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Abstract book

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OA-53

Using technology to build a regulatory ecosystem across Africa to help streamline regulatory approval timelines, so doing, unlocking more investment into the continent.

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The use of technology to enhance medicine regulation in Africa, particularly through the establishment of the African Medicines Agency (AMA), will help drive efficiencies within national regulatory agencies. By adopting electronic tools and platforms, national regulatory agencies can streamline their regulatory processes, reducing the time and cost of regulatory review, and enabling faster access to safe and effective medicines.

Electronic submission systems, for example, can reduce the need for paper-based submissions, simplifying the review process and minimizing errors. Electronic data capture systems can improve the quality of data collected in clinical trials, reducing the need for manual data entry and enhancing data security. This can enable regulatory agencies to more efficiently and effectively review applications and monitor clinical trials, ensuring the safety and efficacy of new medicines.

Moreover, the harmonization of regulatory requirements across Africa, facilitated by AMA's collaboration with other regulatory bodies, can help reduce the regulatory burden on national agencies. By adopting common regulatory standards and guidelines, national agencies can better align their processes with those of their counterparts in other African countries, reducing duplication and improving efficiency.

Overall, the use of technology and the establishment of a continental regulatory body such as AMA can help national regulatory agencies in Africa improve their regulatory processes, enhance transparency and accountability, and ensure faster access to safe and effective medicines for their populations.

OA-58

Associations between prenatal malaria exposure, maternal antibodies at birth and malaria susceptibility during the first year of life in Burkina Faso

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Background Although infants are thought to be protected against malaria during the first months of life mainly due to maternal antibodies, malaria in early childhood is not uncommon in high-transmission settings and susceptibility to Plasmodium falciparum infections varies between infants. This study aimed to investigate how different categories of prenatal malaria exposure (PME) influence levels of maternal antibodies in cord blood samples and examined the effect of maternal antibody concentrations at birth on subsequent risk of malaria in early childhood.

Methods A birth cohort study (N=661) was nested within the COSMIC clinical trial (NCT01941264) in Burkina Faso. P. falciparum infections during pregnancy and infants' clinical malaria episodes detected during the first year of life were recorded. The levels of maternal IgG and IgG1-4 to 15 P. falciparum antigens were measured in cord blood by quantitative suspension array technology.

Results Results showed a significant variation in the magnitude of maternal antibody levels in cord blood, depending on the PME category, with past placental malaria (PM) more frequently associated with significant increases of IgG and/or subclass levels across three groups of antigens defined as pre-erythrocytic, erythrocytic and markers of PM, as compared to those from the cord of non-exposed control mothers. High levels of antibodies to certain erythrocytic antigens (EBA140, EBA175, MSP142, and MSP5) were independent predictors of protection from clinical malaria while antibodies to VAR2CSA-DBL1-2 and DBL3-4 were significantly associated with an increased malaria risk during the first year of life. Remarkably, ratios of protective-to-risk antibodies above 1 at individual level were associated with protection from clinical malaria during the first year of life.

Conclusion These findings indicate that PME categories have different effects on the levels of maternal-derived antibodies to malaria antigens in children at birth and that, this might drive heterogeneity to clinical malaria susceptibility in early childhood.

OA-59

Achieving equitable leadership in Global Health partnerships: barriers experienced and strategies to improve grant funding for early and mid-career researchers in low- and middle-income countries.

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Background Calls to decolonise global health have highlighted the continued existence of colonial structures in research into diseases of public health importance, particularly in low- and middle-income countries (LMICs). A key step towards restructuring the system is equitable leadership in global health partnerships whereby researchers in LMICs are given the opportunity to successfully secure grant funding to lead and drive their own research based on locally defined priorities.
Methods In February 2022, the Tuberculosis (TB) Centre of the London School of Hygiene and Tropical Medicine (LSHTM) hosted a virtual multi-stakeholder workshop aimed at bringing together funders and early- and mid-career researchers (EMCRs) to identify funder initiatives that have worked to improve equitable leadership, to better understand barriers faced by EMCRs, and collectively brainstorm approaches to overcome these barriers. The workshop transcript was analysed using a deductive thematic approach to identify key emerging themes.
Results The workshop was attended by 140 diverse participants representing funders, research institutions, and researchers from Africa, Europe, Asia, and South America. 83 participants self-identified as early- or mid-career researcher, and 19 as senior scientists, with varied areas of interest including communicable and non-communicable diseases and neglected tropical diseases. Major barriers identified were lack of individual and institutional level support, and flawed funding structures for EMCRs in LMIC settings. Strategies on how equitable leadership can be further facilitated included institutional reforms for funders to facilitate equity, diversity, and inclusion in their partners through consultative engagement, and reshaping how research priorities are defined. Other strategies identified included diversified funding streams for research institutions, promoting south-south partnerships, and dedicated funding for capacity building of EMCRs.
Conclusion Advances to overcome funding barriers in global health speak directly to its decolonisation. Complex changes in practice, which are intentional and require uncomfortable shifts, are urgently required.
Funding: Wellcome Trust Institutional Strategic Support Fund.

OA-62

Improved molecular diagnosis of visceral leishmaniasis (VL) using the mini direct on blood PCR Nucleic Acid Lateral Flow Immunoassay (dbPCR-NALFIA).

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Background Current diagnostic methods for VL include parasitology and serology (with rK39 dipstick test and direct agglutination test). These methods have limitations (patient safety or diagnostic accuracy), and molecular testing is proposed to improve diagnosis. Current molecular tools have high accuracy for detecting VL, however their complexity and high costs make their use unsuitable for endemic areas with limited resources. Consequently, there is a need for a simple molecular diagnostic test that can be implemented in resource limited setting.
Methods We have developed a miniaturized direct-on-blood PCR nucleic acid lateral flow immunoassay (mini-dbPCR-NALFIA) as an innovative, easy-to-use molecular assay for the diagnosis of VL in these particular settings. Unlike other simplified molecular methods, such as LAMP, the mini-dbPCR-NALFIA does not require DNA extraction and utilizes a handheld, portable thermal cycler powered by a solar-charged power pack enabling to perform the test without any laboratory infrastructure. Reading of results is done using a rapid lateral flow strip. In the present study we have conducted a laboratory evaluation on the mini db-PCR-NALFIA to determine its diagnostic accuracy. Patient samples (N=146) with suspected VL were tested using the mini db-PCR-NALFIA and compared to conventional PCR (reference test). Sensitivity and specificity represented the accuracy. Cohen's k determined the degree or agreeableness between the mini db-PCR-NALFIA and other diagnostic tests (PCR and rk39 rapid test).
Results Compared to qPCR, the mini db-PCR-NALFIA for VL had a sensitivity of 95.83% (95% CI, 88.30%-99.13%) and a specificity of 97.22% (95% CI, 90.32% - 99.66%). The agreement between both tests was excellent (k-value: 0.93). The Limit of Detection of the platform is around 10 parasites per microliter of blood (spiked with promastigotes).
Conclusion The VL-mini-db-PCR-NALFIA has a very good diagnostic performance and is now ready for large field evaluations in disease endemic countries.

OA-68

Implementation of integrated health-checks for TB-affected households in Zimbabwe

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Background Tuberculosis (TB)-affected communities are often highly vulnerable, with social, economic, and biological factors increasing risk of TB and other chronic conditions, whilst impeding healthcare access. Traditional approaches to TB contact tracing do not address non-TB related health needs.
Methods Nested in an EDCTP-funded TB household contact (HHC) cohort (ERASE-TB), we invited HHC (aged ≥10 years) and people with TB (aged ≥18 years, at treatment completion) to participate in a health-check. The health-check was collaboratively developed and, in addition to TB, included conditions which have high local prevalence (e.g. HIV, hypertension), are associated with TB (e.g. undernutrition, diabetes, mental health, alcohol and smoking), or were of importance to the community (e.g. vision). Testing was performed using point-of-care tools. Participants with a positive result were referred; linkage to care was assessed. The health-check component was funded by Wellcome Trust.
Results From 197 households, 482 HHC and 60 people with TB participated in the health-check. Reasons for non-attendance among people with TB included having moved away, death and not having time. 62% HHC and 32% people with TB were women. 2.4% people reported currently/recently taking TB preventative therapy. Overall, 15% HHC and 31% people with TB were living with HIV, of whom 9% were diagnosed through screening. Six percent of HHC and 27% people with TB were underweight; 22% HHC and 12% people with TB had hypertension; 3% HHC and 13% people with TB had diabetes; 31% HHC and 41% people with TB had mental health symptoms; 15% HHC and 19% people with TB had visual impairment. Most chronic conditions were previously undiagnosed. Successful linkage to care varied by condition.
Conclusion Members of TB-affected households experience a high burden of chronic conditions. Inclusion of strategies to identify and address these factors within TB screening may reduce TB incidence and improve health.

OA-83

Early Bactericidal Activity of Meropenem, Ertapenem, Amoxicillin/Clavulanate and Optimized Rifampicin in Pulmonary Tuberculosis

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Background Repurposing established antibiotics for TB has been successful, notably for fluoroquinolones, linezolid, and clofazimine. Meropenem co-administered with amoxicillin/clavulanate (A/Clav) demonstrated early bactericidal activity (EBA) in clinical trials (Diacon 2016; de Jager 2020; de Jager 2022). This study evaluated different regimens of carbapenems, A/Clav, and rifampicin, alone or in combinations.
Methods This phase 2a, open-label, randomized trial recruited 132 HIV-negative adults with newly diagnosed, smear-positive, rifampicin-susceptible pulmonary TB. Participants received 14 days of treatment in one of 8 experimental arms, or standard-of-care (HRZE). EBA was determined with mixed effects modelling and reported as change in time (hours) to sputum culture positivity (TTP0-14) of samples collected overnight with 95% confidence intervals. Adverse events (AE) were assessed daily.
Results A/Clav 2x1000/62.5mg orally twice daily showed no activity. TTP0-14 of other drugs in combination with A/Clav was, for meropenem 6g over 6 hours(6Mero6): 58.02 hours (18.72-192.92), meropenem 6g over 1 hour(6Mero1): 58.13 hours (27.26-121.83), meropenem 3g over 1 hour twice daily(3x2Mero): 60.07 hours (19.89-884.71), and meropenem 4g over 1 hour(4Mero1): 35.28 hours (25.31-84.74). Ertapenem 1g daily intravenously (ErtaIV) or intramuscularly (ErtaIM) was not active. The activity of rifampicin 35mg/kg daily plus A/Clav was 136.92 hours (103.21-400.64) and HRZE 134.30 hours (106.28-160.23). In 58 participants, 111 adverse events were reported. Most commonly diarrhoea (15 participants: four ErtaIM, three ErtaIV, four 6Mero6, two rifampicin, one each A/Clav and HRZE), injection site reactions (six participants: four ErtaIM, one each 6Mero6 and 3x2Mero), and raised transaminases (four participants: A/Clav, ErtaIM, Erta IV, rifampicin). Three SAEs occurred (pneumonia in ErtaIV, haemoptysis in rifampicin and 6Mero1) unrelated to treatment.
Conclusion Rifampicin-based treatments showed the highest EBA. A/Clav and meropenem given at 6g per day, in single or divided doses, had higher EBA than lower doses, and shorter infusions were better tolerated. Ertapenem-based treatments and A/Clav alone showed no anti-TB activity.
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OA-87

Research ethics committees in Mozambique: operational and functional characteristics evaluated from a self-assessment tool in 2019

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Background In the past decades, Africa witnessed increased biomedical research and transnational collaborations making the continent vulnerable to exploitation. Research ethics committees (REC) are the cornerstone; however, many lack an accreditation system. A self-assessment tool can be feasible for reviewing processes and policies against recognized standards. This study aimed to describe Mozambique's RECs network and its operational and functional characteristics.
Methods A descriptive cross-sectional study was conducted. In 2019, Mozambique had seven RECs; the study population was the president of each existing REC. A self-assessment tool developed by researchers from Africa was used. Participants were recruited by telephone, and after informed consent, the questionnaire was emailed to each participant and returned to the investigators. A descriptive statistical analysis was done to describe the frequency of the events.
Results The existing seven RECs in 2019 accepted to participate in the study. A total of six RECs has a policy for appointing the president. The most common criteria for the president's selection were prior training in ethics (six), followed by prior research experience (five). Regarding resources, only one of the seven RECs reported having a yearly budget, and only one has a full-time administrative staff. The reported number of RECs that meet as a full committee to review research studies once a month was four, and two referred meeting once a week. All the RECs stated they have policies for protocol reviewing. Out of seven, six RECs have a policy on expedited review, on how decisions are made and communicated to investigators.
Conclusion This study is the first attempt to document Mozambique's RECs network. The process of self-assessment raises knowledge regarding strengths and challenges. Results can serve as a quality improvement mechanism detecting specific areas needing upgrading and as a reference on how they are operating compared to others.

OA-92

Clinically relevant enantiomer specific R- and S-praziquantel pharmacokinetic drug-drug interactions with efavirenz and ritonavir: Implications for HIV and schistosomiasis co-infection

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Background HIV and schistosomiasis are the most widespread infections worldwide. The two diseases share the same epidemiological space, especially in poor regions where endemicity is high. Co-infections are therefore common. We conducted a clinical study to determine the effect of efavirenz and ritonavir on the pharmacokinetics of R- and S-praziquantel (PZQ) in healthy male participants. The aim was to increase knowledge towards the safe and efficacious use of PZQ especially in cases of coinfection and mass drug treatment programs where HIV status and concomitant drug intake is not considered prior to administration.
Methods We conducted a non-randomized, open-label, single-dose, one sequence crossover study with 2 arms. A single oral dose of 40 mg/kg PZQ followed by a daily oral dose of either 400 mg efavirenz or 100 mg ritonavir was given to participants for 14 consecutive days. On day 14, they ingested a single 40 mg/kg dose of PZQ. We measured plasma levels up to 12 h on day 1 and day 14. Samples were analyzed by LC-MS. Pharmacokinetic analysis was conducted in WinNonlin to determine the primary endpoints (plasma T1/2, Cmin, and AUC).
Results Efavirenz had a significant effect on the pharmacokinetics of PZQ ($p < .05$), reducing the AUC by 4-fold (1213.15 vs. 281.35 h·ng/ml for R-PZQ and 5669 vs. 871.84 h·ng/ml for S-PZQ). Ritonavir had no significant effect on R-PZQ but increased the AUC 2-fold for S-PZQ ($p < .05$) (4154.79 vs. 7291.05 h·ng/ml).
Conclusion Our study showed clinically significant drug-drug interactions involving PZQ and efavirenz that should be considered in the treatment of schistosomiasis in regions where efavirenz-based ART is common. Using PZQ in HIV patients needs investigation, as there is a risk of both treatment failure and adverse effects because of induction and inhibition. Strategies to avoid these detrimental DDI should therefore be explored.

OA-97

Facilitators and barriers to infant HIV post-natal prophylaxis (PNP), a qualitative sub-study of the PROMISE-EPI trial in Lusaka, Zambia

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Background Infant post-natal prophylaxis (PNP) is used to prevent HIV transmission through breastfeeding. In Zambia, the national recommendations include a three-drug prophylaxis, composed of a dispersible tablet of zidovudine (AZT) and lamivudine (3TC) and a syrup of nevirapine (NVP). The PROMISE-EPI study, modified the PNP regimen to lamivudine only, initiated at 6 weeks and continued until 12 months to all HIV exposed uninfected infants of virally unsuppressed mothers. Our aim in this study was to identify barriers and facilitators to this extended PNP, a keystone toward an effective prevention.
Methods Individual interviews and focus group discussion were conducted with PROMISE-EPI participants who had received the two PNP regimens, health care providers and PROMISE-EPI staff. Sessions were recorded, transcribed verbatim and translated from local languages into English. An initial code-book was designed and then adapted on the basis of the emerging themes, to allow a descriptive thematic analysis.
Results More barriers to PNP adherence were identified with triple drug prophylaxis than with lamivudine. These barriers were related to the formulation and bitter taste of AZT/3TC tablets. The ready to use formulation and sweet taste of lamivudine syrup were appreciated by mothers. Extended PNP proposed in the PROMISE-EPI study was globally well accepted and strategies were found to increase adherence. Adherence to PNP appeared to be better than the mothers' adherence to their own antiretroviral therapy.
Conclusion Accompanying HIV infected mothers and giving them the choice of the PNP to prevent transmission via breastfeeding (type of PNP regimen and extended PNP in non-adherent mothers), may be one of the keys to reducing the burden of pediatric HIV infection in low and middle income countries.
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OA-98

Creating a whole that is more than the sum of its parts: an emerging collaboration between clinical trial units in UK, West and East Africa

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Background MRC The Gambia and MRC Uganda joined London School of Hygiene and Tropical Medicine (LSHTM) in 2018 to form a family of institutions committed to high quality research. Each institution supports Clinical Trials through a formally-constituted Clinical Trials Unit (CTU) or equivalent resources, where the function is to provide end-to-end support for high quality clinical trials (CTs). Until recently, the three CTUs worked as islets, supporting only trials involving their respective institutions as sponsor or partner. In late 2022, the CTUs started a dialogue with the aim of creating regionally-based yet internationally-networked hubs. Our ambition is to leverage the strengths of each CTU and enhance support for high quality CTs through collaborative working and coordinated sharing of resources, expertise and training.
Methods We applied an informal SWOT (Strengths, Weaknesses, Opportunities, Threats) analysis. This identified Strengths where one CTU might take the lead, Weaknesses where a CTU needed support from the others, and where there were Opportunities to be gained from collaboration. We also discussed limitations that might pose Threats to achieving our aims. We adopted principles of equitable partnership. Early conversations took place remotely, followed by in-person meetings which helped to build relationships, deepen contextual understanding and identify specific areas for collaboration.
Results Preliminary collaborative activities underway to foster interdependence between our CTUs include: i) running joint seminar series, ii) co-developing an electronic trial Masterfile (eTMF) system compliant with international standards, iii) developing a searchable database of all trials at LSHTM, iv) working towards shared digital infrastructure for the design, implementation, management and analysis of trials and shared human resources.
Conclusion Collaboration is key for successful clinical trials. Through leveraging unique strengths and counteracting individual weaknesses of three geographically dispersed CTUs, we will create a strong networked trials capacity that is more than the sum of its parts.

OA-99

Evaluation of the safety and efficacy of dihydroartemisinin-piperaquine for intermittent preventive treatment of malaria in HIV-infected pregnant women: a multi-centre, double-blind, placebo-controlled trial (MAMAH project)

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Background Malaria during pregnancy is an important driver of maternal and neonatal health especially among HIV-infected women. In Africa, at least one million pregnant women are annually co-infected with Plasmodium and HIV. The interaction between the two infections is particularly deleterious during pregnancy, leading to an increased risk of malaria and HIV viral load. Intermittent preventive treatment in pregnancy (IPTp) with sulphadoxine-pyrimethamine is recommended for malaria prevention in HIV-uninfected women but it is contraindicated in those HIV-infected women on cotrimoxazole prophylaxis (CTXp).
Methods A randomized, double-blind, two-arm, placebo-controlled trial to evaluate the safety and efficacy of dihydroartemisinin-piperaquine (DHA-PPQ) for IPTp was conducted in HIV-infected pregnant women receiving CTXp, antiretroviral drugs and long lasting insecticide treated nets in five sites from Gabon and Mozambique. Women attending the first antenatal care clinic visit, resident in the study area and with a gestational age ≤28 weeks were randomized to receive either monthly IPTp with DHA-PPQ or placebo. The three day IPTp administration was always done under direct observation. Women were followed up until one month after the end of pregnancy.
Results A total of 666 HIV-infected pregnant women were enrolled in the trial between September 2019 and November 2021. The prevalence of maternal peripheral parasitemia at delivery (primary study endpoint) was unexpectedly low during the study period and no significant differences were found between groups. However, the composite of Plasmodium infection (detected by any diagnostic test during pregnancy or delivery) was significantly decreased in the DHA-PPQ group (RR=0.48, 95CI 0.27-0.84; p=0.010). There were no differences in the prevalence of adverse pregnancy outcomes and serious adverse events across groups.
Conclusion In a context of low malaria transmission, adding monthly IPTp- DHA-PPQ to CTXp in HIV-pregnant women is safe and it is associated with a decreased risk of clinical malaria and overall Plasmodium infection in pregnancy.

OA-102

Reactivation of oncogenic herpesviruses is associated with co-infections causing severe inflammatory presentations in HIV-infected patients from Gugulethu, South Africa

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Background The gamma-herpesviruses Kaposi's sarcoma-associated herpesvirus (KSHV) and Epstein-Barr virus (EBV) both have oncogenic potential, particularly in immunosuppressed patients such as in Human Immunodeficiency Virus (HIV)-infected individuals. Both oncogenic viruses display latent and lytic lifecycles with differing outcomes for associated pathologies. Co-infection with SARS-CoV-2, the causative agent for Covid-19, poses additional unknown risks of cancer development, affecting already vulnerable populations. Indeed, in South Africa, the Covid-19 pandemic occurs against the backdrop of high HIV, tuberculosis and non-communicable disease burdens as well as highly prevalent herpesviruses infections, such as EBV and KSHV. Mounting evidence points to potential interplay between several co-infections and reactivation of opportunistic herpesvirus infections.
Methods This study therefore assessed the risk of KSHV and EBV lytic reactivation in the context of SARS-CoV-2 and HIV infection in a patient cohort (n=400) enrolled at the Gugulethu ART clinic in Cape Town, South Africa, between September 2020 and April 2023.
Results While almost all patients displayed positive EBV serology, 40% were seropositive for KSHV. About 70% of the cohort was SARS-CoV-2 seropositive already before national Covid-19 vaccination roll-out, demonstrating high prevalence of SARS-CoV-2 in this population. KSHV seropositive patients (with or without positive SARS-CoV-2 serology) were followed up every 6 months to measure reactivation of KSHV and EBV in the peripheral blood. We found that oncogenic herpesvirus reactivation primarily occurred in patients with underlying uncontrolled inflammatory conditions, potentially caused by SARS-CoV-2 infection, which exacerbated clinical outcome.
Conclusion While the design of this study cannot distinguish if disease synergy exists between KSHV and/or EBV and Covid-19 nor if either viral infection is indeed fuelling the other, these data point to potential contributions of oncogenic herpesvirus infection to clinical outcome, particularly in the South African context of high disease burden which warrants further investigation.
This study was funded by the EDCTP (Training and Mobility Action TMA2018SF-2446-KSHV/HIV morbidity).

OA-183

Dynamic of molecular and resistance markers prevalence of Plasmodium falciparum during the seasonal malaria chemoprevention campaign in school aged children in Bandiagara, Mali.

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Background Recently, the World Health Organization (WHO) has recommended to extend the seasonal malaria chemoprevention (SMC) with Sulfadoxine-pyrimethamine plus amodiaquine (SP-AQ) strategy to school aged children and to use alternative artemisinin-based combination therapies (ACTs). There is less data on the efficacy of ACTs in SMC and their impact on the selection of drugs resistant parasites. The aim of this trial was to assess the efficacy of Dihydroartemisinin-Piperaquine (DHA-PPQ) in school aged children during and after SMCs and to assess the prevalence of resistance markers to ACT, amodiaquine and piperaquine.
Methods We conducted a randomized trial from September to December 2020 including 345 children of 6-15 years old. Study participants were randomized in 1:1:1 ratio to receive monthly 3 consecutives doses of DHA-PQ, SP-AQ or control drug (Albendazole). Study drugs were administrated for 3 consecutive days at each SMC round. All drugs were administrated under direct supervision of a study pharmacist. Dried blood specimens (DBS) were collected at the start of each SMC round and 7 days after the first dose of SMC. Dynamic of malaria parasites prevalence and the resistance markers to drugs were assessed by molecular assays in DHA-PQ, SP-AQ and control arms over 4 months of SMC and 8 months following SMC using q-PCR assay.
Results Preliminary data from 100 participants showed a significant decrease in the prevalence of Plasmodium falciparum parasites carriage from 67% to 10% at days 1 and 31 after the first SMC round. The prevalence remained low during SMC follow-up period. Molecular assays of resistance markers are ongoing. Full results will be presented at the meeting.
Conclusion DHA-PPQ is suitable for SMC, assessment of parasites prevalence and resistance markers selection is ongoing.

OA-189

Building capacity for HIV cure research in Ghana - The H-CRIS experience

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Background Cure research is the new frontier in the fight against HIV as prioritized by organizations like the International AIDS Society, the EDCTP and the National Institutes of Health. However, though 70% of people living with HIV are in Africa, the literature shows that very little of the current cure research efforts involve African scientists or patients. Important questions such as how co-infections like malaria, helminths, tuberculosis, and different HIV clades affect the viral reservoir can only be answered in Africa, to ensure that an eventual cure is effective and appropriate for African patients.
Methods With support from the EDCTP through a senior fellowship grant in 2019, we set up the HIV Cure Research Infrastructure Study (H-CRIS) at the University of Ghana with partnership from Washington University in St Louis and Amsterdam University Medical Centre. Our approach was to leverage the initial EDCTP grant, to obtain more grants to sustain the cure research training.
Results Through H-CRIS, we have set up a cohort of 390 patients with HIV that we monitor on a regular basis for viral load, CD4 counts, co-morbidities and other parameters. We have trained 3 postdoctoral scientists, 2 PhD students, 3 MPhil students and 10 research assistants in HIV cure research methods. We have collected data on patient perspectives on cure research, performed laboratory screening of compounds towards cure, and obtained additional funding to perform cutting edge studies on how co-infections such as tuberculosis and hepatitis impact the HIV reservoir. Through mentorship and guidance of trainees, we have quadrupled the initial EDCTP grant by obtaining additional funding of over 2 million dollars from various sources to sustain the cure research.
Conclusion We will share our model of starting and sustaining a basic and translational HIV cure research programme which is feasible and replicable in other Africa settings.

OA-195

Spatial clustering, hotspot analysis and temporal distribution of the seventh Ebola Virus Disease outbreak in Uganda

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Background Uganda is an ecological hot-spot with infectious disease transmission belts which exacerbates its vulnerability to epidemics. Its proximity to the Congo Basin, influx of refugees and the intrusion of humans into ecological areas formerly occupied by animals and other pathogen carriers, has resulted in an increased risk of Ebola virus disease (EVD) over the last two decades. This study aimed to determine the spatial clustering, hot spot analysis and temporal distribution of the recent EVD outbreak in Uganda.
Methods The study used an ecological design based on the 2184 subcounties in Uganda as the spatial units. Initial exploratory analysis used measures of spatial autocorrelation in the R statistical package. Using the Anselin's Local Moran test cluster detection method, spatial autocorrelation was applied to determine the presence of statistically significant clusters and hotspots.
Results Overall, 142 confirmed cases of Sudan virus disease (SVD) were reported, of which 55 died (CFR: 39%), and 87 recovered. In addition, 22 deaths among probable cases were reported in individuals who died before samples could be taken (overall CFR: 47%). Overall, nine Ugandan districts were affected by this outbreak: Bunyangabu, Jinja, Kagadi, Kampala, Kassanda, Kyegegwa, Masaka, Mubende, and Wakiso. When the number of permutation test was set to 9999, Moran's I = 0.37261, P = 0.0085, and was significant at significance level of 0.01. Spatial cluster analysis identified two most likely cluster; one large multi-centered cluster in districts of Mubende and Kassanda with 13 locations and one cluster in Rubaga division in Kampala district.
Conclusion Substantial spatial clustering of EVD was detected at sub-county level in the recent outbreak at two districts of Mubende and Kassanda in the central region of Uganda. This study identifies hotspot areas for efficient implementation of early-targeted interventions for the prevention and control of the outbreak.

OA-196

Development of a CAA/CCA duplex test for improved diagnosis of human schistosomiasis

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Background Schistosomiasis is caused by infection with parasitic worms, schistosomes, and affects hundreds of millions people worldwide. The detection of schistosome circulating cathodic and anodic antigens (CCA and CAA) has proven to be highly valuable in diagnosing intestinal and urinary schistosomiasis. Within the freeBILy project, a CCA/CAA duplex test was developed which detects both antigens simultaneously to improve the diagnostic accuracy and potentially identify Schistosoma spp based on CAA/CCA ratios.
Methods CAA and CCA were incorporated into the current laboratory-based UCP-LF test platform utilizing a duplex test-format; i.e. a single prototype device with two parallel lateral flow (LF) strips. Test performance was evaluated using banked sample sets (serum and urine) from two different Schistosoma endemic areas using standardized protocols. Samples were available from both cross-sectional as well as school-age children based population studies. In a subset, CCA/CAA ratios were determined.
Results CAA-levels in urine were lower compared to CAA-levels in serum, both for S. mansoni (Sm) and S. haematobium (Sh). Significantly more CCA was observed in Sm urines compared to Sh urines. In urine the CCA/CAA ratio for Sm was significantly higher compared to the CAA/CCA ratio for Sh, while no differences were observed in serum. Species could not be identified unequivocally based on the CCA/CAA ratio.
Conclusion Combined detection of CAA and CCA improved diagnostic accuracy and showed added value compared to detection either antigen separately, particularly in Sh settings where the POC-CCA performance is limited. Identification of Schistosoma species based on the CCA/CAA ratio seems challenging due to multiple factors. Generally, CAA and CCA levels in serum and urine show marked differences which would benefit from further focused in-depth studies.

OA-208

Evaluating the impact of computer-assisted x-ray diagnosis and other triage tools to optimise Xpert orientated community-based active case finding for TB and COVID-19 (XACT-19)

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Background Almost 40% of persons newly diagnosed with TB are unreported. Detecting cases in TB/HIV endemic communities have been restricted by a lack of sensitive and user-friendly point-of-care (POC) diagnostic tools. Computer-aided detection (CAD) has been recommended by the WHO for screening for TB, however, implementation of CAD in community-based active case finding (ACF) is unclear. We aimed determine the adjunctive role of CAD in Xpert-orientated community-based ACF for TB.
Methods In this ongoing, EDCTP-funded (RIA2020S-3295), open-labelled randomised controlled trial (RCT), high-risk persons (symptomatic and/or HIV-infected) with presumed TB were recruited from TB/HIV endemic communities in South Africa and Zambia (Zimbabwe is an additional site). Using a low-cost mobile van staffed by three healthcare workers and equipped with an ultra-portable x-ray and GeneXpert® system, participants were randomized into either 'CAD + POC Xpert' (Arm 1: CAD followed by Xpert MTB/RIF Ultra in CAD-positive participants using a CAD4TB v7 threshold of 10 [South Africa] and 50 [Zambia] based on prior population-specific calibration), or 'POC Xpert alone' (Arm 2: POC Xpert MTB/RIF Ultra only). The primary outcome was time to detection of microbiologically proven TB (Xpert and/or culture positivity). Here we present an interim trial progress report.
Results From Feb 2022, a total of 505 participants have been enrolled (256 [50.7%] from South Africa and 249 [49.3%] from Zambia). 26.9% (136/505) of participants were HIV-infected (median CD4 of 609). 33/505 (6.5%) tested positive for TB (25/256 [9.8%] in South Africa and 8/249 [3.2%] in Zambia). 15 participants underwent screening to detect 1 case of TB. Of TB-positive participants, 7/33 (21.2%) were smear positive.
Conclusion Community-based ACF detected a high burden of TB, of which a significant minority (~20%) was probably infectious. These data have implications for ACF strategies in high burden settings.

OA-217

Introducing a priority review voucher in the EU to encourage neglected disease product development

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Background Despite their huge burden, there are insufficient prevention or treatment tools available for neglected diseases due to limited market profitability. We propose that the European Union (EU) create a new incentive to encourage neglected disease product development by rewarding developers with a tradeable voucher for the accelerated assessment of a second, more profitable, product.
Methods We used annual monitoring reports (2015-2021) from the European Medicines Agency (EMA) and IQVIA data on pharmaceutical sales to estimate the value of earlier introduction of pharmaceuticals in the EU. We analysed the sales of international blockbuster products (2015-2022, quarterly data, in USD) in EU countries. We explored the complementarity of the voucher program with existing EMA programs such as PRIME and EU-M4all. The voucher could grant early scientific dialogue with the regulator (as PRIME does) and access to an EMA scientific opinion with the WHO and national regulatory authorities of target countries (as EU-M4all does). This program would complement the Global Health EDCTP3 joint undertaking as well. We interviewed stakeholders to discuss the features for such a programme, based on the lessons learned from the United States of America (USA).
Results Our research suggests that accelerated assessment in the EU would save developers on average six months of regulatory time (including clock stops). We estimated that this would give the voucher a value of around 100 million EUR, similar to the average value of vouchers in the USA. We proposed that EU and USA voucher programs be compatible, together granting a total reward of 200 million EUR.
Conclusion The EU is contributing to tackling neglected diseases through different initiatives. Our results suggest that a priority review voucher programme in the EU would be a valuable additional contribution and could help to accelerate the development of new and improved products for neglected diseases.

OA-218

Enhanced effect of seasonal malaria chemoprevention when coupled with nutrients supplementation for preventing malaria in children under five years old in Burkina Faso

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Background In rural African settings, most of the children under the coverage of Seasonal Malaria Chemoprevention (SMC) are also undernourished at the time of SMC delivery, justifying the need for packaging malarial and nutritional interventions. This study aimed at optimizing the impact of SMC by coupling the intervention with nutrients supplementation for preventing malaria in children in Burkina Faso.
Methods A randomized trial was carried out between July 2020 to June 2021 in the health district of Nanoro. Children under SMC coverage were randomly assigned to one of the three study arms SMC+Vitamin A (SMC-A) or SMC+Vitamin A+ Zinc (SMC-AZc) or SMC+Vitamin A+ PlumpyDoz(tm) (SMC-APd), a Medium Quantity - Lipid-based Nutrient Supplement. Children were followed up for one year including an active follow-up period for 6 months followed by a 6 months passive follow-up period. At each visit, physical examination was performed. Capillary blood sample was collected for malaria diagnosis by Rapid Diagnosis Test.
Results In total, 1059 children were enrolled i.e. 353 children per arm. Adding nutritional supplements to SMC had an impact on all-cause morbidity. More specifically, a reduction of morbidity odds of 24%, adjusted OR=0.76 (0.60 – 0.94) in SMC-APd arm compared to control arm. A reduction 23% (adjusted OR=0.77 (0.61 – 0.97)) in the odds of having uncomplicated malaria was observed in SMC-APd arm but not with Zc arm adjusted OR=0.82 (0.65 – 1.04) compare to control arm. Even better, a reduction of 52%, adjusted OR= 0.48 (0.23 – 0.98) in the odds of having severe malaria was observed in SMC-APd arm compared to control arm. Unlike clinical episodes, no effect of nutrient supplementation on cross sectional asymptomatic infections was observed.
Conclusion Adding nutritional supplements to SMC significantly increases the impact of this intervention for preventing children from malaria and other childhood infections.

OA-223

Myocardial structure and function assessed by cardiac magnetic resonance in adolescents with perinatal-acquired HIV infection taking antiretroviral therapy

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Background HIV in adolescents with perinatal HIV (PHIV) is associated with an increased risk of cardiac disease, which is not well characterised. We characterised myocardial structure and function in adolescents with PHIV and established on antiretroviral therapy (ART) using advanced imaging with cardiac magnetic resonance (CMR).
Methods We conducted a cross-sectional study in PHIV aged 10-19 years taking antiretroviral therapy and an HIV-negative comparison group in Harare, Zimbabwe. Participants underwent a 3-Tesla CMR examination including assessment of myocardial structure and function (cine) and myocardial fibrosis (late gadolinium enhancement, LGE). Groups were compared using unpaired t-test, and potential predictors were assessed with multiple linear regression.
Results Forty-four participants were included in the analysis (n= 23 with HIV; 52% female and 21 uninfected controls; 48% female]). Participants with PHIV were older [median (IQR) 18 (16-19) vs 15 (13-17) years; p=0.002] compared to uninfected controls. They also had lower height-for-age and weight-for-age z-scores [Mean (SD), -1.84 (1.0) vs 1.17 (1.0); p=0.044] and [-1.35 (1.4) vs -0.21 (1.4); p=0.011] respectively. In the PHIV group, median age at HIV diagnosis was 5.5 (IQR, 4-8) years and 18 (82%) were virally suppressed (<19 copies/ml). The PHIV group had a larger indexed left ventricular (LV) mass [Mean (SD), 39.2 (5.4) vs 35.3 (6.4) g/m2; p=0.047] and LV end-diastolic volume [75.0 (8.2) vs 67.5 (12.5) mL/m2; p=0.026] compared to controls. LV and right ventricular systolic function measured by either ejection fraction or strain was normal in both groups, and no LGE was observed. No association of LV systolic function was observed with age, sex, and HIV viral load.
Conclusion In this interim analysis, an increased indexed LV mass and end-diastolic LV volume in the PHIV group relative to those HIV-negative may suggest LV structural changes. Recruitment is ongoing and comprehensive regression modelling shall be performed.
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OA-225

Optimising second line anchor drug options for children with HIV in Africa: 96 week results of the CHAPAS-4 randomised trial

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Background Paediatric second line antiretroviral therapy (ART) formulations are limited. CHAPAS-4 (ISRCTN22964075), a 2X4 factorial randomised trial investigated efficacy and safety of 4 anchor drugs.
Methods Children from Uganda, Zambia and Zimbabwe on non-nucleoside reverse transcriptase inhibitor-based regimens, requiring second line ART, were randomised to dolutegravir (DTG) or ritonavir-boosted darunavir(DRV/r), atazanavir(ATV/r) or lopinavir(LPV/r) dosed according to WHO weight-bands. Primary endpoint was week-96 viral load(VL)<400copies/mL. We hypothesised ATV/r would be non-inferior to LPV/r(12% margin); both DRV/r and DTG superior to LPV/r and ATV/r arms combined (superiority threshold p≤0.03; multiple comparisons). Analysis was intention-to-treat, based on logistic regression. Results of second randomisation (tenofovir alafenamide(TAF)-based vs. SOC backbone) will be reported separately.
Results 919 children aged 3-15years (54%male, median[IQR] viral load 17,573copies/mL[5549, 55,700]; CD4 count 669[413, 971]) were randomised and spent 98% of time on allocated regimen. At week-96 208/226(92.0%) on DTG, 203/230(88.3%) on DRV/r, 193/229(84.3%) on ATV/r, 180/223(80.7%) on LPV/r had VL<400c/ml. DTG was superior to LPV/r and ATV/r (adjusted difference 9.7%[4.8, 14.5],p<0.0001); DRV/r showed a trend to superiority to LPV/r and ATV/r (5.6%[0.3, 11.0],p=0.04); ATV/r was non-inferior to LPV/r (3.4%[-3.4, 10.2],p=0.33). Results were similar for VL<60copies/mL and <1000copies/mL and at weeks 48 and 144. CD4 count improved in all arms. More grade 3/4 adverse events(AE), predominantly hyperbilirubinemia, occurred for ATV/r vs LPV/r(p<0.0001); DTG had fewer AE vs. LPV/r(p=0.02). There was no evidence of excess weight-gain. Improvement in growth parameters were lowest with LPV/r. Renal and bone health was similar between arms. One child died (treatment-unrelated); 3% had serious adverse events.
Conclusion These results supports current WHO guidelines for preferred and alternative second line ART. In the future children will require second line ART after first line DTG. Ongoing development of child-friendly boosted DRV and ATV will be key to ensure robust treatment options are available for children in Africa.

OA-235

Antibody responses to endemic coronaviruses in South Africa

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Background Understanding pre-existing, cross-reactive immunity to SARS-CoV-2 is important for pan-coronavirus vaccine design. Since pre-existing T cell immunity has been associated with prior infection by circulating, endemic human coronaviruses (hCoVs), there has been recent interest in mapping hCoV exposure and immunity. However, few of these studies have been performed in Africa, where hCoV exposure may differ. We measured antibodies to endemic hCoVs in South African adults and adolescents, to gain insights into baseline exposure across different age groups.
Methods Using an established ELISA, we measured IgG specific for HKU1, 229E, OC43 and NL63 in pre-pandemic plasma from adolescents (n=14, ages 15-19) and adults (n=13, ages 20-50). A technical repeat was included for each sample, and samples were randomised within each assay plate. Data were analysed using non-parametric statistical tests.
Results In preliminary findings, antibodies specific for NL63, an alphacoronavirus, were detected in all adults and most adolescents (93%). Interestingly, fewer participants had antibodies to the other human alphacoronavirus, 229E, with IgG detected in 54% of adults and 50% of adolescents. Antibodies to the betacoronavirus, HKU-1, were present in all participants. We found no differences in the magnitude of responses between adults and adolescents for NL63, 229E and HKU-1, although a weak association with age was observed for NL63 (p=0.04, r=0.39) and HKU-1 (p=0.04, r=0.4). Finally, antibodies against OC43, another betacoronavirus, were measured in a subset (n=9) of adult participants, with responses detected in all.
Conclusion Our data suggest childhood exposure to endemic coronaviruses, such that adolescents already have detectable antibodies. Importantly, hCoV 229E may not circulate as frequently in South Africa compared to the global north, where reports confirm durable and detectable 229E antibody responses in adults. These geographical differences in exposure have important implications when considering the SARS-CoV-2 shift to endemicity, and the design of pan-coronavirus vaccines.

OA-240

Determining whether mass vaccination campaigns with fractional-dose PCV10 (PNEUMOSIL) could accelerate group protection against pneumococcal transmission in sub-Saharan Africa

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Background In settings with low routine coverage of pneumococcal conjugate vaccines (PCVs), mass campaigns targeting multi-age cohorts (MAC) might accelerate herd protection but would be costly. Mass campaigns using fractional dose PCV would decrease cost and increase access, but their effect on pneumococcal carriage is unknown.
Methods We conducted a cluster-randomized trial in Niger to evaluate the effect of mass campaigns on pneumococcal carriage. 63 villages were randomized in a 3:3:1 ratio to receive mass campaigns targeting children aged 1-9 years with a single full dose of Pneumosil, a single 1/5 fractional dose, or no campaign. We conducted surveys among 2268 households before and 6 months after vaccination. Data were collected about household composition and sociodemographics; a nasopharyngeal swab (NPS) was collected from a child aged 1-9 years. NPS were collected in STGG media and stored at -80°C within 8 hours of collection. Culture and Quellung reactions were performed in Kilifi, Kenya, in accordance with WHO-recommended procedures.
Results Pre-vaccination results are currently available; post-vaccination results will be available in September 2023. In the baseline survey, 2223 children were included, with median age of 4 years (IQR 2-6). Median household size was 7 (IQR 5-10), and a median of 4 people (IQR 2-5) slept in the same room as the child. 41% of children received 3 recorded doses of PCV in EPI, which increased to 80% when considering self-report. Baseline pneumococcal carriage prevalence was 87%, and the prevalence of vaccine-type (VT) carriage was 17%. Serotypes 19A, 19F, 23F, and 6A accounted for 74% of VT carriage. The most common non-VT serotypes isolated were 34, 11A, 23B and 16F.
Conclusion Eight years after PCV13 introduction, residual VT carriage was 17%, which is lower than expected. The effect of MAC mass campaigns on VT carriage will be known in September 2023.
Funding: EDCTP

OA-252

East and Southern African consortium for outbreak epidemiology training (ENTRANT)

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Background East and Southern African countries are susceptible to disease outbreaks, and vulnerable to public health emergencies due to constrained health systems. We aim to promote the development of a critical mass of epidemiologists to work with National Public Health Institutes and Ministries of Health to strengthen response capacity.
Methods The East and Southern Africa Consortium for Outbreak Epidemiology Training (ENTRANT) programme was established with funding from EDCTP and Africa CDC, to provide epidemiological training and mentorship to early- to mid-career public health professionals working in the region. ENTRANT is coordinated by a consortium of institutional partners relevant to outbreak response in the region, and supported by an independent Advisory Committee comprising experts in capacity strengthening in sub-Saharan Africa. A competitive application process was implemented to identify high-calibre public health professionals for entry into the programme. Fellows undertake MSc Epidemiology at London School of Hygiene and Tropical Medicine (LSHTM) followed by further focussed short course multidisciplinary training on the emergence, spread and response to pandemics. Fellows receive mentorship from experienced epidemiologists in their home country, and take part in regular transferable skills training and networking activities.
Results From a total of 324 applications, 15 public health professionals (eight female, seven male) from Botswana, Ethiopia, Kenya, Tanzania, Uganda and Zambia have been awarded Fellowships. To date, six have completed their MSc Epidemiology training, with the remaining Fellows due to complete in October 2023. Fellows who have completed formal training have gone on to work for Ministries of Health and public health research institutions. Fellows at all stages of the programme have formed a strong network through regular meetings and networking events.
Conclusion The ENTRANT programme has been successfully established. Further funding will be sought to further expand the programme and promote a long-term mutually-supporting network of outbreak and pandemic control practitioners.

OA-270

Skin diseases and their frequency patterns in skin camps in PEP4LEP implementing districts in Tanzania, preliminary results

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Background Skin diseases are common human illnesses globally. Improved diagnostic skills of health staff working in underserved communities may uncover a wide range of diseases, including skin Neglected Tropical Diseases (NTDs). Integrated skin screening is an approach used in PEP4LEP, a research project in Ethiopia, Mozambique, and Tanzania that is aimed at identifying the most effective and feasible method for screening people at risk of developing leprosy and administering chemoprophylaxis. We present preliminary results on the skin diseases and their frequency patterns as found during integrated skin screening in communities in three Tanzanian districts.

Methods Data on the skin diseases identified and the frequency of diagnosis were collected in the skin camps that took place in Morogoro, Mvomero, and Lindi districts in Tanzania as part of the PEP4LEP study

Results A total of 7,721 participants were screened from July 2020 to January 2023 in 74 skin camps, 4,871 (63.1%) had skin conditions. A total of 77 (1.0%) contacts were newly diagnosed with leprosy. Frequently detected skin diseases were: tinea capitis (2,230 cases, 29.0%), pityriasis versicolor (1,173, 15.2%), and atopic dermatitis (610, 7.9%). Apart from leprosy, other diagnosed skin NTDs included: scabies (695, 9.0%), and onchocerciasis (54, 0.7%). These findings are preliminary as recruitment is still ongoing, an in-depth analysis is expected towards the end of the project.

Conclusion Integrated skin screening in community skin health interventions contributes to reducing the barriers to the identification and management of skin conditions, including skin NTDs like leprosy.

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OA-271

Stakeholders' perspectives and willingness on use of SMS reminders and mobile money incentives to reduce loss to follow-up among presumptive TB patients in Uganda

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Background Loss to follow-up of presumptive TB patients is a major challenge towards the realization of the End-TB strategy. SMS reminders and mobile money (MM) incentives have shown promise by improving health outcomes. However, there is limited knowledge on whether these interventions can increase linkage to care/treatment for presumptive TB patients in Uganda. We explored views about using SMS reminders and MM incentives in improving linkage to care of presumptive TB patients.

Methods A qualitative study was conducted, involving; 20 key informants with health workers (HCW), 25 in-depths interviews with presumptive TB patients and 8 focus group discussions with TB patients. Interviews were audio recorded and transcribed verbatim. Data was analyzed using Atlas.ti V12.0.

Results Almost all respondents viewed SMS as not a good communication channel to remind presumptive TB patients to complete diagnosis. They expressed concerns that the SMS reminders could lead to unintended disclosure of one's TB status if they were accessed by another person. Also mentioned the existing fatigue with SMS from telecom companies hence most likely to ignore/delete any messages coming in without reading, lack of real-time interactive communication and not useful for patients who can't read. Phone calls were preferred to SMS because they are private, foster a two-way communication in real-time and felt that a phone call is personal and makes them feel that the HCW cares about them. There were divergent views on MM incentives, majority disagreed to MM sent before the patient comes to the health facility as it may tempt the patient to divert it rather than the intended use.

Conclusion The findings from this study showed limited preference of the SMS reminders. As we embrace mHealth, the human interaction between patient and HCW needs to be maintained. MM sent to the patient prior to the clinic visit, might be diverted.

OA-272

Health system costs of decentralized TB diagnostic testing with Molbio Truenat MTB/RIF vs. hub-and-spoke GeneXpert MTB/RIF in Mozambique and Tanzania

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Background Diagnostic testing for TB needs to optimize access, turnaround time and thus time to treatment initiation and cost. Point of care (POC) testing optimizes the former, but additional costs beyond the test cost alone might be drivers of overall cost in a POC testing strategy, especially in low-and-middle-income settings.
Methods We estimated the health system cost per participant tested for TB on-site via the novel Molbio Truenat MTB/RIF platform (Molbio Diagnostics, Verna, Goa, India) versus the hub-and-spoke standard of care, predominantly off-site testing with Xpert MTB/RIF (Cepheid, Inc., Sunnyvale, CA, USA). We used a health systems perspective, nested in a pragmatic, cluster-randomized trial across 29 clinics (15 intervention, 14 standard of care) among four sites in Mozambique (Sites A and B) and Tanzania (Sites C and D). We estimated ranges for health service delivery costs using trial expense reports, facility assessments, and project staff interviews.
Results The estimated cost per participant tested using on-site Molbio Truenat was $53 (95% credible interval: $45-$63) in Mozambique [$55 ($47-$64) for Site A and $57 ($50-$64) for Site B], and $42 ($35-$50) in Tanzania [$41 ($36-$47) for Site C and $48 ($39-$57) for Site D]. For the standard-of-care (hub-and-spoke) arm, the cost per participant tested was $40 ($35-$45) in Mozambique [$35 ($33-39) for Site A and $48 ($45-$52) for site B], and $21 ($19-$24) in Tanzania [$23 ($21-$24) for Site C and $20 ($18-$22) for Site D]. Equipment and staffing costs for testing were higher in the decentralized arm, as many of these costs were shared between clinics in the standard-of-care arm. Costs for consumables, training, and communication were comparable across arms.
Conclusion From a health system perspective, decentralized molecular testing for tuberculosis is more expensive than using a hub-and-spoke approach.

OA-286

Plasma concentrations of first line antituberculosis drugs in infants with HIV and severe pneumonia: A pharmacokinetic sub-study of the Empirical Trial

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Background Infants living with HIV are at high risk of tuberculosis and death. Optimal antituberculosis therapy is essential for favourable clinical outcomes particularly in severely ill children. Using WHO-recommended weight-band dosing, younger children weighing <8kg are at risk of suboptimal exposures. We aimed to evaluate plasma concentration of first line antituberculosis drugs in infants with HIV.
Methods EMPIRICAL trial (#NCT03915366; EDCTP2-funded (RIA2017MC-2013)) is a randomized controlled trial evaluating empirical antituberculosis and cytomegalovirus treatment in infants with HIV hospitalized for severe pneumonia in 5 African countries. Eligible infants aged <1 year, weighing ≥3kg, on antituberculosis treatment had a blood sample taken 2-hours post-dose at days 30, 90 and 180 in a pharmacokinetic sub-study. Antituberculosis drugs were dosed according to WHO weight-bands using fixed-dose-combination dispersible tablets of rifampicin(15mg/kg)/isoniazid(10mg/kg)/pyrazinamide(35mg/kg) 75/50/150mg with ethambutol(20mg/kg) 100mg. Antiretroviral-naïve infants initiated treatment in accordance with national guidelines. We compared C2hr plasma concentrations for rifampicin, isoniazid, pyrazinamide, and ethambutol with published Cmax references.
Results Forty-nine infants of whom 21 were female, median (range) age 6.1(2.5-13.5) months and weighing 5.3(3.4-8.7) kg were included in the analysis of study day 30. The geometric mean (CV%) C2hr for rifampicin, isoniazid, pyrazinamide and ethambutol were 3.66(161) mg/L, 2.80(102) mg/L, 22.27(97) mg/L, and 0.56(101) mg/L, respectively. The C2hr values were substantially below adult reference Cmax for rifampicin [ref in adults (10 mg/kg dose): 8-24 mg/L] and ethambutol [ref: 2-6 mg/L], slightly lower for isoniazid [ref: 3-6 mg/L], and within range for pyrazinamide [ref: 20-60 mg/L].
Conclusion Plasma levels of first-line TB drugs in infants with HIV and severe pneumonia were low compared to adults. This is consistent with other studies showing that infants and younger children do not achieve adult references for first-line TB drugs at current recommended doses. Our data support considerations for optimising dosing of first-line TB drugs for infants.

OA-317

A multi-component integrated HIV/HTN care model improves hypertension screening and control in rural Uganda: A cluster randomized trial

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Background The prevalence of hypertension (HTN) is increasing among people with HIV (PHIV) across sub-Saharan Africa. However, little data exist on the effectiveness of integrated HIV and HTN care delivery systems on blood pressure [BP] screening and control.
Methods We conducted a cluster-randomized trial among PHIV (≥18 years) to evaluate a multicomponent integrated HIV/HTN care model (intervention) versus standard-of-care (control) in 52 health centres (HCs, 2/district and 26/arm) in rural Southwestern Uganda (NCT04624061), with districts as unit of randomization. The intervention included: 1) health worker training on integrating HTN care, 2) promoting HTN screening and care; 3) introduction/improvement of NCD registers, patient care cards, and HTN data capture in electronic medical records; 4) WhatsApp messages for coordination among providers and district health teams. Both arms received BP machines, NCD registers, patient cards, and buffer HTN medicines. Evaluation included: cross-sectional surveys administered annually to a random sample of patients in each HC. Primary endpoints were recent HTN screening and HTN control (<= 140/90 mm Hg) at 24-months. We examined differences in screening (intervention vs. control) within subgroups and change in HTN control (BP<140/90mmHg) from 12-to-24-months within intervention clinic participants with HIV and HTN. Analyses were adjusted for clustering.
Results Among 3,603 PHIV (2,114 intervention; 1,489 control; 53% women; 47% aged ≤40years) surveyed at 24-months, HTN screening was 76% in intervention vs. 22% in control clinics; risk ratio (RR)=3.44 (95%CI:2.50-4.72; p<0001). Effects were seen for women (RR=3.16), men (RR=3.84), adults aged 18-40years (RR=4.29), and adults aged 41+years (RR=2.96). In the intervention arm, HTN control improved from 33% at 12-months to 57% at 24-months for a risk difference=24% (95%CI:17-30%; p<0.001).
Conclusion The integrated HIV/HTN care model dramatically improved overall HTN screening and BP control among PHIV and HTN. This presents opportunities to reduce NCD related morbidity and mortality and improve HIV/HTN care.

OA-322

Bridging the research gaps on AMR in sub-Saharan Africa - A One Health approach

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Disease outbreaks and management are a huge challenge for public health systems worldwide. With globalization, spread of pathogens through trade and travel increases the demand for suitable medicines. At the same time, the excessive use of drugs in veterinary and human medicine leads to a reduction in effectiveness and even to the development of resistances. Antimicrobial resistance (AMR) has become a major problem worldwide. While most high-income countries have already developed a strong surveillance system for AMR, low- and middle-income countries have an urgent need for monitoring AMR. This, as well as the coinfection with neglected tropical diseases (NTDs), remains a significant challenge, especially across sub-Saharan Africa.
The aim of this project is to strengthen the capacity across 7 Sub-Saharan African countries for improved management of AMR and NTDs. The focus here lies on identifying the linkages and transmission of AMR between humans, animals and the environment in a One Health context. In order to better control AMR, academic and research institutions from the eight participating countries have developed 6 work packages (WPs) to build the local capacity to identify the main transmission routes.
The WPs include screening for AMR in humans, environment and livestock, employing surveillance and genetic mapping of circulating AMR strains; investigating relationships between helminthic infections and drug resistant bacteria; developing capacities for point of need diagnostics of AMR and NTDs using mobile labs for field application; identifying any changes in antimicrobial use and AMR incidence during the COVID-19 pandemic in Sub-Saharan African contexts; controlling communicable disease transmission, by identifying and improving existing hygienic practices at the human-animal-environment interface; and building capacity for sustainable leadership in antimicrobial stewardship (AMS).
With the established consortium, this project proposes unique solutions for AMR/AMS through the development of both knowledge and technological infrastructure from a large, diverse, multidisciplinary team.

OA-333

Kinetics of antibody in Ebola survivors following specific anti-Ebola treatment in the Democratic Republic of the Congo

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Background The use of specific anti-Ebola monoclonal antibodies has increased the survival rate of Ebola patients. The present study aimed to assess their impact on antibody response in EVD survivors.
Methods We conducted a cohort study among survivors of the tenth EVD outbreak in DRC. All participants were treated with monoclonal antibodies (Ansuvimab, Inmazeb, or ZMapp) or an anti-virus (Remdesivir). The antibody levels against Ebola Glycoprotein, Nucleoprotein, and Viral protein antigens using Luminex technic, measured during the EVD acute phase were confronted to those analyzed during the study follow-up. The primary outcome was the antibody level over time. Both linear and logistic regression models were used to assess the association between antibody levels and the main relevant exposures.
Results Among the 358 analyzed for antibody response, 23·7% were seronegative for at least two antigens at the discharge from the Ebola Treatment Center. The antibody trend showed an up-to-down trend but a continuous decrease in an overall linear evolution. The quantitative modeling has shown a significant decrease in antibody levels for NP, GP, and VP-40 ($p<0·001$) with the fastest decrease for glycoprotein. The factors that are significantly associated with the lower antibody rate for NP were Ansuvimab ($p=0·001$), male ($p=0·016$), and higher CT value ($p<0·001$). The probability of being positive for at least two antigens was 53% for Ansuvimab, 73% for Inmazeb, 76% for Remdesivir, and 78% for ZMapp.
Conclusion The US FDA-approved monoclonal antibodies Ansuvimab and Inmazeb have both been effectively administered to EVD patients. According to the analysis of the patient's antibody kinetics, one-fourth of them were seronegative on the day of discharge, and the majority rapidly lost their antibodies over time. These findings highlight the issue of how monoclonal antibodies could affect the control of EBOV reservoir in survivors who may be at risk for EBOV reactivation.

OA-344

Clinical development in Burkina Faso of novel malaria vaccines based on the Pfs48/45 antigen

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Background Malaria transmission blocking vaccines (TBV) hold the potential to block malaria transmission in the population thereby contributing to malaria elimination by producing specific antibodies against functionally important proteins expressed during parasite development in the mosquito. The Plasmodium falciparum Pfs230 and Pfs48/45 proteins are leading candidates for a malaria TBV, while the Circumsporozoite Protein (CSP) remains the leading candidate for an anti-infection Vaccine.
Methods A scalable and reproducible product process in Lactococcus lactis was developed for two candidates: R0.6C (a first-generation TBV) and ProC6C (a novel fusion protein, developed as a multi-stage malaria vaccine). Preclinical development led to a dual-adjuvant design for clinical evaluation, where the antigen is absorbed to Alhydrogel® and either administered directly or mixed at the bedside with the Matrix-M™ Adjuvant. A first-in-human Phase 1 study, conducted in Burkina Faso adults, evaluated R0.6C and ProC6C (at two dose levels, 30/100 µg) formulated on Alhydrogel® alone or in combination with Matrix-M (15/50 µg).
Results This clinical study demonstrated that both antigens, regardless of dosage, on either formulation were safe and well tolerated. Serology conducted against the immunogen, demonstrated that the addition of Matrix-M enhanced the immune response in adult Burkinabes, compared to Alhydrogel® alone. The functional antibody response, evaluated by an independent laboratory, demonstrated that R0.6C induces sporadic transmission reducing antibodies (TRA). In comparison, ProC6C induced significant transmission reducing antibodies (>75% TRA in > 75% of the cohort).
Conclusion These results demonstrate that malaria proteins, produced L. lactis and when formulated on Alhydrogel® alone or in combination with Matrix-M are safe, well tolerated and immunogenic. The immunogenicity of ProC6C and its functional antibody response, lays the foundation for further clinical development of this novel chimeric antigen. This project is part of the EDCTP2 Programme supported by the European Union and Developing Countries Clinical Trials Partnership (Grant number RIA2018SV-2311).

OA-345

The 1,000 Global Research Studies Challenge: Developing nursing, midwifery and community health workers' research leaders to transform global healthcare

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Background Low- and middle-income countries (LMICs) across Africa face significant health challenges and yet there is vast disparity in where research happens across the globe. Nurses, midwives, and community health workers are the predominant healthcare provider in most care settings and so should be supported, trained and enabled to undertake research that can deliver evidence to improve health outcomes in their communities.
Methods Global Research Nurses, part of The Global Health Network, is teaming up with the Nursing Now Challenge and other partners worldwide to utilize research as a leadership opportunity for nurses, midwives, and community health workers in LMICs. The goal of this collaboration is to register 1,000 research studies led by these healthcare professionals and provide them with the necessary skills and opportunities to generate new evidence that can improve health outcomes in low resource settings, supporting Health for All. Each study will deliver new skills and opportunities within the workplace, whilst generating missing data, supporting Health for All. The Global Health Network, a WHO collaborating centre and vast community of practice will provide the scaled support and mechanisms for the studies to be designed, operated, and reported. The Nursing Now Challenge campaign aims to improve health globally by creating leadership development opportunities for nurses and midwives.
Results The initiative will empower nurses and midwives to lead and innovate in healthcare and enhancing their professional development by delivering research leadership skills in the workplace. The program will provide lasting research capacity, achievable leadership and career development opportunities, and a comprehensive plan to ensure that it can work and leave strong, lasting impact.
Conclusion By increasing the capacity for nursing, midwifery and community health workers' research, this challenge will help to elevate these professions and demonstrate their crucial role in addressing African and global health challenges.

OA-358

Innovative Access Approach to Translate R&D into Impact for Preschool-Aged Children Suffering from Schistosomiasis

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Background Based on the 2021-2030 WHO Neglected Tropical Diseases (NTDs) Roadmap, schistosomiasis elimination as public health challenge will require treatment of all populations at risk, as well as development of innovative products such as a pediatric medication to target specifically preschool-aged children. Access to treatments for NTDs is currently based primarily on philanthropic donations from pharmaceutical companies which have significantly contributed to decrease endemicity while ensuring access to targeted populations. However, new access models to provide innovations are a prerequisite to ensure long-term sustainable and equitable access to all at country level, strengthening country ownership and empowerment in the fight against NTDs.
Methods Together with international stakeholders, the Pediatric Praziquantel Consortium is elaborating the various elements of an innovative procurement-based mechanism addressing the "4 As" of an access framework based on Availability, Affordability, Accessibility and Acceptability of the potential new pediatric treatment option, once it will be registered.
Results This is a new access path in the NTD community with many gaps to fill. Some elements have been already defined such as the establishment of a high-quality local manufacturing ensuring adequate production, a tailored regulatory approach allowing introduction of the product in countries, and a pricing structure leading to affordability. However other elements such as the demand path, the procurement mechanism and its funding remain critical gaps to be addressed with the support of the countries and international stakeholders.
Conclusion Innovations needed to address the WHO 2030 Elimination agenda will also require an innovation in their accessibility as today this aspect of the value chain is the new valley of death hampering the translation of NTD R&D into impact.

OA-359

Latent Tuberculosis Infection among people with Diabetes Mellitus in Uganda and Tanzania

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Background People with Diabetes Mellitus (DM) are at increased risk for TB and those who have latent TB infection (LTBI) might be indicated for TB preventive therapy. We examined the prevalence and determinants of LTBI among people with DM as part of the PROTID project in Uganda and Tanzania.
Methods A total of 2005 participants with DM were screened for LTBI at four sites in Uganda and Tanzania. LTBI was diagnosed using the tuberculin skin test (TST) with a cutoff of 10mm and or a positive QuantiFERON-TB plus (QFT-plus) after excluding ATB.
Results The overall prevalence of LTBI was high at 56.3% (lowest at 35.1% in Moshi, Tanzania, and highest at 77% in Kampala, Uganda). 780/2005 (38.9%) had a positive TST, 862 (43.0%) had a positive QFT-plus, and 515 (25.7%) had both a positive TST and QFT-plus. There was a good agreement of 72% (k=0.42; 95% CI: 0.38-0.46) between the two tests. On multivariable analysis, those aged between 36-45 [AOR=2.38 (CI: 1.44-3.92)]; 46-55 [AOR=1.98 (CI: 1.26-3.13)]; and 55 years and above [AOR=1.48 (CI: 0.95-2.29)]; previous TB [AOR=1.85(CI:1.15-2.99, p=0.01)], contacts with TB disease [AOR=1.51(CI:1.16-1.96)] were associated with increased odds of LTBI positivity while Female gender [AOR=0.59(CI: 0.48-0.73), p<0.001] and HIV positivity [AOR=0.66(CI:0.47-0.93), p=0.02] were statistically not associated with LTBI positivity. Overweight and obese DM patients had increased odds of LTBI [AOR=1.85 (1.02-3.35) p=0.04 and AOR=2.18 (1.19-3.97) p=0.01] respectively. Known factors such as current BCG scar, smoking, or alcohol use were not associated with LTBI in this population.
Conclusion People with DM in East Africa are at a high risk of LTBI. Early detection and treatment of LTBI in this population could help prevent the progression to active TB and reduce morbidity and mortality associated with TB in people with DM.
Funding: EDCTP

OA-365

Capacity building as a response to emerging and re-emerging infectious diseases in Africa

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Background Emerging and re-emerging infectious diseases (EREIDs) are evolving global health challenges especially to highly vulnerable health systems in Sub-Saharan Africa (SSA). EREIDs may arise from any viral, bacterial, fungal, protozoal, helminthic or prion pathogens. Importantly, the EREIDs challenge in the backdrop of widespread antimicrobial resistance complicates disease control processes. The vision of the Consortium for Development of Sustainable Research Based Fellowship Training on Infectious Disease Epidemiology and Biostatistics in Africa (IDEA Fellowship) is to strengthen capacity building in infectious disease field epidemiology through pragmatic fellowship training, with the objective to train the next generation of infectious disease field epidemiologists in conducting disease surveillance, outbreak investigations and timely response, and translating data into evidence-based practice in Uganda and Africa.
Methods Through a consortium approach, the IDEA Fellowship Programme has involved key stakeholders to implement the first national infectious disease field epidemiology Master's programme. The consortium led by Busitema University has 8 complementary, but synergistic partners: Uganda National Public Health Institute; Ministry of Science, Technology and Innovation; Uganda National Health Laboratory and Diagnostic Services; Uganda Virus Research Institute, Mbale Clinical Research Institute; Infectious Diseases Institute. The Open University, UK is our Northern Partner.
Results The first national formal curriculum on Infectious Disease Epidemiology and Biostatistics was developed, approved and is being implemented. Through a fair, gender-balanced, rigorous, and competitive 24 months fellowship programme, we recruited 15 African early-to-mid career scientists of whom 13 are currently progressing well in their Fellowships. 13 emerging and re-emerging infections in Uganda are being profiled. The fellows are organising a training conference in which 20 district level epidemiologists and biostatisticians will be trained in Uganda.
Conclusion The IDEA Fellowship Programme is a paradigm for the development of a critical mass of scientists in Infectious Disease Epidemiology and Biostatistics in Africa.

OA-408

Clinical Trial Capacity building from scratch: The WANECAM 2 Experience in Niamey, Niger

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Background The West African Network for Clinical Trials of Antimalarial drugs second edition (WANECAM2) is an Africa-Europe consortium funded by EDCTP2. In collaboration with Novartis and Medicines for Malaria Venture WANECAM2 is contributing to the development of KAF156-LUM SDF and improving clinical studies capacity in the sub-Region. A novel team was identified in Niger, where clinical trial capacity is lagging and was targeted for focused capacity building.
Methods A series of trainings in clinical trial procedures, GCP and GLP were provided by the MRTC-team in July 2019 in Bamako, Mali. A second GCP training was done on site in Niamey, Niger by the MRTC in November 2019 where the entire Niger team participated. Two Niger Biologists visited the MRTC for training and certification in August 2022 while one physician received advanced training in clinical trial procedures, embedded in one of the Mali trial sites. Three nurses were trained on the REDcap platform on medication data entry. One PhD student and one MSc student were registered at USTTB, Mali. Site visits of WANECAM2 teams in Burkina-Faso were organized for the Niger leadership.
Results From November 2019 to December 2020, with on-site assistance from two experienced physicians and one laboratory certified technician from Mali, the Niger team conducted a Phase IV in vivo study on the efficacy of Artesunate-Pyronaridine versus Artemether-Lumefantrine and enrolled 240 participants. A second study on biological parameters completed in May 2022 with a total of 1052 participants enrolled. Quality control and data analysis are underway. A new building was refurbished and fully equipped.
Conclusion A new study team and infrastructure was built from scratch in Niger through South-South collaboration and is ready to contribute to an upcoming Phase III trial.
Funding: WANECAM2 which is part of the EDCTP2 (RIA2017T-2018 WANECAM2).

OA-429

High Mortality in African infants living with HIV hospitalized with severe pneumonia

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Background Children with advanced HIV disease (AHD) are at an increased risk of morbidity and mortality. We describe mortality rates among infants with AHD hospitalized with severe pneumonia.
Methods EMPIRICAL is an ongoing Phase II-III, open-label randomized factorial (2×2) trial supported by EDCTP (GA RIA2017MC_2013/#NCT03915366) to assess the impact of empirical treatment against cytomegalovirus and tuberculosis in infants living with HIV hospitalized with severe pneumonia. The primary endpoint is all-cause mortality at 15-days and 12-months post enrolment. Recruitment is on-going and includes 22 hospitals from 6 African countries (Côte d'Ivoire, Malawi, Mozambique, Uganda, Zambia, Zimbabwe).
Results In March 2023, 431 infants had been recruited and 429 were included in analysis. Their median age was 4.36 months (IQR, 3.18-7.08) and 49% were female; 164 (38%) had a history of maternal and/or infant prophylaxis for prevention-mother-to-child-transmission (PMTCT); 306 (71%) were newly diagnosed of HIV during hospitalization; Median HIV viral load and CD4% were 6.3 logs copies/mL (IQR, 5.8-7.0) and 14.4% (IQR, 9.9-21.6) respectively. 196 (46%) of the infants died within a 6 months follow up period (2.16 months (IQR, 0.26-6.16), 110 (56%) in the first admission and 86 (44%) after it. The main register causes of death are pneumonia 91 (46%), sepsis 32 (16%) and gastroenteritis 10 (5%). An in-depth analysis of deaths is ongoing, including minimally invasive tissue sampling, microbiological and histopathological evaluation.
Conclusion Children living with HIV and severe pneumonia have a very high mortality, both during the initial hospitalization and after hospital discharge. Measures focused on earlier identification and treatment as well as focused on decreasing post-discharge mortality are urgently needed. EMPIRICAL will report on the survival benefit of cytomegalovirus and tuberculosis treatment at trial conclusion. Emphasis should be put into reducing missed opportunities for PMTCT; strengthening early infant diagnosis and antiretrovirals initiation for those who fail PMTCT.

OA-442

Legislative, Educational, Training, Institutional and Social impact evaluation of the BERC-Luso Project in the Portuguese-Speaking African Countries

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Background The Biomedical Ethics and Regulatory Capacity Building for Portuguese Speaking African Countries Project (BERC-Luso) was a four-year initiative that aimed to enhance biomedical ethics and regulatory capacities in Angola, Cape-Verde, Guinea Bissau, Mozambique, São Tomé and Príncipe, and Portugal. The project established a network of National Ethics Committees (NCEs), National Regulatory Authorities (NRAs), and experts in biomedical research, developed a comparative legislative study, and created educational programs to promote capacity building. The digital repository in Portuguese language served as an example for similar projects and supported complementary actions beyond the project's term.
Methods A set of indicators was developed to measure the project's impact, and the evaluation was carried out through public and grey literature and event reporting. The indicators were linked to concrete actions that leveraged institutional, legislative, and capacity-building development. Score points were attributed to each indicator, with calculation of score mean values.
Results In all partner countries, a high level of success (78.59%) was achieved by meeting the goals set at the beginning of the project via the roadmap. A total of 311 activities were developed, impacting at least 3,848 professionals from different backgrounds. Over 172 hours of training were delivered, and the project registered mass dissemination through television broadcast, radio, and media in at least six countries.
Conclusion Overall, the BERC-Luso Project had a significant impact on every participating country, visible through the long-lasting effects of the successful implementation of the bottom-up and top-down approaches. The project trailblazed capacity building in ethical and regulatory revision in the partner countries, but there is still a need for further investment in legislative, institutional, and training levels to reinforce the implementation of best practices.

OA-445

A phase II/III multicenter randomized clinical trial evaluating the safety and efficacy of a single and three-day albendazole-ivermectin fixed-dose versus albendazole to treat soil-transmitted helminthiases

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Background The widespread use of benzimidazole-class anthelmintics for the control of soil-transmitted helminths (STH) is challenged by the suboptimal efficacy of the drugs used (especially against Trichuris trichiura and Strongyloides stercoralis), and the possible emergence of anthelmintic resistance. A new fixed-dose combination of albendazole and ivermectin (FDC) is a promising solution. Here we report the results of an EDCTP-funded multicenter Phase II/III adaptive randomized clinical trial (ct.gov: NCT05124691) to evaluate the safety and the efficacy of the FDC given as a single-dose (FDCx1) or 3-day regimen (FDCx3) compared to albendazole (ALB) single-dose for the treatment of T. trichiura, hookworm and S. stercoralis in individuals aged between 5 to 17 years in Mozambique, Ethiopia and Kenya.
Methods The phase II component was designed to assess the safety of FDCx1 and FDCx3 in 3 weight groups in Kwale, Kenya. The main outcome was safety, assessed by recording the type of adverse events, frequency, duration, severity, and relationship to study drugs. The results were then evaluated by the DSMB to proceed with the phase III efficacy trial. The main endpoint of phase III was defined as the cure rate for each of the 3 species of STH, measured 21 (+/- 7) days post-treatment using duplicate Kato-Katz thick smears.
Results A total of 993 participants were recruited during Phase II (n=128) and Phase III (n=865). For Phase II, 27 (21.1%) received ALB, 50 (39.1%) FDCx1, and 51 (39.8%) FDCx3. The safety analysis included 124 participants. No severe adverse events were observed in the study. The percentage of participants with adverse events was 4 (17%) for ALB, 10 (20%) for FDCx1, and 12 (24%) for FDCx3. Most were mild gastrointestinal adverse events in the three treatment arms.
Conclusion The results of the phase III trial are being now analyzed and will be presented in the meeting.

OA-451

Spirometry, diffusion capacity, absolute lung volumes and PET/CT findings upon completion of tuberculosis treatment - preliminary findings of StatinTB/ExtendTB trial

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Background Morbidity and mortality rates after successful completion of a six-month course of tuberculosis (TB) treatment remain elevated. Persistent lung inflammation (PLI) on 18F-FDG-PET/CT has been associated with TB relapse and may also lead to post-TB lung disease (PTLD).
Methods The ongoing EDCTP-funded StatinTB trial (RIA2017T-2004; NCT04147286) evaluates safety/efficacy of 40 mg atorvastatin to reduce PLI after TB treatment in HIV-/HIV+ adults measured by 18F-FDG-PET/CT with extended total follow-up of 96 weeks (ExtendTB, NIH-funded). We report findings at time of enrolment into StatinTB/ExtendTB of the first 106 participants. Participants with clinical response to TB treatment and a negative sputum culture for TB at 16 weeks were screened after completing 24 weeks of treatment for drug-sensitive TB. Complete pulmonary function and PLI were measured using EasyOne Pro®Lab and PET/CT. PLI was defined as total lung glycolysis (TLG)≥50 SUVbw*mL. StatinTB/ExtendTB are conducted according to ICH-GCP.
Results Of the 106 participants (32% women) aged 32.5±7.0 years who underwent PET/CT, 20.8% were HIV+, 57.5% smokers, 28.3% had previous TB; 13.2% reported ongoing cough, 3.8% chest pain and 8.5% shortness of breath. PLI was present in 49.1% of participants (mean TLG of 209±161 SUVbw*mL). Diffusing capacity of the lung for carbon monoxide (DLCO) was consistently reduced in participants with PLI (DLCO%Pred 73.4% vs. 93.7%; p=0.0002) as was FVC%Pred (82.1% vs. 94.9%; p=0.0004); FEV1%Pred was 82.1% vs 94.9%, p=0.0004. After accounting for other variables including HIV and smoking, every one percent increase in DLCO%Pred remained independently associated with a decrease of 4.7 SUVbw*mL of TLG (p=0.017).
Conclusion PTLD is present in half of participants. Impaired DLCO is associated with PLI in adults after completing a 24-week treatment regimen for drug-sensitive TB. This highlights the need for treatment optimisation during and after TB treatment to reduce PTLD with persistent lung inflammation.

OA-464

Clinical predictors of tuberculosis in children – a prospective study in five low-middle income countries

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Background Paediatric Tuberculosis (TB) is associated with significant morbidity and mortality. Despite advances in methods of microbiological detection, diagnosis relies heavily on clinical and radiological features.
Methods Children (<15years) with suspected TB from 5 low-middle income countries were prospectively enrolled. Baseline demographic and clinical data, and specimens for microbiological testing were collected. Participants were categorised as confirmed, unconfirmed or unlikely TB, according to NIH consensus definitions. Odds ratios were calculated using multivariable logistic regression analyses comparing 1) confirmed vs unlikely TB, and 2) TB disease (confirmed and unconfirmed TB) vs unlikely TB.

Results Of 974 children enrolled, 842 (86.4%) had sufficient data for diagnostic classification; 28.4% (239/842) had confirmed TB, 34.2% (288/842) unconfirmed TB, and 37.4% (315/842) unlikely TB. The median age was 5.2 years (IQR, 1.9 to 9.1), with 48.9 (412/842) <5 years and 11.6% (98/842) <1 year. Overall, 15.8% (133/842) were children living with HIV (CLHIV) with almost half (47.7%, 63/133) antiretroviral treatment naïve. Malnutrition was present in 22.3% (188/842). Reported symptoms were similar across groups. Children with confirmed TB had the highest prevalence of positive Tuberculin Skin Test results, TST (61% [134/239] vs 49% [129/288] in unconfirmed group and 42% [125/315] in unlikely group) and chest radiograph (CXR) findings attributable to TB (45% [108/239] vs 30% [87/288] and 13% [41/315]). Regression analysis found associations between confirmed TB and TST positivity (OR 6.36, 95%CI 3.52-11.50), CXR (OR 2.57, 1.33-4.97) and number of symptoms (OR 1.27, 1.05-1.52 for each additional symptom reported); and TB disease and CLHIV (OR 2.92, 1.60-5.34), TST positivity (OR 4.07, 2.63-6.31), CXR (OR 2.26, 1.39-3.67), and number of symptoms (OR 1.26, 1.09-1.45 for each additional symptom reported).
Conclusion From one of the largest childhood cohorts, over half of children with TB disease were diagnosed based on clinical and radiological features alone. Findings reflected the well-described symptomology of paediatric TB.

OA-484

Improving rapid detection of 2nd line drug resistance in Mycobacterium tuberculosis with Xpert MTB/XDR and MolBio 2nd line

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Background Rapid detection of resistance to key drugs such as fluoroquinolones (FQ) and bedaquiline (BDQ) is essential for appropriate management of multi-drug resistant tuberculosis (MDR-TB). . Molecular tests available require either infrastructures not available in peripheral laboratories in low resource countries, or do not detect resistance to BDQ. Recently, two tests have been developed: GeneXpert MTB/XDR (Cepheid, USA) detecting resistance to isoniazid (INH), FQ and ethionamide (ETH), and TrueNat XDR (Molbio Diagnostics, India) for detection of resistance to INH, FQ and BDQ.

Methods In the EDCTP-funded project (DIAMA) aimed at developing culture free approaches for diagnosis and management of MDR-TB patients, we assessed the performances of these tests in field conditions compared to phenotypic drug-susceptibility testing (pDST) and whole genome sequencing (WGS) using 1711 unique samples consecutively collected in the Sub-Saharan African region (Benin, Cameroon, DRC, Ethiopia, Guinea, Mali, Nigeria, Rwanda and Senegal).

Results Using a composite reference standard comprising pDST and WGS, Xpert-XDR showed a sensitivity of 87.3% for INH, 37.8% for ETH and 66.7% for FQ, with a respective specificity of 96.5%, 98.3% and 99.7%. For TrueNat, the sensitivity was 88.1% for INH and 47.4% for FQ, with a specificity of 85.7% for INH, 97.7% for FQ and 98.5% for BDQ.

Conclusion These tests showed promising results, particularly as screening test for detection of resistance to FQ and BDQ.

OA-490

Safety, reactogenicity and immunogenicity of MTBVAC in newborns in a TB endemic area: a phase 2a randomized, double-blind, dose-defining trial

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Background New safe and effective TB vaccine strategies to replace infant BCG vaccination are needed urgently. We evaluated the safety, reactogenicity and immunogenicity of three doses of the live-attenuated Mycobacterium tuberculosis (Mtb) vaccine candidate, MTBVAC, in comparison to BCG in South African newborns.

Methods Healthy infants, HIV-unexposed, BCG-naïve newborns without history of close TB contact were randomly allocated into three sequential cohorts to receive a single intradermal dose of BCG (SSI, 2.5×10^5 CFU) or MTBVAC (2.5×10^4; 2.5×10^5 CFU; or 2.5×106 CFU).

Results 228 pregnant women consented, and 99 newborns were enrolled. Seventy-eight infants across all 3 cohorts had local reactions, all rated mild, except one grade 2 erythema. Induration, swelling, and erythema was more common with increased MTBVAC dosage. Induration and swelling were more common in MTBVAC 2.5x106 than in BCG and reactogenicity in MTBVAC 2.5x105 was same as BCG. Twelve infants experienced 14 vaccine-unrelated SAEs including one death due to bronchopneumonia. Eight infants commenced TB treatment for unconfirmed pulmonary TB (BCG n=4 and MTBVAC 2.5x104 CFU n=4) and one for unconfirmed TB meningitis (BCG). MTBVAC was highly immunogenic at all 3 doses, inducing predominantly Th1-cytokine-expressing CD4 T-cells, which peaked at day 56 and waned thereafter. The 2.5×105 and 2.5×106 CFU MTBVAC doses were more immunogenic than BCG, inducing very similar response magnitudes and phenotypes. Vaccination with any MTBVAC dose resulted in QFT conversion in most infants at Day 56, but these responses waned and reverted to QFT-negative in more than half by the end of the 1-year follow-up period.

Conclusion MTBVAC appeared safe and well tolerated and immunogenic at doses between 2.5×10^4 CFU and 2.5×106 CFU in South Africans newborns. The 2.5×105 CFU MTBVAC dose was selected for the ongoing phase 3 trial in a high TB prevalence setting.

OA-498

PedMAb1 clinical trial: Safety assessment of CAP256V2LS to prevent breastmilk HIV transmission in HIV-1 exposed uninfected neonates

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Background Breastmilk optimizes child survival in low-middle income high HIV prevalence settings. However, breastmilk transmission of HIV-1 continues to contribute to residual vertical HIV transmission. The Phase 1 PedMAb clinical trial aims to define the optimal doses, ideal combination and timing of subcutaneous (SC) administration of two HIV-1 broadly neutralizing antibodies (bNAbs), VRC07-523LS and CAP256V2LS, separately or in combination, to prevent breastmilk transmission of HIV-1 in high incidence regions such as South Africa. The trial is being conducted at the South African Medical Research Council Chatsworth Clinical Research site and the RK Khan hospital. Here we first report the reactogenicity and safety events of CAP256V2LS for the first time in infants.

Methods Between 1st September and end of October 2022, 8 eligible HIV exposed uninfected infants received 5mg/kg CAP256V2LS SC, within 72 hours of birth. All infants were observed for 4 hours post-dose, and followed up face-to-face at days 3, 14 and 28 post-dose for primary objective safety assessments, and until 6 months for secondary objective. A pictorial study diary handed to mothers and collected at day 14 post-dose helped mothers document reactogenicity and early adverse events (AEs). An internal study safety committee reviewed all safety data every two weeks. The Division of AIDS Table, version 2.1. July 2017, was used to grade AEs.

Results No reactogenicity events were observed at 4 hours or over the first 3 days post-dose. Thirteen AEs were documented during the 28-days post-bNAb administration, mostly common illnesses (except for low absolute neutrophils, a palatal cyst and an uncomplicated umbilical hernia); other 20 AEs were recorded during the following 5 months. AEs were deemed unrelated to study product.

Conclusion CAP256V2LS administered SC at 5mg/kg to infants within 72 hours of birth is safe. The trial is proceeding to test bNAb's safety at a higher dose (10mg/kg).

OA-504

Towards an arsenic-free oral treatment for human African trypanosomiasis due to Tb rhodesiense: a new tool for disease elimination

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Background T.b. rhodesiense human African trypanosomiasis (r-HAT), the zoonotic, acute form of sleeping sickness in Eastern Africa, is lethal if untreated. Today only one arsenic-based, neurotoxic drug, melarsoprol, is available for intravenous treatment of advanced meningo-encephalitic disease, the most frequent presentation seen by health services. A new oral treatment would simplify HAT elimination as proposed by WHO. Fexinidazole was approved in 2018 as the first oral drug to treat T.b. gambiense HAT but was not yet evaluated for r-HAT.

Methods A single-arm clinical trial beginning October 2019 in the two main known foci in Malawi and Uganda tested fexinidazole for r-HAT as an alternative to existing treatment. Complementary actions included training of prescribers and laboratory technicians of peripheral health facilities to improve diagnostic capacity, and ethnographic research to understand health-seeking behaviours of populations at risk. These studies supported the creation of community awareness materials and activities.

Results The primary efficacy result of the clinical trial was achieved with no related deaths during hospitalisation: 0 (C.I.=0.0-8.43%), against a benchmark of 8.5% lethality attributable to melarsoprol. Training covered health staff from twelve provinces in Uganda and three in Malawi, beyond initial plans. Two ethnographic studies provided updated information about perceptions of communities at risk regarding r-HAT, leading to four articles. Posters and leaflets were developed and disseminated in health facilities and community gatherings.

Conclusion Fexinidazole has shown to be a good alternative to existing treatments for oral treatment of both stages of r-HAT. It will be submitted for EMA regulatory review in preparation for use in endemic countries. Disease awareness has increased among health staff and populations living in endemic areas of Uganda and Malawi. We expect fexinidazole to be deployed in 2024 as a new r-HAT therapeutic.

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OA-506

Working towards better guidance for studies that involve African healthy volunteers in the context of the VolREthics initiative

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Background There are well-recognised ethical guidelines for biomedical research, though a lack of specific guidance for studies targeting healthy volunteers. Noting this, the Ethics Committee of the French National Institute for Health and Medical Research (Inserm) convened an initiative to propose elaboration of good practices to protect health volunteers in research, VolREthics. Online discussions and workshops were held at international and regional levels since February 2022 to debate experiences and best practices. This abstract presents the summary of findings from the African regional perspective.
Methods An online Sub-Saharan Africa workshop was convened in May 2022. A pre-workshop questionnaire to capture the regional context better was distributed, and notes during the event taken. Feedback from all regional meetings and plans for developing international guidance were discussed at a workshop in Brussels, April 2023, with representatives from regulatory agencies, manufacturers, research institutions and funders, ethicists and healthy volunteers.
Results 78 people from 21 (14 African) countries and 3 healthy volunteers attended the African workshop, 39 completing questionnaires. Concerns raised included inadequate community engagement, informed consent, feedback of results and guidance on/compensation for secondary use of data, plus economic and/or educational vulnerability of participants. The risk of exploitation or harm, and potential for compromised scientific validity of studies was also mentioned. Proposed solutions were better oversight through legislation and competent ethics committees, national guidelines for compensation, appropriate conditions for confinement, improved dialogue between stakeholders, and innovative learning and engagement to build trust in collaboration with relevant partners such as The Global Health Network's African communities of practices.
Conclusion This important initiative has established momentum for closing gaps in how studies enrolling healthy volunteers are conducted ethically and equitably. Further discussions with colleagues from other regions involved in VolREthics should enrich the approach toward sound good practices.
Sponsorship: European Commission, EDCTP, Inserm, Anrs-Inserm, EEIdF

OA-510

Contribution of the BREEDSAFCA project to the sustainable evolution of research participants protection in Cameroon

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Background In Cameroon, ethics review has made remarkable progress since 2009 thanks to a stronger political will and support from national and international partners. This progress however remains limited because existing regulations are not fully elaborate on ethical/administrative evaluation of clinical research and the protection of participants. The coverage and decentralization of the national ethics review system is still limited to ensure the evaluation and monitoring of protocols according to recommended standards while respecting socio-cultural particularities of communities.
Methods The first phase of the BREEDSAFCA (Building Capacity for Research Ethics Evaluation and Drugs Safety Monitoring) project was implemented in Cameroon from 2018 to 2022 with funding from EDCTP to contribute to; among others aims to strengthen the regulatory framework of Cameroon's ethical and administrative evaluation of clinical research, and to improve the national coverage with Research Ethics Committees (RECs). An assessment of the needs in terms of coverage and functioning of ethics committees as well as the reinforcement of regulatory aspects was conducted and the results presented to the competent actors.
Results The progress attributable to the BREEDSAFCA project included; the increase of regions covered by an ethics committee from 2 to 6 out of the 10 Cameroon regions; contributing to the development of the law on the protection of health research participants; the development of master SOPs for the establishment and functioning of RECs and for ethical and administrative review of research protocols; the training of existing RECs members in Cameroon in the evaluation of research protocols, the setting up of independent RECs financing system; and the providing of office space for all officially existing RECs.
Conclusion The BREEDSAFCA project contributed to improving the regulatory framework of the ethics review system in Cameroon, the national coverage of regions by ethics committees and strengthening the capacity and skills of ethics committees to evaluate protocols.

OA-533

UKCDR: Enhancing Coherence, Collaboration, and Joint Action in the UK Research Funding Landscape and Beyond

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UKCDR, the UK Collaborative on Development Research, amplifies the value and impact of research for global development by promoting coherence, collaboration, and joint action among UK research funders. For over a decade, UKCDR has been providing UK research funders with tools, analysis, and good practice to support their evidence-informed decision-making processes to address global challenges.

An underlying principle for effective collaboration and cooperation is the notion of equity. In partnership with ESSENCE on health, we have developed a good practice document supporting funders, institutions, and academics with recommendations on how to embed equity in research partnerships. Following this and of relevance to the work of EDCTP, we are analysing the types of partnerships funders of research for development are developing, the extent to which equity has been defined and/or put into practice, and lessons learned on how to support equitable relationships between research funders to guide future partnership development processes.

Among other strengths of UKCDR is our mapping and analysis work which has provided funders with crucial information on the research landscape on a variety of topics to help shape funding responses. This is exemplified by our COVID CIRCLE initiative (delivered in collaboration with GloPID-R) which features an online tool containing details of more than 20,000 projects awarded by more than 300 funders globally in relation to COVID-19 – which proved to be a valuable tool in helping funders, policymakers, and researchers understand research gaps and potential areas for collaboration to deliver a more effective and coherent global research response to the pandemic. Following its success, we are expanding this work (titled Pandemic PACT) to cover a wider range of epidemic prone diseases and broader epidemic and pandemic research preparedness activities – thereby enhancing collaboration and coherence at a larger scale.

Funding source: various funders (incl UK research funders, government)

OA-544

T cell responses to SARS-CoV-2 infection and vaccination in people living with HIV

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Background A major emphasis as the pandemic progresses is understanding durability of SARS-CoV-2 immune responses in key populations. Some vaccines elicit suboptimal immune responses in people living with HIV (PLWH). Despite viral suppression by ART, incomplete CD4 T cell reconstitution and residual immune activation may compromise immune memory in PLWH. We monitored SARS-CoV-2 infection and vaccine-induced T cell responses in PLWH.

Methods SARS-CoV-2-specific cellular immune responses were measured in healthcare workers who received a single dose Ad26.COV2.S in the Sisonke trial, a phase 3B implementation study. We assessed the durability of spike-specific T cell responses at baseline, 6 and 24 weeks after vaccination, in 78 PLWH and 191 HIV-uninfected individuals.

Results At baseline, 62-75% of participants had existing spike-specific CD4 T cell responses, while 26-28% had CD8 responses, indicating prior infection. There were no significant differences in responses between HIV-uninfected participants and PLWH. Six weeks after vaccination, this increased to 95-96% and 45-66% for CD4 and CD8 Spike T cell responses, respectively; with response magnitudes significantly higher after vaccination in all groups, including PLWH. In those without prior infection, while there was a similar proportion of responders in both groups for CD4 responses, there were significantly fewer PLWH who mounted a CD8 T cell response at 6 and 24 weeks. CD8 response magnitudes were also significantly lower in PLWH. However, in those with an existing baseline spike response, there was no difference between the groups, indicating that a compromised primary response could be recovered by a second spike exposure.

Conclusion We detected transient defects in T cell immunity in PLWH who were well-suppressed. Inadequate T cell responses or accelerated waning of vaccine responses in PLWH may increase risk of severe disease. Understanding the longterm durability of immune memory to SARS-CoV-2 in PLWH is critical for guiding vaccination policy.

Funders: EDCTP and SA-MRC.

OA-601

Acceptability and feasibility of the future introduction of intermittent preventive treatment for malaria in infants in Massinga district, southern Mozambique

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Background Children under five years are at high risk for malaria illness and death. In 2022 the WHO updated and expanded its recommendation for Perennial Chemoprevention of Malaria (PMC), i.e. the delivery of regular doses of sufadoxine-pyrimethamine (SP), integrated within existing Expanded Immunization Programmes (EPI), to prevent malaria in children under 2 years of age living in moderate-to-high transmission settings. To assess the perceived acceptability and feasibility of future PMC intervention
implemented in Massinga District (Mozambique), from the health care workers, caregivers and community perspectives.

Methods We conducted a mixed methods study between June and July 2022. We collected 56 KAP questionnaires with health care workers (HCWs) of the 15 participating facilities and 32-recorded semi-structured interviews with HCWs, caregivers and community healthcare workers (CHWs). For quantitative data, we performed descriptive statistics. Qualitative data were transcribed, analyzed and synthetized through rapid qualitative analysis.

Results All respondents agreed on the heavy burden of malaria in children. Most HCWs (51.8%) were aware that malaria in children could be prevented through tablets (experience from SP in pregnant women). Administering PMC during a vaccination session was perceived as easy and feasible by 92.9% of HCWs. HCWs agreed on the high (89.3%) caregivers' care seeking behaviour in case of fever in children. However, 60.7% agreed that distance and lack of transport poses barriers accessing health facilities. Overall, the integration of PMC in routine EPI services was perceived as relevant. Community members reported trusting healthcare interventions and HCWs as well as CWHs. Caregivers expressed their willingness to participate in active peer mobilization while community members emphasized the need for continuous community engagement to enhance acceptability and influence initially reluctant caregivers.

Conclusion PMC in children was perceived as acceptable by HCWs, caregivers and different community actors, as a strategy to prevent malaria and avoidable care seeking. Structural and logistical barriers were anticipated. Involving key community members in active mobilization was perceived as paramount.

OA-652

Safety and tolerability of favipiravir for the treatment of Lassa fever: A randomized controlled open label phase II clinical trial

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Background Lassa fever (LF) is a severe re-emerging infectious disease caused by the Lassa virus (LV). LF is a priority disease on the World Health Organization's R&D blueprint and affects a large number of countries in West Africa, with Nigeria carrying the highest case burden in the world. Current treatment options are limited to supportive care and the antiviral drug ribavirin. However, evidence for the efficacy of ribavirin in LF is poor. A recent study showed that in vivo plasma concentrations do not suffice to exert a relevant antiviral effect. New drugs for LF treatment are therefore urgently needed but no therapeutic trials have been conducted for this indication in the past decades. Favipiravir is a broad-spectrum antiviral registered for pandemic influenza that has also been clinically evaluated for other viral infections. It shows potent activity against LV in pre-clinical studies. To evaluate the safety and tolerability of favipiravir as repurposed drug in the treatment of LF, a phase II clinical trial was conducted.

Methods LF patients were recruited at the Irrua Specialist Teaching Hospital and the Federal Medical Centre of Owo in Nigeria, which are the worldwide largest LF treatment centres. Blood sampling for virological, serological and immunological analyses, hematology and biochemistry as well as clinical assessments were done on days 1, 2, and then every other day until the end of the study.

Results In total, 40 LF patients were included in the trial between 2021 and 2022. Results on cure rates, safety and tolerability of this first GCP compliant phase II clinical trial will be presented to provide first insights into this new treatment option for LF.

OA-667

HIV self-testing uptake and linkage to HIV care among male fisherfolk in two fishing communities in rural Uganda: early results from the PEST4MEN study

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Background HIV self-testing (HIVST) can improve HIV testing rates among highly mobile populations including the male-fisherfolk, but this is not well documented. We assessed HIVST uptake and linkage to HIV care among male fisherfolk in rural Uganda.
Methods The peer-led HIVST intervention for men (PEST4MEN) was conducted among male fisherfolk in two fishing communities in Kalangala and Buvuma island districts in central Uganda, between July and September 2022. Before intervention implementation, 22 men were selected from existing social network groups and trained to serve as male HIV self-test kits distributors or "peer-leaders". Each peer-leader was then requested to nominate up to 20 men from their social networks, who were screened for eligibility and administered a baseline interview if they were eligible. Eligible men had to be 15+ years, self-report a HIV-negative or unknown HIV status and not tested for HIV at least three months prior to enrolment. After the baseline visit, men obtained free oral HIV self-test kits from their peer-leaders and used them to self-test for HIV. We assessed uptake of HIVST and linkage to HIV care among first-time HIV-positive testers using STATA (version 16.0).
Results Of 475 men screened for study eligibility, 400 (84%) were eligible and administered a baseline interview. Ninety percent (361) completed a follow-up interview. Of these, 98.3% (355) obtained at least one kit from their peer-leaders; 99.1% (352) used them to self-test for HIV. Of the 352 self-testers, 9.4% (33) tested HIV-positive; 81.8% (27) were first-time HIV-positive testers. Of the 27 first-time HIV-positive testers; 40.7% (11) went for confirmatory HIV testing, 10 were confirmed as HIV-positive and 9 were linked to HIV care.
Conclusion Our peer-led HIVST intervention achieved high rates of HIV testing uptake and identified a high proportion of previously undiagnosed HIV-positive male fisherfolk but linkage to confirmatory HIV testing was sub-optimal.

OA-686

Advancing research on epidemic prone-pathogens: "Integrated Services for Infectious Disease Outbreak Research" (ISIDORe)

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Well before the COVID-19 pandemic, health experts from around the world identified major gaps in global preparedness for infectious diseases. In the EU, among others, investment was made in life sciences research infrastructures and infectious disease networks that federate facilities offering scientists access to cutting-edge research services, and that could be mobilized in times of crisis.
As one of the first actions of the European Health Emergency preparedness and Response Authority (HERA), the ISIDORe programme, "Integrated Services for Infectious Disease Outbreak Research", was launched in 2022.
ISIDORe is a new approach to epidemic preparedness and response research in Europe. It assembles and provides free access to an unprecedented One Health-driven integrated portfolio of cutting-edge research resources, dedicated to the study of any epidemic-prone disease.
Coordinated by ERINHA ("European Research Infrastructure on Highly Pathogenic Agents"), ISIDORe involves all the major European Research Infrastructures and networks in the field of biomedical research, from the most fundamental (e.g. structural biology) to the most applied (e.g. vaccine development and clinical trials), including social sciences. The ISIDORe programme has two overarching goals: i) to support rapid research responses to outbreaks and epidemics and ii) to contribute to the preparedness to any epidemic-prone pathogen threat. In line with its goals, during its first year ISIDORe contributed to fighting the rise of the SARS-CoV-2 variants through its dedicated call for proposals, and advance Mpox research.
The preparedness programme supports research on the pathogens with epidemic potential from RG 4 pathogens (such as Marburg virus, Nipah virus, Hendra virus, Lassa virus, CCHF virus) to pathogen X, including respiratory pathogens and vector-borne pathogens. This mechanism enabled transdisciplinary projects to be conducted, to improve preparedness, and accelerate research and innovation during times of emergencies.
We aim at showcasing the results of ISIDORe-supported research projects and ongoing opportunities for free access.

OA-713

Achieving the ISO9001 Certification: A Milestone in Quality Management for the National Research Ethics Committee: the Case of the Senegalese National Research Ethics Committee

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Background Quality management is crucial for ensuring research ethics practices' integrity and efficiency. The National Research Ethics Committee (CNERS) of Senegal has made strides by becoming the first African National Research Ethics Committee (NREC) to achieve ISO9001 certification. This globally recognized certification validates compliance with quality standards for managing systems and organizations. It also signifies the organization's commitment to continuous improvement, monitoring, and evaluation of policies and practices, particularly amidst the recent COVID-19 pandemic.
Methods This initiative is part of the EDCTP-funded BCA-WA-ETHICS-II project, aimed at strengthening research ethics capacities in West Africa. The CNERS' ISO9001-2015 certification process included the development of a quality management system from early 2022, including a thorough assessment of the CNERS's quality management system, which included a series of internal and external audits conducted by Bureau Veritas. Significant capacity building was undertaken, during which 15 CNERS members were trained in ISO9001-2015 quality management standards and received ISO9001 Internal Auditor certification.
Results The CNERS successfully completed the first stage of the audit in October 2022. Subsequently, with a quality management expert, they developed several quality management documents, including quality policy guidelines, process cartographies, work plans, and customer satisfaction evaluation tools. The final (certification) audit took place in March 2023, involving a comprehensive review of the CNERS's quality management documents and interviews with administration and committee members. The CNERS achieved the ISO9001-2015 certification in March 2023, becoming the first African NREC to do so.
Conclusion The CNERS' ISO9001-2015 certification sets a valuable precedent for other African NRECs. The system offers multiple benefits, including enhanced customer satisfaction, service delivery, organizational credibility, internal quality management structure, communication, and responsiveness to unforeseen circumstances. It is relevant in the governance and management of NRECs, particularly post-COVID-19, where scientific research requires rigor and compliance with the principles of medical, public health, artificial intelligence, and research ethics.

OA-715

Receipt of intravenous co-amoxiclav challenges eligibility screening for the PediCAP Trial in Johannesburg, South Africa

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Background In 2020, updated South African guidance on management of children with community-acquired pneumonia were published by the South African Thoracic Society. These guidelines recommend intravenous co-amoxiclav as first-line therapy for children hospitalised with World Health Organisation (WHO) defined severe pneumonia. We evaluated how this guideline change impacted on participant enrollment into the PediCAP Trial (https://projectpedicap.org/) at the Trial site in Johannesburg, as receipt of intravenous co-amoxiclav is an exclusion criterion for PediCAP enrollment.
Methods A line list of all paediatric admissions to the Johannesburg PediCAP site is maintained, to facilitate screening for age-eligible paediatric patients with respiratory illness on weekdays. The total number of children hospitalised at the site, the total number of respiratory admissions, and the characteristics of children screened for PediCAP were assessed descriptively.
Results From 15 July 2021 to 15 May 2023, 11,998 children were hospitalised at the study site. On PediCAP screening days, 4,829 age-eligible children were hospitalised, 2,377 (49.2%) of whom had respiratory admission diagnoses. Five-hundred, twenty-seven children underwent point-of-care C-reactive protein (CRP) testing for eligibility screening into PediCAP and 239 (45.4%) were enrolled. A clinician decision to initiate intravenous co-amoxiclav was a common reason for non-eligibility (in 316 [13.1%] of 2,417 children). Formal CRP levels were significantly higher in children enrolled into PediCAP compared to those treated with intravenous co-amoxiclav (median 51.0 mg/L [Interquartile range (IQR), 29.0-111.0] vs. 18.0 mg/L [IQR, 5.0-57.5]; corrected P-value<0.001).
Conclusion National guideline recommendations to use intravenous co-amoxiclav as first-line therapy for children hospitalised with severe pneumonia have impacted participant recruitment into PediCAP at the Trial site in Johannesburg. Significantly lower CRP levels in children treated empirically with intravenous co-amoxiclav indicates a disparity between clinician prescribing and the likely aetiology of disease in children hospitalised with severe pneumonia at the study site, warranting optimisation of antimicrobial stewardship practice.

OA-721

Leveraging Digital Platforms to Support a Sustainable National Research Information Management System for Research Ethics and Regulation in Uganda

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Background In Uganda, complex clinical research projects that require regulatory oversight are a growing phenomenon. Although there are functional national regulatory agencies (NRAs) to provide oversight, various constraints, including the lack of a robust digital platform to facilitate their work make them inefficient. This scenario has necessitated the establishment of a sustainable digital system to support the work of the NRAs and research ethics committees (RECs). Against this background, the EDTCP-II grants supported a project on Scaling up the Capacity of RECs in Uganda (SCRECU), 2019-2022, and facilitated further development of a National Research Information Management System (NRIMS) which had been developed with support from an earlier EDCTP grant. The overarching objective of SCRECU was to build sustainable capacity for the NRIMS with capabilities of facilitating multi-REC ethical reviews, national registration of research protocols, and their subsequent monitoring by NRAs and RECs.
Methods We trained RECs personnel on the use of NRIMS for online protocol submissions and management; post-approval processes and enrolment of RECs. We provided the RECs with ICT equipment and followed them up to ensure utilization. We tested the effectiveness of the NRIMS, evaluated its adoption, and developed guidelines for its operationalization.
Results We trained the chairperson, an administrator, and an IT officer from each of the 26 RECs in Uganda on the use of NRIMS and equipped them with Internet services and other relevant tools. Our study demonstrated the affordability of NRIMS and how digital tools can be leveraged to strengthen ethics and regulatory capacity in resource-constrained settings. The study also generated an inventory of equipment required for the operationalization of an NRIMS. The NRIMS has registered over 13,000 users, received over 6,000 applications, and granted 2,500 approvals online. The NRIMS has enhanced institutional workflows, reduced paperwork by over 95%, and turnaround time for protocol approvals by 50%. It has enhanced research ethics regulatory capacity in Uganda.
Conclusion The NRIMs has revolutionized and strengthened research ethics and regulation in Uganda. It provides a secure, web-based solution for efficient submission, review, approval, and monitoring of research projects. Its success in Uganda provides a paradigm shift for other NRAs in sub-Saharan Africa.

OA-722

Assessment of Naturally Acquired Humoral Immunity against malaria protecting against Controlled Human Malaria Infection (CHMI)

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Background A successful malaria vaccine should, depending on the targeted stage of the malaria life cycle, induce both humoral and cellular immune responses. Naturally acquired immunity (NAI) against malaria is thought to target mostly the blood stage and protects individuals against symptomatic and severe disease, but often fails to protect against infection per sé. A better understanding of the mechanisms of NAI and its role in all stages of the life cycle might lead to improved vaccine design of the next-generation malaria vaccine.
Methods In Lambaréné, Gabon, a study was conducted in which semi-immune individuals underwent repeated controlled human malaria infections (CHMI) using direct venous inoculation of fully viable cryopreserved Plasmodium falciparum (Pf) sporozoites (PfSPZ, strains NF54 and 7G8). Participants were randomized into two arms allocated 1:1. In arm A, participants were infected using Pf strain 7G8 followed by five infections with Pf strain NF54. In arm B, participants were infected four times with Pf strain NF54 followed by one infection with Pf strain 7G8 and finally one infection with NF54. Here, we investigate the immune response against Pf antigens potentially relevant for the protective immune response against malaria. Selected antigens were expressed using mammalian or bacterial expression systems and subsequently purified. Humoral immune response was assessed by indirect ELISA.
Results In total 56 participants were enrolled. Their average age was 28 +/- 6 years. Most participants were male (82%). At baseline, Pf-specific antibodies ranged from 5 to 100 µg/ml in plasma, with a predominance of antibodies against blood stage antigens, such as AMA1 and merozoite surface proteins. The antibody responses against these antigens showed minor fluctuations during follow-up.
Conclusion The investigation is ongoing, and further antigens will be investigated. Specifically, the dynamics of antibody responses throughout the study period, also regarding antibody isotype and function, will be presented.

OA-724

Interrogation of an Multi Drug Resistant Tuberculosis outbreak using Whole Genome Sequencing

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Background The spread of drug-resistant strains which has been reported to be attributed to primary transmission threatens TB control and prevention programs. Previous molecular epidemiological studies have reported that the dynamics of tuberculosis transmission varies geographically. After a reported increase in drug resistant TB cases in the West Coast region of the Western Cape Province, South Africa, the aim of this study was to identify transmission hotspots and possible outbreaks of drug-resistant tuberculosis within this region.
Methods Spoligotyping and Sanger sequencing of first line drug resistance conferring mutations of drug resistant strains in the region over 5 years (2008-2012) identified a multidrug-resistant tuberculosis (MDR-TB) outbreak of the X-family, mainly located in the Northern parts of the region. Whole genome sequencing (WGS) was done on all available strains (n=177) to establish the phylogenetic relationships of this outbreak.
Results Through WGS and Sanger sequencing of first line drug resistance conferring mutations of drug resistance, we found identical mutations conferring resistance to the 4 first-line drugs used in tuberculosis treatment in this lineage 4.1.1.3 cluster, including a rare katG315 double mutation. This is indicative of transmission of MDR-TB. Isolates belonging to this outbreak, but with different additional mutations conferring to resistance to second-line drugs were also identified, indicating that pre-XDR-TB are primarily acquired from this existing MDR strain genotype. XDR-TB has not yet been seen, as this outbreak peaked before the introduction of new generation anti TB drugs.
Conclusion Monitoring and interrogation of drug resistant TB outbreaks plays an important part in our understanding of the drug resistant TB epidemic to ultimately eradicate TB disease worldwide.

OA-739

High-levels of HIV drug resistance persist in ART-experienced patients post-dolutegravir rollout in KwaZulu-Natal, South Africa

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Background HIV drug resistance (HIVDR) remains a major threat to achieving sustainable viral suppression on antiretroviral therapy (ART). In South Africa, dolutegravir (DTG) is the preferred first-line ART backbone since its rollout in December 2019.
Methods We curated HIVDR genotypic data obtained from the National Health Laboratory Service (NHLS) for ART-experienced patients with virological failure (i.e., consecutive viral loads ≥1,000 copies/mL) receiving HIV-care at public-sector health facilities in KwaZulu-Natal (KZN) province, South Africa. We estimated levels of HIVDR from genotypes processed between January 2018 and June 2022, and assessed temporal trends of HIVDR across 11 districts of KZN, prior to- and following DTG-rollout in South Africa.
Results Of 4,069 genotypes curated, 3,511 (86.3% CI 85.2–87.3) had HIVDR mutations, with most resistance mutations occurring among adult females aged >15 years, p=0.01. Despite an annual decrease in protease inhibitor (PI)-specific mutations (p=0.0001), about one-third of genotypes had ≥3 drug-class resistance mutations, mainly nucleoside, and non-nucleoside reverse transcriptase inhibitor (NNRTI) mutations. Only 50 genotypes had integrase resistance data, from which 9 (18.0%) had intermediate to high-levels of resistance to DTG. Overall, rural districts had fewer HIVDR genotypes (598/4069, 15%) but with higher HIVDR prevalence (88.1% CI 85.3–90.6) compared to densely populated peri-urban and urban districts.
Conclusion Six in every seven genotypes from patients with virologic failure had HIVDR mutations despite DTG-rollout, with persistent NNRTI resistance. Thus, whilst introduction of DTG is expected to alleviate HIVDR burden, a sub-population of people may not fully benefit from DTG-use due to multi-drug resistance, at which point PI-based ART is warranted. Higher proportions of HIVDR in rural districts and among adult women, highlight regions and individuals needing priority HIV care. Overall, these findings urge strengthening of HIV services in public healthcare systems to ensure sustainable DTG-use in first-line and subsequent ART regimens.

OA-765

Molecular diagnostic tests specificities and their contribution for HAT postelimination monitoring in Burkina Faso and Côte d'Ivoire

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Background Elimination of gambiense Human African Trypanosomiasis (gHAT) as public health problem has been achieved in countries like Côte d'Ivoire and Burkina Faso. The World Health Organization (WHO) has set targets for interruption of transmission of gHAT by 2030. In this context, the performance of diagnostic algorithms for early detection of HAT re-emergence remains to be assessed.
Methods Our study represents a further step in the analysis on 8,648 dried blood spots collected during HAT rapid diagnostic tests (RDT) screening in gHAT historical foci in South West Burkina Faso and Centre West Côte d'Ivoire. We assessed the specificity of three molecular tests on 1,000 randomly selected samples from each country. We performed the Trypanozoon subgenus-specific m18S qPCR and RIME LAMP and the Trypanosoma brucei gambiense-specific TgsGP qPCR.
Results No parasites were detected using parasitological investigations. The overall seroprevalence based on positivity to at least one RDT was 1.19% (103/8648, (0.83-1.55%). The specificities of m18S qPCR and TgsGP qPCR were 99% (990/1,000, 98.9-99.8%) and 99.8% (998/1,000, 95.5-100%) respectively. The RIME LAMP test was negative for all 1,000 specimens (specificity 100%).
Conclusion All molecular tests qPCR m18S, qPCR TgsGP and RIME LAMP showed high diagnostic specificity. A previous study demonstrated low analytical sensitivities for qPCR m18S and qPCR TgsGP (respectively 1,000 and 10,000 trypanosomes/mL) while that of the RIME LAMP (100 trypanosomes/mL) was in the range of parasitaemias commonly observed in HAT patients. However, none of the three tests was entirely suitable for high-throughput use. To decide what is the best algorithm for HAT post-elimination monitoring, data on costs for all possible algorithms including serological and parasitological diagnostics need to be considered, according to the epidemiological context.
Funding from the EDCTP2 Programme supported by the European Union (Project DRIA-2014-306-DiTECT-HAT).

OA-770

Treatment Outcomes of Low-Level Viremia Among Adults Living with HIV on Dolutegravir-Based First Line Antiretroviral Therapy in Botswana

Ontlametse T Bareng[1,2,*], Sikhulile Moyo[1,3], Mbatshi Mudanga[4], Kagiso Sebina[4], Catherine Koofhethile[1,3], Wonderful Choga[1,2], Irene Gobe[2], Modisa Motswaledi[2], Docas Maruapula[1], Natasha Moraka[1,2], Rosemary Musonda[1], Joseph Nkomo[5], Dinah Ramaabya[5], Tony Chebani[5], Penny Makuruetsa[5], Joseph Makhema[1,3], Simani Gaseitsiwe[1,3]

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Background We evaluated the treatment outcomes of individuals experiencing low-level viremia (LLV) on dolutegravir (DTG) based first-line antiretroviral therapy (ART) in Botswana by determining the trends of LLV over a period of 6 years.
Methods We used a large national observational cohort of individuals (aged≥18yrs) who initiated on DTG-based first-line ART for at least 3 months from June 2016 to December 2022. The prevalence of viral suppression (VL ≤50copies/mL), low-level viremia (VL:51-999copies/mL) and virologic failure (VF) (any VL>1000copies/mL) were estimated among PLWH. The prevalence of LLV was further classified into LLV ranges (low-LLV:VL:51-200copies/mL, medium-LLV:201-400copies/mL and high-LLV:VL:401-999copies/mL). Univariate and multivariable Cox proportional hazards regression determined whether LLV (exposure) is associated with VF (outcome).
Results Among 50,742 PLWH who have at least one VL measurement during the follow-up, the overall prevalence of LLV by duration strata was 2.2%, 1.8%, 1.7%, 2.3%, 3.1%, 3.7% and 3.9% at 0.25-<0.5, 0.5-≤1, 2, 3, 4, 5, 6+ years respectively. By LLV ranges, ≥90% had low-LLV in each duration strata. A total of 539 had reported LLV at year 0.25-<0.5 whereby 529(98.1%) had single instance of LLV, 9(1.7%) with 2-consecutive-LLV (confirmed) and 1 (0.2%) had at-least-3-LLV(persistent) measurements. The prevalence of PLWH with confirmed-LLV was 9.1%, 9.0%, 7.3%, 6.4%, 9.1% and 8.4% at 0.5-≤1, 2, 3, 4, 5, 6+ years of the follow-up period, respectively. The prevalence of persistent-LLV increased from 0.2% to 7.0% from year 0.25-<0.5 to 6+. PLWH with LLV had an increased risk of VF (adjusted-Hazards-Ratio [aHR] 2.65; 95%CI 2.16-3.26) at a later visit compared to suppressed VL group. High-LLV and persistent-LLV were the main LLV factors associated with VF.
Conclusion The prevalence of LLV ranging from 1.7-3.9% was found in this cohort. Having a high or persistent-LLV is associated with a high risk of subsequent VF. Intensified clinical monitoring strategies are warranted for individuals with LLV.

OA-779

Beneficial Non-Specific Effects of Oral Polio Vaccinations Campaigns – Did one drop save more lives than anyone could have imagined?

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Background In the last three decades, more than 2,500 national vaccination Campaigns with Oral Polio Vaccine (C-OPV) have distributed more than ten billion doses of OPV to children in the effort to eliminate wild poliovirus. C-OPVs have been demonstrated in several studies to reduce all-cause under-3-year mortality by ~25-35%, suggesting that C-OPV has beneficial non-specific effects (NSEs). We triangulated the evidence with different data sources and analytic approaches.
Methods We used Health and Demographic Surveillance System data from several countries to compare all-cause and cause-specific under-3-year mortality after and before C-OPVs in Cox proportional hazards model adjusted for other campaign interventions and calendar year. We modelled the counterfactual number of deaths averted by C-OPVs. We distinguished between C-OPV administered alone and other campaign interventions.
Results In urban Bissau, Guinea-Bissau, between 2002-2014 C-OPVs reduced all-cause mortality by 25% (95% CI: 15-33%). In Chakaria, Bangladesh, between 2004-2019, the estimate was 31% (10-48%). In rural Burkina Faso between 2012-2016, C-OPV reduced mortality and hospitalisations (composite outcome) by 36% (6-56%). Limited effect was observed on all-cause mortality (5% (95% CI: -4-13%) reduction) in Navrongo, rural Ghana, between 1996-2015. However, C-OPVs were more frequent than in previous analyses and effects differed by routine vaccinations and age groups. In all studies, apart from Bangladesh, the effect of C-OPV was more beneficial in males than females. Based on the Guinea-Bissau results, OPV averted 10% (5-15%) of all childhood deaths during the analysis period. No similar effects were found for other campaign interventions.
Conclusion There is now compelling evidence that C-OPVs have beneficial NSEs. OPV is planned to be stopped in 2026. Based on the existing evidence, this may paradoxically increase child mortality. It is urgent that we find ways to mitigate the potential negative impact. One drop may have saved more lives than anyone could have imagined.

OA-801

Surveillance of respiratory viruses in Gabon during the Covid-19 pandemic

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Background Acute respiratory infections are a major global burden, with pneumonia being the leading cause of death. However, very little information has been available on their causative agents in Africa. In Gabon, Central Africa, although COVID-19 has been extensively studied since the pandemic emerged, the other respiratory viral diseases have been paid less attention compared to COVID-19 and no surveillance study has been conducted in the country. Therefore, this study aimed to reveal the situation of respiratory viral diseases in Gabon during the COVID-19 pandemic.
Methods A total of 582 nasopharyngeal swab specimens were collected from SARS-CoV-2 negative patients with respiratory illness in several provinces of Gabon during the period from March to December, 2020. Viral RNA was extracted and screened by RT-qPCR for major 17 respiratory viruses. Epidemiological analysis was performed using patient demographic information and the detected viruses were analyzed genetically.
Results Of 582 samples, 156 were positive (26%) for eight viruses: enterovirus (EV), human rhinovirus (HRV), human coronavirus OC43, human parainfluenza virus 3 and 4a, adenovirus, influenza A virus (IAV) and human metapneumovirus. Genotyping of HRV based on 5'UTR and VP4/VP2 sequences identified all genotypes (A, B, and C). Gabonese hMPV and IAV strains were classified as group A and H3N2 respectively. Moreover, hMPV was detected for the first time in Gabon in this study.
Conclusion This study revealed the circulation and distribution of respiratory viruses during the COVID-19 pandemic in Gabon. In particular, detection rate of EV in this study was higher than that reported in 2014 in Gabon. This study reports for the first time in Gabon the molecular characterization of HRV, hMPV and whole genome of IAV strains. Further investigation would be required to validate the effect of the COVID-19 pandemic on the incidence of other respiratory viral diseases.
Funding source: JSPS

OA-815

A community approach to re-thinking the principles of good randomized controlled trials: informative, respectful, collaborative, feasible and well-managed

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Background The Covid pandemic has illustrated a substantial need for good Randomized Controlled Trials (RCTs) to better understand the benefits and hazards of medical interventions. The Good Clinical Trials Collaborative (GCTC) has created new guidance to promote and enable high-quality, ethical RCTs.
Methods In 2020, the Collaborative convened two workshops with a diverse, global, multi-disciplinary, multi-stakeholder group of 84 members to design the guidance. Draft content was reviewed at workshops, exploring scientific and ethical considerations, clinical contexts and quality management. After public consultation, the Guidance was finalized and published on www.goodtrials.org in 2022.
Results The agreed Five Principles of Good RCTs are that they are designed to produce scientifically sound answers to relevant questions, respect the rights and well-being of participants, are collaborative and transparent, are appropriate for their context, manage quality effectively and efficiently. The Guidance is underpinned by considerations that help a trial to fulfil its ethical responsibilities regarding participants, future and current patients. It is designed to support all RCTs in all settings to be relevant, informative, and provide sound answers to clear questions, thereby driving the development of better interventions and the delivery of future care. For professionals, the Guidance can be a tool to prompt and justify tailored applications of the principles in a particular setting. However, the Guidance can also aid community engagement by improving understanding of what a good RCT looks like – and why – for non-professional audiences.
Conclusion We hope that this Guidance can be a foundation of common understanding that good healthcare is informed by good evidence from good trials – and that it can help improve the standards of clinical trials and the way we collectively learn from and utilize their results.

OA-900

A bilingual training platform in data management and sharing to support open science across the EDCTP Networks of Excellence

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The EDCTP Regional Networks of Excellence (NoE) have been increasing capacity for knowledge and training in data management and sharing as part of EDCTP2. The aim of this new work was to enhance and leverage the EDCTP Knowledge Hub to support secondary data analysis that could be utilised across all four NoEs. The hub would provide overarching content, as well as deeper-dive training materials allowing networks to develop tailored in-person sessions addressing local use cases.
This training initiative is a joint project of the EDCTP NoEs, The Global Health Network and the Infectious Diseases Data Observatory (IDDO) and has several components: enhanced online modules in English and French covering an essential curriculum in data management and sharing; dissemination through a Data Management and Sharing Technical Working Group consisting of NoE members to ensure that content meets their training needs; additional resources for local face-to-face training developed from the online training course, with tools and case studies made available alongside the online training package for download and use.
The content and delivery of this training have been tailored specifically for the needs of the EDCTP NoEs, enhancing knowledge on data management and sharing to support secondary analysis that responds directly to the clinical research context of sub-Saharan Africa. Leveraging the powerful web-based training platform, this initiative draws on experience from across EDCTP NoEs and partners to deliver a comprehensive curriculum in both English and French.
As the EDCTP NoEs continue to strengthen their capacity and look towards more advanced data management and sharing solutions that fit their context, this training platform will provide sustainable knowledge and training foundations for supporting this growth in expertise, aligned with the EDCTP NoE aims of research collaboration to further raise the quality of clinical research and practice across sub-Saharan Africa.

OA-901

Comorbidities in children and adolescents growing up with HIV: the need to focus beyond viral suppression

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The scale-up of antiretroviral therapy (ART) has resulted in large numbers of children with perinatally-acquired HIV who would have died in early childhood with untreated HIV, reaching adolescence and adulthood. However, it is becoming known that children growing up with HIV are at risk of multisystem co-morbidities, despite ART. In Africa (where 90% of the world's children with HIV live), the majority of the current cohort of older children and adolescents with HIV did not start ART in infancy, and HIV viral suppression rates are lower than those observed in adults. These factors increase the risk of co-morbidities. Children with HIV experience a range of comorbidities including cardio-respiratory, musculoskeletal and neurocognitive disease.
While there is awareness of the burden of chronic comorbidities in adults who are ageing with HIV, there is much less awareness of the burden of comorbidities in children growing up with HIV. Thus, HIV management guidelines and programmes have hitherto focused almost exclusively on achieving viral suppression. These comorbidities result in considerable disability and have wide-ranging effects such as poorer adherence, lower educational attainment and premature mortality. Addressing these comorbidities is critical for the well-being of children as they enter adulthood. The talk will summarise the existing evidence on the range and spectrum of co-morbidities, underlying drivers and draw out the outstanding research agenda.

OA-902

Fair partnerships as a key to empower African R&D stakeholders to advance equitable and sustained access to quality health products

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To maximize the impact of the findings of clinical research, long-term plans for equitable access to new, innovative health products should be included right from the outset of R&D planning. This is a complex undertaking, that requires multilayered, coordinated interventions across various disciplines and sectors, including but not limited to pharmaceutical regulation, ethical oversight, technology transfer, intellectual property ecosystem, market dynamics, production capacity, supply systems, communities engagement etc. Partnerships grounded in the principles of fairness, respect, care and honesty as per TRUST Code (A Global Code of Conduct for Equitable Research Partnerships), and established with a thorough comprehension of the process of decolonization of global health research, are essential pre-requisites for enabling African clinical researchers, their research centres and partners to achieve these ambitious objectives. In particular, fair and collaborative partnerships will (i) enable defining a regional and continental clinical research agenda that prioritizes the population unmet health needs, and (ii) facilitate the generation of evidence and translation of research findings into concrete access to new products to all those in need, including through rapidly-available multisource and/or biosimilar quality-assured formulations.

Once fair governance mechanisms are established, collaborations -including in the clinical research field- should be empowered to adopt a systematic approach that addresses the interconnectedness of R&D with the legal, regulatory and policy determinants of access. Such an approach should include comprehensive planning from the start, addressing provisions for, among other things, quality-assurance, surveillance, sustained supply, technology transfer and market shaping. To achieve this broad scope, from R&D to ensuring product quality, availability and affordability to all, these collaborative partnerships must not be limited to researchers alone. They should actively involve regulators and policymakers within the local pharmaceutical systems. By engaging all relevant stakeholders, we could create a more comprehensive and effective framework to achieve equitable access to healthcare products.

OA-903

Breaking Barriers, Bridging Knowledge: Inclusion of Women in clinical research by Addressing Gender and Diversity Regional Gaps in Clinical Research Capacity in Africa

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Despite advancements in medical research worldwide, there are still gender and geographical inequities in clinical trials, with a disproportionate underrepresentation of women and marginalised groups. In order to overcome these obstacles and fill information gaps, there is a need to enhance clinical research capabilities in Africa, promoting women's participation, and valuing diversity. To close the knowledge gap and promote inclusivity, capacity-building efforts enable women in Africa to assume leadership roles in clinical research. The gender imbalance is exacerbated by historical prejudices, job difficulties, and cultural expectations, which prevent the progress of inclusive and diverse medical knowledge. As a result, Trials of Excellence in Southern Africa is implementing training for female PhDs aimed at nurturing a generation of skilled and knowledgeable women researchers and leaders who will drive advancements in medical research and will present it as a case study.

Initiatives to enhance capacity are essential for women to assume clinical research leadership positions. These programmes should offer skills development, leadership training, and mentoring opportunities. To achieve this, it is necessary to invest in financing, education, and infrastructure for a supportive research atmosphere.

In most African societies, cultural norms are a barrier to women in leadership positions. A more inclusive research environment should be created by raising awareness within communities of the value of women's contributions and challenging traditional gender stereotypes. Breaking barriers calls for partnerships for capacity-building initiatives and resource sharing and expertise. Additionally, institutional support, including gender-sensitive policies and flexible work schedules, can help women succeed in research.

Beyond gender equality, empowering women to conduct clinical research is essential for expanding medical knowledge and enhancing healthcare outcomes in Africa. By addressing gender and diversity gaps in research leadership, we can bridge knowledge disparities, break barriers, and build a more inclusive and resilient healthcare system for the continent.

OA-904

Role of pathogen genomics in Public Health: Lessons from HIV and COVID-19 towards pandemic Preparedness

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The invaluable lessons learned from the application of pathogen genomics during the HIV and COVID-19 pandemics hold significant implications for pandemic preparedness. These insights can shape our strategies to tackle future infectious disease outbreaks and reinforce global health readiness. Firstly, the understanding of transmission dynamics gained through genomic surveillance has highlighted the importance of early detection and rapid response. By closely monitoring viral mutations and genetic diversity, public health authorities can swiftly identify emerging pathogens, track their spread, and implement containment measures.

Secondly, the successful evaluation of interventions and treatment success using genomics data emphasises the need for evidence-based decision-making. Pathogen genomics provides real-time information on the effectiveness of therapeutics and vaccines, allowing the refinement of treatment strategies. By leveraging these insights, future pandemic responses can be more agile and effective, saving lives and reducing the burden on healthcare systems.

Furthermore, the identification of SARS-CoV-2 variants and their geographic distribution has demonstrated the importance of a globally coordinated surveillance network. Early detection and characterisation of variants enable the development of region-specific public health measures and targeted vaccination campaigns. Building international collaborations and data-sharing mechanisms will be crucial in facilitating a rapid response to emerging variants in future pandemics. Moreover, the ethical considerations surrounding pathogen genomics underscore the necessity of establishing robust ethical frameworks in pandemic response

Lastly, the collaborative efforts demonstrated during the HIV and COVID-19 pandemics underscore the significance of global partnerships in pandemic preparedness which should be strengthened. International cooperation, knowledge exchange, and resource-sharing are essential in addressing global health challenges effectively.

In conclusion, lessons from HIV and COVID-19 genomics have far-reaching implications for pandemic preparedness. Integrating pathogen genomics into public health systems can revolutionise disease control efforts, optimise outbreak response, and foster a proactive approach to tackling emerging infectious threats and mitigating the impact of future pandemics.

ABSTRACTS OF SCIENTIFIC SYMPOSIA

Scientific symposia 1.1

Ensuring that Children with HIV in Africa survive and thrive

Organiser: University College London (United Kingdom)
Chairs: Victor Musiime (Uganda) and Bwendo Nduna (Zambia)
Presenters: Mutsa Bwakura-Dangarembizi[1], Hylke Waalewijn[2], Veronica Mulenga[3]

[1]University of Zimbabwe, Zimbabwe, [2]University of Cape Town, South Africa, [3]University of Zambia, Zambia

Around 1.5 million children live with HIV in Africa, of whom ~52% are receiving antiretroviral therapy (ART). Safe, effective options are needed for children requiring second-line ART, allowing them to thrive and survive into adulthood. The CHAPAS partnership recently completed the CHAPAS-4 phase III factorial randomised trial investigating second-line ART in children in Uganda, Zimbabwe, Zambia. This symposium will explore beyond primary efficacy/safety outcomes, including details of nutrition, growth, bone/renal health and metabolic changes. Detailed pharmacokinetic data will inform doses for new convenient paediatric fixed-dose dispersible tablets. We report how the collaboration has strengthened clinical trials capacity of partner organisations, individual researchers, and adapted to enable completion of a high-quality trial, overcoming multiple challenges presented by the COVID-19 pandemic.
Themes:

1. Surviving: pharmacokinetic sub-studies of ART drugs were efficiently nested within the trial, including new TAF/lamivudine paediatric FDCs. Drug-drug interactions between TAF and ritonavir-boosted protease inhibitors (PIs) or dolutegravir provided exposures previously shown to be effective/well-tolerated in adults. Results will inform ART guidelines, including for children requiring concurrent TB treatment.
2. Thriving: detailed presentation on nutritional status and bone health of children assessed using a range of measurements (growth, bio-electrical impedance measuring fat/protein changes), laboratory (renal/bone, lipids) and imaging (dexa-scans, calcaneal ultrasound) techniques, according to randomised treatment: (darunavir/ritonavir(DRV/r), atazanavir/ritonavir(ATV/r), lopinavir/ritonavir(LPV/r), dolutegravir(DTG); and tenofovir alafenamide(TAF), abacavir(ABC)/zidovudine(AZT)-based backbone). Children receiving LPV/r showed poor growth versus comparison drugs ($p<0001$). Growth was better with TAF compared to ABC/ZDV($p=0.0002$), with no excessive weight-gain observed with DTG+/-TAF over >2years.
3. Partnerships: capacity strengthening of partner organisations including expanding trial infrastructure beyond main research centres, through 'hub and spoke' within-country mentoring and early-career researcher development (7 PhD; 3 Masters' students). Teams rose to the challenges in the face of the COVID-19 pandemic, providing innovative support for children and their families. Target recruitment of 919 children was met; with only 11(0.01%) lost-to-follow-up.

Scientific symposia 1.2

Partnerships for implementation research to optimise the impact of Seasonal Malaria Chemoprevention in West and Central Africa: the OPT-SMC project

Organiser: Université de Thiès (Senegal)
Chairs: Jean Louis Ndiaye (Senegal) and Corinne Merle (Switzerland)
Presenters: Jean-Louis Ndiaye[1], Nnenna Ogbulafor[2], Christian Kompaore[3], Bienvenu Camara[4], Mady Cissoko[5], Aissata Kone[5], Fatimata Sall [6]

[1] Université de Thiès, Sénégal, [2]National Malaria Elimination Programme, Nigeria, [3]Programme National de Lutte contre le Paludisme, Burkina Faso, [4]Maferinyah Research Center, Guinea, [5]Programme National de Lutte contre le Paludisme, Mali, [6]Université de Thiès, Sénégal

The OPT-SMC partnership was established in response to WHO's call in 2018 that access to proven core malaria interventions should be improved as a matter of urgency, in order to reverse the slow-down in progress in malaria control that had been observed since 2015. One of the key WHO recommendations was that in Sahelian countries where transmission is highly seasonal, the large-scale implementation of seasonal malaria chemoprevention should be extended to all suitable areas, aiming at full coverage. Between 2018 and 2022, SMC has been scaled-up with support from donors and national programmes, with SMC programmes in 14 countries reaching 45million children by 2021 and 48million in 2022. But SMC is complex to deliver, optimal impact requires the number and timing of cycles to be adapted to the local seasonal pattern to ensure children are protected throughout the periods of greatest malaria risk, and while high levels of SMC coverage are possible with door-to-door delivery, strategies to be adapted to the local context. The OPT-SMC partnership supports national malaria programmes to identify barriers to full coverage of SMC and take steps to overcome them, through implementation research and by strengthening partnerships between implementing countries to share learning. This symposium will discuss experiences of building a regional partnership for implementation research on SMC, we will share results from projects Nigeria and Burkina Faso, Mali, Guinea and Senegal, review
lessons learned, and discuss priorities for operational research on the control of seasonal malaria.

Scientific symposia 1.3

A paradigm shift towards local and gender balanced leadership, promoting equitable partnerships and next generation African leaders

Organiser: Centro de Investigação em Saúde de Manhiça (CISM, Mozambique)
Chairs: Rella Zoleko Manego (Gabon) and Innocent Valea (Burkina Faso)
Presenters: Charles S Mgone[1], Ghyslain Mombo-Ngoma[2], Dearie Okwu[2], Jessica Dalsuco[3]

[1] Former Executive Director of EDCTP, Tanzania, [2]Centre de Recherches Médicales de Lambaréné, CERMEL, Gabon, [3]CISM, Mozambique

Capacity development is one of the five EDCTP objectives. In the last two decades major investments have been made in human capacity and infrastructure development in sub-Saharan countries. However, career development of young scientists, especially women, remains a challenge. Higher education training opportunities have been targeted traditionally within global north academic institutions. This favors the flight of human capital and impedes long-term sustainability of local capacity development.
An efficient collaborative approach with sub-Saharan universities and creation of local training and further career opportunities for young scientists require additional efforts but would better support access to opportunities. Grant specific goals for the global south institutions have traditionally been geared towards achieving time bound project targets, rather than sustainable outcomes. Encouraging a long-term perspective for clinical research in institutions and regions, as well as researchers, is key.
Today it is necessary to shift the paradigm of traditional North-South collaboration, fostering equitable partnerships and building on existing local leadership capacities. This entails going beyond a single project perspective, and developing a long-term development strategy, supporting new policies and best practices, involving women and local communities in decision making process to ensure gender balance, cultural appropriateness and social responsibility of research programs.
Multi-partner consortia supported by EDCTP including diverse stakeholders such as academia, global health organizations, pharmaceutical companies, and sub-Saharan Africa research institutions are key to driving the necessary paradigm shift to true sustainability of the African clinical trial ecosystem, offering an unprecedented space for direct dialogue. The objective of this symposium is to showcase how two EDCTP grantees, PAMAfrica and SINDOFO, have joined forces to propose an innovative approach for capacity building. Capitalizing on local expertise and inclusion of women to foster South-South collaboration and mutual South-North capacity building strengthens gender equity within, and sustainability of, the trial ecosystem in the long term.

Scientific symposia 2.1

Making diagnostics accessible – beyond diagnostic platforms and assays

Organiser: Foundation for Innovative New Diagnostics (FIND, Switzerland)
Chairs: Katharina Kranzer (United Kingdom) and Alberto Garcia-Basteiro (Spain)
Presenters: Marta Cossa[1], Immaculate Kathure[2], Marguerite Massinga Loembe[3], Achilles Katamba[4], Pedro da Silva[5], Celso Khosa[6]

[1]Manhiça Health Research Centre, Mozambique, [2]Ministry of Health, Kenya, [3]African Society for Laboratory Medicine, ASLM, Ethiopia, [4]Makerere University, Uganda, [5]National Priority Programmes (NPP), South Africa, Instituto Nacional de Saúde (INS), Mozambique

Timely and appropriate diagnosis and treatment is the key to reducing TB mortality, morbidity and to prevent transmission. However, almost half (4.3 million) of the estimated 10 million individuals who develop TB and more than two-thirds of those with MDR/RR-TB remain undiagnosed globally each year. Key reasons include inadequate access to existing TB diagnostics, which additionally perform poorly in key population groups such as children and people living with HIV. Additionally, there is poor access to rapid TB drug susceptibility testing to diagnose and effectively treat MDR/RR-TB.
Potential interventions to close these important gaps in the TB diagnostic care cascade include i) decentralisation of diagnostic platforms to ensure near-patient testing ii) diagnostic algorithms for individuals for whom TB is more difficult to diagnose specifically people living with HIV and children and iii) alternative non-sputum based non-invasive sample types such as urine, stool, and tongue swabs. It is important for TB programmes to rapidly implement interventions found to have been successful in research studies to ensure wider benefit to people affected by TB. Scale-up requires collaboration between researchers, policymakers, and programmers. Often new intervention or diagnostics are piloted within TB programs before full scale-up allowing to learn important lessons during the initial implementation phase.
This symposium will discuss different strategies to enhance access to effective TB diagnostics, including decentralisation of two point-of-care platforms, a diagnostic algorithm for people living with HIV admitted to hospital and the practical implementation of a rapid drug susceptibility test to allow individuals with MDR/RR-TB to be started on more timely, appropriate treatment. We will also explore opportunities provided by different sample-types in those unable to produce a sputum sample. Importantly lessons learned from pilot projects scaling up near patient testing will be presented by National TB Programme and Laboratory service managers, with subsequent discussion.

Scientific symposia 2.2

From the bench to the field: contextual complexities in access and delivery of new health technologies in African health systems

Organiser: University of Health and Allied Sciences (Ghana)
Chair: Jürg Utzinger (Switzerland)
Presenters: Olumide Ogundahunsi[1], Margaret Gyapong[2], Garry Aslayan[3], Cecilia Oh[4]

[1]University of Medical Sciences, Nigeria, [2]University of Health and Allied Sciences, Ghana, [3]TDR Geneva Switzerland, [4]UNDP Access and Delivery Partnership, Thailand

Research and development of new health technologies take place in controlled environments to generate empirical evidence of efficacy and fitness for purpose. Beyond the proof-of-principle and trial stages, new technologies must be introduced and scaled-up in real-life contexts that exist in communities, within health systems and populations in general. This symposium will highlight critical capacities for the access to, and delivery of, health technologies including drugs and vaccines. Building on historical and contemporary perspectives, the speakers will illustrate the contextual dimensions of introducing new or improved medical interventions in typical African health systems.
Speakers will address their topics from the perspective of what was missing on the eve of the Sustainable Development Goals, what is being done now and what is required to make access to, and delivery of, new health technologies a success, highlighting challenges and opportunities. Being leaders in various fields and holding critical positions in their institutions and globally, it is expected that the presentations, discussions and take-home messages will facilitate commitment of the various institutions to contribute to the attainment of the Sustainable Development Goals (SDGs).

Scientific symposia 2.3

Working toward impactful clinical trials through collaborative research in South Saharan Africa: The example of the EDCTP NoEs

Organiser: EDCTP Regional Networks of Excellence and The Global Health Network (United Kingdom)
Chairs: Souleymane Mboup (Senegal), Francine Ntoumi (Congo) and Bernard Kikaire (Uganda)
Presenters: Francine Ntoumi [1], Jolivet Mayela[1], Leonard Numfor[1] , Gauthier Mesia [1], Bernard Kikaire[2], Rodrigues Matcheve[3], Assan Jaye[4], Jean Pierre N'Guessan[4], Badou Gaye[4], Bai Lamin Dondeh[4], Frank Kagoro[5,6], Elvis Temfack[5,6]

[1]CANTAM, Congo/Cameroon, [2]EACCR, Uganda, [3]TESA III, Mozambique, [4]WANETAM, Senegal/Ivory Coast, [5]TGHN, Tanzania/United Kingdom, [6]Africa CDC, Ethiopia/Cameroon

Background The capacity to conduct clinical trials in sub-Saharan (SSA) remains very low. The few institutions able to carry out ICH-GCP research operate in silos, or through individual partnerships with European counterparts. This symposium aims to discuss the progress of the European Union EDCTP 2-supported programme established to address this gap.
Methods The NoEs (CANTAM-Central, EACCR-East, TESA-South and WANETAM-West Africa) have built institutional and individual capacity for conducting GCP-ICH research through training and mentorships, improving south-south and north-to-south collaborations, critical infrastructural upgrades to support research in the poverty-related diseases. The networks also developed Knowledge Hubs (KHs) hosted at The Global Health Network Platform to host, translate, and disseminate training and resources.
Results The NoEs have achieved significant results, including securing over 20 million Euros in additional funding from EDCTP and other agencies through grant applications. They have closely worked with other EDCTP-funded consortia and supported major continental programs such as the Africa Research Agenda and the new ecosystem for health research and data science with Africa CDC. The NoEs have been 15189-ISO-accredited and are at the forefront of conducting clinical trials on TB, HIV, and Malaria vaccine efficacy involving volunteers from Europe and Africa. They have provided comprehensive training and mentorship, graduating 20+ post-docs, 30+PhDs, and 20+ MSc students. Over 1,000+ trainees in short courses and 50+ Clinical Research Associates and Monitors have been trained and involved in monitoring studies. The KHs have a global user base of 8,000+ individuals from 72+ countries.
Conclusion The NoEs have established effective governance structures to support consortium activities. After a decade, the NoEs have become robust collaborative research platforms and an SSA flagship of EDCTP in facilitating clinical research skills and capacity building. To ensure continued success, it is recommended that each NoE develops a clear plan for the sustainability of their endeavours.

PA-6

Provider and user acceptability of integrated treatment for the control of malaria and helminths in Saraya, southeastern Senegal

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[1]London School of Hygiene & Tropical Medicine, United Kingdom, [2]Université Cheikh Anta Diop, Senegal, [3]Université de Thies, Senegal, [4]Saraya Health Centre, Senegal, [5]Université Gaston Berger de Saint-Louis, Senegal

Background Integration of vertical programmes for the control of malaria, schistosomiasis and soil-transmitted helminthiasis has been recommended to achieve the elimination of malaria and neglected tropical diseases (NTD) by 2030. Given the dearth of studies on the acceptability of the integrated approach, we conducted this qualitative study within the context of a randomized controlled trial to explore the perceptions and views of parents/caregivers of at-risk children and healthcare providers to determine their acceptability of the integrated malaria-helminth treatment approach.
Methods Randomly selected parents/caregivers of children enrolled in the trial, health care providers, trial staff, malaria and NTD programme managers were interviewed using purpose-designed topic guides. Transcripts obtained from the interviews were coded and common themes identified using content analysis were triangulated. Fifty-seven study participants comprising 26 parents/caregivers, 10 study children aged ≥10 years, 15 trial staff, four health care providers and two managers from the Senegal Ministry of Health were interviewed.
Results Thirty-eight of the participants (66.7%) were males and their ages ranged from 10-65 years. Overall, the integrated malaria-helminth treatment approach was considered acceptable but the study participants expressed concerns about the taste, smell and side effects associated with amodiaquine and praziquantel in the combination package. Reluctance to accept the medications was also observed among children aged 10-14 years, due to peer influence and gender-sensitive cultural beliefs.
Conclusion Addressing concerns about the taste and smell of amodiaquine and praziquantel is needed to optimize the uptake of the integrated treatment programme. Also, culturally appropriate strategies need to be put in place to cater for the inclusion of children aged 10-14 years in this approach.

PA-16

Strengthening research ethics oversight in Botswana - The case of University of Botswana

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Background The University of Botswana (UB) received a grant from the European and Developing Countries Clinical Trials Partnership (EDCTP) from 2011 to 2013. The overall aim of the grant was to strengthen capacity for ethical review and promote ethical conduct of research at UB. This paper presents findings from a study that evaluated the impact associated with the implementation of the grant on the research ethics processes at UB.
Methods Through a document review, the funded project plan, including targets, tasks and milestones, were assessed against the met deliverables, achievements and impact associated with the project.
Results The grant enabled the establishment of a Research Ethics Office, which is now a permanent structure, providing ethics oversight to all research conducted by the University research community. In addition, an IRB Administrative Officer was hired to coordinate the activities of the IRB and now heads the Research Ethics Unit. The grant also facilitated the acquisition of office equipment that contributed to improving the operations of the committee, including speeding up the ethics review process and communication with stakeholders. Standard Operating Procedures and guidelines on human research were developed, and several workshops held for graduate students and university staff. Furthermore, the grant facilitated IRB staff and some committee members to attend short courses on research ethics in South Africa, hence enhanced their skills and knowledge. Finally, key government stakeholders responsible for the issuance of research permits were involved in a workshop that reviewed and streamlined the review process and reduced the turnaround time for issuance of research permits.
Conclusion The EDCTP grant was critical in strengthening the research ethics oversight structures at the University of Botswana. These structures and processes have the potential to serve as a best practice model for other Universities intending to establish Research Ethics units in Botswana and beyond.

PA-21

Accuracy of GeneXpert Ultra for diagnosis of childhood tuberculosis within national public health systems in West Africa – a multicentre pragmatic study

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Background We conducted a pragmatic evaluation of GeneXpert Ultra ('Ultra') for diagnosis of childhood tuberculosis (TB) within national public health systems in West Africa.
Methods In this cross-sectional study, children (<15 years) with presumed pulmonary TB were consecutively recruited and evaluated at three tertiary hospitals in Benin, Ghana, and Mali. Bivariate random-effects models were used to determine the pooled sensitivity and specificity of Ultra against a microbiological reference standard ([MRS]; liquid culture) and a composite reference standard ([CRS]; culture-confirmed TB and unconfirmed TB).
Results Overall, we enrolled 193 children with a median (IQR) age of 3.2 (1.1 - 8.9) years, 88 (46%) were female, and HIV prevalence was 36/142 (25%). 32 (17%) children had confirmed TB, 39 (20%) had unconfirmed TB, and 122 (63%) had unlikely TB. Using MRS, the pooled sensitivity and specificity of Ultra were 55% (95% CI: 28 - 79%) and 95% (95% CI: 88 - 98%), respectively. Ultra demonstrated sensitivity and specificity of 50% (95% CI: 16 - 84%) and 95% (95% CI: 85 - 99%), respectively, using sputum, as against sensitivity of 46% (95% CI 17 - 77%) and specificity of 93% (95% CI: 87 - 97%) for gastric aspirate. Against the CRS, the pooled sensitivity and specificity of Ultra decreased to 17% (95% CI: 4 - 53%) and 93% (95% CI: 87 - 96%), respectively. Using sputum, sensitivity and specificity of Ultra were 24% (95% CI: 7 - 50%) and 94% (95% CI: 82 - 99%), respectively, compared with sensitivity of 14% (95% CI: 5 - 30%) and specificity of 91% (95% CI: 82 - 96%) using gastric aspirate.
Conclusion The suboptimal sensitivity of Ultra in children with TB investigated routinely within national public health systems in West Africa constitutes a major challenge.
Funding: EDCTP-West African Networks of Excellence for TB, AIDS & Malaria.

PA-29

Molecular surveillance of pfhrp2/pfhrp3 gene deletion among asymptomatic individuals in Southern Ghana using highly sensitive digital PCR

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Background Malaria remains a major public health concern, especially in the tropics and subtropics where disproportionately high disease burden occurs annually. The World Health Organization recommends parasitological confirmation of suspected malaria cases by either Giemsa stained microscopy or rapid diagnostic tests (RDT) before treatment. The most sensitive RDT used for malaria diagnosis targets histidine-rich protein 2 (HRP2), an antigen unique to Plasmodium falciparum. HRP2 based RDTs also detect histidine-rich protein 3 (HRP3), a structural homolog sharing multiple epitopes with HRP-2. This notwithstanding, there are reports of the deletion of the pfhrp2/pfhrp3 gene and it impact on performance. To improve on the detection of the deletion, this study aimed to investigate the prevalence of pfhrp2/pfhrp3 gene deletion using novel digital PCR (dPCR) in Southern Ghana. The dPCR assay provides absolute quantification of the target gene without a need for a calibration curve.
Methods Community-based cross sectional study was conducted at three districts (i.e., Nkwanta South, Sekyere South and Ga South) in Southern Ghana. A total of 1134 whole blood samples were obtained from asymptomatic individuals in the aforementioned study sites.
Results After screening for Plasmodium falciparum with varATS multicopy gene, 304 samples were selected from Nkwanta South (54.6%, n=166), Ga South (28.3%, n=86) and Sekyere South (17.1%, n=52) and were typed for the presence/absence of the target gene using digital PCR. The assay detected deletion in pfhrp3 gene with 0.3%(n=300) of the isolates examined reported to have a deletion. Unlike pfhrp3, no deletion was observed with respect to pfhrp2.
Conclusion Our findings validate the novel dPCR assay as a is high-throughput and highly sensitive tool for molecular surveillance of pfhrp2/pfhrp3 gene deletion in Ghana.

PA-35

"Slash and Clear" as an effective vector control technique for onchocerciasis in Cameroon

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Background Onchocerciasis (river blindness) is still endemic in parts of Africa, causing skin, eye, and brain disease. The cornerstone intervention for onchocerciasis control is community-directed treatment with ivermectin (CDTI), but therapeutic coverage remains sub-optimal in several endemic communities. The "Slash and Clear" (S&C) vector control technique has been proposed as an environmentally-friendly alternative tool to supplement CDTI.

Methods We conducted repeated cross-sectional entomological studies in Nachtigal, an onchocerciasis-endemic village located beside a fast-flowing segment of the Sanaga River in Cameroon. Blackfly breeding sites were mapped and monthly blackfly biting rates (BR) assessment, initiated at the Nachtigal riverbanks using the human landing-catch approach. Blackfly catching for BR measurements were done for three consecutive days (7:00 to 18:00 daily) every month, by the same two catchers, switching every hour. On March 1st 2023 (a timepoint marking the transition from dry to rainy season), we implemented the S&C intervention at the Nachtigal rapids. Physically-fit village volunteers were trained and supervised in the destruction of the breeding sites using machetes and the removal of potential substrates for blackfly breeding from the river. Post-intervention BR were assessed two weeks after the S&C, and changes in BR were calculated.

Results Following S&C, monthly BR went from 28,000 in February 2023 to 13,888 bites per person in March 2023 (50.4% reduction). In contrast, in the absence of S&C, BR were 31,108 in February 2022; rising to 36,053 in March 2022 (15.9% increase) with the returning rains. Therefore, compared to the natural evolution of blackfly abundance and nuisance, the S&C intervention engendered 50.4+15.9=66.3% decrease in the BR at the Nachtigal riverbanks.

Conclusion Our study demonstrates the significant impact of a community-based S&C vector control approach on blackfly biting rates. Coupled with good CDTI coverage, reducing the blackfly population would break the onchocerciasis transmission cycle and accelerate its elimination.

PA-40

Evaluation of Lassa virus (LASV) specific IgG or IgM antibodies among HIV patients in the Northwest region of Cameroon

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Background Individuals living with HIV are susceptible to other infections due to poor or weakened immune system. Viral haemorrhagic fever caused by Lassa Virus (LASV) has been endemic in parts of West Africa. About four lineages have been discovered in Nigeria a country bordering Cameroon. The porosity of the borders and increased movement across West African countries put Cameroon at risk of LASV. Interestingly, there has not been any report of Lassa fever in Cameroon. Here we evaluated, the seroprevalence of LASV antibodies among HIV patients in Cameroon.

Methods Serum samples obtained between December 2021 and April 2022 from 330 HIV-positive consented patients were tested for LASV IgG and/or IgM antibodies specific for LASV nucleoprotein and/or prefusion envelope glycoproteins using ReLASV® Pan-Lassa IgG/IgM ELISA Test Kit according to the manufacturer's instructions. Data were analysed using SPSS and GraphPad.

Results Analysis of these samples showed that IgG and IgM antibodies were detected in 2.4% (8/330) and 1.8% (6/330) samples respectively. All the IgM positive samples were also positive for IgG. Our data showed that both IgG and IgM antibodies do not depend ($p>0.05$) on age, gender and duration on antiretroviral therapy (ART) though the prevalence was high in age group <25 years, males, and those who had taken ART for <5years. The mean OD of both IgG (0.06 Vs 0.03) and IgM (0.88 Vs 0.04) were significantly higher ($p< 0.05$) between LAVS positive and negative cases.

Conclusion Our results are the first to detect LASV antibodies in Cameroon. With increase movement and porosity of the border, it is plausible that exposure to LASV is inevitable. This has direct implications for understanding the transmission risk, mitigation, and eventually the prevention and control of LASV in Cameroon. Our results indicate the urgent need to extend LASV surveillance in other part of Africa.

PA-45

Lassa Fever Outbreak Investigation, Suakoko District, Bong County, Liberia, 2023

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Background Lassa fever causes morbidity and mortality in Africa. An estimated 100,000 to 300,000 cases of Lassa virus infection and 5,000 fatalities occur in West Africa annually. Lassa fever accounts for 10%–16% of hospital admissions in Liberia and Sierra Leone annually. On the 6th of January 2023, the Bong County Health Team confirmed Lassa fever in a student nurse at Phebe Hospital, Liberia. Five additional cases were reported before the 15th of January 2023. We investigated the source, magnitude, identified and traced contacts, and implemented control measures.

Methods We reviewed medical records from December 2022 in the hospital, and interviewed health workers and contacts. We modified the case definition, listed contacts, followed up for 21 days using checklist, and tested suspected cases. We performed descriptive analysis using Microsoft Excel 2016. Results were presented in frequencies, proportions, and median and displayed in tables, graphs, and maps.

Results A total of 15 persons were suspected and tested for the Lassa virus from January 6 - 31, 2023. Of these, 53.3% (8/15) were positive for the Lassa virus, with a case fatality rate of 25% (2/8). Fifty percent (4/8) were health workers. The median age range for the cases was 34 (6-48) years. Males accounted for 62.5% (5/8). Seventy-two contacts were listed, 4.2% (3/72) of the contacts became cases. Forty-two percent (3/7) of the additional cases were health workers linked to the index case. Fifty percent of the cases were imported from other counties. The index was a student nurse who worked in the hospital on December 12, 2022, on a missed Lassa fever case.

Conclusion The outbreak was sporadic, however among the health workers it was hospital-acquired due to a missed case of Lassa fever and improper hygiene measures. We recommend training and supplies for health workers, especially affiliating students.

PA-46

COVID-19 surveillance data analysis, Monze district, Zambia, 2022

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Background COVID-19 remains a public health threat globally. As part of control measures, the Zambian government integrated it into the IDSR, hence the need to regularly analyse COVID-19 data to inform decisions. This analysis was done to assess COVID-19 descriptively, and to generate hypothesis of factors associated with its mortalities in Monze district.

Methods Between 31st October 2022 and 9th December 2022, we conducted a cross-sectional review of COVID-19 cases and mortalities for the period 1st June 2020 to 30th June 2022. Data were extracted from COVID-19 line list and analysed using EpiInfo. Results were presented in tables and graphs.

Results Between June 2020 and June 2022, Monze district recorded 3141 cases of COVID-19, where 54.2% (1702/3141) were females however, 66% (51/77) of males died of COVID-19 compared to females. The median age was 31 years (IQR 22 – 43) with case fatality rate of 2.5% (77/3141). Most 71.3% (2239/3141) of those who were infected reside in urban area. Majority 28.4% (891/3141) of cases were from 21 – 30 years whilst most 53.2% (41/77) of mortalities were from 71 years and above. Most 29% (912/3141) of cases and 32.5% (25/77) mortalities occurred in June 2021. Sex and age were associated with COVID-19 mortalities.

Conclusion More females were infected whilst more males died from COVID-19. The most infected age group was 21 – 30 years. Higher mortalities were recorded in the age group 71 years and above. Majority of the cases were from urban areas. Most cases and mortalities occurred in June 2021. Further studies are required to determine higher reported cases among females, urban settings, 21-30 age group and deaths in the elderly.

PA-49

Lassa fever outbreak investigation in Weija-Gbawe municipality, greater Accra region, Ghana, 2023

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Background Lassa fever, an acute viral haemorrhagic and zoonotic disease has high case-fatality among hospitalised patients. We investigated an outbreak of Lassa fever in Weija-Gbawe Municipality to determine its magnitude, trace case-contacts, identify the source, and suggest preventive and control measures.
Methods A descriptive study involving reviews and observations was conducted within Weija-Gbawe municipality, from 1st March to 25th March 2023. Hospital and community case searches were done. Suspected case was any person with illness of gradual onset with unexplained acute fever (temp >37.5oC) with one or more of following: malaise, headache, sore throat, cough, nausea, vomiting, diarrhoea, myalgia, oedema, sudden convulsion, bleeding, spontaneous abortion following fever, chest pain, hearing loss, history of contact with excreta of rodents or epidemiological linked to a case of Lassa Fever from 13th February 2023 within the Greater Accra Region. Attack and case-fatality rates were calculated. Case-contacts were identified, line-listed, blood samples taken to confirm Lassa fever, and monitored 21 days from day of last contact with a confirmed case. A nearby market where most of the inhabitants purchase food stuffs was inspected for waste disposal and food storage. Traps were set for rodents in the market and their body fluids, excreta sent for laboratory investigation.
Results Of 62 cases and contacts listed, the overall attack and case-fatality rates were 11.3% (7/62) and 14.3% (1/7) respectively. Mean age of cases was 33.5 years (± 7.1). Majority, 71.4% (5/7) were female. Waste and food stuff were poorly kept and accessible to rodents in the market. Laboratory investigation on rodents was negative for Lassa fever.
Conclusion The outbreak was contained with low mortality. Health workers and community were sensitized on Lassa fever, its mode of transmission and preventive measures. The municipal health director should disinfect homes of confirmed cases and the health facility.

PA-55

Two-step malaria RDT detection PfHRP2/pLDH and point-of-care tests for bacterial infections for the management of febrile diseases in children under-5 years in Burkina Faso

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Background In low and middle incomes countries such as sub-Saharan Africa, the management of febrile diseases remains challenging given the lack of practical diagnostic tools to screen the real cause of fever and the limits of malaria rapid diagnostic tests. In order to improve the management of febrile diseases in children under 5 years, this study has been conducted.
Methods The study was conducted at the Field Station of Sigle, set-up by the Clinical Research Unit of Nanoro. All patients from 6-59 months attending the outpatient clinic of the health facility of Bologho in the health district of Nanoro, with documented fever or history of fever within the pass 7 days were invited to participate to the study. Participants were randomized either the intervention package (e-Algorithm or RDT-decisional algorithm arm(RDT-DA)) or routine system. The intervention package was constituted by the following PoC tests: two-step malaria RDT detection PfHRP2 and pLDH, CRP, white blood cells (WBC) count, oximetry, Group A Streptococcus, and Salmonella/Shigella.
Results Antimalarial prescription was 42.05% (164/390) in e-Algorithm arm, 43.65% (172/394) in RDT-DA and 52.30% (232/392) in standard practice system [risk difference (RD): -10.25% (p p<0.001) for e-Algorithm and -8.65% (p<0.001) for RDT-DA). Antibiotics were prescribed in 46.92% (183/390) in e-Algorithm arm, 50.25% (198/394) in RDT-DA arm and 76.28% (299/392) in routine system [RD: -29.36% (p<0.001) for e-Algorithm and -26.03% (p<0.001) for RDT-DA]. The reduction of antibiotic prescription greater in children without malaria [RD:-64.79% (p<0.001) for e-Algorithm arm and -61.62% (p<0.001) for RDT-DA algorithm arm].
Conclusion Implementation of two-step malaria RDT and PoC tests for bacterial infections has potential to improve the management of febrile diseases in children under 5 years and reduce inappropriate prescription of antibiotics. Nevertheless, the use of CRP test is not suitable differentiate bacterial to non-bacterial infections in children with malaria.

PA-65

Facilitators and barriers to integrated malaria prevention in Wakiso district, Uganda: a photovoice study

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Background Malaria continues to cause significant morbidity and mortality particularly in Sub-Saharan Africa. Appropriate combinations of non-chemical and chemical methods of malaria vector control in the context of integrated vector management have been recommended by the World Health Organization. Integrated malaria prevention, which promotes the use of several malaria prevention methods holistically, is being explored. The aim of the study was to explore facilitators and barriers to using integrated malaria prevention in Wakiso district, Uganda.
Methods The qualitative study employed photovoice among 20 community members in Kasanje Town Council, Wakiso District. The photos taken by participants for a period of 5 months using smartphones were discussed monthly with the researchers. The discussions were audio-recorded, and resulting data analysed using thematic analysis with the support of NVivo (2020).
Results Various conventional and non-conventional measures were being used for preventing malaria such as: insecticide treated nets; clearing overgrown vegetation; draining stagnant water near houses; mosquito coils; smouldering of cow dung; insecticides; plant repellents near houses; as well as closing doors and windows on houses early in the evening. Facilitators to using several malaria prevention methods holistically included: low cost and convenience of some methods such as slashing overgrown vegetation; and support provided for certain methods such as receiving free mosquito nets from the government. Barriers to using several malaria prevention methods holistically included: inadequate knowledge of some methods such as housing improvement; allergic reactions to chemical-based methods such as insecticide treated nets; unaffordability of some methods such as insecticide sprays; and inaccessibility of certain methods such as body repellents.
Conclusion Several barriers to using integrated malaria prevention were identified. These barriers need to be addressed so as to contribute to malaria prevention efforts in endemic communities.

PA-66

Electronic monitoring devices are feasible and acceptable for adolescents living with HIV in Zimbabwe

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Background Adherence to antiretroviral therapy (ART) among adolescents living with HIV (ALWH) is lower than other age-groups, which leads to viral non-suppression. Electronic monitoring devices (EMDs) can improve adherence. EMDs provide daily information about medication intake which can be used to identify those at risk of treatment failure. The use of EMDs by ALWH has been limited in both research and clinical practice. We conducted a mixed methods study to assess field operationalisation and acceptability of EMDs among ALWH in Zimbabwe.
Methods ALWH enrolled in a clinical trial investigating the effect of weekly vitamin D supplementation on bone health in Harare were randomly selected to use the EMD for 24 weeks to take the trial drug. No feedback on EMD-recorded vitamin D adherence was given to participants. 16 participants were purposively selected for qualitative interviews to explore acceptability of using the EMD.
Results Of the 97 participants enrolled, 50 (52%) were female and age range was 11–20 years. All participants used the EMD to store and take vitamin D. One EMD was destroyed in a house fire, 5 recorded low battery (after a median 19 weeks) and were brought back in time for recharging. 36 EMDs lost connectivity with the server for ≥ 14 days during the study, of which 8 spontaneously restored connectivity. The 28 participants whose EMDs lost connectivity were recalled for manual data upload. No data was lost as the EMD can record and save pillbox events when offline. Participants found the EMD easy to use. Older adolescents (16-20 years) preferred the EMD to traditional ART pillboxes because it was discreet and prevented inadvertent HIV disclosure.
Conclusion EMDS are feasible and acceptable for ALWH in Zimbabwe. This study has informed a clinical trial investigating effectiveness of EMDs paired with text message reminders for ART adherence.
Funder: EDCTP

PA-69

Performance of ultra-sensitive malaria rapid diagnostic test to detect Plasmodium falciparum infection in pregnant women in Kinshasa, the Democratic Republic of the Congo

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Background Low peripheral parasitemia caused by sequestration of Plasmodium falciparum in the placenta hampers the diagnosis of malaria in pregnant women, leading to microscopy or conventional rapid diagnostic tests (co-RDTs) false-negative results. Although mainly asymptomatic, maternal malaria remains harmful to pregnant women and their offspring in endemic settings and must be adequately diagnosed. Ultra-sensitive RDTs (uRDTs) are thought to be more sensitive than co-RDTs, and their diagnostic performance was assessed in the present study in pregnant women living in Kinshasa, a stable malaria transmission area in the Democratic Republic Congo.
Methods To assess and compare the performances of both co-RDTs and uRDTs, 497 peripheral blood samples were tested using microscopy and quantitative polymerase chain reaction (qPCR) as the index and the reference tests respectively. The agreement between uRDT, co-RDT, microscopy and qPCR was determined by Cohen's Kappa test.
Results The median parasite density by qPCR was 292 p/µL of blood [IQR 292 (49.7-1,137)]. Using qPCR as the reference diagnostic test, microscopy was the least sensitive test [55.7% (95% CI: 47.6-63.6)], followed by co-RDT [81.7% (95%CI:74.7-87.3)] and uRDT [88% (95% CI:81.9-92.6)]. The corresponding specificity was respectively: 98.5% (95% CI:96.6-99.5), 95.2% (95% CI:92.5-97.2) and 94.4% (95% CI:91.4-96.6). The agreement between qPCR and uRDT was almost perfect (kappa=0.82). For parasite density (qPCR) below 100p/µL, the sensitivity of co-RDT was 62% (95%CI:47.1-75.3) compared to 68% (95%CI:53.3-80.4). Between 100 and 200p/µL, the sensitivity of co-RDT tended to be lower compared to uRDT: 89.4%(95%CI:66.8-98.7) versus 100%(95%CI:82.3-100) for uRDT. In both cases, microscopy was lower, with 20% (95%CI:10-33.7) and 47.3% (95%CI:24.4-71.1) respectively.
Conclusion uRDT tended to be more sensitive than co-RDT in the detection of malaria in pregnant women. Therefore, it has the potential to improve malaria management in pregnant women. Microscopy shows poor performance for the diagnosis of malaria in pregnancy.

PA-70

Utility of the loop-mediated isothermal amplification assay for the diagnosis of visceral leishmaniasis from blood samples in Ethiopia

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Background Rapid and accurate visceral leishmaniasis (VL) diagnosis is needed to initiate prompt treatment to reduce morbidity and mortality.
Methods Here, we evaluated the performance of loop-mediated isothermal amplification (LAMP) assay for the diagnosis of VL from blood in an endemic area in Ethiopia.
Results LAMP was positive in 117/122 confirmed VL cases and negative in 149/152 controls, resulting in a sensitivity of 95.9% (95%CI: 90.69–98.66) and a specificity of 98.0% (95%CI: 94.34–99.59), respectively. The sensitivity of the LAMP assay was 95.0% (95%CI: 88.61–98.34) in HIV-negatives and 100% (95%CI: 85.18–100.0) in HIV-positives. Compared with microscopy, LAMP detected 82/87 (94.3%, 95%CI: 87.10–98.11) of the microscopy1 cases and was negative in 11/27 (40.7%, 95%CI: 22.39–61.20) of the microscopy2 cases. Compared with the rK39 serology, LAMP detected 113/120 (94.2%, 95%CI: 88.35–97.62) of the rK391 cases and was negative in 149/154 (96.8%, 95% CI: 92.59–98.94) of the rK392 cases. However, when compared with microscopy only, rK39 detected 83/87 (95.4%, 95%CI: 88.64–98.73) of the microscopy1 cases and negative in only 12/27 (44.4%, 95%CI: 25.48–64.67) of the microscopy– cases. There was an excellent agreement between rK39 and LAMP (Kappa 5 0.91, 95%CI: 0.86–0.96). Furthermore, an algorithm using rK39 followed by LAMP would yield a sensitivity of 99.2% (95%CI: 95.52–99.89) and a specificity of 98.0% (95% CI: 94.34–99.59).
Conclusion The findings demonstrate that LAMP assay is an accurate and rapid molecular assay for VL diagnosis, including in HIV-1 co-infected patients, in an endemic setting.

PA-71

TB household contacts screening in Mozambique, Tanzania and Zimbabwe

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Background Mycobacterium tuberculosis (Mtb) transmission among households contributes significantly to the tuberculosis (TB) burden. Understanding TB risks and the prevalence of Mtb infection in affected households may help designing strategies for case-finding and targeted prevention. The EDCTP-funded ERASE-TB study aims to validate new diagnostic tests in a cohort of household contacts (HHCs) of adults with infectious pulmonary TB.
Methods 2,101 HHCs ≥10 years of age were enrolled across three sites in Mozambique, Tanzania and Zimbabwe and are being followed up for 24 months. Enrolled HHCs undergo 6-monthly symptom screening, physical examinations and chest X-ray (CXR). HHCs with symptoms presumptive of TB and/or a CXR suggestive of TB undergo sputum-based tests, i.e., Xpert MTB/Rif Ultra /culture. At each visit, novel diagnostics, e.g. TAM-TB and Xpert Host Response (Cepheid), are conducted and blood and urine samples stored in a biorepository. The biorepository will be used for future investigations of new diagnostics applying a case-control design. Testing for Mtb infection is done at baseline using interferon-gamma release assays (IGRA; SD Biosensor).
Results An average of 2.4 contacts per household were recruited. The median age was 26.7, 62% were females, 321 (15%) were living with HIV, and 44 (14%)of these were newly diagnosed. One-quarter of the enrolled HHCs were children aged 10-18 years. At baseline, 355 (17%) had TB-related symptoms and 5% CXRs suggestive of TB. The prevalence of pulmonary TB was 0.7% while the prevalence of Mtb infection was 54%. Follow-up of study participants is ongoing.
Conclusion Despite COVID-19 related interruptions, the targeted enrolment size of 2100 HHC was achieved. While a considerable proportion of HHC had Mtb infection at baseline or had symptoms and/or CXR findings suggestive of TB, less than 1% were diagnosed with TB. This is a relatively high HIV prevalence, albeit mostly known and on treatment.

PA-74

Efficacy of single dose albendazole for the treatment of soil-transmitted infections among school children in Southern Ethiopia

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Background Targeted mass drug administration (MDA) of single-dose albendazole to the at-risk population as preventive chemotherapy or deworming is recommended by WHO to halt transmission of soil-transmitted helminth (STH) in endemic countries. We assessed the effectiveness of single-dose albendazole distributed through a school-based MDA program against hookworm, ascaris lumbricoides, and trichuris trichiura STH infection.
Methods 984 STH-positive school children from two rural woredas in southern Ethiopia were enrolled. Stool samples were examined before MDA and at weeks 4 and 8 post-MDA. Efficacy was assessed using cure rate (CR) and egg reduction rate (ERR).
Results The proportion of children who were cured of any STH parasite at week 4 and week 8 of post-MDA were 46% and 43.3%. The CR was 97.2%, 71.5%, and 49.5% for hookworm, ascaris lumbricoides, and trichuris trichiura respectively at week 4 post-MDA. The ERR at week 4 was 98.8%, 84.5%, and 68.3% for hookworm, ascaris lumbricoides and trichuris trichiura respectively. The observed CR (97.2%) and ERR (98.8%) for hookworm were above the WHO efficacy threshold (CR ≥95%, ERR ≥90%). However, CR (71.5%) and ERR (84.5%) for ascaris lumbricoides were lower than the WHO efficacy threshold (>95%) indicating a reduced efficacy. The CR (49.5%) for trichuris trichiura was below the WHO efficacy threshold (>50%) but the ERR (68.3%) was above the WHO efficacy threshold (>50%). The CR of ascaris lumbricoides in younger children was significantly lower compared to the older children (64.4% versus 74.2%, p=0.006).
Conclusion We found a reduced efficacy of single-dose albendazole against ascaris lumbricoides and doubtful for trichuris trichiura but efficacious in treating hookworm. Therefore, alternative treatment options are needed for the effective elimination of STH as a public health problem by 2030.
Funding: This study was supported by the EDCTP2 program as part of the PROFORMA project (Grant number CSA2016S-1618).

PA-78

Drug transporter expression in healthy South African women exposed to pre-exposure prophylaxis (PrEP)

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Background Effectiveness of oral and topical Pre-exposure prophylaxis (PrEP) is dependent on adequate drug delivery and availability to cells and tissues targeted by HIV. PrEP formulations tested in African women, have produced varying results in preventing HIV infections. Drug transporter protein expression and function are proposed regulators of PrEP disposition. Additionally, ARV-specific drug transporters and inflammation are known modulators of drug transporter expression and function, affecting drug efficacy.
Methods We determined if there was concordance between drug transporter mRNA expression in the blood and female genital tract (FGT) of 45 women taking oral PrEP as Truvada® over 6 months. Additionally, we determined the associations between drug transporter mRNA expression, inflammation, and plasma tenofovir. mRNA expression of six drug transporters P-gp, MATE-1, MRP-2, MRP-4, OAT-1, and OAT-3 was conducted using quantitative RT-PCR. Cytokines were measured using multiplexed technology.
Results Correlation analyses showed moderately significant associations between OAT-1 mRNA expression in the blood and FGT at baseline ($rs<1$, $p=0.0004$), 3 months ($rs<1$, $p=0.0001$) and 6 months ($rs<1$, $p=0.048$). This was also observed for P-gp, MATE-1, MRP-2 and MRP-4 but only after PrEP initiation at 3 and 6 months ($rs<1$, $p<0.05$). Linear mixed models showed trending associations between cytokines and drug transporter expression: IL-1β and MCP-1 and OAT-1 and OAT-3 ($p<0.1$); IL-1Rα and TNF-α and MRP-2 and MRP-4 ($p<0.1$); MIP-1β and MATE-1 ($p<0.1$). No significant associations were observed between drug transporter mRNA expression and plasma tenofovir at 3 or 6 months.
Conclusion Our results suggest that drug transporters may be similarly expressed in the blood and FGT. Furthermore, inflammation may alter drug transporter expression, which can modify PrEP disposition. Collectively, our data may be used to better understand factors that affect PrEP efficacy and better understand PrEP pharmacokinetics to guide implementation of optimal PrEP dosages to ultimately prevent HIV especially in vulnerable, at-risk African women.

PA-79

Perspectives of Stakeholders on Post-Trial Access (PTA) Arrangements: the case of Ethiopia

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Background The increasing number of clinical trials in developing countries providing solutions to the high burden of diseases leads to the vulnerability of study participants and their communities and access to the trial results. In CIOMS, Post-trial access (PTA) is defined as the obligation of sponsors, researchers, host government and other relevant stakeholders, including the community and the research ethics committees to make any intervention or product developed, and knowledge generated, for the study participants or community available as soon as possible. This study explores the stakeholders' perspectives on post-trial access and how PTA arrangements could be feasibly and sustainably incorporated into clinical trials in Ethiopia.
Methods A qualitative study was conducted on stakeholders involving principal investigators, institutional review board (IRB) members; regional ethics review committee (RERC) members; national ethics review committee (NEC), regulatory agency members, and funding organization using face-to-face in-depth interviews and thematically analysed.
Results Our analysis shows that the majority of the study participants do not know about PTA and its implementations, responded lack of binding regulations/laws, the weak collaboration between different stakeholders, and the lack of follow-up of clinical trials. Moreover, most participants pointed out the possibility of study participants and their community exploitation because of PTA statements in the current clinical trial approval and authorization processes.
Conclusion Therefore, we recommend revising the available working documents/guidelines by including PTA, capacity building at different levels, and establishments of independent bodies facilitating the arrangements of PTA and follow-up of its implementations.

PA-80

Specificity of serological screening tests for diagnosis of gambiense human African trypanosomiasis in Côte d'Ivoire and Guinea

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Background Serological tests play a crucial role to diagnose gambiense human African trypanosomiasis (HAT) by preselecting individuals for microscopic examination, and, in the near future, by directly identifying patients for treatment. Variability in reported specificities, the introduction of new rapid diagnostic tests (RDT) and the hypothesis that malaria decreases RDT specificity, led us to evaluate the specificity of 5 HAT screening tests.
Methods Venous blood samples from 1095 individuals from Côte d'Ivoire and Guinea were tested with commercial (Bioline HAT 2.0, HAT Sero-K-SeT, CATT/T.b. gambiense) and experimental (HAT Sero-K-SeT 2.0, DCN) HAT screening tests and with a malaria RDT. Individuals negative with all 5 HAT tests were considered HAT free, while positives underwent microscopy. HAT case definition was based on trypanosome detection by microscopy.
Results One HAT case was detected. Test specificities (n=1094) were: CATT/T.b. gambiense [98.9% (98.1-99.4%), p<0.0001] > HAT Sero-K-SeT [86.7% (84.5-88.5%), p<0.002] > Bioline HAT 2.0 [82.1% (79.7-84.2%), p=0.0113] > HAT Sero-K-SeT 2.0 [78.5% (76.0-80.9%)] and DCN [78.2% (75.7-80.6%)]. Bioline HAT 2.0 and DCN include 2 test lines, and specificities of line 1 [respectively 83.7% (81.4-85.8%) and 80.6% (78.2-82.9%)], corresponding to ISG-65, were significantly lower (p<0.0001) than with line 2 [respectively 95.8% (94.4-96.8%) and 94.5% (93.0-95.7%)]. The ISG-65 line therefore significantly decreased overall test specificity. Although all the HAT tests were less specific in malaria positive than in malaria negative individuals, differences (p values >0.08) were not significant.
Conclusion CATT/T.b. gambiense is more specific than HAT RDTs. The HAT Sero-K-SeT is more specific than second generation RDTs which all contain ISG-65, either as a separate test line (Bioline HAT 2.0 and DCN) or within a single "mixed antigen" test line (HAT Sero-K-SeT 2.0). To improve specificity, removing ISG-65 from experimental RDTs or ignoring the ISG-65 line should be considered, if test sensitivity is not significantly impacted.

PA-81

Bridging the gap: aligning research efforts with disparities in burden of disease - experiences of early-career researcher conducting investigator-initiated trial in a low-income country

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Background Low-income countries bear 90% of the worldwide burden of disease yet there is underrepresentation of research addressing priority issues for low-income countries. Lack of research skills exacerbate the problem. While calls support locally driven research, investigators initiating RCTs in low-income countries encounter barriers, preventing RCT execution. We use our investigator self-initiated trial to provide some of our experiences, in executing a trial in a low-income country.
Methods We are conducting a large RCT to determine the effect of text messaging plus motivational interviewing on sustaining breastfeeding, among 275 women living with HIV.
Results We first assessed the feasibility of the large trial. We submitted multiple grant applications for the pilot trial and secured enough funds within three years. Some awarded funds were returned due to grant timeframe conditions. The pilot trial capitalized on existing research infrastructure. In 2020, we secured the EDCTP2 grant for the large trial. Lack of infrastructural support negatively affected the budget. The pilot trial was exempted from ethics fee. The large trial was approved by ethics before the EDCTP action period, due to tight funding timeframe. We secured funds elsewhere for ethics fee. Each study was approved within three months. The Western Cape Government, Department of Health (WCDH) has a National Health Research Database assisting researchers with applications submission for review by the Provincial Health Research Committee granting access to provincial healthcare facilities. WCDH approved each study within six months. We recruited from a healthcare facility, serving a small pool of our target population which prolonged pilot trial recruitment. We use Research Electronic Data Capture at no cost.
Conclusion Enabling environments improve efficiency of trial execution. Leveraging on existing research infrastructure optimize use of available resources. Small research grants should consider flexible funding timeframes. Collaboration with stakeholders in routine healthcare facilitates facility access for research.

PA-82

Advanced Field Epidemiology Training (FETP) program delivered through blended learning in three west African Portuguese speaking countries

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Background A consortium of African and European Universities, National Institutes of Public Health and Research Centers proposed a project to implement a Master's in Field Epidemiology via blended-learning platforms based at University of Cape Verde. The field training is implemented with the National Institutes of Public Health of each country where strengthening of the local health systems in perspective. Thus, the presentation will describe the experience of implementing a blended-learning advanced field epidemiology training, the defining strategies for the internship and the first outputs produced by Epi Fellows.
Methods The overall project will be described as well as processes in developing the curriculum and its accreditation at different levels and the establishment of International Steering Committee. We describe the recruitment of students, how sites for training were selected as well as the outputs of the first student internships.
Results A total of 55 applications were received and 15 students were selected (6 from Cape Verde, 6 from Guinea-Bissau and 3 from São Tomé & Príncipe). Through a consultative process and field visits, tutors were identified for each student in their country of origin as well as field training sites considered relevant to enhance experiences and capacity of trainees in health surveillance and outbreak response at ministerial, municipality/district and hospital/health facility levels. The expected outputs from field training were defined and the 3 products of the first internships, focusing on the evaluation of the national health information systems of each country, the epidemiological surveillance from a one health perspective, the focus on antimicrobial resistance and outbreak investigations are critically described.
Conclusion The practical training in the countries of origin complemented with theoretical training offered online will allow better insertion and retention of the trained cadres in their countries of origin and contribute for health system strengthening.

PA-85

Innovation for global health at Novartis: two decades of progress in science and partnering

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Background The Novartis Institute for Tropical Diseases (NITD) and EDTCP were both launched in 2003 and similarly pursue scientific advances underpinned by international research collaborations. Moreover, EDCTP-supported institutions directly enable therapeutic R&D at Novartis. To highlight the approach of a large pharmaceutical company and inform cross-sector research collaborations, we sought to describe Novartis' experiences in novel drug discovery for poverty-related and neglected diseases emphasizing the critical role of partnering.
Methods We analyzed NITD's history, progress, and lessons learned over two decades in the context of recognized health priorities in Africa and enabling research partnerships.
Results NITD was established as a public-private partnership involving Novartis and the Singapore Economic Development Board. Scientific priorities evolved to keep pace with the changing epidemiology of disease in global low resource settings and currently organize around two main groups of pathogens: protozoan parasites responsible for malaria, kinetoplastid diseases, and cryptosporidiosis; and emerging viral threats including coronaviruses, flaviviruses, and henipaviruses. A decisive enabler has been durable collaborations with public, private, and academic partners to jointly advance early science and translation of fundamental discoveries, and several major anti-malarial trials are ongoing with EDCTP support. Innovation at Novartis is exemplified in cryptosporidiosis, a high-burden diarrheal disease in childhood. Novartis scientists learned about cryptosporidiosis through the landmark Global Enteric Multicenter Study, which included EDCTP-supported researchers, and discovered a potent inhibitor of the parasite PI(4)K lipid kinase to treat the disease. The front-running compound is approaching phase II clinical development and we will explore partnership to enable definitive trials to bring this therapy to pediatric patients in Africa.
Conclusion Partnerships have enabled scientific progress at NITD over the past twenty years and we expect international collaboration to be equally instrumental to the delivery of innovative therapies needed to address the most pressing global health problems anticipated over the next decades.

PA-89

Professional career pathways are needed to combat a declining workforce and lack of competency-based training in clinical research in Africa

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Background Six sub-Saharan African nations are in the top 10 globally for losing over 50% of their medical graduates to work abroad. Insufficient training and career advancement options hinder retention, harming sustainable development. Evidence-based research training is needed to improve research capacity and retention.
Methods The Global Health Network (TGHN) and the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) collaborated to create an Evidence-led Essential Research Skills Training Curriculum (EERSTC). The study surveyed 7,176 individuals from 153 countries worldwide, with 54% of respondents from Africa. The EERSTC showed effectiveness in developing research skills among novices. The curriculum recommends specific modules for clinical research training programs.
Results TASK Research Academy used selective modules from the EERSTC to develop a training course that uses storytelling, simulations, and interactive case studies to teach core competencies. Since its launch in August 2022 the course has enrolled 127 novices, with 82 having completed it. 98% of students believe the course improved their confidence in their ability to work in clinical trials, while 90% indicated that it helped them create career opportunities. The academy plans to further develop bi-chronous clinical research career pathway programs for research-naive individuals. These role-focused career pathway programs will be based on the suggested EERSTC modules and will use the latest digital technologies to create simulation-based training. By providing industry-ready training that emphasizes practical application, graduates will be prepared to start working immediately.
Conclusion To achieve the Sustainable Development Goals by 2030, Africa requires research capacity building to attract sponsors and promote clinical research. Lack of research experience is a significant barrier to entry. Training that aligns with industry needs and core competencies can equip the next generation of researchers and support and African research culture, easing entry barriers and combatting workforce deficiencies.

PA-91

strengthening capacity of research ethics committees for review of research protocols with complex and emerging study designs in Uganda

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Background There has been significant increase in research in Uganda, in response to the increasing burden of emerging and re-emerging infectious diseases. Research should be supported by a robust and pragmatic research regulatory framework to assure safety and wellbeing of research participants, high ethics and scientific standards. Research Ethics Committees (RECs) oversee the conduct of research, hence should possess technical expertise for timely and high-quality review of research protocols. We aimed to strengthen capacity of RECs to review research protocols with complex and emerging study designs.
Methods Baseline assessment of self-reported competence of REC members in complex and emerging study designs informed development of a curriculum and subsequent training. Trainees were evaluated using pre- and post-training tests with a pass mark of 60%.
Results Baseline assessment involved 55 REC members; 57% were male. Competence was lowest for controlled human infection models and reverse pharmacology, and highest for cluster randomized studies and implementation science. Competence in other designs was scored below 50% including; evaluation of technologies and digital health interventions, step wedged design, case control studies, ecological studies, phase I-III clinical trials, and adaptive platform trials. Training was delivered to 77 REC members, 55% female, 71% took the pre-test and 44% took the post-test. The lowest and highest scores were lower for the pre-test compared to the post-test (27% and 75% vs 62% and 93% respectively). There was an increase in proportion of trainees who scored above the pass mark in the post-test compared to the pre-test (82% vs 35%) and an increase in the average score in the post-test compared to the pre-test (70% vs 54%).
Conclusion Training resulted into improved REC members' knowledge on complex and emerging study designs. We recommend regular training of REC members in science and ethics and evaluation of quality of review of research protocols.

PA-93

SARS-CoV-2 Infection-Acquired Seroprevalence and Pfizer/BioNTech BNT162b2 vaccine-induced antibody response among Schoolchildren in Hawassa, Ethiopia

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Background With the persisting low vaccination intake, particularly in children of low-and middle-income countries (LMICs), sero epidemiological studies are urgently needed to guide and tailor COVID-19 pandemic response efforts in schools and to place mitigation strategies for future post pandemic resurgence. However, there is limited data on SARS-CoV-2 infection-induced and vaccine-induced humoral immunity in schoolchildren in LMICs, including Ethiopia.
Methods We assessed and compared the infection-induced antibody response at two time points and the BNT162b2 (BNT) vaccine-induced antibody response at a single time point in schoolchildren from Hawassa, Ethiopia using an in-house anti-receptor binding domain (RBD) IgG ELISA assay.
Results Over a five-month period, the seroprevalence of SARS-CoV-2 infection-induced antibodies in unvaccinated schoolchildren (7-19 years) at the two blood sampling points increased by more than 10% from 51.8% (219/419) during the first week of December 2021 (pre-Omicron wave) to 67.4% (60/89) by the end of May 2022 (post-Omicron wave). A significant correlation (P=0.001) was found between anti-RBD IgG seropositivity and a history of COVID-19-like symptoms. Compared to the levels of SARS-CoV-2 infection-induced anti-RBD IgG antibodies before vaccination, higher levels of BNT vaccine-induced anti-RBD IgG antibodies were observed even in SARS-CoV-2 infection-naïve children of all age groups (P = 0.0001). A single dose of the BNT vaccine was shown to be adequate to elicit a strong antibody response in children with pre-existing anti-RBD IgG antibodies comparable to that of SARS-CoV-2 infection naïve children receiving two doses of BNT vaccine. The BNT vaccine was well-tolerated by all recipients (111), with no serious adverse events reported.
Conclusion A single dose BNT vaccination could be considered for children with prior SARS-CoV-2 infection when a shortage of vaccine supply is a limiting factor to administer two doses irrespective of their serostatus. Albeit small size of the study participants, the BNT vaccine is immunogenic and safe for schoolchildren.

PA-95

The development of culturally-congruent mental health evaluation guidelines for an African context centering gender, socioeconomic, and health equity

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Background Africa experiences great mental illness burden due to highly prevalent impoverished living conditions and a double burden of disease, exacerbated by COVID-19's socioeconomic decline and systematic inequalities augmentation, rendering mental healthcare inaccessible. Mental health in Africa is under-researched, accounting for 2% of global research, mirroring gaps in mental healthcare with 84% fewer specialized providers than the global average. The WHO reports that only 45% of African States have a mental health policy complying with international human rights. Stereotypes such as witchcraft are attributed to mental illnesses, increasing stigma and discrimination. Currently, no mental health research review guidelines specific to sociocultural and gender aspects exist. High rates of gender and social inequalities in Africa necessitate their inclusion when evaluating research. Ethics committees are strategically positioned to ensure the scientific and ethical rigour of mental health research.
Methods Thirteen tools evaluating mental health research, programmes, policies and sex- and gender-sensitive considerations were systematically reviewed. Data extracted and adapted to the African context yielded a 54-item assessment tool.
Results A 54-item assessment tool, created categorized into Research governance, Background and justification, Methodology and Ethical impact of the research. It will guide the process of mental health research protocol evaluation taking into account ethical, gender, and sociocultural factors in Africa.
Conclusion This will enhance health equity in Africa, bridge gaps in mental health research, prevent discrimination, facilitate the achievement of the 3rd and 5th SDGs, and guarantee the African Charter on Human and Peoples' Rights 16th Article, entitling humans to the highest attainable mental health state. The tool applies to mental health research protocols review and explores various dimensions such as team competency, cultural congruency of the methodology, perpetual respect for participant dignity, autonomy, and rights, gender and intersectionalities- based sensitivity of data collection, analysis, and dissemination.
Funding: EDCTP funded project - BCA-WA-ETHICS II

PA-96

Surveillance of hematological and biochemical changes following mass Ivermectin and Albendazole administration for the control of lymphatic filariasis in endemic communities of Tanzania

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Introduction Ivermectin and Albendazole (IA) are drug combinations used in mass drug administration (MDA) to halt transmission of lymphatic filariasis (LF) in endemic communities. Safety data on haematological and biochemical changing patterns following MDA is limited. We investigated changes in such parameters among individuals exposed to IA during MDA in rural Tanzania.
Methods An analytical cross-sectional study was conducted amongst 498 individuals whose blood samples were collected before and after MDA. Complete blood count, renal and liver function tests were done at day 0 and 7. Wilcoxon signed rank and McNemar tests were used to compare the median and proportion of individuals with abnormal values respectively, before and after MDA.
Results The overall findings indicate changes in some parameters after IA intake. The median values of haematological parameters to include RBC, Hb, and HCT decreased and MCH and MCHC increased significantly in both FTS positive and negative individuals following MDA ($p<0.05$). Platelet counts to include PDW, MPV and PLCR all increased after drug intake in both groups ($p<0.05$). Biochemical parameters to include ALT and BilD decreased in both groups whilst AST increased in FTS positive (from 24.4 U/L to 25.35 U/L, $p=0.01$) and decreased in FTS negative individuals (from 24.95 U/L to 24.55 U/L, $p=0.04$). A significant proportion of individuals had haematological parameters below reference range (RBC 8.2%, $p=0.01$; Hb 23.5%, $p=0.002$; HCT 32.9% $p<0.001$; MCH 9.8%, $p<0.001$; and MCHC 0.5%, $p<0.001$). Sex was the only predictor of low Hb levels with females at a higher risk of experiencing low Hb than males (aOR: 3.16, 95% CI= 1.29-7.76, $p=0.01$).
Conclusion Our findings demonstrate that haematological changes may occur following IA MDA. No significant changes in biochemical (kidney and liver function test) parameters were observed after drug use. Overall, the observed abnormalities were minor with minimal clinically relevant safety concerns.

PA-104

Prevalence and Associated risk factors of two human schistosomiasis among school children in two endemic communities of Southern Nigeria

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Background Schistosomiasis remains one of the most prevalent neglected tropical diseases, especially in Nigeria which has the greatest number of infected people worldwide. School-aged children are the most vulnerable, as they participate in water contact activities that expose them to free-swimming cercariae released by infected snail species in freshwater; hence most studies target this age group. A cross-sectional study was conducted among 466 participants from two communities in South-west Nigeria to investigate the risk factors associated with high prevalence of the two human schistosome infection.
Methods Urine and stool samples were collected from consenting school children in Ilie and Ore communities of Osun State, Nigeria. Schistosoma haematobium eggs were detected in the urine using the urine filtration technique, while S. mansoni eggs were detected in stool using the Kato–Katz thick smear technique.
Results The overall prevalence of schistosomiasis was 40% (185/466), with 31% and 10% infected with S. haematobium and S. mansoni, respectively. The multiple logistic regression analysis revealed that water contact activities i.e washing and fishing ($X2 =7.52$; $p< 0.06$; $X2 =19.54$, $p =0.000$) knowledge of schistosomiasis ($X2 =12.7$; $p= 0.00$) blood in the urine ($X2 =37.8$; $p< 0.00$) were the significant risk factors associated with schistosomiasis in these communities.
Conclusion This study revealed that schistosomiasis is still prevalent in endemic communities of southern Nigeria. Factors predicting schistosomiasis were related to water contact activities (fishing and washing) knowledge of schistosomiasis, previous infection, and blood in the urine. These findings highlight the need for mass drug administration, health education, and community mobilization to significantly reduce the prevalence and morbidity of schistosomiasis in these communities.
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PA-105

Mapping the timeliness of routine vaccination among 12-35 months old children in The Gambia: a spatial modelling study

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Background The timeliness of routine vaccination is usually estimated at the national level or for large regions. Such estimates often conceal epidemiologically relevant variations and make it difficult to identify pockets of untimely vaccination which could benefit from targeted interventions. Here, we demonstrate the utility of geospatial modelling techniques in generating highly-detailed maps of vaccination timeliness. Additionally, we investigate the spatial relationships between the prevalence of delayed vaccination and the estimated number of children with delayed vaccination at the second and third-administrative levels in The Gambia.
Methods We obtained cluster-level childhood vaccination data from the 2019-20 Gambia Demographic and Health Survey. Using the third dose of pentavalent vaccine (PENTA3) and the first dose of measles-containing-vaccine (MCV1) as examples, we mapped early and delayed vaccination at 1x1 km resolution. We utilized a fully Bayesian geostatistical technique with a binomial likelihood built on a suite of publicly available geospatial covariates and implemented using the integrated nested Laplace approximation—stochastic partial differential equation (INLA-SPDE) approach.
Results Our analysis revealed early PENTA3/MCV1 were less prevalent compared to delayed vaccination, with a largely uniform spatial pattern across the country. Delayed PENTA3/MCV1 showed substantial subnational inequalities, with certain areas located in the central and eastern end of The Gambia, having the highest pockets of children with delayed vaccination compared to coastal areas. We also found that districts and wards located in the central and eastern, in addition to coastal parts of The Gambia showed a spatial overlap of having both the highest prevalence and absolute number of children with delayed PENTA3 and MCV1 vaccinations.
Conclusion Our results offer decision-makers a tool to better understand where strengthening vaccine delivery systems might have the greatest impact.
Funding: This project is part of the EDCTP2 Programme supported by the European and Developing Countries Clinical Trials Partnership (grant number TMA2019CDF-2734-TIMELY).

PA-107

Efficacy status of artemisinin-based combination treatment of falciparum malaria in Lagos, Nigeria

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Background Artemisinin resistance is a major limitation against malaria control. Routine monitoring of the efficacy of artemisinin-based combination (ACT) treatment is required to ensure early detection and response to drug resistance. This research evaluated therapeutic response to directly observed treatment with artemether-lumefantrine (AL) in participants infected with uncomplicated falciparum malaria.
Methods The study was conducted in Ijede, a sentinel site in southwestern Nigeria. Microscopy, rapid diagnostic test and 18S ribosomal ribonucleic acid (rRNA) polymerase chain reaction (PCR) methods were used to diagnose Plasmodium falciparum. Primary outcomes were clinical and parasitological cure rates at day 28. Secondary outcomes included patterns of fever and parasite clearance. Parasite genotyping using merozoite surface proteins 1 and 2 markers was performed at baseline and at the time of recurrence of parasitaemia to differentiate between recrudescence and new infections.
Results Of the 79 participants enrolled, 58 completed the follow-up to day 28. Clinical observations and microscopy showed no early treatment failure whereas 18S rRNA PCR analysis identified parasite DNA in 37% (23/62) of participants followed up on day 3. However, this did not correspond to treatment failure in subsequent follow-up days. Based on Kaplan–Meier survival estimate, day 28 cumulative incidence of success of AL treatment was 96.6%.
Conclusion This finding demonstrates sustained in vivo efficacy of AL as first-line treatment of uncomplicated malaria in the study area. Investigations are underway for ex vivo genotyping of resistance markers to validate the efficacy status of ACT in this population.

PA-113

Pharmacogenomics of drug-drug interactions in malaria-HIV con-infections: effects on generic artemether-lumefantrine therapy used in Ghana for malaria treatment

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Background Malaria/HIV co-infection (MHC) is a public health challenge which may present with worse health outcomes due to interactions. Coadministration of artemether lumefantrine (ALU) and antiretroviral therapy may have potential drug-drug interactions that can affect the course of treatment for both diseases. Generic ALU medications are used in Ghana for malaria treatment after RDT or microscopy diagnosis. ALU is metabolized by the enzymes CYP2B6, CYP3A4/5, CYP2A6 and UGTs which can be affected by pharmacogenetics. A better understanding of the effects of MHC on ALU drugs could help prompt treatment, and control of malarial parasites among HIV-infected patients. This study evaluated effects of MHC on ALU drugs used in antimalarial treatment and pharmacogenetic influences on their efficacy.
Methods To compare metabolite profiles and treatment outcome in patients on generic ALU for uncomplicated malaria and MHC, this study has recruited about 218 participants. However, we currently have complete preliminary metabolite and genomic data on 52 participants. Blood was taken for microscopy, genotyping using iPLEX Gold microarray and PCR-RFLP, and metabolite analysis using LC-MS/MS.
Results Median parasite density was 2119.42/uL, 760.10/uL, 0/uL and 0/uL on days 1,2,3 and 7 for malaria-only participants and 7322.52/uL, 3928.60/uL, 0/uL and 0/uL for MHC participants. Plasma concentrations of dihydroartemisinin (DHA) ranged from 3.30-35.85ng/ml. Desbutyl-lumefantrine (DBL) concentrations ranged from 7.8ng/ml-40.44ng/ml on days 3 and 7. Decreased concentrations of lumefantrine, DBL and DHA were observed across CYP2B6 *1/*1, CYP2B6 *1/*18/*1/*6, CYP3A5 *1/* and CYP3A5 *1/*3/*1/*6/1*/*7 carriers for MHC participants. However, MHC carriers of non-functional haplotypes CYP2B6*6/*6 or *6/*18 or *18/*18 showed increase in lumefantrine, DBL, artemether and DHA concentrations.
Conclusion Pharmacogenetic variations affected ALU plasma concentrations although blood parasites were eliminated by day 3 in malaria monoinfected and MHC participants. This however shows there is potential drug-drug interactions between ALU-ART components which can influence the progression of either disease.

PA-114

Addressing causes and underfunding of neglected disease of Low-Income Countries (LICs) synergizing national and EU funding

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Background Despite a worldwide decrease, sub-Saharan Africa (sSA) still has high incidence and the highest percentage of under 5 deaths (55%) in the world. This is due to several causes, including high incidence of infectious disease, often neglected or underreported, lacking effective treatments or vaccines. During our activities on Typhoid fever, Sclavo Vaccines Association (SVA) and Fondazione Achille Sclavo (FAS) came across increasing evidences in sSA of marked morbidity and mortality due to an unreported disease in children and HIV patients: invasive Non-Typhoidal Salmonellosis (iNTS)
Methods SVA and FAS, two nonprofit Italian institutions devoted to supporting development of vaccines for LICs, committed to catalyze funds and a group of institutions to fight this disease of the most vulnerable. The institutions applied for national and European funding, receiving first a validation at the local level, followed by funding from the EC and EDCTP. This stepwise approach created the necessary know-how to prepare solid projects, supporting a valid candidate vaccine fit for use in LICs. The projects synergistically address reasons why this disease is neglected: low epidemiology knowledge and disease awareness, lack of candidate vaccines and financial commitments.
Results Two projects were rejected at the national and EU level: finally a grant was obtained in Italy from the Tuscany Region (S-Afrivac) concentrating on epidemiology, disease modeling and vaccine and assay development. The successful conclusion of this project worked to open doors for two EU grants: the H2020 EC Vacc-iNTS and the EDCTP Pedvac-iNTS projects. Within 4 years, these projects multiplied tenfold the funds devoted in the EU to iNTS vaccine development.
Conclusion The validation of targeted projects against neglected diseases at the national level followed by synergistic submission to European Agencies in appropriate calls addressing all causes of neglection may significantly increase success in fighting these modern plagues of LMICs

PA-117

Digitization of research ethics committees in Africa: vector of efficiency and quality

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Background Research is an essential component of the response to health challenges such as weak health care systems and high disease burden that Africa faces. In addition to these challenges, the advent of health emergencies has led to a significant increase in the number of protocols for review by Research Ethics Committees (RECs). The majority of RECs in Africa still use paper-based review systems with long lead times for authorization. Regarding the major role assigned and the desired efficiency of the CERs, the digitization of the protocol ethics review process is a necessity for scientific development.
Methods We conducted a literature review using key words related to the digitization of RECs in Africa and used the experiences of RECs in Benin that are in the process of digitization through to the AMELIORER Project (2021-2023) entitled "Enhancing Research Ethics and Regulatory Capacities in Benin" and funded by EDCTP (CSA2020ERC-3086).
Results The digitization of committees on the continent has brought light to their operations by facilitating dynamic and efficient ethics review. It has contributed to improving the quality of review through standardization and harmonization of ethics review procedures and reduction administrative workload and costs. However, RECs are facing digital learning challenges and technological capacity (availability of computer equipment and quality connectivity).
Conclusion For a more effective and dynamic research framework in Africa, it is essential to support RECs to implement and overcome the challenges inherent in the digitization process.
The funding source: CSA2020ERC-3086

PA-118

Safety monitoring during mass drug administration: Adverse Events following the use of Ivermectin, Diethylcarbamazine and Albendazole for the control of lymphatic filariasis in Kenya

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Background In Kenya Mass Drug Administration (MDA) intervention with single dose of Diethylcarbamazine Citrate (DEC) and Albendazole (ABC) commonly referred to as DA. has been in use since 2002 the control of Lymphatic Filariasis(LF), however no safety surveillance has been conducted before. Recently, the Neglected Tropical Disease (NTD) Program, piloted the use of Ivermectin (IVM), Diethylcarbamazine and Albendazole known as IDA triple therapy in two highly endemic counties.
Methodology This was a longitudinal community-based cohort event monitoring 10,010 and 10, 411 eligible participants in Kilifi and Mombasa Counties respectively. Adverse event monitoring and grading was actively done at 24 hours, 48 hours and at day 7 following mass drug administrations. The collected data was analysed for incidence, types, and predictors of adverse events.
Results A total of 5807 and 3102 AEs were reported by 2839 and 1621 individuals in the IDA and DA groups, respectively. The incidence of experiencing one or more AEs was significantly higher ($p<0.0001$) in IDA (27.3%; 95%CI, 26.4%-28.2%) compared to DA (16.2%;95%CI, 15.5–16.9%) group. The three most AEs reported among those who took IDA were dizziness (15.9%), drowsiness (10.10%) and headache (6.5%), compared to DA that reports dizziness (5.9%), headache (5.6%) and loss of appetite (3.3%). Female sex, taking ≥ 3 tablets of DEC or IVM, older age, taking concurrent medications, ≥3 tablets of DEC, and type of meal taken before MDA were significant predictors of AEs. The AEs were systemic, mild to moderate and transient.
Conclusion Both the dual Therapy with DA and triple therapy with IDA were generally safe and well as MDA regimens for Elimination of LF. The incidence of experiencing one or more type AEs is about two-fold higher with IDA than with DA. The integration of safety monitoring during MDA is critical for the timely detection and management of reported AEs.

PA-119

Evaluation of global lung function initiative reference equations in healthy Gambian children

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Background Spirometry testing in respiratory disease research, diagnosis, and management relies on reference equations. The Global Lung Function Initiative (GLI) reference equations are based on data from 26 countries, but sub-Saharan African populations are largely under-represented. This study assessed the appropriateness of GLI equations (African-American, southeast Asian, others/mixed, Caucasian, and northeast Asian) in healthy Gambian children.
Methods Healthy children were recruited for spirometry tests using a hand-held spirometer. We compared mean z-scores of forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) obtained from each GLI reference equation with a value of 0 using one-sample t-tests. We assumed that if the GLI predictions were optimal, the measured z-scores of the healthy Gambian children would have an average value of 0 and a standard deviation of 1.
Results Out of 91 children, 86 (94.5%) had valid spirometry results per ATS/ERS criteria. The median age (IQR) for participants with valid results was 11.3 years (8.1-13.7), with 34 females and 52 males. Mean z-scores for FEV1 and FVC were closest to 0 with the African-American reference equation (FEV1: -0.91±0.87; FVC: -0.97±0.93) and lowest with the northeast Asian reference equation (FEV1: -2.43±1.21; FVC: -2.80±1.39). The proportion of children with FEV1 and FVC z-scores below -1.64 (LLN) was lowest with the African-American reference equation (FEV1: 18.6%; FVC: 23.3%) and highest with the northeast Asian reference equation (FEV1: 75.6%; FVC: 79.1%). Mean z-scores for FEV1 and FVC were significantly lower than 0 for all GLI reference equations.
Conclusion African-American GLI reference equation showed best fit, while the northeast Asian equation was the worst in this study. However, none of the GLI equations adequately represented Gambian children's lung function. Locally derived reference equations are needed.
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PA-121

Relative growth rates for height among children and adolescents living with HIV on antiretroviral therapy

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Background Perinatally acquired HIV is a treatable chronic condition such that through antiretroviral therapy (ART), children with HIV (CWH) are now surviving to adulthood. However, CWH often exhibit impaired growth. We aimed to identify the height growth patterns among CWH and determine age at peak-height-velocity (PHV).
Methods This is a secondary analysis of data collected prospectively in the ongoing VITALITY randomised controlled trial in Zimbabwe (EDCTP: VITALITY-RIA2018CO-2512). The trial has recruited 840 CWH (11-19 years) established on ART for at least 6 months, to determine whether vitamin-D3/calcium supplementation improves bone mass and strength with follow-up to 96 weeks. Height is measured at 12-week intervals with currently (31-March-2023) 135 participants having completed 96-weeks of follow-up. Weight and height for age were calculated using 1990-UK-reference values, with Z-score≤-2 classifying those underweight and stunted. Analysis of height trajectories was performed using the Superimposition by translation and rotation (SITAR) adjusting for size, pubertal-timing and growth-rate and fitting the mean and velocity curves by sex.
Results We recruited 447(53.2%) females and 393(46.8%) males and followed them up for 1.37(IQR:1.15-1.1.61) years; at baseline median (IQR) age was 15(13-17) years and 30.0%(n=252) were stunted. CHW were taking ART for median (IQR) 9.8(6.3-12.3) years of their lives and 81.9%(n=688) were on an ART regimen containing tenofovir-disoproxil-fumarate. Lifetime fracture prevalence was 5.9%(n=50). At baseline (n=840), mean (SD) height-for-age was -1.70(1.06) and -1.22(1.05) for males and females respectively. Over 48-weeks (n=780), median (IQR) height gains were 3.3(1.1-5.9) cm and 1.2(0.3-3.5) cm for males and females separately. Age at PHV was 15.0 years (PHV:8.2cm/year) and 13.2 years (PHV:5.6cm/year) for males and females respectively.
Conclusion There is a high prevalence of stunting among CWH in Zimbabwe. Both males and females showed delayed PHV compared to regional estimates (females:11.8, males:14.4 years), raising concerns for persistent height deficits in adulthood known to impact human capital and function in later life.

PA-131

The contribution of neutrophils and their soluble markers to lung pathology in tuberculosis disease

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Background Tuberculosis is a leading infectious disease killer. It primarily affects the lung, accompanied by tissue damage from excessive host inflammation. Neutrophils are implicated as primary mediators of this tissue destruction. This study aims to access neutrophils and their soluble mediators in relation to TB-induced tissue damage.
Methods Fifty-three (53) patients with confirmed TB were recruited. Neutrophil numbers in sputum and blood were assessed using microscopy and automated counting. Soluble mediators were analysed in sputum and plasma by ELISA. Participants were classified as having mild (n=24) or severe (n=29) lung pathology at baseline based on a median chest X-ray Ralph score of 70%. Lung recovery was also assessed at 6 months of TB therapy with 14 participants classified as having good recovery and 15 having poor recovery based on overall change in Ralph score.
Results Plasma MMP9 levels at baseline were significantly higher in patients with severe [median (IQR) = 404548 (272166 - 465789) pg/ml] compared to mild [median (IQR) = 94461 (43194 – 168716) pg/ml] lung pathology (p=0.0277). Plasma MPO levels in both groups decreased significantly by week 2 (p=0.0287) and week 8 (p=0.0110) treatment respectively. Patients with severe lung pathology at baseline had significantly higher levels of circulating MPO compared to those with mild pathology [median (IQR) = 208913 (146125 - 239403) pg/ml and 106366 (69207 - 146633) pg/ml] (p=0.0432). No difference was seen in analytes between good and poor lung recovery patients.
Conclusion Severe lung pathology was associated with high plasma MMP-9 and plasma MPO at baseline. No difference was seen in good and poor lung recovery groups at 6 months but should be assessed at later time-points. Understanding how neutrophils and their associated protein markers drive lung pathology and subsequent long term post-TB lung disease could inform, whether and which HDT may support better treatment outcome.

PA-133

Significant reduction in blackfly bites following implementation of Slash and Clear: An option to consider for onchocerciasis elimination in areas of persistent transmission

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Background Although "Slash and Clear" has proven effective in reducing blackfly densities in low transmission foci, the impact of this strategy in high transmission settings with large rivers and important vector densities remains to be demonstrated.
Methods A controlled before-and-after community-based intervention comprising two arms (Bayomen as control site and Biatsota as intervention site) was carried out in the Mbam Valley (Centre Region, Cameroon). In each arm, baseline blackfly densities were collected over one year using the human landing method. The intervention consisted of destroying the trailing vegetation where blackflies breed. Blackfly densities were collected post-intervention to assess the impact of the intervention. Before the intervention, a total of 36,273 and 29,041 blackflies were collected in Bayomen and Biatsota, respectively.
Results After the intervention period, the total blackfly density in the intervention site decreased from 29,041 to 20,011 (31.1% reduction), while an increase of 2·7% was observed in the control site (from 36,273 to 37,248). The Poisson mixed regression model shows that the reduction was significantly greater in the intervention site than in the control site (p<0.0005).
Conclusion This study showed that "Slash and Clear" approach is feasible and has a significant impact on vector densities in a high transmission setting. Further studies are needed to investigate the long-term impact of this vector control approach, and how this promising strategy can be scaled-up and sustained until elimination of onchocerciasis.

PA-134

Averting Campylobacteriosis through management of environmental health: end route for reducing the environmentally mediated Campylobacteriosis in South Africa

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Background Campylobacteriosis is the lexicon used to denote the group of infectious diseases caused by several species of Campylobacter. A form of Campylobacteriosis of significant public health importance is Campylobacter enteritis. Campylobacter species are increasingly being recognized as leading agents of gastroenteritis. In South Africa, it has been suspected that Campylobacter infection could be endemic. Freshwater environments are under pressure from climate change and consequent drought, change in conditions and migration of new species into these systems. Environmental management and managing environmental risk factors will control and prevent the epidemic or at least could significantly reduce the vulnerability of communities to Campylobacteriosis. This study provides knowledge-based recommendations for controlling and preventing Campylobacteriosis in South Africa.
Methods Collection of secondary data of at least five years of culture-confirmed cases of Campylobacter infection in two Municipalities in the Eastern Cape was conducted to establish community infection and infection rates. River water samples were also collected and analysed for Campylobacter spp. In addition, this study utilized a literature review and interviews of residents to identify local environmental risk factors of Campylobacteriosis in the two populations.
Results Campylobacter infection could be endemic in the Eastern Cape region of South Africa. Direct contact and consumption of surface waters faecal-contaminated local rivers are likely risk factors for Campylobacteriosis. Also, protecting surface water from access by animals is critical to interrupting the transmission of Campylobacter from animals to humans in these rivers.
Conclusion Campylobacteriosis in South Africa may be environmentally mediated. Rivers in South Africa are platforms for transmission of Campylobacter spp., and so prevention of Campylobacteriosis can be achieved by reducing their Campylobacter burden by protecting these platforms from contamination. The findings of this study are policy levers to mitigate Campylobacteriosis risk in South Africa.

PA-136

Optimizing approaches in the control of neglected tropical diseases: Highlighting women's roles in research for policy and planning in control of urogenital schistosomiasis in Cameroon

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Background This research highlights the role of natural, cultural and structural gaps which shape sickness experiences and social stigma of women with manifestations of female genital schistosomiasis (FGS), a neglected gynaecological condition resulting after untreated infection with urogenital schistosomiasis. We focus on using women's shared experiences without them emerging as victims, but as voices for change, all activists and collaborators in the quest of their human rights, good health, and representation. Women take ownership and present their own interpretations capturing expressive, and symbolic aspects as persons living with a neglected tropical disease.
Method Focusing on ethnography and specific case studies of women manifesting symptoms of FGS within endemic rural fishing communities in Cameroon, we present illness experiences of women affected by FGS, drawing from a narrative method, and information on health service provision around FGS, to show the role of women and their histories in research on health, a frequently neglected angle.
Results Our results show how gendered power dynamics in decision making, and gendered experiences such as the need to manage menstrual health; as well as structural gaps, combine to bring an FGS mental health toll. Sub-fertility brings a heavy psychosocial toll from external blame and rejection, exacerbating the burden affected women experience of internalized stigma and the mental challenge of not being able to fulfill cultural standards, leading to exclusion.
Conclusion Gender-analysis is used to highlight missing gaps, and context embedded understanding which could be used to address neglected tropical diseases and their related psychosocial burden. With context-specific experiences portraying co-morbidity with mental ill-health and FGS as a neglected tropical disease, there is a need to prioritize women's voices and mental-health management at policy level through a person-centred approach.
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PA-139

Impact of molecular diagnostic tools for community-based active case-finding: a multicentre randomised controlled trial

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Background Tuberculosis (TB) disease remains undiagnosed or unreported in approximately 4.2 million people annually. To address these "missing millions", we assessed the feasibility and impact of a scalable model for transmission-interrupting, community-based active case finding (ACF) in major cities of four African countries: Cape Town, South Africa, Lusaka, Zambia, Harare, Zimbabwe, and Maputo, Mozambique.
Methods In peri-urban informal settlements using a 1:1 randomised controlled trial (stratified by country), we performed ACF using a low-cost mobile clinic fitted with a portable 2-module Xpert system and compared a point-of-care (POC) Xpert to a standard-of-care centralised laboratory Xpert with sputum culture used as a reference standard. At the Cape Town site, those with microbiologically confirmed TB received infectiousness studies, including smear microscopy, chest x-ray (CXR) and cough aerosol sampling (CASS).
Results Of 4193 rapidly screened individuals, 1977 were identified as at risk for TB and received targeted screening and randomisation to either POC Xpert (n=988) or centralised Xpert (n=988). Across all sites, 97 (4.9%) of 1977 participants had microbiological confirmation of TB; 53/531 at the Cape Town site (10.0% TB positivity rate; 29/53 [54.7%] culture-positive). Xpert identified 75% (22/29) of all culture-positive samples. 40/53 participants had all infectiousness studies performed, and 26/40 were identified as probably infectious (defined as cavities on CXR [n=26] and/or smear-positivity [n=9] and/or CASS-positivity [n=3]). Xpert identified almost all probably infectious cases (25/26 [96.1%]).
Conclusion Community-based active case-finding using portable molecular-based diagnostic tools reliably detects probably infectious, minimally symptomatic TB patients. These data inform key elements of ACF strategies needed to bridge the gap to find, treat and end TB.

PA-142

High SARS-CoV-2 seroprevalence among pregnant women in Allada and Natitingou (Benin) in 2022

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Background In Benin, as of April 12, 2023, 28,014 cases and 163 deaths of coronavirus disease (COVID-19) had been notified. COVID-19 disease has been associated with an increased risk of preterm birth, caesarean delivery and maternal morbidity. However, few studies have evaluated the extent of SARS-CoV-2 infection among pregnant women in sub-Saharan African countries. In this EDCTP-funded COVID-19 surveillance project, we aimed to determine SARS-CoV-2 seroprevalence and identify factors associated with seropositivity among pregnant women in Benin.
Methods A cross-sectional study was carried out between April and June 2022 in Allada, a middle-size city in southern Benin, and Natitingou, a city located 500 kilometres North. Pregnant women in their third trimester of pregnancy were recruited at study antenatal care clinics. A rapid diagnostic test for detection of IgG/IgM against the receptor binding domain of SARS-CoV-2 spike protein was performed, and socio-demographic and clinical characteristics of the participants were recorded.
Results A total of 861 women were included in the study. Mean age of study participants was 26.4 years, and their mean gestational age was 35.0 weeks. SARS-CoV-2 antibodies were detected in 75.7% (95%CI 75.6%-78.6%) of non-vaccinated participants. Only 6.7% (95%CI 5.15-8.62%) of the participants reported to had been vaccinated against COVID-19. Unvaccinated participants from Allada who had at least one previous morbidity had an almost three-fold increased risk of presenting SARS-CoV-2 antibodies (OR=2.89 [1.19-7.00]). None of the participants had been diagnosed/tested for COVID-19 during their pregnancy.
Conclusion The SARS-CoV-2 virus has circulated greatly among pregnant women from Benin. Despite none of the participants had been diagnosed with COVID-19, three out of four participants presented SARS-CoV-2 antibodies, suggesting that COVID-19 cases were asymptomatic or remained undetected by the national surveillance systems.

PA-146

Descriptive epidemiology of Lassa fever at a new hotspot in north-central Nigeria, January-December, 2022

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Background Lassa fever is an acute viral hemorrhagic zoonotic disease. The epicentre of Lassa in Nigeria is Ondo and Edo but recently, there has been an upsurge in Benue State. This is in addition to an emerging pattern of all year transmission representing a drift from peak period of November-April. In this study, we described the epidemiology of Lassa fever in Benue State from January-December 2022.

Methods We conducted a secondary analyses of Lassa fever data obtained from Surveillance outbreak response management analysis system (SORMAS), Benue State, Nigeria over a 12 month period (January-December). Data on total reported cases, tested positive, mortality and sociodemographic characteristics was extracted and analysed.

Results A total of 264 suspected cases were reported within the study period; of these, 34 (12.9%) were confirmed by laboratory diagnosis with 11 deaths and case fatality rate (CFR) of 32.4%. Of the total confirmed cases, 22 (64.7%) were male while the median age range 30-39 years had the highest number, 78 (29.5%) of confirmed cases. Majority, 29 (85.3%) of the confirmed cases within the study period occurred in Makurdi, the State capital. The seasonal trend of Lassa fever from epi-curve was propagated with peak from January to February.

Conclusion There was a very high burden and endemicity of Lassa fever in Benue State with an unprecedented highest CFR ever recorded among the 36 States of Nigeria which has become the new hotspot in the country especially Makurdi the State capital and young active working population more affected. Lassa fever transmission occurs all year-round with peak from January-February. There is need to develop preparedness plans and define thresholds for Lassa fever epidemic.

PA-148

Co-payment mechanism in Uganda: Awareness of healthcare personnel and Implications on availability of Artemisinin agents in private drug outlets

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Background Affordable medicines facility-malaria (AMFm) program and subsequently Co-payment mechanism were developed to help increase access to quality assured Artemisinin Combination Therapies (ACTs) in seven countries in sub-Saharan Africa. We explored through a qualitative study, experience of healthcare personnel on Co-payment mechanism and the implication on access and availability of ACTs in private drug outlets in Uganda.

Methods In each drug outlet, data was collected from pharmacists through key informant interview. The interview covered, (i) awareness of the co-payment mechanism, (ii) Knowledge of quality assured artemisinin combination therapies (QAACT), (iii) stocking of QAACTs, (iv) dispensing price of QAACTs), and (v) determinants of dispensing price of QAACTs. Data was managed using Atlas.ti and analysed using framework methodology.

Results From 25 key informant interviews, five themes emerged, (i) considerations taken while stocking antimalarial agents, (ii) access and purchasing behaviour of clients, (iii) antimalarial dispensing, (iv) awareness of QAACT, and (v) awareness of Co-payment mechanism. None of the respondents was aware of Co-payment mechanism and QAACT (green leaf ACT). Duocotecin brand of ACTs (non-QAACT) was the most stocked antimalarial agent. Every seven in ten drug outlet clients request to purchase ACTs without a prescription and preferred buying cheaper brands. Drug outlets stocked and sold both ACT and non-ACT antimalarial agents. Most drug outlet clients cannot afford buying a full dose of an ACT. None of the respondents considered using Co-payment mechanism while stocking ACTs.

Conclusion There is lack of awareness of Co-payment mechanism and QAACT among pharmacists. There was reportedly no difference in the dispensing price between QAACT and non-QAACT. The dispensing of less than a full dose of ACTs to drug outlet clients is a common practice. The Ministry of Health needs to create awareness through public campaigns on the Co-payment mechanism in the country.

PA-150

Madagascar's experience with the introduction of Typhoid fever conjugated vaccines

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Background Structured typhoid fever surveillance data are critical to inform policy and recommendations on introduction of safe and efficacious typhoid conjugate vaccines (TCV). Here, we describe how a multi-year and multi-site facility based typhoid surveillance and a demonstration introduction of the Vi-CRM197 TCV in Madagascar helped to generate representative population level burden of typhoid fever to inform TCV introduction decisions by the Ministry of Health.
Methods Leveraging the facility based typhoid surveillance, we aim to implement a demonstration mass vaccination project where approximately 58,000 children between 9 months and 16 years of age will be vaccinated using Vi-CRM197. Feasibility of vaccine introduction, vaccine uptake and hesitancy, and effectiveness of the vaccine in preventing typhoid fever will be assessed using a population census, a hybrid surveillance including enhanced facility-based surveillance and active fever surveillance.
Results During the baseline census, we enumerated a total of 158,770 individuals in Itasy and Analamanga regions. Of the total population, 58,195 (37%) are age eligible for vaccination. Community engagement with community leaders, healthcare professionals and local stakeholders was conducted and the vaccination campaign is planned for Q3/2023. Hybrid surveillance will be used to estimate vaccine effectiveness and impact in preventing typhoid fever and antimicrobial resistance (AMR).
Conclusion Census and enhanced community engagement are essential to build community trust and participation in public health interventions. Demonstration projects for vaccine introduction supported by systematic disease surveillance are key to inform policy decisions for TCV introduction.
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PA-151

PEP4LEP Case detection delay reliability or measurement consistency testing in Mozambique, Ethiopia, and Tanzania – preliminary results

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Background Detection delay is defined as the period between onset of first signs and symptoms of leprosy and the time of diagnosis, comprising of a 'patient delay' and a 'health-system delay' and reliability refers to the consistency of a measure. Three types of consistency are considered: over time (test-retest reliability), across items (internal consistency), and across different researchers (interrater reliability). For the case detection delay (CDD) two are applicable: test-retest reliability and interrater reliability.
Methods The study was conducted in Ethiopia, Mozambique and Tanzania. The CDD questionnaire was administered to 79 leprosy patients. One month later, another researcher re-administered the CDD questionnaire with these same patients. Interrater reliability was assessed using the intra class correlation coefficient (ICC). The test-retest reliability was assessed among 69 leprosy patients by determining the CDD at one month difference, both times using the same rater, and then we determined the reliability by looking at the Pearson correlation between the two sets of CDD data.
Result Results from 79 leprosy patients show that, 3 (3.8%) were children under 15 years of age and 25 (31.6%) were women. Interrater reliability: the first interviews led to a mean CDD of 24.0 months (95% CI =17.1 - 30.9). The second interviews, also led to a mean CDD of 24.0 months (95% CI =17.7 - 30.3). For the test-retest reliability, the mean CDD of the first and second interviews were 16.5 (95% CI =13.6 - 19.5) and 16.9 (95% CI =13.8 - 20.1) respectively: the interrater reliability measured with ICC was 0.89 (95% CI of 0.84 - 0.93). Test-retest repeatability coefficient was 0.90 ($p = 0.01$).
Conclusion The PEP4LEP CDD tool to determine the case detection delay of newly diagnosed leprosy patients, was validated in the three African countries showing that both test-retest and interrater reliability measurements demonstrated good reliability of the instrument.

PA-152

Epigenetic alteration of M. tuberculosis strains during exposure to cholesterol reveal unique methylome motifs

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Background Mycobacterium tuberculosis, the causative agent of Tuberculosis (TB) is a notorious pathogen that is responsible for the highest mortalities from a single bacterial pathogen worldwide. Many studies have revealed that cholesterol contribute to M. tuberculosis pathogenesis with unique transcriptome changes implicated to cholesterol metabolism in genetically diverse clinical strains of M. tuberculosis complex (MTBC). Hence, the current study was aimed at investigating epigenetic changes associated with cholesterol metabolism since these changes may provide novel targets for development of TB treatments.
Methods The laboratory M. tuberculosis strain, H37Rv together with the recently identified Lineage 8 clinical strain were cultured in 7H9 broth and minimal media supplemented with cholesterol as the main carbon source. DNA was extracted using the Cetyltrimethylammonium bromide method followed by clean-up using Zymo DNA concentrator kit. Long read whole genome sequencing was performed in a PacBio SMART sequencer for complete methylome characterization using the RS Modification and Motif Analysis protocol and annotated further using DistAMo by selecting methylated genes with a significant z score (≥2 or ≤-2).
Results The highest significantly methylated motifs, CTCCAG, CTGGAG and VNCYGVNYR coding for Rv2060, rseA and Rv1175 genes, respectively, were detected in H37Rv grown in normal 7H9 broth while an additional CYGVNYR motif was detected during growth in cholesterol-rich media. This was in contrast to RNCYGVNYR motif detected in the Rv3632 gene for Lineage 8 strain during grown in 7H9 broth compared to CBBV, CTACCCGVC, GATNNNNRTAC, GNCTACSCA, GTAYNNNNATC, GVGGYMVCR and CACGCAGHNH motifs detected for pks8, Rv2459, PE_PGRS16, vapC22, fadD2, sseA, ackA genes, respectively.
Conclusion These findings suggest "unique" epigenetic regulation in clinical strains of MTBC compared to the laboratory H37Rv, which may explain their virulence traits. The precise characterization of MTBC methylation profiles in cholesterol-rich environments could open new avenues for the development of treatments since cholesterol is essential during M. tuberculosis pathogenesis.
Funding: EDCTP

PA-153

Use of antibody-based biomarker to assess the risk of human exposure to Aedes mosquito bites and infection of Dengue in North-eastern Tanzania

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Background Global expansion of Arboviral diseases transmitted by Aedes mosquitoes is alarming. As seen by the frequent reports of the emergence and re-emergence of dengue, zika and chikununya infection.
There is a growing interest in the use of biomarkers for exposure to mosquito bite, including Aedes Nterm-34 kDa, as a proxy for Aedes-borne diseases risk. The objective of this study was to assess whether IgG antibodies against Nterm-34 kDa peptide was associated with the level of human exposure to Aedes mosquito bites and risk of dengue infection.
Methods Three longitudinal surveys were conducted during rainy season (June 2021), dry season (September 2021) and short rainy (January 2022) in three villages in Bondo, Tanga. The study included children aged between 2-10 years and adolescents/adults aged 11-70 years. Face-to-face interviews were conducted. A pre-tested questionnaire was used to collect information regarding demographic characteristics and mosquito bite prevention measures. The developed questionnaire was uploaded in the system and data was collected electronically using Open Data Kit (ODK) application. Collected blood samples were tested for the presence of IgG antibodies against Aedes Nterm-34kDa using ELISA test.
Results Results showed that the medians of specific IgG antibodies levels were significantly different in three seasons (p=0.009; Kruskal-Wallis test). Dengue positive participants presented a higher level of anti-salivary IgG compared with dengue negatives (p=0.02; non-parametric Mann–Whitney test).
Conclusion Anti-Nterm-34kDa IgG antibodies is important correlate of human exposure to mosquito bite, thus the antibodies are important indicator to measure the risk of dengue infection.
Funding: This study is part of the EDCTP2 program supported by the European Union (grant number TMA2019PF-2694-SABOT).

PA-154

Perceptions of frontline healthcare workers on their "duty to care" during the COVID-19 pandemic in Mozambique

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Background The COVID-19 pandemic placed healthcare workers worldwide under significant physical and psychological stress due to increased workplace demands causing fatigue and burnout. In addition, shortages in personal protective equipment (PPE) were commonly, leading to fears for their own personal safety. The pandemic also renewed ethical questions about how to reconcile healthcare workers´ duty to care with concern for their personal health, safety, and well-being. Our study aimed to explore this dynamic from the perspectives of frontline healthcare workers.
Methods We conducted a mixed-methods, descriptive study in which we carried out semi-structured, in-depth interviews in April-June 2022, with frontline healthcare workers at four hospitals in Maputo Province, Mozambique. Qualitative interviews were audio-recorded, transcribed and entered into Microsoft Excel for content analysis. Quantitative data was entered in REDCap with descriptive analysis in SPSS.
Results We interviewed 53 frontline workers (physicians, nurses and assistants). When asked about their ethical responsibility to provide care during a pandemic, 20 (38%) respondents affirmed that, despite the risk, they had an obligation to care for patients with COVID-19, even without PPE, due to their professional commitment. Eighteen participants (34%) stated that they were not obligated to provide patient care, without PPE, due to the risk of contracting the virus. The remaining 15 (28%) said that they would take care of patients in rare situations. Thirteen (25%) respondents reported first-hand knowledge of examples during the pandemic in which patients were discriminated against in the health care setting, received poor care, or had health workers who refused to provide them care all together.
Conclusion Our findings show that frontline healthcare workers in Mozambique were divided as to the limits of their professional responsibility to care for patients with COVID-19. Risk management strategies for highly infectious diseases like COVID-19 must be reformulated to improve service delivery while safeguarding providers.

PA-164

Acceptability and feasibility of tuberculosis diagnostic sample collection in young children presenting with presumptive tuberculosis in Cape Town, South Africa

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Background Due to diagnostic challenges in childhood tuberculosis (TB), the World Health Organization (WHO) has recommended the use of non-sputum-based samples, including stool. This study evaluated the feasibility and acceptability of different TB diagnostic sampling procedures.
Methods In a prospective observational cohort study, we collected clinical data from children presenting with presumptive pulmonary tuberculosis (PTB). At enrolment, collection of TB diagnostics samples included respiratory samples (gastric aspirate, induced sputum and expectorated sputum), blood, urine and stool. Questionnaires on the acceptability and feasibility were collected from caregivers and healthcare workers (HCWs). A social scientist observed the collection of samples and performed qualitative interviews with HCWs.
Results We conducted 59 diagnostic and acceptability questionnaires of children's experiences of TB diagnostic sample collection. Sample collection was successful in 59% for urine, 36% for stool, 74% for blood and 72% for any respiratory sample. Overall, more than half of the caregivers felt that stool (86%), urine (75%), blood samples (67%) and respiratory samples (57%) were convenient for their children.
We observed sample collection in 32 children. HCWs had specific challenges with collecting urine samples from young girls due to the leaking urine bags. Children of all ages were resistant when collecting respiratory samples. In children aged 7-12 years, HCWs faced difficulties with collecting stool samples. These children felt embarrassed providing stool samples due to increased self-awareness. HCWs found blood samples easiest to collect, followed by respiratory samples, urine and stool. Even though blood sample collection was observed to cause more discomfort and pain.
Conclusion Although urine and stool samples seem a good non-invasive alternative sample for TB diagnosis in children, remaining challenges hamper the feasibility and acceptability of these specimens, which will need to be considered for future studies.

PA-165

Adherence to medication and clinic care experience among pregnant and breastfeeding women living with HIV in the Kilimanjaro region, Tanzania

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Background Adherence to antiretroviral treatment (ART) among HIV-positive pregnant and breastfeeding women is influenced by various context-specific factor. This study aimed to investigate clinic experience and adherence among pregnant and breastfeeding women living with HIV. This cross-sectional study was conducted among pregnant and breastfeeding women living with HIV who were receiving care at selected health facilities in Kilimanjaro region.
Methods Data were collected through face-to-face interviews using a semi-structured questionnaire. We analyzed data using descriptive statistics to describe levels of adherence. Differences in adherence rates between pregnant and breastfeeding women were assessed using chi-square tests.
Results The study included 100 breastfeeding women and 42 pregnant women. Self-reported adherence to antiretroviral therapy (ART) among pregnant and breastfeeding women was 94%, while pharmacy refill data indicated adherence rates of 57%. Although not statistically significant, pregnant women were found to be more adherent compared to breastfeeding women by 57.14%, (p = 0.987). Women who were satisfied with clinic care also tended to be more adherent, with a rate of 57.45%, (p = 0.248), compared to those who were not satisfied. Fifteen percent of the participants reported having to travel a long distance to access the clinic, despite other facilities nearby. This was attributed to concerns about stigma, lack of comfort, and unfriendly healthcare workers. Eighty percent of the women understood the importance of adhering to ART. However, only 37% had attended workshops or training sessions at the clinic on adherence to ART and medications.
Conclusion This study highlights the importance of ensuring access to healthcare services for pregnant and breastfeeding women living with HIV. Despite the high level of understanding of the importance of adherence to ART, only few women had attended workshops or training sessions on adherence to ART. Efforts should be made to increase participation in training and education programs to improve adherence to ART.

PA-166

Circulating anodic antigen (CAA) detection in pregnant women and their child during Schistosoma haematobium infections in Lambaréné, Gabon

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Background The detection of schistosome-derived antigens in urine is a highly effective diagnostic approach for controlling schistosomiasis. It offers greater sensitivity compared to parasitological methods and involves a more convenient, user-friendly lab-based method. This diagnostic approach is particularly advantageous for pregnant women and young children, as early detection of active infections can lead to prompt treatment with Praziquantel (PZQ). The freeBILy clinical trial in Gabon (NCT03779347) evaluated the accuracy of the circulating anodic antigen (CAA) test for detecting Schistosoma haematobium (Sh) infections in pregnant women as well as an endpoint measure for PZQ efficacy.
Methods The accuracy of the upconverting particle lateral flow (UCP-LF) CAA urine test was comprehensively evaluated using a cross-sectional design and comparing it against urine filtration (UF) and PCR. Subsequently, Sh-positive pregnant women were enrolled in sub-study and received a single dose of PZQ either immediately (intervention) or after delivery (control) to assess the safety of PZQ use during pregnancy and to monitor the kinetics of CAA levels following PZQ administration. Finally, in an observational, longitudinal study mothers and their newborns were followed to determine the incidence of schistosomiasis in infants with accurate diagnostics.
Results A total of 733 pregnant women were enrolled in this study with mean age 25.3 years. The prevalence of schistosomiasis measured by the respective tests was 18% (UF), 19% (UCP-LF CAA), and 12% (PCR). Compared to the composite reference standard, the sensitivity of UCP-LF CAA was 71.8%, with 64% and 68% for UF and PCR, resp.
Conclusion Preliminary data show a high prevalence of schistosomiasis among pregnant women. Furthermore, the UCP-LF-CAA test was more sensitive than conventional microscopy, which contributed to the improved health of pregnant women as they were treated during pregnancy. PZQ treatment had no deleterious effects on mother nor child, and administrating it to pregnant women can be considered to be safe.

PA-167

Characterization of HIV-1 reservoirs in children and adolescents: A systematic review and meta-analysis toward pediatric HIV cure

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Background The virostatic effect of antiretroviral therapies (ART) infers viral persistence in sanctuaries, with a high likelihood of reactivation off-treatment. This systematic review and meta-analysis aimed at estimating the global burden of archived drug resistance mutations (ADRMs), the size of reservoirs and their determinants in paediatrics.
Methods Were included, randomized and non-randomized trials, cohorts and cross-sectional studies of HIV reservoirs in vertically-infected participants, published in English/French between 2002-2022. As primary outcomes, we evaluated the prevalence of ADRMs and estimated the size of reservoirs (HIV-1 DNA copies/10 6 cells) in paediatrics. Subgroup analysis were performed to further characterize the data and the meta-analysis was done through random effect models.
Results Overall, 50 studies from 17 countries worldwide were included encompassing 2569 vertically infected participants (aged 2-days to 19-years; 52.81% females). There were limited data on the quantitative characterization of viral reservoirs in SSA, and sensitive tool as ddPCR for characterizing viral reservoirs were not implemented in the most sub-Saharan Africa (SSA) countries. Overall prevalence of ADRMs was 37.80% [95%CI: 13.89–65.17], with 48.79 [95%CI: 0–100] in Africa, 42.08% [6.68-82.71] in America, 23.88% [95%CI: 14.34–34.90] in Asia, and 20.00% [95%CI: 10.72–31.17] in Europe; without any difference between infants and adolescents (p=0.656). Starting ART before 2 months of age limited the size of HIV-1 DNA (p=0.054). Participants with long suppressed viremia (>5years) had lower rates of HIV-1 DNA (p=0.027) whereas pre-/post-ART CD4 ≤29% and pre-/post-ART viremia ≥5Log were all found associated with higher rates of HIV-1 DNA (p=0.038, p=0.047, p=0.041 and 0.035 respectively).
Conclusion Our findings underscore high levels of ADRMs in paediatrics worldwide, with a higher reservoir driven by delayed ART initiation, shorter period of viral suppression and immuno-virological failures. Thus, strategies for paediatric HIV functional cure should target adolescents/children with very early ART initiation, high immunity and long-term viral suppression.

PA-172

Impact of Global Health Research in Africa under the EDCTP-funded "one-health" public-private partnership PANDORA-ID-NET-1

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Background New emerging and re-emerging infectious diseases continue to cause loss of life around the world. For a rapid, effective, and robust response to these outbreaks, a multidisciplinary public-private consortium "ONE HEALTH", PANDORA-ID-NET-1 of 22 partner institutions (13 African and 9 European) led by Fondation Congolaise pour la Recherche Médicale was created following an EDCTP (2016) call.
Methods PANDORA-ID-NET-1 implements its activities by area and by transversal activities through 4 regional hubs (West, East, Central, and South Africa) for the development of intervention teams with rapid, mobile laboratory services, capable of responding to epidemics of emerging and re-emerging infectious diseases, and of carrying out inter- and intra-epidemic actions.
Results Expected impact: Global visibility of this essential network that provides accelerated evidence for the optimal clinical management of patients and guides the public health response to any serious infectious epidemic.
Medium-term impact: Improved capacities for the detection and epidemiological surveillance of new or re-emerging infectious disease threats originating in Africa or elsewhere.
Long-term impact: Capacities of the 4 regions to develop and conduct high-quality clinical trials and research on emerging infectious diseases.
Conclusion PANDORA-ID-NET-1 had an impact on research in many African countries of 4 regional hubs. He has been an important tool for improving capacity to respond to outbreaks of emerging and re-emerging diseases for public authorities and aims to support the Africa CDC in its action. Through its many activities, workshops, capacity building, interventions in response to Lassa Fever in Sierra Leone, Chikungunya outbreak in Republic of Congo, Arenavirus surveillance in Zambia, Monkeypox studies in Nigeria, Europe's response largest Monkeypox outbreak and currently against Covid-19 pandemic in Sub-Saharan Africa, the Global Response or epidemiological, genomic surveillance in Congo and in antimicrobial resistance and, has made more 222 publications, more 20 in The Lancet (https://www.pandora-id.net/) and joining different initiatives.

PA-173

COVID-19 vaccines uptake among healthcare workers within primary healthcare facilities in an urban setting in Uganda

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Background Vaccination is one of the most successful public health interventions for preventing infectious diseases. A successful vaccination program depends on high coverage, and health care workers (HCWs) play a pivotal role in ensuring high uptake of vaccines in the population. COVID-19 vaccines have been proven to be efficacious, and vaccination campaigns have been ongoing, however there is a perceived high vaccine hesitancy even among health care workers in Uganda. This study aimed at describing the facilitators, barriers to and level of uptake of COVID 19 vaccines among healthcare workers in primary healthcare facilities in an urban setting in Uganda.
Methods We conducted an online cross-sectional survey among healthcare workers in private and public healthcare facilities in Entebbe municipality between July 2021 and August 2021. Data was collected using an online questionnaire. Uptake of the vaccines among healthcare workers was analysed as proportions, and logistic regression was used to analyse barriers and facilitators to uptake of COVID 19 vaccines.
Results The study enrolled 360 participants, with 61.7% (n=222) females. A total of 236 (65.6%) healthcare workers had received at least one dose of COVID 19 vaccine with higher uptake among females 64%(n=151). Age above 40 years (OR 4.29), participating in COVID 19 vaccine related activities (OR 4.18) and having had a negative SARS-COV-2 test result (OR 1.79) increased the odds of having been vaccinated. Working in either a private for profit (OR 0.23) or a private not for profit (OR 0.19) reduced the odds of having been vaccinated. History of having cared for a COVID 19 patient and having a positive SARS-COV-2 test result did not influence the uptake of the vaccines in the study population.
Conclusion Vaccine uptake among healthcare workers was close to the World Health Organisation (WHO) recommended uptake of 70% by mid-2022.

PA-182

A three-phase supportive capacity building in implementation research: the case of SAVING Consortium

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Background A key objective of the EDCTP SAVING Consortium was to build Institutional and Individual capacity in Implementation Research (IR). The aim was to equip institutions along the Access and Delivery Value Chain to identify and address bottlenecks hindering delivery of new medical interventions including vaccines using IR.
Methods A Capacity Needs Assessment was carried out and results used to plan the capacity building approach. All trainees were enrolled and undertook a specialized Massive Open Online Course (MOOC) on IR. The MOOC was adapted to suit availability needs of trainees. Trainees were then taken through three in-person 5-day residential IR workshops. The workshops covered proposal development, preparation of documentation for ethical approval, and Report/manuscript writing. The workshops involved presentations by experienced facilitator/investigators within the consortium with supportive sessions where trainees put into practice what they had learnt. Each workshop was interspersed with a period of six weeks during which the trainees completed the required outputs. A unique feature adapted from an earlier TDR funded study included embedding of Research Scientists in each of the teams to provide on-going support during and in between workshops. Senior Consortium Investigators provided back-up support.
Results The needs assessment showed that 64.1% of 78 respondents considered themselves beginners with regards to experience in IR. By the end of workshop 1, four proposals addressing bottlenecks identified had been successfully drafted by three teams from stakeholder institutions. After workshop 2, three proposals were submitted for ethical review and approvals obtained. All three teams are currently at various stages of data collection and analysis.
Conclusion This hands-on model for Institutional training in IR is effective as it ensures that trainees obtain needed support as their capacity is being built. They "learn by in doing" in real time, while capacity and confidence is built in a sustained manner.

PA-185

Unique neutrophil responses in persons living with HIV who remain persistently TB, tuberculin and IGRA negative

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Background Persons living with HIV (PLHIV) have a greater risk of tuberculosis (TB). Nevertheless some PLHIV who live in high TB environments remain persistently TB, tuberculin and interferon gamma release assay (IGRA) negative (HITTIN). HITTIN are a subset of persons more commonly referred to as "resisters"(RSTR) since they are inferred to resist persistent infection with Mycobacterium tuberculosis (Mtb). Multiple genetic and genomic studies are underway to elucidate the genetic and immunological components contributing to this "resistance". Neutrophils have been shown to be able to control Mtb infection with neutrophil extracellular traps (NETs) highlighted as an important form of cell death in some RSTRs. We investigated the differential gene expression (DGE) in response to Mtb H37Rv infection after 1h and 6h in neutrophils from HITTIN (PMNHITTIN) compared to neutrophils from persons who are so-called latently infected with Mtb, are PLHIV, with no TB history and test persistently IGRA and tuberculin positive (PMNHIT).
Methods Neutrophils were isolated from 17 HITTIN and 11 HIT and infected with Mtb H37Rv for 1h and 6h. RNA was extracted and sequenced. Isolated Mtb H37Rv infected (1h,6h) and non-infected (1h,6h) neutrophils were plated and stained for microscopy with Hoechst 33342 (nuclei) and PL2/3 (nucleosomal complex of Histones 2A,2B and chromatin). After imaging and processing we calculated the log transformed ratio of the NET area change at 6h to 1h in uninfected and infected samples.
Results No significant DEG was observed between PMNHITTIN vs PMNHIT after 1h infection with Mtb. There was significant DEG after 6h Mtb infection with an enrichment of genes for NETosis. Microscopy showed lower NET formation in PMNHITTIN vs PMNHIT after 6h infection with Mtb.
Conclusion These results emphasize the role of neutrophils in the early innate immune response to Mtb. Further research is required to examine the relationship between neutrophils and the documented T-cell response to determine the role of neutrophils in the RSTR phenotype.

PA-188

Motivations for participation and decision-making processes for participants in malaria controlled human infections studies in Kenya: A cross-sectional study

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Background Controlled human infection studies (CHIS) that involve the deliberate infection of healthy volunteers with a pathogen are increasingly being conducted in endemic developing countries in Africa, including Kenya. This study investigated the motivations for and extent of consultation of potential CHIS participants with others before participation in two malaria CHIS in Kenya.
Methods Participants who had come for screening into two malaria CHIS were approached to complete a researcher-administered pre-enrolment questionnaire from 2020-2022. The questionnaire captured participants demographic characteristics, motivations for participation, and extent of consultation with others before deciding to join the study, among others.
Results 215 participants completed the questionnaire, of which 70% were males, 51% married, 38% aged between 21-24 years, 63% staying with at least a child at home, 24% having past research experience, 16% unemployed, and 53% having primary-level education. Among the motivations for deciding to participate in the study, pre-enrolment health checks (188/215, 87%), contribution towards potential malaria vaccine development (150/215, 70%), and study financial compensation (110/215, 51%) were the most reported. 153(71%) indicated that they would still participate without any compensation. 54%(116/215) of the participants indicated that they sought the opinions of others before deciding to participate in the study, with the category of persons most consulted being spouses 47%(55/116), parents 41%(48/116), friends and colleagues 34%(39/116) and former CHIS participants 32%(37/116). These findings are largely in support of our findings from earlier qualitative studies and comparable to findings reported by participants in CHIS and phase I clinical trials in developed countries.
Conclusion Most potential participants in Kenya are motivated by different factors before deciding to participate in of malaria CHIS, and the majority also consult with others in deciding whether to participate. These findings can provide key stakeholders important information in the design, evaluation and conduct of CHIS in similar settings.

PA-193

Simple imaging system for optical label-free identification of bacterial clinical isolates in Low-Resource Settings (LRS)

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Background Only 1.3% of the sub-Saharan African diagnostic laboratories are performing clinical bacteriology. To improve this, diagnostic tools in LRS should be simple, affordable and maintenance-friendly, in contrast with the expensive machinery used in high-income countries, such as mass spectrometer for identification. Lensfree imaging is a label-free identification technique that can be performed directly on colonies growing on agar plates, with low-cost instrumentation.
Methods We report here the very first clinical assay of a wide-field lensfree imaging device, namely 24mm x 36mm, for identification down to species. Considering this large field of view, several hundreds of colonies can be analysed simultaneously. A database of over 250 clinical bacterial isolates was collected at LHUB-ULB, gathering respiratory (20% of isolates), urine/genital tract (20%) and skin/wound (20 %) samples, as well as positive blood cultures (40 %). Partially coherent light emitting diodes (wavelengths 550nm and 940nm) illuminated microbial cultures growing on Mueller Hinton agar at 36°C. Clinical isolates were labelled through MALDI-TOF mass spectroscopy. To optimize supervised learning, various deep learning models, pre-trained or not, were developed and compared.
Results Over 11.000 colonies were collected in the database that focused on 5 species (Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis). From these, different deep learning models were trained with at least 1800 samples per species. As a result, the algorithms yielded unambiguous identification of each species, with at least 90% accuracy.
Conclusion This very first database paves the way towards a future imaging device for the diagnosis of bloodstream infections in LRS, within the SIMBLE project. As a second stage, a second database is to be acquired, in Africa, on positive blood cultures.

PA-199

Investigating the relationship between numerical skills and malaria: implications for prevalence and control behaviours in Central Africa.

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Background Malaria remains a significant public health problem, particularly in sub-Saharan Africa, where an estimated 90 percent of all malaria cases and deaths occur. Various medical and non-medical interventions have been implemented to prevent and reduce the spread of the disease, including availability of drugs, public health policies, and health-seeking behaviours. The effectiveness of these interventions depends greatly on the ability of individuals to understand and appropriately implement the preventive measures. Numeracy, or the ability to understand and use numerical information, has been shown to be an important factor in health decision-making and behaviour. We study the effect of numeracy on malaria control behaviours and prevalence in central Africa.
Methods Malaria control behaviours were assessed using sleeping in bednets, pregnant women taking antimalarial drugs, and taking a child to a medical facility when suffering from fever and cough. The average plasmodium falciparum parasite rate (PfPR) in children between the ages of 2 and 10 was the indicator of prevalence of malaria. The study was based on a sample of 5 Central African countries (Cameroon, Chad, Democratic republic of Congo and Gabon) and 62 administrative level one regions. The study utilized pooled OLS regression to determine the relationship between numeracy and malaria control behaviours as well as prevalence.
Results Numeracy influences malaria control behaviours positively. Higher numerical skills increase likelihood for engagement in malaria control behaviours. In addition, bednet access and education positively influence bed net utilization and IPTp uptake. However, media exposure negatively influences IPTp uptake. Regions with high levels of humidity have higher levels of bednet usage and treatment seeking but have lower levels of IPTp uptake.
Conclusion The findings suggest that improving numerical skills may have implications for malaria prevention and control efforts.

PA-201

Species identification and drug susceptibility testing of non-tuberculous mycobacteria isolated among presumptive tuberculosis patients in Lambaréné, Gabon

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Background Non-tuberculous mycobacteria are increasingly recognised as causative agents of opportunistic and device-associated infections in humans. In Gabon, data is scarce, as species identification and drug susceptibility are not performed in most laboratories. The objectives of our study were to identify the relative frequencies of non-tuberculous mycobacteria species circulating and to determine their genotypic susceptibility pattern regarding the antibiotics most commonly used to treat NTM infections among presumptive tuberculosis patients.
Methods This cross-sectional prospective study was conducted at the CERMEL TB laboratory from January 2020 to December 2022 to generate drug susceptibility data on NTM species identified from presumptive TB patient specimen sent to the National TB Reference Laboratory. The drug susceptibility to macrolides and aminoglycosides and the NTM subspecies identification were performed using the genotype NTM-DR kit.
Results Among 524 culture-positive specimen, 146 (28%) were NTM. The predominant group was Mycobacterium avium complex, MAC 80/146 (54.8%), of which M. intracellular 53/146 (36.3%) and M. avium 27/146 (18.5%)); followed by Mycobacterium abscessus complex, MABC 38/146 (26.0%), of which M. abscessus subsp. abscessus 20/146 (13.6%); M. abscessus subsp. massiliense 10/146 (7.0%); and M. abscessus subsp. bolletii 8/146 (5.4%)). All MAC were genotypically fully susceptible to macrolides and aminoglycosides. All five isolates of MABC showed polymorphisms both of the erm (41) and rrl genes, both coding for macrolide resistance.
Conclusion All MAC isolates were fully susceptible to macrolides and aminoglycosides, thus confirming their role in NTM treatment. However, resistance-conferring polymorphisms indicate limited susceptibility of M. abscessus complex isolates against both drug classes; requiring further investigation to comprehensively determine M. abscessus drug susceptibility. The study results presented here shall guide clinicians to better manage treatment. Routine susceptibility testing is not available.

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ELISA quantification of bNAbs in Dried Blood Spots (DBS) from Infants in the PedMAb trial

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Background The rate of mother-to-child-transmission of HIV-1 through breastfeeding remains high in Africa. Studies in neonatal macaques have provided proof of principle that broadly neutralizing antibodies (bNAbs) can protect from infection. The PedMAb trial aims to provide pharmacokinetic (PK) and safety data of passively administered bNAbs (VRC07-523LS or CAP256V2LS) in neonates. To overcome challenges associated with limited blood volume draws from infants as well as sample transportation from remote places, we validated the use of dried blood spots (DBS) for establishing PK data.
Methods Five adult and 10 cord blood samples were spiked with varying known concentrations (1, 10, 100 and 1000µg/mL) of CAP256V2LS or VRC07-523LS. Spiked blood was blotted onto DBS cards and dried overnight. Quantification was done via ELISA using the respective anti-idiotype antibodies as coating antigens.
Results The best elution protocol was selected from adult spiked DBS based on higher extraction efficiency and the lower coefficient of variation for both antibodies and next validated on cord blood DBS. To account for the whole blood derived eluate, ELISA parameters were optimised through changing key parameters such as anti-ID coating concentration, blocking buffer, incubation temperature and number of washes. Performance of the ELISAs displayed a lower limit of detection and specificity of 0.39µg/mL and 90.7% for CAP256V2LS and of 0.18µg/mL and 98.1% for VRC07-523LS. Specificity was assessed against 108 plasma from HIV-exposed uninfected infants. Given that existing bNAb PK data are from plasma samples, we defined a correction factor to transform DBS values into plasma values. DBS values also corrected by sample-matched haematocrit, which differs from adults and over time, has the best match with sera values (13% error).
Conclusion Overall, this study validates DBS sampling for the PK assessment of passively administered bNAbs in neonate and infant blood in the PedMAb trial, and for future use in other neonatal trials.
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PA-206

Breaking the silence of female genital schistosomiasis in Ghana's health system: A case of health workers within the FAST project

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Background Female Genital Schistosomiasis (FGS) remains one of the most critical and neglected topics in Neglected Tropical Diseases (NTDs) and the health of women and girls worldwide. Health workers' knowledge of FGS is vital to the prevention and management of the disease. This study, therefore, conducted implementation research to identify and address the FGS knowledge gap among health workers in Ghana.
Methods This study was a 3-year (2020 -2022) implementation research study applying a pragmatic uncontrolled quasi-experimental study design. The study involved a baseline assessment, an intervention phase involving the training of health workers about FGS and an endline assessment. A mixed-method approach was applied to data collection. The qualitative data involved 20 In-depth Interviews while the quantitative data involved 116 health workers. NVIVO 12 and STATA 14 were used for qualitative and quantitative data analysis, respectively.
Results Before the intervention, there was little knowledge about FGS among health workers as most participants only understood FGS as merely urogenital schistosomiasis in females. Based on the baseline assessments, an FGS education intervention in the form of training of health workers and distribution of FGS educational materials was carried out. The impact of this intervention enhanced health workers' awareness and management of FGS. However, access (availability and affordability) to praziquantel (the main drug used in treating and preventing schistosomiasis) was cited as a challenge.
Conclusion The FGS intervention has improved health workers' awareness and understanding of FGS. However, there is a need to improve access to praziquantel to facilitate FGS management. In addition, a holistic strategy encompassing all stakeholders at the individual, community, and health-system levels is required to improve the general knowledge and management of FGS.

PA-213

Enhancing protocol compliance in large pragmatic drug trials implemented in resource-limited settings: Experience from the PregnAnZI-2 Trial in The Gambia

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Background The PregnAnZI-2 trial was conducted in The Gambia and in Burkina Faso to evaluate the efficacy of intrapartum azithromycin (AZI) to reduce neonatal sepsis and mortality and maternal infections. Overall, 11,983 birthing parents and their newborns (6,735 participants for Gambia Site) were recruited into the study and randomized at a 1:1 ratio to receive either AZI or placebo. The independent trial monitoring was conducted by the Clinical Trials Unit of the Medical Research Council Unit The Gambia at LSHTM and we report here the main quality measures implemented in the trial and the subsequent protocol deviations observed in The Gambia site.
Methods As part of quality control measures, the trial implemented frequent retraining of trial staff on study procedures, electronic data capture systems with integrated real-time eligibility and data quality checks, and pre-prepared drug blisters numbered similarly as the randomization list and envelopes. We conducted a total of 20 monitoring visits (a site initiation visit, 18 interim monitoring visits and close out visit) and captured all the protocol deviations identified in a purposively developed database.
Results Overall, there were 55 protocol deviations (PDs) identified in The Gambian site among the 6,735 women enrolled, giving a PD rate of 0,82% per participant. This affected the percentage allocation for the other variables. The most common PDs were missed or out-of-window visits (53% [26/49]) and wrong sequence in treatment allocation (29% [14/49]). PDs related to inappropriate consenting, or inclusion of ineligible participants represented 12% [6/49] and all other deviations 4% [3/49].
Conclusion With robust quality control measures, frequent onsite monitoring, and by tapping into the potential of electronic data capture systems, research teams can efficiently implement large clinical trials of high quality with very few protocol deviations in resource-limited settings.

PA-219

Implementing molecular diagnostics for soil transmitted helminths in a multicentric clinical trial: external quality assessment in the EDCTP_STOP project

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Background The EDCTP_STOP project is a multicentric clinical trial (ALIVE trial ct.gov: NCT05124691) that aims to interrupt the transmission of soil-transmitted helminths using novel treatment regimens. While cure rate measured by microscopy is the primary efficacy outcome, limitations in sensitivity after successful treatment pose a challenge. Nucleic acid amplification tests are a promising alternative. One objective in the EDCTP_STOP project is to assess real-time polymerase chain reaction (qPCR) as a secondary efficacy outcome, which necessitates implementing an external quality assessment scheme (EQAS).
Methods The Helminth External Molecular Quality Assessment Scheme (HEMQAS), provided by the Dutch Foundation for Quality Assessment in Medical Laboratories (SKML), was implemented in the study. The sample distribution consists of blinded ethanol-preserved stool samples to assess DNA extraction, and purified DNA samples in stabilizing buffer to assess the amplification technique. Four consortium partners participated in the 2022 assessment. LUMC scored 99% (91/92 targets correctly identified). KEMRI scored 74% (68/92 targets). CISM scored 99% (75/76) and ULE scored 100% (62/62 targets).
Results For stool samples, the outcomes demonstrated that ineffective DNA extraction caused multiple false negative outcomes, particularly for Trichuris trichiura. Pipetting-error during DNA extraction may explain false positive outcomes. For DNA samples, false negative outcomes most likely resulted from handling errors. Systematic errors such as qPCR channels used to detect targets may account for false positive outcomes as spectral overlap in a multiplex qPCR may cause incorrect data interpretation. The use of validated positive control DNA elucidated which primer and probe pairs required optimization.
Conclusion These outcomes facilitated targeted molecular optimization per trial site prior to testing trial samples. Participating in an EQAS facilitates capacity building by identifying training and laboratory validation needs, and ensures reliable reproducible results.

PA-220

AccessAfrica guidelines on post-trial access in SSA

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Post-trial access, according to research ethics guidelines, refer to the responsibility of sponsors and researchers, in coordination with other stakeholders such as the regulators from the host country, to ensure (continued) access to the knowledge generated and study intervention -- when proven safe and effective -- by the research participants and the community. Guidelines stress that the responsibility is more pronounced in clinical trials in low-resource settings. However, in spite of what guidelines say, post-trial access remains largely unactualized. To date, there are only general statements from international guidelines and very few countries with some kind of regulation requiring post-trial access. With the increased offshoring of clinical trials especially in low and middle income countries, this situation is untenable. To address this lacuna, AccesAfrica first did interviews, surveys, focus group discussions and a review of the literature -- both white and grey -- to understand the state of affairs but also to explore feasible solutions. The result of this work culminated in the AccessAfrica Guidelines on Post-trial Access in Sub-Saharan Africa. The Guidelines provide general principles and stakeholder-specific articles that expound on post-trial access as a multi-stakeholder responsibility. The Guideline is also co-created through the of stakeholders from different Sub-Saharan countries. It is this guideline we wish to launch and introduce to a wider audience by presenting it in this EDCTP forum.

PA-224

Impact of diabetes mellitus on tuberculosis treatment outcome

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Background Diabetes mellitus (DM) maybe a risk factor for tuberculosis (TB) and negatively affect outcome of treatment. We investigated the impact of DM on TB treatment outcome in a longitudinal study.
Methods The diabetic status of all microbiologically confirmed TB patients was determined at baseline (t0). The DM group consisted of known DM and on anti-diabetics (TBDMt) and newly diagnosed DM patients who were monitored by clinicians for three months without DM treatment (TBDMnt). Bacterial clearance at days 0, 7, 14, 28 and 56 were analysed by molecular bacterial load assay (MBLA) and HbA1c levels at three (t1), and six (t2) months during TB treatment, and 3 months post-treatment (t3). Clinical examination including X-ray was done.
Results A total of 559 TB patients were followed, 49 (8.8%) were diabetic with 36 (6.4%) TBDMt and 13 (2.4%) TBDMnt. The HbA1c of the TBDMt showed significant decrease in median-HbA1c from t0 to t3 (p=0.029) but still hyperglycemic. The TBDMnt cohort showed a significant decline in median-HbA1c from t0 to t1 (p=0.006), and remained normoglycemic. The TBDMt cohort had more infiltrations in the lower lung fields than the TB-only cohort (p=0.02). Analysis of 354 serial sputa collected from 59 cases (42 TB-only and 17 TBDMt cases) showed that the average bacterial load of the TB-only cohort at diagnosis was significantly higher than TBDMt cohort (p=0.03). However, after 56 days of TB treatment, the bacillary load of TBDMt cohort was significantly higher (p=0.04) using TB-MBLA. Time of sputum conversion from positive to negative as measured by TB-MBLA was shorter in TB-only participants (66 days) than TBDMt participants (88 days). Genotyping of mycobacterial isolates showed that Mycobacterium africanum Lineage 6 was associated with TBDMt cohort (p=0.023).
Conclusion Our findings suggest delayed mycobacterial clearance among DM cohorts and DM may predispose individuals to TB caused by distinct lineages.

PA-231

Specialized massive open online course on implementation research: The case of SAVING Consortium

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Background The EDCTP SAVING Consortium aimed to build Institutional and individual capacity in Implementation Research (IR). This was to enable Stakeholder Institutions along the Access and Delivery value chain identify and address implementation bottlenecks hindering delivery of new medical interventions such as vaccine. As a first step in the capacity building, there was a need to tailor the Massive Open Online Course on IR to the availability needs of the target institutions.
Methods Initial consultations were held with trainees to agree on the mode of training that would be most impactful. Extensive consultations were held with local organizers of the MOOC to discuss adapting the mode of training to suit the Consortium. A variety of approaches were considered based on earlier experience with other institutions. The MOOC was held weekly over a 5-week period with 3 to 4 hours at each sitting. This was alternated with a free week to enable members see to their other duties at their institutions. Two modules were taken at each sitting. During each training session, members watched the videos together with onsite facilitators who were Senior Investigators in the Consortium and who were IR trainers. Each video was followed by an interactive session during which facilitators clarified any unclear areas providing practical examples. Trainees took the assessments immediately. Outstanding assessments were completed before the next in-person session. All 5 models were completed in three sessions over a 5-week period.
Results By the end of the 5-week period, out of the total of 53 participants who enrolled, 41 successfully completed the MOOC and gained TDR certificates of completion by the end of the period.
Conclusion This model for undertaking the MOOC is a good choice for participants who require IR training but who have very busy work schedules like participants in our setting.

PA-234

Digital adherence tools with personalized adherence feedback: a promising guide for adherence counselling among children and adolescents living with HIV in Tanzania. A mixed-methods study

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Background Adherence to treatment is a challenge to people living with HIV (PLHIV). Therefore, interventions are highly needed to assist PLHIV in adhering well to medication. Digital adherence tools (DAT) that offer real-time intervention are promising due to their ability to timely detect non-adherence and provide an opportunity for counselling. We tested DAT to understand the need for tailored adherence feedback among children and adolescents living with HIV (CALHIV) in Kilimanjaro, Tanzania.
Methods We conducted a mixed methods study among CALHIV with their caregivers. Participants completed a survey at study entry to collect disease, treatment, and adherence background information. Then, they used the DAT for one month. The DAT included (1) using Wisepill box that records lid opening as medication intake, (2) receiving reminder SMS and (3) receiving adherence feedback after one month based on reports generated by the DAT. The feedback sessions lasted for maximum 30 minutes and focused on identifying possible solutions to the non-adherence patterns. After that, we conducted exit interviews, in-depth interviews and focus group discussions. We did descriptive and thematic content analysis.
Results We included 20 children (0-14 years) and 20 adolescents (15-19 years). Median adherence measured with DAT was 98.5% among children and 72% among adolescents. Most participants understood the feedback graph, liked the feedback content and thought receiving adherence feedback and counselling would improve their future adherence. Participants explained that feedback reports provided great accuracy in discussing adherence behaviour with counsellors and nurses. However, 25% of adolescents did not agree with the feedback as it indicated they did not open the pillbox while they had. This was mostly due to technical and connectivity challenges.
Conclusion DAT with personalized feedback on adherence is a promising intervention to improve counselling and disease management among CALHIV. Our upcoming randomized clinical trial will assess in detail its effectiveness in improving adherence.

PA-244

Capacity building for female scientists in East Africa

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Background Women are under-represented in academic careers, particularly in research. The challenges they face include difficulties in balancing family/life responsibilities and work, lack of adequate mentors, financial challenges, and bias in the provision of opportunities. In sub-Saharan Africa, the proportion of women scientists is even smaller. The Capacity Building for Female Scientists in East Africa (CaFe-SEA) program is funded by EDCTP through the Partner States' Initiated Activity. It aims to equip female scientists from under-represented countries with knowledge and skills for research in infectious diseases.
Methods The program is delivered by the Eastern Africa Consortium for Clinical Research (EACCR) through universities within the region. Scholars were selected through a competitive process, and each was attached to an EACCR partner institution. CaFe-SEA is multidisciplinary program delivered through five tracks including laboratory sciences, an interface between non-communicable diseases and communicable diseases, maternal and child health and health-behavioural sciences. The scholars receive training in cross-cutting courses like epidemiology and biostatistics, bioethics, research management, and leadership, GCP-ICH, GCLP and scientific writing.
Results The project enrolled 8 female scholars from South Sudan, Burundi, Ethiopia, Rwanda, Zanzibar, Uganda, Kenya, and Tanzania. All scholars are registered at universities in their home countries except the South Sudan scholar who has registered in Uganda. All scholars have been attached to EACCR mentors working with their university supervisors. They have developed their proposals and are in the process of obtaining ethics approval before initiating field activities. The main challenges faced are managing family and PhD studies by some of the scholars and learning English for the scholars from Burundi and South Sudan.
Conclusion The early achievements the CaFe SEA project demonstrate the possibilities of supporting African female scholars to become distinguished scientists.
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PA-247

Novel cytokine signatures for Tuberculosis diagnosis and treatment monitoring

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Background Currently available sputum-based diagnostic tools for Tuberculosis (TB) are expensive, time-consuming, and not suitable for children and people living with HIV (PLHIV) who cannot produce sputum or are paucibacillary. A long turnaround time delays treatment and increases transmission. There is therefore an urgent need for new, rapid, and inexpensive non-sputum-based tests for identifying patients with tuberculosis. The aim of this study was to identify new cytokine signatures to screen or triage patients with tuberculosis disease and for monitoring anti-tuberculosis treatment.

Methods Expression levels of 48 cytokines were measured in serum collected from a prospective cohort of 260 adults with presumptive TB. Patients were classified at diagnosis as TB or with other respiratory disease (ORD) using GeneXpert MTB/RIF Ultra. Confirmed adult TB patients had samples collected at baseline, 1, 2, 4 and 6 months of treatment. Mean fluorescent intensities of cytokines were compared between TB and ORD patients and diagnostic accuracy of individual and cytokines combinations were determined using area under the receiver operating characteristic curve (AUC). The best cytokine signatures were determined using multivariate logistic regression models using CombiROC package in R-statistics.

Results 32/48 cytokines were differentially expressed in adult TB compared to ORD patients. The best signatures defined by combiROC algorithm were MIG alone, IL-2Ra+MIG, and IL-16+MIG and these could diagnose TB from ORD with AUCs of 0.918 (91% sensitivity and 83% specificity), 0.921 (92% sensitivity and 79% specificity), and 0.918 (91% sensitivity and 82% specificity) respectively. All identified biomarkers were found to significantly reduce during treatment suggesting a potential value for treatment monitoring.

Conclusion We identified three parsimonious signatures that identify TB patients with high diagnostic accuracy, that showed potential for treatment monitoring. Moreover, these were identified in serum samples eliminating the need for in-vitro stimulation, thus reducing time to obtaining results.

PA-249

Training Epidemiologists and Biostatisticians for enhanced response to disease outbreak and epidemic in West Africa: approach and progress

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The COVID-19 pandemic has more than ever demonstrated the urgent need to train more skilled epidemiologists and biostatisticians in Sub-Sahara Africa to reverse the deficiency of reliable epidemiological data while efficiently monitoring, analyzing, and interpreting these data to inform public health policy and decision-making. The project "Training Epidemiologists and Biostatisticians for enhanced response to disease outbreak and epidemic in West Africa" (TEBWA, 2021-2024), supported by EDCTP2, aims to enhance West Africa's research capacity in epidemiology and biostatistics to respond efficiently towards diseases outbreaks and emerging (and re-emerging) infectious diseases. Specifically, the project aims to (i) train fifteen skilled postgraduate biostatisticians and infectious disease epidemiologists in West Africa; (ii) strengthen the ability of young scientists from West African countries to manage epidemic disease outbreaks, and (iii) strengthen regional and international cooperation in Biostatistical and epidemiological research. The project is coordinated by the University of Abomey-Calavi (Benin) in partnership with the London School of Hygiene and Tropical Medicine (LSHTM, UK) and the Benin National Agency for Primary Health Care (Benin). Fifteen young Africans (7 women and eight men) from eight countries (Benin, Ghana, Togo, Mali, Liberia, Guinea, Niger, and Cote d'Ivoire) have been recruited. They are currently following a master's degree in either Biostatistics or Epidemiology and public health interventions. They are further taking online courses with the LSHTM. The project TEBWA also provides its fellows with a special mentoring program where fellows benefit from the rich and extensive experiences and networks of their mentors (from Africa and Europe). This mentorship program is key for their career development after the end of the project. The fellows are also supported in subscribing to several scholars and practitioners' societies. The fellows are currently doing their research on various topics related to diseases such as COVID-19, Lassa Fever, Malaria, Cholera, Measles, Ebola, etc.

PA-255

Genetic profiling of plasmodium falciparum antigenic biomarkers among asymptomatic pregnant women on intermittent preventive treatment with sulfadoxine-pyrimethamine from Southwest Nigeria

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Background The genetic complexity of Plasmodium falciparum is a contributory factor to the emergence of drug-resistant parasites. WHO recommends intermittent preventive treatment of malaria in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) to reduce the deleterious effects of maternal and neonatal malaria in high transmission settings. However, asymptomatic malaria still persists in areas of endemicity despite IPTp-SP regimen. The study evaluated the allelic profiles of Plasmodium falciparum merozoite surface proteins (Pfmsp-1, Pfmsp-2), glutamate-rich protein (Pfglurp) and multidrug resistance-1 gene (Pfmdr-1) in pregnant women on IPTp-SP regimen from southwest Nigeria.
Methods 100 PCR-confirmed Plasmodium falciparum isolates, comprising visit 1 (V1) (n = 52), Delivery (n = 31) and Cord blood (n = 17) were randomly selected from EDCTP2 funded study (Trial no. 98867 IPTp-SP resistance in Nigeria TMA 2015 CDF – 973). Genomic DNA was genotyped using nested PCR. The Pfmdr-1 gene was further evaluated using restriction fragment length polymorphism (RLFP) at codon 86 with Apo1 restriction-digestion enzyme. Allelic frequencies, proportions and multiplicity of infection was calculated. Statistical significance was considered at $p \leq 0.05$.
Results Isolates from V1 confers 21.2% (Pfmsp-1), 32.7% (Pfmsp-2) and 9.6% (Pfglurp) distinct alleles, while delivery samples had 45.2% (Pfmsp-1), 32.3% (Pfmsp-2) and 6.5% (Pfglurp) allelic types. Cord isolates recorded the highest alleles; 70.6% (Pfmsp-1), 58.0% (Pfmsp-2) and 5.9% (Pfglurp). The MOI for V1 was 2.7, 2.1 and 1.1 for Pfmsp-1, Pfmsp-2 and Pfglurp. Delivery and cord isolates recorded 3.2, 1.9 and 2.7, 1.9 for Pfmsp-1 and Pfmsp-2 respectively; but had monoclonal Pfglurp alleles. The Pfmdr-1 wild/mutant allelic combination (N86Y) was present in 11.8% (V1), 61.3% (Delivery) and 58.8% (Cord blood) $p \leq 0.05$. Single point mutation (86Y) was only present in 5.9% cord isolates.
Conclusion Antigenic falciparum strains with N86Y Pfmdr-1 mutations may limit the efficacy of intermittent sulfadoxine-pyrimethamine prophylaxis of malaria during pregnancy in southwest Nigeria.

PA-257

'Nothing about us without us': Multi-country adolescent patient-led recruitment information in the Long-Acting Treatment in Adolescents (LATA) trial – an animated video to compliment 'traditional' participant information

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Background Participant information sheets and consent forms (PIS&C) in paediatric/adolescent clinical research are predominantly produced by adults. They are long and complex, meeting ethics, regulatory, and where applicable, pharmaceutical industry requirements, rather than the target audience. Young people report they do not understand much of the information provided, so do not read it, and rely on conversations with trusted Healthcare Providers. LATA (NCT05154747) being conducted by the BREATHER Plus Consortium, is the largest randomised trial of long-acting injectable antiretroviral therapy in virologically suppressed adolescents aged 12-19 years living with HIV-1 (ALWH). LATA has 'Youth Trials Boards (YTB)' in the participant countries (Kenya/South Africa/Uganda/Zimbabwe) that consist of supported, structured groups of ALWH who are active partners in the development and delivery of LATA, which started enrolment in May 2023.
Methods YTB members attended a global digital meeting to explore what information their peers need to give proper informed consent/assent and what medium would best deliver this.
Results The group agreed a short, engaging video would provide core information on how the medicine works, the injection experience and trial requirements. Youth engagement specialists worked with animators to develop a concept and provisional script. The process included ongoing 'science and youth' checks. YTB members lent their voices to ensure the video was in local languages. The final video was 5-6 minutes long (u-tube link to follow). All the national ethics committees have approved the video.
Conclusion The LATA video compliments the traditional PIS&C and was made through genuine youth engagement. The process allowed the young people to decide the format and content, whilst ensuring it correctly represented the trial. While this video is an adjunct to the PIC&S, in future, videos such as this could replace much of the lengthy complex language provided to trial participants, this merits further discussion with ethics committees and regulators.

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Addressing low uptake of COVID-19 vaccines in the Volta Region of Ghana

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Background As part of the EDCTP SAVING (Sustainable Access and Delivery of New Vaccines in Ghana) Consortium's implementation research (IR) capacity-building objective, capacity was built among partner institutions to develop IR proposals to address implementation challenges that affect the effective delivery and uptake of new medical interventions. The University of Health and Allied Sciences in Ghana is therefore using the IR approach (baseline to inform intervention and endline assessments) to address the low uptake of COVID-19 vaccines in the Volta Region of Ghana, despite the availability of the vaccines. This abstract focuses on the baseline assessment of the factors associated with the uptake of COVID-19 vaccines in the Volta Region of Ghana.
Methods The baseline assessment used a cross-sectional mixed-methods (quantitative and qualitative) design. A simple random sampling technique was used to collect quantitative data from community members aged 15 and above with a questionnaire, while in-depth interviews and focused group discussions were conducted among key stakeholder groups. Quantitative data were analyzed using frequencies, percentages, bivariate, and logistic regression analyses with STATA version 16, while thematic analysis of qualitative data was done using Nvivo software.
Results A total of 440 adults were sampled for the study, and the majority of them were female (58.73%). Less than 59% of the respondents had received the vaccine. 60% experienced adverse events after receiving the vaccine, and 36% reported adverse events as a reason for not receiving the vaccine. It was difficult to vaccinate the educated community members. Significant factors associated with COVID-19 vaccine acceptability include sex ($\chi2=9.643$; $p=0.002$), age ($\chi2=10.956$; $p=0.012$), marital status ($\chi2=47.331$; $p=0.001$)
Conclusion Addressing sociodemographic factors associated with COVID-19 vaccination uptake can aid in achieving herd immunity. This would require targeted health education focusing on individuals with less likelihood of accepting the COVID-19 vaccines.
Funding: EDCTP Saving Project

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Overcoming challenges in vaccination campaign during COVID-19: lessons learned from the TyVEGHA study

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Background Conducting vaccine studies in resource-poor settings comes with challenges. These challenges could include lack of infrastructure for cold chain management, accessibility of vaccination centres, the community's behaviour towards researchers, and political interference. In a pandemic situation e.g., during the Covid-19 peak, overcoming these barriers was difficult. To ensure more than 80% coverage during the field implementation of a Typhoid Conjugate vaccine (TCV) Trial in Ghana (TyVEGHA), we developed strategies to overcome these challenges.
Methods The study team identified the strength and weaknesses of the community and established a community advisory committee to help guide the conduct of the trial. This committee included chiefs and prominent members of the community, religious leaders, local health administrators, and community activists many of whom were employed as field workers.
Communication was done in many forms, i.e., through the local media, fieldworkers moving from home to home, using communication vans at the marketplaces, and mounting platforms of religious groups. Five satellite sites were identified and integrated into the strategy for the primary campaign. Personnel from these sites were recruited, and sheds were built for the study to bring the vaccination closer to hard-to-reach communities.
Vaccines were deployed daily from the main trial centre in cool boxes with thermometers and additional cooling elements. Small community durbars with queen mothers as ambassadors led the discussion on the importance of the typhoid vaccine and the need for participation in the study.
Results With support from the community an average of 500 children were screened daily. 20,052 (87.2% of eligible children) were vaccinated, with less than 10% of those screened, hesitant to receive the vaccine. No major vaccine related issues occurred during primary vaccination.
Conclusion Good communication strategies and community participation with a sense of community ownership was the primary force for the successful vaccination campaign.
Funding: EDCTP

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Enhancing referral and participation in surveillance through facilitated participatory training in Asante Akim Agogo, Ghana: The TyVEGHA experience

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Background Deployment of large-scale surveillance in low-income settings can be challenging. Meanwhile, the inclusion of pharmacists, health centres, over-the-counter medicine sellers (OTC), and herbal clinic practitioners as referral agents for health programs has the potential to improve access to healthcare services, increase enrolment in surveillance programs, and improve patient outcomes. We report here the participation of these important players in a large-scale vaccine deployment: Typhoid Vaccine in Ghana (TyVEGHA) programme in a rural setting in Ghana.
Methods We published elsewhere the concept of the severe typhoid fever programme (SETAPlus). In brief, we trained pharmacists, OTC agents, and herbal medicine sellers within the catchment area of the TyVEGHA study to support referral of eligible participants to Agogo Presbyterian Hospital-Trial Site. Facilitated (through incentives and community-sensitization) Participatory Training (FPT) was conducted to support the partnership and understanding of referral processes for eligible participants. The owners/caretakers were trained in the use of digital thermometers, bench aids and logs for referral and enrolment. Refresher training was conducted every six-months to ensure sustained knowledge/skills. We assigned study members to supervise their activities and facilitate referral process. Finally, we conducted monitoring activities twice-a-week to certify compliance with good clinical practice and adherence to protocol.
Results Prior to the use of FPT in July-2022, the number of providers identified was 36. This number increased to 48 as of April 2023 (within a period of nine month), with 137 participants being referred for enrolment, blood draw, and subsequent follow-up. However, only 79% of the total facilities identified are currently referring participants due to challenges including inconsistent operation of OTCs, unrealistic incentive expectations and proxy drug purchases.
Conclusion FPT using health agents and community sensitization increased referral for participation in the TyVEGHA study. The study highlights the potential advantages of including these as referral points for health programs.

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Assessing the feasibility and adherence of video observed therapy among Tuberculosis patients in Lambaréné: A pilot study

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Background Tuberculosis (TB) is a significant public health concern in many low-middle income countries, including Gabon, where adherence to TB treatment is often poor. Video Observed Therapy (VOT) has been proposed as an alternative to traditional directly observed therapy (DOT) to improve adherence to TB treatment. This pilot study aimed to assess the feasibility and adherence of a new approach, Video Observed Therapy, among TB patients in Lambaréné, Gabon.
Method A pilot study was conducted from October 2018 to January 2020 among 20 TB patients in Lambaréné. Participants were trained to record and send videos of their drug intake. The feasibility, adherence, and factors that could affect adherence were assessed. The main outcome measure was the proportion of expected videos received from participants. Good adherence was defined as having sent at least 85% of the expected videos.
Results Out of the 2684 videos expected, we received 2282 (85%). 85% (17/20) of the participants reported internet connectivity as the primary reason for not sending videos, 70% (14/20) of participants forgot to record the video, 65% (13/20) reported smartphone dysfunction and 50% (10/20) of participants had good adherence to VOT. Adherence to VOT was associated with having a smartphone at inclusion (p-value=0.019) and the level of education (p-value=0.029). Poor adherence was associated with going out of the network coverage area (p-value=0.01).
Conclusion This pilot study showed that VOT was feasible and acceptable among TB patients in Lambaréné, Gabon. Adherence to VOT was moderate, with internet connectivity and technical issues being significant barriers. Efforts should be made to improve access to stable internet connectivity, technical support, and education among TB patients to increase adherence to VOT.

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Altered Mycobacterium tuberculosis (Mtb)-specific T-cell responses in comorbid tuberculosis and type 2 diabetes mellitus

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Background Tuberculosis (TB) is one of the leading causes of death from a single infectious agent with approximately 1.4 million deaths annually. Efforts to eradicate TB are threatened by diabetes mellitus (DM), which confers a greater than a 3-fold TB disease risk. Both TB and DM are accompanied by marked immunologic changes, however, changes in Mtb-specific T-cell functional responses remain poorly characterised. We compared Mtb-specific CD4+ and CD8+ T-cell functional responses among patients with LTBI-DM (21), DM (16), ATB (19) and ATB-DM (04).
Methods Peripheral blood mononuclear cells were stimulated with ESTA-6/CFP-10 peptide pools or PHA, and characterised Mtb-specific CD4+ and CD8+ T cell functional memory (CD45RA/CCR7), activation (HLA-DR), exhaustion (PD-1) and apoptosis (Bcl-2) profiles by flow cytometry. Data were analysed using FlowJo v.10.8.2 and Prism v.8.4.
Results Central memory CD4+/CD8+ T cells were decreased in ATB [median (IQR): 30.80 (20.70-34.80)] compared to DM [41.35(36.63-57.13)] (P<0.0001)/(P=0.0388) and LTBI-DM [45.60(38.75-50.40)] (P<0.0001)/(P=0.0028) patients. Effector memory CD8+ T cells were decreased in DM [21.50(15.18-30.28)] compared to LTBI-DM [32.00(23.45-43.80)] (P=0.0193) patients. TEMRA CD4+ phenotypes were decreased in ATB [1.17(0.88-2.83)] compared to LTBI-DM [0.70(0.30-1.26)] (P=0.0040) and DM [0.99(0.41-1.34)] (P=0.0057) patients. CD4+ T cell HLA-DR expression was upregulated in ATB [2.49(1.12-3.49)] compared to LTBI-DM [1.16(0.89-1.43)] (P=0.0016) and DM [1.63(0.99-2.33)] (P=0.0235) patients. CD4+/CD8+ T cell PD-1 expression was upregulated in LTBI-DM [1.77(1.49-2.94)] compared to DM [1.63(0.95-2.07)] (P=0.0499) and ATB-DM [0.62(0.33-0.94)] (P=0.0381) patients. Finally, CD4+ T cell Bcl-2 expression was increased in ATB [4.17(2.99-5.87)] compared to LTBI-DM [2.08(1.44-3.71)] (P=0.0077) patients.
Conclusion ATB decreases CD4+/CD8+ T-cell central memory while DM decreases CD8+ T-cell effector memory compromising immune surveillance and production of effector cytokines against TB. DM upregulates TEMRA, cells less protective against Mtb. CD4+/CD8+ T cells are exhausted possibly due to persistent inflammation and Mtb-exposure but remain anti-apoptotic. Loss of PD-1 mediated inhibition in DM could promote severe TB disease.

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Lessons learned from a phase 2 diagnostic clinical trial in seven Sub-Saharan African countries

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Background The Covid-19 pandemic led to severe health systems collapse, as well as logistics and supply delivery shortages across sectors. For example, delivery of PCR related healthcare supplies was massively delayed during the COVID crises. A rapid and accessible SARS-CoV-2 molecular detection method in low resource settings offers many advantages. The aim in this study was to validate a novel isothermal amplification method for rapid detection of SARS-CoV-2 across seven sub-Sharan African countries and build capacity onsite.
Methods In this multi-country phase 2 diagnostic study, 3,231 clinical samples at seven African sites were tested with two reverse transcription Recombinase-Aided Amplification (RT-RAA) assays targeting the SARS-CoV-2 Nucleocapsid (N) and RNA-dependent RNA polymerase (RdRP) genes. Testing was performed in a mobile suitcase laboratory within 15 minutes. All results were compared to reference real-time RT-PCR.
Results All sites passed the initial quality control before screening the clinical samples in a single-blinded clinical trial. Four sites demonstrated good to excellent agreement between RT-RAA and PCR, while three sites showed fair to moderate results. The sensitivities for RdRP varied depending on Ct and study site (Ct values <30 ranged 60.5 – 100%; Ct values 30-35 ranged 23-90%; Ct values >35 ranged 3.6- 46.3%). Various factors regarding the setting and test operator were shown to have an effect on the test accuracy.
Conclusion Overall, the RdRP based RT-RAA test showed the best assay accuracy. Lessons learned from this study to assure test accuracy across various sites include the implementation of standardized operation procedure, in-person continuous training for staff, and enhanced quality control measures.

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Differences in risk factors between a high and low vertical HIV transmission setting: Implications for elimination of new paediatric HIV infections

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Background Roughly 1.3 million infants are exposed and 150,000 newly diagnosed with Human Immunodeficiency Virus (HIV) annually. Estimates of Vertical HIV transmission (VHT) rates vary by setting. In this study, we assessed the risk factors for VHT among infants born to women living with HIV in Tanzania and Mozambique.
Methods Between October 2019 and August 2021, data was collected from pregnant women living with HIV who participated in the LIFE study [RIA2016MC] at 28 obstetric health facilities in Tanzania and Mozambique. VHT was assessed up to month 3 of age in all infants. At baseline, demographics and clinical characteristics were collected to assess risk factors for VHT. Mixed effects models adjusted for health facility clustering were used to calculate risk ratios.
Results In total, 6,509 women living with HIV and their 6,605 exposed infants were included in the study. VHT up to month 3 of life was 2.69% (95% CI: 2.21, 3.24) in Mozambique, significantly higher than the 0.62% (95% CI: 0.35, 1.00) observed in Tanzania (RR: 4.45, 95% CI: 2.63, 7.99). On average, Tanzanian women were significantly older, attended antenatal care more frequently, and had been on antiretroviral treatment for a longer period. After adjusting for these factors, virologic non-suppression at delivery was the principal risk factor for transmission (RR: 35.7, 95% CI: 19.2, 73.1). In Mozambique, 31.0% of all mothers were not suppressed at delivery compared to 8.1% in Tanzania; only 8.9% (11/124) infants who acquired HIV by month 3 had mothers who were virally suppressed at delivery.
Conclusion We observed a striking difference in VHT between countries. Lack of viral suppression at delivery was the main risk factor for VHT, highlighting the need for better understanding the individual, community, and health system factors associated with lack of viral suppression in pregnant and lactating women living with HIV.

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Changes in standard care overtaking research: the case of the East African Point-of-Care (EAPOC) Viral Load Monitoring study in Kilimanjaro and Arusha regions, Tanzania

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Background The proportion of virologically suppressed (83%) people living with HIV (PLHIV) in Tanzania is below the 95%-target. Enhanced adherence counselling (EAC) is given when the viral load (VL) is >1000 copies/ml. Centralised laboratory VL monitoring hinders reaching the 95%-target due to challenges like long turn-around times. Point-of-care (POC) tests may overcome this. The aim was to assess the feasibility of POC monitoring.
Methods We assessed pre-feasibility during preparations of the EAPOC-study, a cluster randomised trial on the effectiveness, acceptability, and feasibility of POC-VL monitoring using m-PIMA in East Africa. M-PIMA gives results within 70 minutes, displayed as <800 copies/ml, or if above 800, an actual number. We used the 'Measurement Instrument for Determinants of Innovations' (MIDI) framework to determine feasibility comprising determinants of (1) the innovation, (2) the end-users, (3) the organisation, and (4) the socio-political context. We deployed the MIDI on narratives from meeting minutes, informal conversations, emails, and WhatsApp conversations. We did a thematic framework analysis to identify themes.
Results Considering the innovation, POC was expected to be complex, and there was unclarity in the need for centrifuges. Regarding end-users, nurse counsellors think they can give results rapidly, have beliefs about better treatment outcomes, understand the process and need training. Themes related to the organisation included time availability, re-arrangement of clinic staff to use POC inside the counselling room, counsellors' self-efficacy, and cartridges' availability. A central socio-political theme was a change of standard care in study sites whereby EAC was done at VL>50 copies/ml.
Conclusion We identified challenges that may hinder the feasibility of POC for viral load monitoring. We recommend having good manuals and thorough training of staff, well-defined staff duties and available time and a good supply of cartridges. In addition, we advocate for POC devices that display VL copies as low as 50 copies/ml.

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Introduction of the malaria vaccine RTS,S in the Volta region of Ghana: approaches and challenges

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Background The Ghana-based SAVING consortium aims to identify and address implementation challenges for the delivery of new medical interventions, such as RTS,S, the malaria vaccine introduced in Ghana in 2019. Inoculation is at 6, 7, 9 and 24 months of age. The lifesaving potential of the vaccine can be limited by its effectiveness and implementation issues.
Methods In November 2022, a qualitative study, employing in-depth interviews of five managers, three health workers and two community health volunteers was performed on: steps and challenges in introducing RTS,S; acceptability of RTS,S among health workers and community members; vaccine coverage.
Results There was a cascade training approach on RTS,S in the 10 districts that received RTS,S; the national centre trained staff at regional level. The region then trained the districts, which then trained the frontline healthcare workers and widely informed the population about RTS,S. In general, the training was perceived as adequate and well deployed. Acceptance of RTS,S by the healthcare workers and the population was good in spite of some misconceptions and a low perceived need for the vaccination. Awareness among the population and one health worker about the low level of effectiveness of the vaccine was limited. Vaccination coverage for the 4th dose of RTS,S was 40.1% among the eligible children (as of June 2022). A large drop-out rate between dose 3 and 4 was observed.
Use of the Med Safety Mobile App: the Regional Health Administration/Directorate introduced this MedApp in collaboration with the Food and Drug Authority. The motivation of the health delivery system to make full use of the MedApp was limited. In the visited district hospital, the MedApp was not being used.
Conclusion The encountered challenges are common to other vaccines, including COVID-19 vaccines. Governments and stakeholders should take note of the existing evidence to anticipate these issues.

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A multicentre, phase III, randomized study to evaluate efficacy and safety of VPM1002 in comparison with BCG in prevention of Mycobacterium tuberculosis infection in infants.

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TB was declared as an emergency disease in 1993, approximately 2 billion people are affected and 1.6 million people die yearly. Children contribute to 10-15% of global TB while estimated death is 200,000 yearly. TB prevention is important to reduce infant mortality and currently BGC vaccine is used for prevention. BGC efficacy and protection against TB Meningitis and Miliary disease is sub-optimal by 64-86% and 73% vs 77% respectively. As BCG clearly has inadequate efficacy against most forms of childhood and adult TB, there is an ongoing drive to develop more effective vaccines.
A novel vaccine VPM1002 is introduced to counterbalance the deficit. VPM1002 is a genetically modified Mycobacterium bovis Bacille Calmette-Guérin (BCG) strain. Despite its widespread use, BCG has been ineffective at stopping the spread of TB. To improve the immunogenicity of BCG, two genetic modifications were implemented leading to the development of VPM1002. Firstly, the hly gene from Listeria monocytogenes encoding for the listeriolysin O protein (LLO) was integrated into the BCG Danish genome. LLO disrupts the phagosome, thereby facilitating antigen translocation into the cytoplasm to allow for efficient presentation to CD8+ T cells. In contrast to BCG, where immune responses are mediated via the major histocompatibility complex (MHC) II pathway, the expression of LLO in VPM1002 allows for the enhancement of MHC I responses, thereby closely resembling the natural mechanism of protection against Mycobacterium tuberculosis. To ensure optimal LLO activity in an acidic phagosomal environment, the urease subunit C gene of BCG was subsequently inactivated.
SIIPL in collaboration with VPM has designed a Phase III study, which is currently ongoing in five Sub-Saharan African countries to evaluate efficacy and safety of VPM1002 in comparison to BCG. 6940 newborn infants are enrolled with 1:1 allocation. The follow-up is currently ongoing. So far, no safety concerns have been reported.

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Juvenile toxicity program to support use of Cipargamin (KAE609) in paediatric patients with severe malaria

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Background Severe malaria is a life-threatening disease with intravenous artesunate as the only recommended first line therapy. Global annual incidence of severe malaria is ~2 million cases with a case fatality rate >5% (despite antimalarial treatment) in endemic regions. Children under 5 years of age account for ~80% of all malaria deaths. Consequently, early evaluation of efficacy and safety in children <5 years of age is of paramount importance for the development of severe malaria therapies. KAE609 (Cipargamin) is a potent and fast-acting schizonticidal drug. Data are presented here from nonclinical juvenile toxicity studies with Cipargamin that supports early inclusion of paediatric patients in Phase II studies.

Methods Repeated-dose toxicity studies in juvenile animals were conducted to support enrolment of paediatric patients from 6 months to 12 years of age. The rat is a sensitive toxicological species, and parenteral administration was used for ease of administration to young animals and to maximize systemic exposure. Effects from birth through to sexual maturation were assessed by administration on days 4 to 11 or days 20 to 27 of age with ~3 months of recovery. Endpoints included clinical observations, assessments of sexual maturation, oestrous cycling and reproductive capacity, clinical pathology, toxicokinetic analyses and histopathology.

Results Toxicological findings for Cipargamin in juvenile rats were comparable with earlier toxicity studies in adult animals. No indication of developmental or reproductive risks were observed that preclude use of Cipargamin in paediatric patients.

Conclusion The juvenile toxicity studies fully assessed the nonclinical safety profile of Cipargamin and enable inclusion of the planned paediatric population in Phase II studies.

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Aetiology and antimicrobial resistance profile of maternal infections in Blantyre, Malawi; analysis of data from a maternal infection surveillance project

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Background There is a high prevalence of infections and sepsis in pregnancy in Malawi, with evidence of a rising incidence of antimicrobial resistance. Lack of resources to inform the organism-specific therapy of maternal infections results in a significant proportion of maternal deaths being due to infections and sepsis. Through the implementation of a microbiology services for obstetrics patients, we aimed to describe the epidemiology and antimicrobial resistance profile of maternal infections in a tertiary hospital in Blantyre, Malawi, and investigate the impact of maternal infections surveillance platform on pregnancy outcomes.

Methods Data on pregnant women from a maternal infections surveillance project serving a tertiary hospital in Blantyre, Malawi from 1 February 2021 to 30 March 2023 was used for the analysis. Descriptive statistics were used to describe the prevalence of infection and antimicrobial resistance. The association between infection from different samples and adverse delivery outcomes (a composite created through theory-driven grouping of a priori defined variables) was tested using multivariate logistics regression.

Results Preliminary analysis on urine sample data for 347 patients shows the prevalence of infections in urine in this population was 41.2% (95% CI of 36.0% to 46.4%), with up to two-thirds (57.3%) of the patients being on at least one empirical antibiotic on admission. 29.2% of the cultures grew Escherichia coli, and 8.2% grew Klebsiella pneumoniae. There were high levels of antimicrobial resistance demonstrated by the commonest isolates, especially Pseudomonas aeruginosa. Infection in urine was associated with adverse delivery outcomes 1.95 (95% CI 1.24 to 3.10, p=0.004). Having a culture result significantly informed the choice of antibiotic prescribed to a patient.

Conclusion These results suggest that having an infection in urine is associated with a greater prevalence of adverse delivery outcomes. Additional studies of a prospective nature are required to rigorously investigate this association.

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Building capacity of the regional referral hospitals in Uganda to conduct ethical reviews in research. A case of Masaka and Jinja regional referral hospitals

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Background Regional Referral Hospitals (RRHs) are mandated by MoH to conduct research to provide evidence-based care to patients, however most lack the knowledge and skills. These provide mostly tertiary care to patients and serve as referrals for several districts under their catchment. Eastern Africa Consortium for Clinical Research (EACCR) through its HIV work package builds capacity for conducting ICH-GCP complaint research in the region.
Methods Two RRHs from two regions in Uganda with high volumes of patients were considered: Masaka RRH and Jinja RRH located in Central and Eastern Uganda respectively.
Results The needs assessment done to identify the research capacity gaps, showed that the hospitals lacked Institutional review board (IRBs) to guide and evaluate research protocols. Memorandum of understanding were signed between Masaka and Jinja RRHs and the EACCR HIV work package. The parties agreed to train and build capacity of the members of the IRBs to review protocols and establish IRB offices in Masaka and Jinja RRHs.
Over 10 staff from each of the two hospitals were trained in good clinical practice, Research management, protocol reviews and research bioethics during pandemics. Masaka RRH had their IRB office refurbished with lockable cabins, a computer, and a printer scanner. The administrators received a one-weeks mentorship attachment to the IRB office at UVRI to learn IRB office operations. The IRB in Masaka and Jinja were guided to develop Standard Operational procedures (SOPs) as reference documents for operations. The IRB Office in Jinja had their office renovated and lockable -movable cabins were installed.
All these RRHs are in the process getting accreditation from Uganda National Council of Science and Technology (UNCST). UVRI IRB continues to provide peer mentorship to these two IRBs.
Conclusion When accredited, the two hospitals will use the patients and cohorts' data for health research to answer research questions affecting communities in Uganda.

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Plasmodium falciparum antimalarial drug resistance: population-based spatio-temporal evolutionary trends in Uganda

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Background Antimalarial drug resistance threatens global malaria control efforts. Critical resistance-mediating mutations include those in the targets for sulfadoxine-pyrimethamine, transporter proteins and propeller domain of P. falciparum Kelch-13 protein that are associated with artemisinin partial resistance.
Methods To gain insight into antimalarial drug resistance trends, we surveyed vital P. falciparum polymorphisms from 10-16 health facilities across Uganda from 2016-22. We further assessed for evidence of evolutionary selection of resistant isolates by evaluating diversity in genomic regions flanking resistance loci.
Results Five mutations in the targets of sulfadoxine (PfDHPS 437G, 540E) and pyrimethamine (PfDHFR 51I, 59R, 108N) were prevalent (80-100%). The prevalence of PfDHFR 164L and PfDHPS 581G mutations, which mediate higher level antifolate resistance, varied between sites and over time. The PfDHFR 164L mutation was most common in southwestern and central Uganda (>20-75%), with increasing prevalences from 2016-17 to 2022, and increases were also seen in other parts of the country. The PfDHPS 581G mutation was also most common in the four sites in southwestern and central Uganda, although significant changes were not detected. Mutations in PfCRT and PfMDR1, associated with aminoquinoline resistance, were increasingly uncommon. The PfCRT 76T allele was detected in western Uganda bordering the Democratic Republic of Congo. The PfMDR1 86Y mutation, which was previously very common, was absent from 2018-2022. The 1246D mutation decreased, with 0% prevalence in 2022. Four PfK13 mutations (675V, 469Y, 469F and 561H), remain highly prevalent by 2022, compared to our earlier reports. Regarding evolutionary selection, isolates with antifolate and aminoquinoline resistance-associated alleles showed similar diversity to wild-type isolates, in genomic regions flanking the resistance loci.
Conclusion These results suggest limited evidence of recent selection of antifolate resistance, consistent with stable transmission of resistant isolates; and continued recovery of aminoquinoline sensitivity in Uganda.

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Prevalence of parasite resistance amongst pregnant women receiving intermittent preventive treatment in pregnancy with Sulfadoxine-Pyrimethamine (IPTp-SP) in malaria endemic communities in Southwestern Nigeria

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Background The devastating effect of malaria in pregnancy (MIP) is mitigated by periodical administration of intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine (IPTp-SP). Possibility of emergence of Plasmodium parasites resistant to SP portends a threat to pregnant women living in malaria endemic regions. This was an EDTCP2 funded study to assess the effect and prevalence of Plasmodia resistance to SP in selected Nigerian communities.
Methods Consenting pregnant, gestational age 16-29 weeks, having met the inclusion/exclusion criteria were enrolled into one of the 5 study centres within Ikenne and Remo North LGA, Ogun State. Subjects were screened for malaria using microscopy, RDT and PCR, from enrolment to delivery. Positive malaria parasite samples were further analysed for Plasmodium falciparum dihydrofolate-reductase (Pfdhfr) and Plasmodium falciparum dihydropteroate-synthase (Pfdhps) mutations. All result were entered into REDCap® database and statistical analysis done using Microsoft Excel® 2019 and Stata 17®.
Results A total of 520 women, mean gestational age of 21 weeks were enrolled. Participants had average of 4 visits and 4 doses of SP before delivery. The prevalence of malaria parasitaemia was 2.9%, 4.8% and 35.5% using microscopy, RDT and PCR analysis respectively. There were 87 (19.4%) clinical malaria and 361 (80.6%) asymptomatic cases during the study. A total of 114 malaria positive samples were analysed for mutations. 51.8% were positive for mutations, while 4-points mutations were most prevalent (14.0%) and 4.4% had all 10-points mutations for Pfdhfr and Pfdhps. There were significantly more Pfdhfr mutations than Pfdhps and significantly higher mutations at enrolment.
Conclusion The prevalence of clinical malaria was low considering Nigeria is endemic for the disease, but high asymptomatic cases. Higher Pfdhfr/Pfdhps mutations were seen at enrolment. This study is the first to report the use of 6 doses of IPT-SP and all 10-points mutations for Pfdhfr/Pfdhps, which are definitive markers for SP resistance.

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Study Coordinator Training Programs Should Give Attention to Particular Clinical Trial Knowledge and Skill Domains for a Holistic Set

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Background Clinical trial knowledge and skills significantly influence the quality of clinical trial conduct. This article assesses the confidence of the ClinOps study coordinators' training program trainees in the various clinical trial knowledge and skill domains.
Methods Eighty-nine participants from 19 countries in Africa and South Korea participated in this cross-sectional study before commencing the training program for study coordinators. We assessed their confidence in several domains, such as clinical trial phases, regulations, ethics, data management, informed consent, project and financial management, internal and external team management, investigational product management, investigational site files (ISF), safety reporting, and patient recruitment and retention on five scales from "1" (Not Confident) to "5" (Extremely Confident). We compared the differences in confidence on various domains using the Kruskal Wallis test and pairwise Wilcoxon rank test with Bonferroni p-value adjustment. We also assessed factors associated with the baseline confidence of the trainees and the contribution of baseline confidence to a successful course completion using logistic regression, and Fisher's exact test, respectively.
Results Confidence in conducting a trial complying with ethical principles, informed consent process, securing approval, and managing ISF were relatively high among the trainees. However, the confidence of participants in financial, project, and external partner management, as well as closing out a trial was low. The differences in confidence in the various domains were statistically significant. After the training, the trainees' confidence was significantly increased in all the domains, though the confidence in the four domains remained relatively low.
Conclusion Training efforts aiming to augment the knowledge and skills of study coordinators should give better attention to financial, project, and external partner management, as well as closing out a trial to ensure study coordinators with holistic clinical trial knowledge and skills.

PA-292

The effectiveness of real-time electronic adherence monitors in improving ART adherence and viral load suppression in persons living with HIV: a systematic review and meta-analysis

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Background In this review we assessed the efficacy/effectiveness of real-time electronic adherence monitors (R-EAMs) in improving ART adherence and viral suppression among persons living with HIV (PLHIV).
Methods We searched the following databases: MEDLINE, Embase and Global Health for publications up to 11 October 2022. Controlled studies investigating R-EAMs as an intervention to improve adherence and/or viral load suppression in PLHIV were included. We assessed study quality using the Cochrane risk-of-bias tool for randomized control trials (RCTs) and the Newcastle-Ottawa Scale for cohort studies. A narrative synthesis and meta-analysis was conducted to synthesize results. This study is registered with PROSPERO, number CRD42022365596.
Results Out of 638 papers identified, 8 were included (6 from Africa and 1 each from USA and China). 6 of the studies were randomized control trials (RCTs), and 2 were cohort studies. No studies demonstrated an improvement in viral load suppression. However, 2 studies; a RCT in China (mean adherence - 96.2% vs 89.1%), and a crossover cohort study in Uganda (mean adherence - 84% to 93%) demonstrated an improvement in ART adherence. In terms of ART adherence, the common effects model (4 RCTs) showed a pooled standard mean difference of 0.1886 [0.0154; 0.3618, p = 0.0328] suggesting that the intervention had a small positive effect. However, the mixed effects model demonstrated no effect with a mean difference of 0.1596 [-0.2174; 0.5366, p = 0.4068].
Conclusion There is emerging evidence on the effectiveness/efficacy of R-EAM based digital adherence tools in improving HIV treatment outcomes. However, due to the heterogeneity of population groups, intervention designs, and adherence measurement instruments, the results of this review need to be interpreted with caution. Therefore, more studies need to be conducted to determine the effectiveness of this novel intervention; additionally, outcomes, measurement instruments, and evaluation frameworks need to be standardized.

PA-294

Evaluation of a novel GeneXpert host gene transcription assay for rapid diagnosis of childhood Tuberculosis – A multi-centre prospective study in lower middle income countries

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Background Underdiagnosis in children with tuberculosis (TB) results in high mortality. Novel tests using child-friendly samples and increased accuracy are needed. Cepheid's MTB-Host Response Cartridge (MTB-HR) measures a three-gene transcriptomic signature on fingerprick-blood shows promising results in adults.
Methods RaPaed-TB was a prospective multi-site cohort diagnostic accuracy study recruiting children <15 years in five countries, and the first to assess MTB-HR in children. Standardised microbiological, radiologic, and clinical criteria were used to define TB status. MTB-HR was tested at baseline and at months 1,3, and 6.
Results Of 633 children with a valid MTB-HR result, 202 (31.9%) had culture-confirmed and 207 (32.7%) unlikely TB. MTB-HR differentiated children with culture-confirmed TB from those with unlikely TB with area under the curve (AUC) 0.85 (95%CI: 0.80-0.89), sensitivity 59.8% (50.8-68.4), and specificity 90% (95%CI 85.5-94.0). The sensitivity of the MTB-HR was higher among children with disseminated TB (75.0%, 95%CI 57.8-87.9) compared to those with sole pulmonary/extrapulmonary disease (56.5%, 95%CI 44.0-68.4, and 50.0%, 95%CI 26.0-74.0). AUCs were comparable between age groups at 0.82 for <1 year (95%CI 0.68-0.95), 0.86 for 1-5 years (95%CI 0.77-0.95), 0.78 (95%CI 0.67-0.88) for 5-10 years, and 0.88 (95%CI 0.81-0.96) for 10-14 years of age. AUC was lower in children living with HIV (CLHIV) at 0.70 (95% CI 0.45-0.95) vs. 0.84 (95% CI 0.80-0.90) in those without, and higher in children with severe acute malnutrition (SAM; 0.91, 95%CI 0.80-1.00 vs. 0.83, 95%CI 0.78-0.88). MTB-HR normalized over time in children treated for TB while remaining unchanged in those with unlikely TB.
Conclusion The MTB-HR showed good diagnostic accuracy for culture-confirmed TB including key subgroups. The diagnostic yield, ease of capillary blood-sampling, and short time-to-result on the widely available GeneXpert platform makes the MTB-HR a promising tool for TB diagnosis in children and subsequent reduction of child TB mortality.

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Intermittent preventive treatment (IPT) of malaria in pregnancy with mefloquine may reduce nevirapine levels among HIV-infected women

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Background Sub-Saharan Africa is the region with the highest burden of malaria and HIV worldwide, being pregnant women the most vulnerable populations. Mefloquine (MQ) for intermittent preventive treatment (IPTp) of malaria in pregnancy has shown to significantly reduce malaria-related adverse maternal outcomes. However, while effective in HIV-uninfected pregnant women, results from an EDCTP-funded placebo-controlled trial assessing the safety and efficacy of IPTp-MQ among HIV-infected pregnant women showed that MQ recipients had a two-fold increased risk of HIV mother-to-child transmission (MTCT) compared to the control group. In this analysis we aimed to determine the antiretroviral (ARV) drug levels among a sub-sample of pregnant women participating in the aforementioned trial by treatment arm.
Methods ARV drug levels were determined by UPLC/MS/MS methodology (LLQ 2.5ng/mL, for all drugs) in venous and cord blood samples of 249 pregnant women enrolled from 2010 to 2012 in Manhiça, Southern Mozambique.
Results No significant differences in the maternal and foetal levels of nevirapine (NVP), lamivudine (3TC) and zidovudine (AZT) were found across groups. However, maternal levels of NVP tended to be decreased in MQ recipients compared to the placebo one among the subset of women transmitting the HIV to their infants (344.64 [558.99] vs 926.4 [619.67], p=0.054).
Conclusion Our findings suggest potential pharmacological interactions between MQ and NVP that warrant caution in the administration of antimalarial drugs to HIV-infected women on ARV treatment.

PA-297

Characterising the vaginal virome of women living with and without HIV using sequence independent single primer amplification

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Background The cervicovaginal mucosa is inhabited by an ecosystem of bacteria, fungi and viruses, which likely interact with each other. The vaginal virome may influence vaginal immunity directly, or though modulation of the bacterial component via bacterial-phage dynamics. These interactions may play an important role in sexual and reproductive health outcomes. However, it is predicted that over 60% of the human DNA virome has not yet been identified, and the RNA virome is even less explored, nor has the impact of HIV on the vaginal virome composition been described.
Methods We optimised viral particle extraction from vaginal swabs. We then optimised a Sequence Independent Single Primer Amplification (SISPA) approach to enable deep sequencing of the viral metagenome that decreases the GC and genome size bias introduced by commonly used methods such as Multiple Displacement Amplification and Rolling Circle Amplification, while also yielding a greater diversity of near-complete metagenome-assembled genomes.
Results SISPA was able to recapitulate almost exactly the relative abundance of a viral mock community. Storing swabs in universal transport media (UTM) directly after collection and treating the sample with a 18G needle prior to viral particle extraction resulted in the greatest yield of viral nucleic acid and subsequent read depth, over storing swabs dry or in a 1:1 dilution of UTM and SM buffer. We have applied this method to vaginal swabs from Sub-Saharan African women with and without HIV.
Conclusion This work lays the ground work for project TMA2020CDF-3192, which will assess the interaction of vaginal virome and bacteriome in pregnant women with HIV in sub-Saharan Africa and risk of preterm birth.

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Predicting disease effect on the pharmacokinetics (PK) of sustained and immediate release formulations by applying physiologically based pharmacokinetic (PBPK) modelling

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Background 5-flucytosine (5FC) is used for the treatment of cryptococcal meningoencephalitis (CM) in patients with advanced HIV. The current dosing is four times a day involving high risks of low adherence and not adapted for severely ill patients. To address this, a sustained release (SR) pellet formulation was developed. Two PK studies in healthy subjects were performed, evaluating the immediate release (IR) and SR formulations. To estimate the SR formulation exposure of 5FC in patients, PBPK modelling was applied.
Methods A healthy population was generated in PK-Sim [3,4] and modified to include the following disease components: 1) increased (20%) intestinal permeability as a consequence of "leaky" intestine, 2) decreased (20%) intestinal permeability as a consequence of damaged microvilli intestine, 3) diarrhoea due to faster transit time in small intestine (20%) and large intestine (50%), 4) diarrhoea due to higher water volume in large intestine (50%) and 5) severe malnutrition.
Results The main risk in exposure with the SR formulation compared to IR formulation is for diarrhoea caused by fast transit time, resulting in a 10% lower ratio (SR/IR) exposure compared to a healthy population. This can be explained by the shorter time available for absorption in diarrhoea, affecting the SR formulation to a greater extent than the IR formulation.
Conclusion Switching from an IR to SR formulation for the treatment of CM is not predicted to impact exposure in a patient population, except for patients with fast transit diarrhoea.
Funding: This project is funded by the EDCTP2 programme supported by the EU, with additional funding from the Swiss Agency for Development and Cooperation (SDC), MSF International, and other private foundations and individuals. The findings and conclusions contained herein are those of the authors and do not necessarily reflect positions or policies of the aforementioned funding bodies.

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Lyophilization and field based stability of ID93 + GLA-LSQ, a single-vial adjuvanted subunit tuberculosis vaccine candidate

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Background ID93_GLA_LSQ is one of the adjuvanted-recombinant protein vaccines that are in clinical development for the prevention of pulmonary TB. The current composition comprised of two vials, one containing the antigen and one containing an adjuvant, which is' bedside mixed' immediately prior to immunization. Hence, this study developed a strategy for the presentation of the vaccine as a single vial through conjugation and lyophilization. The study also evaluated the field-stability of these samples stored at room temperature in five health facilities in Nigeria.
Methods Lyophilization process was developed to have a single vial of co-mixed(coVL) and conjugate(ConjVL). The physicochemical stability and biological activity stability were evaluated for three months at 4ºC and 37ºC. The parameters evaluated include cake quality and melting point for the powder, while the reconstituted liposomes were assessed for liposome reformation, particle size, GLA and QS21 concentration and the integrity of ID93. The samples were stored in five health centres to assess the stability of the formulation outside cold chain for nine months.
Results The assessment of the stability parameters for coVL and ConjVL, showed that they were stable at 4°C and 37°C. Moreover, the two formulations maintained their biological activity at the two storage conditions for three months, however, the conjugated formulation still maintained higher memory T cell cytokine recall response in the in vitro whole blood assay as observed with the liquid formulation. The two formulations stored at average daily room temperature of 29.3-30.7°C in five health centres across South –Western geopolitical zone of Nigeria maintained the cake quality and melting points for the nine months with less than 20% reduction in GLA and QS21 across the sites and the particle size growth was also less than 50%.
Conclusion This work presents development of thermostable adjuvant-containing subunit tuberculosis vaccine in developing country.
Funding: This work received funding support from EDCTP

PA-305

FC gamma receptor gene polymorphisms and reservoir size in HIV patients in Ghana

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Background Fc gamma receptors (FcγR) are cell surface glycoproteins that bind to the Fc portions of immunoglobulin IgG antibodies to elicit diverse effector functions. Polymorphisms in different FcγR genes have been associated with HIV infection and vaccine trial outcomes. Some studies have suggested that FcγRIIa may be a marker of latent reservoir size, however, this remains controversial. Hence whether FcγRIIa and other Fc receptors have functional consequences on the size or reactivation capacity of the reservoir needs to be investigated.
Methods In this pilot study, single-nucleotide polymorphisms (SNPs) in FcγRIIIa, FcγRIIa, and FcγRIIb genes were determined by Sanger sequencing in 50 HIV-infected ART-suppressed individuals. HIV reservoir size was determined by quantifying total HIV DNA (vDNA) and cell-associated unspliced (US) HIV RNA by qPCR. Association analysis was performed using three coding SNPs, one per gene (FcγRIIIa-rs396991, FcγRIIa-rs1801274, and FcγRIIb-rs1050501).
Results The median reservoir size as estimated by vDNA copy number was 116 (range, 1 - 5798) copies/million cells and US RNA was detectable in 15 out of the 50 samples. Our analysis found the median reservoir size was almost 3 times larger in males compared to females who are suppressed (p=0.038).
Conclusion Reservoir size was observed to be larger in younger patients compared to those older, however, not statistically significant. However, there was no significant associations between the FcγR SNPs and HIV vDNA or US RNA. Studies in larger cohorts are necessary to explore associations between FcγR polymorphisms and HIV reservoir.
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PA-306

ADOPT: the implementation research program introducing the potential new paediatric treatment option into schistosomiasis control programs in endemic countries

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Background Current programs to control schistosomiasis mainly target school-aged children and rely on mass drug administration centered on primary schools. Alternative drug distribution platforms need to be identified to ensure equitable access to the potential new treatment option for pre-school aged children, once registered.
Methods The Paediatric Praziquantel Consortium has developed an operational research program with the aim to identify and describe robust yet flexible drug distribution platforms and delivery modalities that can easily be adapted to different settings. Called ADOPT program, the approach includes a rigorous acceptability and perception assessment as basis for small-scale pilot studies to evaluate and compare potential delivery platforms and access strategies in terms of feasibility, costs and coverage. Insights and lessons learnt from this phase will inform and guide the roll-out of the most promising approaches.
Results Working with partners in three countries, social science studies were already conducted to establish a baseline of acceptability and perception of paediatric schistosomiasis and its potential new treatment, and to inform the social mobilization strategy. Following the systematic assessment of a range of potential distribution platforms, a restricted number per country has been prioritized. Standard protocols for the pilot studies are currently under development and will be submitted to ethics review committees to start the pilots soon after obtaining a positive opinion from regulatory authorities. Practical aspects including the determination of the correct drug dose in settings without access to scales, drug administration to small children, and training needs are also explored.
Conclusion High geographic and population coverage will only be achieved if the social mobilization is effective, the drug distribution platform has universal reach, and staff are adequately trained. A toolbox with a selection of tested protocols and guidance documents for their adaptation will facilitate rapid expansion both inside study countries and by other interested partners.

PA-307

Effect of albendazole 400 and 800 mg on hypermicrofilaremic loiasis and eosinophilia: preliminary results of a phase IIb, randomized, single-blind clinical trial in northern Gabon

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Background Albendazole (ALB) is used safely for the reduction of Loa (L.) loa microfilaremia. However, there is no official recommendation. ALB could be used routinely in onchocerciasis outbreaks in case of coendemicity with loiasis, in order to make hypermicrofilaremia carriers eligible for mass treatment with ivermectin. The purpose of this study is to compare the efficacy and safety of two ALB treatment regimens in the management of hypermicrofilaremic loiasis.
Methods The study was conducted in the Woleu-Ntem region of northern Gabon. Clinical, haematological and parasitological data were collected. Patients were divided into 3 groups: 2 groups of hypermicrofilaremia (≥8000 mf/mL) treated with 400 mg and 800 mg for 30 days and a control group consisting of patients with low microfilaremia (<8000 mf/mL) treated with ALB 400 mg for 30 days. Microfilaremia and adverse events were investigated and monitored weekly until day 30.
Results In total, 72 patients were included and followed for 30 days on daily ALB administration. The control group had 38 patients. In the two experimental groups, 16 received ALB 400 mg and 18, ALB 800 mg. L. loa microfilaremia and eosinophilia were measured at day (D) 0, 2, 7, 14, and D30. Clinical data were monitored daily before each ALB dose administration. Microfilaremia decreased at D30 in 82.3% of hypermicrofilaremic subjects to below 8000 mf/mL. No serious adverse events were recorded; 30.0% had clinical manifestations after ALB, and for 20.0%, the main adverse event recorded was pruritus. No difference between the two groups of hypermicrofilaremic patients was observed in the reduction of microfilaremia and the occurrence of clinical manifestations. Eosinophilia decreased in all groups with no difference between two experimental groups.
Conclusion ALB 400 mg/800 mg for 30 days, decreased significantly reduces microfilaremia/eosinophilia/symptoms and can be used for eligibility of microfilariae carriers for mass treatment with ivermectin.

PA-309

Comparing the accuracy of inflammation detection using the lateral flow point of care Genital InFlammation Test (GIFT) interpreted by visual inspection versus automated reader

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Background Sexually transmitted infections (STIs) and bacterial vaginosis (BV) are highly prevalent risk factors for HIV infection, partly driven by genital inflammation. We have developed a novel true point-of-care inflammation lateral flow assay called the Genital InFlammation Test (GIFT). GIFT detects the presence of elevated genital inflammatory cytokines to screen for asymptomatic STIs/BV cases that are missed in settings where syndromic management is practiced. Novel point-of-care tests (like GIFT) must benchmark their performance against the guidelines specified by the WHO's REASSURED criteria, which includes being equipment-free. This study compared the performance of human eye reading of the GIFT device to an automated device reader.
Methods Bio-banked lateral vaginal wall swabs collected from 10 women were tested for the presence of inflammation biomarker bands (IL-1alpha, IL-1beta) on GIFT devices, which were visually assessed by two independent researchers for band intensity (using G-scores between 0-10). Visual inspection of G-score band intensity was benchmarked against cytokine concentrations measured by commercial ELISA. G-score visual assessments were compared with band intensity measurements using an automated device reader (AXXIN-AX-2X-S™).
Results Significant concordance was observed between visual (G-scores) for IL-1alpha and IL-1beta and automated reader intensities (rho=0.96, p<0.0001 and rho=0.89, p=0.0003, respectively). However the automated reader enabled test line detection at lower cytokine concentrations (<300pg/ml) than visual inspection. A three-country field study of the GIFT device in 675 women is currently being conducted in South Africa, Zimbabwe and Madagascar. Data from real world use of the GIFT device will confirm the value of including an automated reader in result interpretation.
Conclusion This laboratory evaluation of the GIFT device performance, assessed visually or using an automated reader suggests that the reader may offer a sensitivity benefit over visual reading at lower vaginal cytokine concentrations, while accuracy will be comparable at higher concentrations.

PA-310

User perspectives on Molbio MTB for use as a decentralized Point-Of-Care diagnostic test in Mozambique and Tanzania

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Background Timely and appropriate diagnosis and treatment are key to reduce tuberculosis (TB) mortality, morbidity and prevent transmission. However, almost half (4.3 million) of the 10 million annual TB cases remain undiagnosed. Incorporating patients' preferences when implementing of a point-of-care (POC) strategy for TB diagnosis may facilitate scale-up and impact. This qualitative study explores the values and preferences of patients, healthcare providers and decision makers regarding a POC TB diagnostic strategy using the Molbio TrueLab platform in Mozambique and Tanzania.
Methods We conducted semi-structured interviews with patients (20-24/country), professional users (laboratory staff, nurses, clinicians, 10/country) and decision makers (3/country). Direct observations of the testing procedures and usability surveys in staff operating the platform were also conducted.
Results Preliminary findings show that Molbio TrueLab platform and TB assays are easy to use (System Usability Scale score= 82.5/100). During observations, the most frequently error was forgetting to check for internal control line of the cartridge (n=6/9). Providers appreciated the possibility of identifying TB and rifampicin resistance on site, without having to transport samples for centralized testing. Patients preferred the same-day results and fast initiation of treatment when samples were investigated by Molbio. However, some view waiting longer time for the results as an acceptable trade-off if results are more accurate. While some patients described difficulties producing the sputum sample, most thought that sputum was the only samples which could be investigated for TB. In terms of the diagnostic process, patients valued the support and counselling from staff. Fears of being stigmatized after diagnosis were common.
Conclusion The Molbio platform and TB assays were perceived as easy to use by health providers, and an alternative for TB diagnosis at the POC that was not just acceptable but also preferred by patients in Mozambique and Tanzania.

PA-311

Vitamin D status and the risk of malaria among under-five children in Africa

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Background Vitamin D deficiency (VDD) and malaria are conditions of public health importance whose burden is still rising among children globally and in sub-Saharan Africa (SSA). Animal studies have found evidence of the association between VDD and various outcomes, including malaria. However, few observational studies quantifying the effect of VDD or vitamin D insufficiency (VDI) on malaria in humans exist. This study aimed to examine the effect of vitamin D on malaria risk among children in SSA.
Methods This analysis utilised data from a prospective birth cohort in Entebbe, Uganda and a community-based cohort in Kilifi, Kenya. Univariate and multivariable Poisson regression with robust standard errors, logistic, and linear regression models were used to estimate the effect of vitamin D on malaria (incidence/risk/antibodies), respectively.
Results Of the 2493 children analysed, 42.0% had VDD/VDI (25(OH)D levels<75nmol/L). After adjusting for age, sex, iron deficiency (ID) and country, there was some evidence of an association between VDD/VDI and malaria incidence at 6 months following vitamin D measurement (ARR:1.18;95%CI:0.98-1.42;p=0.072). Malaria risk and incidence results were similar. After adjusting for age, sex, ID, inflammation, and cohort, there was strong evidence of an association between VDD/VDI and higher log anti-AMA-1 (Adjusted β:0.25;95%CI:0.08,0.43;p-value=0.004). Some differences in the relationship between VDD/VDI and malaria antibody levels were seen between cohorts.
Conclusion Low vitamin D levels are associated with increased malaria incidence and *P.falciparum* antibodies. The results of this analysis were consistent with the evidence from animal studies and did not support the clues found in some existing observational studies. These results suggest that VDD/VDI may play a role in advancing malaria infection, but the malaria antibody results could be due to reverse causality. Further research is warranted to confirm the malaria incidence/risk results and address the direction of causality between VDD/VDI and malaria antibodies using Mendelian randomisation.
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PA-313

Folic acid, vitamin B12 and homocysteine profiles in young non-pregnant and pregnant women living in a malaria endemic area: a secondary analysis of trial data

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Background The safety of iron and folate supplementation in young women living in malarious areas, before and during their first pregnancy, is uncertain as both nutrients can alter malaria risk.
Methods Folate biomarkers were assayed by ELISA in sera of 541 never pregnant women (mostly adolescent) enrolled in a periconceptional controlled trial of weekly iron/folic acid supplementation in rural Burkina Faso (Funded by AREF-EDCTP). Of these 315 become pregnant during the trial, with 226 remaining non-pregnant. **Results** For paired samples mean homocysteine and folic acid concentrations increased between both baseline and early pregnancy (p<0.0001), and baseline and late pregnancy (p<0.0001), although B12 concentration only increased by late pregnancy. In those remaining non-pregnant with paired samples (n=133), homocysteine and folic acid decreased between baseline and end of study (respectively 59.0±24.0 versus 56.5±25.8, (p=0.001; and 39.9±8.3 vs 33.7±7.00 nmol/L, p=0.0001, [(t test]). Vitamin B12 concentrations did not change between enrolment and end assessment (189.32±32.83 vs 189.45±32.95 pmol/L, p=0.97, [t test]). Malaria parasitaemia prevalence was 54.0% in pregnant women in early pregnancy and 41.8% in women remaining non-pregnant women at end assessment. In pregnant women mean B12 concentration was lower in those with parasitaemia (170.9± 25.4 vs 181.1± 25.8 pmol/L, p<0.01). In non-pregnant women these values were 34.0 ±6.4 vs 33.2±7.0 nmol/L (p=0.56) for folic acid; 193.5±31.8 vs 189.9±30.9 pmol/L (p= 0.57) for B12, and 53.6±24.4 vs 58.1±28.0 µmol/L, p=0.40, [t tests]) for homocysteine. In pregnant or non-pregnant women folic acid and homocysteine concentrations did not differ by malaria status.
Conclusion In conclusion, concentrations of folate biomarkers increase from early in pregnancy, with a negative association of malaria parasitaemia with vitamin B12 concentration. In non-pregnant women folic acid and homocysteine decrease at end of study with no association of malaria.

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The kinetics of M.tb-specific CD4+ T cell response during HIV infection

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Background HIV infection is the most significant risk factor for developing active tuberculosis (TB). Even during the first year of infection, when CD4+ T cell counts are still well maintained, people living with HIV (PLWH) have an increased risk of TB. Previous studies have demonstrated that the rapid depletion of M.tb-specific CD4+ T cells during early HIV infection may contribute to the onset of TB in PLWH.
Methods We measured M.tb-specific CD4+ T cell responses longitudinally in 17 participants selected from the CAPRISA 002 study. We assessed five timepoints: Prior to HIV infection (median: 6.5 months, IQR: 10-4), 3 months after HIV infection (IQR: 3-3.75), 1 year after infection (IQR: 11-12), during chronic infection (median: 60 months, IQR: 40-71) and approximately 2 years after antiretroviral therapy (ART) initiation (IQR: 31-98.5 months). PBMCs were stimulated with M.tb antigens, and we used intracellular cytokine staining and flow cytometry to measure the frequency of M.tb-specific CD4+ T cells.
Results All 17 participants exhibited an M.tb-specific CD4+ T cell response prior to HIV infection (median: 0.2%, IQR: 0.09-0.47). Three months after HIV infection, M.tb responses were undetectable in 35% of the participants (n=6). In this group, M.tb-specific responses re-emerged in 4/6 participants during chronic HIV infection and were maintained 2 years after ART initiation. In contrast, in another group of participants (n=9) M.tb-specific CD4+ T cells were well maintained early after HIV infection. Moreover, the majority of participants in this group (6/9) had only minor fluctuations in their M.tb-specific responses throughout the course of HIV infection and after ART.
Conclusion Our data supports previous findings showing that there is an early depletion of M.tb-specific CD4+ T cells within the first year HIV infection. This may explain the heightened risk of TB in PLWH even prior to significant immune suppression.

PA-325

The Pediatric Praziquantel Consortium: Our development journey to provide treatment to pre-school aged children

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Merck KGaA, Germany, on behalf of the Pediatric Praziquantel Consortium

Background Schistosomiasis, highly prevalent in tropical regions, affects over 240 million people. Praziquantel (PZQ) is considered the standard-of-care treatment. However, around 50 million preschool-aged children (PSAC) remain untreated in public health programs, mainly due to the lack of a child-friendly formulation. In 2012, the Pediatric Praziquantel Consortium was established to provide a treatment tailored for PSAC. This work has resulted in the development of arpraziquantel: a novel (oro)dispersible tablet containing L-PZQ, the biologically active PZQ enantiomer. The 150 mg tablets are small, allow precise dosing and have improved taste properties.
Methods The new formulation was developed by Astellas (Japan) and Merck KGaA, Darmstadt, Germany. Farmanguinhos (Brazil) has established drug product production while Universal (Kenya) is preparing for local manufacturing. Phase I, II and III clinical trials have been completed. The latter was conducted in Côte d'Ivoire and Kenya in PSAC (3 months to 6 years) infected with Schistosoma mansoni or Schistosoma haematobium. 288 PSAC were treated with a single dose of arpraziquantel or PZQ. The primary endpoint was clinical cure at week 3.
Results High cure rates close to or above 90% were achieved in Schistosoma mansoni-infected children at a dose of 50 mg/kg, and in Schistosoma haematobium-infected children at 60 mg/kg. Egg reduction rates were very high (~99%) across all groups. The safety profiles of arpraziquantel and PZQ were similar, and no new safety issues were identified.
Conclusion Phase III results indicate that arpraziquantel is efficacious, well-tolerated, and shows improved palatability among PSAC. Through Merck KGaA, the Consortium has applied for a scientific opinion from the European Medicines Agency under the EU-M4all procedure for high-priority medicines intended for markets outside the European Union. A positive opinion would facilitate the inclusion of arpraziquantel in the WHO list of prequalified medicinal products as well as regulatory approvals in endemic countries.

PA-336

Diagnostic accuracy of computer-aided detection of tuberculosis on chest X-rays and C-reactive protein as tuberculosis triage tests at health facilities in Lesotho and South Africa

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Background To improve tuberculosis (TB) case-finding, rapid, low-cost, non-sputum TB screening tests need to be developed with, WHO-defined target product profile criteria of, sensitivity of 90% and specificity of 70%. The TB TRIAGE+ ACCURACY study evaluated artificial intelligence-based computer-aided detection software (CAD4TB) and point-of-care C-reactive protein (CRP) in presumptive TB patients attending health facilities in South Africa and Lesotho.
Methods Between April 2021 and March 2022, we conducted a prospective study enrolling adults (≥ 18 years) with one or more TB symptoms; cough, fever, night sweats, weight loss. Participants received a CRP blood test, digital chest X-ray for CAD4TB (version 7) and produced one sputum sample for Xpert MTB/RIF and Xpert MTB/RIF Ultra testing and one for liquid TB culture. Primary endpoint was receiver operating characteristic analysis (ROC) of CAD4TB and CRP against a composite microbiological reference standard (CRS: Xpert MTB/RIF Ultra and liquid culture).
Results We enrolled 1392 participants, median age was 45 years, 54% were women, 48.6% were HIV-infected, 23.8 % had a history of TB, 87.9% were able to produce sputum. 126 (10.3%) participants were found to be TB positive. The ROC for CAD4TB and CRP against CRS showed an AUC of 0.89 (95% CI 0.86-0.92) and 0.80 (95% CI 0.76-0.84), respectively. The threshold for CAD4TB was defined as ≤27 with a sensitivity of 91% and specificity of 71%, the threshold for CRP was ≤7mg/L with a sensitivity of 90% and specificity of 39%.
Conclusion CAD4TB, but not CRP, achieved the minimum sensitivity and specificity for a triage test for pulmonary TB defined by WHO's target product profile. The performance of both tests did not differ significantly by HIV status, but was significantly lower in patients with a history of TB compared to those with no history of TB.
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PA-340

A systematic review of the efficacy of artemisinin-based combination therapy (ACT) in people living with HIV (PLHIV) diagnosed with uncomplicated Plasmodium falciparum malaria in Africa

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Background Africa bears the highest double-burden of HIV and malaria worldwide. In 2022, 25.6 million people were living with HIV (PLHIV) and 228 million malaria cases were diagnosed in Africa. Malaria patients co-infected with HIV are considered at a higher risk of failing malaria treatment according to the WHO. This review aims to assess the treatment outcomes following artemisinin combination therapies (ACTs) in PLHIV.
Methods The literature search was conducted up to April 2022 in the following databases: MEDLINE, EMBASE, Web of Science, Cochrane Central, WHO Global Index Medicus and Clinicaltrials.gov. Studies describing any malaria treatment outcomes or antimalarial drug exposure (area under the curve, concentration) in PLHIV treated for falciparum malaria infection were eligible for inclusion.
Results A total of 26 eligible articles were screened of which 19 studies (2003-2017) from six countries were included in this review; this represented >3,000 malaria episodes in PLHIV across various transmission settings. Antimalarial treatments studied were artemether-lumefantrine [AL] (n=16), dihydroartemisinin-piperaquine (n=7), and artesunate-amodiaquine (n=1); PLHIV were treated with efavirenz (EFV, n=11), nevirapine (NVP, n=9), atazanavir-ritonavir (n=1), trimethoprim-sulfamethoxazole (n=6), lopinavir/ritonavir (LPV/r, n=4), or were untreated (n=3). Compared with no HIV patients, EFV reduced exposure to all antimalarial components (n=2), LPV/r increased lumefantrine exposure (n=1); NVP reduced artemether exposure only (n=2). There was no evidence of increased risk of recrudescence in PLHIV compared to patients without HIV (n=7), but for AL, PLHIV receiving LPV/r appear to have a lower risk of recurrence when compared to no HIV (n=1), or PLHIV on NVP or EFV (n=2).
Conclusion Limited data on ACT treatment outcomes or drug exposure in PLHIV exist, and the effect of antivirals appears inconsistent in the literature. Considering the heterogeneity in study designs, our findings support conducting an individual patient data meta-analysis to explore the impact of ARVs on antimalarial treatment.

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Diagnostic accuracy of published host blood transcriptomic tuberculosis signatures in a low burden hospital setting

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Background Several host blood transcriptomic signatures have shown promise as tuberculosis (TB) diagnostic candidates, supporting the use of such biomarkers in prototype RNA-based point-of-care tests. Further validation of these signatures across different clinical and endemic settings in relevant patient cohorts is required to ascertain their global applicability. We aimed to evaluate the accuracies of published TB transcriptomic signatures in discriminating TB disease from lower respiratory tract infections (LRI) and latent tuberculosis infection (LTBI) in a low-burden hospital setting.
Methods We evaluated the accuracy of 20 candidate blood transcriptomic TB signatures in diagnosing TB in 86 individuals (18 TB, 19 LRI, and 49 LTBI) recruited at Oslo University Hospital, Norway. Gene expression was measured using the fluidigm microfluidic qRT-PCR platform on Paxgene blood RNA samples collected at inclusion. The diagnostic performance of the signatures was assessed by area under the receiver operating characteristic curve (AUC-ROC).
Results When a head-to-head comparison of the accuracies of the signatures was made between the study groups (TB vs LRI and TB vs LTBI) similar diagnostic performance was observed for the Sweeney 3-, Francisco 2-, Gjøen 7-, and Roe 3- gene signatures (AUC between 0.78 and 0.89). GBP1 and GBP5 were the most accurate individual genes (AUC ≥ 0.80), differentiating TB patients from individuals with LRI and LTBI. However, new 3- and 5-gene combinations, improved the accuracy in distinguishing TB from LRI (AUC=1.00, Sensitivity and specificity of 100%) and TB from LTBI (AUC=0.99, Sensitivity = 93.3%, Specificity = 97.9%), respectively.
Conclusion Host blood transcriptomic TB signatures primarily identified in studies from high TB-burden settings showed equivalent diagnostic potential in a low-burden hospital setting. New combinations of transcripts with improved diagnostic accuracy, met the minimal WHO target product profile thresholds for non-sputum-based triage TB tests, and warrant further investigation in larger, prospective, and diverse patient cohorts.

PA-351

HIV-1 genotypic susceptibility to second generation non-nucleoside reverse transcriptase inhibitors among patients failing antiretroviral therapy in Cameroon: Implication for the long-acting therapies in Africa

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Background Long-acting therapies combining second generation non-nucleoside reverse transcriptase inhibitors (2Gen-NNRTI) with integrase inhibitor (INSTIs) such as cabotegravir, have demonstrated potent activity in treatment-experienced HIV-infected patients. In our context it has already been shown that less than 1% of patients are resistant to INSTI. However, there is not data on cross-resistance events between first (EFV and NVP) and 2Gen-NNRTI (Etravirine, Rilpivirine,Doravirine). This study aimed to evaluate 2Gen-NNRTI resistance and their susceptibility in patients failing antiretroviral treatment (ART) in Cameroon.

Methods An observational study was conducted at the Chantal BIYA International Reference Centre among patients failing ART from 2020-2023. Genotypic resistance testing was interpreted using Stanford HIVdb; penalty scores of drug resistance were ≥60 (high-resistance), 30–59(intermediate-resistance), <30(susceptible). Acceptable threshold for potential drug-efficacy was set at >50% at population-level.

Results A total of 670 patients were enrolled including 366 failing first-line (1stGen-NNRTI based) and 304 second-line (protease-inhibitors) regimens. Median viremia was 54889 [9,867–231,470] copies/ml and ART-duration was 17[15–25] months. Prevailing 2Gen-NNRTI mutations were: Y181C (22.24;149/670%) and G190A (18%;120/670). Overall rate of resistance to NNRTI was 88.81% [with 91% (334/366) failing first-line and 85% (261/304) failing second-line; p=0.03]. Drug susceptibility was 54.93% (Etravirine); 46.87% (Rilpivirine), 40.60% (Doravirine). Following susceptibility profile, patients failing on Efavirenz-based regimens were more susceptible to 2Gen-NNRTI (OR=0.42[0.21–0.84]; p=0.004), while those failing after receiving EFV and NVP were less-susceptible to 2Gen-NNRTI (OR=4.4[1.16–14.81]; p=0.02). CRF02_AG was the prevailing subtype (68.31%), without any significant effect on any 2Gen-NNRTI susceptibility.

Conclusion After ART-failure in Cameroon, there is a high-level of cross-resistance to 2Gen-NNRTI. However, etravirine retains residual efficacy in half of the population. Etravirine represents the most suitable 2NNRTI for combination with INSTI as part of long-acting ART, pending a stratified approach to identify eligible patients in RLS.

PA-352

Detectable low-level viremia among people living with HIV in Cameroon suggests a revised threshold for viral suppression: Evidence in the era of dolutegravir-based ART

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Background Transitioning to dolutegravir-based therapy in Cameroon has improved viral suppression (VS) rates, known as low-level viremia (LLV) <1000copies/ml. However, there is a growing number of patients experiencing VS with detectable LLV, indicating risk of virological failure. This study aimed to characterize the distribution of LLV and associated factors in the Cameroonian context.

Methods A laboratory-based study was conducted among treatment-experienced patients monitored for HIV plasma viral load (PVL) from January 2020 through April 2022 at the Chantal BIYA International Reference Centre (CIRCB), Yaoundé-Cameroon. PVL was measured using the Abbott m2000RT-PCR. Among patients with LLV, levels of PVL were stratified into 4 cut-points: <50, 50-200, 201-500, and 501-999 copies/ml, with p<0.05 considered statistically significant.

Results Overall, 14970 patients were enrolled: 72.5% were female; 14219 adults, 466 adolescents, 285 children. By ART-regimens, 3411 were on NNRTI-based, 505 on PI/r-based and 11054 on DTG-based ART. Median [IQR] duration on ART was 36[27-39] months. Overall VS (<1000 copies/ml) rate was 88.8% (13291/14970) (95% CI: 88.2-89.3), and stratification in this population showed 1.5% (207/13291) with 501-999 copies/ml, 3.3% (445/13291) with 200-500 copies/ml, 10.8% (1439/13291) had 50-200 copies/ml, and 84.2% (11200/13291) with <50 copies/ml, p<0.0001. By ART-regimens, detectable LLV (50-999copies/ml) was 13.9% (1540/11054) with DTG-containing versus 14.1% (551/3916) with other ART-regimens, p=0.81. By age, detectable LLV was 13.8% among adults versus 16.9% mchildren/adolescents, p=0.01. Most importantly, the trend overtime of detectable LLV between 50-200 copies/ml increased significantly from 65.2% (534/819) in 2020, 70.7% (678/958) in 2021 and 72.2% (227/314) in 2022, p=0.001.

Conclusion Even though VS rate appears encouraging, there is a significant increasing proportion of patients with detectable LLV in this DTG-era. Of note, LLV with 50-200 copies appears highly predominant, suggesting a revision of threshold for VS at a maximum of 200 copies/ml in resource-limited settings like Cameroon.

PA-357

COVID-19 monitoring in Cameroon reveals men and elderly persons at risk of prolonged duration of positivity: a contribution toward Long-COVID

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Background The novel Coronavirus 2019 pandemic brings about overwhelming demographic, social, and economic damage worldwide. Evidence on disease progression (COVID-19) and viral clearance time remain limited in resource limited settings. Such understanding is crucial for public health control measures at both individual and community-levels. We evaluated the viral clearance of SARS-CoV-2 infection and factors associated with positivity duration in COVID-19 cases in Cameroon.
Methods A prospective cohort-study of SARS-CoV-2 positive cases was conducted from March 2020-October 2021 in Yaounde-Cameroon (representing the first-three waves). RT-PCR was carried out on the participants using nasopharyngeal swabs. SARS-CoV-2 positivity duration was evaluated from the first to last positive PCR-test before a negative result. Epi-info V.7.0 and Graphpad Prism Version 6 was used for data analyses with $p<0.05$ considered statistically significant.
Results A total of 282 participants were enrolled; mean age was 41±14 years, 62.1% were males, and 15.6% (42/282) symptomatic cases with 59.0% (25/42) having cough. The overall median of positivity duration was 15 [IQR: 9-23] days. Positivity duration was significantly higher in males (16 versus 14 days, $p=0.03$) and people aged >40 years (15 versus 14 days, $p=0.02$). Positivity duration was not affected by presence or absence of symptoms ($p=0.80$) and so significant correlation was found with viral load ($r=0.03$; $p=0.61$). Considering baseline (24.7±7.2Ct) and last viral load (29.3±5.9 Ct), the ΔCt (4.6±1.3) and positivity duration (15 days) revealed a kinetic in viral decay of 0.3±0.087 Ct/day.
Conclusion In this African setting, the positivity duration of 15 days is in accordance with viral clearance around 2 weeks for optimal confinement at community-level, with men and/or the elderly experiencing prolonged infection. Given the viral decay (0.3 Ct daily), we suggest personalized control periods in accordance with baseline viral loads.

PA-362

Towards explainable AI-based decision support in predicting SARS-CoV-2 breakthrough infections in a SSA context

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Background Vaccinated persons are still prone to SARS-CoV-2 breakthrough infection since vaccines do not offer 100% protection. Thus, quick decision-making on identifying high-risk persons prone to COVID-19 breakthrough infection is essential for effective medical care and cost saving. We explore how one can use Explainable Artificial Intelligence (XAI) to create a decision-making tool that can aid medical professionals in detecting patients prone of SARS-CoV-2 breakthrough in South Africa and beyond.
Methods A dataset obtained from an intervention study on volunteers with cardiovascular disease (CVD) risk factors conducted in Cape Town, South Africa, comprising symptoms and feedback from 257 persons — 203 were vaccinated and 54 not — was used for the investigation. Two machine learning algorithms: Deep Multilayer Perceptron (Deep MLP) and the XGBoost classifier were trained on the dataset. The Shapley Additive Explanations (SHAP) was used to investigate the most critical variables influencing breakthrough infection from the ML models' results. Lastly, a decision-support tool for detecting patients prone to breakthrough infection that leverages the ML model with the best results was created.
Results The results show that the XGBoost model performed better (F1= 0.86; AUC = 0.74; G-Mean=0.71; MCC=0.49). Body temperature, total cholesterol, glucose level, blood pressure, waist circumference, body weight, body mass index (BMI), haemoglobin level, and physical activity per week are the most critical variables influencing breakthrough infection.
Conclusion We established threshold values for each of them so that we could classify every new value as either high or low, and used these to construct an XAI model that combines machine learning and rule-based reasoning to predict if a patient is prone to breakthrough and provide a rationale/justification for the prediction made.
Funding: This research was partially supported by a grant from the South African Medical Research Council (SAMRC).

PA-364

Knowledge and reporting of adverse events following childhood immunization among health workers and caregivers at Mengo hospital, Kampala

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Background Although all vaccines used in National Immunization Programmes are safe and effective, no vaccine is completely risk-free and adverse events occasionally occur after an immunization. Failure to report adverse events following immunization (AEFI) can lead to death and misconceptions about vaccine safety hence vaccine hesitancy. Alleged vaccine quality and safety issues must be dealt with rapidly and effectively. This study assessed level of knowledge and reporting of AEFI among healthcare workers and caregivers at Mengo Hospital, Kampala.
Methods A health facility-based mixed-methods cross-sectional study design was used. Eligible participants were caregivers of children and healthcare workers. Qualitative data were collected through self-administered questionnaires. Focus group discussions (FGDs) among caregivers and Key informant interviews (KII) among healthcare workers collected data on knowledge and reporting procedures of AEFIs. Level of knowledge of AEFI was assessed using the Likert scale and logistic regression was used to analyse the association of different factors with reporting of AEFI. Qualitative data were analysed manually into themes.
Results A total of 388 participants enrolled with mean age (SD) of 28.75 (5.65) years and 51.8% were female. Over two-thirds (61.3%) had poor knowledge about AEFIs. Less than half (41.8%) had ever reported an AEFI to the hospital. Unemployment (OR= 1.628), good knowledge of AEFI (OR=1.572), and parity less than four (OR= 2.070) were found to increase odds of reporting of AEFIs. From the 7 KII and 6 FGDs, we found that most healthcare workers and caregivers had good knowledge of AEFIs but the majority had never reported nor knew the procedure for reporting of AEFI.
Conclusion The reporting of AEFIs was low among caregivers in Kampala. There is need to sensitize caregivers about the necessity to report AEFIs.
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PA-372

Evaluation of the prevention of mother-to-child transmission of HIV programs at the second immunization visit in Burkina Faso and Zambia, countries with different HIV epidemics

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Background Monitoring indicators for prevention of mother-to-child transmission of HIV programs (PMTCT) is key to assessing the progress toward elimination of mother-to-child transmission (MTCT) of HIV. Using a patient-orientated innovative strategy based on the second visit in the expanded program on immunization (EPI-2) visit at 6-8 weeks, we assessed PMTCT indicators in Burkina Faso and Zambia.
Methods From December 2019 to September 2021, the PROMISE-EPI study (Clinical Trial: NCT03870438) assessed women attending EPI-2 at primary health care facilities in Burkina Faso and Zambia with their children about their exposure to PMTCT interventions. Women living with HIV viral load was measured using GeneXpert® HIV RNA, and their children were tested for HIV using GeneXpert® HIV Qual.
Results Overall, 25093 were enrolled from Burkina Faso and 8961 women from Zambia. Almost, all women attended at least one antenatal care visit, the median number of visits was 4 (IQR: 3-5) in both countries. Among Women diagnosed with HIV at EPI-2, 4.5% and 1.7% were not aware of their HIV status, in Burkina Faso and Zambia, respectively. Among those aware of their HIV positive status, 95.8% and 99.2% were on ART in Burkina Faso and Zambia respectively. Among WLHIV on ART, 75% and 79.2% achieved a viral load suppression (Viral load < 1000 copies/mL) in Burkina Faso and Zambia respectively. Infant post-natal prophylaxis was administered from birth until EPI-2 to 60.9% and 89.7% of HIV exposed children in Burkina Faso and Zambia, respectively. In Burkina Faso, only 60/192 (31.3%) of HIV exposed children were sampled for early infant diagnosis and 3 (1.6%) received a result by EPI-2. In Zambia, these figures were 879/1465 (64.0%) and 9.9% (145/1465) respectively.
Conclusion This evaluation strategy could strengthen program monitoring and help identifying gaps to be addressed on the last mile towards elimination of MTCT of HIV.

PA-375

Feasibility of a programmatic mass drug administration campaign for malaria in Southern Mozambique

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Background Malaria Mass Drug Administration (MDA) is recommended to reduce malaria in low transmission settings, with a target coverage of ≥80%. This study assesses the feasibility of a programmatic MDA (pMDA) pilot implementation in southern Mozambique.
Methods The National Malaria Control Programme implemented pMDA in Chidenguele (Gaza Province), where the estimated population is 59,271. Two rounds of door-to-door distribution (using satellite maps with previously enumerated households (Reveal® platform)) with fixed points were conducted between December 2022 and February 2023. Household coverage was estimated with both district census data and satellite number of expected households. All eligible individuals ≥6 months received a full therapeutic 3-day-course of dihydroartemisinin-piperaquine. Individual data collection was conducted during round 1 (R1), which was changed to aggregated data at the household level in round 2 (R2). Community engagement and human resources were also strengthened between the two rounds. The target number of households to be reached by team/day was 25/30 in R1 and 15 in R2.
Results When using census data, household coverage (households reached over targeted) increased from 59.4% (8799/14818) in R1 to 94.3% (13972/14818) in R2, while with the satellite estimates, it increased from 62.5% (8799/14075) to 99.3% (13972/14075). Population programmatic coverage (individuals treated over total population) increased from 40.9% (24237/59271) to 69.8% (41347/59271). Treatment rate among present individuals (operational coverage) decreased from 91.3% (24237/26541) to 85.1% (41347/48588).
Conclusion Collecting aggregated data, decreasing the household target per day per team and using fixed-points at the end as a recovery strategy helped improve operational performance. However, reaching an 80% programmatic coverage is challenging even with high rates of household visitation and operational coverage, mainly due to absences and exclusions.
Funding: This project is funded by the EDCTP2 Programme.

PA-378

Implementation research outcomes of a programmatic mass drug administration campaign for malaria in southern Mozambique: results from a community and health staff survey

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Background Mass Drug Administration for malaria consists of administering antimalarial drugs to the whole population in a defined area, irrespective of infection status. The World Health Organization recommends it to reduce transmission in low transmission settings. To ensure that MDA is effective, at least 80% of the target population should be reached.
Methods Between December 2022 and February 2023, two rounds of programmatic MDA (pMDA) were implemented by the Mozambican National Malaria Control Program in the administrative post of Chidenguele (Manjacaze district, Gaza province), where the estimated population is around 59,000. To evaluate the coverage, adherence, acceptability, adoption and appropriateness of the pMDA delivery strategy, a cross-sectional community survey and a survey to the health staff involved in the implementation were conducted.
Results Data routinely-collected during the pMDA show that population programmatic coverage (individuals treated over total population) was 69.8% (41347/59271), while according to the cross-sectional survey, 73.9% (569/770) of respondents reported having taken the medication. 84.2% (648/770) of community respondents thought that the campaign could help decrease malaria in the community, and 91.3% (703/770) thought that taking the medication regardless of malaria infection was acceptable. Among community respondents that were aware of the pMDA campaign (686/770), 76.5% (525/686) stated they knew about its objectives. 88% (22/25) of surveyed health staff reported to be very willing to collaborate and comply with procedures and with the intervention prior to the start of the implementation and 73.1% (19/26) agreed that the designed intervention was adequate to meet the objectives of the program.
Conclusion Overall, the pMDA delivery strategy was accepted by both the community and the implementers. Community and stakeholder engagement were essential to ensure a successful campaign implementation.
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PA-379

Effect of soil-transmitted helminth infections on haemoglobin level in Plasmodium infection among children and young adults living in rural areas of Gabon, Central Africa

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Background Plasmodium infection remains a public health issue in endemic areas, with anaemia being one of the main indicators of disease morbidity. In areas co-endemic for helminths, both infections very often occur in the same individual and interactions have been reported. The present analysis aimed to assess the effect of helminth infections on haemoglobin concentration in Plasmodium infection in a population of children and young adults living in rural areas of Gabon.
Methods The study was longitudinal where participants were followed for six months. Urogenital schistosomiasis (UGS), soil-transmitted helminths (STH), and filariasis were assessed by microscopy at baseline and at month six. Plasmodium infection status and haemoglobin concentration were assessed at month six, only. Anaemia was defined using the recommendation of the WHO.
Results A total of 217 participants were included in this analysis. Of them, 73% (160, 95%CI: 67–79) were anaemic. Anaemia was associated with Plasmodium infection (p-value=0.04), but not with UGS (p-value=0.12), STH infection (p-value=0.16), and filariasis (p-value=0.59). Adjusted to age, sex, ascariasis, and UGS, participants with Plasmodium infection had an odds of 2.44 (95%CI: 1.07–6.13) of anaemia, compared to those without Plasmodium infection. In the stratified analysis on STH and adjusted to age and sex, participants with Plasmodium infection had a significant decrease in haemoglobin concentration as compared to those without (β= -0.90, 95%CI: -1.36 – -0.43, p-value<0.001) among participants infected with STH, while no difference was observed between both groups among participants negative for STH (p-value=0.051).
Conclusion Our results reveal a high prevalence of anaemia making it a serious public health issue in our community. We found Plasmodium infection as the main parasitic infection associated with anaemia in our community, with STH infections showing a protective effect on the reduction of haemoglobin concentration in Plasmodium infection.
Funding source: Deutsche Forschungsge-meinschaft (DFG), grant number: MO 1071/12-1.

PA-380

Advancing rights-based knowledge production in sexual and reproductive health by early-career researchers for advocacy: experience of implementation of a mentorship program in francophone Africa

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Background Few early-career researchers are working on rights-based knowledge production in sexual and reproductive health (SRH) in francophone Africa. To accelerate the generation and dissemination of evidence in the field of SRH and rights, young researchers need support. One form of support is the setting up of a mentorship program embedded in a researchers' network.
Methods We designed and implemented a mentorship program aiming to produce six original articles in SRH with a right-based perspective. Articles accepted were published in a special edition of a specialized peer review journal. The process included design and strategic dissemination of call for applications, three-stages selection process of mentees, identification of mentors according to the research topic of the mentees and building of six mentor-mentee dyads. It was completed by competency-based trainings on scientific writing and advocacy (in-person workshop and webinars), in-person/remote meetings and email exchanges between each mentee-mentor dyad and internal peer-review of manuscripts before submission to the journal.
Results We selected six mentees (four women and two men) with medical, midwifery, demography and social sciences background. Their mean age was 35.2 and only two published a paper as first author. The addressed topics were related to identity effects of differential gender socialization on first child and marriage aspirations of adolescents, delivery experience, modern contraception use among adolescents and abortion. All the manuscripts are currently in the peer-review process for publication. The research results will be used to support advocacy activities in each context.
Conclusion This mentorship program provides early-career researchers with research and advocacy skills. The network set up is an enabler for the continuous production of knowledge and its effective use to drive change for the benefit of the region's communities.

PA-382

Trends in sulfadoxine-pyrimethamine resistance molecular markers among Plasmodium falciparum isolates before and after adopting seasonal malaria chemoprevention in Nanoro, Burkina Faso

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Background Despite various efforts to control malaria among children, the disease remains a leading cause of morbidity and mortality worldwide. In the Sahel region, including Burkina Faso, seasonal malaria chemoprevention (SMC) using Sulfadoxine-Pyrimethamine (SP) and Amodiaquine has been implemented since 2014. However, introducing this new strategy may lead to the spread of Plasmodium falciparum resistance to SP. This study analyses the mutations in SP resistance genes, dihydrofolate reductase (Pfdhfr) and dihydropteroate synthase (Pfdhps) before and after adopting SMC in Burkina Faso.
Methods Dried blood spots obtained from previous studies conducted in Nanoro from 2010 to 2020 were randomly selected. Out of this selection, 769 Plasmodium falciparum isolates were retained, with 299 collected between 2010-2012 before the SMC adoption and 470 collected between 2018-2020 after the SMC implementation in 2014. The Pfdhps and Pfdhfr genes were amplified using nested PCR, and mutations that confer resistance were identified by sequencing the resulting products.
Results The prevalence of Pfdhfr triple mutations (CIRNI) increased from 44.4% before the adoption of SMC to 84.4% following its implementation ($p<0.0001$). There were no mutations at codon Pfdhps 540; those at Pfdhps 581 remained rare and were reported exclusively after the SMC implementation (2.8%). The prevalence of haplotypes observed for the Pfdhps gene did not differ significantly over time. However, the Pfdhps haplotype quadruple mutant VAAKGS recently reported in Nigeria was found only in 2020 (1.4%). The combined Pfdhfr/Pfdhps quadruple mutant IRN/AAKA was the most common and increased following SMC implementation (44.9% vs 16.5%; $p<0.0001$).
Conclusion After the SMC implementation, the prevalence of Pyrimethamine resistance markers increased significantly, while no difference was observed for Sulfadoxine resistance markers. Nevertheless, the detection in 2020 of the emerging Pfdhps haplotypes highlights the need to monitor SP resistance continuously.
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PA-383

Comorbidity-related inequality in COVID-19 deaths in Eastern Uganda: Implications for priority setting for equitable access to pandemic vaccines

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Background Evidence-based priority setting for accessing vaccines optimises the impact of roll-out during pandemics. However, in low-resource settings, policy decisions are less informed by evidence.
Methods We collected retrospective (April 2020 – March 2021) and prospective (April – September 2021) data at Mbale and Soroti Regional Referral Hospitals in Eastern Uganda. The study received ethical approval from Mbale Regional Referral Hospital Research Ethics Committee (MRRH-REC) and Uganda National Council for Science and Technology (UNCST). We computed risk ratios to assess the risk of mortality associated with lack of vaccination and the presence of comorbidity. We also estimated the Concentration index along the gradient of increasing comorbidities. We used STATA version 17 for data analysis.
Results We included 1847 hospitalised patients with a Polymerase Chain Reaction (PCR) confirmed COVID-19. The majority (94% [1736/1847] were adults (≥18 years) and males (1108/ 1847 (60.0%). Generally, over a quarter (34.5% [637 / 1847]) had at least one comorbidity, and it was common in adults (97.5% [621/637]. Common comorbidities were Hypertension (322/1847 [17.4%]), Diabetes Mellitus (214/1847 [11.6%]), Malaria (85/1847 [4.6%]), HIV (19/1847 [1.03%]) and Tuberculosis (5/1847 [0.27%]). Mortality was 16.2% [300/1,847] and increased with comorbidities (no comorbidity:100/300 [33.3%]), any one comorbidity: 125/300 [41.7%]) and multiple comorbidities: 75/300 [25%]). Mortality was more concentrated in the group with multiple comorbidities (Concentration index: -0.33, $p=0.000$); (RR: 3.8 [95% CI: 3.04, 4.73). The uptake of safe and efficacious vaccines was at 2.1% [38/1,824], but vaccine uptake lowered the risk of mortality by 11% (RR: 0.89 [95% CI: 0.45, 1.75].
Conclusion Comorbidities and mortality were rare in patients below 18 years. In Uganda, adults aged 18 years and above with comorbidities were prioritised in the fifth position for vaccine access. During priority setting for COVID vaccines, more weight should be allocated to comorbidity status.

PA-384

Lassa fever vaccine trial preparedness: preliminary findings of a targeted community-based epidemiologic study in Nigeria

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Background Developing a vaccine to prevent Lassa Fever (LF), caused by Lassa virus (LASV), is a World Health Organization priority. We describe preliminary findings of a LASV epidemiologic study in Nigeria to inform preparation for CEPI/EDCTP funded phase 2 LF vaccine trial.

Methods We conducted a community-based cross-sectional study at 10 randomly-selected primary healthcare centers in Abuja Municipal Area Council (n=6) and Ikorodu (n=4). A total of 630 participants aged ≥ 18 years were enrolled between February-September 2022. Socio-demographics, willingness to participate in a future LF vaccine trial, and knowledge of LF were assessed in questionnaires. Blood and urine samples were collected for laboratory analyses, including LASV antibody assays using Zalgen ReLASV Pan-Lassa Combo NP/Prefusion GP IgG/IgM ELISA kits.

Results Of 630 participants, 434 (69%) were female and the median age was 38 years (interquartile range 28-50). LASV IgG seropositivity was detected in 51 of 176 (29.0%) participants so far tested; further testing is underway. Most participants (87%) were knowledgeable about LF and radio/television was the most commonly reported source of information (63%). Willingness to participate in a future LF vaccine trial was affirmed by 580 (93%) participants and 99.7% (574/576) were willing to provide biological samples. Potential protection from LF was the most common reason for willingness to participate (78%). Among 22 (4%) unwilling participants, the most common reason was fear of harm by the vaccine (36%).

Conclusion Our findings suggest substantial LASV exposure and eagerness to participate in a LF vaccine trial in two Nigerian locations with previously limited epidemiologic data. Radio and television-based messaging that emphasizes the safety of vaccine trial participation and the potential protective value of a licensed LF vaccine may improve recruitment for the imminent phase 2a LF vaccine trial in Abuja, Nigeria.

PA-386

High exposure to SARS-CoV-2 in rural Southern Mozambique after 4 waves of COVID-19: community-based serosurveys

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Background In the same month the WHO declared COVID-19 a pandemic (March 2020), the first case was reported in Mozambique, and by April 2023 the country had seen four waves of COVID-19 233,334 with cumulative positive cases and 2,242 deaths. We conducted community-based serosurveys in the Manhiça district to assess the evolution of exposure after successive COVID waves.

Methods Four seroepidemiology surveys separated by ~3 months were conducted between May 2021 and June 2022. In each, 1,200 individuals residing in Manhiça District were randomly selected from the Demographic Surveillance System, stratified equitably into four age groups (0-19, 20-39, 40-49, ≥60 years). Blood samples were collected and analyzed by commercial Elisa kit (Wantai) for the detection of total antibodies (IgM and IgG).

Results Overall, 4,579 participants had blood samples collected, of which 3,346 were tested. The prevalence of SARS-CoV-2 antibodies increased over time from 27.6% (184/666) in serosurvey one to 63.6% (595/936) (p: <0·001) in serosurvey two, reaching 91.2% (700/768) (p: <0·001) and 91.1% (1017/1117) (p: 0·941), in the third and fourth serosurveys, respectively. Higher antibodies detection was observed among individuals aged 20-39 years in serosurveys one, three, and four (32%, 96.1% and 94.3% respectively), but age group 40 – 59 years during serosurvey two (66.8%). A high seroprevalence (85.7%; 156/182) was still observed among individuals who had not been vaccinated at the time they were enrolled in serosurvey 4. The pattern of increasing seroprevalence was related to the occurrence of COVID-19 waves.

Conclusion Our data demonstrate increased seroprevalence levels after each serosurvey from 27% to 91%, showing universal exposure to SARS-CoV-2 of the general population residing in the Manhiça District after four COVID-19 waves. High seroprevalence were also observed among unvaccinated and vaccine ineligible (<18 years) individuals reaching over 90% at the last serosurvey.

PA-388

Placement for transformative clinical trial skills to sustain chain reaction-like model of expanding human capital for accelerating development of safe, efficacious, accessible and affordable anti-Tuberculosis

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Background High burden of Tuberculosis (TB) in Africa justify continued need for development of safe, efficacious, accessible and affordable anti-TB. Paradoxically, the continent contributes <3% of global clinical trial outputs. Lack of appropriate trainings has been cited as important factor. Therefore, this project aimed to strengthen capacity of the fellow and peers in clinical trial designs, operational planning, conducting, management and reporting.
Methods EDCTP funded and linked the fellow to Pan-African Consortium for Evaluation of Antituberculosis Antibiotics (PanACEA) at University of St. Andrews. The fellow and supervisors developed 12 months training plan with five objectives fitting precisely into the ongoing SimpliciTB-OptiRiMoxTB trial to evaluate short treatment regimen for drug-susceptible TB. Intensive field work activities have been conducted at Kibong'oto Infectious Diseases Hospital-Tanzania, followed by National Health Services (NHS) Scotland, Helse-Nord TB-Initiative (HNTI)-Malawi and other PanACEA sites. The fellow attended meetings including PanACEA Annual 2022 meeting and The Union World Conference on Lung Health.
Results Skills of clinical trial designing and operational planning were imparted during development of OptiRiMoxTB protocol version 1.0. Developed drug management plan provided skills on handling of investigational medicinal products to ensure quality, safety and efficacy. Obtained ethical and regulatory approvals and reflective report on community engagement during clinical trials transformed the fellow on ethical consideration and safety. Reflective report from experiential visits at NHS and HNTI, in-person Good Clinical Trial training and developed Manual of Procedures have imparted clinical trial conducting and management skills. Developed manuscript of OptiRiMoxTB protocol has strengthen fellow's scientific reporting skills during clinical trials.
Conclusion The acquired transformative skills prepared the fellow for further sustaining chain reaction-like model of expanding human capital with clinical trial skills for TB and other poverty related diseases through short course trainings of almost 100 peers and personal career development hence increasing clinical trials leadership in Africa.

PA-390

Evaluation of the Saline Gargle Collection Method for the Molecular Detection and Sequencing of SARS-CoV-2 in Botswana

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Background Inadequate sampling poses challenges in the COVID-19 diagnostic cycle. Nasopharyngeal swabs are gold-standard but often associated with patient discomfort, require trained healthcare workers (HCW), and are resource intensive. The saline gargle (SG) method has proven to be acceptable for respiratory pathogen detection. We performed a prospective cross-sectional study to evaluate the SG method against the nasopharyngeal and oropharyngeal (NO/OP) method in the molecular detection and next generation sequencing (NGS) of SARS-CoV-2 in Botswana.
Methods Eligible participants aged ≥5 years, who were close contacts of a positive case, and/or presented with clinical symptoms of COVID-19, were recruited December 2021- January 2022, and July-September 2022. NP/OP samples were HCW-collected followed by SG collection where participants swished and gargled 5ml sterile 0.9% saline for 20 seconds. Samples collected December 2021-January 2022 underwent nucleic acid extraction and RT-PCR while samples collected July-September 2022 were tested with GeneXpert SARS-CoV-2 Assay. McNemar exact test was used to analyze comparability of testing with significance set as $P<0.05$.
Post-recruitment, random sampling of 10 lab-confirmed SARS-Cov-2 positive stored sample pairs underwent NGS.
Results Of 127 pairs, 25 matched samples tested positive for SARS-CoV-2 on both sampling methods. Additionally, SG had 6 false negatives and one sample which was positive but negative with NP/OP. Statistical analysis revealed some evidence of a difference in the detection of SARS-CoV-2 between SG and NP/OP samples ($p=0.031$). SG showed an overall sensitivity of 81.25% (95%CI 68.8%-96.0%).
NGS was successful in 16 samples, 10 SG and 6 NP/OP. The 5 matched successful pairs revealed similar genomic strains (73-100% relatedness). All samples had mutations of high affinity to ACE2 receptor in the Spike gene suggesting circulation of Omicron variant.
Conclusion The SG method is a reliable and logistically easier alternative for SAR-CoV-2 detection and NGS to contribute toward efforts of COVID-19 surveillance in Botswana.

PA-391

Self-efficacy of menstrual health and school attendance among Ugandan secondary school girls

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Background Menstrual health (MH) is a public health issue in low- and middle-income countries impacting adolescent girls' education. This study aims to measure MH self-efficacy and its association with school attendance among girls in Wakiso and Kalungu districts of Uganda.
Methods Participants were Secondary 2 girls enrolled in the ongoing MENISCUS cluster-randomized trial evaluating the impact of a multi-component MH intervention on education, health, and well-being outcomes in 60 secondary schools. Baseline data on demographic and socioeconomic status (SES) was collected through a self-administered questionnaire in March-June 2022. School attendance was measured as a girl missing 2 or more school days during the term due to menstruation, MH self-efficacy was measured using the 26-item Self-efficacy in Addressing Menstrual Needs Scale (SAMNS) with scores categorized into tertiles. Logistic regression was used to assess the association.
Results There were 3,673 girls with a median age of 16 years, of which 2,123 (55.8%) were day scholars, as opposed to boarding students, and 762 (20.0%) were of the lowest SES. The prevalence of missing 2 or more days in term due to menstruation was 830 (22.6%). Missing school due to menstruation was associated with lower SES (OR=1.93, 95%CI: 1.57, 2.36), being a day student (OR 1.53, 95%CI:1.31, 1.70), being older than 15 years (OR = 1.62, 95%CI:1.38, 1.89), and attending government school (OR = 1.27, 95%CI:1.08, 1.49). Missing school for 2 or more days due to menstruation was strongly associated with being in lower menstrual health efficacy after controlling for SES, age, student type (day/boarding), household size, and school ownership (Government/Private) (OR=1.68, 95%CI:1.39, 2.04, P=0.0053).
Conclusion Results indicate that lower MH self-efficacy significantly affects girls' school attendance. Missing school results in underperformance in the curriculum and decelerates education for the girl child. Supporting these girls through menstruation could improve self-esteem and promote school completion.

PA-394

Access to diagnosis of bloodstream infections in low-resource settings: evaluation of the improved "Turbidimeter" prototype to detect bacterial growth in manual blood culture systems

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Background In low-resource settings, blood culture bottles (BCBs) are often visually inspected for signs of growth. We developed a "Turbidimeter" to objectively assess growth based on the presence of broth turbidity. The first generation Turbidimeter detected growth in four out of ten bacterial species (i.e. three Enterobacterales and one Streptococcus sp.) in simulated blood cultures inoculated with spiked horse blood. Here, we present the results of the second generation Turbidimeter.
Methods Home-made BCBs (30 ml Tryptone Soy Broth with 0.3 mg/ml sodium-polyanethole sulphate) were inoculated with 2 ml of fresh human blood spiked with 20 different microorganisms (i.e. five Enterobacterales, three non-fermenting Gram-negative bacteria, two staphylococci, one Enterococcus sp., four streptococci, two fastidious organisms and three yeast spp). The BCBs were incubated in Turbidimeter modules inside a conventional incubator for 20-96 hours; measurements were done every 30 seconds. Growth detection was based on the decrease of transmitted and increase of scattered light. We compared growth detection between the first and second turbidimeter generation (improved design with new LED and detector).
Results Growth was detected in 80% of 118 BCBs tested, showing full detection of all enterococci, streptococci, and non-fermenting Gram-negative bacteria (100%), and partial detection of Enterobacterales (84%), staphylococci (88%), fastidious organisms (17%) and yeast (67%). Compared with the first prototype, growth detection improved considerably. Six microorganisms that remained undetected before, were now (partially) detected: 100% growth detection of BCBs with Staphylococcus aureus, Burkholderia cepacia and Pseudomonas aeruginosa and 17% of BCBs with Candida albicans, Haemophilus influenzae and Neisseria subflava.
Conclusion The second generation Turbidimeter showed improved growth detection (17-100% of BCBs) compared with the first prototype. Field testing will be conducted within the EDCTP2-funded SIMBLE project from May 2023 until end of 2024 in Benin and Burkina Faso, to evaluate performance and ease-of-use for future implementation in field laboratories.

PA-401

Demographic surveillance in low-resource settings during COVID-19: Lessons learnt from the Typhoid cluster randomised trial in Ghana

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Background Setting up a robust typhoid demographic surveillance system (DSS) in low-resource areas will help in characterizing, and defining priorities and strategies for typhoid control activities such as the deployment of new conjugate typhoid vaccines. The study describes the DSS methodology, data, strengths and use in achieving high vaccine coverage.
Methods Enumeration areas (EAs) were used as the clusters for the Typhoid Conjugate Vaccine Trial in Ghana (TyVEGHA) study. The existing EA maps had two main limitations: they did not capture the structures and the boundaries were not clearly defined. We employed drones to take spatial pictures of the study area and generated GIS maps with well-defined boundaries. With the GIS maps, enumerators located and enumerated every participant in each structure within a cluster. A census form, developed on Commcare running on tablets, was used to capture the demographic, socio-economic and WASH attribute information of participants and households. For purposes of the mass vaccination, each participant in the study area was given a census identification (ID) card.
Results Overall, demographics of 73,625 individuals (i.e., 55,881 during baseline and 17,744 during the first update) from 15,029 households (13,266 for baseline and 1,764 for first update) were recorded. It was observed that 1,125(1.95%) birth, 343(0.59%) death, 2,219(3.84%) in-migration and 1,101(1.91%) out-migration occurred in the TyVEGHA catchment area between the baseline and first update. The eligible participants for the TyVEGHA trial during the baseline was 22,539/55,881 (40.33%). Due to the robust DSS, we observed a high vaccine coverage rate of 88.36% (20,323) including screen failures. Overall, 4.7% (961 per 20,323) queries were detected and quality control guidelines were used to resolve all queries weekly.
Conclusion Setting-up robust demographic surveillance in low-resource areas is necessary for improving the dearth of reliable data for planning health and socio-economic interventions and achieving high vaccine coverage rates.

PA-404

Neutrophil associated markers in sputum to predict postTB lung impairment

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Background Tuberculosis (TB) is the #1 bacterial killer worldwide. Despite of successful antibiotic treatment, exacerbated patients did not regain sufficient lung capacity and develop postTB lung disease (PTLD). We hypothesized, that neutrophils play an important role in disease exacerbation and associated marker can be used for early detection of PTLD.
Methods 25 confirmed MDR-TB Patients were recruited, sputum samples were taken over 6 months and analyzed for neutrophil associated proteins by ELISA. TB severity was assessed at baseline and month 6 using spirometry (lung function) and x-ray (lung pathology). Patients were categorized in mild and severe diseased by using Ralph score (threshold 40 pts) or spirometry (threshold FVC<0.85*LLN.FVC or gli.FEV1.zscore<-2).
Results 16 patients (64 %) had a stable severe impairment in lung function and no improvement after 6 month was observed. In contrast, x-ray pathology was improving in 10 patients (40 %) and remained stable severe in 10 patients (40 %). Ralph scores were significantly higher in patients with impaired lung function. Neutrophil associated marker significantly declined under antibiotic treatment. Patients with stable severe impairment have significantly increased MMP8 sputum concentrations at baseline ($p = 0.017$) and increased concentrations of Calprotectin ($p = 0.008$), MPO ($p = 0.034$), ELA2 ($p = 0.031$) and NGAL ($p = 0.01$) at week 2. In addition, Calprotectin ($p = 0.005$), MMP8 ($p = 0.011$) and NGAL ($p = 0.03$) concentrations were increased in males at month 4, while no sex differences in x-ray pathology was observed.
Conclusion Early postTB lung impairment was associated with neutrophil proteins in acute TB and elucidate the impact of neutrophils on disease progression and immune pathology. These proteins will be further analyzed as targets for Host Directed Therapies to reduce oxidative stress, tissue degradation, as well as immune modulators to prevent PTLD.
Funding: Funded by German Center for Infection Research

PA-407

Supporting women leadership in global health research

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Background According to WHO only 25% of women in the health workforce are in senior positions. Underrepresentation of women in leadership positions in biomedical research has contributed to gender bias in research questions, study designs, and outcomes. In 2019 IAVI published a report on factors inhibiting women's careers in STEM in Africa with the Academy of Sciences and developed a framework to enhance gender transformative processes in HIV biomedical research.
Methods Building on its previous work, IAVI conducted an operational study across nine of its partner clinical research centers (CRCs) in Africa to understand the barriers and enablers for growth in leadership in 2022. A gaps assessment was conducted through a cross-sectional survey and key informant interviews of male and female staff from nine African partner CRCs in Kenya, Uganda, South Africa and Zambia.
Results Out of the 58 respondents, 65.6% agreed that recruitment at their institutions demonstrate gender parity, but the distribution across disciplines does not necessarily represent gender balance. According to 50%, leadership positions at their institutions are representative of institutional gender make-up. 75.8% agreed that their institution would benefit from additional resources and training for on gender equity and inclusion issues. Key influences women researchers' career choices associated growth in leadership included family responsibilities, socio-cultural biases casting women in supportive roles, unawareness of networking opportunities, and personal perceptions on leadership abilities.
Conclusion Recommendations from the needs assessment are being used to develop targeted strategies to address structural, institutional, and individual mindsets and promote a gender transformative environment within IAVI's CRC partner network under the leadership of a technical working group. The strategies will include awareness creation and sensitization in the workplace, targeted programs including coaching, mentorship and peer learning, as well as targeted support to women enhance women's participation in networking and learning opportunities.

PA-410

Adverse pregnancy and birth outcomes of DTG-based ART regimen roll-out in Ethiopia. A retrospective multicenter cohort study

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Background Dolutegravir (DTG) containing antiretroviral regimen (ART) has been rollout for pregnant and breastfeeding women in Ethiopia since April 2020. However, no data was reported on the new regimen's pregnancy and birth outcome safety.
Methods A retrospective cohort study was conducted in 14 hospitals across Ethiopia. Data were collected from the routine prevention of mother-to-child HIV transmission recording charts and participant medical charts. Eligible participants were HIV Positive pregnant women enrolled in the PMTCT care and later their infants. The primary outcomes were any adverse pregnancy outcome (abortion, intrauterine fetal death, preterm birth, and maternal death) and any adverse birth outcome (stillbirth, early neonatal death, low birth weight, infant death).
Results A total of 2653 pregnant women enrolled in the PMTCT care. Among these, 38 (1.5%) of the pregnancies end up with abortion, 10 (0.4%) intrauterine fetal death and 20 (0.8%) gave birth to a dead fetus. Among the live births, 5 (0.2%) newborns died before one month of age, and 8 (0.4%) died after one month. There were two maternal deaths, one before and one after birth, due to obstetric complications. 87(4.9%) and 80(4.7%) of the women gave birth before 37 weeks of gestation and <2500 gm birth weight, respectively. 55.6% and 29.3% of the women used DTG and efavirenz-containing ART regimens for PMTCT, respectively. The remaining 15.1% used other ART regimens. The rate of adverse pregnancy outcome was significantly lower ($p<0.002$) among women who received a DTG-based ART regimen (2.2%) than efavirenz based (4.7%) or other ART regimens (9.4%). The rate of adverse birth outcome was lowest ($p=0.059$) for DTG (4.7%) compared to efavirenz- based (5.1%) or other ART regimens (6.5%).
Conclusion DTG-containing ART regimens for pregnant women has a better pregnancy and birth outcome safety profile than efavirenz-based or other ART regimens.

PA-415

Challenges in implementing guidelines for CD4 and viral load testing and implications for clinical management of HIV+ pregnant women and their newborns in southern Mozambique

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Background Antiretroviral therapy (ART) for HIV is recommended for all pregnant women on a life-long basis. Despite the critical importance of viral suppression for treatment success, data on virologic results remain limited in Mozambique. Viral load routine testing is crucial to monitor viral suppression. The study aimed to estimate the proportion of HIV-infected pregnant women with CD4 and viral load results and their newborns with PCR in Southern Mozambique.
Methods This cross-sectional study uses retrospective clinical record data from Aug/2019 to Aug/2020 of pregnant women on ART in 11 primary Health Facilities of Manhiça District. We randomly selected 500 paper files for each group, including 399 pregnant women and 417 newborns. Data collection used a structured questionnaire inserted into a Tablet and imported into RedCAP database. Descriptive statistical analysis was performed using SPSS v21.
Results The pregnant women were young (52%), 25-35 years old. The newborns were delivered in the maternity (99.3%) with a mean weight of 3069 (SD=480.7) gr and received Nevirapine prophylaxis (96.6%). A CD4 test was requested in 98.2% of the women; 83.2% had CD4 results, and the mean of CD4 was 468.7 (SD=478.6) cells/mm3. Regarding viral load, 80.5% of pregnant women entered the first antenatal visit on ART, only 19.9% had the viral load test requested, and only 9.8% had viral load results in their clinical files. For PCR, 99.8% of the newborns had the PCR exam requested in their first month of life; 95.4% had the results in their clinical files, and 1.9% were positive for HIV.
Conclusion The study shows low compliance with Viral load monitoring recommendations at the antenatal visit in a context of a high proportion of pregnant women entering the first antenatal visit with ART. Strategies to improve viral load monitoring should be implemented for better care of mothers and newborns.

PA-416

Chronic kidney disease prevalence among antiretroviral therapy naïve patients in Lagos, Nigeria

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Background Antiretroviral therapy (ART) has improved the survival of people living with HIV (PLWH). With improved lifespan, there is increased risk of Non-communicable diseases (NCDs), notably Chronic kidney disease (CKD). This study aims to determine CKD's prevalence and associated factors among ART-naïve PLWH in Nigeria.
Methods This is a secondary data analysis of ART naïve PLWH enrolled over six years (2014 – 2019) at a large treatment center in Lagos. Data collected include sociodemographic characteristics, weight, height, concurrent co-morbidities (hypertension, diabetes mellitus, and tuberculosis), and HIV-specific factors (WHO clinical stage, viral load, and CD4 counts). CKD was defined as an estimated glomerular filtration rate less than 60ml/min/m2 using the three equations [Body surface area corrected Cockcroft Gault (BSA-CG), Modification of Diet in Renal Disease (MDRD), and Chronic kidney disease Epidemiology Collaboration (CKD-EPI)]. Ethical approval was obtained before the study commencement.
Results A total of 2782 PLWH were included in the study, with a mean age of 37.9 (± 9.8) years. A significant proportion of study participants were females (62.2%), had at least secondary school education (58.8%), were married (54.8%), employed (85.7%), and did not consume alcohol (76.6%). Hypertension (21.1%) and tuberculosis (6.1%) were the predominant co-morbidities. A significant proportion of participants were in WHO stages 1 or 2 (55.5%), had CD4 counts less than 500 cells/mm3 (75%), and were virally suppressed (71.7%). The age-standardized prevalence of CKD was 10.0% (8.6 – 11.4), 17.2% (15.4 – 19.0), and 13.1% (11.5 – 14.7) using the BSA-CG, MDRD, and CKD-EPI equations, respectively. Increasing age and anaemia were found to predict the presence of CKD, irrespective of the equation used.
Conclusion The prevalence of CKD is relatively high, and age and anaemia were significant predictors. Therefore, comprehensive care is needed to ensure close monitoring of PLWH for CKD and associated predictive factors.

PA-422

Development and deployment of lateral flow antigen test for COVID-19

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Background The ongoing COVID-19 pandemic, caused by SARS-CoV-2, continues to pose serious threat to global health while devastating world economy and lifestyles. Mass testing is critical in mitigating spread of the disease since it allows for prompt clinical and well-tuned public health interventions. However, the standard test for COVID-19 - based on PCR- requires trained personnel, expensive instruments and reagents, takes hours to provide results and is often available only in centralized laboratories. This limits the number of tests that can be done, especially in low- and middle-income countries. Thus, there is an urgent need for rapid point-of-care diagnostic tests. In this regard, we are developing a lateral flow antigen test which we envisage will be affordable, easy to use and will not need skilled personnel, expensive reagents nor machines.
Methods We are leveraging on an innovative high-throughput wheat germ cell free expression system to generate several COVID-19 antigens derived from locally circulating SARS-CoV-2 sequences. Using these antigens, we shall produce monoclonal antibodies in mice and the most efficient capture and detector pairs of antigen specific antibodies will be mounted on lateral flow test strips. We shall then evaluate the implementation outcomes- feasibility, acceptance, and cost effectiveness and user friendliness- of the lateral flow antigen test to inform adaptation and future scale up.
Results These results are preliminary. We have generated five contextualised COVID-19 (RBD, S, N, M and E) antigens. Production of monoclonal antibodies for use in lateral flow antigen test is ongoing. Data on test reliability and implementation outcomes will be shared in due course.
Conclusion Our development will facilitate ramping up of testing even in resource-constrained settings. Additionally, this venture will strengthen the domestic capacity in diagnostic technology for COVID-19 and other emerging infectious diseases since the prototype could be readily adapted to any emerging pathogen.

PA-424

The INTEGRATE Study: an adaptive platform trial for the development of new interventions to combat Lassa Fever in West Africa

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Background Lassa fever (LF) is a viral haemorrhagic fever responsible of 5000 deaths per year in West Africa, with in-hospital mortality at 12%. Ribavirin is the only treatment available with worrying toxicity, questionable efficacy and low access because of its high cost. Consequently, there is an urgent need for new drugs to treat LF patients.
Methods The INTEGRATE study is a platform, multinational, multicentre, sequential, seamless phase II-III, controlled, randomised, superiority trial in open-label parallel arms. Its primary objective is to compare the efficacy of each Investigational Medical Product (IMP) to Standard of Care Drug (SCD) to prevent death or organ failure in hospitalized patients with confirmed LF. The primary endpoint is the proportion of patients presenting no clinical aggravation between D0 and D14. All hospitalized patients, including pregnant women, are eligible for enrolment. The total follow-up period is 28 days. Three interim analyses are planned, with a total study population of 218 patients per arm. A co-sponsorship will be assumed by ANRS-MIE and the Irrua Specialist Teaching Hospital (ISTH).
Results Trial inclusions will begin in Nigeria in April 2024 at the Federal Medical Centre Owo and at ISTH. Other West African sites (Liberia, Benin, Guinea and Nigeria) will join the platform as they complete a site preparedness program currently undergoing. The first IMP to be evaluated will be the repurposed drug Favipiravir, compared to the SCD Ribavirin. The second IMP will probably be the antiviral ARN 75039, which has shown promising results in pre-clinical phases and is currently in phase I evaluation.
Conclusion The ribavirin treatment for LF is still debated in term of safety, efficacy and affordability. The INTEGRATE study will provide evidence on new drugs efficacy in order to treat patients and reduce the burden of LF.
Funding: Acknowledgment to EDCTP for funding this study.

PA-425

Educational experiences, needs, and impact among children and adolescents living with HIV in the Kilimanjaro region in Tanzania

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Background Early HIV testing and treatment is crucial to the survival and long-term well-being of children and adolescents living with HIV. In Sub-Saharan Africa, the risk of HIV transmission and infection among children and adolescents, especially young girls is high. Tanzania adopted the test and treat, where all children and adolescents who tested positive for HIV are initiated into care, though adherence to medication and viral suppression is challenging. Strategies to overcome adherence challenges include education provisions at the clinics. In this study, we assessed the educational content provided, the needs of children and adolescents, and its impact on viral load suppression (VLS).
Methods A cross-sectional study was conducted among 286 children and adolescents living with HIV on ART in Kilimanjaro, Tanzania. Socio-demographic characteristics, clinic educational contents, and viral load results were collected using semi-structured questionnaires. Numerical and categorical variables were summarized using descriptive statistics. We compared the educational contents and adherence with VLS using chi-square tests to find the difference between groups.
Results Among 286 participants recruited: 142 (33.3%) were children and 143 (33.4%) were adolescents. Their median age was 9 (7-12) and 18(16-18), and there were 145 males and 141 females. Among 101 who received education content at the clinics, 68(67%) received education on the importance of taking medication and improving adherence. Of those who received adherence education 48(71%) had VLS while 22(69%) of those who never received adherence education were suppressed(P=0.852). Other 141 children and adolescents reported needing educational seminars at the clinics on adherence, safe sex practices, reproductive health education, and entrepreneurship.
Conclusion Continuous education provision at clinics is vital to improve health and adherence among children and adolescents. Further strategies to incorporate health education in clinics should be implemented even with little evidence of improving VLS from this study.

PA-426

Genetic profiling of molecular markers of antimalarial resistance in areas targeted for school-based malaria chemoprevention strategies in North-Eastern, Tanzania

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Background Recently, WHO has recommended expansion of the malaria preventive chemotherapies to include intermittent preventive treatment of school children (IPTsc). However, there is concern due to the emergence and spread of partial artemisinin resistance based on PfKelch13 mutations in Eastern Africa. This study was conducted to determine the baseline prevalence of molecular markers of artemisinin-based combination therapies (ACTs) and Sulfadoxine-Pyrimethamine (SP) resistance prior to implementation of IPTsc intervention in a highly malaria endemic area.
Methods Pre-intervention assessment of the prevalence of molecular markers of artemisinin, partner drugs, SP resistance and Histidine Rich Protein 2/3 (HRP 2/3) genes deletion was conducted in Handeni and Kilindi districts from July 2020-December 2021. The districts implemented programmatic IPTsc trial using Dihydroartemisinin-Piperaquine. Dried Blood Spot were collected from children (5-15 years). DNA was extracted from malaria positive samples using commercial kits. NGS sequencing was used for the analysis of molecular markers.
Results Out of the SNPs detected at low frequency in the Pfkelch13 gene (A578S, K568T, N489Y), none have been validated as molecular markers of artemisinin partial resistance, majority 95.5% (340/356) was the wildtype. The majority of Pfcrt haplotype (n=356) was CVMNKTHFIMCGI (75.5%), other occurred at low frequency, CVIETTHFIMCGI (11.8%), CVIETTHFIMCGT (7%), SVMNTTHFIMCGI (0.8%), SVMNTTHFIMCGT(2.2%). Pfmdr1 haplotypes (n=355) NYSND (71.5%) and NFSND (20.6%) were predominant; others were at low frequency. Quintuple Pfdhfr-Pfdhps haplotypes (n=134) was at high frequency (70.1%). Parasites with HRP2 and 3 gene deletion was detected in 4.5% (15/335) and 20.9% (70/335), respectively.
Conclusion The lack of validated artemisinin resistance markers is reassuring and confirms targeted areas are suitable for malaria chemoprevention implementation. The baseline assessment is essential in implementing drug resistance monitoring during scaling up of the IPTsc intervention.
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PA-431

Schistosome's infection among pregnant women in the rural highlands of Madagascar: a call for public health interventions in neglected vulnerable populations

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Background Schistosomiasis is a waterborne disease with high morbidity in Sub-Saharan Africa countries, including Madagascar. Mass drug administration is the main public health control strategy for the disease. Even though recently recommended to all age groups and pregnant women, school-aged children are most targeted due to a lack of prevalence data on other vulnerable populations, including pregnant women. This study has the objective to estimate the prevalence of Schistosome's infection in pregnant women in the highlands of Madagascar to inform the control strategies in the country.
Methods This cross-sectional study was conducted using baseline data on pregnant women enrolled in a cluster randomized controlled trial freeBILy (fast and reliable easy-to-use-diagnostics for eliminating bilharzia in young children and mothers). Women were recruited between April 2019 and February 2020 at one of the 42 included Primary Health Care Centers when attending routine antenatal care services during the second or third pregnancy trimester. The urine-based UCP-LF-CAA (Up-Converting Phosphor – Lateral Flow) test was used for the detection of Schistosome infections. The prevalence was estimated for the overall sample and stratified by women characteristics.
Results A total of 4328 urine samples were collected. Of these, 55.9% [CI95%:53.6-58.2] were positive for Schistosome's infection. The prevalence of Schistosome's infection was 55.0% [CI95%:52.9%-57.0%] among pregnant women living in rural settings, 62.2% [CI95%:53.3-70.4] among those with no formal education, and 54.4% [CI95%:52.2-56.6] among those working as farmers. The prevalence increased with age, ranging from 51.6% (CI95%:48.7-54.4) among 16-19 years old to 62.3% (CI95%: 59.4-65.1) among 30-49 years old.
Conclusion Our study shows a high prevalence of Schistosome's infection among pregnant women in the rural highlands of Madagascar. Public health interventions including pregnant women are urgent to progress toward the elimination of schistosomiasis as a public health problem by 2030.

PA-435

Long-term immune response in children vaccinated with BK-SE36/CpG blood stage malaria candidate vaccine in a malaria hyperendemic and seasonal area of Burkina Faso

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Background BK-SE36/CpG is a lyophilized formulation of recombinant Plasmodium falciparum serine repeat antigen 5 adsorbed to aluminium hydroxide gel and reconstituted with the TLR9 adjuvant, CpG-ODN (K3). In the primary study in malaria-exposed adults and children living in Burkina Faso, the vaccine showed acceptable safety and immunogenicity profile. The 5-10 years old cohort was chosen for a follow-up study to evaluate the long-term persistency of the immune response.
Methods In the primary trial, participants were randomized to receive three doses of either BK-SE36/CpG or the control vaccine at 0, Week 4 and 16. The trial was completed in January 2020 (Day 365). The follow-up study consisted of a single visit conducted 3 years after enrolment (~24 months following D365). All children who participated in the 5-10 years-old cohort were invited for a short medical examination and a blood sample was collected for parasitological and immunogenicity measurement.
Results 44 children out the 45 in the primary trial provided consent for the follow-up study. The proportion of children with detectable anti-SE36 IgG titres in the BK-SE36/CpG arm as compared to the control arm remained high (82.8% vs. 46.7% in control group). The differences in the geometric mean of anti-SE36 IgG titers were statistically significant for vaccine arms at any timepoint: D140 (4 weeks after Dose 3: $p<0.001$), D365 ($p<0.001$) and Year 3 ($p=0.039$). Compared to baseline, antibody titres were 60 and 3.6 times higher at D140 and Year 3, respectively.
Conclusion BK-SE36/CpG induced high level of antibody responses in 5-10 years-old. The antibody response persisted/or remained high at Year 3. There were some indications that the antibody response can be boosted by natural infection, which may explain the sustained level of antibody titres obtained in this follow-up study.

PA-441

Establishing an enabling environment for women's participation in HIV prevention trials among hard-to-reach fishing communities along Lake Victoria Uganda

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Background Women are disproportionately affected by HIV/AIDS in Sub-Saharan Africa. Women's participation in HIV prevention research is associated with men/spousal influence. The willingness of women to participate in HIV prevention research is challenged by negative influences from the male fraternity as primary decision-makers. The UVRI-IAVI HIV Vaccine Program (UVRI–IAVI) engaged both low and high-risk women in HIV vaccine trials and epidemiological preparedness studies. We document experiences of engaging women in HIV prevention research among fishing communities in Uganda.
Methods From 2002-2022, Good Participatory Practices (GPP) plans provided a framework of activities that aimed at enhancing male support for women's participation in research. Community gate keepers and male targeted platforms of engagement were implemented. Women supported disclosure packages, community based male champions of women's participation, and spousal invitations for HIV risk reduction and appreciation at the research site were conducted. Games and sports activities involving men were organized as advocacy platforms with free treatment extended to spouses and children. Tokens of appreciation benefitting families were offered to female participants at different milestones in studies. Myths and misconceptions surrounding women participation were addressed in communities.
Results Between 2002-2022, improved trends in women enrolment and retention were registered when their spouses were involved. Community based structures for male champions promoting advocacy for women participation in research have been established. General community appreciation for women HIV risk and vulnerability assessment form a basis for their consent to women participation in research with emerging trends in adult advocacy for women's participation in HIV prevention research.
Conclusion Advancing women participation in research greatly contributes to the global HIV research efforts for new HIV prevention options.

PA-443

A decade of trends in HIV infection among pregnant women in southern Mozambique

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Background Monitoring HIV infection rates is needed to guide health interventions and assess their impact, especially in highly vulnerable groups to the infection such as pregnant women. This study describes the trends of HIV infection over 10 years in pregnant women attending antenatal care (ANC) clinics in southern Mozambique.
Methods Data collected as part of three studies undertaken between 2010 and 2021 in HIV-infected pregnant women attending the ANC clinic were analysed. HIV incidence was estimated between prevalence points using two validated methods, one based on mortality rates and the other on survival information after HIV infection. Trends over time were obtained by fitting a second-order orthogonal polynomial regression model.
Results Overall, 10392 pregnant women attending their first ANC visit were included in the analysis. There was a decrease of the HIV prevalence from 33.9% (95% CI: 30.9-36.9%) in 2010 to 21.4% (95% CI: 19.6-23.2%) in 2021, after a peak of 35.3% (95% CI: 30.1-40.8%) in 2016. Regarding maternal age, prevalence of infection was highest in women aged 20-25 in 2010 progressively increasing in older women being the highest in 35-40 year old women in 2021. HIV infection incidence increased from 3.7 per 100 person-years during 2010-2016 to 10.1 per 100 person-years in 2018-2019, decreased to 6.2 per 100 person-years in 2020-2021.
Conclusion In the last decade, there was an initial increase of the prevalence and incidence of HIV followed by a downward trend, in this area of southern Mozambique. This encouraging trend may be attributable to the massive expansion of antiretroviral therapy during 2010-2021 in Mozambique. However, the burden HIV remains unacceptably high in this particularly vulnerable group, calling for a need to strengthen HIV preventive strategies to ending HIV/AIDs in the country.

PA-446

Advanced HIV disease package implementation during community-based active TB-case finding

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Background A package of care reduces mortality from advanced HIV disease (AHD) but is poorly implemented. We are assessing feasibility of its implementation, using point-of-care Omega VISITECT CD4 (VISITECT) to identify CD4>200cells/µL or ≤200cells/µL, within two TB-triage studies in South Africa and Lesotho. During near-facility passive case-finding (TB TRIAGE+ ACCURACY, n=1,392), implementers found AHD package implementation feasible, despite challenges. Here, we report feasibility and outcomes during community-based active case-finding within the ongoing TB TRIAGE+ TRIAL (current n=3,304).

Methods All people living with HIV (PLHIV) are offered VISITECT testing, and if CD4≤200cells/µL a urine Alere Determine tuberculosis lipoarabinomannan (TB-LAM) and Immy cryptococcal antigen (CrAg) test. Same-day community initiation of anti-retrovirals, cotrimoxazole and TB-preventive therapy is provided. We assessed procedural compliance and have conducted one group discussion with implementers in South Africa.

Results Between September 2022-April 2023, in South Africa and Lesotho respectively, 416/1306 (31.9%) and 439/1998(22.0%) of enrolled participants were PLHIV, among whom 16/416 (3.8%) and 20/439 (4.6%) newly diagnosed. In South Africa and Lesotho respectively, 331 (79.6%) and 368 (83.8%) among PLHIV received VISITECT, and in 23 (6.9%) and 32 (8.3%) VISITECT indicated CD4≤200cells/µL. In South Africa and Lesotho respectively, TB-LAM was performed in 23/23 (100%) and 32/32 (100%), and CrAg in 23/23 (100%) and 30/32 (93.8%). TB-LAM and CrAg were positive in 1 (4.3%) person in South Africa. Since April 2023, VISITECT testing was interrupted following batch recall due to suboptimal specificity. The main challenges reported (long procedural duration and results reading of VISITECT) reflected findings from facility-based implementation. However, implementers did not recommend the package after the recall.

Conclusion During community-based provision of the AHD care package, compliance with most procedures was good. The principal barrier was VISITECT inaccuracy, leading to overreporting of CD4≤200cells/µL and interruption of testing. An accurate, rapid, user-friendly point-of-care CD4-test is necessary for community implementation of this package.

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PA-447

ALERRT capacity strengthening programme – knowledge brokering across international networks to support co-development and enhance regional research capabilities

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Background Strong expertise exists within regional and international research networks, so active sharing has the ability to improve the research capabilities of study teams and broader communities of researchers; transferring knowledge and tacit learning between organisations, disease areas and settings. As part of the African coaLition for Epidemic Research, Response and Training (ALERRT) consortium, we harnessed The Global Health Network's well-regarded mechanisms for building a community of practice and connecting teams, research programmes and networks; enabling 'know-how' to move effectively between them.

Methods Key to this approach is the dynamic pairing of the digital platform and the structured regional initiatives. With the collaboration of multiple research networks, including PANDORA-ID-NET, EACCR, CANTAM, TESA, REDe, core resources and training materials generated by the study teams are reflected back on the platform; enhancing the learning and the utility afforded by these to as many other researchers and teams globally.

Results A range of mediums is used to deliver and disseminate skills-based and research implementation learning. This includes i) Toolkits for setting up practical workshops and supported learning sessions to enhance the institutional research environment; ii) hosting Webinars, to ensure a wider opportunity to engage healthcare professionals in research efforts, key lessons and recommendations; iii) Study profiles which include protocols and patient information sheets, which can be readily downloaded and modified by others to raise standards and speed up research; and iv) new eCourses identified through workshops, collaborative partners, and the research programmes themselves; authored by regional experts. This approach amplifies the expertise housed within any one research programme, scaling the applicability of methods and processes.

Conclusion By actively convening excellence between networks, organisations, diseases and settings, the ALERRT community continues to deliver sustainable impact to other researchers well beyond the immediate consortium partners.

PA-450

Laboratory diagnosis of Pneumocystis jirovecii in HIV-positive infants with severe pneumonia using non-invasive samples

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Background The laboratory diagnosis of P. jirovecii pneumonia (PCP) is typically based on microscopic observation of cysts and trophic forms on deep respiratory specimens. In low-income countries, access to bronchoalveolar lavage is limited, particularly for children, and PCP is usually a clinical diagnosis in HIV-positive infants. The use of different laboratory tests on more easily-obtained upper respiratory and venous blood samples could enhance laboratory-confirmed PCP diagnosis.
Methods PCP-PED is an ongoing ancillary-study of the EMPIRICAL trial (#NCT03915366), supported by the EDCTP2 Program and the European Union (TMA2020CDF-3217), which recruits HIV-positive infants hospitalized with severe pneumonia from 8 hospitals in Mozambique. Nasopharyngeal aspirates are processed for direct immunofluorescence microscopy (IFM) to detect P. jirovecii cysts and for quantitative polymerase chain reaction (qPCR) targeting kex-1 gene (Genesig real-time PCR kit). Plasma samples will be used for serologic quantification of (1-3)-β-D-glucan (BG) and Human Krebs Von Den Lungen-6 (KL-6) antigens.
Results In interim analysis as of March 2023, 61/151 (40.4%) participants recruited have qPCR and IFM results. Median age was 4.0 [IQR, 3.1-6.3] months and 47.5% (29/61) were female. Median HIV viral load and CD4% were 6.0 logs cp/mL [IQR, 5.9 - 6.9] and 13.5% [IQR, 10.0-19.6], respectively. qPCR was positive in 45.9% (28/61) and 39.3% (11/28) were on cotrimoxazole prophylaxis prior to hospitalization. The median P. jirovecii fungal load on positive samples was 13,304 copies/mL [IQR, 3,975-61,484]. Among participants with positive qPCR, 25% (7/28) were IFM positive. All participants with negative qPCR results were IFM negative; no participants with positive IFM had negative qPCR results.
Conclusion Positivity rates for qPCR were higher than for IFM, suggesting superior sensitivity for P. jirovecii detection. Future analysis will focus on qPCR/IFM correlation, BG and KL-6 results, and P. jirovecii PCR fungal loads to attempt to differentiate colonization and infection.

PA-452

Molecular surveillance for polymorphisms associated with Artemisinin-Based Combination therapy resistance in Plasmodium falciparum isolates from southern Brazzaville and beyond in the Republic of Congo

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Background Emergence and spread of P.falciparum strains resistant to artemisinin-based combination therapies (ACTs), poses a significant threat to global malaria control efforts. Therefore, the close monitoring of molecular markers is essential as an early warning system to detect the emergence and spread of resistance. This study aims to assess the prevalence of haplotypes of the Pfcrt, Pfmdr1 and PfK13 resistance markers in isolates from the south of Brazzaville and beyond, in the Republic of Congo.
Methods Between March and October 2021, a cross-sectional study was conducted in rural and urban areas of the south of Brazzaville and beyond in individuals aged 1-83 years with microscopic P. falciparum infection. Parasite DNA was extracted using Qiagen kit and all samples were screened to confirm P. falciparum infection by nested PCR. Restriction Fragment Length Polymorphism was used for the detection of single nucleotide mutation within the Pfcrt, Pfmdr1 genes of the parasite, and detected mutations were further confirmed using Oxford nanopore sequencing platform, while PfK13 gene mutations were investigated by sequencing.
Results Among 329 samples with confirmed P. falciparum infection, the overall prevalence of the 76T (Pfcrt), 86Y (Pfmdr1) and 184F (Pfmdr1) mutations were 26.7%, 5.3% and 23.9% respectively. The Pfk13 wild type was found in 98.3% isolates while, 1.7% isolates had a mutation in the Pfk13 domain (4 synonymous mutations and 1 non-synonymous mutation, A578S). No significant difference was observed between rural and urban data.
Conclusion These results indicate low prevalence of mutations within the Pfcrt, Pfmdr1 genes of P. falciparum and no validated Pfk13 mutation associated with artemisinin drug resistance in this study setting, suggesting that ACTs remain effective in the area, but required continuous surveillance.

PA-453

Building an innovative long-term collaboration for strengthening the research capacity, the research environment and the scientific leadership in Mozambique

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The Manhiça Health Research Center (CISM)is a well-established research center with a strong and consolidated research capacity into communicable diseases prevalent in Mozambique, with particular focus on the main causes of morbidity and mortality. Since its creation, CISM has grown within the framework of a bilateral cooperation programme between the Mozambican and Spanish governments and with support from the Hospital Clinic (HC) and the University of Barcelona (UB) to fight diseases and protect the health of vulnerable populations through research, healthcare and training.
In 2008 the Manhiça Foundation was created representing one of the most important events in the development of the Centre because it entitled CISM to a Mozambican legal framework, which facilitates its sustainability and long-term autonomy. In 2010, as part of this strategy for integration and country ownership, the Foundation for Community Development and Eduardo Mondlane University joined as partners. And in 2015, the Barcelona Institute for Global Health replaced the HC and the UB.
One of the key strategies of this partnership to build CISM's research environment has been the training of staff through the joint development of capacity building and strengthening activities. After 27 years of successful collaboration, a Training Fellowship Programme has been established to train young African graduates wishing to develop their career as researchers; the program provides hands-on training within research projects implemented at CISM. Many training courses and workshops have been developed to train clinical researchers, technicians, data managers, etc.; and networks with other Sub-Saharan African countries have been established to strengthen research capacities (e.g., TESA). All these efforts succeeded in awarding 114 postgraduate degrees in collaboration with North and South universities all over the world for both African and international students: 63 doctorates and 47 master; more than 140 research and training internships; and more than 10 funded collaborative projects.

PA-454

External factors affecting recruitment in a global paediatric pneumonia trial: lessons learned from PediCAP

Kamla Pillay

St George's University, United Kingdom, On behalf of the PediCAP Consortium

Background Pneumonia in children is common worldwide and is associated with significant morbidity and mortality. PediCAP is an ambitious randomised controlled trial (ISRCTN63115131) with the aim of determining the optimal duration and formulation of amoxicillin and co-amoxiclav for children aged 2 months to 6 years with severe community acquired pneumonia in sub-saharan Africa.

Methods Recruitment occurred across thirteen sites in Uganda, Zambia, Zimbabwe, South Africa and Mozambique. Virtual monitoring of recruitment was led by the Medical Research Council Clinical Trials Unit (MRC-CTU). The recruitment target was set to 1100 in the main trial, PediCAP-A, and 120 in the pharmacokinetic substudy, PediCAP-B.
Results A total of 987 patients were recruited to the main trial between December 2020 and May 2023 (2 in 2020, 216 in 2021, 528 in 2022 and 241 in 2023). Recruitment is currently ongoing. Several external factors affected recruitment speed over this period. The SARS-CoV-2 pandemic led to staff redeployment, local lockdowns which affected patterns of respiratory disease and delayed ethical approval timelines. An Ebola epidemic further exacerbated these challenges in some sites. Changes in national empirical antibiotic guidelines to a non-protocol antibiotic caused a significant reduction in children eligible for recruitment in South African sites. Constant communication between the MRC-CTU and the sites was needed in order to respond to these barriers to recruitment. Additional virtual meetings and updates were scheduled to maintain trial safety during concomitant outbreaks of infectious diseases. Decisions to close sites affected by changing empirical guidelines was made when recruitment was thought to be permanently affected, given that other sites were recruiting well.
Conclusion Unforeseeable challenges are inevitable in global RCTs. Pragmatic responses to these challenges allows recruitment to trials like PediCAP to continue safely while maximizing the chance of reaching the recruitment target, therefore enabling more impactful results.

PA-455

Bedside ultrasound for the diagnosis of tuberculosis in HIV-positive infants hospitalized with severe pneumonia

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Background Tuberculosis (TB) diagnosis is challenging in children, particularly in infants, contributing to high TB-related mortality. Up to 30% of infants with pulmonary TB have concurrent extrapulmonary disease, with findings that can frequently be detected with ultrasound. A protocol of focused assessment with sonography for HIV-associated TB (FASH) at six abdominal and thoracic positions has shown promise for diagnosis in children and adults, but few infants have been included in published studies.
Methods EMPIRICAL (#NCT03915366) is a randomized, controlled trial funded by EDCTP (RIA2017MC-2013) recruiting HIV-positive infants <12 months hospitalized with severe pneumonia without current/past TB diagnosis or exposure. All participants have Xpert Ultra (stool, nasopharyngeal aspirate) and urine LAM testing, and in an ongoing blinded diagnostic ancillary study at 5 hospitals in Mozambique, FASH is performed. An interim descriptive analysis was done for participants no longer active in the trial as of April 2023.
Results For the 39 participants included, the median age was 3 months (IQR:3.17-5.13), 48.7% were female, and the median CD4% was 13% (IQR:9.90-17.55). There was ≥1 positive FASH finding in 10/39 (25.6%); all had pericardial effusion 10/39 (25.6%), with focal splenic lesions and ascites also noted in 2/39 (5.1%) and 1/39 (2.6%), respectively. No participants had pleural effusion, focal liver lesions, or abdominal lymphadenopathy. In participants with laboratory-confirmed TB, 42.9% (3/7) had ≥1 positive FASH finding. There were 2 positive FASH findings in 7.6% (3/39) participants, of whom 66.7% (2/3) had laboratory-confirmed TB.
Conclusion Positive FASH findings were frequent in HIV-positive infants hospitalized with severe pneumonia and even more common in the subset of participants with laboratory-confirmed TB, with pericardial effusion noted on all positive FASH exams. Future analysis will attempt to define which abnormalities on FASH exam are most predictive of TB disease and assess the use of FASH to monitor TB treatment response.

PA-456

Field testing of a novel point-of-care Genital InFlammation Test (GIFT) in low- middle-income countries in Africa: aiming to prevent HIV infection and improve reproductive health

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Background Sexually transmitted infections (STIs) and bacterial vaginosis (BV) are major risk factors for HIV infection and reproductive complications in women living in sub-Saharan Africa, in part because of inflammation associated with these conditions. In women, most STIs and BV are asymptomatic, and therefore not diagnosed in low and middle income countries (LMICs), where etiologic testing is not common and infections are treated based on presence of signs or symptoms (syndromic management). To improve STI/BV case finding in LMICs, we have been developing a true point-of-care low cost lateral flow test based on inflammation biomarkers – called the Genital Inflammation Test (GIFT) – to screen women who would benefit from further etiologic testing.
Methods Through an EDCTP2 RIA2020I funding mechanism, the first version of the GIFT device has been developed in South Africa and is currently being evaluated in three parallel clinical studies in South Africa, Zimbabwe and Madagascar. Field testing is intended to inform optimisation of the final prototype device.
Results The GIFT-Africa consortium (www.GIFT-Africa.org.za) includes a cross-disciplinary team of experts, including those working on design, optimisation, manufacture and laboratory validation of the first in field GIFT device, clinical performance in each region compared to inflammation biomarkers measured by ELISA, STIs measured using NAATs, and BV measured by Nugent. In addition to assessing sensitivity/specificity in different LMIC settings, implementation of the GIFT device into reproductive health services will be evaluated using: in-depth interviews with patients and healthcare professionals (user experience); discrete choice experiments with end-users; cost, budget impact and cost-effectiveness analyses, and; a DELPHI survey to evaluate key stakeholder recommendations for implementation.
Conclusion The GIFT device is positioned to cost-effectively increase STI/BV case-finding, but also to improve STI/BV management for women in LMICs, who are at high risk of HIV infection and reproductive complications.

PA-459

The effect on treatment outcomes of baseline resistance to pyrazinamide after 6-months of BPaMZ in the SimpliciTB Clinical Trial

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Background The combination of bedaquiline, pretomanid, moxifloxacin, and pyrazinamide (BPaMZ) provides the shortest duration of treatment required to sterilize mice in relapsing mouse models. SimpliciTB was an open-label study to evaluate the safety and efficacy of 4-months BPaMZ (4BPaMZ) compared to standard therapy (4HRZE/2HR) in DS-TB participants. The trial also included a cohort of DR-TB participants who received 6-months BPaMZ (6BPaMZ). The primary efficacy endpoint was time to culture negative status through 8 weeks; the key secondary endpoint was relapse-free cure at week 52. The proportions of patients with culture conversion by 8 weeks and of favorable outcome at week 52 (MITT analysis) for 4HRZE/2HR, 4BPaMZ and 6BPaMZ were 47.3%, 84.1%, 85.7% and 93.1%, 85.3%, 83.1%, respectively. The lower rates of favorable outcomes in BPaMZ arms were largely due to higher rates of hepatotoxicity-related trial discontinuations, in which PZA may have contributed.
Methods Using Kaplan-Meier (KM) and Cox PH models adjusting for socio-demographic and clinical factors, we explored the effect on outcome of baseline resistance to pyrazinamide (BRZ) in the DR-TB group of participants.
Results 55 of 152 (36.2%) participants in the DR-TB cohort had BRZ based on phenotypic and genotypic drug susceptibility testing. Time to negative sputum culture for patients with and without BRZ was not statistically significantly different (aHR=0.79, 95% CI (0.54,1.15) p= 0.22). Relapse-free cure was documented in 42/51 (82%) participants with and 68/79 (86%) participants without BRZ (unadjusted Chi-sq test p=0.57).
Conclusion PZA resistance at baseline did not impact outcomes at week 8 or week 52 in DR-TB patients treated with BPaMZ. A regimen of pretomanid, moxifloxacin with a potent diarylquinoline could present an efficacious and better tolerated therapeutic alternative for DS- and DR-TB patients and should also be explored as a therapeutic option for DS-TB.

PA-463

Phase 1b randomized, controlled, double-blinded, age de-escalation trial to evaluate the safety, reactogenicity and immunogenicity of BK-SE36/CpG malaria vaccine in Burkinabe healthy adults and children.

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Background BK-SE36/CpG is a recombinant Plasmodium falciparum vaccine candidate targeting blood-stage parasites. The P. falciparum SE36 protein was expressed in E. coli, adsorbed to aluminium hydroxide gel, and reconstituted with CpG adjuvant. An acceptable safety profile of the BK-SE36/CpG vaccine was previously showed in healthy malaria-naïve Japanese adults. The aim of the Phase Ib study reported here was to assess the safety and immunogenicity in healthy malaria-exposed African adults and children.
Methods A double-blind, randomized, controlled, age de-escalating, clinical trial was conducted in an urban area of Ouagadougou, Burkina Faso. One hundred and thirty-five healthy participants aged 21-45 years, 5-10 years, and 12-24 months were randomized 2:1 to receive three vaccine doses of BK-SE36/CpG (BK) or rabies vaccine. Subjects were monitored within 7 and 28 days following each vaccination for solicited and unsolicited adverse events. Severe and serious adverse events were collected throughout the study duration (12 months). Immune responses were measured at baseline, 28 days after each vaccination, and at trial end.
Results Of the one hundred thirty-five subjects enrolled, one hundred thirty-four received all three scheduled vaccine doses. Five Grade 3 events unrelated to vaccination were reported in three subjects (3%) in the BK arm. Five SAEs reported, all due to severe malaria, were judged unrelated to the study vaccine. BK induced higher mean anti-SE36 antibody titers compared to control, with higher titers post-Dose3 compared to post-Dose2. A stronger immune response was observed in younger cohorts (12-24-month-old > 5-10-year-old > 21-45-year-old). In all cohorts, epitope mapping of sera from BK vaccinees showed predominant reactivity with the synthetic peptides that are lied into intrinsically unstructured regions.
Conclusion The BK-SE36/CpG vaccine was well-tolerated and immunogenic in all age groups. These results pave the way for further proof-of-concept studies with larger cohorts to demonstrate the efficacy of the vaccine.

PA-466

Factors associated with coverage of three doses of Intermittent Preventive Treatment of malaria in infants with Sulfadoxine-pyrimethamine: a cross-sectional community-based survey in Sierra Leone

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Background Intermittent Preventive Treatment of malaria in infants (IPTi) is a malaria control strategy consisting of the administration of sulfadoxine-pyrimethamine alongside routine immunizations. IPTi has been renamed as Perennial Malaria Chemoprevention (PMC), accounting for its recently recommended expansion into the second year of life. Before starting a pilot implementation on PMC, the currently implemented strategy was assessed in children in selected areas of Sierra Leone.
Methods A cross-sectional, community-based, multi-stage cluster survey was conducted in 2021 in three districts in Northern and northwestern provinces of Sierra Leone among 10-23 months old children. IPTi coverage was calculated using percentages and 95% confidence intervals weighted for the sampling design and adjusted for non-response within clusters. Factors associated with iPTi coverage including malaria RDT were assessed.
Results A total of 720 children were recruited. Coverage of three IPTi doses was 50.57% (368/707; 95% CI 45.38 – 55.75). Adjusted for all other studied covariates, older children (OR per month increase 1.07, 95% CI 1.02–1.11, P-value 0.0056), those who slept under a mosquito net the previous night (OR 1.76, 95% CI 1.22–2.53, P-value 0.0029) and those whose caretaker was paid-employed (OR 2.74, 95%CI 1.11, 6.74, P-value 0.0290) were more likely to have received the complete three IPTi doses. Children whose caretakers were males (OR 0.50, 95% CI 0.28–0.91, P-value 0.0251), residing in Port Loko district (OR 0.40, 95% CI 0.19–0.87, P-value 0.0212) and those with a positive RDT result (OR 0.57, 95% CI 0.39–0.82, P-value 0.0035), were less likely to have received complete three doses of IPTi.
Conclusion In this survey, IPTi coverage was around 50%. A positive health behaviour possibly explains the association with use of mosquito nets. This implies that positive health behaviour messaging is key in improving coverage of IPTi, a key malaria prevention strategy.

PA-472

Malaria prevalence in pregnant woman in Southern Mozambique

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Background Malaria in pregnancy is a significant public health concern in Mozambique, with significant maternal and fetal morbidity and mortality. According to WHO, Mozambique is one of the countries in sub-Saharan Africa most affected by malaria in pregnancy, although malaria cases are decreasing in some parts of the country. Interventions are necessary to reduce the burden of malaria in Mozambique. The present study evaluates the prevalence of malaria infection among pregnant women and describes its profile.
Methods This is a cross-sectional study with women attending antenatal care in 11 primary Health Facilities of Manhiça District and Massinga Distrital Hospital between August 2021 and April 2023. All pregnant women were systematically screened for malaria with an ultrasensitive Rapid Diagnostic Test (HS-RDT); if positive, malaria infection was confirmed by microscopy. We also assessed malaria symptoms. Data were collected using a predefined questionnaire entered into a RedCAP database, and descriptive analysis was done using SPSS v21.
Results We screened 17661 samples of pregnant women who attended routine antenatal care at any visit. From this, 286 were positive, with a Malaria prevalence of 1.6%. Of these, 221 (77.3%) were confirmed by microscopy. Malaria-confirmed women presented between 20-29 years of age (86.4%) and in the second trimester of pregnancy (65.9%). About 25% were asymptomatic for malaria, mostly (64.4%) under 20 years old and from Massinga district (68.9%).
Conclusion This study reports a low malaria prevalence in pregnant women attending antenatal care facilities in the study area. A quarter of these women were asymptomatic at the time of diagnosis. Therefore, adjusting the information and preventive measures for these women from areas of low malaria transmission is essential.

PA-476

Investigating the contribution of Mycobacterium tuberculosis specific Th22 responses to TB resistance

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Background Tuberculosis (TB) resisters refer to adults from high burden TB areas who, despite exposure to Mycobacterium tuberculosis (Mtb), consistently test negative for TB infection. There is recent evidence for IFN-γ-independent mechanisms associating with the resister phenotype. We have previously characterised IL-22 and Th22 responses to Mtb, and we investigated whether Mtb-specific IL-22 T cell responses may contribute towards resistance to Mtb infection.
Methods We studied a cohort of HIV-infected and uninfected individuals with latent TB infection (LTBI; n=50). In addition, we recruited HIV-uninfected healthcare workers in regular contact with TB patients (sustained workplace TB exposure of >5 years). Participants were screened for Mtb infection using tuberculin skin test (TST) and IFN-γ release assay (IGRA) and classified into resisters (TST-IGRA-; n=25) or those with LTBI (TST+IGRA+; n=25). Blood was stimulated with Mtb antigens and cryopreserved. Flow cytometry was used to determine the Mtb-specific CD4 T cell cytokine responses (IFN-γ, IL-17 and IL-22).
Results Mtb-specific Th22 cells, producing IL-22 in the absence of IFN-γ or IL-17, were present at high frequencies in LTBI, and contributed 50% of the total CD4 response to Mtb, comparable in magnitude to the IFN-γ response. HIV-infected persons, who have a heightened risk of TB even at well-preserved CD4 counts, had 3-fold lower Th22 responses, similar to the reduction in Th1 responses. In ongoing studies, we are examining Mtb-specific IL-22 T cell production in individuals who are resistant to Mtb infection, to determine the potential contribution of this Th subset to the resister phenotype.
Conclusion We have shown that the Mtb-specific Th22 subset is distinct from both Th1 and Th17 cells and make a major contribution to the overall T cell response to Mtb. These important data warrant further study of the role of Th22 cells in the resistance and control of Mtb infection.
Funding: EDCTP

PA-477

Building a national network for inpatient pediatric clinical research in Mozambique

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Background Universidade Eduardo Mondlane (UEM) and Hospital Central de Maputo (HCM) were invited to join a consortium of established pediatric research groups from 5 other sub-Saharan Africa countries in a proposal for the EMPIRICAL trial, which received EDCTP funding in 2019 (RIA2017MC-2013). At that time, HCM and UEM did not have an active pediatric research team, nor a history of collaboration on a pediatric clinical trial.
Methods A research office was established on the HCM pediatric wards. Procurement and laboratory cooperation was established with another Mozambique recruiting site, Centro de Investigação em Saúde de Manhiça. Dedicated and part-time staff were hired, including an HCM pediatrician and nurse. Comprehensive research training was conducted, and the first EMPIRICAL patient was recruited in May 2020. Due to slow recruitment across the consortium, UEM agreed to extend to an additional 3 hospitals in Maputo, again including Ministry of Health staff at each new site. Recruitment was similarly extended to the principal referral/academic hospitals in the other regions of Mozambique with inclusion of Hospital Central de Beira in 2020 and Hospital Central de Nampula in 2021, in partnership with Universidade Católica de Moçambique and Universidade Lúrio. This network has led recruitment in EMPIRICAL, is participating in four pharmacokinetic substudies and an autopsy substudy, and has 2 local ancillary studies, one with EDCTP Career Development Fellowship support (TMA2020CDF-3217).
Results The infrastructure and capacity established through EMPIRICAL has been leveraged for additional pediatric inpatient research opportunties, with UEM leading 4 hospitals participating in the EDCTP-funded PediCAP trial (RIA2017MC-2023), and 2 hospitals in the UNITED-meningitis diagnostic study.
Conclusion A successful pediatric inpatient research network was quickly established in Mozambique with donor support that facilitated capacity building, and a model that prioritized inclusion of Ministry of Health hospital staff in research teams with inter-institutional collaboration to achieve national coverage.

PA-478

Machine Learning Based Modeling of Malaria: A Systematic Review

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Background Malaria remains a major global health challenge, with millions of people affected annually. Traditional methods for predicting malaria outbreaks are limited by factors such as cost, availability, and accuracy. The application of machine learning techniques has emerged as a promising alternative for modeling and predicting malaria outbreaks. This systematic review aims to evaluate the current state of research on machine learning-based modeling of malaria.
Methods A comprehensive search was conducted in several databases, including PubMed, google scholar, and Web of Science, to identify relevant articles published between 1992 and 2022. The search terms included "machine learning," "predicting," and "modeling" in combination with "malaria," We included studies that focused on machine learning techniques for predicting malaria outbreaks and assessed the strengths and weaknesses of the models.
Results Preliminary analyses showed that studies used different machine learning techniques, including artificial neural networks, decision trees, linear regression, random forest, and support vector machines to predict malaria outbreaks and identify the main factors that determine outbreaks. Most of the studies used a combination of environmental and socio-economic factors, such as temperature, rainfall, and population density, to predict malaria outbreaks. The prediction accuracy of the models ranged from 80% to 95%, depending on the machine learning technique used and the dataset.
Conclusion Machine Learning techniques have shown promise in predicting malaria outbreaks by incorporating environmental and socio-economic factors. The strengths of the models included high accuracy and the ability to predict outbreaks before they occur. However, the limitations of the models include the need for extensive data and the difficulty of generalizing the models to other settings. Further research is needed to address these limitations and to optimize the machine learning-based models for predicting malaria outbreaks.

PA-480

Capacity development of applied epidemiologists in Eastern Africa Region (CDAE): progress, challenges, and lessons learned

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Background Capacity Development of Applied Epidemiologists (CDAE, 36-months programme, seeks to create a networked cohort of highly competent professional with master's degree in Epidemiology or Biostatistics (EPI fellows) and strengthens the supervision capacity of targeted universities to effectively deliver programmes in Epidemiology or Biostatistics. In this paper, we describe the progress made, challenges encountered, and lessons learned.
Methods The African Population and Health Research Center leads the programme in partnership with Amref International University (private university) and Jaramogi Oginga Odinga University of Science and Technology (public university), both in Kenya, and Lund University in Sweden. We conducted a highly competitive and rigorous recruitment process which attracted highly qualified applicants from diverse backgrounds.
Results We received 706 applications from 21 countries from which 15 EPI fellows were admitted. They completed their course work and participated in two Joint Seminars, designed their research proposals, defended, and received ethical approval (collection of data is ongoing). Concurrently, 20 supervisors were trained on quality supervision for two weeks to ensure EPI fellows received adequate support and guidance throughout the programme. The programme however encountered several challenges including: high number of qualified applicants but limited funding, adherence to timelines, unequal learning conditions, and difficulty in reaching out to other stakeholders. Some lessons included: high demand for the programme in Sub-Saharan Africa (SSA), concurrent training of EPI fellows and supervisors provides interaction opportunity, expansion need for the programme, and greater synergy in collaborations (academia and industry).
Conclusion CDAE is critical for strengthening public health systems in SSA. This programme provides a blueprint for other countries seeking to build the capacity of their public health workforce. As we draw near the end of the programme, "what next" discussions are ongoing. Our programme demonstrates the importance of public-private partnerships and drawing synergies from various institutions to deliver seasoned epidemiologist.

PA-481

Incidence of Mycobacterium Tuberculosis Infection among Healthcare Workers in HIV clinics in North Central Nigeria

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Background Healthcare workers (HWs) in Low-Middle Income Countries (LMIC) are at increased risk of Mycobacterium tuberculosis infection considering the huge burden of TB, HIV, and the inadequate infection control practices in these settings. Nigeria, a LMIC has a 44.8% prevalence of IGRA positivity among HWs. However, the incidence of M tuberculosis infection is still uncertain. We measure the incidence of M tuberculosis infection using serial testing with IGRA among HWs as a surrogate for assessing effectiveness of TB infection control and document the cumulative risk and incidence rate of M. tuberculosis infection among HWs in Nigeria.
Methods A prospective cohort study was conducted among HWs in facilities with dedicated HIV clinics in north-central Nigeria. HWs of varying cadre who voluntarily consented were enrolled over a period of 4 months, and TB exposure assessed using an interviewer-based questionnaire. All were screened with IGRA at baseline and only those with negative IGRA results were followed-up with serial IGRA testing at month 6, 12 and 24.
Results 641 HWs with negative IGRA results at baseline were followed up. The mean age of participants was 38.4 years (SD9) with majority being women (65%). The cumulate risk of M. tuberculosis infection at 6, 12 and 24 months were 22%, 13% and 14% respectively. However, the incidence rate at month 6, 12 and 24 time points were 44.4/100 person years (py), 39.6/100 py and 31.2/100 py respectively. When stratified by type of clinic (i.e. HIV clinic vs non HIV clinic), we found no statistical difference in the cumulative risk and incidence rate ($p>0.05$).
Conclusion There is a high incidence of M tuberculosis infection in HWs in Nigeria which remains fairly stable after 1 year. Working in HIV clinics is not associated with increased risk. There is urgent need for implementation of effective TB infection control in Nigeria.

PA-494

Socioeconomic determinants of early health care utilisation and association with malaria hospitalisation among under five years children in Manhiça, Mozambique

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Background Malaria is one of the significant health problems in the world, and the greatest burden of the disease is concentrated in Africa, which accounts for about 95% of cases. The World Health Organization indicates that early seeking for treatment is crucial to avoid worsening the disease and, consequently, death. This work evaluated the factors that influence early health care-seeking (EHCS) behaviour in children under five years old and the effect of EHCS on hospitalisations.
Methods We conducted a health facility-based observational longitudinal study over 5 years, starting in January 2015 where confirmed P. falciparum (Pf) malaria cases were identified in an ongoing morbidity surveillance system established in Manhiça district hospital and 5 referral health centres by Manhiça Health Research Centre. Using the first visit for all children that visited a Health Facility (HF) with fever or history of fever in the previous 24 hours and confirmed Pf malaria, we defined EHCS as a visit to an HF within 48h after the onset of fever. We used multilevel logistic regression to identify the factors related to EHCS and the association between EHCS and hospitalisation.
Results Of 66620 under 15 years old children screened only 1603 meet all inclusion criteria. A kilometre increase in the distance to a health facility reduced the odds of EHCS by 11% (aOR=0.89; CI: [0.83-0.95]; p=0.001). EHCS reduced the odds of hospitalization (aOR=0.56; 95% CI: [0.34 -0.93]; 0.024) and year increase in the year of the visit increased the odds of hospitalization by 66% (aOR = 1.66; 95% CI: [1.41-1.93]; $p<0.001$).
Conclusion Increasing the distance to HF reduced the likelihood of EHCS, whereas EHCS reduced the risk of hospitalisation. Maulana and Calanga lead the hospitalisation cases in the study area in children with malaria and cases of delay in health care seeking.

PA-496

Bridging the Gap: Training Needs Assessment for Clinical Trials Assessors and Inspectors and implementation of targeted capacity building in Tanzania

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Background The Covid-19 pandemic and other emerging diseases increased the need to conduct clinical trials (CTs) to investigate appropriate treatments or prevention measures. One of the main barriers for conducting CTs in Africa is delays in regulatory and ethics reviews. Furthermore, existence of inadequate regulatory inspections of CTs to evaluate the integrity of data submitted to health authorities, protect patient safety, and assess the adequacy of site/sponsor quality systems to achieve the same. To this end, the ASCEND project assessed the level of competency and training needs for evaluating clinical trial applications (CTAs) and conducting clinical inspections in Tanzania. Moreover, to recommend interventions to bridge the gap.
Methods A descriptive cross-sectional study was conducted from February to June 2021 using an online survey to collect information on training needs and competencies. The population was 130 respondents from research, regulatory and academic institutions.
Results Out of 130 approached respondents, only 69.2% (90/130) participated. The most common qualification of the respondents was a master's degree (59%). Bachelor degree and PhD holders stood at 21% and 20%, respectively. The findings indicated that 94% of the respondents needed training on assessment of clinical data, 92.2% on product quality, 92.6% on statistical data, and 81.2% on understanding and using the checklist for Good Clinical Practice (GCP) inspection.
These findings were used to develop two accredited short courses 70-hours (7-credits) each. The courses were CTAs assessment and GCP inspection. Consequently, 2-weeks short courses were conducted. Pre- and Post- course tests were administered to assess the training impact.
Conclusion A pool of proficient assessors is important for quality reviews of CTAs and in timelines reduction. The short courses conducted were successful, and increased a pool of competent assessors and GCP inspectors in Tanzania. For further strengthening the regulatory capacity, additional training is recommended.

PA-500

Prevalence and genomic characterization of typhoidal and non-typhoidal Salmonellae in Ghana

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Background Salmonella are a group of facultative anaerobic bacteria that belong to the family of Enterobacteriaceae. The common serovars are Salmonella enterica subsp. enterica serovar Typhi which causes typhoid fever and the non-typhoidal Salmonellae (NTS) which are associated with gastroenteritis. Data on the epidemiology and genomic characteristics of Salmonellae in sub-Saharan African countries are limited.
This study describes the epidemiology and genomic characterization of Salmonellae in Ghana.
Methods A prospective incidental hospital-based surveillance study among patients presenting with febrile illness from May, 2016 to April, 2023 was conducted in the Asante Akyem District of Ghana and Komfo Anokye Teaching Hospital. Blood cultures were processed for identification of Salmonella using standard bacteriological techniques. A subset of Salmonella isolates were confirmed using real-time-PCR amplification targets for S.Typhi and invasive NTS. The concentration of DNA were quantified using nanodrop and shipped to Eurofins Genomics for illumina based sequencing. Raw reads were assembled and analysed using Pathogenwatch web tool.
Results The study enrolled 6,557 participants between the ages of 1 and 95 years of which 51.7% were males. The prevalence of Salmonella Typhi and NTS were 0.14% (95%CI: 0.096 – 1.5) and 0.33% (95%CI: 0.21% - 0.5%) respectively. Male gender (adj OR; 95%CI = 1.6; 0.93-2.75) and age group below 15 years (Adj OR; 95%CI=3.94; 1.67-9.3) had higher odds of infection with Salmonella Typhi. A subset of 42 Salmonella Typhi isolates sequenced, identified the predominant genotype as 2.3.2 (54.1%) followed by 3.1.1 (42.9%). Of 17 iNTS isolates sequenced, Typhimurium (10; 62.5%), Enteritidis (5; 31.3%), Poona (1; 6.2%) and Saintpaul (1; 6.2%) were identified. Common resistance markers identified were chloramphenicol resistance (catA1; 10/50), sulphonamides resistance (sul1; 10/50), beta-lactam (9/10) and trimethoprim (dfrA; 10/50).
Conclusion The increasing rate of resistance and endemicity of infections emphasize the need for the introduction of vaccines to reduce disease burden.

PA-507

Genomic surveillance of infectious pathogens in the Republic of Congo

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Background Deadly emerging infectious pathogens pose an unprecedented challenge to health systems worldwide, especially in the Republic of Congo, where health care infrastructure is limited. Thus the COVID-19 pandemic has been an opportunity to improve the national genomic platform that could be expand to all circulating pathogens serving surveillance, prevention and response actions. This work aimed to establish the genomic platform for the effective control of infectious pathogens in the Republic of Congo.
Methods By 2021, we established the Oxford Nanopore Technology platform for the first time in the Republic of Congo to respond firstly to the COVID-19 pandemic and secondly to other pathogens like Plasmodium falciparum, Mycobacterium tuberculosis, HIV and others. Between April 2020 and August 2022, a total of 1200 oropharyngeal samples were tested positive for SARS-CoV-2 by RT-PCR. Of these samples, 589 with Ct< 28 were selected for sequencing by ONT next generation sequencing (NGS). All the complete sequenced genomes were submitted on GISAID for publication, and variants were identified using Pangolin and Nextclade nomenclature.
Results A total of 381 SARS-CoV-2 whole genomes were successfully sequenced and submitted on GISAID. Our results revealed the circulation of 21 SARS-CoV-2 variants in the Republic of Congo during the study period, with the presence of variants of concern such as alpha (B.1.1.7), delta (B.1.617.2) and Omicron (B.1.1.519). Four waves of the virus epidemics were observed during this study period. The B.1.640.1 variant was reported for the first time in the Republic of Congo through this study, and was observed to be spreading locally and regionally.
Conclusion This work contributed to monitor in a daily basis the spread of SARS-CoV-2 in the country to support the national containment strategies of the pandemic. This established platform is serving for the identification of other pathogens that could represent a threat of public health.

PA-511

Utility of host transcriptomic biomarkers in the diagnosis of spinal tuberculosis

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Background Spinal tuberculosis (TB) is a potentially severe form of TB that accounts for 50% of all musculoskeletal TB cases. The condition presents with non-specific symptoms often resulting in delayed diagnosis. Therefore, there is an urgent need for new tools that can aid early diagnosis. Host transcriptomic biosignatures have shown promise in the diagnosis of pulmonary TB and may be useful in spinal TB. We aimed to evaluate the utility of selected published host transcriptomic signatures for the diagnosis of spinal TB and monitoring of treatment response.
Methods The study was conducted at a tertiary hospital in the Western Cape, South Africa. A total of 26 genes were evaluated in participants with confirmed spinal TB (n=24) and mechanical back pain (n=17) using qRT-PCR on RNA extracted from Paxgene blood. Receiver Operating Characteristic (ROC) curves and General Discriminant Analysis were used to evaluate the diagnostic potential of individual genes, as well as gene combinations.
Results Preliminary analysis of four individual genes (GBP5, DUSP3, BATF2 and SERPING1) indicated their potential as diagnostic candidates with areas under the ROC curve (AUCs) ranging from 0.83 to 0.87. The four-gene signature (GBP5+DUSP3+SERPING1+BAFT2) was able to diagnose spinal TB with a sensitivity of 87.5% (95% CI, 67.6%-97.3%) and a specificity of 66.7% (95% CI, 29.9%-92.5%) in a resubstitution classification matrix. However, after leave-one-out cross validation, the sensitivity was 79.2% (95% CI, 57.8-92.9%) while the specificity was 66.7% (CI, 29.9-92.5). A significant difference ($p \leq 0.05$) was observed in the expression of all four genes at baseline and 12 months of treatment.
Conclusion Our preliminary results highlight the potential of the selected genes as candidate biomarkers for spinal TB diagnosis and monitoring of treatment response however, further investigation is warranted to validate these findings.

PA-512

Behavioural predictors of uptake of HIV and pregnancy prevention products among adolescent girls and young women and female sex workers in Kenya and Uganda

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Background UPTAKE is a programme to accelerate access and facilitate adherence to effective and innovative long-acting technologies to prevent HIV and unintended pregnancy among Adolescent Girls and Young Women (AGYW) and Female Sex Workers (FSW) through behavioural science in Kenya and Uganda. We identified characteristics which predict the use of HIV and pregnancy prevention products and measured the strength of preferences.
Methods A quantitative survey was administered to 326 AGYW and 334 FSW in both countries. Descriptive, inferential, and segmentation analysis was applied to reveal user-preferences, behavioural patterns and the predicting factors of product uptake.
Results Product usage, particularly for HIV prevention, was lower among AGYW than FSW. Although awareness of long-acting prevention products including implants and intra-uterine devices (IUDs) was high among both groups, uptake remained low, primarily due to perceived side effects. For pregnancy prevention, the male condom was most used among both AGYW and FSW, followed by injectables. For HIV prevention, male condoms were most used, followed by oral pre-exposure prophylaxis (PrEP). Effectiveness and easy accessibility were the most highly valued product features.
The influential factors driving and predicting uptake varied by product. At the 0.05 significance level, risk preference, stigma, Intimate Partner Violence (IPV), locus of control, peer influence, subjective risk, country, and age appeared significant in influencing uptake of various products. Segmentation was only found influential for the uptake of implants and male condoms among AGYW.
Conclusion More than half of participants are aware of long-acting contraceptive products, though only 17% of AGYW and 22% of FSW used implants, and less than 2% used IUDs. Furthermore, very few recognised the ring as a HIV prevention method, and none used it. Behavioural interventions should be tailored by product and respond to the key influential factors to increase awareness and bridge the gap between awareness and uptake.

PA-513

Experience with AVAREF regulatory procedure to facilitate clinical trial startup in sub-Saharan Africa

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Background The African Vaccine Regulatory Forum (AVAREF) is a network of African national regulatory authorities (NRAs) and ethics committees (NECs) with an objective of improving access to medicines by reducing and standardizing review and approval times for clinical trial applications, while also optimizing quality of regulatory processes across sub-Saharan Africa (SSA)[1]. It utilizes joint reviews and parallel CTA submissions to NRAs, NECs and Institutional Review Boards (IRBs).
Methods Novartis piloted use of the AVAREF procedure for a Phase 2 clinical study in malaria patients involving 7 countries/13 sites in SSA.
Results A letter of intent for a scientific advice meeting was submitted to AVAREF to trigger the procedure start. The meeting occurred 2 months later with participation of experts from SSA. One NEC identified for inclusion in the procedure did not agree to participate.
The timetable was agreed by all parties, which facilitated CTA parallel submissions. However, differences in understanding of the procedure emerged. Despite scheduling of a face to face joint review meeting including all parties to discuss questions on the CTA, two NEC approvals were received prior to the joint review. Validation questions requesting sequential approvals by IRBs/ECs were also received. The procedure is currently ongoing, and the pilot will inform the path for future EC/HA submissions in SSA.
Conclusion AVAREF procedure holds promise to reduce lengthy sequential NEC and NRA approval timelines in SSA. It also provides a forum for open discussion of study-related questions and for scientific advice in SSA. Attention is warranted to further clarify the review process and expectations for NECs, in particular.

PA-514

Immunomodulatory activities of atorvastatin on PBMCs from successfully treated TB patients presenting with or without persisting lung inflammation - preliminary findings of StatinTB trial

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Background Post-TB lung disease (PTLD) is a neglected chronic lung condition that occurs despite successful completion of TB treatment. Statins have broad-range immune-modulatory and anti-inflammatory properties with a potential to reduce PTLD and improve symptoms. In our ongoing StatinTB trial (RIA2017T-2004; NCT04147286), we evaluate safety and efficacy of 40 mg atorvastatin to reduce persistent lung inflammation (PLI) after TB treatment in HIV-/HIV+ adults measured by 18F-FDG-PET/CT. Here we aim to investigate the ex vivo immunomodulatory activities of atorvastatin on peripheral blood mononuclear cells (PBMCs) from treated TB patients following M. tuberculosis infection.
Methods At the end of TB treatment, enrolled study participants were subjected to PET/CT scan and. PBMCs were collected at baseline and treated ex vivo with atorvastatin overnight followed by infection with M. tuberculosis (Mtb) HN878 strain. At 24 hours post infection, PBMCs were subjected to flow cytometry to evaluate inflammatory cell surface markers and cell populations. Confocal microscopy was performed to measure phagosome maturation (Rab-7), phagolysosome fusion (Cathepsin-D and LAMP-3) and autophagy (LC3B). CFU and Tunnel assays were conducted to measure intracellular Mtb growth and apoptosis.
Results Ex-vivo treatment of PBMC with atorvastatin significantly reduced the intracellular growth of Mtb as measured by CFU assay. Atorvastatin treatment significantly reduced the expression of inflammatory cell surface markers (CD11b and CD16) and decreased classical monocyte (CD14+CD16-) population measured by flow cytometry. The colocalization coefficient of Mtb with the phagosome marker (Rab-7), phagolysosome markers (Cathepsin-D and LAMP-3) and autophagy marker (LC3B) were significantly enhanced by atorvastatin as measured by confocal microscopy. Apoptosis was significantly increased by the treatment of atorvastatin.
Conclusion As a host protective mechanism atorvastatin induces phagosome and phagolysosome maturation, autophagy and apoptosis in Mtb-infected PBMCs.

PA-516

Association of HIV and mycobacterial lineage on five-year TB treatment outcomes in Mali

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Background Factors associated with long-term TB treatment outcomes are not well understood. The aim of our study was to determine the association of mycobacterial lineage and HIV co-infection on mortality and TB recurrence five years after first-line TB treatment in Bamako, Mali.
Methods Between 2015-2022, we conducted a longitudinal cohort study enrolling adults with smear-positive rifampicin-susceptible pulmonary TB. After diagnosis, patients were followed at 1 month (M), 2M, 5M and 6M to determine treatment outcome. Spoligotyping was used to determine baseline lineage classification (M. tuberculosis (L4), and M. africanum (L6)). After treatment completion, patients were evaluated every 6 months for five years to determine their clinical status. Univariate and multivariate logistic regression was used to identify factors associated with treatment outcome.
Results Of the 1,283 patients enrolled, 911 (71%) were male and 116 (9%) were co-infected with HIV. BMI <18.5 (aOR: 1.4, 95% CI: 1.1-1.9) and HIV co-infection (aOR: 2.9, 95% CI: (1.8-4.8) were associated with initial treatment failure. Among the 684 patients maintained for the entire 5-year follow-up, 72 (11%) died and 35 (5%) developed recurrent TB. Baseline L4-infected patients were not more likely to die than L6-infected patients (51% vs 26%, p=0.79) or develop recurrent TB (54% vs. 31%, p=0.58). HIV was not associated with death (p=0.58) or TB recurrence (p=0.32). Among all recurrences, 8 (23%) recurred within 1 year after treatment completion, 25 (71%) within 18 months, and 28 (80%) within 2 years. We were not able to obtain a recurrent TB sputum sample.
Conclusion Neither HIV co-infection nor mycobacterial lineage was associated with 5-year mortality or TB recurrence. Only half of the patients completed follow up and we were limited by the inability to differentiate TB relapse from reinfection. Future analyses that can differentiate relapse from reinfection may be helpful.

PA-518

A comparative study of the Force and multiplicity of infection in children under Seasonal Malaria Chemoprevention or not in intense malaria transmission area of Banfora

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Background P. falciparum parasite genotyping in longitudinal studies was described as a suitable manner for measuring outcomes of interventions and to estimate the force of the infection.
Methods This study was designed to compare the force and multiplicity of infection (FOI and MOI) in children on SMC (<5 years) or not (5 to 12 years) in Banfora, an area of intense malaria transmission in Burkina Faso. Both groups received supervised curative doses of artesunate (AS) or dihydroartemisinin-piperaquine (DHA-PQ) to eliminate existing parasites. Parasite DNA was extracted and then analyzed by nested PCR to detect and genotype P. falciparum parasites. Both active (biweekly sampling at home) and passive (sampling at health center visits) case detection were used to ensure that a high proportion of infections were captured.
Results A total of 458 PCR-detected P. falciparum positive samples were collected and 87.99% were positive for msp2 gene. There were no differences in MOI (p=0.80) and FOI (p=0.09) between the two DHA-PQ and AS treatment cohorts. The mean values of FOI and MOI were 2.00 [1.82-2.18] and 2.98 [2.83-3.14] respectively. In comparison, there was no statistically significant difference (p=0.92) between the mean values of the FOI of subjects on SMC (1.98 [1.57-2.39]) and those who were not (2.00 [1.82-2.21]). The same was true (p=0.75) between the MOI of subjects on SMC (3.03 [2.69-3.38]) and the other group (2.97 [2.79-3.15]). With a fever and parasitemia >5000 trophozoites/µL, the value of the polyclonality in passive detection was 57.69% [43.26-70.99] and the difference with that in active detection (2.28% [1.06-4.62]) was statistically significant (p<0.01).
Conclusion Both FOI and MOI were not age-dependent, despite current malaria control methods that target children under five years. This would suggest that the SMC did not provide specific protection on these children living in an area of very high transmission.

PA-521

Operationalization of an electronic submission and management platform in Tanzania for streamlining the ethics review process

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Background An effective regulatory system is crucial for fostering ethical conduct and generation of high-quality research outputs. A wide range (14-396 days) of time-to-ethical and regulatory approval has been reported in East Africa. Since 2002, the number of applications received by the Tanzania National Ethics Committee (NEC) increased from 75 to an average of 450 applications per-year by 2022, increasing demand for robust and rapid ethics approval system. Through support from EDCTP-funded projects, we implemented and operationalised the electronic system (REIMS) for submission and management of ethics review process.
Methods Prior to implementation, an audit was conducted to ascertain needs and potential benefits. IT experts were sourced in Tanzania to revamp, customise, and simplify the existing Research Ethics Information Management System (REIMS). Mixed methods were used to assess performance and effectiveness of REIMS among users. An online customer satisfaction survey was carried out. Quantitative data on review timelines and approvals, NEC meeting minutes and institutional progress reports were analysed.
Results The number of clinical trials received by the NEC from July 2020 to June 2022 increased and during 2022, NEC approval timelines took an average of 75 days, with timelines of up to 180 days. Sixty respondents replied to the online user survey in October 2022. Customer satisfaction with REIMS was at 86.7%, with users requesting integration with payment systems and allowing multiple access for project team members per protocol. The system was customised to accommodate submission of progress reports for passive monitoring and the generation of signed ethics clearance certificates integrated with a barcode.
Conclusion Online ethics review systems improved communication, transparency and consistency of the clearance process. The applicant is alerted of the status of their protocol thus increasing trust and confidence by the users of the review process. The time-to-approval has been shortened since operationalisation of e-system.

PA-522

Performance of alternative bacteriological measures of response to MDR-TB therapy during the initial 16 weeks of treatment

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Background Treatment for Multi-Drug Resistant Tuberculosis (MDR-TB) is long and costly. Currently, there are limited effective and affordable treatment response monitoring tools. We set to evaluate the performance of alternative bacteriological measures of response to therapy during the initial 16 weeks of MDR-TB treatment.
Methods In a prospective study of MDR/RR-TB in Uganda, all smear-positive participants were enrolled for treatment response monitoring using Concentrated Fluorescent Microscopy (CFM), Fluorescein-di-acetate (FDA) AFB vital smear microscopy, and 16S rRNA-based assay in a Molecular bacterial load assay (TBMBLA) and Mycobacterial Growth Indicator Tube (MGIT) as alternative bacteriological measures. Pooled early morning and spot sputum samples were processed at weeks 0 (pre-treatment), 2, 4, 6, 8, 12, and 16. Solid culture, Middle Brook 7H11 selective (MB7H11S) colony-forming units were used as the standard measure of treatment response. Bacteriological conversion to negative by the alternative tests was assessed against MB7H11 at weeks 12 and 16 of treatment.
Results A total of 59 participants were enrolled, of whom 58 provided sputum samples at baseline. Participants were; 64% male, median age (IQR) 33 (28.6-37.4), 44% HIV-positive, and 78% on ART. The underweight (BMI<18.5kg/m2) was 61% and the median BMI (IQR) was 18.1 (17.3-18.6). Bacteriological positive at baseline were n (%); CFM 49 (84.5), FDA 40 (69.0), TB-MBLA 32 (60.4), MGIT 51 (87.9), and MB7H11S was 47 (81.0). Bacteriological conversion to negative at week 12 and week 16 respectively were CFM 92% and 98%, FDA 98% and 98%, TB-MBLA 98% and 100%, MGIT 95% and 93%, MB7H11S 96% and 98%.
Conclusion Our data show that concentrated fluorescent smear microscopy, fluorescein-di-acetate smear microscopy, TBMBLA, and MGIT culture as suitable alternative measures of response to therapy among MDR-TB patients. Efforts should be made to make such methods available for the timely monitoring of patients on MDR-TB regimens.

PA-526

Chronic non-communicable diseases in patients with pulmonary tuberculosis in the city and province of Maputo, Mozambique, 2021-2022

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Background The prevalence of Non-communicable Diseases (NCDs) in countries where Tuberculosis (TB) and HIV/AIDS are still major challenges rises concerns for public health. Mozambique faces an epidemiological transition and the overlap of TB, HIV and NCDs may have implications for the control of the three diseases.
The objectives of this study were to determine the prevalence of diabetes, obesity and arterial hypertension and the associated risk factors in patients with pulmonary tuberculosis in the city and province of Maputo, south Mozambique.
Methods A cross-sectional study was conducted in four Health Centers from March 2021 to July 2022. All new cases of pulmonary tuberculosis confirmed by bacilloscopy (BK) or GenExpert, and with or without HIV, were recruited and tested for diabetes by measuring glycosylated haemoglobin (Hb1Ac). The arterial blood pressure and body mass index (BMI) were measured, and socio-demographic variables were collected through a questionnaire. The data were entered into the REDcap platform and analysed using the SPSS version 20.
Results Of the 402 patients TB subjects, 62.2% were male, with a mean age of 38 years. The prevalence of Diabetes (HbA1c > 6.5%) was 12.7%. Regarding hypertension, systolic hypertension (SBP>140 mm Hg) was 16.9%, and diastolic hypertension (DBP >110mm Hg) was 29, 9%. The Obesity (BMI > 25) was 13.7%. In overall subjects, HIV was positive in 41.3%. Regarding the risk factors for chronic diseases, 11.7% had a family history of Diabetes, 50.7 % had alcohol habits, 19.9% had smoking habits and 74.6% did not practice physical activity.
Of the HIV positive patients, 30.7% had systolic hypertension and 19.3% diastolic hypertension, 16.3% diabetes and 14.5% obesity.
Conclusion The prevalence of diabetes and arterial hypertension in TB patient is high compared to other African countries. Thus, is recommended to establish an integrative screening service for NCDs screening in patients with Pulmonary Tuberculosis.

PA-527

Beta-cell function and insulin resistance in adults with different patterns of diet: a cross-sectional study in northwestern Tanzania

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Background The diabetes burden in sub-Saharan Africa is high, but data on the relative importance of insulin resistance and beta-cell dysfunction there is scarce. We investigated the association between dietary patterns with insulin resistance and beta-cell dysfunction among HIV-infected and HIV-uninfected adults in Mwanza, Tanzania.
Methods In a cross-sectional study, insulin resistance and beta-cell function were measured from plasma insulin and glucose during an oral glucose tolerance test. Diet data were collected using a validated food frequency questionnaire, and dietary patterns were derived by principal component analysis and reduced rank regression. Socio-demographics, smoking, alcohol taking, and physical inactivity data were collected using structured questionnaires. Logistic regression analysis was used to assess the association between insulin resistance, and beta-cell dysfunction with dietary patterns adjusting for potential confounders.
Results Of 462 participants, the mean age was 42 (±12) years, 58% were females, and 60 % were HIV-infected. The proportion with insulin resistance was 43% and 35% by the Matsuda index and HOMA-IR, respectively. Beta-cell dysfunction was present in 37%, 43%, and 43.3% by the insulinogenic index, HOMA-β, and oral disposition index, respectively. Higher adherence to a carbohydrates-dense diet pattern was associated with more insulin resistance by HOMA-IR (aOR 3.7, 95% CI 2.2; 6.3) and Matsuda index (aOR 6.2 3.4; 11.2), and less beta-cell dysfunction by HOMA-β (aOR 0.4 0.2; 0.6) and insulinogenic index (aOR 0.5 0.3; 0.9). Higher adherence to the vegetable-rich pattern was associated with insulin resistance by the Matsuda index (aOR 2.2 1.3; 3.7).
Conclusion Carbohydrate-dense pattern increases the risk of insulin resistance but decreases beta-cell dysfunction. Higher adherence to a vegetable-rich pattern increases the risk of insulin resistance. Further studies to look at glucose metabolism and why a vegetable-rich pattern has an odd effect in sub-Saharan Africa are warranted.
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PA-530

Association of Tumor involvement at diagnosis, type of treatment administered and Human Leucocyte Antigen with endemic Burkitt's Lymphoma survival rates in northern Uganda

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Background This study addresses the problem of the paucity of literature on survival rates and its determinants among eBL patients from Sub-Saharan Africa. Endemic Burkitt Lymphoma (eBL) is one of the most important cancers disproportionately affecting children. It is a B-cell tumor and the most common childhood cancer in many countries in equatorial Africa, including Uganda. To fill this gap, we proposed to study whether the extent of tumor involvement at diagnosis, the type of treatment administered, and a patient's immune response regulating genes called Human Leucocyte Antigen (HLA) are associated with five-year survival rates among a group/cohort of Burkitt Lymphoma children hospitalized in Uganda between 2011 and 2015.
Methods We performed a cross-sectional study of 316 eBL cases previously treated at St. Mary's Hospital Lacor between the period of 2011-2015. We reviewed medical records to abstract data for screening and enrolment of participants. Participant-five-year survival rate since diagnosis was the main outcome and the extent of tumor involvement at diagnosis, type of treatment administered, and Human Leucocyte Antigen (HLA) were the independent variables.
Results Of 316 enrolled participants, the age range of the participants was 0–15 years. Of the 303 (95.8%) that had their tumor staged at the time of hospitalization, 17% (5/303) had their tumors staged as Category One, and 98% (298) staged as Category Two. The proportion of surviving children was 265 (0.84) compared to 51 (0.16) that died at the time of hospitalization. Survival status at the end of treatment was not associated with the tumor category at the time of hospitalization.
Conclusion When completed, the results of this study shall highlight the factors affecting the survival of eBL children in Uganda which is important information for developing meaningful follow-up strategies with an increased focus on survivorship beyond routine disease surveillance.

PA-539

Developing hands-on skills on tuberculosis sponsor responsibilities and clinical trial management for END-TB in Sub-Saharan

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Background The END TB strategy recommends scaling up of research training and capacity by growing the workforce of scientists in tuberculosis (TB) endemic settings skilled in "development and rapid uptake of new TB tools and "interventions" and "research to optimise implementation and impact". The SimpliciTB consortium aimed to develop the skills, confidence and international competitiveness of African research leaders engaging in TB while extending network of African sites capable of performing high quality clinical trials in TB.
Methods Through co-leadership and partnership with St Andrews University, University College London from United Kingdom; Radboud University Medical Center-The Netherlands and TB Alliance-United States mentorship was provided to the senior clinical research fellow and clinical research & development fellow based at Kibong'oto Infectious Diseases Hospital in Tanzania to execute sponsor and trial management responsibilities for a new clinical trial of anti-TB therapy to be delivered in four African countries: Gabon, Malawi, Mozambique and Tanzania.
Results From January 2022- April 2023, achievement in capacity development include design of the potential regimen for a phase III TB clinical trial, and development of the protocol titled: "A pragmatic trial with optimized dose of rifampicin and moxifloxacin for the treatment of drug susceptible pulmonary tuberculosis (OptiRiMoxTB)". The Operational team meeting was successfully formulated comprising of two categories i) sponsor category with international principal investigators as co-chairs, trial manager and associated core groups including biostatistics and data management, pharmacy and drug management, microbiology and biomarkers, finance and administration and ii) Trial sites each bringing at least the site PI, and site coordinators. Trial-governance including the data safety monitoring and steering committees are set. All sites have submitted ethical and regulatory clearance to their respective bodies and authorities.
Conclusion Despite challenges, the preparatory phase has completed and enrolment of participants expects to start in the second quarter of 2023.

PA-540

Activation profile of peripheral Mycobacterium tuberculosis-specific CD4+ T cells associate with high-resolution imaging findings in Tuberculosis household contacts

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Background High-resolution imaging has permitted identification of lung pathology related to asymptomatic subclinical disease state. However, current diagnostic tests do not permit to identify asymptomatic individuals with early TB disease. We and others have shown that the activation profile of Mtb-specific CD4 T cells is a robust biomarker to identify active TB cases. Our aim was to define if such blood-based flow cytometric relates to radiographically defined subclinical TB.
Methods Our cohort consisted of 137 tuberculosis household contacts who had undergone 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) imaging, which identifies anatomical abnormalities and elevation of FDG uptake indicative of ongoing inflammation. We measured the frequency, activation and polyfunctional profile of Mtb-specific CD4+T cells using flow cytometry, and the profile of Mtb-specific CD4 responses was related to the FDG uptake quantified by standardized uptake value (SUVmax) and visual score (VS). A 6-month follow-up sample and PETC/CT were obtained on 35 participants.
Results While the frequency and polyfunctional capacity of Mtb-specific CD4+ T cells show no relationship with the degree of inflammation in the lung, HLA-DR expression on Mtb-specific CD4+ T cells positively associated with both SUVmax ($p < 0.0001$, $r = 0.45$) and VS ($p < 0.0001$, $r = 0.44$). Moreover, longitudinal analysis shows that dynamic change in HLA-DR expression on Mtb-specific CD4+ T cells (ΔHLA-DR) over 6 months mirrors SUVmax and VS changes ($p = 0.017$, $r = 0.46$ for ΔSUVmax and $p = 0.004$, $r = 0.54$ for ΔVS).
Conclusion Our data demonstrate that a simple flow cytometry-based assay, measuring the activation level of peripheral Mtb-specific T-cells, could act as a surrogate marker to identify asymptomatic individuals with TB-associated lung inflammation. This could aid in the development of new tools to 1) identify those most at risk of TB progression and 2) assist targeted enrolment into efficacy trials of new TB vaccines.

PA-541

Underrepresentation of clinical trials in Africa: A call for social justice and equitable participation

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Background Despite having 18% of the world's population and 25% of the global disease burden, Africa contributes less than 5% of clinical trials. The continent's population is predicted to grow by 2 billion by 2038; creating an unexploited market for clinical trials which are critical to the development of new medications, improving patient access and achieving health equity. Making trials equitable entails ensuring that they are carried out in populations that would benefit from them and who have the disease characteristics of interest. Justice and equity in trials have the potential not just to benefit vulnerable populations, but also to strengthen the value, quality, and generalizability of trials outcomes. Using data from two major global trial registries, we describe inequitable representation of clinical trials in Africa.
Methods A cross sectional analysis of both interventional and observational studies registered on ClinicalTrials.gov trial registry before 1st May 2023) and WHO International Clinical Trials Registry Platform (ICTRP). Trends across regions were compared in both databases.
Results Among 450,550 trials registered in ClinicalTrials.gov database, 16,430 (3.6%) were conducted in Africa. Globally, there has been a steady increase in the number of trial registrations in ICTRP during the 1999–2021 period, however, Africa continuously registered the least number of trials over the years, 13,208/781, 080 (1.7%).
Conclusion Current underrepresentative research in Africa contributes to widening the gap of health inequities and necessitates radical changes. There is need for equity, and social justice in clinical trial representation in Africa, with a deliberate effort to prioritize diversity, inclusion, and ethical conduct in research studies. Together, Africa research institutions and collaborating partners such as EDCTP can increase the number of trials conducted in Africa to improve capacity of African nations to conduct clinical trials and improving health outcomes in vulnerable populations.

PA-543

Evaluation of host serum biomarkers from successfully treated TB patients presenting with or without persisting lung inflammation - preliminary findings of StatinTB trial

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Background Despite the availability of anti-TB treatment, successfully treated TB patients remain with persisting lung inflammation regardless of HIV status. Lung inflammation has been linked with robust or imbalanced host immune responses which exacerbate tissue necrosis. Soluble host biomarkers have been shown to correlate with the development of lung inflammation at different stages of anti-TB treatment which further affect sputum conversion in these patients.
In our ongoing StatinTB trial (RIA2017T-2004; NCT04147286), we evaluate safety and efficacy of 40 mg atorvastatin to reduce persistent lung inflammation after TB treatment in HIV-/HIV+ adults measured by 18F-FDG-PET/CT. Here we aim to explore the expression profile of host serum biomarkers from successfully treated TB patients with or without persisting lung inflammation.
Methods Study participants were screened for sputum conversion at month-4 and month-6 of anti-TB treatment. Enrolled participants were subjected to PET/CT scan, where Arm A=TLG<50SUVbw*ml (minimal lung inflammation) and Arm B=TLG≥50SUVbw*ml (persisting lung inflammation). A total of 71 participants (Arm A=42, Arm B=29) were evaluated in this study. Serum samples were collected after 1-week washout period following completion of anti-TB treatment. A panel of 48 biomarkers were evaluated using Luminex multiplex platform (Bioplex200).
Results Twenty soluble biomarkers were differentially expressed between Arm A (TLG<50SUVbw*ml) and B (TLG≥50SUVbw*ml). These included 9 pro-inflammatory biomarkers,1 anti-inflammatory cytokine, 5 growth factors, 2 pleiotropic mediators and 3 chemokines. Using ROC curve, 14 biomarkers were identified as potential individual candidates to distinguish between Arm A and Arm B with AUC ranging between 0.702-0.833 where sensitivity ranged between 58.6-69.0% and specificity ranged between 71.4-81.0% at specific cut-off values.
Conclusion This study highlights that successfully treated TB patients remain with persisting lung inflammation. These patients further present with different soluble biomarker profiles which may be driven by lung inflammation.

PA-545

Diagnostic evaluation of a loop-mediated isothermal amplification test for yaws

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Background Yaws, caused by the bacterium Treponema pallidum subsp. pertenue (TPE) is a neglected tropical disease targeted for eradication by 2030. It is endemic in 15 countries across West Africa, the Pacific, and Asia. The clinical and serological tools currently used to detect yaws are hindered as many other bacteria, especially Haemophilus ducreyi (HD), can cause similar lesions. Molecular tools, such PCR, can differentiate yaws from other organisms causing skin lesions, but are expensive and require trained technicians and specialised laboratory facilities. There is therefore a need for alternative diagnostic tests that can provide rapid and accurate diagnosis of yaws within endemic countries. The LAMP4yaws project is a diagnostic accuracy study of a combined Treponema pallidum (TP) and HD loop mediated isothermal amplification (TPHD-LAMP) test conducted in three yaws-endemic countries in West Africa (Cameroon, Côte d'Ivoire and Ghana).
Methods We screened 3104 individuals with clinically suspicious skin lesions and tested these individuals with point of care serological tests. In total we recruited 517 participants with serologically-confirmed yaws in Cameroon (n=20), Côte d'Ivoire (n=97) and Ghana (n=400).
Results Overall 361 were male (69.8 %) and the median age was 9 (IQR: 4-14). Each participant provided two swabs: the first was tested for TP and HD using the TPHD-LAMP test at local district laboratories and the second was tested for these pathogens using qPCRs conducted at the national reference laboratory in each country. Alongside this we developed the first ever external quality control scheme for molecular diagnostics of yaws which could be applied to both LAMP and qPCR testing.
Conclusion We will present data on the sensitivity and specificity of the TPHD-LAMP test compared to reference standard qPCR, alongside a mixed-methods evaluation of the quality-assurance, acceptability, feasibility and cost-of the LAMP assay to determine its potential as a tool for national yaws programs.

PA-557

Feasibility randomised clinical trial on the effect of N-acetylcysteine efficacy, safety and tolerability in reducing adverse-drug-events among adults receiving multidrug resistant-tuberculosis regimen in Tanzania

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Background There is a limited capacity to conduct research particularly the clinical trials in sub-Saharan Africa. Furthermore, it was uncertain whether a clinical trial would be designed and executed in Tanzania to confront the challenges of infectious diseases. We proposed to conduct a clinical trial among multidrug resistant tuberculosis (MDR-TB) patients with the mains components of toxicity reduction and capacity development in clinical trials in Tanzania.
Methods Established clinical trial unit was equipped with standards of operations, clinical trialists, laboratory scientists, and mid-level personnel and create a rapid response infrastructure at Kibong'oto Infectious Diseases Hospital in Tanzania. Concurrently we conducted a feasibility N-acetylcysteine (NAC) trial, a phase 2b randomized open labelled superiority trial with three parallel groups and a primary endpoint of occurrence of adverse drug reaction at any time during treatment for MDR-TB. Patients were randomised to either a control arm, or an interventional arm of NAC 900mg daily, or an interventional arm of NAC 900mg twice-daily administered during the intensive phase of MDR-TB treatment.
Results From September 2021 -, October 2022, KIDH mobilized relevant personnel to execute the clinical trial. The site screened 70 MDR-TB and 66 were randomised in three arms with each of 22 participants. Trial participants that completed trial procedures in control arm,900mg daily and 900mg twice arms were 21 (95%), 18(82%) and 18 (82%) respectively. Common adverse drug events reported in trial participants included hyperuricemia 50, alanine and or aspartate transaminases 82, arthralgia 18, anemia 8, dyspepsia 7, mucocutaneous skin reaction 4 and peripheral neuropathy 3. Total severe adverse events were 8 and all were resolved
Conclusion We have demonstrated that it is feasible to design and conduct the clinical trial in Tanzania.
Funding: This study received financial supports EDCTP_2 program supported by the EU project through the Senior Fellowship Scheme TMA1463

PA-559

Use of stools for childhood tuberculosis diagnosis using GeneXpert Ultra in Bamako, Mali

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Background The diagnosis of childhood tuberculosis is still a challenge in the world because children are generally paucibacillary moreover obtaining sputum is very difficult. Most of the existing diagnostic tests for tuberculosis are based on sputum sampling in symptomatic tuberculosis patients. The objective of this work was to detect mycobacteria by Gene Xpert MTB/RIF Ultra in the stools of children samples.
Methods We conducted a cross-sectional study between January 2022 and June 2022on the diagnosis of tuberculosis by the Xpert MTB / RIF Ultra test from the stools. All Children under 15 years suspected of having tuberculosis from the pediatric department were included in the study. Stools samples have been collected and tested by xpert in the P3 laboratory of tuberculosis and hemorrhagic fevers of UCRC. In addition, sputum samples were also collected for Xpert MTB/RIF Ultra. The variable diagnostic performance was calculated.
Results We enrolled twenty-two (22) children suspected of tuberculosis. The average age of the children was 21.72 ±21.93 months. The sex ratio was sex (3,4) in favor of the male and 14% (3/22) of the patients had positive HIV status. After carrying out the Xpert MTB/RIF Ultra test from stools and sputum, 45% (10/22) of stools were positive and among the sputum 40% (9/22) were positive. The positive predictive value (PPV) and the negative predictive value (NPV) of the test Xpert MTB/RIF Ultra stool and sputum were 47,62% and 47,83%) and for sputum 45,83% and 45.45% respectively.
Conclusion Considering these results, the Xpert MTB/RIF Ultra test performed on stool may be an alternative for the diagnosis of childhood TB in the absence of a good sputum sample.

PA-565

Low rates of virological failure and HIV drug resistance among HIV-infected children at the mother-child centre in Yaounde, Cameroon: lessons following transition to dolutegravir

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Background Virological failure (VF) in pediatrics remains challenging in sub-Saharan Africa (SSA), reaching alarming rates in Cameroon. With limited evidence in the era of transition to pediatric dolutegravir (DTG)-based antiretroviral therapy (ART), we sought to evaluate predictors of virological response and HIV drug resistance (HIVDR) among children within the Cameroonian context.
Methods A facility-based study was conducted among HIV-infected children aged 6 months to 10 years at the Chantal BIYA Foundation's Mother-Child Centre in Yaoundé-Cameroon, from November 2022 through April 2023. Plasma viral load (PVL) and HIVDR were performed at the Chantal BIYA International Reference Centre. VF was defined as two consecutive PVL>=1000 copies/ml at one month interval under active adherence counselling/support (daily reminder and psychosocial supports by phone calls/SMS). Predictors of virological response were determined, with $p<0.05$ considered statistically significant.
Results A total of 318 HIV-infected children were enrolled; median [IQR] age was 8 [5.75-9] years and sex ratio was 1:1. Regarding ART-regimens, 299 (94%) were on DTG-based, 16 (5%) PI/r-based, 3 (1%) NNRTI-based regimens; and mean duration on ART was 5.57 ± 2.57 (min-max: 7-10) years. Based on PVL results, 37 children were virally unsuppressed (PVL>=1000 copies/ml), giving a rate of 11.6% non-viral suppression. Non-viral suppression was significantly higher with poor adherence ($p<0.001$) and living out of the town ($p=0.018$). After active adherence counselling/support, 30 adherent children were resampled and 3 had PVL>= 1000 copies/ml, indicating 0.99% (3/311) rate of VF. Among the 3 experiencing VF, HIVDR mutations were found in 2: L74V (1/3), K103N (1/3), M184V (2/3), P225H (1/3); indicating an overall rate of 0.66% (2/302) HIVDR. Neither PI nor INSTI mutations were found.
Conclusion Children are experiencing good treatment with transition to DTG-containing ART together with active adherence support, leading to less than 1% VF and HIVDR. This strategy contributes in achieving the third 95 in children and preserves future pediatric therapeutic options in SSA.

PA-566

Acceptability and feasibility of a pilot malaria prevention strategy for children under two years in Sierra Leone: a mixed methods study among Health Care Workers

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Background Despite evidence of its safety and efficacy in preventing infant malaria, Sierra Leone is the only country worldwide to have deployed the WHO-recommended Perennial Malaria Chemoprevention (PMC) strategy at the country level. The MULTIPLY project is evaluating extending PMC into the second year of life and strengthening PMC delivery through outreach services. We aimed to assess the acceptability and feasibility of this pilot approach among Health Care Workers (HCWs).
Methods This was a cross-sectional mixed methods study conducted from January–February 2022 in three districts (Bombali, Port Loko and Tonkolili). A self-administered questionnaire was used among 144 HCWs and 42 CHWs actively involved in under-5 care in selected facilities (n=25). In addition, in 9 selected facilities of Bombali district, structured observations were conducted, 9 facility in-charges responded to a semi-structured individual interview as well as 13 HCWs and 4 key informants. Descriptive analysis was performed on the quantitative data, qualitative data was analyzed thematically, followed by a mixed methods analysis.
Results Respondents had good knowledge (score 16.4 out of 21) of the causes, symptoms and prevention of malaria. Most (93.5%) perceived PMC as an effective strategy. PMC integration alongside routine immunization was perceived as reducing HCW and caregiver costs and time-associated burden. HCWs trusted that PMC expansion through increased doses would lead to improved health outcomes. However, several existing logistical and structural barriers were documented, including stock-outs of drugs and vaccines, unavailability of supplies for PMC administration, transportation for caregivers accessing facilities and HCWs delivering outreach services, and the anticipated increase in workload due to additional reporting tools.
Conclusion HCWs reported positive experiences and perceptions of PMC integrated alongside routine immunisations and the overall anticipated acceptability of the pilot strategy. Findings suggest that innovative implementation strategies will be key to overcoming the feasibility barriers identified.

PA-569

Evaluation of the effect of intermittent preventive treatment of malaria in pregnancy five years after the update of the national policy in Burkina Faso

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Background Since 2014, Burkina Faso has adopted the new policy of intermittent preventive treatment of malaria in pregnancy with sulfadoxine-pyrimethamine (IPTp-SP). We assessed the effect of the 3-dose strategy of IPTp-SP on reducing the prevalence of malarial infection, low birth weight (LBW) and maternal anaemia at delivery, as well as associated risks factors in the health district of Yako, 5 years after the update of the national policy.
Methods A cross-sectional study was carried out among recently delivered women in health facilities of Yako from July to December 2019. Sociodemographic characteristics, medical and gynaeco-obstetrics history were collected using a standardized questionnaire. We performed a microscopy and measured the haemoglobin level (Hb) by HemoCue. A multivariate logistic analysis was conducted with a significance of $p < 0.05$.
Results Overall, 614 women were included. The average age was 25 ± 6 years and the majority of women (74.59%) were married, illiterate (53.83%) and housewives (69.56%). Over 92% of them said they slept under an insecticide-treated bet net (ITNs). The prevalence of malaria infection was 10.93%. The average birth weight was 2942.2 ± 462.28 grams and 11.06% were born with LBW (birth weight < 2500 grams). The use of the ITNs significantly reduced the risk of LBW, unlike the maternal age (<20 years), hypertension and the female sex of the new-born. Anaemia (Hb < 11.0 g/dl) was found in 54.77% of women, and this anaemia was severe (Hb < 8.0 g/dl) in 5.92% of cases. Young maternal age, maternal fever, malaria infection as well as a history of stillbirth were significantly associated with the risk of severe anaemia. There was no association between the number of doses of SP received and the risk of LBW.
Conclusion The coverage of the IPTp strategy seems to have been improved. Studies on parasite drug resistance are needed.

PA-574

Prevalence and factors associated with malaria infection in children aged 10 to 23 months in Togo in 2022

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Background Intermittent Preventive Treatment in infants (IPTi) is a strategy to prevent malaria in children living in moderate-to-high malaria transmission areas through administration of a full therapeutic course of sulfadoxine-pyrimethamine. MULTIPLY is a multicentric project aiming at implementing IPTi in three sub-Saharan Africa countries. Before IPTi implementation in Togo, we conducted a survey to estimate malaria and Plasmodium infection prevalence in children aged 10 to 23 months (U2).
Methods A cross-sectional household survey was conducted in Haho district between Jan– Feb (dry season) 2022. Three-stage cluster random selection was carried out. Vaccination status, insecticide-treated bed net use, and children's demographic characteristics were collected. Malaria infection was defined as positive malaria rapid diagnostic test and estimated with its 95% confidence interval (CI). A mixed-effects logistic regression model was used to assess factors associated with malaria infection. Survey data was weighted to reflect the sampling design.
Results A total of 685 children (51.8% male) were included with a mean age of 17 months. Eight out of ten slept under bed net the night before the interview. The prevalence of Plasmodium infection was 32.1% (95% CI: 28.6–35.7) of which a half had clinical symptoms. In the multivariable model, low educational level of the household head (primary: aOR=1.78 and no formal education: aOR=1.70; p=0.038; ref = secondary or above), presence of more than one under five years children in the household (aOR=1.47; p=0.031) and living at >5 km from the nearest health facility (aOR=1.52; p=0.042) were associated with malaria infection.
Conclusion While the survey was conducted in the dry season, one third of U2 children had malaria infection. IPTi can be a promising strategy to reduce malaria burden in this vulnerable population. Strengthening outreach services and more targeted health communication could play an important role in protecting children against malaria.

PA-577

The WHO Research Framework: Developing a highly adaptable framework designed to work for all clinical research

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Background To drive improvements in health we need more and better evidence derived from data from the whole spectrum of health research, and from every healthcare setting. Essential research is not being conducted because researchers can be daunted by overwhelming regulations and confusion over how to apply existing guidelines. Here we describe the development of the WHO Research Framework Tool, an innovative decision-tree application designed to guide researchers to relevant, appropriate guidance tailored for their specific study design, to ensure scientific and ethical standards are met, in a manner proportionate to risk.
Methods A prototype Framework Tool developed by a Core Group of researchers has been iteratively tested and refined by a Review Group. Comprised of researchers from varied health research backgrounds and healthcare settings, Review Group members were invited to use real study examples to test the tool's algorithms, and feedback on the questions, and guidance generated. Testing of the application is now being widened to include stakeholders across The Global Health Network's global North and South collaborations and WHO Regional and Country Offices to ensure it is globally and locally relevant.
Results The Framework Tool will be presented, and more researchers invited from different geographical locations, methodological and therapeutic research groups to contribute to expanding the types of study designs included and its further refinement.
Conclusion Different types of evidence are needed to understand, prevent, treat and manage health problems, within an ecosystem of research. This tool will enable researchers in all research settings to navigate complex regulations and locate relevant guidance to support them in setting up high-quality, accurate, safe, and ethical health research studies regardless of type. This approach also ensures anyone has the opportunity to be involved in developing a fit-for-purpose tool that may be shaped by progress in research methodologies within global health.

PA-580

Capacity development to facilitate delivery and uptake of a new medical intervention: Fexinidazole oral treatment for the elimination of human African trypanosomiasis

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Background T.b. gambiense human African trypanosomiasis (g-HAT) is a neglected tropical disease targeted by the World Health Organization (WHO) for elimination by 2030. The first all-oral treatment for g-HAT, fexinidazole (developed by DNDi), received a marketing authorization in DRC in December 2018 and was included as first-line treatment in the new WHO-HAT treatment guidelines and added to the 2019 WHO-Essential Medicines Lists. DNDi collaborated with WHO to support five HAT-endemic countries through EDCTP2.
Methods The project focused on healthcare capacity-strengthening and coordination support for the appropriate use of fexinidazole, and fexinidazole surveillance and national pharmacovigilance systems support, including for the timely and efficient reporting of adverse reactions through the HAT Platform as a communication mechanism, trainings, and reinforced pharmacovigilance channels. Regarding fexinidazole surveillance, selected health facilities' health workers were trained on WHO-HAT treatment guidelines and safety notification, including choice of internationally compatible software with Vigibase repository. Support to national pharmacovigilance systems was provided to five target countries (DRC, Guinea, Angola, CAR, and South Sudan) through baseline assessments, set-up, and training of five national and six regional pharmacovigilance units in the DRC coordinated with the DRC national PV team.
Results During the last two years of the project, 630 healthcare workers from 243 facilities were trained on the new WHO-HAT treatment guidelines, including fexinidazole, in the five target countries. 556 HAT patients were treated with fexinidazole, and notifications of adverse events were sent to WHO and national pharmacovigilance systems. In addition, the five national pharmacovigilance systems were equipped and trained.
Conclusion This project enabled the reinforcement of five countries' national pharmacovigilance systems and development of collaborative networking to extend safety surveillance to all drugs. Healthcare workers in all five countries were trained in the use of fexinidazole, and HAT patients are now being effectively diagnosed and treated.

PA-581

Population-based surveillance of anti-sars-cov-2 antibodies according to vaccine-status in Cameroon: evidence from the EDCTP perfect-study

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Background Anti-SARS-CoV-2 vaccine remains a global health priority but there is scarcity of evidence on post-vaccine response from sub-Saharan Africa countries. Our objective was to assess the overall rate of SARS-CoV-2 immunity and its association according to vaccine-status and types of vaccines administered in the Cameroonian context.
Methods A population-based sero-survey was conducted from February through July-2022 among individuals screened for COVID-19 at the Chantal BIYA International Reference Centre-(CIRCB) in Yaoundé-Cameroon. Socio-demographic, clinical features and vaccine status were collected; SARS-CoV-2 antibodies were tested on plasma using Ninonasal™ COVID-19 IgG/IgM assay. Statistical analyses were performed, with $p<0.05$ statistically significant.
Results Of the 1713 participants enrolled, median [IQR] age was 39 [31–48], 57.1% (978/1713) men, 1.6% (27/1713) had flu-like symptoms and 19.7% (337/1713) had previously SARS-CoV-2 positive. Regarding vaccination, 67.6% (1158/1713) had received at least one dose (48.5% Pfizer, 24.9% Johnson&Johnson, 18.0% Moderna; 7.8% AstraZeneca, 4.4% Sinopharm and 0.2% Sputnik-light), of whom 91.9% (1064/1158) fully vaccinated. Median duration post-vaccination was 5 [3–8] months (min: 1; max: 20). Overall rate of anti-SARS-CoV-2 antibodies was 83.9% (1438/1713), with 0.2% (3/1713) IgM, 80.6% (1381/1713) IgG and 3.2% (54/1713) IgM/IgG. Following univariate analysis, the presence of antibodies was associated with female gender (F/M, $p=0.028$), vaccination (Yes/No, $p<0.0001$), complete and partial vaccination ($p<0.0001$ and $p=0.008$ respectively), duration post-vaccination (≤5 />5months, $p<0.0001$), as well as with all COVID-190 vaccines except sinopharm and sputnik ($p<0.0001$, $p=0.0002$, $p<0.0001$, $p=0.024$, $p=0.5$ and $p=0.94$ respectively). Following multivariate analysis, being vaccinated and duration post-vaccination (≤5months) were predictors of the presence of anti-SARS-CoV-2 antibodies (aOR=3.13 [95%CI: 2.39–4.09]; $p=0.0001$ and aOR=2.5 [95%CI: 1.63–3.84]; $p<0.0001$ respectively).
Conclusion The high-rate of COVID-19 antibodies suggests herd immunity at community-level in Cameroon following vaccination. However, rapid fading of antibodies (~5months) calls for strategies to adjust timing for booster-doses while phasing-out vaccines with poor immunity.

PA-583

Revolutionising tuberculosis treatment response monitoring and developing research capacity in Africa: progress and potential of the Tuberculosis Molecular Bacterial Load Assay

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Background Tuberculosis (TB) treatment is long and complex. Here we summarise data from EDCTP-funded studies of the Tuberculosis Molecular Bacterial Load Assay (TB-MBLA) as a TB treatment monitoring tool.
Methods Treatment naïve participants from four Sub-Saharan African countries were assessed for TB diagnosis and treatment response using TB-MBLA compared to liquid culture (MGIT) and other standard-of-care tests.
Results Diagnostic accuracy assessment using MGIT as gold standard showed TB-MBLA sensitivity, specificity, positive-and-negative-predictive values were 99%, 91%, 92% and 99% respectively among presumptive TB cases. TB-MBLA turn-around-time (clinic-laboratory-clinic) was <24h compared to 5-42 days of MGIT culture. 450 participants were assessed for treatment response across four studies. The pre-treatment bacillary load across cohorts was 5.33+1.33log10eCFU/mL which was cleared to zero in over 95% of the participants by month-6 of treatment. TB-MBLA revealed early bacillary load clearance in 7% (32/450) participants who achieved a stable negative TB-MBLA result by week-2 of treatment and was faster than MGIT to identify participants at a risk of disease relapse. High pre-treatment bacillary load =/>6log10eCFU/mL, was associated with failure to convert to negative by month-2 of treatment. Resolution of TB-MBLA-measured sputum bacillary load mirrored cough resolution, reduction of C-reactive protein levels in blood and correlated with MGIT culture time-to-positivity (Spearmans r= -0.5, p<0.0001) during treatment. Like MGIT, TB-MBLA demonstrated that regimens containing rifampicin-35mg/kg and rifampicin-20mg/kg-400mg-moxifloxacin cleared TB bacteria significantly faster than the standard-of-care regimen by month-2 of treatment, p=0.049 and p=0.008 respectively in DS-TB, and highlighted efficacy of bedaquiline-containing all oral regimen for DR-TB treatment. This work produced 5 African PhD graduates plus >500 clinical/laboratory scientists trained in principles of molecular diagnostic development and implementation globally.
Conclusion The data shows that TB-MBLA is a robust assay for TB treatment response monitoring and anti-TB drug development. It has contributed to research capacity building across Africa and beyond.

PA-591

Antimicrobial resistance in bacteria isolated from diarrheal stools in children at the Yirimadio community health center, Mali

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Background Diarrheal diseases constitute a serious public health problem, particularly in developing countries and it is the second leading cause of child mortality. Self-medication and overuse of antibiotics due to the scarcity of complementary diagnostic systems can lead to the development of multi-resistant bacteria causing diarrhea. The objective of this work was to identify the bacteria responsible for diarrhea in children and to characterize their sensitivity to a panel of antibiotics used in Mali.
Methods This study involved 554 children seen in outpatient visits at the Yirimadio community health center and diagnosed with diarrhea. Yirimadio is a peripheral district area of Bamako the capital city of Mali. Stool samples were collected and analyzed by stool culture and antibiotic susceptibility was determined by the disk diffusion method on agar medium.
Results The bacteria responsible for diarrheal were Escherichia coli (31.8%) and Salmonella (2.9%). In Escherichia coli strain, amoxicillin and cotrimoxazole were the most resistant antibiotics, 93.8% and 92.6%, respectively. The Extented Spectrum Beta Lactamase resistance phenotype accounted for 39.8 % in Escherichia coli. A resistance of 12.5% to cotrimoxazole and cefoxitin was found to Salmonella strains.
Conclusion This study showed that Escherichia coli is the most frequent bacteria involved in diarrhea in children under 3 years of age in Yirimadio, which are resistant to amoxicillin and co-trimoxazole, two antibiotics commonly prescribed in this setting.

PA-593

A Lassa fever vaccine trials program in west Africa: advancing a product to licensure in times of outbreak

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Background Lassa Fever (LF) is a growing public health threat in West Africa. Each year, LF kills thousands and about 300,000 people become ill, while approximately 80% of infections are unrecognized. Primary transmission is via rodents, however human-to-human transmission occurs, especially in medical settings. The live attenuated chimeric vaccine candidate, rΔVSVG-LASV-GPC, created by replacing the attachment protein of VSV with that of Lassa Virus, has been shown to be safe and immunogenic in a Ph1 trial (IAVI C102 PACTR202106625781067).
Methods The Lassa Fever Vaccine Efficacy And Prevention for West Africa (LEAP4WA) consortium brings together partners from West Africa, Europe, and the U.S. to advance the development of rΔVSVG-LASV-GPC towards licensure. The program encompasses three pillars: capacity building, community engagement, and clinical trial implementation.
Results The program has identified sites in Liberia, Nigeria, and Sierra Leone with high LF incidence and supports community engagement, infrastructure improvement, and skills development. The LEAP4WA teams have upgraded facilities, trained on Good Clinical Practices, Good Clinical Laboratory Practices, Basic and Advanced Life Support, and developed Standard Operating Procedures. Informed by prospective cohort studies that assessed LF incidence and prevalence and the Phase 1 clinical trial, conducted separately from LEAP4WA, a protocol for the LEAP4WA trial is being developed. Engagement of diverse at-risk communities leverages partners' strong community ties and research traditions, incorporating awareness of LF and rodent control and understanding of research goals and methods.
Conclusion LEAP4WA will enable a Phase 2b safety and efficacy study of the novel vaccine in adults and children in Nigeria, Sierra Leone, and Liberia. This represents a key step in LF vaccine development and accelerates the path to broad access by engaging diverse at-risk communities. This study will lead to a pivotal Phase 3 trial to assess efficacy, with a goal of achieving licensure as a preventive vaccine.

PA-594

CYP2C8*2 impacts desethylamodiaquine concentration upon repeated artesunate-amodiaquine treatment of uncomplicated malaria in Mali

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Background CYP2C8 polymorphisms can impair the metabolism of the antimalarial amodiaquine and influence exposure to the key active metabolite desethylamodiaquine (DEAQ). CYP2C8*2 entailed to slow metabolism phenotype is the most frequent allele in Africa. Here we study the association between CYP2C8*2 carriage and DEAQ D7 drug level for repeated treatments. We conducted a retrospective study on achieved dried blood spot samples and drug level data from West African Network for Clinical Trials of Antimalarial Drugs (WANECAM I) conducted between October 2011 and December 2015 in Bougoula Hameau (Mali).
Methods We analyzed 206 samples and the related data from patients enrolled in artesunate-amodiaquine arm and actively followed for 2 years. DNA was extracted with QIAGEN kit. CYP2C8*2 status was determined by PCR-RFLP. We used DEAQ day 7 plasma concentration data previously measured by High Performance Liquid Chromatography. The set of outliers with extremely high day 7 DEAQ levels were additionally analyzed by Real time PCR for the presence of CYP2C8*3 and *4. Finally, we analysed the association between homozygous genotype, drug level and the timeframe between episodes.
Results Out of 206 patients, 153 patients (74.3%), 40 patients (19.4%) and 13 patients (6.3%) patients were respectively *1/*1, *1/*2 and the *2/*2. During the first treatment, there was no difference in D7 DEAQ drug level between the *1/*1 and *2/*2 groups. However, when retreatment was required less than 35 days after the first intervention, a more intense DEAQ accumulation was observed among *2/*2 carriers, relative to the first episode levels (D7, + 67%), compared with *1/*1 subjects (D7, +16%).
Conclusion We showed that repeated artesunate-amodiaquine administration inside a 35-day post-treatment frame leads to DEAQ accumulation, the effect being significantly higher in patients carrying the reduced function allele CYP2C8*2, suggesting an increased risk of overexposure and amodiaquine toxicity.

PA-595

Hepatotoxicity associated to N-Acetyltransferase type 2 polymorphisms in TB patients with malaria at Jamot Hospital, Yaoundé, Cameroon

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Background Unlike in developed countries, most infectious diseases such as tuberculosis (TB) and malaria continue to cause deaths in low-income countries. Recent studies have shown that hepatotoxicity during TB treatment may be related to the Arylamine N-Acetyltransferase (NAT2) acetylator polymorphism especially in countries with high TB incidence such as Cameroon. The aim of this study was to determine the NAT2 genetic variation associated with hepatotoxicity in TB/Malaria co-infected patients in Jamot Hospital, Yaoundé-Cameroon.
Methods This was a prospective study from April 2018 - March 2019, aiming to evaluate the genetic variation in NAT2 coding region in TB patients with malaria. A total of 336 pulmonary TB patients with or without malaria infection, aged 15 years and above, were included. Each sputum sample was tested by the Ziehl Neelsen method. Whole blood sample was used for malaria detection using Rapid Diagnostic Test and microscopy. DNA was extracted by chelex method, hepatotoxicity by spectrophotometry, and genotyping done by Polymerase chain reaction followed by restriction fragment length polymorphism analyses with enzymes (KpnI, TaqI, BamHI).
Results Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) values were significantly higher among TB/malaria co-infected cases compared to TB mono infected patients (p=0.03, p=0.01 respectively). In the group of mono-infected TB patients, a significant difference was found for ALT values between day 1 and day 90 (p=0.021). Similarly, a significant association was found between the development of hepatotoxicity and the presence of a slow acetylator phenotype in TB-malaria co-infected (p=0.026).
Conclusion The study suggests that TB/malaria co-infections and NAT2 variant phenotype are risk factors for hepatoxicity induction. Therefore, for a more efficient care, evaluation of NAT2 genotypes might be essential to reduce drug interactions and liver toxicity in case of coinfections.

PA-597

Experiences and lessons learnt in the 13 years of the EDCTP funded EACCR Reciprocal Monitoring scheme

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Background In April 2010, East African Consortium for Clinical Research (EACCR) in partnership with the University of Oxford initiated the Reciprocal Monitoring Scheme (RMS). This is an innovative, practical and affordable monitoring scheme whose main aim is strategic quality management of health research for the 23 institutions that form the consortium. The main role of the RMS is to oversee the progress of clinical trials while ensuring that they are conducted, recorded, reported in accordance with approved Protocols, Standard Operating Procedures (SOPs), applicable local and international regulatory requirements and Good Clinical Practice. We share our experiences and lessons learnt in the past 13 years.
Methods Each institution identified one or two experienced monitors who were paired with unexperienced monitors for mentorship and capacity building. Cross-country pairing was done and monitors were allocated studies to monitor. Physical training was periodically done to refresh skills and brainstorm on experiences.
Results A regional pool of 42 monitors were trained and paired from 6 Eastern Africa countries and 5 Northern countries. Seven sponsors have been supported to monitor thirty three (33) studies so far. The scheme offered an opportunity for cross-site sharing of best practices and networking at a cheaper cost compared to using conventional clinical research associates. Dedicating time for monitoring activities remains a big challenge for the study team and monitors.
Conclusion Paired monitoring fostered capacity building and maximized sharing of best practices for quality management of internationally recognized health research. Cross-country monitoring visits promoted networking and dialogue between researchers, communities and other stakeholders.

PA-604

Whole genome sequencing confirmed contamination of Mycobacterium ulcerans-infected lesions by Rhodococcus erythropolis

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Background We describe two contamination cases of Mycobacterium ulcerans clinically infected lesions by Rhodococcus erythropolis, a bacterium of environmental origin with rare cases of human infection.
Methods Two lesion swabs collected from clinically characterized Buruli ulcer-like patients were submitted to molecular (IS2404-PCR) and biological (OA-decontamination + microscopy + culture) analyses for detection and in-vitro culture of Mycobacterium ulcerans (Buruli ulcer etiological agent) respectively.
Results Analysis of DNA extracts from crude samples revealed the presence of M. ulcerans DNA and the sample classified as positive. After 14-days of in-vitro incubation in Löwenstein-Jensen culture media, yellow colonies characteristic of M. ulcerans were observed. However, PCR analysis of culture suspensions revealed no M. ulcerans DNA, while Ziehl-Neelsen staining showed rough red colonies not characteristic of M. ulcerans. Further microbial identification and characterization by MALDI-TOF MS revealed the presence of Rhodococcus erythropolis. The identification was confirmed by whole-genome sequencing (WGS) to establish the genomic link between this originally called Mycobacterium erythropolis and M. ulcerans. Blasting of short reads from WGS confirmed the organism as R. erythropolis. Comparative analysis of whole genome sequences revealed low genomic relatedness between the two organisms with 5.72% average genome coverage using M. ulcerans Agy99 reference genome.
Conclusion This cases illustrates that Buruli ulcer disease may be underdiagnosed due to lesion contamination by R. erythropolis and difficulties in M. ulcerans identification in the routine clinical diagnosis procedure.
Funding: This project was funded by the EDCTP2 programme supported by the EU [TMA2019PF-2693-AGBBU].

PA-609

Pre-established Plasmodium falciparum clearance by Artemether-lumefantrine (AL) versus Artemether-lumefantrine (AL) + atovaquone-proguanil (AP) in mosquito vectors – a Study within the ASAAP Project

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Background In addition to curative treatment against the pathogenic asexual stages of malaria parasites, targeting the transmissible sexual stages is essential to impede the spread of drug resistance. The present study relies on a clinical trial testing the benefits of combining Atovaquone Proguanil (AP) with Artemether-lumefantrine (AL) in the treatment of uncomplicated malaria. AP has been shown to prevent transmission after treatment by affecting parasite development in mosquito vector Atovaquone exhibits additional properties where it persists in the serum of treated patients for days and is also known for hindering parasite development during ookinete to oocyst and oocyst to sporozoite transition. We hypothesize that pre-established P. falciparum infection in mosquitoes may be affected by metabolized drugs in patients' blood when ingested during a blood meal. We therefore tested the effect of the ingestion by mosquitoes of blood from AL versus AL+AP treated patients on pre-established P. falciparum infection.
Methods Eight time points (between Day 0 to Day 28) plasma from 24 patients treated with either AL+placebo or AL+AP has been collected for mosquito feeding. Infectious blood meal was provided to laboratory-reared female Anopheles mosquitoes and infected mosquitoes were exposed 4 days later to a second blood meal containing the plasma from treated patients.
Results We will present the effect of treatment and days post-treatment in patients, measured by comparing the infection prevalence and intensity among mosquitoes after dissection of a subset of exposed mosquitoes. The effect of treatment and time on the dynamics of sporozoite detection and mosquito survival will also be analysed.
Conclusion The present study will provide important data on alternative malaria treatments for their effect on vectorial transmission and will support decision-making for treatment policies.

PA-613

Early Identification of ART missed doses: baseline data from the RETAIN study.

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Background We present baseline data from "Improving RETention and viral load outcomes for people taking Antiretroviral therapy through early IdentificatioN of missed doses (RETAIN)", a cohort study exploring detailed adherence metrics [viral load (VL), electronic adherence monitoring (EAM); tenofovir diphosphate (TDF-DP) concentrations and self-report (SR)] in people on ART, when initially flagged for reduced adherence.
Methods ART-naïve people from three Cape Town ART clinics had adherence monitored by missed doses (EAM), missed clinic visits or by raised VL. At the time of first flagging by any measure, blood was drawn for HIV-1 VL and TDF-DP (indicating dosing over 4-8 weeks); urine collected for tenofovir rapid assay (indicating dosing over 3-5 days). SR adherence and EAM data were collected for the past 30 days. Initial adherence data at the time of first non-adherence are presented here.
Results Between July22 and March23, 61 of 282 people were flagged for poor ART adherence; 45(74%) by missed doses, 14(23%) by missed visits and 2(3%) by raised viral load. All self-reported good adherence (>90% doses taken in past 30 days), however EAM and TDF-DP showed reduced adherence across all groups [43-53% doses taken over past 30 days; suboptimal median (IQR) TDF-DP concentrations: 390 (191-677) fmol/punch (normal range >800fmol/punch)]. 56(92%) had tenofovir in their urine. Only those in the raised VL group had viremia at the time of the visit. Missed doses and missed visit were flagged sooner (35 and 45 days) than raised viral load (114 days).
Conclusion All those flagged for reduced adherence had poor adherence confirmed by objective measures, EAM and TDF-DP concentrations, despite self-reporting near perfect dosing. Positive urine tenofovir reflects dosing near to the study visit (white-coat dosing). Poor adherence was noted most rapidly by detection of missed doses and missed visits; allowing time for adherence support before breakthrough viraemia occurs.

PA-622

Growing the ethical review capacity for health research in The Gambia

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Background Ethics in research is one of the core pillars of responsible conduct of research which promotes good research practices and protects the rights of participants. Good ethical practices in the conduct of research is essential for high quality research. Research has shown a disparity in ethical review capacity in Africa with most countries not having national ethics frameworks with few or none-existing national ethics committees to oversee the conduct of research in these countries.
Methods Since 1947, Medical Research Council Unit, The Gambia at LSHTM was the only research institution in the country conducting biomedical research. The country had one independent research ethics committee that was established in 1980 - The Gambia Government/MRCG Joint Ethics Committee. The committee is the only recognised Ethics Committee (EC) in The Gambia.
While the in-country research ecosystem is registering a significant growth, policies and procedures at national and institutional levels to support the ethical conduct of research are lacking. To fully identify the capacity needs, a situational analysis of the current ethical and regulatory review capacity in academic and research institutions was conducted through the ERC Grant. The assessment was done by administering a questionnaire to academic and research institutions conducting health research. The study also conducted a workshop for institutions that have functional ethics committees during which a focus group discussion was conducted, and a questionnaire administered to have an in depth understanding of capacity gaps that exist within the existing seven committees conducting review in country.
Results Results showed significant gap in the awareness of ethics and regulatory requirements required when conducting research.
Conclusion The findings also showed that there is need for formal training on research ethics and the review process for ethics committees; the need to train a set of ethics administrators and establishing a national ethics secretariat.

PA-631

The immunopathogenic mechanisms of severe cutaneous adverse drug reactions to first line anti-tuberculosis drugs

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Background First-line anti-tuberculosis drugs (FLTD) are the commonest cause of severe immune-mediated adverse drug reactions, including SJS/TEN and DRESS in PLHV. The mechanisms of these life-threatening reactions are poorly understood, making diagnosis and treatment challenging in patients who can ill-afford suboptimal treatment.
Methods We aimed to identify genetic markers for FLTD-induced SJS/TEN and DRESS through HLA, ERAP and KIR typing, and used an integrated single-cell approach involving: i) CyTOF2 (n=8), and ii) ScRNA-seq (n=3) to characterise peripheral blood immune cells activated by offending drug.
Results Rifampicin (RIF)-associated DRESS was commonest. IFN-gamma ELISPOT, optimised for FLTDs, was most sensitive (75%) for RIF-DRESS. RIF-DRESS/SJS/TEN(ELISPOT+) cases were associated with HLA-B*44:03, and single-cell work was restricted to these cases and matched controls. HIV-related chronic immune activation drove expansion of exhausted (CD57+PD-1+TIGIT+) CD8+ T cells in cases and controls. However, a subpopulation of these CD8+ T cells in cases expressed co-stimulation (CD28+CD27+) markers. We confirmed these with ScRNA-seq, as KLRG1lowCX3CR1high CD8+ T-cells with RIF-specific proliferative and cytotoxic capabilities (IFNGhiTNFhiGNLYhiGZMBhiPerforinhi). The V-J junction and CDR3αβ analysis showed a unique TCR repertoire for each case, with predominantly CD8+ oligoclonality. GLIPH2 analysis of TCRβ sequences found eight common T-cell groups across the three cases. Differential gene expression identified the SQVP TCR-motif as having RIF-induced proliferative and cytotoxic profiles. Regulatory T-cells (CD127lowCD25hiCCR4hi) were higher in controls and produced more TGF-beta.
Conclusion This study is the first detailed immunophenotyping work of RIF-DRESS in PLHV; including optimised ELISPOT to identify IFN-gamma T-cells to FLTD, with a strong association between HLA-B*44:03 and RIF-DRESS. We propose that, despite expanded, exhausted CD8+ T-cell populations characteristic of HIV-related advanced immunosuppression, RIF-DRESS patients have drug-specific cytotoxic CD8+ T cells, potentially sharing low-frequency TCR-motifs like SQVP. Increased functional regulatory T-cells may contribute to maintaining tolerance in HLAB*44:03+ controls. Future site-of-disease and in-vitro work is required to better define proposed pathogenic T-cell populations.

PA-643

Bayesian Spatial Analysis of Incomplete Vaccination among Children Aged 12-23 Months in Nigeria

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Background High childhood disease prevalence and under-five mortality rates have been consistently reported in Nigeria. Vaccination is a cost-effective preventive strategy against childhood diseases. Therefore, this study aimed to identify the determinants of Incomplete Vaccination (IV) among children aged 12-23 months in Nigeria.
Methods This cross-sectional design study utilized 2018 Nigeria Demographic and Health Survey (NDHS) dataset. A two-stage cluster sampling technique was used to select women of reproductive age who have children (n=5,475) aged 12-23 months. The outcome variable was IV of children against childhood diseases. Data were analyzed using Integrated Nested Laplace Approximation and Bayesian binary regression models (α0.05). Visualization of incomplete vaccination was produced using the ArcGIS software.
Results Children's mean age was 15.1±3.2 months and median number of vaccines received was four. Northern regions contributed largely to the IV. The likelihood of IV was lower among women aged 25-34 years (aOR=0.67, 95%C.I=0.54-0.82, p<0.05) and 35-49 years (aOR=0.59, 95%C.I=0.46-0.77, p<0.05) compared to younger women in the age group 15-24 years. An increasing level of education reduces the risk of odds of IV. Other predictors of IV were delivery at the health facility (aOR=0.64, 95%C.I=0.53-0.76, p<0.05), and media exposure (aOR=0.63, 95%C.I=0.54-0.79, p<0.05). Mothers' characteristics explained most of the variability in the IV, relatively to smaller overall contributions from the community and state-level factors (p<0.05).
Conclusion The level of IV against childhood diseases was high in Nigeria. However, disparities exist across the regions and other socioeconomic segments of the population. More efforts are required to improve vaccination sensitization programs and campaigns in Nigeria.

PA-649

RLDT - A rapid and simple molecular diagnostic tool to aid surveillance and vaccine evaluation of enterotoxigenic E. coli and Shigella

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Background ETEC and Shigella spp (ES) are the leading causes of diarrhea among children in impoverished areas of the world. Vaccine development for ES has been prioritized and accelerated in recent years. As promising vaccine candidates for ES move toward field trials in endemic areas, an improved understanding of the epidemiology of ES will be critical. A critical constraint is the complex, time constraining and expensive diagnostic methods currently required for detecting ES infections such as bacterial culture for Shigella, PCR of selected E. coli colonies for ETEC etc. These methods are not feasible outside a well-equipped laboratory to provide country-specific burden of ES, and not feasible for assessing vaccine efficacy in the resource poor settings (RPS). Thus, a simple and sensitive detection assay for ES is critical to fill this gap.
Methods We developed a novel simple, rapid (<1hour), sensitive as qPCR, and inexpensive assay, RLDT (Rapid LAMP based Diagnostic Test) at JHU, which can detect ETEC (LT, STh and STp genes) and Shigella (ipaH gene) directly from stool. The assay is stable in ambient temperature, avoids maintaining a cold chain, and is mostly electricity-free.
Results We successfully implemented and evaluated the RLDT assay comparing with current diagnostic assays qPCR, PCR, and culture in several African and Asian countries. With funding from the EDCTP, the Centre for Infectious diseases, Zambia and GRAS from Burkina Faso were able to implement RLDT for surveillance of ES in ~2700 children seeking care to the hospitals with diarrhea. We are currently implementing RLDT in the primary health care facilities in the endemic countries.
Conclusion Given, RLDT is simple, rapid, sensitive, specific, appropriate for RPS and easy to scale up, this assay is an ideal tool to fill the gap for ES disease surveillance, vaccine evaluation and case detection in the endemic countries.

PA-655

Severe pneumonia is associated with worse neurocognitive function among infants living with HIV

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Background Despite reduction of HIV-associated mortality in children with the implementation of antiretroviral treatment (ART), HIV-associated neurocognitive deficits are still of great concern. These are thought to result mainly from intra-cranial HIV-associated pathology. The contribution of extra-cranial infections like pneumonia is not well described. We compared neurocognitive function between infants living with HIV (ILHIV), with and without severe pneumonia.
Methods This EDCTP-funded case-control study (TMA2020CDF-3198) was conducted among ILHIV with severe pneumonia enrolled in the EMPIRICAL trial (#NCT03915366) (cases), and age-matched ILHIV without severe pneumonia (controls). We assessed neurocognitive function using the Bayley's Scales of Infant and Toddler Development-III within 3weeks of hospital discharge or recruitment among cases and controls respectively. We compared demographic and clinical characteristics as well as neurocognitive mean scaled scores between the two groups.
Results Among 66 infants (44 cases and 22 controls) included in the study, 36 (54.5%) were male and the median age was 6 months (IQR = 4.47 - 8.98). There was no difference in age (p = 0.83), sex distribution (p = 0.43), prematurity proportions (p = 0.16), breastfeeding (p = 0.56) proportion on ART and its duration, (p = 0.05, and p = 0.07 respectively), viral load (p = 0.28), or hemoglobin (p = 0.06). The cases had lower weight-for-height z-scores than the controls (-1.73 [IQR = -2.68 – 0.44] vs -0.08 [IQR = -1.85 - 0.85] respectively, p = 0.04). There was no difference in family care indicators between groups. Among infants with complete data, the cases (n=40) scored poorer than the controls (n=18) in all neurocognitive domains; cognitive (p = <0.01), language (p = 0.04), and motor (p = <0.01).
Conclusion Severe pneumonia increases the likelihood of neurocognitive deficits among ILHIV. Interventions reducing the risk and severity of pneumonia may be beneficial in reducing neurocognitive decline in this population.

PA-658

Shigella incidence and resistance to commonly used antibiotics in children under five years of age living in a community setting in Ouagadougou, Burkina Faso

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Background Shigellosis is a major public health problem worldwide. There is no vaccine to control shigellosis, which is the best way to control infectious diseases. To assess the true burden of shigellosis before proceeding with the evaluation of a candidate shigellosis vaccine, a longitudinal study was conducted in children under five years of age in a community setting.
Methods A cohort of healthy children under five years of age from Ouagadougou's peri-urban area was followed for twelve months. Stool samples were collected at scheduled follow-up visits (enrolment, 6-month, and 12-month) and during diarrhoea episodes. Conventional microbiology techniques plus the BD Phoenix M50 (Becton Dickinson) were used for Shigella strains identification. Shigella serotypes were identified using polyvalent antisera or PCR in case of non-serotypeable strains. Strains were tested for sensitivity to standard antibiotics.
Results From the 750 children followed, a total of 2170 stool samples were analysed, of which 236 were diarrhoeal. Shigella spp. was isolated from 64 stools. The annual incidence of diarrhoea was 321.8 per 1000 children (95% CI: 283.2, 365.7). The annual incidence of shigellosis was 87.7 per 1000 children (95% CI: 68.6, 112.0). The fraction attributable to Shigella infection in cases of moderate to severe diarrhoea was 4.7%. Shigella cases were more common in children older than 24 months. All four serogroups of Shigella spp were found and the most common serogroup was Shigella flexneri. All strains showed multidrug resistance. The most observed resistances were to trimethoprim-sulfamethoxazole (82.81%), tetracycline (81.25%), ampicillin (76.56%), nalidixic acid (25%) and chloramphenicol (17.19%).
Conclusion This study determined the burden of shigellosis and confirmed its endemicity in Burkina Faso. The most frequent species was Shigella flexneri. The frequency of multi-antibiotic resistant Shigella spp. strains was very high. Complete typing of isolated strains is needed to guide the development of serotype-based vaccines.

PA-666

Adapting a COVID-19 ELISA for dried blood spot testing in Mali, West Africa

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Background Serosurveillance is an important method to help monitor COVID-19 in the community in Mali. We previously adapted and qualified a two-antigen Enzyme-Linked Immunosorbent Assays for use in local laboratories using venous blood samples (95% CI, 73.9% (51.6-89.8) and 99.4% (97.7-99.9)) respectively as sensitivity and specificity). However, the burden of blood collection set cost can be challenging in resource limited region where alternative source of biological material will facilitate a large scale of COVID19 surveillance. In this study (funded by NIH) we assessed the of dried blood spot (DBS) samples to quantify Sars-Cov-2 antibodies by ELISA using RBD and Spike antigens.
Methods Respectively 248, 226 and 391 volunteers were randomly selected from Sotuba (urban), Bancoumana (town) and Doneguebougou (village). Venous blood and DBS samples were collected, tested in parallel to assess concordance and the performances of the DBS samples. During the optimization phase (n=36), a promising concordance was found. This allowed us to analyze 829 additional samples on the Spike antigen.
Results We had (31/36) of samples that were COVID-19 seropositive (two category kappa 1.0) in both type of samples, suggesting a strong concordance. Analysis of the 829 samples showed a high correlation (Pearson r = 0.9239 p < 0.0001) with 98% concordance between venous blood ELISA and simplified DBS spike ELISA (kappa = 0.92). As performances, the DBS showed a sensitivity of 99% (95% CI, 98%-99%) and a specificity of 99% (95% CI, 93%-100%). It had 100% (95% CI, 99%-100%) as positive predictive value, 88% (95% CI, 79%-94%) as negative predictive value.
Conclusion Overall, DBS elution and testing was comparable to venous blood testing in the Malian population, and this supports it use in large-scale SARS-CoV-2 serosurveillance studies as a valuable alternative to venipuncture. Our perspective is to optimize/adapt DBS serology to other viruses like Zika virus, Ebola virus, Dengue virus, hepatitis viruses.

PA-668

EDCTP/Africa-CDC supported master b-learning Field Epidemiology Program in Cabo Verde: results from field training in strengthening the health information systems of Lusophone West African countries

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Background Africa's weaknesses in responding to public health emergencies triggered the University of Cabo Verde's EDCTP/Africa CDC supported b-learning Field Epidemiology Program (2022-2024), after Mozambique´s and Angola's experiences. The Program targets 15 students from Cabo Verde (CV)(6), Guiné-Bissau (GB)(6) and São Tomé e Príncipe (3). Groups of three students completed their first field training, producing reports focusing on antimicrobial resistance (AMR) and/or One Health Surveillance within existing health information systems (HIS).
Methods During field training students, supported by site supervisors and tutors, selected a HIS, described it, assessed its quality, and identified opportunities for improvements, namely on the possibility to expand its One Health scope.
Results In the three countries, the HIS for human health is structured around the platform District Health Information System 2 (DHIS2) complemented by population-based surveys. Clinical and public health services, disease programs and surveillance systems are supposed to feed their data into the DHIS2, mostly manually, although this does not always happen. AMR is not regularly monitored for lack of laboratory capacity for antibiograms; when done, it is mostly related to tuberculosis. GB is the only country reporting a National HIS Strategic Plan. Private care providers/services are not included in the DHIS2 data/information circuits.
Animal/plant health have separate information systems with variable degrees of sophistication. CV is the only country reporting the development of coordination structures with animal and environmental HIS.
Besides these experiences, students analyzed disease related data (diarrhoeal diseases, malaria, HIV, tuberculosis) and participated in outbreak investigations (shigella, influenza, rubella).
Conclusion Key obstacles to develop One Health Information Systems are siloed structures for human, animal and environmental HIS, but also significant blind spots in human HIS, related to programs and services that do not dialogue with DHIS2, lack of capacity to obtain laboratory-based data and a private sector growing outside relevant data/information circuits.

PA-673

Development of a mobile application to support perinatal period of pregnant women in Nigeria: User-centred design approach

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Background About 99% of global maternal mortality occur in developing countries and Nigeria accounts for 20% of all maternal mortality. Major contributory factors include poverty, distance, cultural and religious beliefs, and ignorance. Mobile health technology (mHealth) is emerging in Africa. While SMS has been the most common intervention, mobile apps have not been explored for maternal care in Nigeria. This study describes the process of design, development, and testing of mobile app for pregnant women in Nigeria.
Methods Using a user-centred design, we conducted semi-structured interviews at each stage of mobile app development with randomly selected pregnant women attending antenatal clinics in Oyo State, Nigeria. The first interview focused on need assessment or empathy, followed by alpha and beta testing of the mobile application prototype at health facilities in Ibadan, Nigeria.
Results The barriers to accessing perinatal care was distance to nearest facility (mean = 3.3km), lack of perinatal education, and cost. Low fidelity prototype of the mobile app was designed with five features (gamified microlearning, lifestyle tracking, clinic connection, financial planning, and chat). Alpha testing showed that 56% (n=7) of pregnant women surveyed considered lifestyle tracking and gamified microlearning as the most useful features of the mobile app. Mobile app increased the level of knowledge of preeclampsia by 179%. User feedback from alpha-testing informed the development of high-fidelity prototype for beta testing. 95.2% of pregnant women surveyed were willing to download the mobile app. The final app developed was uploaded on Google Playstore (MyBelle Pregnancy App) for free download.
Conclusion mHealth apps have the potential to increase access to prenatal information and services in Nigeria and may reduce maternal and childhood mortality. This paper has described the process of development of first indigenous mobile app specifically for pregnant women in Nigeria using user-centred design thinking approach.

PA-675

Navigating the COVID-19 pandemic for participant recruitment and follow-up: Experiences from the PediCAP clinical trial consortium

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Background COVID-19, first reported in Wuhan, China in December 2019, was declared a pandemic in March 2020, causing restrictions of movement of people and goods worldwide. This affected every aspect of life, including the conduct of clinical trials. We highlight the challenges faced by the PediCAP consortium and how we navigated them.
Methods The PediCAP consortium is composed of 14 partners (https://projectpedicap.org/the-consortium/) in Africa and Europe. The EDCTP-funded clinical trial (ISRCTN63115131) is enrolling children aged 2months to 6years with pneumonia in Mozambique, Uganda, South Africa, Zambia and Zimbabwe. Participant recruitment started in December 2020, during the COVID-19 pandemic; and by end of April 2023, 987 of the targeted 1100 participants (89.7%) had been enrolled. The challenges faced by the clinical sites, and measures taken to mitigate them, were obtained from minutes of monthly teleconferences and interviews with site staff, and summarized in themes.
Results The following were reported as challenges and their mitigating measures:

- Delays in obtaining ethical and regulatory approvals: Ethical and regulatory bodies adopted paperless submissions, virtual review meetings, and used online tools to interact with applicants.
- Slow recruitment of participants resulting from reduction in numbers of patients attending hospitals, due to fear of contracting COVID-19, and lockdowns restricting movement. This was solved by adding a partner and satellite sites. Additionally, a no-cost extension of the project was made to allow for extension of the recruitment period.
- Site initiation, protocol training, procurement of trial drugs, and clinical trial monitoring were delayed/problematic. The sponsor adopted virtual platforms and local monitors to mitigate this.
- A need to protect site staff and participants from contracting COVID-19. Country specific COVID-19 risk management plans were developed and implemented.

Conclusion COVID-19 impeded smooth progress of PediCAP trial activities. However, a joint and collaborative effort was key in navigating the challenges.

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Identification P. falciparum antigens associated with reduced risk of malaria during pregnancy

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Background Understanding the immunity against pregnancy malaria can accelerate vaccine development against pregnancy associated malaria. In this study, we investigated immunoreactivity of pregnant women sera to 698 recombinant proteins derived from 3D7 strain of P. falciparum.
Methods The recombinant proteins were expressed using the wheat germ cell-free system, a method used to synthesize high quality plasmodial proteins that elicit immunologically active antibodies. The sera were obtained from a prospective pregnant women cohort between 12-18 weeks of gestation visiting a hospital in Bungoma County, Western Kenya, a malaria endemic region. Pregnancy outcomes were determined during scheduled and unscheduled visits. The immunoreactivity to sera was determined by AlphaScreen assay; a homogeneous high-throughput system that detects protein interactions.
Results Multi definition analysis selected 34 antigenic domains; 23 were Plasmodium falciparum Erythrocyte Membrane proteins (PfEMP1s), 8 merozoite stage proteins (BSPs), 2 Repetitive interspersed family proteins (RIFINs) and 1 surface-associated interspersed gene family proteins This suggests that antibodies targeting PfEMP1s; PfEMP1 – DBL domains and cysteine-rich interdomain regions of PfEMP1 domains (CIDR), and RIFINs are abundantly present in pregnant women of increasing gravida and may be highly associated with protection from malarial anaemia, low newborn birth weight and contribute to positive pregnancy outcomes.
Conclusion Put together, this cohort showed a recognition for antigens across PfEMP1, BSPs and ESPs families suggesting that antibodies to multiple proteins work together in providing functional immunity during pregnancy. Functional assays are currently ongoing to validate these proteins.
Funding: This study is part of the EDCTP2 programme supported by the European Union.

PA-679

Engaging youths on social and ethical issues around bio-banking in Kilifi, Kenya. Use of deliberative consultation workshops

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Background There is increasing attention to bio-banking in health research due to its value in providing rapid turnaround of research results. However, bio-banking in Sub-Saharan Africa is still in infancy and is wrought with many ethical and social-cultural challenges. There's a dearth of research focusing on informed views of young people, who are likely to be the greatest consumers of health research information. At the KEMRI Wellcome Trust Research Programme (KWTRP) with nearly 1.5million biological specimens stored for over 30years, social science research investigated opinions about biobank/ing, and the ethical and social-cultural considerations from diverse stakeholders including youth.
Methods One-day deliberative consultation workshop with 44/47 Young Persons Advisory Group members from three secondary schools in Kilifi County. This aimed at informing and seeking opinions of the youth on the ethical and social-cultural issues of biobank/ing. Activities included discussions about DNA, KWTRP biobank tour, plenary and focus group discussions. Topics discussed included views on sample storage, sharing, consent, assent, and benefits of bio-banking. Data was transcribed, translated to English, and analyzed using thematic analysis.
Results Participants seemed to understand health research and supported bio-banking due to its associated benefits. They emphasized strict adherence to ethical guidelines on sample sharing, especially confidentiality. They supported initial parental consent for continued storage and sharing of samples collected for research while they were minors. Tracing participants who transit to adults, and recall biases were some of the reasons given for not re-contacting minors to re-affirm consent for continued secondary sample use. They also suggested that assent age should be lowered to 9-16years [as opposed to 13-17 years].
Conclusion Engaging the youth in bio-banking was regarded as an important step. Therefore, with careful considerations, youth can be engaged to demystify health research and bio-banking through well-tailored and suited engagement strategies.
Funders: Wellcome Trust, Global Health Bioethics Network and NIH Fogarty.

PA-682

Overcoming diverse challenges associated with innovative multicountry collaborative initiatives: The Kenyan experience of the Prev_PKDL project

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Background The EDCTP-funded PREV_PKDL project was designed to: i) advance the clinical development of a vaccine for prevention of visceral leishmaniasis (VL) / post kala azar dermal leishmaniasis (PKDL) and ii) to gain a greater understanding of the immune determinants of treatment outcome, using multidimensional, multiparameter phenotyping of patient cohorts recruited across the countries of the Leishmaniasis East Africa Platform (LEAP; Ethiopia, Kenya, Sudan and Uganda). Central to the latter objective was the establishment of a distributed Center of Excellence in Flow Cytometry across the collaborating sites (Ethiopia, Kenya, Sudan Uganda and UK).
Methods Accomplishing the project objectives required acquisition of specialised equipment (CytoFLEX LX Cytometer), sourcing and validation of custom antibody panels, specialised training of flow cytometry managers, and renovation of space to develop a Flow Cytometry Laboratory. Study approvals were obtained for implementation at Kimalel and Chemolingot subcounty hospitals in Baringo County.
Results Multifaceted challenges were numerous, including delays in laboratory allocation and renovation, UK VISA issues precluding travel of the flow manager, supply chain delays occasioned by government requirements, late arrival of equipment, relocation of personnel and equipment from initial study site to current site, in-country insecurity and an ongoing curfew in the study area due to cattle rustling. Despite these challenges, the study has been initiated and high quality immunological data obtained from 24% of the target sample size. In addition, six Leishmania isolates have been obtained from splenic aspirates of VL patients enrolled as part of a nested collaboration that seeks to understand how parasite genotype affects clinical status and treatment response.
Conclusion Developing the capacity to conduct in depth immune phenotyping of patients enrolled in clinical studies in East Africa faces many hurdles that can be overcome by perseverance and a common objective.
Funding: This project is part of the EDCTP2 Programme supported by the European Union (RIA2016V-1640).

PA-684

Strengthening national ethics committees in West and Central Francophone Africa: Progress, challenges, and perspectives

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Background National Ethics Committees (NECs) are critically required to ensure rigorous and ethically sound health research. In Francophone Africa, in spite of a rise in the bulk of clinical and biomedical research, and the fact that the region is highly vulnerable to emerging infectious diseases, NECs have not reached the institutional maturity of their counterparts in Anglophone Africa. To address these challenges, the Cameroon Bioethics Initiative (CAMBIN) received funding for strengthening the capacity of NECs in four Francophone African countries: Cameroon, Chad, Mali and Niger.
Methods Through the project called "Strengthening National Ethics Committees in West and Central Francophone Africa (SNECFA)", CAMBIN supported NEC members (1) to write/update their Standard Operating Procedures (SOPs) for the review of research protocols during routine and emergency health situations; (2) register/renew their Federal Wide Assurance number (FWA); (3) develop and/or revise Training and Resources in Research Ethics Evaluation (TRREE) national supplement for their country; (4) disseminate the SOPs and TRREE national supplements and (5) draft a collaboration plan (Mali with Niger and Cameroon with Chad).
Results CAMBIN provided customized training programmes for NEC members. The four NECs have developed their SOPs following the WHO guidelines and are currently using them for the review of research protocols. They all have an active FWA registration – improving their international visibility. The NECs are developing and/or updating their TRREE national supplements. Finally, a groundwork for knowledge sharing, exchange of ideas and good practice between the NECs has been created through the development of two (Mali/Niger and Cameroon/Chad) collaboration plans.
Conclusion The capacity of NECs in Cameroon, Chad, Mali and Niger is being strengthened. The dissemination of the SOPs and the TRREE national supplements within the scientific community will further boost their national and international visibility. Collaboration plans will be implemented in the coming months.

PA-689

Using Plasmodium falciparum field isolates to characterize the molecular factors associated with in vitro resistance to imidazolopiperazine KAF156 and GNF179 in Mali

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Background Not anticipated chloroquine resistance subsequently led to the use of artemisinin-based combination therapies (ACTs) as first-line treatments for Plasmodium falciparum malaria. The discovery of new alternative molecules to ACTs urges after the identification of ACT resistance in many regions, notably in South-East Asia and recently in Rwanda (Africa). There is necessity to understand the mechanism of resistance for new antimalarial drugs and investigate its appearance in field parasites before their deployment in the field. Laboratory strains were used to induce invitro resistance to imidazolopiperazines (IPZs) currently in phase 2b trials and active on all stages of plasmodium species. Nevertheless, it remains to be determined whether these mutations or other can translate into field parasites causing drug resistance.
Methods We exposed P. falciparum clinical isolates along with lab 3D7 strain to 3 successive pressures with 5xIC50 of IPZ (31.85 nM) to select for mutant parasites and assessed their susceptibility to IPZ and reference compound dihydroartemisinin.
Results We identified two recrudescent 3D7 strain (3D7_FS and 3D7_FOM) as well two recrudescent field parasites (EEF407 and EEF408). When performed the dose-response test against these recrudescent 3D7 strain and field parasites as compared to their respective wild types, 55 and 251-fold change in IC50s of 3D7 recrudescent parasites 3D7_FS and 3D7_FOM respectively was observed as compared to their wild types. However, no difference in IC50 of the field parasites and their wild type was observed. Interestingly, the fitness cost for recrudescent field parasites was 2-fold higher than that of the wild type.
Conclusion Drug resistance was observed in lab parasite unlike in field parasite with recrudescent field parasites having a high fitness cost. Sequencing will be used to identify markers associated with drug resistance and pursue the resistance selection in more field isolates.
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PA-690

Women's empowerment and uptake of Sulfadoxine-Pyrimethamine for intermittent preventive treatment of malaria during pregnancy: results from a cross-sectional survey in the Lake endemic region, Kenya

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Background Malaria in pregnancy remains a major public health problem in endemic areas of the sub-Saharan African (SSA) region. However, there is limited understanding of the role of women empowerment in using Sulfadoxine-Pyrimethamine for intermittent preventive treatment of malaria during pregnancy (IPTp-SP) in the SSA region. This study examines the association between women empowerment indicators and optimal uptake of IPTp-SP (3 or more doses) in the Lake endemic region of Kenya.
Methods We used data from a cross-sectional baseline survey of 3154 women aged 15-49 years in Kisumu and Migori Counties who had a live birth in the last two years prior to the study. Data were collected between June to August 2021. We conducted a descriptive analysis to show the distribution of respondents by key background characteristics, and bivariate and multivariate logistic regression to examine statistically significant associations between women empowerment measures (decision-making power, control of assets, education, and employment status) and optimal uptake of IPTp-SP.
Results Of the 3154 surveyed women, 1505 (47.7%) received optimal IPTp-SP dose during their last pregnancy. The Odds for optimal use of IPTp-SP increased among women who had: high decision-making autonomy (AOR=1.31; CI=1.10 — 1.58); 4 or more ANC visits (AOR=3.18; CI=2.64 — 3.84); interacted with a healthcare provider about IPTp (AOR=1.47; CI=1.27 — 1.71); and high knowledge of approaches to prevent malaria in pregnancy (AOR=1.99; CI=1.62 — 2.45).
Conclusion The study findings suggest that maternal health interventions should focus on less empowered women (i.e. women with less decision-making autonomy), women with limited ANC visits and interaction with a healthcare provider, and those with limited knowledge of approaches to prevent malaria in pregnancy because they are less likely to achieve optimal use of IPTp-SP dose during pregnancy.

PA-696

Determination of therapeutic threshold for tuberculosis in a clinical setting using adapted Nominal Group Technique in Southern Africa

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Background Confronted with diagnostic uncertainty when no further testing is available, clinicians will consider the potential harm and benefit of offering versus withholding treatment. However, this could result in high false-positive (FP) and false-negative (FN) treatment decisions. Treatment can be offered if the probability of TB in the patient is above the "therapeutic threshold" (ThT): the probability of disease at which the expected utility of treating and not treating is the same. We adapted the nominal group technique (aNGT), a consensus-building exercise, to estimate ThT in TB.
Methods This was a sub-study of the TB TRIAGE+ study (www.tbtriage.com). We enrolled 123 health professionals (doctors, nurses and program managers) involved in routine management of TB patients in South Africa (SA) and Lesotho. This involved 17 (6 face-to-face and 11 online) interactive sessions with 4-14 participants. Participants elicited, discussed and refined the harms of FP and FN treatment decisions for stable ambulatory patients. They weighed all harms according to their importance in treatment decisions by distributing 100 points. ThT, derived as the sum of the weights of the harms of the FP decision divided by the total weight, was analyzed using a hierarchical beta regression model.
Results One-third of participants had >10 years of professional experience in TB, including 42% medical doctors and 40% nurses. The overall ThT was 37.7% (95% CrI: 35.7-39.8). Observed ThT was lower for Lesotho; 31.3% (vs. SA: 39.8%), sessions discussing harms of FN decision first; 33.2% (vs. FP: 39.9%) and doctors; 34.2% (vs. Nurses: 39.4%, Others: 38.0%) but similar by years of experience and type of session (face-to-face vs. online).
Conclusion The aNGT produced a reliable estimate of ThT. The setting, participant profiles and order of discussion of harms influence ThT. Factors influencing ThT will be explored further in focus group discussions and in-depth interviews.
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PA-697

Evaluation of CAD4TB and point-of-care C-reactive protein as tuberculosis triage tests in a multi-centre facility level study in Southern Africa using Bayesian latent class analysis

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Background Globally, millions of tuberculosis (TB) cases go undetected annually due to underdiagnosis. The WHO recommended rapid molecular tests have limited availability for routine clinical practice in resource-limited settings. This warrants the need for non-sputum-based, easy-to-use, rapid, cheap and accurate triage tests. However, the lack of a perfect reference standard complicates the evaluation of new diagnostic tests. We aimed to estimate the diagnostic test accuracy of computer-aided detection for tuberculosis (CAD4TB) and point-of-care C-reactive protein (POC-CRP) as triage tests for tuberculosis screening at the facility level in a two-centre cross-sectional study (TB TRIAGE+ ACCURACY) corrected for the reference standard bias.
Methods We conducted a secondary analysis of TB TRIAGE+ ACCURACY among 1392 ambulatory patients aged ≥18 years reporting at least one cardinal TB symptom in rural and semi-rural Lesotho and South Africa. Using Bayesian latent class analysis, we estimated the sensitivity and specificity of ten diagnostic tests including CAD4TB version 7 (CAD4TBv7) and POC-CRP. Diagnostic tests based on similar biological mechanisms violate standard model assumptions leading to incorrect estimates. Based on expert opinion, we accounted for potential sources of dependencies among the true pulmonary TB (PTB) and true non-PTB cases. Expert opinion and published data were used to aid in specifying the priors for the unknown model parameters.
Results At an appropriately chosen threshold, CAD4TBv7 meets the WHO target product profiles for a TB triage test with an estimated sensitivity of 97.0% and specificity of 70.0%. POC-CRP can work as a rule-out test for TB, meeting the sensitivity requirement only at 92.0%, but at 39.0% fails to reach the required specificity. Microbiological tests have imperfect sensitivity (range: 77.0% to 84.0%).
Conclusion Evaluation of diagnostic accuracy of triage tests using composite reference standard or standard LCA would give biased results. CAD4TBv7 is a promising triage test while POC-CRP has limitations.
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PA-698

Babies born to mothers with active tuberculosis (TB) have reduced IgG Tetanus and Diphtheria vaccines responses and increased IL-17 production

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Background
Babies born to mothers with active TB (ATB) are at risk of poor clinical outcomes like low birth weight however, little is known about their vaccine responses. We hypothesised that these babies have reduced responses to vaccines compared to babies born to TB-free mothers.
Objectives
i. To determine IgG responses to: BCG, measles, tetanus, and diphtheria vaccines and
ii. To determine TB-specific cytokine responses using QuantiFERON (QFT) plasma.
Methods A longitudinal case-control study; baby-cases (born to mothers with bacteriologically confirmed ATB) and baby-controls (born to mothers without ATB). Quantitative IgG-specific BCG, diphtheria, tetanus, and measles ELISA assays were performed on infant plasma harvested from heparinised venous blood collected on first encounter after birth (month 0), at month 3 and month 6 following immunisation as per the Uganda routine immunisation schedule for children under 1 year. Luminex (5-plex) assay for TB-specific cytokines: IL-17/IL17A, IFN-γ, TNF-α, IL-2 and GM-CSF was also performed on baby QFT plasma. Prism was used for statistical analysis, and $P<0.05$ was considered statistically significant after performing the Mann-Whitney U-test. Data was expressed as medians and interquartile ranges. Fold changes were computed by dividing medians of cases by medians of controls.
Results Fold change analysis revealed that cases had a 0.15-fold decrease in diphtheria antibodies and a 0.69-fold decrease in tetanus antibodies compared to controls (p=0.0281)/(p=0.0122) respectively. No significant difference in BCG and measles antibodies was observed among cases and controls (p=0.9999/p=0.6568) respectively. Also, a 1.23-fold increase in IL-17/IL-17A cytokine response among cases was observed compared to controls (p=0.0142). Finally, no significant difference in IFN-γ, TNF-α, IL-2 and GM-CSF cytokine responses was observed (p=0.4811/p=0.8064/p=0.1668/p=0.3881) respectively.
Conclusion Maternal ATB reduces infant diphtheria and tetanus vaccine responses and causes a 1.23-fold increase in IL-17/IL-17A cytokine responses among exposed infants. Further studies are required to determine the later life response outcomes.

PA-699

Impact of six-month interval praziquantel treatment on the prevalence of urogenital schistosomiasis at village level in the Senegal river basin

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Background Schistosomiasis is a parasitic disease responsible of important morbidity and mortality in sub-Saharan endemic countries. In Senegal, national schistosomiasis control and elimination program has initiated since 2012, annual repeated praziquantel (PZQ) mass drug administration (MDA) in endemic regions in the Senegal River basin (SRB). The impact of annual MDAs is assessed at the health district level. However, considering the focal characteristic of the disease transmission, huge disparities exist at the lowest levels, such as village or contamination site.
Methods This study consisted in following the Schistosoma haematobium infection using microscopic method in a cohort of school-age children in five villages in the SRB. Baseline prevalence was evaluated in August 2020 then 40 mg/kg of PZQ was administered. Six month after, the prevalence and reinfection were evaluated and a second treatment was administered in March 2021 following by a second prevalence and reinfection evaluation six months after.
Results At the baseline, very high prevalence was observed in the villages of Guia (91.2%) and Khodit (90.6%) with Human frequenting irrigation canal while moderate prevalence was noted in the village of Ndiawara (45%), and Dioundou (49%) with Human frequenting the river and also in the village of Mbane (43.1%) near the Lac de Guiers. After two six-months interval treatment, prevalence of Schistosoma haematobium was reduced in all the villages with the lowest reinfection rates noted in children frequenting the Senegal river (25.5%) and the lac de Guiers (36%), while the villages near the irrigation canal, remain hotspots with higher rates of reinfection in children (58%).
Conclusion This study suggests to adept the periodicity of the MDA in the SRB at a 6-month interval in the villages near the irrigation canals, while maintaining the annual treatment in the other villages in accordance with the WHO guideline on control and elimination of schistosomiasis.

PA-700

Investigating the utility and added value of non-sputum-based approaches for diagnosis of tuberculosis in West African children: a study update

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Background Childhood tuberculosis (TB) accounts for 12% of the 10.6 million incident cases of TB globally, and 16% of all TB-related mortality. The majority of childhood TB cases and deaths occur in TB-endemic countries where difficulties with confirming TB diagnosis with conventional sputum-based approaches contribute to poor outcomes. We present the methodological approaches and progress report from a study investigating the added value of non-sputum-based approaches for the diagnosis of TB in children in West Africa.
Methods This is a multi-country study recruiting children (age <15 years) with presumptive pulmonary TB at study sites in The Gambia, Ghana, and Benin. Participants undergo standardised conventional clinical, radiologic and microbiological investigations for TB diagnosis. In addition, early morning stool samples are simultaneously collected for testing with Xpert Ultra ('stool Xpert'), while Computer-aided Detection for TB-version 7 ('CAD4TBv7'; Delft Imaging, Netherlands) abnormality score are derived for their digital chest radiographs (CXR). Bayesian latent class analysis will be used to determine the added value of the non-sputum-based tests in term of relative increases in sensitivity and specificity by combining CAD4TBv7 and stool Xpert results with conventional methods.
Results Recruitment and investigation of eligible study participant have commenced at the three study sites, with more than 100 children enrolled from January 2023 till date. The CAD4TBv7 system has been set up at the Gambia study site. Digital CXR from the two other study sites are de-identified and transferred electronically to The Gambia, using an encrypted internet-based file transfer software, for CAD4TBv7 scoring. A blinded senior radiologist also provides independent assessment of the likelihood of TB on each CXR.
Conclusion This study presents an opportunity to objectively determine how many additional childhood TB cases can be detected if CAD4TBv7 abnormality score and stool Xpert are combined with conventional diagnostic tests.
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PA-702

Collaborative implementation of Laboratory Quality Management System (LQMS), AMR surveillance and stewardship in county hospital laboratories in southeast Liberia – journey so far, lessons learned

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Background Laboratory Quality Management Systems (LQMS), antimicrobial resistance (AMR) surveillance and stewardship (AMS) are important for quality patients' care and safety. Through collaboration between Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) and Liberia's Ministry of Health (MOH); Health Focus GmbH (www.health-focus.de) and Integrated Quality Laboratory Services (www.iqls.net) implemented LQMS, AMR surveillance and AMS in hospitals in southeast Liberia
Methods LQMS implementation started April 2021 with baseline assessment of five hospital laboratories, using WHO's Stepwise Laboratory Quality Improvement Process Towards Accreditation (SLIPTA) check-list. Training topics and Quality Improvement (QI) action plans were developed to address identified gaps. Internal audit of the laboratories was conducted in April 2023, while the final SLIPTA audit is scheduled for July 2023.
For AMR surveillance and AMS, a central bacteriology laboratory was established at the JJ Dossen hospital, Harper, Maryland County; and staff were trained to perform sample analysis (bacteria ID and AST) using standard methods. Steering Committee members in each hospital perform regular AMS ward rounds. Quality indicators of antimicrobial use (i.e. correct compounds, dosage and duration) were assessed before and after AMS ward rounds.
Results At baseline, only the JJ Dossen laboratory reached 1-star SLIPTA threshold; and guidelines for good clinical laboratory practice and quality management were grossly inadequate. Internal audit conducted in April 2023 showed marked improvement in LQMS, with all the laboratories making overall increases in their SLIPTA points. Similarly, there was significant improvement in the antibiotic treatment guideline (due to incorporation of local antibiogram data); completeness of microbiological diagnostics; and clinical outcome.
Conclusion Despite persistent systemic challenges (institutional and human), good collaboration between local and international partners, regular coaching, mentoring and supervision accounted for the successes achieved in this remote, difficult-to-reach part of Liberia. Critical stakeholders were integrated in the project to ensure continuous improvement and sustainability beyond current GIZ funding.

PA-703

Middle East respiratory syndrome coronavirus-a 10-year (2012-2022) global analysis of human and camel infections, genomic sequences, lineages, and geographical origins

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Background The World Health Organization priority zoonotic pathogen Middle East respiratory syndrome (MERS) coronavirus (CoV) has a high case fatality rate in humans and circulates in camels worldwide.
Methods We performed a global analysis of human and camel MERS-CoV infections, epidemiology, genomic sequences, clades, lineages, and geographical origins for the period January 1, 2012 to August 3, 2022. MERS-CoV Surface gene sequences (4061 bp) were extracted from GenBank, and a phylogenetic maximum likelihood tree was constructed.
Results As of August 2022, 2591 human MERS cases from 26 countries were reported to the World Health Organization (Saudi Arabia, 2184 cases, including 813 deaths [case fatality rate: 37.2%]) Although declining in numbers, MERS cases continue to be reported from the Middle East. A total of 728 MERS-CoV genomes were identified (the largest numbers were from Saudi Arabia [222: human = 146, camels = 76] and the United Arab Emirates [176: human = 21, camels = 155]). A total of 501 'S'-gene sequences were used for phylogenetic tree construction (camels [n = 264], humans [n = 226], bats [n = 8], other [n=3]). Three MERS-CoV clades were identified: clade B, which is the largest, followed by clade A and clade C. Of the 462 clade B lineages, lineage 5 was predominant (n = 177).
Conclusion MERS-CoV remains a threat to global health security. MERS-CoV variants continue circulating in humans and camels. The recombination rates indicate co-infections with different MERS-CoV lineages. Proactive surveillance of MERS-CoV infections and variants of concern in camels and humans worldwide, and development of a MERS vaccine, are essential for epidemic preparedness.

PA-706

Clinical and microbiological predictors of healing in Buruli ulcer disease

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Background Among participants with PCR confirmed BU, we examined the relationship between clinical and microbiologic characteristics and wound healing as assessed using three methods for the determination of rate of healing (RoH).

Methods Participants were grouped as fast healers and slow healers based on healing status at 8 weeks. Lesion measurements were obtained with acetate sheet tracings (2D) or Aranz software (3D) fortnightly. RoH was determined using the absolute area (AA), percentage area reduction (PAR) and linear (LM) methods at 4 weeks post-antibiotic treatment. Predicted time to healing was compared to the actual healing time. Baseline clinical and microbiological characteristics were assessed for associations with healing.

Results All three methods for calculating the RoH significantly distinguished between fast and slow healers ($p<0.0001$). The predicted healing time using the LM was comparable to the actual healing time for fast healers ($p=0.34$). Fast healers had shorter median time to healing [6, IQR (4,12)] compared to [24, IQR (20,33)] ($p<0.0001$) for slow healers. More slow healers had positive AFB (121/197(61%) at baseline, positive culture growth [52(46%), higher bacterial load at baseline (median IS404 cps/ml [500 IQR (500,1750) vs (500 IQR (250-2000; $p=0.038$]) and viable Mu 16srRNA (median (IQR) cps/ml [500 (500-,500) vs 0(0,500), ($p=0.003$)]) than fast healers. Slow healing was strongly associated with large (category II and III), plaque, oedematous lesions, longer time to clearance of viable M. ulcerans and development of paradoxical reactions.

Conclusion LM predicted healing time is comparable to actual healing time. Baseline characteristics associated with healing can be considered as markers for healing to facilitate improved disease management to reduce patient and caregiver anxiety.

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PA-707

Report of COVID-19 vaccine safety monitoring in Kano State, Northwestern Nigeria. 2021–2023

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Background Monitoring the safety of vaccines is a global priority and has been a major focus for the WHO. Detecting, notifying, reporting, and investigating adverse events following immunization (AEFIs) requires well-functioning reporting systems. There is substantial variation in the tracking and detection of AEFIs and many countries still report a lower share than would be expected. The global rollout of COVID-19 vaccines has been remarkably successful, with over six billion doses administered. Nigeria has modified its routine vaccine systems for tracking AEFIs related to COVID-19 and began reporting AEFIs related to the COVID-19 vaccination in 2021. Here we present the findings on the COVID-19 AEFI surveillance in the most populous state of Nigeria.

Methods Kano is a northern Nigerian state with an estimated population of over 16 million; 40% live in urban areas while 60% live in rural communities. Line listing of AEFIs by vaccine type detected and reported following COVID-19 vaccination were collected by the Integrated Disease Surveillance and Response (IDSR) team from March 2021 to April 2023.

Results Out of the 19,507,819 total COVID-19 vaccine doses used, 9,321 AEFIs were reported. Majority (31%) of the vaccine doses used were Moderna with 1,514 AEFIs reported. A total of 5,307,312 were Pfizer vaccine doses (27.2%) and 1,282 AEFIs were reported. About 2,260,900 Astrazeneca vaccine doses were used while 30% (5,891,215) of the vaccine doses were Johnson and Johnson with 1,982 and 4,543 AEFIs reported respectively.

Conclusion The highest AEFIs reported were from Johnson and Johnson vaccines. There is need for strengthening and continuous monitoring of AEFIs due to COVID-19 vaccines through robust safety monitoring systems. This will provide timely information helpful in building public trust about the safety of the novel vaccines which will improve COVID-19 vaccine acceptability and coverage in Nigeria, Sub-saharan Africa and globally.

PA-708

Circulating immunoglobulins and the development of transient lymphocytopenia in the phase 1 CAPRISA 012B trial testing HIV monoclonal antibodies

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Background Acute, transient lymphocytopenia that was not clinically significant was observed in the CAPRISA 012B phase 1 clinical trial following administration of broadly neutralizing antibodies (bnAbs)- CAP256V2LS alone or in combination with VRC07-523LS. We undertook an evaluation of this observation and posited that systemic immunoglobulins (Igs), and cytokine profiles in women who develop lymphocytopenia are different to those who did not.
Methods A total of 20 women were included, eight women had developed transient, gradable lymphocytopenia. Plasma Ig isotypes, IgG subclasses and 27 cytokines were measured in women with lymphocytopenia and 12 women without lymphocytopenia at enrolment (prior to bnAbs) and at days 1, 7, 28, 56 post-bnAb administration.
Results IgG subclasses, IgM and total lymphocyte counts were significantly lower prior to bnAbs in women who developed gradable lymphocytopenia than those who did not ($p<0.05$). Significantly higher MIP-1β but lower TNF-α levels from enrolment to day 56 were found in women with gradable lymphocytopenia compared to non-lymphocytopenia women. Additionally, 6 cytokines (IL-6, IL-8, IP-10, MCP-1, G-CSF and IL-1RA) were significantly elevated from enrolment to day 1 post-bnAb administration in women with gradable lymphocytopenia and non-lymphocytopenia ($p<0.05$). Among gradable lymphocytopenia, 9 additional cytokines (TNF-α, MIP-1α, MIP-1β, RANTES, Basic FGF, eotaxin, IFN-γ, IL-17A and IL-4) were significantly elevated at day 1 post-bnAbs compared to enrolment.
Conclusion Transient lymphocytopenia in the CAPRISA 012B trial was a physiological event associated with some inflammatory markers with no apparent clinical effects. Although the development of lymphocytopenia was not clinically significant, baseline immunological markers including relative reduction of IgG subclasses and IgM, reduced lymphocyte counts, and cytokines may identify those at increased risk of developing acute, albeit transient lymphocytopenia in HIV prevention trials.
Funding: European and Developing Countries Clinical Trials Partnership, South African Medical Research Council,
and South African Department of Science and Innovation.

PA-711

Assessment of effectiveness of the RTS,S/AS01 malaria vaccine using the case-control approach: lessons learned from Malaria Vaccine Pilot Evaluation (MVPE) in Ghana, Kenya, and Malawi

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Background The RTS,S/AS01 malaria vaccine was introduced in Ghana, Kenya, and Malawi in 2019. Evaluation includes case-control studies designed to monitor individual-level safety and effectiveness to complement population-level estimates derived from the MVPE. Here, we discuss design and practical considerations for conducting case-control studies to measure vaccine effectiveness against severe malaria, the need for a 4th dose, and for assessment of safety outcomes.
Methods For the severe malaria study we aimed to estimate the effectiveness of the primary 3 doses, and of the 4th dose. We also aimed to estimate rebound, if any, in children who received only the primary 3 doses. Cases were patients with severe malaria admitted to a study hospital, residing in an RTS,S/AS01 implementation area, and eligible to have received the 3rd or 4th dose of the vaccine. The case patient's home is visited to collect data on vaccination status and other details. Four controls are then recruited from the same community, matched closely on date of birth. Vaccination status is determined from home-based records, and from clinic registers. Similar approaches were used for studies of safety outcomes.
Results We share preliminary results and discuss the challenges encountered and lessons learned about implementing a multi-centre case control study for a malaria vaccine, and approaches to data collection which have proved effective, including establishing surveillance, the use of specific case definitions standardized across centres, recruiting closely age-matched community controls, and obtaining reliable information from both cases and controls on potential confounding factors which may be associated with both risk of the outcome and with access to vaccination.
Conclusion Case control studies are an efficient means of monitoring vaccine effectiveness and safety, but require care in design and implementation. The lessons learned from the malaria vaccine pilots will be useful for countries planning introduction of a malaria vaccine.

PA-718

HIV-infected adolescents have alarmingly low adherence levels to ART – a short report from Tanzania

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Background More than eight in ten of the world's 1.65 million adolescents living with HIV live in sub-Saharan Africa. Despite the availability of antiretroviral therapy (ART), there is limited robust data on adherence to ART levels among adolescents, as this group is often neglected in HIV research.
Objective: Our study aimed to estimate and compare adherence levels, based on self-reporting, pharmacy-refill counts and electronic monitoring using a digital adherence tool (DAT) among adolescents living with HIV in Tanzania.
Methods We used three measures to assess adherence levels among adolescents aged 15 to 19 years, residing in Kilimanjaro region, in Tanzania. Median adherence levels were calculated, and optimal adherence was defined as > 95% of pills taken. Adolescents used the DAT, the Wisepill dispenser (RT2000), for one month and were followed-up with a short semi-structured exit-interview. Thereafter, adolescents were interviewed about their experiences with using the Wisepill® device.
Results Median adherence levels were respectively 100% (IQR 93 – 100%), 97% (IQR 85 – 98%) and 72% (IQR 24 – 91%), based on self-report, pharmacy-refill counts and on results from the DAT. Strikingly, out of the twenty participants, the proportion of adolescents achieving 95% pill intake were 70%, 55% and 20% of adolescents respectively.
Conclusion Even based on self-reported adherence, only less than three-quarters of adolescents achieved sufficient adherence to treatment. Therefore, interventions to improve adherence to ART regimen are urgently needed among HIV-positive adolescents, especially in resource-limited settings.

PA-727

Physiologically-based pharmacokinetic modelling of drug–drug interactions between ritonavir-boosted atazanavir and rifampicin in pregnancy

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Background Ritonavir-boosted atazanavir (ATV/r) and rifampicin are mainstays of second-line antiretroviral and multiple anti-TB regimens, respectively. Rifampicin is a strong inducer of CYP3A4, the main enzyme involved in atazanavir metabolism, causing drug-drug interaction (DDI) in those co-infected with HIV and TB, which might be exaggerated in pregnancy. We employed physiologically-based pharmacokinetic (PBPK) modelling to investigate atazanavir pharmacokinetics during coadministration of rifampicin and ATV/r in pregnancy.
Methods A pregnancy PBPK model was developed from a published adult PBPK model by incorporating pregnancy-induced biological changes. Predicted pharmacokinetic parameters in pregnancy were validated with published clinical datasets for once daily (OD) rifampicin 600 mg and clinical data for ATV/r (300/100 mg) in pregnancy (NCT03923231). Predicted atazanavir Ctrough was compared against its protein-adjusted IC90 (14 ng/ml) when simulating the coadministration of ATV/r 300/100 mg OD and rifampicin 600 mg OD in pregnancy. Alternative dosing regimens were also explored.
Results The pregnancy model was considered validated when the absolute average fold error (AAFE) for Ctrough and AUC0-24 of ATV/r 300/100 mg OD and for Cmax and AUC0-24 for rifampicin 600 mg OD were <2, when comparing predicted vs observed data. Similarly, comparison of predicted and observed plasma concentrations of atazanavir and ritonavir in the sparse pregnancy data (NCT03923231) gave AAFE values <2. Pregnancy was predicted to increase the rifampicin DDI effect on atazanavir. For the dosing regimens of ATV/r 300/100 mg OD, ATV/r 300/200 mg OD and ATV/r 300/100 mg BD (all with rifampicin 600 mg OD), predicted atazanavir Ctrough was above 14 ng/ml in 29%, 71% and 100%; and 32%, 73% and 100% of the population in second and third trimesters, respectively.
Conclusion PBPK modelling suggests ATV/r 300/100 mg BD could maintain antiviral efficacy when co-administered with rifampicin 600 mg OD in pregnancy. Clinical studies are warranted to confirm safety and efficacy in pregnancy.

PA-728

Exploring the disposition of select artemisinin combination therapies in the treatment of malaria and malaria parasite kinetics in children with sickle cell disease in Kenya

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Background Children with Sickle Cell Disease (SCD) have decreased spleen function which is responsible for increased susceptibility of SCD patients to malaria and other infections. There is evidence that hemoglobinopathies such as SCD may influence the activity of artemisinin derivatives by altering their accumulation and binding to target molecules within the parasitized erythrocyte. If hemoglobinopathies alter the efficacy of Artemisinin-based Combination Therapies (ACTs) through an attenuated effect of the artemisinin component, further research into dose optimization would be justified. Currently there is no data on the disposition of ACTs and malaria parasite kinetics in children with sickle cell disease in Kenya.
Methods A proposed five-arm open-label, prospective, randomized, clinical trial will be conducted at the KEMRI Kondele Children Hospital in Kisumu, Kenya. Children less than 18 years with SCD and co-infected with P. falciparum will be enrolled based on the set inclusion and exclusion criteria with up to 20 participants in each of the of the five (5) arms. The aim is to evaluate the pharmacokinetics (PK) and pharmacodynamics (PD) of artemether-lumefantrine (AL), artesunate-amodiaquine (ASAQ), Dihydroartemisinin-piperaquine(DHA-PPQ), artesunate-mefloquine and artesunate-pyronaridine (AP) fixed-dose combinations in children with uncomplicated falciparum malaria and sickle cell disease. Samples for PK/PD analysis and malaria will be taken at specified time points. Mathematical modelling based on the following set criteria will be conducted: phenotype- percentage of haemoglobin F, makers of splenic dysfunction, previous exposure to prophylactic antimalaria drug-chlorproguanil and malaria parasite kinetics.
Results The results of this proposed study will bridge the gap of knowledge on the disposition of ACTs in children with SCD as well as help in formulating new or review current treatment for malaria in children with SCD.

PA-730

Impact of additional screening using highly-sensitive rapid diagnostic tests and treatment combined with monthly Sulfadoxine-Pyrimethamine on LBW and peripheral malaria infection: Asser Malaria Study

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Background The burden of MiP remains high with adverse effects on the health of both women and their offspring. In endemic areas, pregnant women are generally asymptomatic with low parasitemia which can be missed by malaria RDTs, but affecting the pregnancy course. We postulate that proactive screening with highly-sensitive RDTs (HS-RDT) and treatment of those found infected using dihydroartemisinin piperaquine (DP), in addition to standard intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine (IPTp-SP) could improve maternal and infant health.
Methods Pregnant women with gestational age of 16 to 24 weeks were randomized to receive screening and treatment with DP and IPTp-SP or IPTp-SP alone until delivery. Biological samples were collected for participant management and study purposes. Primary and secondary end- points were the prevalence of placental malaria, maternal anemia, maternal peripheral infection, and low birth weight.
Results Malaria infection was detected in almost one on four (1/4) of the pregnant women at recruitment. No difference was found between study arms in terms of placental malaria infection (adjusted odds ratio, 1.54 [95% confidence interval, 0.95–2.53]; P = 0.082). At delivery, the prevalence of peripheral maternal infection was slightly lower in the intervention group compared to the one of the control group but the difference was not statistically significant. Increasing number of IPTp-SP doses was associated with a significantly lower risk of peripheral malaria infection and low birth weight.
Conclusion Pregnant women should initiate antenatal care as soon as possible in order to fully benefit of malaria preventives measures. Strategies addressing late attendance to ANC with early start of IPTp-SP among eligible pregnant women should be developed and implemented.
Funding: This project is part of the EDCTP2 programme supported by the European Union (grant number TMA2018CDF-2397-ASSER MALARIA)

PA-734

BCG vaccine to reduce unplanned absenteeism due to illness of health care workers during the COVID-19 pandemic. A multi-center randomised controlled trial (BCG-COVID-RCT)

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Background This present study aimed to test whether providing Bacillus Calmette-Guérin (BCG) vaccine to health care workers (HCW) could reduce non-planned absenteeism due to infectious disease, including COVID-19, by 20% and thereby decrease the potential impact of the COVID-19 pandemic in health care systems in Africa.
Methods We conducted a single-blinded placebo-controlled multi-center randomized trial in Guinea-Bissau and Mozambique between December 2020 and June 2022. Participants were randomized 1:1 to an intradermal standard dose of BCG vaccine or placebo (saline) and followed by telephone interviews every 2 weeks for 6 months. Days of unplanned absenteeism was analysed using Bayesian negative binomial regression yielding relative risk ratios (RRs). The incidence of infectious diseases, COVID-19 infections and all-cause hospitalizations were analysed in Cox proportional hazards models proving hazard ratios (HRs).
Results A total of 668 (Guinea-Bissau, n=503; Mozambique, n=165) HCWs were enrolled in the trial; 95% (636/668) completed follow-up. The RR of unplanned absenteeism for BCG vs placebo was 1.21 (0.52-2.46) in Mozambique, 1.34 (0.75-2.20) in Guinea-Bissau. The HR in the combined analysis HRcombined was 1.29 (0.81-1.94). The incidence of infectious disease episodes yielded a HRcombined of1.18 (0.97-1.45). No protection against COVID-19 infections was observed (HRcombined=1.19 (0.80-1.75). There tended to be a protection from all-cause hospitalization (HRcombined=0.51 (0.13-2.03)).
Conclusion This study did not find that BCG could reduce absenteeism, on the contrary there was a tendency towards a greater risk of self-reported absenteeism, infection episodes and COVID-19 infection. However, BCG tended to reduce the risk of severe of disease in terms of the risk of hospitalizations, aligning with other randomized trials showing protective effects against more severe outcomes.

PA-736

TB infection treatment eligibility among household contacts of microbiologically confirmed pulmonary TB patients in high TB settings

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Background TB preventive therapy (TPT) is recommended to household contacts (HHCs) exposed to active tuberculosis (TB). Among contacts of multidrug-resistant tuberculosis, 80% were deemed eligible for TPT using World Health Organisation (WHO) criteria: HIV-infected, aged <5 years or TB-infection (TBI). This finding questions the need for TBI testing prior to TPT initiation. We determined TPT eligibility among drug-sensitive TB (DS-TB) index households in Lesotho, South Africa, and Tanzania.
Methods We enrolled DS-TB index cases and their HHCs. Index cases were enrolled if aged ≥18 years, microbiologically confirmed with TB within ≤6 weeks of diagnosis. Blood specimens were taken from HHCs aged ≥5 years, HIV-uninfected or unknown status and tested with QuantiFERON-TB-Gold-Plus (QFT-Plus) for TBI. HIV testing was offered to HIV-uninfected HHCs and those who didn't have recent HIV test. Those HIV-infected, aged <5 years, and those with TBI were considered eligible for TPT.
Results We enrolled 340 TB index cases and 964 HHCs [321 Lesotho, 300 South Africa, and 343 Tanzania] from July 2021 to September 2022. HHCs aged <5 years were 14% overall (138/964): [16% (50/321) Lesotho, 3% (9/300) South Africa, and 23% (79/343) Tanzania]. In total, 10% (96/964) of HHCs were HIV-infected, of whom 94% (90/96) were self-reported and 6% (6/96) diagnosed at baseline: [12% (40/321) Lesotho, 13% (39/300) South Africa and 5% (17/343) Tanzania]. Of 624/733 (85%) who tested for TBI, 49% (304/624) were QFT-Plus positive overall: [53% (100/187) Lesotho, 56% (119/212) South Africa, and 38% (85/225) Tanzania]. Overall, the proportion of HHCs eligible for TPT using WHO criteria was 63% [535/855, 95% Confidence Interval 59–66%]: 69% (190/277) Lesotho, 64% (166/259) South Africa, and 56% (179/319) Tanzania.
Conclusion Approximately two-thirds of TB-exposed HHCs were eligible for TPT. Further work on cost-effectiveness of TBI testing should be considered to explore the utility of testing in high burden settings.

PA-737

Genome-wide association study in Ghanaian lymphatic filariasis-affected individuals

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Background Lymphatic filariasis (LF) is a parasitic disease caused by filarial nematodes. An estimated 40 million individuals infected with the filarial nematodes present with the symptomatic LF manifestations of lymphedema (LE) and hydrocele. These symptoms develop in only a subgroup of infected people, and host genetics have been attributed to the disease heterogeneity. Studies that have sought associations between LF and host genetics have focused mainly on candidate genes. The current study aimed to conduct the first genome-wide association study (GWAS) to determine LF susceptibility.
Methods Single nucleotide polymorphism (SNP) data from 3189 participants comprising 1508 LF cases and 1681 asymptomatic controls were analysed in the study. Cases were selected based on the presence of either LE and/or hydrocele while controls consisted of participants who had lived in the endemic community for at least 10 years and had no LE and/or hydrocele. These unrelated participants were genotyped using the Infinium Global screening array with multi-disease drop by Illumina®.
Results Independent signals, rs2245413 and rs2245710 were observed at genome-wide significance ($p<5x10-8$) to be associated with LF. At the HLA locus, SNP rs7742085 located near the HLA-DQB2 gene was identified at genome-wide significance to be associated with LF susceptibility (P = 3.93 x 10-8, odds ratio [OR] = 1.43 [confidence interval {CI} 1.26-1.63]. Other studies have associated these SNPs with renal abnormalities, LE and hydrocele. Additionally, at three non-HLA loci, close to the genes OR5V1 (rs1419637), RNU6ATAC11P (rs2243492), and PAK1 (rs2852388), suggestive evidence of LF associations (P 1.0 x 10-6) were also observed.
Conclusion This first stage GWAS in Ghanaian population identified novel SNPs associated with LF risk, highlighting the potential of GWAS to provide gene candidates for functional analyses as therapeutic targets toward the World Health Organization's 2030 elimination goal.

PA-738

Evaluation of QIAreach QuantiFERON-TB lateral-flow nanoparticle fluorescence assay for TB infection testing among TB household contacts in three high-burden settings

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Background Tuberculosis infection (TBI) testing and treatment are fundamental to achieve TB elimination ambitions. Among household contacts (HHCs) of TB patients, the uptake of TBI testing is limited, in part due to a lack of gold standard test and challenges associated with implementation, which vary by available tests. Our study evaluated the prevalence of TBI among HHCs and determined concordance of QuantiFERON-TB-Gold-Plus (QFT-Plus) to QIAreach QuantiFERON-TB (QIAreach), a new field-friendly lateral-flow-nanoparticle-fluorescence assay.
Methods In a cross-sectional study in Lesotho, South Africa and Tanzania, blood samples were collected from HHCs at an initial household visit using a single lithium heparin tube for paired QFT-Plus and QIAreach processing, testing and interpretation following manufacturer's guidelines. TBI prevalence was determined using QFT-Plus result. We assessed percentage agreement between QFT-Plus and QIAreach using Cohen's Kappa.
Results We enrolled 964 HHCs [321 in Lesotho, 300 in South Africa, and 343 in Tanzania]. Of this, 465 HHCs had paired results, of whom 65% (302/465) were females with a median age of 27 years (interquartile range: 13, 45). TBI prevalence was 51% (236/465). Among HHCs with paired results, 42% (197/465) were positive and 34% (156/465) negative on both assays, while 24% (112/465) had discordant results. Total agreement was 78% [353/451, 95% Confidence Interval (CI): 74 – 82, kappa = 0.5627, $p<0.001$] with a positive agreement of 77% (197/255, 95% CI: 71 – 82) and a negative agreement of 80% (157/195, 95% CI: 74 – 85).
Conclusion Among HHCs in three high-burden countries, we identified a high TBI prevalence. QIAreach demonstrated a moderate concordance against QFT-Plus. However, in the absence of a gold standard test, it is difficult to interpret the implication of this finding. Further research is needed to understand its usability in this population, specifically if it addresses field implementation challenges associated with similar TBI tests.

PA-743

Collision of three pandemics: the effect of tuberculosis and HIV on the epidemiological, clinical, virological, and immunological trajectory of Covid-19 in primary healthcare facility attendees

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Background Covid-19 emerged as global pandemic during the past three years, with an unprecedented impact on public health. SARS-CoV-2 epidemiology was poorly understood, especially in the African context. A particular gap in knowledge was the effect of HIV and tuberculosis (TB) on the outcomes of Covid-19 disease. We implemented a research study that addressed critical questions concerning Covid-19 disease epidemiology in the context of low resource countries with high burden of poverty, and high rates of TB and HIV. This study was highly collaborative, with investigators from Namibia and Botswana working with colleagues in Europe, and with an NGO in Namibia which supported rapid implementation. Here we are reporting on preliminary data since recruitment is ongoing, focusing on the co-infection rates of HIV, TB and Covid-19.
Methods Recruitment commenced in July 2022; we followed a two-pronged approach: first, all primary healthcare facility (PHC) attendees were approached for TB infection, TB disease, Covid-19 and HIV screening. Second, we followed-up Covid-19 patients as diagnosed by the Ministries of Health, and tested these index cases and their households for TB infection, TB disease, Covid-19 and HIV.
Results Preliminary results for the primary healthcare facility component: we enrolled 1523 participants. 840/1523 (55%) were male, 55/1523 (4%) were younger than 20 years, 923/1523 (61%) between 20-40 years old, and 545/1523 (36%) older than 40 years. 246/1523 (16%) were HIV infected. 33/1157 (2.8%) had active TB and 624/1415 (44%) had latent TB infection. 470/1523 (31%) were not vaccinated against Covid-19, and 110/1523 (7%) partially vaccinated.
Conclusion To note is the high active TB prevalence. Future analyses will include investigating risk factors associated with these differential rates. We believe our findings will contribute to the growing literature on Covid-19 in high burden TB/HIV settings, and to the rationale behind universal active TB screening at primary healthcare facilities.

PA-745

Purpose and options for integration of the Genital InFlammation Test (GIFT) into a sexually transmitted infection management pathway using an adapted delphi process

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Background Sexually transmitted infections (STIs) and bacterial vaginosis (BV) are often asymptomatic in women but cause genital inflammation, which increases HIV risk. The Genital InFlammation Test (GIFT) point-of-care device for detecting genital inflammation is being developed and evaluated. We aimed to explore the main purpose of GIFT and potential integration points within World Health Organization (WHO) STI guideline pathways.
Methods An adapted Delphi method was employed to gather input from experts in the field of STI/BV management. Health service providers, programmers, researchers and policy makers were recruited as respondents. The survey was designed with input from the project's International Advisory Board. Round-one had open-ended questions, including on the purpose of GIFT. Themes from round-one informed the round-two survey, which included integration points for the device into guidelines for the management of STIs/BV (WHO, 2021). Responses were measured on a 5-point Likert scale (strongly agree to strongly disagree) to build consensus. Consensus was reached if ≥70% of participants selected strongly agree or agree.
Results A total of 79 experts responded across both rounds. Most participants were aged 25-54 years, and 58% of respondents were female. Feedback from round-one suggested the GIFT device would be best used to screen for inflammation prior to etiological diagnosis. Round-two survey results showed that WHO-recommended syndromic management pathways 3 and 4 (where molecular assays and point-of-care tests are not available) are ideal integration points for the GIFT device in STI management.
Conclusion The GIFT device promises to be a valuable point-of-care screening tool for detecting genital inflammation in asymptomatic women and may be useful to inform the management of women with symptoms. The device would be of greatest value in resource-constrained settings where molecular assays and other rapid diagnostics are lacking. Stakeholder consultations will facilitate its roll-out and use within healthcare systems.

PA-748

Platform for efficient health emergency response of community diagnostic and surveillance laboratories

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Background Early detection of pathogens is of outmost importance for managing epidemic outbreaks. Primary healthcare laboratories in low-and middle-income countries often lack comprehensive diagnostic and surveillance capacities due to limited resources and infrastructures. The Gates Foundation supported the International Centre for Genetic Engineering and Biotechnology (ICGEB) in establishing a platform for the sustainable transfer of diagnostic and surveillance technologies to community laboratories in Africa. The technology transfer is facilitated through an initial testing at ICGEB followed by a multicentric clinical trial in recipient countries, while support for regulatory approval is also provided. This workflow was successfully applied to an isothermal amplification colorimetric molecular assay (RT-LAMP) for RNA viral detection.
Methods The testing of RT-LAMP for SARS-CoV-2 developed by New England Biolabs was based on a multicentric observational and cross-sectional clinical study on 1657 prospective swabs collected in four African countries and Italy. The sample size included 25% negative, 50% positive and 25% weakly positive samples, while extracted RNA was tested in parallel with the diagnostic standard RT PCR. The test was rolled out to six additional African countries and a further optimized version allowing to skip RNA extraction was tested in four countries, such that the current field trial tested 2419 swabs and 589 saliva samples.
Results RT-LAMP from swabs resulted highly specific (98%), with positive predictive value 99%, and 87% sensitive with negative predictive value 70% compared to standard RT PCR. Stratification of RT-PCR data showed superior sensitivity achieved with a cycle threshold (Ct) below 35 (97%), which decreased to 60% above 35. Similar values were obtained with saliva direct testing. The test was approved in Kenya and Nigeria.
Conclusion RT-LAMP performance is comparable to RT-PCR, particularly with medium-high viral loads, hence it can be deployed in resource-limited settings for timely management and prevention of COVID-19 and other diseases.

PA-755

Feasibility and acceptability of stool-based TB diagnosis: perspectives from healthcare providers in Manhiça District, southern Mozambique

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Background Stool-based TB diagnostics (SbTBD) are reported to contribute to increased rates of bacteriological confirmation in children and people living with HIV. However, there is a lack of evidence on perceived feasibility and acceptability of SbTD in TB high burden countries. Within the Stool4TB project, funded by EDCTP, this study aimed to assess healthcare providers' (HPs) perspective on the feasibility and acceptability of SbTD.
Methods A qualitative study was conducted across five health facilities and four communities within the Manhiça District (Mozambique). Twenty-one semi-structured interviews were conducted with HPs, from February 2022 to March 2023. The interviews were transcribed, coded, entered in a matrix and analyzed using the Diffusion of Innovation and symbolic power theories.
Results According to HPs, the SbTD can be suitable for diagnosis of TB in people who have difficulty in producing sputum, especially children; the approach is considered simple, non-traumatic, and feasible supporting sample capture across all age groups. However, according to respondents, the acceptability of this technique might vary among the patients. Refusals might be due to delays in receiving assistance; lack of awareness about the technique; fear and disgust of touching stool; the association of stool with witchcraft and local beliefs about TB transmission. On the other hand, acceptability could depend on: feeling obliged to comply with government recommendations; the good experience with health services, and the expectation of being cured.
Conclusion HPs view Stool-based TB diagnostics as a more advantageous approach in terms of feasibility compared to other diagnostic strategies, such as sputum-based approaches. However, patient acceptability may be compromised due to existing health services challenges and perceptions about stool and TB. Acceptability could be promoted by the dissemination of information about the SbTD, enforcement of awareness raising about TB and SbTD, and increasing experience and trust in the health services.

PA-766

TRANSVAC Trainings: Lessons from 5 years of vaccinology courses, and the transition to an independent program

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Background The development and validation of novel vaccines requires specific expertise in many subjects. Scientists often require specialized training when they enter vaccinology from an adjacent field or advance a vaccine candidate to the next stage of the pipeline. The limited availability of this training represents a key gap in the field. This issue affects academic labs and small biotech companies which lack in-house knowledge regarding specific areas. We have found that access to training opportunities is particularly needed by groups in sub-Saharan Africa, and is critical to strengthening local capacities.
Methods From May 2017 through April 2023, the Horizon 2020 program TRANSVAC2 worked to address these gaps by offering free training courses in addition to scientific services.
Results 14 modules were developed pertaining to various vaccinology subjects, and 31 separate trainings sessions were attended by over 400 trainees from 44 countries—including 19 different low- and middle-income countries (LMICs). Selected applicants were offered seats in the courses with no registration fees and free accommodation.
Conclusion 5 years of hosting the TRANSVAC courses has provided several lessons on the needs of professionals in both the academic and industrial vaccine fields. The course organizers are now transitioning from the European Commission-supported framework to a new operational model. Through this model, we will continue offering established, highly demanded courses to the vaccine community and introduce new trainings, including the development of accessible eLearning modules. This process aims to build upon the experiences and reputation of the program to form a new, sustainable platform for vaccine courses.

PA-767

Prevalence and risk factors of urinary schistosomiasis in northern Malawi - An assessment of mass drug administration and community perceptions of the disease

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Background Vector control, identification of at-risk populations, and the encapsulation of community perceptions remains a prerequisite to planning and designing as well as the implementation of control measures. MDA is the gold stand technique in the control of schistosomiasis in Africa. Hence the objectives of this study were to investigate community perceptions of the disease and determine the prevalence and Risk factors of urogenital schistosomiasis in Northern Malawi.
Methods A total of 1841 in-depth interviews (IDIs) were conducted between April 2022 and May 2023. The study also enrolled 251 participants that responded to the in-depth interview and submitted urine for microscopy. The study also conducted a seasonal snail survey in Karonga, Rumphi, Nkhatabay, and Nkhotakota districts for species distribution and infection status.
Results In general, out of the 1841 study participants involved in the IDIs, less than 20% had a fairly good level of knowledge about the disease, its spread, and prevention techniques. Out of 251 children that were enrolled 87 (34.7%) were found to have S. haematobium eggs. Chi-square analysis established that having a parent in rice farming (p=0.029) occupation is a key risk factors for urogenital schistosomiasis. It was also surprising to note that those schoolchildren who received Praziquantel during MDA had significantly higher prevalence (p=0.010). Furthermore, this study revealed that they are no association between a child involved in MDA advocacy campaigns and a level of knowledge on schistosomiasis transmission. Bulinus and Biomphalaria were found to be the abundant species and Bulinus was found to be the key vector.

PA-768

Prevalence cardio metabolic diseases factors in individuals living in Gabon according to chronic intestinal parasite carriage

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Background Chronic parasitism has been associated with disruption of the gut microbiota which has been linked to cardiometabolic disturbances. While intestinal parasitosis is common in sub-Saharan Africa such as Gabon, there is little data on cardiovascular and metabolic risk factors in Gabon and the impact of chronic parasitism on the frequency of these. The aim of this study was to determine the prevalence of cardiovascular and metabolic risk factors in relation to chronic or non-chronic carriage of intestinal parasites, the type of parasites and the factors associated with Gabon.
Methods This cross-sectional study included participants aged 18-55 years. It was conducted in communities in Gabon using the World Health Organization (WHO) stepwise approach to surveillance of risk factors for chronic non-communicable diseases. Data were collected using the WHO standardised and adapted survey questionnaire. Lifestyle socio-demographic data and medical history of hypertension and diabetes were collected. Anthropometric parameters and blood pressure were measured. Blood glucose and lipid concentrations were also measured. Intestinal parasites were tested by the Kato-Katz and Merthiolate-Iodine Formalin Concentration techniques. Statistical analysis was performed using SPSS version 20.0 software.
Results A total of 894 participants were included. The mean age was 39.38 ± 8.1 years. The prevalence of intestinal parasitic infections was estimated at 33.66%. Dyslipidemia, hypertension and overweight were more frequently encountered, respectively 43.8%; 43.1% and 51.5%. Parasitized participants frequently had dyslipidemia (50.5% vs 40.5%), p = 0.004 hypo HDL-C (38.5%vs 20.6%), p<0.01 and high ultra-sensitive CRP (57.5% vs 42.1%), p < 0.001 compared to non-parasitized. Dyslipidemia, low LDL cholesterol levels were associated with Soil transmitted helminth carriage (61.4% vs 45.9% vs 46.5%), p = 0.01, compared to protozoan carriers and co-infected.
Conclusion The results obtained suggest a relationship between the type of parasite and biomarkers of lipid metabolism.

PA-769

Bayesian spatio-temporal analysis of malaria hotspot in Gabon from 2000 to 2015

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Background At the local level, malaria transmission persists through hotspots. Besides other known factors, the distribution of malaria hotspots may be shaped by environmental variables. However, research focusing on this aspect has been relatively scarce in Gabon. This underscores the need for further investigations to elucidate the specific environmental factors together with a specific intervention, that may contribute to the distribution of malaria hotspots, taking into account the spatio-temporal effect in Gabon.
Methods These data were part of the Demographic Health Survey program from 2000 to 2015. Hotspots of malaria prevalence for cluster of households were identified using the local Getis-Ord Gi* statistic. The effect of covariates on the outcome was assessed using a Bayesian space-time framework with a Binomial model, implemented in the Integrated Nested Laplace Approximation (INLA), using the Stochastic Partial Differential Equations approach (SPDE).
Results A total of 316 clusters were initially considered, out of which 257 clusters with known hotspot status were included in the analysis. Among these clusters, approximately thirty percent were persistent hotspot over time and concentrated in rural areas. Using a spatio-temporal model, association between malaria prevalence hotspot variation and two key factors was found: years and rainfall. Each additional year or amount of rainfall was associated with an increase in the odds of hotspot occurrence (adjusted posterior odds ratio [AOR]: 1.32, 95% confidence interval [CI]: 1.03-1.69 and AOR: 1.15, 95% CI: 1.02-1.30, respectively). Furthermore, the analysis found that clusters of households with high insecticide-treated net (ITN) coverage were less likely to be hotspots (0.19 (95% CI: 0.06-0.61)).
Conclusion These findings highlight the spatio-temporal dynamics of hotspots and the role of the rainfall, in influencing their occurrence. Moreover, the protective effect of high ITN coverage suggests the importance of targeted interventions in mitigating hotspot formation and malaria transmission.

PA-773

Placental foetal–maternal innate immune responses to placental malaria

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Background During malaria in pregnancy (MiP), Plasmodium falciparum-infected erythrocytes sequester in the placenta, causing placental malaria (PM) and poor pregnancy outcomes, including low birthweight, preterm birth, and stillbirth. Mouse data indicate that innate immune response to PM on the placenta's maternal side adversely affects the foetus and in response, the placenta's foetal side mounts an innate counterresponse that improves foetal outcomes. However, this has not been observed in human PM.
Methods We used histological and molecular analyses to characterize the PM status of bio banked placentas and corresponding maternal sera. Molecular tools were used to characterize innate immune responses to human PM in the foetal and maternal sides of the placenta.
Results Histology and molecular assays showed that 50% of women who had no history of MiP and had received malaria chemoprophylaxis, had PM. Among women with MiP history, the PM rate was 70%. RT-qPCR revealed that foetal sides of PM-negative samples had lower levels of Toll-like receptor (TLR)- 4 and 9 when compared with maternal sides of the same placentas. However, in PM-positive placentas, their levels were higher in foetal sides than maternal sides of the same placentas. Moreover, TLR4 was significantly upregulated in maternal sides of PM-positive placentas versus maternal sides of PM-negative placentas. Intriguingly, TLR4 was significantly upregulated in foetal sides of PM-positive placentas versus foetal sides of PM-free placentas. Immunohistochemical analysis revealed that when compared with PM-negative tissue, PM-positive samples expressed markedly higher levels of 8-hydroxy-2'-deoxyguanosine, a marker of oxidative DNA damage. RT-qPCR showed that this was accompanied by the upregulation of p21, a marker of DNA damage repair.
Conclusion Our data indicate that human PM drives differential innate immune response in foetal vs maternal sides of the placenta, and triggers placental oxidative DNA damage. These observations may have implications for the diagnosis and management of PM.

PA-780

Universal testing for TB investigation among household TB contacts in three sub-Saharan African countries

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Background A reliance on symptom-based screening, followed by complicated testing and referral algorithms, has limited the impact of tuberculosis (TB) contact investigation in high-burden settings. Consequently, alternative approaches such as universal TB testing, where household contacts (HHCs) are tested regardless of symptoms, have gained interest. We evaluated a universal Test-and-Treat strategy among HHCs, complemented by linkage to appropriate TB treatment or TB preventive therapy (TPT).
Methods We conducted a cross-sectional pilot study in South Africa, Lesotho, and Tanzania. Index patients ≥18 years, with microbiologically-confirmed TB diagnosed within ≤6 weeks were enrolled. Among all consented HHCs, we aimed to collect sputum samples regardless of whether symptoms were reported or not. In HHCs <10 years, we also followed an algorithm based on WHO paediatric guidelines, where all symptomatic contacts were referred for further evaluation. Sputa were tested using Xpert MTB/Rif (Xpert). As indicated, persons were referred for TB treatment initiation, further investigation or TPT depending on country guidelines.
Results We enrolled 342 index patients and 964 HHCs. The median age of HHCs was 18 years (8-39 years) and HIV status was known among 57%; 16% self-reported being HIV infected. Among the 964 HHCs, 147(15.2%) were symptomatic. The proportion with successful sputum collection was similar in symptomatic and asymptomatic patients. In total, 25(2.5%) HHCs had a positive Xpert; 11(7.4%) among symptomatic and 14(1.7%) among asymptomatic. Of those eligible for TPT according to country guidelines (n=277), 208(75%) were started on TPT.
Conclusion Universal testing for TB among household contacts was feasible and yielded PWTB among contacts who were asymptomatic. Variations in study findings by country suggest the effect of the intervention may vary by setting; a planned cluster randomized trial is underway which will further evaluate the yield of TB and TPT uptake in a larger-scale implementation.

PA-785

Characterization of anti-SARS-CoV-2 humoral immunity among health care workers in hospitals from the islands of Santiago and São Vicente, Cabo Verde

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Background Health Care Workers (HCW) faced a high risk of exposure to SARS-CoV-2.
In the present study, we described the presence and duration of anti-S and anti-N IgG antibodies against SARS-CoV-2 among HCW to evaluate the immunity response induced by either SARS-CoV-2 infection or COVID-19 vaccination.
Methods Case-cohort study of 465 HCW from hospitals from the islands of Santiago and São Vicente, conducted in 2021, of which 217 were cases (SARS-CoV-2 infection) and 248 controls (no SARS-CoV-2 infection). Study participants were followed-up until 6 months after recruitment for longitudinal analysis of antibody dynamics, independently of SARS-CoV-2 vaccination status. ELISA test for anti-N and anti-S1 SARS-CoV-2 IgG antibodies were performed on serum samples using collected at baseline (T0) and at 6 months (T6). Among vaccinated participants, these two time points corresponded to a mean time from vaccination of 115 (SD: 60 days) and 350 days (SD: 74 days) respectively.
Results Of the 396/465 (85%) tested for anti-SARS-CoV-2 antibodies at T0, 36% (n=66/185) of cases and 12% of controls (n=26/211) were positive for anti-N.
Among the vaccinated at T0 165/166 (96%) cases and 200/205 (97%) controls were positive for anti-S1.
The anti-S1 among the case and control group remained high at T6, with 177/179 (99%) cases and 197/198 (99%) controls of HCW tested at 6 months being positive.
Among 250 (67%) vaccinated, who were anti-N negative at T0-,115(32%) remain negative at T6.
Conclusion These findings showed that only 31% of cases had anti-N. The results also showed positive results for IgG anti-N in HCW without previous SARS-CoV-2 infection, which could be considered asymptomatic cases. Most vaccinated participants had Anti-S after vaccination and they remained high during the 6 months of follow-up. Nonetheless, at least (65/354) had a new infection (32 cases, 33 controls).
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PA-786

Socioeconomic inequalities in antenatal care uptake in Mali and Burkina Faso: analysis of districts level data

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Background Disparities in the use of maternal health services are, among other things, a consequence of socio-economic inequalities within and between countries. The insufficient use of antenatal care (ANC) deprives pregnant women of preventive and curative measures to reduce maternal morbidity and mortality. This study aimed to assess the socioeconomic inequalities in the uptake of ≥4 ANC visits in Mali and Burkina Faso (BF).
Methods Data used were from the EDCTP-funded INTEGRATION project (2021-2024), a multicenter cluster-randomized implementation trial of intermittent preventive treatment with sulfadoxine-pyrimethamine delivered through the seasonal malaria chemoprevention channel. At baseline, a 3-stage sampling household survey was conducted among 780 and 810 women in Kangaba (Mali) and Boussé district (BF) respectively. ANC uptake during the last pregnancy and socioeconomic indicators were collected. The wealth index (WI) was calculated using household's ownership of a selected set of assets, dwelling characteristics, type of drinking water source, and toilet and sanitation facilities. Concentration curves were drawn using WI to assess the socioeconomic inequalities in the uptake of ≥4 ANC visits. Finally, Erreyger's corrected concentration indices were calculated to understand the magnitude of these inequalities.
Results Based on the concentration curves, the uptake of ≥4 ANC visits in Mali was concentrated among wealthy households, while in BF there was no difference considering WI. In Mali, inequalities in the uptake of ≥4 ANC visits (concentration index (CI)=0.0627, standard error (SE)=0.019; p<0.01) were in favor of the wealthier households. In BF, we did not see any statistically significant inequalities in the uptake of ≥4 ANC visits (CI=0.0012, SE=0.0102; p=0.90).
Conclusion Socio-economic inequalities in the uptake of ≥4 ANCs was more evident in Mali than in BF where, unlike Mali, ANC visits are free of charge for the women. These findings highlight the ways to increase equity in access to ANC services.

PA-788

Can we escape ESKAPE bacteria: Trends of antimicrobial resistance and single nucleotide polymorphisms in ESKAPE bBacteria in stool during and post TB treatment

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Background TB treatment is prescribed to millions of individuals yearly, and after cure these individuals often develop recurrent post-TB complications. There is little information exists at the intersection of TB and AMR (i.e., resistance in microbes other than M. tuberculosis complex).The ESKAPE group (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter spp.) are considered key taxa in AMR acquisition. K. pneumoniae is a common isolate from blood stream infections in our setting, South Africa.
Methods We used the Next-Gen Antimicrobial Resistance Detection (N-GARD) assay, a novel, multiplex, sequencing technique to profile AMR associated strains and genes present in stool of drug-susceptible and drug-resistant TB cases longitudinally.
Results In both cohorts, no significant changes were seen in the proportion of ESKAPE or AMR associated strains during treatment, but trends were noted. The drug-susceptible cohort showed trends of longitudinal increases in AMR-related strains; Enterobacter cloacae, Klebsiella pnemoniae, Klebsiella varicola. Significant longitudinal decreases in AMR-related gyrA (Escherichia coli), fluctuations in tetD, strB and trends of increased FosA, qnrD, qnrA, Sul3 and SaM2 were seen in the drug susceptible cohort. The drug-resistant cohort showed significant increase in npmA and trends of longitudinal increases of ermA and sul1. We also noticed trends of single nucleotide polymorphisms.
Conclusion Overall, the drug-resistant cohort had more significant changes in AMR-associated genes compared to drug susceptible cohort. These changes in the resistome during TB treatment require future investigation and future studies will involve more targeted analysis of identified trends.
Funding: This project is part of the EDCTP2 programme supported by the European Union (grant number TMA2019CDF-2738-ESKAPE-TB) and is partly funded by the National Research Foundation.

PA-790

Strengthening knowledge translation capacities through partnerships: the data to policy training and mentorship program in Zambia

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Background Knowledge Translation (KT) is "the synthesis, exchange, and application of knowledge by relevant stakeholders to accelerate the benefits of global and local innovation in strengthening health systems and improving people's health". For over 7 years now, the Data to Policy (D2P) program is one of the approaches Zambia has taken to build capacity for knowledge translation. The initiative is a year-long mentorship program that equips health professionals with skills to develop evidence-based policy briefs on public health priority issues. The D2P utilizes epidemiology with economic analysis and modelling to develop informative policy briefs. The D2P program is supported by the Bloomberg Philanthropies through CDC Foundation, and it is implemented by the National Health Research Authority (NHRA) whose functions among other this is research capacity building and KT.
Methods Through a call for applications, eligible health professionals express their interest to participate in the program stating a public health issue they will work on during the mentorship. The NHRA reviews and admits eligible participants to the program. A curriculum of 21 modules and is delivered by trained mentors who are experts in various and appropriate fields. Four to five trainings, close mentor-mentee check-ins, stakeholder engagements, a policy forum and final presentation of policy briefs to policy makers in the Ministry of Health.
Results The policy briefs quantify the public health issue, bring out the cost and quality implications of interventions and policy options, and recommends the most feasible options. A total of 83 people have been trained under D2P and 43 policy briefs have been developed, disseminated and recommendations from some have been considered for policy for different programs.
Conclusion The partnership plays an important role in strengthening the KT capacity and contributes to informed decision making in Zambia.

PA-795

Completion of isoniazid preventive therapy for latent tuberculosis infection among children and adolescents compared to adults living with HIV, Kinshasa, Democratic Republic of the Congo

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Background Little is known about isoniazid preventive therapy (IPT) adherence among youths compared to adults living with HIV in Kinshasa, Democratic Republic of the Congo (DRC).
Methods Retrospective cohort analysis including children, adolescents and adults living with HIV who were treated at US President's Emergency Plan for AIDS Relief (PEPFAR)-supported sites in Kinshasa, DRC, from 2004 to 2020. The primary outcome was the proportion of patients who completed 9 months of daily self-administered IPT. Log-binomial regression was used to identify independent factors of IPT non-completion. Kaplan-Meier analysis was performed for time-to-death analysis.
Results Of 24,121 eligible patients, 1,136 (4.7%) were children (< 11 years), 1,523 (6.3%) were adolescents (11–19 years), and 21,462 (89%) were adults (≥ 20 years). The median age was 6 (IQR:2-8) years for children, 15 (IQR: 13-18) years for adolescents, and 42 (35-50) years for adults. Overall median follow-up (months): 9 (IQR: 7.8-9.2). Among 7,983 of 24,121 PLHIV (33%) who initiated IPT, 63.2% completed treatment. Compared to adults, children and adolescents were less likely to complete treatment (52.3% and 51.1%, respectively vs. 63.0%, p<0.001). Compared to adults, children were 1.29-fold (95% CI: 1.11-1.50, p=0.001) more likely to not complete IPT. Adolescents (vs. adults) were 32% more likely not to complete IPT treatment (RR: 1.32 (1.20-1.45), p<0.001). Independent risks factors for IPT non-completion were male sex: 1.14 (95% CI: 1.06-1.22) and CD4 < 200 vs. > 200/mm3 (RR 1.20 (1.04-1.38, p=0.011). Kaplan-Meier analysis showed improved survival among patients who completed IPT vs. those who did not (p<0.001).
Conclusion Less than two-thirds of people living with HIV complete 9 months of self-administered IPT in DRC. The lower rate of completion among children and adolescents compared to adults is concerning. Further research is needed to identify barriers to IPT adherence in this population, and inform evidence-informed interventions to improve adherence.

PA-803

Institutionalization of Research and Knowledge Translation in Zambia: Advancing Evidence-Based Decision-Making for Improved Health Outcomes

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Background The National Health Research Authority (NHRA) is implementing a program under the name institutionalization of research and knowledge translation (KT) in Zambia as a means to enhance evidence-based decision-making and ultimately improve health outcomes. The institutionalization of research and KT involves the integration of systematic research processes and the effective translation of research findings into policies and practices within the national health system. NHRA recognizes the critical role that research plays in informing health policies, programs, and interventions.
Methods In order to actualize this program, the NHRA utilized a multi-faceted methodology. This involved carrying out a needs assessment of the ten (10) provinces in Zambia to identify the research and knowledge translation gaps for key personnel. Consequently, the NHRA conducted a research priority setting for each of the ten (10) provinces, through stakeholder engagements, to identify and prioritize research topics/areas aligned with Zambia's health needs and policy priorities. NHRA also developed a robust frameworks to assess the impact of research and knowledge translation activities in the provinces.
Results The NHRA has since created Terms of References (TORs) and facilitated the appointment of Research and Knowledge Translation Focal Point Persons (R&KT FPPs) in all the ten (10) provinces to spearhead research and knowledge translation activities within respective provinces. Consequently, with support from CDC foundation, NHRA has engaged the R&KT FPPs in its research and knowledge translation training and KT mentorship programs. The R&KT FPPs have been trained in Research Methods and Scientific Writing, as well as a KT mentorship course dubbed as Data to Policy.
Conclusion With greater funding and partnership, it is hoped that the program will cascade to the lower levels (district, facility and community) within the Ministry of Health for better health outcomes. Undoubtedly, this initiative represents a crucial and timely step towards evidence-based decision-making and improved health outcomes.

PA-805

Assessing the interaction effect between lagged rainfalls and malaria at the local level: an epidemiological study in Burkina Faso health districts

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Background Although Seasonal Malaria Chemoprophylaxis (SMC) was shown to be effective in preventing malaria in children under five years of age, the malaria burden remains high in Burkina Faso, where the transmission patterns are driven by weather factors. The study objective was to determine the length of high transmission periods and then quantify the specific lag time between the peak of the malaria transmission season and rainfall in each health district.
Methods A Hierarchical Bayesian spatiotemporal modelling with negative binomial distribution was used to fit the malaria weekly incidence from 2011 to 2018. Through the posterior exceedance probability, the Richardson risks classification was used to categorize health districts according to the National malaria control threshold. In each malaria risk area, a cross-correlation analysis was used to quantify the temporal association between weekly malaria incidence and rainfalls.
Results There was a spatial and temporal heterogeneity of malaria risk within the same region across the country. Three malaria risk areas were pinpointed through the Richardson classification. High-risk areas or hotspots ((Pr(θ_k>0.19)>0.8), low-risk areas or coldspots ((Pr(θ_k>0.19)<0.8) and medium-risk areas. The average duration of high transmission was estimated at 15 weeks. The malaria incidence rate peaked annually during the rainy season with a lag time of six to fourteen weeks from the beginning of the rainy season.
Conclusion This study provided spatial stratification of malaria risk while quantifying both length of high transmission periods and lag time between malaria peaks and rainfalls. These lag times should be understood and considered by the Health Program Planners when implementing SMC campaigns in the local context for delivering interventions at the right/relevant time.

PA-806

A composite cytokine model to monitor tuberculosis treatment response. A pilot study.

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Background There is an urgent need for biomarkers that predict TB treatment response in clinical practice and research. Despite its poor specificity and sensitivity, sputum microscopy and culture conversion 8 weeks following treatment initiation remains the recommended surrogate for TB treatment response. A blood-based biomarker with the ability to predict TB treatment response will significantly improve research into TB treatment-shortening trials, trials testing new anti-TB therapy and clinical practice where it can potentially aid in early identification of patients at risk of poor treatment outcomes.
Methods We conducted a pilot, nested case-control study to identify potential biomarkers to predict TB treatment response. All participants completed the PredictTB treatment-shortening clinical trial. All available confirmed relapses at the time of this pilot study (17) and one treatment failure participant were included and 54 controls were randomly selected. Multiplex immunoassays were used to measure serum expression of 50 cytokines at baseline, weeks 04, 08 and 16 and 24. In addition, demographic and symptom data, clinical examination parameters and laboratory results were collected.
Results Using baseline and week 8 parameters, we derived a model that discriminated between relapses and controls with an AUC of 0.81, sensitivity of 0.78 and a specificity of 0.85. Parameters that were most useful in discriminating between relapses and controls were changes from baseline to week 8 in TNF-alpha, sIL2R-alpha, IL 12p70, sVEFFR3, sVEGFR1, E-selectin, and MIP-1. In addition to chest pain and diastolic blood pressure; baseline Apo A1, IL-1beta, and Apo C3 also contributed to the model. Our data also validated a previously published treatment response signature.
Conclusion Our results indicate that a multivariable model may be better at predicting TB treatment response compared to current measures. This work is preliminary and will be combined with a larger cohort.
Funders: Predict TB clinical trial- EDCTP2 programme

PA-809

Setting up of a multiplex HRM method for rapid screening of mutations of SARS-COV-2 variants in Burkina Faso

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Background Since its outbreak in late December 2019, SARS-CoV-2 has rapidly evolved and mutated continuously, leading to the genesis of many variants with variable degrees of infectivity and lethality. In the current pandemic context, the rapid sharing of information relating to genome sequences is essential. This study, realized within the Afroscreen program, aimed to implement an open screening technique in several African countries, and to evaluate its usefulness in the monitoring of the SARS-CoV-2 variants circulation in the populations.
Methods This study was conducted from January 2022 to November 2022 within the Afroscreen Program that involves over 20 laboratories in 13 African countries. In Centre MURAZ and Souro-Sanou University Hospital laboratory, all individuals with PCR-positive results were tested with the DISARS-CoV-2MOC/I Multiplex kit for the detection of variants. This tool is a multiplex RT-PCR which simultaneously ensures detection of SARS-CoV-2 and differentiation of the main variants of concern and other variants of interest. The associated artificial intelligence-based software DISoft™ was used to automatically analyze and interpret the results. A subset of the resulting variant detections was compared with sequencing.
Results A total of 7685 samples were tested by the screening tool in laboratories within the Afroscreen Program. In Centre Muraz and Souro-Sanou University Hospital, all 515 positive samples were screened for variant detection. 215 known variants were detected. In Centre Muraz that had access to sequencing, several positive samples were sequenced, and results compared to the screening method. Results of this study are under analysis and will be presented during the conference.
Conclusion The use of the multiplex qPCR kit met the need of the laboratories by providing rapid and reliable results in a short time and at an affordable cost. However, sequencing is still essential to investigate undetermined PCR results samples and to go into variants characterization in depth.

PA-810

Ethiopian plasmodium vivax hypnozoites formation dynamics and their susceptibility to reference antimalarial drugs

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Background One of the key obstacles to malaria elimination is largely attributed to Plasmodium vivax's ability to form resilient hypnozoites in the host liver that cause relapsing infections. As a result, interruption of P. vivax transmission is difficult. P. vivax transmission occurs in Duffy-positive individuals and have been mainly thought to be absent in Africa. However, increasing studies using molecular tools detected P. vivax among Duffy-negative individuals in various African countries. Studies on the African P. vivax has been severely limited because most of malaria control program focus mainly on falciparum malaria. In addition, there is a scarcity of laboratory infrastructures to overcome the biological obstacles posed by P. vivax.
Methods Herein, we established field transmission of Ethiopian P. vivax for routine sporozoite supply followed by liver stage infection in Mali leveraging the EDCTP funded HypnoBio - TMA2017CDF-1892 outcome. Furthermore, we evaluated local P. vivax hypnozoites and schizonts susceptibilities to reference antimalarial drugs. The study enabled the assessment of local African P. vivax hypnozoite production dynamics.
Results Our data displayed the ability of the African P. vivax to produce hypnozoite forms ex-vivo at different rates per field isolate. We report that while tafenoquine (1µM) potently inhibited both hypnozoites and schizont forms; atovaquone (0.25µM) and the phosphatidylinositol-4-OH kinase (PI4K)-specific inhibitor KDU691 (0.5µM) showed no activity against hypnozoites forms. Unlike hypnozoites forms, P. vivax schizont stages were fully susceptible to both atovaquone (0.25µM) and the (PI4K)-specific inhibitor KDU691 (0.5µM).
Conclusion Together, the data revealed the importance of the local platform for further biological investigation and implementation of drug discovery program on the African P. vivax clinical isolates.

PA-813

The role of global health research innovation and impact on nutrition and early childhood development in Rwanda: Scoping review

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Background This paragraph highlights the progress made by Rwanda in enhancing nutrition and early childhood development (ECD). It acknowledges the importance of global health research innovation in further advancing these areas. To address this, a scoping review has been conducted to explore existing literature on the impact of global health research innovation on nutrition and ECD in Rwanda. The review aims to identify current knowledge gaps and suggest potential areas for future research.
Methods A comprehensive search of electronic databases was conducted to identify relevant studies published between 2010 and 2021. The search strategy included keywords related to global health research innovation, nutrition, and early childhood development in Rwanda. Inclusion criteria encompassed studies reporting on interventions, programs, policies, or practices that utilized innovative approaches to improve nutrition and ECD outcomes. Data were extracted and analyzed thematically to identify key findings.
Results A search of 500 articles identified 25 studies that met the inclusion criteria. These studies highlight the significant influence of global health research innovation on nutrition and early childhood development (ECD) in Rwanda. Innovative approaches, such as community-based nutrition programs, mobile health technologies, and interdisciplinary collaborations, have played a crucial role in improving access to nutritious food, enhancing maternal and child health services, and promoting optimal ECD practices. The outcomes of these initiatives include a reduction in malnutrition rates, improvements in child growth and development, and increased awareness and adoption of positive parenting practices.
Conclusion The review highlights the need for innovative approaches to tackling the complex challenges faced by vulnerable populations, such as limited access to nutritious food, healthcare services, and psychosocial support. The paragraph suggests that future research should concentrate on assessing the scalability, sustainability, and cost-effectiveness of these innovative interventions.

PA-819

Funding for Africa's COVID-19 research response – what lessons can be learnt?

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Background Assessments of global investments for COVID-19 research have revealed significant inefficiencies in the research funding process. These include duplicated and uncoordinated research efforts. We present an assessment of the funding for COVID-19 research in Africa during the COVID-19 pandemic response. In this work, which forms part of a DPhil project, we undertake "research-on-research", which involves understanding the research process itself.
Methods Two reviews of the UKCDR and GloPID-R COVID-19 Research Project Tracker were undertaken in 2020 and 2022.
Results Our assessment of funding for COVID-19 research in Africa showed the few research projects being undertaken in Africa were mostly supported by funders in Europe. There was limited focus of research projects on the COVID-19 priorities defined by African researchers. We found a delayed research response in Africa compared to Europe and the United States. Further, we are undertaking qualitative assessments to explore the experiences of researchers and grant managers in African research institutions with obtaining and managing funding for COVID-19 research.
Conclusion Tracking funding for infectious diseases research is essential for identifying opportunities for coordination among research system stakeholders. It also facilitates the identification of research gaps for action to avoid unmet research needs. Striving for resilient health systems through health policies and systems research is crucial for preparedness for future epidemics and pandemics in Africa, a continent with a high burden of infectious diseases and chronic local underinvestment in health.

PA-826

Lung function in children with presumed TB- the RaPaed-AIDA-TB Cohort

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Background The importance of impaired lung function in children after tuberculosis (TB) disease has been described due to it´s potential to impact quality of life and long term outcomes. The WHO recommends the evaluation of lung function for all children with severe TB episodes. Here we describe pulmonary impairment prevalence and type in different subgroups.
Methods RaPaed-AIDA-TB is a prospective multi-country diagnostic validation study conducted in Mozambique, Malawi, South Africa, Tanzania, and India between January 2019 and July 2022. In Mozambique, children aged 7 years and above underwent spirometry at the time of diagnosis, and at months 3, 6, 9, and 12 after diagnosis according to ATS/ERS guidelines. Spirometry values below the lower limit of normality were considered abnormal.
Results At the baseline and month 3 visit, 89% (60/67) of participants presented acceptable curves. 51.6% (31/60) were female, median age was 11.3 (IQR:9.7-12.9). 26% (16/60) were children living with HIV. 16%(10/60) had confirmed TB (cTB), 61% (37/60) had unconfirmed TB (ucTB) and 21% (13/60) had unlikely TB (ulTB). Lung impairment was present in 68% (36/60) of children, with 63% (23/36) restriction, 22% (8/36) obstruction, and 13% (5/36) mixed. The mean FVC z score was lower in the cTB group (-1.65) when compared to the ulTB (-3.11) p value=0.03, and the mean FEV1 z score was also lower in cTB (-2.99) compared to ulTB(-2.08), p value=0.16, although this difference was not statistically significant. Mean FVC and FEV1 z scores for the ucTB were similar to the cTB group.
Conclusion Lung function is impaired in a subset of children with presumed TB, the most predominant type being restrictive. Further data and analysis will describe longitudinal data and associated risk factors.

PA-830

Study of biological reference values in the research sites at the Abdou Moumouni University, Niger

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Background The West the African Network of clinical trial of anti-malarial drug (WANECAM-II) is building a new clinical study team in Niger. There are no country-specific normal ranges for haematology and biochemistry parameters which are required for biological safety assessments in local trial participants. In preparation for upcoming Phase III trials of antimalarial drugs the aim this study was to determine the references values of biological parameters in Niger population and establish ranges of normal reference values for basic biochemical parameters and haematological parameters in the different seasons of the year.
Methods A first cross sectional studies was conducted from September to October 2021 (rainy season) and a second from March to May 2022 (dry season). Venous blood was drawn from consenting participants in appropriate tubes for haematology and biochemistry parameters assessment. Parameters were analysed in three ages groups (3months- to 5 years, 6-14 years and 15-50 years) to refine the laboratory ranges by age-groups and by gender. Data were entered through Redcap, extracted, and analysed by RStudio. A Protocol specific training provided to the investigators before running the study. New calibrated Cobas c311 analyser for biochemistry and SYSMEX for haematology were provided to the team.
Results We enrolled 533 and 519 volunteers with 65.3% and 33.9% male for the first and second cross-sectional respectively. The age group of 15-50 years was most represented with 48.9% in both seasons while the two other groups were at 25% each. The median values of each parameter, the Lower and Upper normal Limit were determined, and a references document for haematology and biochemistry parameters for clinical study purpose was generated. Detailed results will be presented at the Forum.
Conclusion Through these two cross-sectional studies, we established the first biological parameters for safety evaluation ready to be used for the EDCTP-WANECAM-II KALUMA study in Niger.

PA-832

Causes of term stillbirths in Eastern Uganda

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Background Because of scarce accurate data about causes of stillbirths in LMICs s, there is need for up-to-date high quality primary data to assess the burden of stillbirth. In this study, we assessed the incidence and risk factors for term stillbirths in Eastern Uganda.
Methods This study was part of the BabyGel trial a community trial designed to evaluate the effectiveness of household alcohol-based hand rub (ABHR) for the prevention of sepsis, diarrhoea and pneumonia in Ugandan infants. We recruited pregnant women in the community from 37 weeks of gestation. We followed up the participants in the community after birth. The incidence, causes and risk factors for term stillbirths were determined.
Results We enrolled 4061 pregnant women at term, whose mean age was 25.0 years (standard deviation ±6.0) of whom 3722 had delivered. Among the participants, 83.2% (3088/3712) delivered in hospital, 65% (2654/4061) had 7 or less years of education (4001/4059) and 90% (3652/4058) were married or cohabiting. There were 47 term stillbirths of whom 28 (59.6%) were intra-partum and 19 (40.4%) were antepartum. The incidence of term stillbirths was 12.6 per 1,000 deliveries (95% Confidence Interval, CI 8.0 to 17.2). The common underlying causes of term stillbirths were prolonged or obstructed labour (22/47), malaria (9/47), cord abnormalities (prolapse or cord around the neck) (6), other maternal infection (5/47) and unidentified causes (5/47). Women who were older than 35 years were 4 times more likely to have a term stillbirth compared to women who were 35 years or younger [risk ratio, 3.9 (95%CI 1.1 to 13.9)]. Place of birth was not associated with stillbirth.
Conclusion Stillbirths is still a major health problem in Uganda. Labour-related complications and infections remain the commonest cause of stillbirths in Eastern Uganda.

PA-835

Memory B cells and T cell responses to mycobacterial proteins discriminate between Buruli ulcer and Tuberculosis patients in Ghana

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Background Buruli ulcer disease (BUD) and tuberculosis (TB) are both endemic mycobacterial diseases in Ghana. Unlike TB, immune-based tests are unavailable for BUD making early diagnosis of BUD challenging. Here we determined the applicability of immune-phenotyping of lymphocytes and the concomitant invitro stimulation with different mycobacterial purified protein derivatives (PPDs) to discriminate confirmed BUD or TB patients.
Methods Flow cytometry was used to examine the lymphoid cell repertoire in BU patients (n=27) and TB patients (n=20). Also, intracellular cytokines (IFNγ and TNFα) in CD4+/CD40L+T cells were also measured after invitro whole blood stimulation using PPD from M. tuberculosis (PPDMtub) and M. ulcerans (PPDMulc).
Results Proportions of NK-, transitional B-, naïve B-, regulatory B-, memory B-, total T-, type 2 helper T-, naïve cytotoxic T-, and effector memory cytotoxic T-cells significantly differed between BUD and TB patients. In addition, PPDMtub-specific CD4+/CD40L+/TNFα T cells were higher in TB patients whiles PPDMulc specific CD4+/CD40L+/TNFα+ T cells and PPDMulc specific CD4+/CD40L+/IFNγ+ T cells were higher in BUD patients. Receiver operating characteristics (ROC) revealed only moderate capacities for these cell proportions to discriminate between the TB and BUD except for memory B cells. However, the ratios of PPDMtub and PPDMulc-specific T-cell responses (PPDMtub/PPDMulc ratios) for both IFNγ (AUC =0.94, p<0.0001) and TNFα (AUC =0.92, p<0.0001), and memory B cells (AUC =0.90, p<0.0001) showed strong capacity to discriminate between BUD and TB patients.
Conclusion We showed that immunophenotyping of memory B cells and PPDMtub/PPDMulc ratios for TNFα and IFNγ are valid approaches for discriminating of patients with BUD in a country with high M. tuberculosis infection rates and common BCG vaccination at birth.
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PA-836

Antimicrobial resistance patterns and molecular characterisation of shigella isolates from under-five children in Zambia

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Background Shigella is one of the top five causative agents of childhood diarrhoea, particularly in lower-middle-income countries, and is one of the vaccine-preventable diseases prioritised for vaccine development by the WHO. The emergence of antibiotic-resistant strains of Shigella is a major public health concern as it reduces the effectiveness of available diarrhoeal treatment and management options. We performed drug susceptibility testing using the BD Phoenix 100 automated microbiology system on shigella isolates from Zambian children under five years presenting with diarrhoea at selected health facilities.

Methods We tested 86 shigella isolates from children U5 from outpatient and hospitalised children during a Shigella surveillance study in Lusaka and Ndola collected between 2020-2021.

Results A high proportion of the Shigella isolates showed resistance to trimethoprim/sulfamethoxazole (79.1.4%), Ampicillin (56.9%), amoxicillin-clavulanate (49.4), Cefuroxime (55.8.1%), and gentamicin (49.4%). Resistance to Ciprofloxacin was observed in only two isolates. Overall, 83.7% (n=72) of the isolates exhibited resistance to at least one class of antibiotics. This included 59.3% (n=51) resistance to Cephalosporins, 79.1% (n=68) to Sulfonamides, 57% (n=49) to Penicillin, 48.8% (n=42) to Aminoglycosides and 25.6% (n=22) to beta-lactams. Multi-drug resistance (resistance to 3 or more drug classes) was observed in 62.8% (n=54) of the isolates. More MDR was observed in in-patient isolates, 71.4%(n=10/14), compared to 61.1% (n=44/72) in outpatient isolates. At the species level, multi-drug resistance was observed in 25/29 isolates identified as S. sonnei and 24/33 S. flexneri isolates.

Conclusion Our research indicates a high proportion of antibiotic resistance among the Shigella isolates from young children, which has significant implications for managing Shigella infections. The results support the urgent need for action on effective strategies for Stewardship (i.e. revision of guidelines) and interventions such as vaccines to mitigate the evolution and spread of AMR.

PA-841

Intra-collaboration towards a harmonized working environment for clinical trials in Zambia – ZAHRSSP (EDCTP project)

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Background Past years have seen an increase in clinical trials being conducted in Zambia and other countries, which demand for the need to enhance the capacities of ethics committees and regulators to provide ethical oversight. In Zambia, there are multiple institutions tasked with the mandates to provide regulatory oversight over clinical trials, with each having specific legal mandates that include the National Health Research Authority, Zambia Medicines and Regulatory Authority and National Biosafety Authority. As such, clinical trial oversight has been highly segmented causing duplications of efforts, increased turnaround time, worsened by linear approach to submission of applications.

NHRA proposed harmonization of key processes amongst the key regulators within Zambia in the Zambia Health Research Systems Strengthening Project: Working Towards a Harmonized Regulatory Framework Project (ZAHRSSP) implemented by NHRA and supported by EDCTP.

Methods Desk review of existing Acts, guidelines and mandates was done during the implementation of the ZAHRSSP project.

Results a) Capacity building was conducted through provisions of training in research ethics, GCP, and protocol reviews.

b) Transition from linear to parallel submission. In the implementation of ZAHRSSP project, the approach was changed into parallel submissions.

c) Development of new clinical trial guidelines and regulations. The guidelines describe applications procedures for approvals, reviews, and approval of clinical trials. Key aspects of the harmonization process was realigning the submission forms amongst the key regulators.

d) Memorandum of Understandings aimed at harmonizing key processes between NHRA and ZAMRA including conducting of joint clinical trial reviews and inspections.

Conclusion steps have been taken for intra-collaboration towards a harmonized working environment for clinical trials oversight in Zambia with key regulators working together. However, need for sustaining the key collaborations aspects after the ZAHSSP project and ensure actualization of the key aspects of the guidelines, MOUs and regulations.

PA-843

Comparison of knowledge, attitudes and perceptions on vaccine hesitancy between rural and urban communities in Zambia, Cameroon, Democratic Republic of Congo and Gabon

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Background The development of vaccines for SARS-CoV-2 had a major impact on the COVID-19 pandemic, protecting and vulnerable and dramatically reducing mortality and severe morbidity due to SARS-CoV-2 infection in countries where vaccine coverage was high. African countries faced various challenges in rolling out SARS-CoV-2 vaccination campaigns, with poorer access to vaccines, vaccine hesitancy and the logistical challenges of reaching communities in rural areas. Rural communities might have differential access to information that results in different levels of vaccine hesitancy compared with urban populations. The aim of this study was to compare the knowledge, attitudes and practices of urban and rural communities regarding immunisation.
Methods We used a mixed-methods design combining individual surveys with focus group discussions. The 240 participants included healthcare workers and lay members of the community (patient carers & relatives), recruited through participating health centres in both rural and urban locations in each country.
Results Preliminary findings suggest that in urban areas, participants were overwhelmed by the multiplicity and contradiction of information sources. In rural areas, there was less access to information, and participants questioned the rationale for vaccination, less so because of anti-vaxx hysteria, but more because of a rational perception that they were at lower risk of COVID-19 due to to the lower population density. The majority of diagnoses were confirmed in urban settings, but this is deceptive, because that is where the greatest diagnostic capacity is.
Conclusion There are disparities in knowledge, attitudes and perceptions between communities living in urban areas compared to those in villages. An in-depth analysis across all 4 participating countries will be presented. We will demonstrate how EDCTP networks of excellence can be used to implement impactful student-led multi-site research studies at low cost.

PA-844

Comparison of knowledge, attitudes and perceptions on the response to the COVID-19 pandemic between rural and urban communities in Zambia, Cameroon, DRC and Gabon

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Background In the early months of 2020 as the COVID-19 pandemic took hold in Europe, there was much concern about how the pandemic would impact populations in Africa, both in terms of how the infection would interact with endemic diseases, and also with respect to the capacity for public health response. Initial case finding activities centred on urban travel hubs where the infection and transmission risk were highest. Rural communities were considered lower risk but were also given less access to diagnostics and other IPC measures. The aim of this study was to compare the knowledge, attitudes and practices of urban and rural communities regarding the government response to the pandemic.
Methods We used a mixed-methods design combining individual surveys with focus group discussions. The 240 participants included healthcare workers and lay members of the community (patient carers & relatives), recruited through participating health centres in both rural and urban locations in each country.
Results Preliminary analysis suggested that rural dwellers were less satisfied with the government response than those in urban settings. Proactive government management and logistical organisation prevented the spread of the COVID-19 pandemic but there were challenges with respect to communication crisis and financial management. Results from both the individual interviews and focus group discussions across 4 countries will be presented.
Conclusion There were clear gaps identified between the response to COVID-19 between rural and urban communities. The lessons learned should be incorporated into epidemic risk management plan in readiness for response to new and emerging threats. We will demonstrate how EDCTP networks of excellence can be used to implement impactful student-led multi-site research studies at low cost.

EA-11

Bio-potency of ashes from two insecticidal plants against Aedes albopictus larvae in water closets in Nigeria

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Background Abandoned water closets can serve as reservoir habitat for mosquitoes especially the Asian tiger mosquitoes. Botanicals larvicides are among the recommended strategies used in Integrated Vector Management (IVM) of mosquitoes. Biological potency of ashes of scent leaves (Ocimum gratissimum) and lemon grass (Cymbopogon citratus) against larvae of Aedes mosquitoes were assessed.
Methods Aedes albopictus larvae were surveyed and marked in water closet in a university in Niger Delta region of Nigeria. Ashes from the plants were measured in 1g, 2.5g, 5g, 10g and 15g respectively and emptied into the bowl of the closet with stagnant water. Acute and Chronic toxicity were carried out and mortality recorded after 10 to 60 minutes and 6hours to 60 hours respectively. Adult emergence was also used to measure efficacy of treatment.
Results It was observed that larval mortality increased with time in all concentrations of test plants and chronic toxicity showed 100% mortality in all treatments. The 15g of lemon grass concentration recorded the highest mortality of larvae after 30 minutes in the acute toxicity experiment. There was 0% mortality of the larvae in the all the scent leave concentration in the acute toxicity experiment. Lethal time of 50% was 0.58 and 2.7g, and for and 95% was 2.3 and 34.1g for Scent leave and lemon grass ashes respectively ($p<0.05$).
Conclusion These treatments are therefore considered as good materials for local treatment of abandoned water closets to reduce vector populations and chances of increased biting rates in Africa.

EA-15

Next Generation malaria treatments shall be effective against Plasmodium ovale and Plasmodium malariae infections to achieve disease control and elimination goals.

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Background One of the key obstacles to control and eliminate malaria is attributed to non-falciparum malaria parasites such as P. ovale and P. malariae that are not specifically targeted by current malaria intervention tools such as drug treatments. These parasites can respectively cause relapsing malaria and chronic infections and therefore sustain malaria transmission without new infectious mosquito's bite. Despite availability of artemisinin combination therapies effective on P. falciparum; P. malariae and P. ovale are being increasingly detected in malaria endemic countries.
Method Here, we optimized and adapted ex-vivo conditions under which P. malariae can be cultured and used for screening antimalarial drugs. Subsequently, this culture method was used to test compounds such as artemether, chloroquine, lumefantrine, and quinine for ex vivo antimalarial activity against P. malariae and P. ovale. Furthermore, we evaluated advanced lead antimalarial compounds.
Results Our study also revealed high frequency of P. malariae (15%) and P. ovale (7%) infections with a significant reduction in ex-vivo susceptibility to chloroquine, lumefantrine and artemether against P. malariae infections. Unlike these compounds, potent inhibition of P. malariae and P. falciparum was observed with piperaquine exposure. All compounds potently inhibited both P. ovale and P. falciparum.
Furthermore, using advanced lead antimalarial compounds, we identified strong inhibition of P. malariae and P. ovale by GNF179, a close analogue of KAF156 imidazolopiperazines, which is a novel class of antimalarial drug currently in clinical Phase IIb testing. Finally, in addition to GNF179, we demonstrated that the Plasmodium PI4K-specific inhibitor KDU691 is highly inhibitory against P. malariae, P. ovale and P. falciparum.
Conclusion Our data indicated that chloroquine, lumefantrine and artemether may not be suitable for the treatment of P. malariae infections and the potential of piperaquine, as well as new antimalarials imidazolopiperazines and PI4K-specific inhibitor, for P. malariae and P. ovale cure.

EA-60

Public bus travel agencies' knowledge and application of COVID-19 preventive measures in Cameroon

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Background The movement of people contributes to the propagation of COVID-19 between and across communities. In Cameroon like in many other countries, the movement of population is mainly by public bus transports. Due to their hypothetically key role in disease transmission, recommendations for the prevention of COVID-19 in travel agencies were included in the response plan. This study was conducted with funding from FIND to map the knowledge of COVID-19 prevention measures in travel agencies and their practices regarding the implementation of these measures.
Methods This was a cross sectional descriptive study targeting travel agencies in main cities of the West region that include Bafoussam, Dschang, Mbouda, Bangangte, Foumban and Foumbot. Data were collected in June 2022 by a semi-structured questionnaire from heads of travel agencies by trained surveyors. Data were collected to assess the awareness of heads of travel agencies regarding COVID-19 preventive measures and the application of these measures.
Results Of the 61 travel agencies reached, 55 (90.2%) consented to participate. Most of the respondents were heads of travel agencies. All travel agencies were aware of the existence of recommendations on COVID-19 preventive measures, 46 (83.6%) were informed via the local authorities and 35 (63.6%) via media. The most known preventive measures were the obligation of facemask wearing by travelers (54 [98.2%]) and the setting up of a hand washing or disinfection station in travel agencies (53 [96.4%]). Of the travel agencies, 27 (49.1%) implemented at least one of the recommended COVID-19 preventive measures with 18 (66.7%) applying the recommendation on setting up of a hand washing or disinfection station in their travel agency.
Conclusion During the pandemic, the implementation of the recommendations to limit the transmission of the disease was not fully implemented by travel agencies. A monitoring system should be set up to ensure appropriate implementation of recommendations during epidemics.

EA-84

Dissecting the Diagnostic Performance of the Alere Filariasis Test Strip for the Detection of Active Wuchereria bancrofti Infection and Treatment Success

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Background Although the Alere Filariasis Test Strip (FTS) is recommended for surveillance and monitoring of Wuchereria bancrofti infection, the performance characteristics of this tool in post-treatment settings have not been established. To determine the accuracy of the FTS in effectively monitoring treatment of bancroftian infection, we investigated the sensitivity of the test in detecting different subgroups of asymptomatic adult worm-infected individuals at pre-treatment and post-treatment and the specificity of the test in detecting treatment success following therapy.
Methods Plasma samples obtained from the same cohort of individuals (n = 143) with known adult worm and microfilariae (Mf) burdens at pre-treatment and 24 months post-treatment were used. The sensitivity of the FTS was assessed for the detection of microfilaremic and amicrofilaremic subgroups of adult worm-infected individuals at both time points. The post-treatment specificity of the test was assessed in those who cleared both adult worm and Mf burdens 24 months following doxycycline treatment. Seventy-one samples from W. bancrofti-uninfected individuals living in the same endemic areas were also analyzed.
Results The FTS showed significantly greater sensitivity for the detection of microfilaremic adult worm-infected individuals (pre-treatment = 100%; 24 months post-treatment = 95.8%) than amicrofilaremic adult worm-infected individuals (pre-treatment = 65.8%; 24 months post-treatment = 52.2%). The FTS's specificity for successfully treated individuals at 24 months post-treatment was 73.0% (CI = 62.58–81.90), which was significantly less than the specificity of the test for uninfected individuals (95.8%, CI = 88.14–99.12).
Conclusion From our results, the FTS does not satisfy the WHO's minimum diagnostic requirements of 85% sensitivity and 98.8% specificity for identifying amicrofilaremic adult worm-infected individuals and successfully treated individuals at 24 months post-treatment, respectively. Our study highlights the need for high-quality diagnostic tools to provide a more precise endpoint infection threshold and accelerate the achievement of the global elimination target for 2030.

EA-90

Influence of CYP2B6 and CYP3A4 polymorphisms on the virologic and immunological responses of patients treated with efavirenz containing regimen

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Background The objective of this study was to evaluate the effect of CYP2B6 and CYP3A4 polymorphisms on the virological and immunologic responses of patients receiving an efavirenz-containing regimen. A total of 153 HIV-positive patients were enlisted for the current study.
Methods Viral load and median CD4 T cell counts were evaluated at baseline and month 6 (M6). Single nucleotide polymorphisms (SNPs) in CYP2B6 and CYP3A4 genes were genotyped using TaqMan genotyping assays.
Results Interestingly, the AG genotype in CYP2B6 rs2279343 was associated with viral load suppression (VLS) compared to the homozygous AA (OR 2.6; 95% CI 1.3–5.3). Moreover, in the overdominant model, the AG genotype was associated with VLS compared to AA/GG (OR 2.05; 95% CI 1.3–2.9). The AG genotype in CYP2B6 rs2279343 was associated with an increase in CD4 cell count between baseline and M6 ($p = 0.01$). In CYP2B6 rs3745274, CD4 cell count at M6 was higher than that of baseline for GG carriers ($p = 0.04$) and for GT carriers ($p = 0.013$). In contrast, the TT mutant displayed no difference in CD4 cell count at M6 and baseline ($p = 0.3$). In CYP3A4 rs2740574, the TC carriers showed a higher median CD4 count at M6 compared to that of the baseline count ($p = 0.024$), similar trend was noted for CC carriers ($p = 0.004$). In contrast, the TT genotype showed no trend ($p = 0.8$). The best genotypes combination associated with CD4 cell count improvement were AA/AG in SNP rs2279343 ($p = 0.003$) and GG/GT in SNP rs3745274 ($p = 0.002$).
Conclusion Our findings support the fact that CYP2B6 rs2279343 could help in the prediction of VLS and both SNPs rs3745274 and rs2279343 in CYP2B6 and CYP3A4 rs2740574 were associated with immune recovery in Malian HIV-positive patients.

EA-135

Continuous Detection of Isolated Cases of Crimean Congo Hemorrhagic Fever in Uganda-2023

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Background Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic arboviral illness and a geographically widespread tick-borne viral infection. On February 13, 2023, the National Viral Hemorrhagic Fever Laboratory at the Uganda Virus Research Institute received an alert for a suspect VHF case in a 4-year-old male who presented with VHF-compatible signs and symptoms at Kawepe Regional Referral Hospital in Kampala.
Methods By using RT-PCR, a blood sample from the suspected patient was examined for CCHF and found to be positive. Increased anti-CCHFV IgM antibody titers on successive blood samples taken from this patient during serological testing confirmed a recent infection. Following the initial RT-PCR positive result, an epidemiological outbreak investigation was started to find any other suspected patients.
Results From the outbreak, three further CCHF patients were identified following field investigations. One confirmed case person died, (Case Fatality Rate = 25%). The clinical presentation of symptoms was general body weakness (100%), fever (100%), and spontaneous bleeding through the gastrointestinal tract (bloody diarrhea) (75%). By the time of this report, no animal samples or ticks had been collected from the neighborhood as part of the environmental investigation.
Conclusion This is one of the CCHF outbreaks that have been reported in Uganda in recent months. The results indicate that CCHF is endemic in Uganda, with sporadic outbreaks occurring throughout the country. The findings also demonstrate that tick exposure increases the likelihood of human infection. In a developing nation like Uganda, these findings further highlight the significance of having a well-established national Viral Hemorrhagic Fever (VHF) surveillance system and diagnostic capability to quickly respond to secondary cases and identify the first cases of VHF outbreaks. We advocate for improved awareness and education about the disease and its transmission among the public, healthcare professionals, and individuals at high risk of exposure.

EA-147

Analysis of host biomarkers in sputum samples from The Gambia, South Africa, Vietnam, and Peru for the development of a point-of-care triage test for tuberculosis

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Background 4 million tuberculosis (TB) cases are undiagnosed annually. A global host biosignature to distinguish TB from other respiratory diseases (ORD) is required to develop a point-of-care (POC) triage test for TB. Our aim was to identify a global host biosignature for TB in sputum samples.
Methods Sputum samples from HIV negative confirmed TB patients (n=221) or patients with other respiratory disease (ORD) (n=414) were analysed from South Africa, Peru, Vietnam and The Gambia. Cryopreserved native sputum samples from all countries were digested with sputolysin for 15 minutes at room temperature, centrifuged, and supernatants stored at -80oC until analysis. Multiplex cytokine arrays were used to analyse 64 host markers. Analyte levels from sputum digested after freezing were compared with those from paired freshly digested supernatants (n=45) in the Gambian cohort.
Results Levels of TNF-α ($p<0.0001$), MMP-2 ($p<0.0001$), IL-1β ($p=0.0002$), IL-22 ($p=0.0004$) and LIGHT/TNFSF14 ($p=0.0007$) were all significantly higher in sputum from TB compared to ORD patients. A global signature consisting of 12 analytes resulted in an AUC of 0.93, Sensitivity of 81% and Specificity of 91% while a reduced performance was seen for a 7-marker signature (AUC 0.81, Sensitivity 73% and Specificity 76%). A 4-marker signature consisting of GCSF, IL19, IL2 and MMP1 from South Africa and Gambia combined resulted in an AUC of 0.84, Sensitivity of 82% and Specificity of 70%. Fresh samples had significantly higher levels of analytes compared to post-hoc digested sputum.
Conclusion We identified a global signature that reached WHO TPP for a triage test but could not reduce from 12 markers with all countries combined. A 4-marker signature from Gambia and South Africa performed well but did not reach the TPP for a Triage test. Freshly digested sputum was superior to post-hoc digestion, indicating that use of frozen samples was a limitation in this study.

EA-181

Investigation of the relationship between malnutrition and immune status of people living with HIV/AIDS in Fako Division, Southwest Region of Cameroon

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Background The greater efficacy of antiretroviral drugs has directed focus towards improving the lifestyle and longevity of people living with HIV/AIDS (PLWHA). Malnutrition impacts the immune system and is influenced by HIV infection and drugs. The aim of this study was to investigate the effect of malnutrition on the immune status of PLWHA in the study population.
Methods A cross sectional study was conducted among 610 HIV positive participants between the months of May 2019 to November 2020 in HIV treatment centres in Fako Division. A questionnaire was used to collect lifestyle data. BMI was used to classify nutritional status. Venous blood was analysed for haemoglobin levels, some macro- and micro-nutrients (Albumin, total cholesterol, triglycerides, iron, calcium, magnesium and Vitamin D), CD4+ cell count, viral load and some inflammatory cytokines (IL-1, IL-6 and TNF-α).
Results Based on BMI results, 316 (52.8%) participants were malnourished, with 39 (6.5%) being undernourished and 277 (46%) were over nourished (overweight and obese). The majority of the patients were deficient in Vitamin D (74.8%) and serum iron (82.4%). Albumin revealed a positive relationship with CD4 cell count ($r = 0.208$, $P = 0.009$) and a negative relationship with viral load ($r = -0.229$, $P = 0.010$). There was a positive correlation between serum iron and CD4 cell count ($r = 0.250$, $P = 0.044$). Albumin correlated negatively with IL-6 ($r = -0.109$, $P = 0.035$) and TNF ($r = -0.121$, $P = 0.014$). Total cholesterol correlated negatively with TNF-α ($r = -0.269$, $P<0.001$) while calcium and magnesium correlation positively with TNF ($r = 0.108$, $P = 0.029$) and IL-1 ($r = 0.105$, $P = 0037$) respectively.
Conclusion It could be concluded that macro- and micronutrients may considerably modulate the immune recovery of PLWHA, thus affecting the quality of life.
Study received funding from CANTAM (Ref: 2517/FCRM/D/DR/08-18)

EA-184

Lineages diversity and drug resistance of Mycobacterium tuberculosis in Gabon

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Background Tuberculosis (TB) is a major public health issue in resource-limited settings, including Gabon, which it is one of the top 30 countries worldwide with a high burden of the disease. Managing multidrug-resistant TB (MDR-TB) in these settings is challenging due to limited access to rapid diagnostics and drug susceptibility testing. Early detection of drug-resistant TB is crucial to controlling transmission of resistant strains and initiating appropriate treatment. The study aimed to determine the proportion and resistance patterns of pre-extensively drug-resistant (Pre-XDR) and extensively drug-resistant (XDR) TB among MDR-TB patients in Gabon and to identify the distribution of their lineages.
Methods In this cross-sectional study, we collected 92 TB isolates from rifampicin-resistant (RR) patients based on Genexpert. We performed BD MGIT liquid culture and whole-genome sequencing using the MinION according to standard procedures.
Results Our findings showed that the HIV-TB co-infection rate was 14.1%, and the mean age of the participants was 31.94 years. We observed that 65.2% of patients had MDR-TB, 19.6% had Pre-XDR, 14.1% had RR-TB, and 1.1% had XDR-TB. We identified three main lineages, with Lineage 4 being the most common (81.52%), followed by Lineage 5 (14.13%) and Lineage 2 (3.26%). The dominant genotypes were Cameroon, LAM, Harleem, West Africa 1b, and Beijing, accounting for 47.82%, 19.56%, 17.39%, 6.5%, and 4.3% of cases, respectively.
Conclusion Our study reveals a high proportion of Pre-XDR patients, underscoring the need to enhance laboratory capacities to monitor Pre-XDR and XDR-TB patients. This is the first detection of Lineage 2, the most virulent TB strain in Gabon, Further studies are needed to investigate the transmission dynamics of the Lineage 2 TB strain in Gabon. TB programs should prioritize the effective and rational use of second-line drugs for newly diagnosed MDR-TB patients to prevent the emergence of Pre-XDR/XDR-TB strains.

EA-205

Ethical challenges in disclosing genomic research results in a developing country

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Background Disclosure of research results may impose undesirable responsibilities and consequences on the participants. Locally and culturally applicable guidelines for protection of research participants from negative consequences of genomic research results disclosure have been not enunciated in many developing countries. Establishment of such guidelines needs to be guided by preferences of the indigenous research participants. This study therefore attempts to determine potential research participants understanding and expectations of disclosure of genomic research results and its implications to participants in genomic research in Nigeria.
Methods In a cross sectional descriptive study 150 participants were selected by systematic sampling from patients attending the laboratory of Adeoyo Maternity Hospital in Ibadan. Information was collected on socio-demographic characteristics of participants, awareness of genomic research studies, preferences on the mode of disclosure of their result and the recipients of such disclosure. Data were analysed using the SPSS version 17 and presented with the tables of frequencies.
Results Most participants were aware of genomic identification of diseases (68%). The main advantage expected from undergoing genomic testing is awareness of health status (58.7%) and main disadvantage is psychological trauma (71.0%). Respondents (94%) preferred genomic research results be communicated to the study participants and certain third parties (86.7%), mostly next of kins (30.7%) and spouses (20%). Reason for seeking disclosure is to obtain social (37.3%) and medical (22%) support. Participants suggested withholding result on account of mental health status of the recipient (10.7%), incurability of the disease (8.7%) and negative social consequence of the disease (8.7%).
Conclusion This study suggests that research participants welcomes disclosure of genomic research results specifically to certain third parties due to the expected benefits. However the consequences of disclosure should be considered before its undertaking. Genomic research undertakings therefore should consider and document research participants' preferences for disclosure while participants consent is being obtained.

EA-216

Contribution of next generation sequencing (NGS) tools for molecular surveillance of malaria drug resistance markers in Burkina Faso

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Background Antimalarial drug resistance represents an increasing public health concern in Africa. Indeed, since the introduction of IPTp-SP and SMC in moderate-to-high transmission settings, the prevalence of Sulfadoxine-Pyrimethamine and Amodiaquine resistance markers are increasing. This calls into question the effectiveness of these preventive strategies in the future. In this project, we aim to evaluate how NGS tools may contribute to the molecular surveillance of malaria drug resistance markers in target populations in Burkina Faso.
Methods The study will be conducted in Nanoro Health District in Burkina Faso. A retrospective analysis of archived samples collected in 2015 from pregnant women receiving IPTp-SP and in 2016 from their children within the ''COSMIC'' trial. Archived samples collected in 2020 from children participating in a study known as ''In-Host'' project will be included as well. In addition, prospective cross-sectional studies will be conducted in 2023 and 2025 in children and pregnant women, respectively. The identification of P. falciparum infections will be performed by microscopy and qPCR. Resistance markers will be investigated using the AmpliSeq Assay and a sequencer machine (MiSeq, Illumina, USA). The multiple nucleotide sequence alignments method will be used to identify the resistance markers.
Results The expected results include the impacts of IPTp-SP and SMC on the evolution of targeted resistance markers in pregnant women in a 10 year-time and in children under 5 years in a 6 year-time. In addition, the level of P. falciparum resistance to Artemisinin-based combination therapies will be known in the two study groups.
Conclusion Regarding the pressure of antimalarial drugs on the selection of resistance markers, it is necessary to use NGS techniques to monitor these markers and assess current strategies for target populations in order to inform and guide the national malaria control programs.

EA-246

Willingness to use long-acting injectable PrEP among high-risk young women in Kampala, Uganda

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Background Long-acting injectable PrEP (LAI-PrEP) is a new, appealing substitute for oral PrEP especially among individuals for whom daily medication adherence is challenging. However, there are no available data on willingness to use LAI-PrEP among young women in Uganda. Therefore, this study aims at assessing the level and factors associated with willingness to use LAI-PrEP among high-risk young women in Kampala, Uganda
Methods We conducted a cross-sectional study that analyzed data from a cohort of 14-24-year- old high-risk young women enrolled between January and October 2019. Participants were given an overview of the attributes of LAI-PrEP including its dosage and administration. Willingness to use LAI-PrEP was defined as whether an individual was willing to adopt injectable PrEP as an HIV prevention method. The complementary log-log model was used to assess factors independently associated with willingness to use LAI-PrEP.
Results We enrolled and analyzed data for 285 participants with mean age of 19 years, 65.1% reported heavy episodic drinking of alcohol (consuming 6 or more drinks on an occasion as per the AUDIT tool), 68.8% had multiple sexual partners in the past 3 months and only 3.9% were aware of LAI-PrEP at baseline. Overall, 199 (69.8%) participants expressed their willingness to use LAI-PrEP with the most commonly cited advantage being the injection's longer lasting HIV protection. Participants that were divorced/separated (aOR 1.74,95%CI 1.02-2.94) and those with multiple sexual partners (aOR 2.12, 95%CI 1.46-3.09) had higher odds of willingness to use LAI-PrEP while those that were screened as heavy episodic drinkers had lower odds of willingness to use LAI-PrEP (aOR 0.61,95%CI 0.42-0.89).
Conclusion Our findings suggest that LAI PrEP, as an alternative to daily oral PrEP, may be used to supplement current evidence-based HIV prevention programs. Therefore, programs for scaling-up LAI-PrEP for AGYW should integrate HIV testing services with sensitization to create awareness of its potential.

EA-263

Association between birth interval and stunting in children under 5: an analysis of data from the 2018 DHS in Guinea

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Background stunting remains a public health problem in sub-Saharan Africa. Several factors could explain it but its relationship with the birth interval remains underestimated in the sub-region. The objective of this study was to analyze the association between birth interval and stunting in children under five years of age in Guinea.
Methods We analyzed secondary data from 2746 participants aged 0-59 months from the 2018 Guinea Demographic and Health Survey (DHS) in whom anthropometric measurements and information on the birth interval were provided. The generalized estimating equations approach was used using Stata version 16.1 software to calculate the unadjusted and adjusted odds ratios with their confidence interval and the significance level set at 5%.
Results Of the 2746 participants in our sample, 31.80% had stunting and this proportion was higher in children who had a short birth interval (< 24 months) 36.81% compared to those who had a long birth interval (≥24 months) 28.03%. After adjusting for age, sex of children, duration of breastfeeding, maternal height, number of antenatal care, region, and household socioeconomic status, the odds of stunting were 48% higher among children who had an birth interval of less than 24 months compared to those who had an birth interval ≥ 24 months (adjusted OR= 1.48; 95% CI = [1.22 - 1.79]).
Conclusion A short interval between births contributes to increasing the burden of stunting, hence the need to strengthen birth spacing policies in order to improve the nutritional status of children under five.

EA-264

Age and locality are among the risk factors contributing to high prevalence of anemia in the Bata district of Equatorial Guinea

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Background Anemia is a serious global health problem particularly in malaria and Soil-transmitted helminths (STH) co-endemic areas, where those parasitic infections can influence the anemia severity. The present analysis aimed to assess the prevalence and associated risk factors of anemia in malaria and STH co-endemic areas.
Methods We conducted a cross-sectional survey between October 2020 and January 2021 in the Bata district. Venous blood was collected for hemoglobin levels assessment using the HemoCue Hb201. Anemia was defined based on the WHO threshold. Plasmodium infection was diagnosed using the microscopy technique and the Kato-Katz technique was used for STH egg identification in stool samples. Multiple logistic regression analysis was performed to assess factors associated with anemia.
Results A total of 339 participants were included in this analysis, with a mean age of 24.4 (SD=23.7) and 64 (19%) aged less than 5 years. A total of 187 (55%) participants were female, while 119 (35.1%) and 79 (23.3%) of them lived in peri-urban and rural areas, respectively. The prevalence of anemia was 77% (95%CI: 72 – 82). Among the anemic population, severe anemia represents 6% (17/262), while moderate and mild anemia represents 60% (157/262) and 34% (88/262), respectively. Anemia was associated with age (p<0.001) and locality (p=0.03). Compared to participants aged 1-5 years, those aged 6-14 years (aOR=0.39; 95%CI: 0.14 – 0.95, p-value=0.048) and those aged more than 14 years (aOR=0.18; 95%CI: 0.06 – 0.41, p-value<0.001) had a lower odd of anemia. Compared to urban areas, peri-urban areas had a high odd of anemia (aOR:1.15; 95%CI:1.24 – 4.87, p-value=0.01).
Conclusion Anemia prevalence is high in the Bata district calling for more research on the determinants of the disease in the country. Our results indicate old age and peri-urban areas as the main factors associated with anemia in the Bata district.

EA-265

Factors affecting the access, delivery and adherence to RTS,S vaccination schedules of the expanded programme on immunization among caregivers in Ghana

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Background WHO recommended the RTS,S/AS01 malaria vaccine for widespread use for children in regions with moderate to high plasmodium falciparum malaria transmission after data from a pilot study revealed the vaccine was safe, significantly reduces severe life-threatening malaria, and can be administered effectively in real-life childhood vaccination settings. This study is consistent with the work of the SAVING Consortium, which builds on the Access and Delivery Partnership value chain framework and emphasizes the importance of high-quality implementation and delivery research as a crucial tenet for the efficient distribution of new medications. Factors that influence primary caregivers'(PCGs) adherence to the RTS,S vaccination schedules as well as health professionals' access to and administration of the RTS,S vaccine were explored.
Methods The larger study "Dynamics of Healthcare Utilization in the Context of RTS,S/AS01 Vaccine Implementation in Ghana" provided the secondary data for this study. Completed transcripts of 45 PCGs and 24 health professionals were imported into NVivo 12 for theme categorization and analysis.
Results Facilitators of adherence were benefits of RTS,S vaccine and trust in the health system and health workers. Barriers to adherence were social activities and other engagements. PCGs preferred fewer vaccination visits with more vaccines because frequent visits disrupt their daily activities. Health workers perceived that the phased introduction of the pilot and delay in its start affected the initial implementation and fuelled rumours. These rumours, though widespread, did not have much effect on uptake after reinforced education.
Conclusion Education and sensitization increased trust and promoted adherence to the RTS,S vaccination schedules. PCGs preference for less vaccination visits should be considered. Future introduction of new vaccines such as the R21/Matrix-M vaccine as well as subsequent roll-out of RTS,S vaccine should leverage on these enablers for implementation success.

EA-300

Barriers and facilitators for implementation of Good Clinical Practice in a Randomized Control Trial in limited resources settings: The example of freeBILy in Madagascar

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Background To fight neglected tropical diseases (NTD), clinical trials implemented in endemic settings are crucial. This requires high standards of Good Clinical Practice (GCP) to ensure participant safety and reliable data. Yet, the local implementation can be challenging due to limited resources, remote study sites, or inexperienced staff. This study aims at assessing barriers and facilitators to implement GCP in limited resources contexts through the example of the clinical trial freeBILy.
Methods A mixed-methods design was used: quantitative data to measure frequencies and extent of GCP nonconformities were extracted from the trial database, while qualitative data were collected among trial staff (n=30) through in-depth interviews and focus group discussions. A closed questionnaire captured background information of the staff. Statistical analysis with R® includes classification of nonconformities by error type and severity, as well as regression analysis of sociocultural factors associated with nonconformities. Qualitative data are being analyzed following a thematic approach. Triangulation of the data will be performed.
Results From a random sample of 500 study IDs of enrolled women, a total of 331,349 data entries have been retrieved from the database and organized to proceed with the regression analysis. The informed consents of the same 500 women were manually reviewed. A total of 30 nurses and midwives with a median age of 30 years (IQR: 29, 34) were qualitatively interviewed. The majority were female (77 %) with a university degree (100%), fluent in French (86 %), and had received GCP training in the last 2 years (97%).
Conclusion Our preliminary data show that the involved staff were well educated and regularly attended GCP trainings, challenging the stereotype of inexperienced staff in SSA. Further analysis will assess association of specific factors with frequencies and type of nonconformities in order to inform implementation strategies of future trials.

EA-301

Understanding the barriers and facilitators of Mass Drug Administration (MDA) in persistent Schistosomiasis hotspots along Lake Albert, Hoima District, Western Uganda

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Background The WHO updated the Neglected Tropical Disease roadmap for 2021–2030 includes new goals of elimination of schistosomiasis as a public health problem in all endemic countries. Despite heightened efforts over the past decade, the roadmap indicates critical action in addressing the barriers to Mass Drug Administration (MDA), the primary method of control, is still required; including improvement in adherence by the populations in persistent schistosomiasis hotspots. One such hotspot is the shoreline of Lake Albert, Uganda, where schistosomiasis control relies on annual MDA provision to school-aged children (SAC) and adults. An overemphasis on regular treatment, without comprehensively addressing the bottlenecks that result in low uptake of treatment in these high-risk populations, is likely to prevent the elimination of schistosomiasis as a public health problem.
Methods An ethnographic study design using in-depth interviews (53), key informant interviews (14), focus group discussions (14) and participant observation was conducted in two study sites along Lake Albert. Thematic content analysis was used during data analysis.
Results The study revealed that the size, taste and smell of the drug, along with its side-effects, coupled with high levels of ignorance and illiteracy about the benefits of participation in MDA, remain reasons for persistent low uptake of praziquantel by some members of the population. Conversely, lived experience of improved health through participation and knowledge of the dangers of the disease if not treated, facilitated treatment uptake.
Conclusion The importance of social influence in crucial knowledge attainment was clear through positive attitudes to localised sensitization by community drug distributors (CDDs); and by extension the reported roles of well-informed mothers in the uptake amongst SAC. We recommend a need for good community engagement strategy that provides continuous education and sensitization; integration of schistosomiasis by the government in primary healthcare activities, through improved recruitment and training provision for CDDs.

EA-316

Macrophages differentiation and Mycobacterium tuberculosis complex lineages influence the response to tyrosine kinase inhibitor Imatinib

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Background Mycobacterium tuberculosis complex (MTBC) success in evading the host immune response is critical to its survival. MTBC phosphorylates tyrosine kinase (TK), such as STAT3, to alter macrophage differentiation into a permissive phenotype that promotes its intracellular survival. This project investigates how macrophage subsets control clinical MTBC lineages in response to host-directed therapeutics (HDT) imatinib currently in clinical trials.
Methods Venous blood from healthy donors was used for monocyte extraction. Monocytes were differentiated into M1/IFN-γ, M2/IL-4, and M2/IL-13 by incubating with GM-CSF and M-CSF for 6 days, followed by 2 days with either IFN-γ, IL-4, or IL-13. Macrophages subsets were infected with reporter-gene-tagged clinical isolates of M. tuberculosis lineage2 (Mtb-L2), lineage4 (Mtb-L4), and M. africanum lineage6 (Maf-L6) at an MOI 5 in the presence or absence of Imatinib. Intracellular bacterial load quantification was done daily by measuring fluorescence, luminescence, and absorbance on SpectraMax i3x. Culture supernatants were collected on day 7 post-infection. Critical cytokines concentration was measured using ELISA, and all statistical analysis was done on GraphPad Prism Version9.
Results M1/IFN-γ macrophages control Mtb-L4 growth significantly than other lineages ($p<0.01$) with higher expression of TNF-α, IL-6 and IL-12. In contrast, M2/IL-4 macrophages contain Maf-L6 growth better than Mtb-L4 and Mtb-L2 with increased expression of IL-10 ($p<0.01$), while M2/IL-13 macrophages were permissive to all three MTBC lineages and express the lowest levels of TNF-α, IL-6 and IL-12. Imatinib stimulated M1 macrophages intracellular growth restriction of all three MTBC lineages but did not affect the M2/IL13 and M2/IL4 macrophage growth control of all MTBC lineages tested.
Conclusion Our study shows macrophage differentiation subsets affect response to different clinical MTBC lineages infection and their response to Imatinib. The development of new HDT should account for macrophage subsets and different circulating MTBC lineages.

EA-318

Comparative analysis of multiplex immunoassays for host biomarker profiling in tuberculosis diagnosis and TB treatment response

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Background Proteins such as cytokines, chemokines and growth factors play critical roles in biological processes. These act as disease biomarkers in the study of various infectious diseases. Dysfunction or dysregulation of these biomarkers may cause a variety of pathophysiological conditions. Consequently, biomarker profiling and related technologies are essential for biological studies, disease diagnosis, monitoring of treatment response and drug discovery. Many multiplexing platforms are available for the detection of these biomarkers. There is limited independently published information about the reliability of most of the platforms available in the market. The objectives of this study were to assess the abilities of the Luminex, Meso Scale Discovery (MSD) and the Curiox Drop-Array system in the detection of biomarkers in spiked sera.
Methods We assessed the abilities of three multiplex technologies; Luminex, MSD and the Curiox Drop-Array system in the detection of five cytokines, interleukin (IL)-2, IL-6, IL-10, Tumour necrosis factor alpha (TNF-α) and Interferon gamma (IFNg), in the same set of spiked serum samples. Experiments on each platform were performed as recommended by the kit manufacturer. We assessed the concentration of each analyte detected by each platform Vs. the expected actual concentrations.
Results For samples with known low and high cytokine concentrations, all platforms were able to discriminate between low Vs. high expression, however, the actual concentration for each cytokine varied greatly amongst the three platforms. Our data revealed MSD as the most sensitive amongst the platforms compared, and Curiox as the most suitable for high-throughput multiplexing, when employed alongside a Luminex platform.
Conclusion Although quantitative differences were found between the platforms assessed, the relative concentrations detected were comparable, showing that all three platforms were suitable for analyzing trends in multiple cytokine profiles. Further studies, including comparison with ELISA are ongoing.

EA-320

Optimisation of RNA extraction methods for small blood volumes for future use in TB host transcriptomic biosignature applications

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Background Whole-blood-based transcriptomic methods have limitations, including in the amount of blood required for standard RNA blood collection tubes. This is particularly relevant to individuals with difficulty in providing large volumes of blood, such as children. Furthermore, the cold chain required for storing blood tubes is problematic in field applications and in remote settings. It is therefore important to optimise RNA extraction techniques to allow for the isolation of high quantity and quality RNA from small blood volumes, and samples that are easier to collect and store under field conditions. Thus, the aim was to evaluate the quantity and quality of RNA extracted from small volumes of whole blood including dried blood spots (DBS) using three commercial extraction kits, to determine suitability for future use in RT-PCR-based experiments.
Methods Total RNA was extracted from small blood volumes (500µl, 100µl, 50µl) and DBS samples using the GenElute™ Total RNA Purification, PureLink® RNA Mini, and Tempus™ Spin RNA Isolation Kits. The yield, purity and integrity of the resulting RNA was assessed with fluorometry, spectrophotometry and agarose gel electrophoresis respectively.
Results An average of 2321 ± 456.30 ng and 336.3 ± 113.6 ng RNA was obtained from 500 µl of blood with the Tempus™and PureLink® kits respectively. Overall, the RNA isolated with both kits were intact and of high quality. RNA isolated from lower blood volumes (100 µl, 50 µl and DBS) using all three kits, was not of sufficient quantity or quality.
Conclusion Preliminary findings indicate that the quantity and quality of RNA isolated from 500µl of blood using either the PureLink® or Tempus™ kits may be sufficient for downstream transcriptomic analysis. Upon completion, our findings may be valuable in future studies that are conducted in individuals with difficulty in providing large volumes of blood such as children.

EA-324

CYP2B6*6 heterozygosity mediates slow P. falciparum clearance in malaria patients treated with Artemether-Lumefantrine

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Background Emerging artemisinin resistance threatens the effort to eliminate malaria; artemisinin resistance investigation emphasizes parasites' genetic modification as the leading cause of treatment failure. But CYP2B6*6 is vital in determining Artemisinin pharmacokinetics hence treatment outcome. Interindividual variability may mediate variable responses to artemisinin therapy among malaria patients.
Methods We recruited 100 symptomatic malaria patients aged five and above; who had P. falciparum infection and prescribed Artemether-Lumefantrine. We established their parasite load change during a 3-day treatment using the quantitative Polymerase Chain Reaction (qPCR) technique. We determined the prevalence of CYP2B6*6 Single Nucleotide Polymorphism among the patients and assessed the relationship with parasitological outcome.
Results 63% of patients had detectable parasites by qPCR, 54% had slow parasite load reduction, and 24% had parasite fold reduction of <100, while 5% of the individuals had > 10000 parasites/µL at day 3. Genotype frequency for CYP2B6*6 was 43% GG, 17%TT and 40% GT. Heterozygosity was associated with slow parasite clearance; P=0.02. The majority of the males were heterozygous.
Conclusion Most patients had delayed parasite reduction after Artemether-Lumefantrine therapy; this is more prevalent among CYP2B6*6 heterozygous individuals. Delayed parasite load reduction could be due to the slow activation of artemisinin to its active metabolite by CYP2B6*6 heterozygous patients. Such patients will have subtherapeutic levels of the active drug, unable to clear the parasite in the required treatment duration at the recommended dosage of artemisinin. The difference in treatment outcomes between different genotypes indicated that host genetic variability could determine treatment outcomes or confer selection pressure against artemisinin and the partner drug.
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EA-328

Descriptive epidemiology of mpox outbreak in Bayelsa state, Nigeria

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Background Mpox disease formally known as Monkeypox is an ongoing public health emergency of international concern associated with high morbidity/mortality with current global burden of 88122 cases, 1,211 probable cases with 148 deaths and CFR =0.17%. In Nigeria, Bayelsa State reported the first mpox case in 2017. However, there is limited information on the epidemiology of mpox in the State. This study therefore aimed to explore the overall prevalence, trends of mpox disease in Bayelsa State.
Methods We reviewed surveillance data on mpox cases from the Bayelsa State Ministry of Health, between November 2017 to March 2023. Data was cleaned and analysed using Stata (v15.0) while results were presented with Descriptive statistic and charts.
Results A total of 242 Mpox cases were reported in eight local government areas (LGA) of Bayelsa State, with majority (64.9%) being males, and below age twenty (34.6%) and from Yenagoa (64.2%), the state capital. The mean age (±SD) was 24.4 (±14.7). Meanwhile, 97.9% of patients did not travel out of their LGA in the two weeks preceding symptom onset. The proportion of mpox cases was markedly reduced consistently from 47.8% in 2017 to 6.6% in 2018 and 4.1% in 2020, with an upsurge of 50.0% in 2022. Out of the 242 cases, 43.4% were classified as discarded case, 35.1% confirmed cases, 21.5% suspected cases with 1 death and CFR =1.2%. Most of the cases (84.6%) had primary or no education, and 46.5% were pupil/student engaged in low-income occupations. The disease is symptomatic in majority (86.8%) of the cases, 10.8% of affected patient presented with Cutaneous eruption.
Conclusion The findings suggest local transmission dynamics propel Mpox mostly among those with low income and limited education. Strengthening laboratory diagnostics and outbreak response capacity is therefore recommended.

EA-334

Potential hindrance of soil-transmitted helminthiasis elimination in Central Africa as a consequence of co-infection with loiasis: a case study in the Centre Region in Cameroon

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Background Soil transmitted helminthiasis (STH) remains a major public health problem worldwide. WHO has recommended a number of strategies for the control of STH, but due to logistical and financial constraints, only school-based deworming using Albendazole/Mebendazole is frequently used. However, this does not take into consideration other age groups who share similar risk and rate of infection, and the drugs used showed reduced efficacy on certain species of soil-transmitted helminths. Some trials have demonstrated that the combination of Albendazole/Mebendazole and Ivermectin a better potential for the interruption of transmission of STH. However, the introduction of ivermectin in the treatment regimen presents a high risk of occurrence of potentially fatal serious adverse events (SAEs) occurring after administration of ivermectin among individuals heavily infected with loiasis. This study aimed to investigate the proportion of individuals coinfected with STH and loiasis, in order to determine which proportion of the population would be at-risk of SAEs if the regimen including ivermectin was used.
Methods A cross-sectional survey was conducted in 2022 in three health districts (Awae, Akonolinga and Okola) in the Centre Region of Cameroon. Capillary blood and stool samples were collected for the diagnosis of loiasis and STH, respectively. Calibrated thick blood smears were prepared for the enumeration of Loa loa microfilariae in the blood, and stool samples were analyzed by the Mini-FLOTAC and Kato-Katz methods.
Results Overall, 660 individuals were tested for both loiasis and STH in the three health districts, of which 23 (3.5%; 95%CI: 2.3-5.2) were coinfected. The overall coinfection rate was 5.3% (95% CI: 2.3-11.7) in Okola, 3.9% (95%CI: 2.3-6.5) in Akonolinga and 2.2% (95%CI:0.9-5) in Awae. Of the coinfected individuals, 69.5% (95%CI: 49.1-84.4) had light L. loa infection while 26.1% (95%CI: 12.5-46.5) had moderate infection and 0.04% (95%CI: 0.007-21) had heavy infection.
Conclusion The risk of developing SAEs remains in the population.

EA-367

Profile of molecular markers of Plasmodium falciparum resistance to Sulfadoxine-Pyrimethamine in southern Brazzaville and beyond, in the Republic of Congo

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Background Growing resistance of Plasmodium falciparum to Sulfadoxine-Pyrimethamine threatens the effectiveness of the intermittent preventive treatment during pregnancy with Sulfadoxine-Pyrimethamine (IPTp-SP) in malaria endemic areas. WHO recommends discontinuation in case of ineffectiveness as determined by over 95% and 10% prevalence of K540E and A581G mutants respectively. The objective of this study was to determine the prevalence of molecular markers of P.falciparum resistance to SP in the parasite population circulating in the south of Brazzaville and beyond, in the Republic of Congo.
Methods Two parallel surveys including hospital and community based cross sectional studies were carried out in the south of Brazzaville and beyond (urban, rural areas) between February 2021 and September 2022, to characterize the molecular markers of P.falciparum resistance to SP (dhfr and dhps). Restriction Fragment Length Polymorphism was used for the detection of single nucleotide mutation within the dhfr and dhps genes of the parasite, and detected mutations were further confirmed using Oxford nanopore sequencing platform.
Results High prevalence of mutations was reported for dhfr gene: N51I (100%), C59R (79.9%), S108N (100%), N164L (0.9%), and dhps gene: A437G (89.5%), K540E (42.4%), A581G (42.1%). The prevalence of the quintuple mutant (N51I+ C59R + S108N + A437G + K540E) and sextuple mutant (N51I+ C59R + S108N + A437G + K540E + A581G) were reported for 32.9% (111/337) and 20.8% (70/337) of the participants respectively while all the seven investigated mutations were reported in only one participant (0.3%). dhfr and dhps mutations were more prevalent in rural compared to the urban areas.
Conclusion These results indicate high prevalence of mutations within the dhfr and dhps genes of P. falciparum in south of Brazzaville and beyond in the Republic of Congo, which might threaten the effectiveness of IPT-SP in this area.

EA-370

Mycobacterium tuberculosis (Mtb) associated immune activation and exhaustion profile to predict active tuberculosis disease and monitor treatment response among presumptive tuberculosis patients.

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Background Tuberculosis (TB) is the leading cause of mortality from a single infectious agent, killing 1.514 million people annually. The currently available sputum-based tests still present challenges. For this reason, blood-based biomarkers remain an important target for improved TB diagnosis. We therefore evaluated the abilities of selected blood cytokines and proteins for identifying active pulmonary tuberculosis (PTB) among presumptive PTB participants and monitoring anti-TB treatment response.
Methods Presumptive PTB participants (n=161) were enrolled in Kampala, Uganda, and blood for serum and paxgene was collected. The concentrations of 27 host cytokine biomarkers, serum immune activation and exhaustion markers and their protein expression were evaluated using the Luminex, ELISA, and RT-PCR platform respectively. Participants were classified as having PTB or other respiratory diseases (ORD) using standard microbiological and clinical tests. Patients with ORD were sub-classified as having latent TB infection (LTBI) or no-LTBI using the QuantiFERON Gold-plus test.
Results: There was differential serum expression of PD1, FOXp3, and CD80 among presumptive PTB patients and during treatment of active PTB disease. Singly, host biomarkers including IP10, IL6, IL2, IL1β, TNFα, IFNγ, and IL12p70, were significantly different among presumptive PTB participants. A bio-signature comprising IP10+IL6+TNFα+IL1β+IL1ra+IL12p70 best diagnosed PTB disease with an area under the ROC curve of 90. Among those on anti-TB treatment, a signature comprising time to positivity (TTP)+TNFα+PDGF-BB+IL9+GCSF best predicted month 2 culture conversion with a sensitivity and specificity of 82%. Differential gene expression of PD1, HLA-DR, and CTLA4 among presumptive PTB patients was observed.
Conclusion We identified blood host biomarkers that were differentially expressed among presumptive PTB participants and had the potential for predicting PTB disease and monitoring anti-TB treatment response among confirmed active PTB patients. Point-of-care tests such as lateral flow platforms for predicting PTB stages and treatment monitoring could be developed using these biomarkers.

EA-376

Saliva as a tool for SARS-CoV-2 genomic and immunological surveillance in the Republic of Congo

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Background The design of this study was intended to evaluate the use of saliva as a reliable non-invasive tool for the genomic and immunological surveillance of SARS-CoV-2 infection in the Republic of Congo.
Methods During this cross-sectional study, the active infection was determined by detecting SARS-CoV-2 RNA using RT-PCR in 220 paired saliva and oropharyngeal samples (OPS), and by sequencing SARS-CoV-2 genome using the Oxford nanopore technology. The detection of anti-SARS-CoV-2 IgG antibody was done in 148 pair saliva and plasma samples using an in-house developed ELISA, and the reproductivity of the assay based on Saliva were assessed in two independent laboratories.
Results Overall, saliva (22/220) and OPS (23/220) showed similar rates of viral detection (p= 1.00). The sensitivity and specificity of detecting SARS-COV-2 active infection in saliva were 95.7% (95%CI: 79.0–99.8%) and 100% (95%CI: 98.1–100%) respectively, with the mean cycle threshold values similar to those of oropharyngeal samples (p>0.05). The genome sequencing revealed a mean coverage of 95.5 ± 2.8 %, finding omicron as the main variant. The anti-SARS-COV-2 antibody detection in saliva showed a sensitivity of 92.0 % (95%CI: 85.0–96.0%) and specificity of 93.3% (95%CI: 78.0–99.2%) compared to plasma. There was a high agreement in antibody detection results between FCRM and ITM laboratories (Cohen's kappa 0,94; p = 0.0001).
Conclusion These findings demonstrate that saliva can be used as a surrogate to Oropharyngeal or plasma for surveillance of SARS-COV-2 infection in the Republic of Congo.

EA-377

Investigating the West African circulating Mycobacterium tuberculosis complex lineages' response to new anti-tuberculosis treatment approaches

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Background Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis complex (MTBC). An estimated 10.6 million cases and 1.4 million deaths were recorded in 2021. There are nine MTBC lineages worldwide, all of which are found in Africa. Some of the lineages are distributed globally (lineage 2 and 4) while other are restricted to certain geographical location, M. africanum is mainly found in West Africa. Despite this diversity, drug-susceptible TB is treated with the same antibiotics' combination for six months. MTBC lineages' genetic diversity has been shown to affect the treatment response. Therefore, new drugs accounting for this diversity are needed to control TB.
Methods Whole genome sequences (WGS) data MTBC isolates from The Gambia were used to harness the genetic mutations for structural bioinformatics analysis. Representative isolates of the major MTBC lineages were transformed using a reporter gene-tagged plasmid to confer luminescence and green fluorescence protein expression to the bacilli. The direct effect of anti-tuberculosis drugs was tested in the presence of the bacteria to determine the minimum inhibitory concentration (MIC) and the half maximal inhibitory concentration 50 (IC50) of each drug against the transformed MTBC lineage. The MIC and IC50 values were then aligned with the genetic variation in each lineage.
Results We analysed 285 WGS samples and showed that the single nucleotide polymorphism with genes associated with drug resistance differ in MTBC lineages. M. africanum lineage6 showed lineage specific mutation in the rpoB, fabG1, and gyrBA genes while M. tuberculosis lineage 4 only showed lineage specific mutation in katG gene. The MIC and IC50 of rifampicin, isoniazid and moxifloxacin differ in MTBC lineages.
Conclusion In conclusion, the genetic variation of drug-susceptible West African MTBC isolates were aligned in vitro response to antibiotics. This pipeline will be used to evaluate the impact of MTBC lineages' genetic mutation on existing and new anti-TB drug response.

EA-395

Effect of mass testing, treatment and tracking on malaria prevalence among children in the Pakro sub district of Ghana over a two-year period

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Background Global efforts to scale-up malaria control interventions are gaining steam. These include the use of LLINs, IRS, Intermittent Preventive Treatment and Test, Treat and Track. Despite these, the drive for malaria elimination is far from being realistic in endemic communities in Africa. This is partly because asymptomatic parasite carriage, not specifically targeted by most interventions fuel transmission. There is a need to use alternative strategies that target asymptomatic parasitaemia. We report the impact of malaria mass testing, treatment and tracking (MTTT) on prevalence of asymptomatic parasitaemia over a two-year period in Ghana.
Methods 5800 individuals in 7 communities in the Pakro sub-district of Ghana participated in this study. Community-based health volunteers moved from house-to-house testing participants using RDTs and treating positive cases with ACTs quarterly.
Results In the intervention arm, the prevalence of asymptomatic parasitaemia significantly decreased from 22.9% (95% CI: 19.8, 26.1) in March 2020 to 6.5% (95% CI 5.9, 7.0) in March 2022 among all the participants. Also, a significant reduction in parasitaemia was observed during the July season 2020 to 2021 ($P<0.001$). Interestingly, there was no significant decline in asymptomatic malaria during the season of November between 2020 and 2022. In the control arm, the parasitaemia increased from 30.3% (95% CI: 24.1, 36.5) in March 2020 to 41.4% (95% CI: 32.8, 50.0) in March 2022. Similar trends were observed for participants ≤15 years and ≥15 years. In the intervention arm the prevalence of moderate anaemia reduced from 4.2% in March 2020 to 1.2 % in March 2022.
Conclusion This study suggests that implementing MTTT could reduce the prevalence of asymptomatic parasitaemia in children under 15 years of age over time. However, care should be taken when planning MTTT as the asymptomatic parasitaemia prevalence varies across season. There is a need to reduce the times interval between interventions.

EA-402

Predictors of archived HIV-1 drug resistance mutations in cellular reservoirs of virally suppressed adolescents: The EDCTP READY-Study TMA2025-CDF1027

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Background Even though 92% of people receiving antiretroviral treatment (ART) have achieved viral suppression (VS) globally, adolescents with perinatal HIV-infection (APHI) have challenges in sustaining VS, probably due to HIV-1 archived drug resistance mutations (ADRMs). Our objective was to investigate on ADRMs among APHI on VS in Cameroon.
Methods An analytical study was conducted in 2021 among 38 consenting APHI on VS at the Chantal BIYA International Reference Centre (CIRCB) in Yaoundé-Cameroon. Proviral-HIV-1 DNA was extracted from buffy coat, DNA extracts were amplified, purified and sequenced by capillary electrophoresis. Generated proviral sequences were used to analyse ADRMs on HIVdb.v9.0. Molecular phylogeny was performed with MEGA v10x and data were analysed with a significance threshold of 5%.
Results A total of 30 samples were successfully amplified, of which 28 sequences were obtained and one sequence was excluded due to APOBEC3G mutations. Sex ratio M/F was 3/4; median age was 14 years [IQR: 13-16.5]. Regarding ART, twelve (42.9%) were on first line, and the most common regimens were TDF+3TC+EFV and TDF+3TC+ATV/r; and 64.3% (18/28) were fully adherent. Regarding ART response, 92.9% were at WHO clinical stages 1/2; median CD4 was 642 [IQR: 421-769] cells/mm3; 32.1% (09/28) had undetectable viraemia. The prevalence of ADRMs was 59.2% (16/27), of which main DRMs by class were M184MV/I (25%), T215Y/IL/FS (15.9%) for nucleoside reverse transcriptase inhibitors (NRTIs); K103K/N (25.7%), A98A/G (14.3%) for non-NRTIs; I54V and V82VA (3.7% each) for PI/r. Second line of ART were associated with ADRMs (p=0.001). ADRMs were found in detectable (66.6% i.e. 12/18) versus undetectable viraemia (44.4% i.e. 04/09), p=0.58. Seven HIV-1clades were found, with CRF02_AG being prevalent (67.8%).
Conclusion Despite VS, APHI harbour ADRMs, which underscore high risks of subsequent ART failure, even with undetectable viraemia. Limiting emerging ADRMs suggest targeting APHI on second-line ART, after previous exposure to NRTI-containing regimens.

EA-403

Multi drug resistant invasive non-typhoidal Salmonella in children from two rural communities in Ghana

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Background Nontyphoidal Salmonella causes more than 1.2 million annual deaths worldwide, the majority in resource-limited countries such as sub-Saharan Africa. Nontyphoidal Salmonella have also become increasingly resistant to antibiotics and are the most frequent cause of bacteraemia in sub-Saharan Africa. Recent data suggests that the burden of the disease is highest in children below 5 years of age.
Methods Within this study, we collected Salmonella from blood samples of children below 5 years of age in two rural communities in Ghana. Strains were identified by biochemical methods and confirmed using the VITEK 2 System. Serotyping and antibiotic susceptibility testing was performed. Further, isolates were subjected to sequencing using a NextSeq 500 Illumina machine.
Results In total 3,159 blood culture samples were collected. of which 72 (2%) tested positive for NTS. A total of 49 Salmonella isolates were serotyped and four different serovars were detected, namely S. Typhimurium (n=29, 59%), S. Dublin (n=10, 20%), S. Enteritidis (n=9, 18%) and S. Westphalia (n=1, 2%). Multidrug resistance was observed in 24% (n/N=11/46) of the isolates tested. MLST analysis confirmed the serovars and sequence types S. Typhimurium (ST313/ST19) being most common followed by S. Enteritidis (ST11/ST1479) and S. Dublin (ST10).
Conclusion The substantially high level of multidrug resistance and emerging fluoroquinolone resistance seen in the invasive Nontyphoidal Salmonella poses a challenge to current treatment strategies. Hence the need for increased surveillance and the development of effective antimicrobial stewardship programs to combat the spread of MDR iNTS in Ghana.

EA-414

Social burdens and benefits of participating in malaria vaccine efficacy trial within a human infection study in Kenya: A qualitative study understanding the experiences of study participants

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Background It is acknowledged that Human Infection Studies (HIS) can accelerate discovery of promising therapies, but this particular research design presents significant ethical, social and cultural challenges, particularly on LMICs. Over the last eight years, embedded social science and ethics research on ongoing malaria HIS examine some of these contextually sensitive challenges. We conducted an embedded social science study in an ongoing malaria vaccine efficacy trial within a HIS in coastal Kenya to further document how experience of participation varied across different malaria HIS.
Methods We conducted 3 focus group discussions and 20 interviews, with 38 male and female HIS participants after vaccination, and during residency, between October 2022 and February 2023. Voice recordings were transcribed, translated, and analyzed using thematic analysis.
Results HIS volunteers reported a range of previous benefits and burdens of study participation. In general [during the in-patient stay], there was raised anxiety around COVID-19 testing, where positivity was an exclusion criteria, considering the need to observe and mitigate for prevention measures such as physical distancing and exit from study participation. Although weekly payments were preferred, their disbursement had logistical and administrative delays and requirements that resulted in strained relationships between participants, family members and the study team. Similar to previous studies participants appreciated using funds from the financial compensation for immediate household needs during the in-patient stay, access to medical screening and general care during in-patient stay.
Conclusion In this preliminary analysis, we highlight the need for HIS teams to carefully consider, striking a balance between potential burdens vs benefits, in the design and conduct of studies, while also being proactive in documenting and responding to unanticipated issues emerging during the study that could affect study participants wellbeing.

EA-438

Women's acceptance and willingness-to-use self-sampling devices for cervical cancer screening in Uganda

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Background Cervical cancer is the commonest cancer of women in Uganda. Over 80% of women diagnosed in Mulago a national outpatient and teaching hospital have advanced diseases. Pap smear screening, on an opportunistic rather than systematic basis, is offered free in the gynecological outpatients' clinic and the postnatal/family planning clinic. One of the objectives of the study was to obtain women's knowledge, acceptance and willingness to use self-sampling before the development of the cervical cancer screening intervention with a self-sampling device.
Methods The study employed a qualitative approach. This was conducted among women and community representatives through Focus Group Discussions. This study was conducted in the districts of Kampala, Mukono, and Wakiso in Uganda to obtain women's input before starting the development of cervical cancer screening intervention with a self-sampling device.
Results The majority of the women expressed positive responses towards a self-sampling device as a very good initiative and were willing to use it if proved effective. Women share perceived benefits as promoting privacy, saving time spent at the clinic, preventing stigma, and solving transport concerns hence promoting cervical cancer screening. Women further preferred self-sampling over standard practices because of no embarrassment and not seem painful. The preferred ways to inform women about the results of self-sampling included designated counselling rooms at health facilities, on the phone if the results are negative, and one-on-one.
Conclusion Self-sampling is a crucial initiative and will be welcomed by women however, there is a need to engage, sensitize and involve the target population like policymakers, health workers, politicians, local leaders, policymakers, women leaders (groups), and any other key influential individuals at the community level on the benefits and how to use it before it is rolled out for buy-in.

EA-460

Impact of Covid-19 pandemic on the prevalence of surface contaminants associated with healthcare waste management in a hospital in Yaounde, Cameroon

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Background An estimated 40% of Nosocomial infections have been attributed to cross-infection via the healthcare personnels' hands, which could result either directly and/or indirectly from touching contaminated surfaces and patient contact. The COVID-19 pandemic has been a stark reminder of the importance of basic infection prevention measures (hand washing, disinfection/decontamination, Personal Protective Equipment use) when providing patient care. Hence, illustrates the importance of establishing the prevalence of nosocomial contaminants found on fomites from March to August 2020 at the Biology, Emergency Departments and Disposal site of a hospital in Yaounde.
Methods In a cross-sectional study, 736 swabs were collected from trash bins (infectious and non-infectious) and surfaces (tables, sinks, chairs, countertops, desks, patient beds and bed stands) of all aforementioned sites. Inoculated on Mueller-Hinton agar, contaminants were isolated and, identified using Gram staining, classical biochemical tests (oxidase, catalase, coagulase, germ tube and Kligler Iron Agar) and grown on specific media (Hektoen Enteric Agar, Mannitol Salt Agar and Potatoes Dextrose Agar).
Results There was a high prevalence of surface contaminants (78.9%) especially for non-infectious bins (90.3%). Their mean frequencies were significant for sampled surfaces of the Biology Department, and only sampled beds of the Emergency ward indicating their equal potential to cause infections. In addition, highly touched surfaces were prone to S. aureus contamination (22.4%), a constituent of the human hand microbiota which suggests that the staff' hands could be the main vector of surface contamination in analysed units. In May, contaminants' frequencies dropped (24.9%) due to increase in the awareness of basic infection control measures amongst staff, staff rotations, changes in work hour schedules and hospitalisation beds' availability.
Conclusion The concept of environmental bacterial reservoir is a reality. Improvement strategies include interventions to reduce/contain the shedding of pathogens and, improving the efficacy of cleaning/disinfection of hospital surfaces and hand hygiene.

EA-475

Transmission of a replication-competent vector rVSV-ZEBOV Ebola vaccine: a phase 2 trial

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Background Live attenuated, including viral vector, vaccines may be transmitted to others. Benefits of secondary transmission include increased vaccine coverage and accelerated achievement of herd immunity. In contrast, risks include vaccine evolution to wild-type pathogens e.g., oral polio vaccine and risks of adverse events in vulnerable populations.
Recently, we reported the shedding of the rVSVΔG-ZEBOV-GP vaccine in children's saliva, suggesting potential secondary transmission to relatives. In this phase 2 vaccine trial, we investigate the secondary transmission of the rVSVΔG-ZEBOV-GP vaccine to the vaccinees' relatives in Gabon.
Methods One hundred sixty-three relatives of our study vaccinees (Gabonese children aged 1-12 years old) were enrolled to assess the transmission of the rVSVΔG-ZEBOV-GP vaccine, compared to another live attenuated vaccine containing the Oka strain of the varicella-zoster virus. They were followed up on days 0, 2 or 3, 7, 14, 21, 28, and 56 post-vaccination. Clinical symptoms and signs were observed, and samples were collected during the study visits. Relative plasma and saliva were tested by RT-PCR for presence of rVSV RNA, alongside antibody titers' determination.
Results Quantifiable rVSV RNA was detected in plasma in a low proportion of relatives on days 2 or 3; there was no detection in the saliva of relatives at any visit. These data will be aligned with titers of anti -ZEBOV-GP and further interpreted. No adverse event was observed in the relatives.
Conclusion rVSVΔG-ZEBOV-GP vaccine virus is transmissible to relatives or close contacts of vaccinees, based on the RT-PCR Ct values, favoured by virus shedding in vaccinated individuals. The implications of this finding require further consideration.
Funding: IMI, VSV-EBOPLUS consortium

EA-505

Heterologous immunity induced by the viral vectored vaccine rVSV-EBOV-GP

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Background Heterologous immunity is the induction of an immune response to an unrelated pathogen upon exposure to a different pathogen, involving memory T cells and B cells response. Studies showed that BCG-immunization would induce resistance to Listeria infection and increase B cells and T cells responses. Viral vectored vaccine are promising and vaccine platform that favour the induction of cellular immune responses beyond potent humoral immune responses. We investigate the potential of the rVSV-EBOV-GP vaccine to induce heterologous immunity through immune mechanisms involving cellular immune responses and a network of cytokines.
Methods We investigate the effect of the vaccination with rVSV-EBOV-GP on the childhood vaccines, including TB, Polio 1,2,3 serotypes, Diphtheria, Bordetella pertussis, Hepatitis B, Yellow fever, Measles, Influenza type B, which are part of the expanded program on immunization in Gabon. We analyzed samples of 120 children enrolled in Phase 1/2, a randomized, controlled, open-label trial. Among them, 80 received the rVSV-EBOV-GP vaccine, and 40 received the Varicella-Zoster vaccine.
Results Antibody titers or cellular immune responses against TB, Polio 1,2,3 serotypes, Diphtheria, Bordetella pertussis, Hepatitis B, Yellow fever, Measles and Influenza type B are being evaluated before vaccination and at days 7, 28, 56, 180 and 365 after vaccination. We also measured adaptive cytokines IFNγ, IL-5, IL-12, IL-13, IL-10, IL-17A, IL-22 at the corresponding time points.
Conclusion Cellular and cytokines immune responses are reliable biomarkers that could be used to assess vaccine candidate efficacity and vaccine heterologous induced-immune response.

EA-528

Investigation on rheumatic diseases in children recipients of two live attenuated viral vaccines: A phase 2 trial

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Background Rheumatic diseases, including juvenile idiopathic arthritis, are chronic inflammatory conditions affecting children. There have been concerns regarding the potential role of live attenuated viral vaccines in triggering rheumatic diseases. This phase 2 trial aimed to investigate the association between two live attenuated viral vaccines and the development of rheumatic diseases in children.
Methods A randomized, controlled open-label trial was conducted involving children aged 1-12 years who were eligible to receive live attenuated viral vaccines for heterologous rVSV-ZEBOV-GP Ebola or varicella. Participants were randomly assigned to receive the vaccine. A muscle-skeleton examination, FBCs, ESR, CRP, HLA-B27, IgM, RF, and ANA were accessed on Days 0,1,2/3, 7, 14, 21, 28, 58, 180, and 365 routinely. The primary outcome was the development of rheumatic diseases, within the follow-up period.
Results 120 children were enrolled in the trial, with 80 in the rVSV-ZEBOV-GP group and 40 in the varicella group. The mean age at enrolment was 6.46 years, and the study population consisted of an equal distribution of gender. The follow-up period, days 1, 2/3, 7, 14, 21, 28, 58, 180, and 365 showed no significant differences in the incidence of rheumatic diseases between the two vaccines clinically. Some participants complained of arthralgia (1.9%), however, it was associated with plasmodium falciparum. For the rest of the inflammatory markers, analysis has been completed and will be available timely.
Conclusion In this phase 2 trial, there was no evidence to suggest that administering two live attenuated rVSV-ZEBOV Ebola and Varicella, was associated with a risk of rheumatic diseases in children. The noted pseudo-signs of rheumatic diseases like arthralgia and body ache were strongly linked to Malaria infection. These findings provide reassurance regarding the safety profile of rVSV-ZEBOV-GP Ebola and varicella concerning rheumatic diseases in children.

EA-562

Epidemiology of HIV and Helminth co-infection among pulmonary tuberculosis patients at Jamot hospital in Yaoundé, Cameroon

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Background Tuberculosis (TB), HIV and Helminths are serious overlapping public health problems in sub-Saharan Africa. This triple burden may lead to accelerated disease progression. Although HIV is integrated in TB programs in Cameroon, data on TB-helminth co-infection still remains limited. This study was aimed at determining the prevalence of helminths and their associated factors among pulmonary tuberculosis patients at Jamot hospital in Yaoundé, Cameroon.
Methods This was a cross sectional study conducted at the Jamot hospital in Yaoundé, Cameroon from April 2022 to March 2023 with participants aged 18 years and above. A well designed questionnaire was used to capture sociodemographic data, clinical history and risk factors for TB, HIV and helminth infections. Sputum, stool and blood samples were collected from each consenting participant. Sputum was examined using auramine microscopy. Stool was examined using the kato-katz and Mini-FLOTAC techniques. Blood was used for HIV serology according to guidelines. TB-uninfected healthy controls were also recruited and their blood and stool samples similarly analysed.
Results A total of 321 sputum smear-positive TB patients (72% males and 28% females) and 65 healthy controls (54% males and 46% females) were included in this study. The prevalence of TB-HIV co-infection was 13.4% (43/321). The prevalence of any helminth infection among TB patients was 13.5% (37/274) and 7.7 % (5/65) among controls. The most prevalent helminth species in this study was Ascaris lumbricoides (62%, 23/37), followed by Trichuris trichuria (19%, 7/37), Strongyloides stercoralis (5.4%, 2/37), and hookworm (2,7%, 1/37). TB-HIV-Helminth triple co-infection was found in 3 cases.
Conclusion The prevalence of TB-HIV and TB-Helminth co-infection is similar. This emphasizes the fact that diagnosis and treatment of helminth infections should be integrated in TB control programs in Cameroon for a better management of the disease.

EA-585

Acute flaccid paralysis surveillance data analysis, Western Region One, The Gambia: 2018-2022

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Background Acute flaccid paralysis (AFP) is a sudden onset of paralysis or weakness in any part of the body in a child <15 years of age. It is caused by both infectious and non-infectious agents. The Wild Poliovirus is the most common infectious cause of AFP in children <5 years of age. There is no known medical treatment other than vaccination for prevention. The epidemiology of non-polio enteroviruses (NPEVs) remains largely unexplored in West Africa including the Gambia. This study aims to describe the characteristics of patients reported with AFP in Western Region One of the Gambia, between 2018 and 2022 and evaluate the AFP surveillance using the WHO-recommended indicators.
Methods The study employed a retrospective records review of the AFP surveillance data of Western Region One from 2018 to 2022 recorded in the national AFP surveillance database. Data were analysed using SPSS version 20.
Results A total of 35 cases of AFP were reported within Western Region One from 2018 to 2022. 64% (23/35) were males and 43% (15/35) were below 5 years of age. The non-polio AFP reporting target (1/100,000 population aged <15 years per year) was achieved throughout the five years. All AFP cases had adequate stool samples. 8 confirmed cases of (NPEVs) were reported and 56% (20/35) of the cases had up to five doses of the Oral Polio Vaccine. The lowest (14%) number of cases was reported in 2020, during which no case was reported between February and August.
Conclusion The AFP surveillance system is sensitive. All reported cases were investigated, and two stool samples were collected from each case, at least 24 hours between stool collection and within 14 days after the onset of paralysis. Active AFP searches should be strengthened to improve case detection in the region and health workers should be trained on AFP surveillance indicators.

EA-586

Prevention of Tuberculosis in people living with Diabetes Mellitus - the PROTID project

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Background Diabetes mellitus (DM) increases the risk of tuberculosis (TB) and will hamper global TB control due to the dramatic rise in type 2 DM in TB-endemic settings. Current guidelines don't recommend TB preventive therapy (TPT) for people with DM due to an absence of evidence.
Methods PROTID is the first randomized, double-blind trial to evaluate the efficacy and safety of 12 weekly doses of rifapentine/isoniazid (3HP) as TPT in people with DM who have latent tuberculosis infection (LTBI, n=3000), with a parallel cohort (n=1000) to measure TB risk in individuals with DM tested negative for LTBI. PROTID, run in Uganda and Tanzania, will also examine optimal ways of screening for active and latent TB, evaluate quality of DM and DM-TB care, establish cost-effectiveness and population impact, and archive samples for pathophysiological studies.
Results As of May 2023, 1890 participants have been screened, of whom 56.2% were LTBI-test positive, 8.5% HIV-infected, 0.5% diagnosed with TB disease and 4.9% reported previous TB. 740 participants (39.2%) have been enrolled in the trial, and 377 in the parallel cohort. Among those screened (mean age 55.8 years, 71.7% female), the mean duration of DM was 8.8 years; 38.2% were overweight and 32.2% obese, with 26.8% on insulin and a mean HbA1c of 9.4%. Further characterization showed hypertension (62.7%), myocardial infarction (1.0%), stroke (3.4%), foot amputations (5.0%), visual loss (60.9%), and peripheral neuropathy (76.9%).
Conclusion PROTID will provide essential evidence regarding prevention of DM-associated TB, and DM care in sub-Saharan Africa. Its initial results show a high burden of TB and LTBI and common HIV co-infection among people with DM in Tanzania and Uganda. DM is characterized by inadequate glycemic control and frequent complications, underlining the need for interventions to improve access and quality of DM care.

EA-603

Efficacy of albendazole against hookworms and its in vitro activity by the egg hatch test in Northwest Ethiopia

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Background Soil-transmitted helminths (STHs) are common in the tropics and subtropics. Although mass drug administration programs remain the cornerstone for STHs control, continuous monitoring of benzimidazole efficacy in areas where albendazole or mebendazole are periodically given is warranted to detect early emergence of resistance in human STHs. The aim of the study was to evaluate the efficacy of albendazole against hookworms in primary school children using coprological examination and to compare the results with the in vitro egg hatch test (EHT) technique.
Methods Stool samples were collected from 90 hookworm-positive children at baseline and 21 days after treatment with albendazole in Bahir Dar Zuria district, northwest Ethiopia, from December to March, 2023. Cure rate (CR) and egg reduction rate (ERR) were calculated using Kato-Katz technique. Hookworm eggs were collected individual at baseline to perform the EHT using an egg concentration protocol. Approximately 50 eggs per well were incubated for 48 hours in triplicates with four concentrations of thiabendazole (0.05 uM, 0.1 uM, 0.5 uM and 5 uM); control wells were also included. The hatching percentage was calculated for each concentration after correcting the data with controls.
Results Only one of the 90 samples tested had a moderate infection; the rest had light infections. The CR was 81.1% and the mean ERR was 94.4%. Eleven children had an ERR of less than 90%, 4 between 90 and 95% and the remaining higher than 95%. In relation to EHT, the highest concentration (5 uM) resulted in the death of all eggs whereas most of the eggs survived at the lowest concentration (0.05 uM). Hatching percentages ranged from 3.9 to 30.3% in 0.5 uM concentration and 47.5-74.9% in 0.1 uM concentration.
Conclusion Based on our findings, EHT at a single concentration of 0.1 uM could be used to estimate benzimidazole effectiveness in vitro.

EA-605

Acceptability and feasibility of perennial malaria chemoprevention for children under two years: a mixed method pre-implementation assessment in Togo (MULTIPLY project)

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Background The WHO recommends the administration of Perennial Malaria Chemoprevention (PMC) alongside the Expanded Immunization Program (EPI) for children under two years. As part of MULTIPLY, a pilot-oriented research project, we described the context and assessed the perceived acceptability and feasibility of PMC implementation by key stakeholders and community actors in Haho district (Togo).
Methods We conducted a pre-implementation mixed methods study (11/2021-02/2022). All district Healthcare workers (HCW) (n=188) of 27 health facilities and a sample of Community Health Workers (CHW) (n=43) were invited to respond to a self-administered questionnaire. Structured observations were conducted in 4 health facilities along with semi-structured interviews with 8 HCWs, 4 facility-in-charges, 4 district health system representatives, 2 CHWs, 16 caregivers and 10 community actors. Descriptive analysis was performed on the quantitative data; qualitative data were analysed thematically. Results will be triangulated following a mixed-methods analytical approach.
Results Overall HCWs and CHWs perceived PMC as relevant in the context of high malaria burden at district level. They had a good level of knowledge about malaria and its prevention (93.5% perceived bednets as effective). HCWs foresaw good community acceptability of PMC, due to its integration with the EPI. Although some HCWs poorly understood the rationale of PMC if children are not sick, they also believed PMC would be effective, given the positive perceptions of the preventive malaria treatment during pregnancy. Several structural and operational challenges were foreseen (e.g. distance barriers for accessing health facilities, lack of materials for PMC administration, or lack of dedicated human resources). Results from the community perspective will be further analysed and compared with these health-system insights to have a complete overview of PMC acceptability and feasibility pre-implementation.
Conclusion At district level in Togo, pre-intervention acceptability of PMC was encouraging, overall. Potential barriers to the feasibility of the strategy were identified.

EA-619

Global evidence, local adaptation (GELA): equitable partnerships to support evidence-informed guideline recommendations for newborn and young child health in three countries in sub-Saharan Africa

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Background Despite progress in newborn and child health, most countries in sub-Saharan Africa have not met the Sustainable Development Goals for under-five mortality. Clinical practice guidelines (CPGs) bridge the gap between research evidence and clinical practice. High quality CPGs directly impact patient care, funding and access to health services. Partnerships with governments, researchers and the public are key to success in this field. The objectives of The Global Evidence, Local Adaptation (GELA) Project partners with ministries of health in South Africa, Nigeria and Malawi to maximise the impact of research on health care through increasing capacity to use global research to develop locally relevant CPGs for newborn and child health.
Methods We have begun implementing our research and capacity strengthening programme, using adaptation methodology and digital platforms to support delivery of contextually-appropriate recommendations. We apply principles of equitable partnerships with national CPG groups, including policy makers, epidemiologists and civil society including continuous communication and co-creation.
Results Steering Groups were convened, and prioritization exercises completed. Priority topics are proceeding to the evidence synthesis stage to be packaged for use in guideline meetings. Guideline members are participating in project-related training. We have completed a landscape analysis of CPGs in newborn and child health identifying gaps in guidelines availability and opportunities for strengthening guideline quality. Evaluation activities are ongoing including knowledge translation tracking and evaluation of capacity needs for decision-makers.
Conclusion The GELA project is on course to achieve its targets. Our success is enabled through partnering with ministries in Malawi, Nigeria and South Africa, the WHO HQ and Afro regional office and civil society groups and a project team of African and international leaders in evidence-based healthcare. Ongoing evaluation will help us learn what works well to reduce waste and save resources for guideline adaptation and may be scalable to other countries like ours.

EA-625

Effects of anti-malarial prophylaxes on maternal transfer of Immunoglobulin-G (IgG) and association to Immunity against Plasmodium falciparum infections among Children in a Ugandan birth Cohort

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Background The in-utero transfer of malaria specific IgG potentially plays a role in provision of immune protection against malaria in children. This study established the effect of IPTp on in-utero transfer of malaria specific IgG and the associated immune protection against malaria in the first birth year of children in Uganda.
Methods We screened a total of 637 cord blood samples from a double blinded randomized clinical trial on Sulfadoxine-Pyrimethamine (SP) and Dihydroartemisinin-Piperaquine (DP) IPTp in a Ugandan birth cohort; study conducted from Busia, Eastern Uganda. Luminex assay was used to measure the cord levels of IgG sub-types (IgG1, IgG2, IgG3 and IgG4) against 15 different P. falciparum specific antigens, with tetanus toxoid (t.t) as a control antigen. Man-Whitney U test (non-parametric) in STATA (ver15) was used in statistical analysis. In addition, Multivariate cox regression analysis was used to determine the effect of maternal transfer of IgG on the incidence of malaria in the first birth year.
Results Mothers on SP expressed higher IgG4 levels against erythrocyte binding antigens. Placental malaria did not affect expression of cord antibodies. Higher levels of total IgG were associated with increased risk of malaria; AHRs: 1.092, 95% CI: 1.02-1.17 (Rh4.2); 1.32, 95% CI: 1.00-1.74 (PfSEA); 1.21, 95%CI: 0.97-1.52 (Etramp5Ag1); 1.25, 95%CI: 0.98-1.60 (AMA1); 1.83, 95%CI: 1.15-2.93 (GLURP) (GLURP), and 1.35, 95%CI: 1.03-1.78 (EBA175). Children born to poor mothers had the highest risk of malaria (AHR: 1.79, 95% CI: 1.31-2.4).
Conclusion Malaria prophylaxis in pregnant mothers using either DP or SP does not affect expression of antibodies. Poverty and gestational malaria are risk factors of malaria infections in children. Malaria antibodies are not protective in endemic areas.

EA-639

Using Periodic intensification for routine immunization (PIRI) to strengthen vaccination against Human papillomavirus in a conflict affected region in Cameroon

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Background Over the years, the incidence of Human papillomavirus infections in Cameroon is on the rise (most prevalent in cervical cancer) with an estimate of 2770 new cases/ year and 1787 deaths/year in women according to 2021 reports. In 2023, national statistics indicate that cervical cancer accounted for 20.9% of cancers affecting women while 2.9% of men were diagnosed with HPV-related infections. Vaccination against HPV is effective in reducing the burden of the HPV associated diseases, nonetheless 19% (Dhis-2) of girls aged 9years in Cameroon were immunized against HPV in 2022. In Cameroon, following introduction of vaccination against HPV in boys in January, 2023, Periodic Intensification of routine immunization was used to strengthen vaccination against HPV in girls and boys in 03 health districts of the Southwest region.
Methods Microplans and lists of lost to follow up children were elaborated at health area level to identify areas with poor routine immunization performance prior to the intervention. There was also media sensitization, stakeholder meetings organized at health area and district level with local authorities. There after PIRI was conducted by each health district in 03 rounds using CHWs and healthcare providers accepted by the community. Study data was obtained from the district health information software and regional performance reports.
Results A total of 3401 girls and 2161 boys age 9years were vaccinated in which the region gained 8 points for girls and boys respectively when compared to 2 and 3 points the region gained in 2021 and 2022 through the same intervention.
Conclusion successful implementation of PIRI in 03 health districts with high level implication of community actors in the conflict affected Southwest region contributed to an improvement in HPV vaccination performance.
This activity was funded by UNICEF

EA-659

Serum proteogenomic profiling of CXCL10 and Zika Virus RNA in pregnant women at Nigerian tertiary teaching hospitals

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Background CXCL10 has been shown to increase up to 200-fold during ZIKV infection in pregnant women and is associated with the pathogenesis of ZIKV. This research aimed to investigate the relationship between Zika virus (ZIKV) infection and overexpression of C-X-C motif chemokine 10 (CXCL10) in pregnant women.
Methods The study investigated a total of 62 serum samples from pregnant women in Nigerian tertiary teaching hospitals who were positive for Zika virus IgM using RTqPCR.
Results Seven samples were confirmed by PCR for the presence of ZIKV RNA, indicating a prevalence of 11.1%. The quantity of ZIKV RNA detected in the seven serum samples ranged from 1.0 x 10^2 to 11.6 x 10^3 copies/ml. Further analysis revealed that CXCL10 was overexpressed in four out of the seven ZIKV-positive samples, with an increase of 4-, 24-, 27-, and 126-fold. These findings suggest a link between ZIKV viremia and CXCL10 overexpression in pregnant women. Additionally, the study identified age, gestational age, and ZIKV-related symptoms as risk factors for CXCL10 overexpression in pregnant women infected with ZIKV. Gene expression analysis revealed regulation values ranging from 1.0 to 126.2 among samples positive for ZIKV RNA.
Conclusion The findings of the study provide new insights into the pathogenesis of ZIKV infection in pregnant women and suggest that CXCL10 may serve as a biomarker for the disease. Future studies may investigate the potential of CXCL10 as a therapeutic target for ZIKV in pregnant women. Overall, this research highlights the importance of understanding the immunological and virological factors involved in ZIKV infection during pregnancy.

EA-661

Novel case finding for drug resistant TB among pastoral communities, a case of Kazo district, Ankole region, south-western Uganda

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Background Uganda is one of the 30 countries with a high burden of TB in the world. According to the 2014-2015 National TB prevalence survey, 39% of people with cough for two or more weeks did not seek treatment. Similarly, there was an estimated 1500 people (range 820-2300) with Drug resistant TB (DR TB) in 2018 but only 34% were notified. While Ankole region in South-Western Uganda detected 36 DR TB cases from April 2022 to March 2023, Kazo District, a majorly pastoral community diagnosed 2. Additionally, in 2021/2022, Kazo District had a case detection rate of 46% (Target 90%). There was need to improve TB case finding and therefore pairing Health workers and village health teams (VHT) to screen for TB in community hotspots was initiated.
Methods Microplanning meetings were held with the District Health Team and USAID LPHS Ankole (TASO). A review of the District TB register was done. Hotspot mapping was done with community participation while prioritising areas with previously high TB notification. Buremba, Kyampangara and Nkungu were selected. In each hotspot, a professional health worker and a VHT were paired to do household health education, TB screening using MOH designed tools and sputum sample collection for 3 days. Samples were tested using Gene-Xpert. All diagnosed clients were started on respective treatment.
Results A total of 524 households were reached,1526 people were screened for TB. Presumptive TB was identified in 220/1526(14.4%) and 15/220 (6.8%) (8 male and 7 female) confirmed with TB. Of these, 13 (87%) were from Buremba. Out of the 13 clients,7(53.8%) (3 male and 4 female) had Rifampicin resistant TB.
Conclusion Pairing Village Health Teams with Professional Health workers in community hotspot screening leads to high TB yield. These data provide a paradigm for optimal active TB case finding in hard to reach communities.

EA-693

Recovery of full susceptibility to deltamethrin of resistant mosquitoes after pre-exposure to pireronyl butoxide: a call for the use of second generation nets in Gabon

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Background Bed nets are the main tools used in vector control of malaria. However, insecticide resistance is a looming threat on their efficacy and the gains obtained over the years. Thus, a better understanding of the resistance profile of vectors is a prerequisite towards the implementation of vector control measures adapted to local settings. We therefore aimed to evaluate the resistance of mosquitoes to various insecticides and the effect of the synergist piperonyl butoxide (PBO) on pyrethroid resistance.
Methods Anopheles gambiae s.l larvae were collected in Lambaréné and reared until adult emergence. The susceptibility of adult mosquitoes to deltamethrin, permethrin, bendiocarb and malathion was tested using the WHO protocol with additional testing performed for permethrin and deltamethrin with mosquitoes pre-exposed to PBO.
Results An. gambiae s.l. mosquitoes were resistant to permethrin 0.75% and deltamethrin 0.05% with mortalities of 11% and 72% respectively, after 24 hours. Resistance to permethrin was of high intensity with mortality of 47% with permethrin 3.75% and 88% with permethrin 7.5%. The combination PBO+permethrin 0.75% resulted in a 4-fold increase in mortality to 44%. The intensity of resistance to deltamethrin is considered moderate with a mortality with deltamethrin 2.5% of 86% in the tests performed. The combination PBO+deltamethrin 0.05% resulted in a complete recovery of susceptibility with a mortality of 100%. Finally, mosquitoes were resistant to bendiocarb and susceptible to malathion with mortalities of 75% and 100% respectively.
Conclusion The results obtained in this study confirm the high intensity of resistance of Anopheles to pyrethroids. However, the improvements observed with the use of PBO in terms of mortality rates suggest that second generation bed nets which are impregnated with PBO could be useful tools for vector control. These results also allow us to consider the use of malathion in combination with other insecticides to mitigate resistance.

EA-709

NK cell determinants of immunity to Mycobacterium tuberculosis in humans

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Background Natural killer (NK) cells respond to pathogen-infected and neoplastic cells by directly killing target cells and secreting immunoregulatory cytokines. Our understanding of the role of NK cells in tuberculosis (TB) pathogenesis remains incomplete.
Methods To gain a better understanding of peripheral blood NK cell functional changes that occur during progression to TB disease, NK cells were characterised using a CyTOF-based intracellular cytokine staining (ICS) assay in a cohort of Mycobacterium tuberculosis-exposed adolescents who were followed up over two years. To explore NK cell characteristics in human tissues, NK cells were also characterised in postmortem cohorts of TB patients who succumbed to disease, and non-TB controls who died from trauma. We characterised NK cell phenotypes and cytotoxic potential in postmortem samples from the lung, hilar lymph nodes, bronchoalveolar lavage (BAL), spleen, and peripheral blood mononuclear cells (PBMC).
Results Functionality scores (using Combinatorial Polyfunctionality analysis of Antigen-Specific Subsets – COMPASS) of peripheral blood NK cells were lower at distal timepoints from TB diagnosis in progressors relative to controllers. However, NK cell functionality scores of progressors increased significantly above controllers at timepoints closer to TB diagnosis. A cytokine neutralization assay suggested that peripheral NK cell cytokine and cytotoxic marker expression during TB disease were dependent on T cell bystander activation via IL-2. NK cells in peripheral blood of TB patients displayed mature, activated phenotypes, expressing higher levels of cytotoxic molecules than non-TB controls. In contrast, NK cells in tissues were phenotypically immature, and were particularly enriched in the lung of TB cases relative to non-TB controls.
Conclusion We observed marked differences and between peripheral blood and tissue NK cells, where enrichment of phenotypically immature and hypo-cytotoxic (expressing low levels of cytotoxic molecules) NK cells in the lung of TB cases potentially reflects a cause and/or consequence of disease pathogenesis, which requires further investigation.

EA-732

Lung function trajectories in South African children with pulmonary tuberculosis – a prospective cohort study

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Background Post-tuberculosis lung disease is a topic of global interest. There is scarce literature on paediatric post-tuberculosis lung disease. The objective of this study was to investigate the impact of pulmonary tuberculosis (PTB) in children by longitudinally measuring lung function (spirometry and oscillometry) trajectories in children with confirmed, unconfirmed tuberculosis or non-PTB lower respiratory tract infection (non-PTB LRTI).
Methods Children < 15 years of age, with suspected pulmonary tuberculosis who had not received more than 72 hours of anti-tuberculosis therapy were enrolled. Spirometry and oscillometry were done at 0, 3, 6 and 12 months; non-PTB LRTI had lung function testing for up to 3 months.
Results 173 children had at least 1 successful lung function test, 105 had spirometry and 169 had oscillometry. The median (IQR) age at enrolment was 96 (63-130) months; 52% were male and 13% were HIV infected.
Less than 5% of the children had positive bronchodilator responsiveness at baseline in all groups. More than 60% of the children with confirmed or unconfirmed PTB and a third of children with non-PTB LRTI had restrictive spirometry pattern at baseline. Children with confirmed TB had a lower z-FVC at 12 months, higher z-R6, compared to unconfirmed TB, median (IQR) -1.7z (-2.4 to -0.7) and -0.9 z(-1.4 to -0.5), p=0.015 for z-FVC and 0.2 (-0.9, 1.1) and -0.3 (-0.9, 0.7), p=0.367 for z-R6, respectively.
Conclusion Children with confirmed TB had lowest zFVC and highest z-resistance at 6Hz at 12 months. Restrictive pattern was the most predominant abnormal spirometry pattern, with very few being bronchodilator responsive.

EA-749

Gender power dynamics in healthcare decision-making: A cross-section study in Southern Malawi

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Background Gender is a social determinant of health. Gender power dynamics can impact women's and children's health outcomes. The Demographic and Health Survey (2015) showed that 68% of women participated in decisions about their own healthcare in Malawi, but there is a lack of information on the socio-determinants and gender attitudes associated with primary health decision-making. This study aims to examine these factors during the male clinic days (health education activities) in four healthcare facilities in Southern Malawi.
Methods We included men who participated in the male clinic days between August and November 2022. The main outcome of interest was the extent of women's participation in their own healthcare. We designed a questionnaire that included the Gender-equitable Men Scale (GEM), which measures attitudes toward gender equality on a scale of 0 to 1. In addition, we collected socio-demographic, relationship, and family-related variables. Univariable and multivariable analyses revealed the association between the main and the other variables.
Results 422 men were included in this study. The average GEM score was 0.53 (0.37-0.67; 95% CI: 0.004). Among the participants, 64.2% (271/422) reported that their female partners did not have the final say in healthcare decisions. When female partners assumed primary decision-making roles (35.8%, 151/422), men reported higher levels of gender-equitable attitudes compared to cases where men were the primary decision-makers (0.57 vs 0.47, p=0.004). Factors such as higher education level, location, formal employment, and male village chiefs emerged as the main socio-determinants associated with women's decision-making role in health.
Conclusion This study emphasizes the significance of socio-economic factors and gender-equitable attitudes in healthcare decision-making. This suggests the need for targeted interventions involving both men and women in discussions about healthcare decisions.

EA-753

Covid-19 in children: Immune response to SARS-CoV-2 infection in children under 5, Guinea-Bissau

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Background Children under the age of five are generally more susceptible to respiratory viral infections, but during the pandemic there have been many reports that children have a low risk of severe SARS-CoV-2 infection. It has been questioned to what extend children have been infected with SARS-CoV-2. We therefore conducted a survey to determine the prevalence among children under 5 years of age in Guinea-Bissau and investigate potential risk factor related to COVID-19 infection.
Methods This is a cross-sectional study, carried out in children under 5 years of age in the study area of the Bandim Health Project, a health and demographic surveillance system located in Guinea-Bissau, between April and July 2022. SARS-Cov-2 antibodies were investigated using rapid diagnostic tests (OnSite Rapid Test, CTK Biotech, USA) to determine the prevalence. Risk ratios (RR) were calculated with 95 % confidence intervals using binomial regression.
Results The study included 831 children. The overall prevalence of SARS-Cov-2 antibodies was 51% (423/831). The prevalence was lowest among the youngest children aged 6-11 months. Older children had significant higher RRs, ranging from 1.47 (12 -23 months) to 1.80 (48-59 months). Other risk factors included whether the child had attended school/kindergarten: RR=1.33 (1.15-1.54); whether child had been ill during the pandemic: RR=1.22 (1.03-1.44); whether someone had died in the house, RR=1.40 (1.15-1.70) and children whose guardian (usually the mother) had attended school for more than five years, RR=1.49 (1.26-1.75).
Conclusion Confirmed cases of SARS-CoV-2 in Guinea-Bissau only represent about 0.5% of the population. However, this study indicates extensive circulation of SARS-CoV-2 since more than half of children under five year of age tested positive for SARS-CoV-2. Age of the child, deaths occurred in the house and education level of the guardian were all associated with previous SARS-CoV-2 infection.

EA-759

Assessment of Adherence with Intermittent Preventive Treatment using Sulphadoxine-Pyrimethamine among Pregnant Women in Osun State, Nigeria

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Background Malaria in pregnancy (MIP) is a major public health concern in sub-Saharan Africa, often associated with poor pregnancy outcomes. A package of interventions, including the SP-IPTp strategy, has been recommended. The uptake of at least three doses of SP-IPTp starting from the second trimester until delivery, at one-month intervals, has remarkably ameliorated the risks associated with MIP. Nevertheless, optimal uptake is somewhat elusive during antenatal care. Hence, this study aimed to assess the extent of adherence with SP-IPTp and plasma levels of sulphadoxine among pregnant women.
Method This was a cross-sectional study among consented pregnant women across 3 sites, each of primary, secondary and tertiary health facilities, in Osun State. Validated antenatal records were employed to assess the uptake of SP-IPTp. Besides, venous blood samples were collected to determine the plasma levels of sulphadoxine.
Results A total of 483 pregnant women ≥30 weeks gestation with a mean age of 30.4 ±5.3 years were enrolled. Of which 30.1% of the women were primigravidae, 25.7% were secundigravidae and the remaining were multigravidae. The result indicated 49.2%, 38.2% and 12.6% of the participants had received one, two and three doses or more, respectively. The antenatal record further showed that 46.7% received a dose of SP-IPTp within the last 56days from the day of sample collection. The difference between the plasma levels of sulphadoxine of those who had their last uptake of SP within 28days and those who had exceeded 28days was statistically significant ($p<0.0001$), the median (IQR) of 9.9 (0.38-33.1)ug/mL and 0.86 (0.05-8.7)ug/mL, respectively and the level is below the LLOQ after 56days.
Conclusion Utilization of the SP-IPTp intervention is still very low, and adherence appears inadequate. Findings in this study reveal that more advocacy on the IPTp-SP strategy and the implementation of directly observed therapy at various antenatal clinics are necessary.

EA-762

Prevalence of Pfcrt K76T mutation years after chloroquine withdrawal in Lagos, Nigeria

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Background Antimalarial drug resistance is a major drawback to malaria elimination agenda. In response to widespread chloroquine (CQ) failure, Nigeria's Health Ministry outlawed the drug for uncomplicated malaria treatment in 2005. Several studies have consistently reported a reversal to CQ susceptibility by Plasmodium falciparum years after hiatus. However, non-adherence to treatment guidelines and anecdotal repurposing of CQ potentially encourage the persistence of drug pressure favoring the fitness of the mutant allele. In this study, we investigated the existing prevalence of a point mutation at position 76 associated with P. falciparum chloroquine resistance.
Methods Sixty-three P. falciparum isolates were collected from Oriokuta Health Centre, Ikorodu, Lagos, during the drug therapeutic efficacy assessments conducted in 2021. Deoxyribonucleic acid (DNA) was extracted and malaria positivity was confirmed by Pf 18S rRNA. Subsequently, the DNA samples were assayed by polymerase chain reaction (PCR) and restriction fragment length polymorphisms (RFLP) to determine the prevalence of Pfcrt-K76T mutation.
Results RFLP analysis identified 39/63 (62%) wild-type K76 and 24/63 (38%) mutant 76T genotype.
Conclusion Our finding points to an evolving epidemiology of Pfcrt K76T alleles. There appears to be an indication of a potential decline in the frequency of 76T mutation. However, this requires further substantiation using advanced variant validation tools in a larger parasite population.

EA-771

An economic evaluation of a test-and-treat strategy for schistosomiasis control in pregnant women and young children (freeBILy)

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Background There exists a remarkable knowledge gap on the effectiveness of schistosomiasis control interventions for pregnant women and children below 5 years of age, resulting in a lack of public health policies and initiatives targeted to these vulnerable groups. We address this gap with the freeBILy trial in Madagascar, which evaluates a test-and-treat strategy (POC-CCA testing and PZQ treatment) in pregnant women and their young children against the status quo.
Methods We model the cost-effectiveness of the strategy in comparison to three alternatives: PZQ treatment after a Kato-Katz positive result, presumptive treatment if symptomatic, and preventive chemotherapy. We develop separate models for pregnant women and their young children, which include deterministic and probabilistic sensitivity analyses. Notably, in the model for pregnant women, we employ health-related quality of life (HRQoL) as a metric to represent the health outcomes of the compared strategies. HRQoL was derived from the administration of EQ-5D-3L questionnaire to 500 pregnant women enrolled in two trial training sites at four time points, twice before and twice after giving birth. While this data will not be considered for the estimate of intervention effectiveness, it provides invaluable information for the economic evaluation. HRQoL was also estimated alongside Gabon freeBILy trial among 630 pregnant women and used in the sensitivity analysis.
Results Preliminary results point to a potential increase in HRQoL in the intervention group (POC-CCA testing and PZQ treatment) in comparison to the control group in Madagascar. However, these results will have to be validated against trial effectiveness measures. In addition, the final cost estimates of the compared strategies will determine the cost-effectiveness of the evaluated strategy.
Conclusion The results will inform policy about which strategy to prioritize given resource constraints in Madagascar and similar settings.
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EA-777

Establishing and navigating community engagement during the COVID-19 pandemic: lessons learned from Zambia

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Background In Zambia, from March 2019, strict adherence to public health guidelines during implementation of essential or COVID-19 related research studies inadvertently impacted the conduct of community engagement (CE). We share our experience of establishing and navigating CE in a TB research study pivoted to include COVID-19 in Zambia.
Methods Different approaches were adapted to solicit CE for different study phases. Phone-based individual conversations (n=6) with community representatives and district health officials, and phone-based group discussions (n=4) with community members were held to obtain initial COVID-19 community experiences and informed protocol development. In addition, low-risk face-to-face meetings (n=8) were held with community members, following COVID-19 guidelines, to deepen understanding of the community experiences. Prior to study commencement, meetings (n=4) with community representatives were held, leading to formation of a COVID-19 Community Team (CCT) to guide study implementation. Meetings with the CCT (n=5), health facility staff (n=3), and sensitization activities (n=20) were held during implementation, and these CE activities were evaluated using observations (n=8), individual interviews (n=8) and focus group discussion (FGD: n=5).
Results Community engagement helped researchers to identify information and knowledge gaps and dynamics, local experience, and supported interaction between community and the health facility. Further, establishing the CCT generated community agency for COVID-19. However, phone-based conversations and discussions, though useful, were limited in quality by poor network, limited number of participants on a single call, and limited ownership of a working phone. Face-to-face CE activities were also undermined by strict adherence to COVID-19 public health and institutional guidelines that prevented social etiquette (e.g. handshakes) and more extended community interactions.
Conclusion Although establishing and navigating CE during the COVID-19 pandemic was feasible, the reach and quality of community engagement was compromised by COVID-19 restrictions. Therefore, a combination of the remote and face-to-face research approaches is required going forward.

EA-792

C-reactive protein and high-sensitivity C-reactive protein levels in asymptomatic intestinal parasite carriers from urban and rural areas of Gabon

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Background Chronic carriage of intestinal parasitic infections (IPIs) can induce chronic inflammation and dysbiosis, which are risk factors for non-communicable diseases. The objective of this study was to determine the relationship between IPI carriage and inflammation in a population of volunteers living in Gabon.
Methods A cross-sectional study was conducted from September 2020 to November 2021 in asymptomatic participants aged 18 years and over, residing in different areas: Libreville (urban area) and, Koula-Moutou and Bitam (rural areas). The detection of IPIs was carried out using microscopy technics. Inflammation markers, C-reactive protein (CRP), and high-sensitivity C-reactive protein (hsCRP) were measured.
Results Overall, 518 participants were included, 64.5% (n=334) of whom resided in urban area and 35.5% (n=184) in rural areas. The median age was 35 years [27; 46]. The prevalence of asymptomatic IPIs was 29.9% (n=155), with a significantly higher frequency in rural areas than in urban area (adjusted OR 6.6 [CI 3.2-13.8], p<0.001). Protozoa were more frequent than soil-transmitted helminths (STHs) in both areas: 81.6% (n=40) in urban area and 69.8% (n=74) in rural areas. STHs were predominant in rural areas (48.1% (n=51) than in urban area (22.4%, n=11). High concentrations of hsCRP and CRP were significantly more frequent in inhabitants from rural areas (23.4% (n=43) and 56.5% (n=104), respectively) compared to those from urban area (11.1% (n=37) and 34.5% (n=116), respectively) (p<0.001). They were more frequent in parasitized individuals (22.6% (n=35) for hsCRP; p=0.002, and 52.9% (n=82) for CRP; p=0.003); notably STHs carriers (65.9% (n=27) for hsCRP, and 36.6% (n=15) for CRP) (p<0.001) contrary to protozoa carriers and coinfected individuals.
Conclusion This first study carried out in Gabon showed that asymptomatic IPIs increase CRP and hsCRP levels, especially STHs. Other biomarkers of inflammation must be analyzed to confirm the relationship between asymptomatic IPIs and chronic inflammation in Gabon.

EA-802

High Dose Vitamin D3 in vitro has no Impact on Neutrophil and Monocyte Antimicrobial Functions

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Background Vitamin D3 (vit.D3) plays an important role in immune responses, and deficiency has been linked to inflammation and higher susceptibility to infections. In vitro studies using pure cell cultures demonstrated vit.D3's contribution to microbial killing capacity of macrophages. However, the effect on neutrophils is poorly described. We assessed the effect of high dose vit.D3 in vitro on activation and microbial killing capacities of neutrophils and monocytes under near-physiological conditions using fresh whole blood from adult healthy donors.
Methods Whole blood was exposed to Mycobacterium bovis Bacille Calmette-Guérin (BCG) and Lipopolysaccharide (LPS) post treatment with 100 nM vit.D3 for 2hr, 6hr, and 24hr. Cellular phenotyping by flow cytometry was performed to quantify expression of neutrophil (CD16bri14low) and monocyte (CD14bri16low) activation markers (CD11b, CD62L), bacterial phagocytic capacity, and reactive oxygen species (ROS) production. Interleukin 8 (IL-8) and myeloperoxidase serum levels were quantified using ELISA, and correlated with intracellular killing capacities by performing colony forming unit (CFU) analysis.
Results Vit.D3 had no significant direct effect on CD11b/62L expression, phagocytic capacity, ROS production, inflammatory marker expression (IL-8, MPO) and killing efficacy independent of the pre-treatment durations. This may reflect differences in vit.D3 concentrations used and kinetics of vit.D3 mediated response patterns in the cells studied when compared to previous reports. Although these results cannot be extrapolated onto in vivo conditions as vit.D3 effects under physiological conditions can be more complex, the whole blood assay proves a valuable tool to analyse host responses ex vivo in patient cohorts. This assay is employed in our ongoing EDCTP funded 96-week randomized placebo-controlled clinical trial (VITALITY) involving high-dose vit.D3 supplementation (20,000 IU/week) in HIV positive adolescents to assess effects on neutrophil and monocyte antimicrobial responses.
Conclusion An interplay of background effects of HIV and other comorbidities need to be considered as they may influence overall benefits of vit.D3 in this population.

EA-807

West African Consortium for Clinical Research on Epidemic Pathogens (WAC-CREP): Sub-Regional Collaborative Model to Strengthen Health Systems for Emerging Infectious Diseases (EIDs)

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The devastating impacts of the sub-regional Ebola Virus Disease (EVD) outbreak clearly demonstrated a significant need to foster collaboration, build human capacity, strengthen laboratory infrastructure, promote community participation in outbreak response, and formulate strategies to harmonize ethical and regulatory pathways to successfully implement clinical trials on vaccines, therapeutics and diagnostics. This sub-regional concept led to a gathering of scientific leaders from the highly impacted EVD countries in the Republic of Guinea to identify a regional approach as the most ideal model to promote complex multi-site cross-border clinical trials, share information on case management during outbreak response, conduct capacity building workshops on regulatory and ethical challenges during public health emergencies (PHEs), identify and strengthen core laboratory systems, share biological samples, and create suitable platforms to share research findings for the mutual benefits of the vulnerable citizens of the sub-region. Accordingly, the West African Consortium (WAC) for Clinical Research on Epidemic Pathogens (WAC-CREP) was borne out of this shared interest by researchers from Liberia, Guinea, Sierra Leone and later Mali and Cote D'Ivoire to advance regional preparedness for global health security by sharing regional research, best practices, and evidence to inform infectious disease policies.
To-date, the consortium has supported the launch of a sub-regional multi-country clinical trial for EVD vaccines, conducted five successful sub-regional scientific conferences and sub-regional training workshops, developed strategic plan to strengthen sub-regional health systems, conducted sub-regional technical and policy expert meeting on EVD survivors, recruited Ministers of Health (MoHs) to serve as Ambassadors, and collaborated on grants, among others. The success of this sub-regional collaborative model clearly demonstrate the benefits of regional collaboration to mitigate emerging infectious diseases (EIDs) of poverty, especially in low and middle-income countries (LMICs).

EA-811

High malaria and arbovirus IgM/AgNS1 seropositivity in children with acute febrile illness in Libreville, the capital city of Gabon

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Background Acute febrile illness (AFI) management represents a challenge in sub-Saharan Africa where appropriate tools for the screening are often lacking. The aim of this study was to determine the prevalence of single and co-infection of malaria and arbovirus in children with AFI in a malaria sentinel site, Gabon.
Methods From July to December 2022, patients with AFI and presenting at the malaria sentinel were screened for malaria and dengue (DENV), Chikungunya (CHIKV) and Zika (ZIKV). Malaria was diagnosed using microscopy, while arbovirus infections were investigated with RDT detecting specific IgM (CHIKV and DENV); NS1 antigen and IgM for ZIKA by. Haematological parameters were analysed.
Results A total of 524 acute febrile cases were included, their median age was 60 [24.0-132.0] months. The prevalence of malaria was 38.9% (n=199/524), P.falciparum was the only plasmodial species detected. Arbovirus RDT positivity rate was 39.1% (n=205/524). Overall, 184 (35.1%) participants were tested positive for ZIKV, 86 for NS1 antigen; 72 for ZIKV specific IgM and 26 for both NS1 antigen and IgM. DENV specific IgM was detected in 42 (8.0%) patients while CHIKV IgM rate was 0.6% (n=3). Considering the number of detected infections, 187 (35.7%) patients were infected by one pathogen, 92 (17.6%) by two and 19 (3.6%) by three pathogens. Co-infections were frequent, Malaria-Zika virus infection predominated (17.3%, n=92). The median Hb level was different according to the type of infection, it was the lowest in case of co-infection (p=0.03). The median platelet count was significantly lower in case of coinfection, patients were at 8-fold higher risk of having thrombocytopenia (OR: 8.7; IC95% [5.3- 14.2], p<0.01).
Conclusion Arbovirus circulation is important in Gabon. There is a need for an adequate biological diagnosis of non-malaria AFI.

EA-817

Relationship between Microbiome and Clinical outcome in Buruli ulcer disease

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Background Previous studies have demonstrated secondary microbial infection of Buruli ulcer (BU) lesions before, during and after treatment. However, there is limited data on the resistance profile of these organisms and their influence on the development of paradoxical reactions. The present study aimed to investigate the microbiome and resistance profile in BU lesions during therapy and at the onset of a paradoxical reaction (PR).
Methods We investigated the bacteria diversity in patients with PCR confirmed BU from 5 endemic districts within central Ghana. Samples were collected longitudinally from lesions and compared to normal skin flora in literature. Microbiological analyses including isolation of bacteria, species identification and antibiotic susceptibility testing (AST) were performed using the VITEK 2 system.
Results Of the 38 participants, 66 bacteria (Actinobacteria – 2.5%, Firmicutes – 48.1%, Proteobacteria – 49.4%) were isolated from BU lesions relative to healthy skin. Staphylococcus spp was dominant at baseline. There was a marked reduction in the number of isolates after treatment with Pseudomonas spp and Staphylococcus spp being the dominant bacterial isolates. Baseline AST profile revealed organisms in BU lesions were highly resistant to tetracycline (55%), benzylpenicillin (52%), and trimethoprim-sulfamethoxazole (26%). Organisms isolated after treatment completion showed high level of resistance to tetracycline (79%), benzylpenicillin (65%) and rifampicin (59%). Of note, 4/8isolates were Methicillin Resistant Staphylococcus aureus (MRSA). Opportunistic pathogens including Staphylococcus spp, Enterococcus spp and Klebsiella pneumoniae were isolated from 6/38 patients that developed PR.
Conclusion Infection with BU alters the skin microbiome of patients. Most BU lesions are colonized by polymicrobial organisms resistant to commonly used antibiotics in Ghana. Our study demonstrated the presence of opportunistic pathogens in BU lesions that developed paradoxical reaction, suggesting a possible relationship.
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EA-821

Prevalence and characteristics of archived HIV drug resistance among virologically suppressed individuals living with HIV in Botswana

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Background The prevalence and impact of baseline archived HIV-1 drug resistance mutations (HDRMs) in people with HIV (PWH) switching to new regimen is not well understood. The aim of this study was to evaluate HDRMs among virologically suppressed individuals on NNRTI based ART in Botswana before they were switched to new dolutegravir (DTG) based ART.
Methods We included a total of 4524 virologically suppressed PWH (aged >18 years) on ART with viral loads <400 copies/ml who were recruited into an HIV cohort, the Botswana Combination Prevention Project, in Botswana between 2013 and 2018. The near full-length HIV-1 proviral DNA pol sequences were analysed for the presence of NRTI and NNRTI DRMs. The Stanford HIV drug resistance database was used for identification of HDRMs.
Results Among the 4524 virologically suppressed individuals, the majority (72%, 3267/4524) were female, with median age of 40 years [interquartile range (IQR): 34-48]. The overall prevalence of DRMs was 16.4% (742/4524, 95% CI: 15.3% - 17.5%). Females had a higher proportion of DRMs than males (12.1% vs. 4.3%, respectively). The prevalence of NRTI resistance was 2.9% (129/4524, 95% CI 2.4% - 3.3%), while the majority of DRMs were associated with NNRTI resistance at 15.1% (685/4524, 95% CI: 14.1% - 16.2%). The NNRTI mutation E138A which confers resistance to etravirine and rilpivirine was the most common (9.3%, 419/4524), followed by K103N (1.6%, 74/4524) which is associated with efavirenz and nevirapine resistance. The most common NRTI associated mutation was M184V (1.1%, 48/4524) followed by M184I (0.8%, 37/4524) which confer resistance to 3TC and emtricitabine.
Conclusion We report a prevalence of archived HDRMs in this cohort of 16.4%. Further research is warranted to understand the impact of the observed archived HDRMs on the efficacy of DTG based regimen.

EA-824

Impact of Multi-Class Antiretroviral Drug Resistant Variants on Newly Approved Antiretroviral Therapy (ART) Among People Living with HIV in Botswana

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Background To evaluate for potential alternative antiretroviral therapy (ART) among people living with HIV(PLWH) who have multi-drug resistance (MDR) variants, we determined resistance to second-generation non-nucleoside reverse transcriptase inhibitors (NNRTIs): Doravirine (DOR), Etravirine (ETR) and Rilpivirine (RPV), and entry inhibitors: Maraviroc (MVC), Enfuvirtide (T20) and Fostemsavir (FTR).
Methods A total of 7473 HIV sequences were analysed, MDR was defined as resistance to •2 drug classes. The Stanford HIV drug resistance database was used for determining DOR-, ETR- and RPV-resistance. MVC-resistance was determined by evaluating for CXCR4 coreceptor usage using geno2pheno and WebPSSM. FTR-resistance was evaluated using previously reported FTR-resistance mutations. T20-resistance was determined according to the 2022 IAS resistance mutations update. Predictors of MDR were determined using the univariate and multivariate logistic regression hazard models.
Results The prevalence of PLWH with MDR was 682/7473 (9.1 %: 95 % CI; 8.3-9.6). Within the MDR group, resistance to the four drug classes was as follows: NNRTIs (84.6%), NRTIs (83.9%), PIs (55.3%) and INSTIs (6%). High prevalence of resistance to second generation NNRTIs was observed within MDR group: RPV (79.3%), ETR (63.6 %) and DOR (67.1%). Within entry inhibitors, 7.9 % (31/391) CXCR4 coreceptor usage was observed, indicating low prevalence of MVC-resistance. A total of 113/626 (18.1 %) MDR individuals presented FTR-resistance. T20-resistance was observed in 313/623 (50.2 %) of MDR individuals. ART experience, virologic failure at VL> 400 copies/mL and being male were significantly associated with developing MDR.
Conclusion The study reports high prevalence of resistance to second generation NNRTIs and T20 in individuals with MDR HIV variants which reduces their potential use as alternative therapy for this group of PLWH. In contrast, low prevalence of FTR-and MVC-resistance allows for their potential use although we suggest genotypic testing prior to use of these drugs to avoid selection of ineffective ARV regimens.

EA-837

A combined health care provider and lay patient and public involvement and engagement in APT sepsis and LACTATE studies. A case for Malawi

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Background Patient and Public Involvement (PPI) significantly contribute to clinical and implementation science research to make it relevant, acceptable, and beneficial to the public concerned. Research poses challenges to the lay public contributors to understand Medical Jargon, procedures, processes, and practice. Yet the need for their contribution towards research that is context specific remain critical. We formed a combined professional committee including medical professionals and lay members of the Public to contribute to the conduct of LACTATE and Active Prevention and Treatment of Maternal Sepsis (APT Sepsis) studies.
Methods The research team contacted health care providers, staff, and fellow PPI members to help identify and nominate sepsis survivors, carers, and spouses to survivors to contribute to LACTATE and APT SEPSIS studies. Health care providers experienced in Maternal and Fetal health were contacted to be part of the committee. The committee reviews Study document, receive implementation updates and discuss progress of studies in a combo approach. Health care providers provide a learning platform to lay public contributors to understand medical jargon and contribute effectively to clinical research while the public contributors provide personal, community and public perspectives about research and care services. Together they shape the research conduct.
Results Twelve members, both lay public contributors and health care professionals formed a strong committee in Maternal and Fetal health research group. No negative power imbalances have been observed within the members. The committee successfully informed the development of participant information sheet for LACTATE Study, provided guidance on dissemination of the APT sepsis study during the intervention phase. More protocols use the committee to guide the development and implementation of the research studies.
Conclusion Combining health care professional and lay public contributors is feasible and effective in contributing to research. Combination approach provides instant learning.

EA-840

Infectiousness of pregnant women in the seasonal malaria transmission zone of Saponé in Burkina Faso

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Background Burkina Faso has a high burden of malaria in pregnancy despite mass deployment of insecticide-treated nets (ITN) and use of intermittent preventive treatment in pregnancy (IPTp). Understanding how pregnant women contribute to the infectious reservoir will enable development of tools to effectively address malaria transmission.
Methods A community-based longitudinal cohort with mosquito infection assays was carried out in pregnant women in Saponé Health District, central Burkina Faso. Pregnant women who were parasite positive were followed monthly after their antenatal care visits (ANC). Venous blood samples were collected for direct membrane feeding assays (DMFA) prior Sulfadoxine-Pyrimethamine (SP) dosing and on day 7 or 14 post DMFA to assess infectiousness to mosquito.
Results A total of 63 pregnant women were enrolled in the survey. 153 mosquitoes feeding experiments were conducted and 7,736 mosquitoes were dissected. 3.9% of feeds were infectious to mosquitoes with 18,3 % of mosquito infection rate and 3.6% oocyst prevalence per infected midgut.
Conclusion Key findings related to parasite and gametocyte density, duration of infection and mosquito exposure will be presented during the conference to address the hypothesis that pregnant women under IPTp may still constitute a significant source of mosquito infection.

EA-845

Cross-reactive anti-SARS-CoV-2 antibody detected in plasma from pre-COVID-19 pregnant women in Yaoundé are not neutralizing

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Background Our study aimed to determine the neutralizing capacity of anti-SARS-CoV-2 antibodies found in the plasma of pregnant women collected during the pre-pandemic period to COVID-19 in three settlements in Cameroon.
Methods A total of 1,590 archival plasma from pregnant women during pregnancy (574) and at delivery (657) were tested for COVID-19 using the Abbott Panbio TM COVID-19 IgG/ IgM rapid diagnostic test. Samples from 120 (9.75%) women were collected from the rural area, 663 (53.86%) in the peri-urban area, and 448 (36.40%) in an urban area at different antenatal visits. To ascertain our findings, randomly selected IgG & IgG/M positive samples (70) were further tested by the Luminex technology specific for viral N and S proteins. The neutralizing capacity of 21 samples with the highest titers against the S protein were assessed against the founder SAR CoV-2. Data was summarized in proportions.
Results During pregnancy with the Luminex technology, 12.50% (4/32) and 3.13% (1/32) of pregnant women were seropositive to the S-protein and N/S proteins respectively. At delivery, 50% (10/20) of women were seropositive for anti-coronaviruses IgG directed against the S-protein only and 15% (3/20) while had antibodies against the N&S protein. A transplacental transfer of protective S proteins from the mother to the child was found in 60 % (3/5) of the tested dyads. During the neutralization assay, 0% of these antibodies found in these pregnant women before the pre-pandemic period at COVID-19 were neutralizing to the ancestral strain.
Conclusion This study provides evidence of existing of cross-reactive anti-SARS-CoV-2 antibodies among pregnant Cameroonian women in the Pre-COVID-19 eras but are not neutralizing against the ancestral virus.
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