

EDCTP Stakeholder Meeting on Neglected Infectious Diseases

Online Consultation Feedback

1 Introduction

EDCTP set up an online consultation to gather views from stakeholders ahead and directly following the meeting. The comments and recommendations informed discussions at the respective meeting, provided input for the final meeting report and where appropriate shall contribute to EDCTP strategy in this field. The open consultative process involved a broad range of stakeholders from academia, industry, foundations, non-governmental organisations, civil society, governments and other interested parties working in the field of NIDs.

The feedback from the online consultation is presented in this document as they have been submitted.

2 Online Consultation Feedback

Prof Peter Aaby

Statens serum Institut Denmark

Current status of the field

Research in public health is very disease/deficiency specific and the corresponding interventions are also assumed to be specific. We are not using the broader learning capacities of the immune system; for example, we have shown that live vaccines reduces child mortality far more than can be explained by the prevention of the targeted specific diseases.

Future Directions

Interventions need to be tested in demographic surveillance sites which have the possibilities of documenting long-term positive and potential negative effects of interventions. We have shown in randomised trials among low-birth-weight children that BCG reduces neonatal mortality with 40%. It is there a problem that donor policies (GAVI) increasingly encourage wastage control which means that vial of BCG are only opened when 10-12 children are present to be vaccinated. This leads to higher age of vaccination and therefore less benefit of the vaccination.

The role of EDCTP

EDCTP should emphasise that interventions should have an impact on overall mortality/morbidity and not just on disease-specific prevention. For example, IPTi has been shown to reduce malaria with ~30% but there is no evidence that is reduces infant mortality.

Dr Pilar Aparicio

National Centre of Tropical Medicine - Institute of Health Carlos III Spain

Current status of the field

The most important challenge in the prevention and control of NIDs in Sub-Saharan Africa is to integrate all activities related to these fields in the health systems of the countries. To get this objective would be necessarily to strength the health workers training on these diseases and to get better tool for diagnosis, treatment and control activities. The majority of these diseases are transmitted by insect vectors, including mosquitoes, black flies, sand flies, and tsetse flies. Others are spread by contaminated water or soil infested with worms. Improving our



knowledge of how to control these factors in the specific environmental and sanitation conditions of sub-Saharan countries is truly a difficult challenge.

Future Directions

Diagnostics are needed to identify infected patients for treatment, to conduct surveillance of treatment effectiveness, and for assessing outcomes in drug and vaccine efficacy trials. Diagnostics and biomarkers should be able to identify active infection as well as stage or form of disease. For all NID organisms, development of new or better drugs is a research priority. Ideally, assays for related or multiple NIDs might be performed on the same platform so as to simplify infrastructure needs as well as to allow for testing for multiple agents in areas where co-infections commonly occur.

Prophylactic vaccines may not be viable for NTDs of low incidence or prevalence; however, with the immunopathology associated with many NTDs, these diseases might be appropriate targets for therapeutic vaccines. Additionally, for diseases that are also present in an animal reservoir, there is potential to reduce disease incidence in humans indirectly by vaccinating these animals.

As many NTDs are transmitted by invertebrate vectors, a greater understanding of the interaction between vector and parasite is also important. Such research may be useful to identify potential targets for parasite growth and survival within the vector and transmission to the human host.

Shared field resources could be used to assess preventive or therapeutic interventions, for developing vector management strategies and can serve as resources for a variety of intervention studies. Efforts to incorporate research capacity into program intervention sites should be considered as a cost-effective way to both conduct research and assess the effectiveness of public health/program interventions.

Develop data bases containing information on approaches that have proven unsuccessful as well as those that have succeeded. Databases might also include a list of specimens (parasites, vectors, DNA, etc.) available in repositories that have been well characterized and can be used for a variety of purposes (ie.: drugs and vaccines).

To get good collections of whole infectious organisms or organism components (especially for difficult to maintain/prepare organisms) could be very useful for scientific community. **The role of EDCTP**

A "critical mass" of investigators is essential for progress in any research endeavour. Strategies to attract and retain investigators for NID research need is a good contribution of EDCTP, especially given the high degrees of complexity of carrying out research in these diseases that may deter investigators from entering or staying in the field.

EDCTP can support and stress the importance of international collaborative efforts in order to assure the relevance and appropriateness of proposed research and to enhance targeted, cost-effective goals. Also EDCTP can play an important role on support translational research topics (e.g., diagnostics). EDCPT can value better communication between basic researchers and program/intervention investigators. Control programs and research programs in individual NIDs could benefit from better linkages. EDCTP can stimulate creative, ethical approaches to facilitate harmonization between intervention programs and research. Solving complex problems, such as drug development and vector management strategies will require interdisciplinary research approaches, and EDCTP could encourage these approaches.



Mrs Katy Athersuch

MSF Access Campaign Switzerland

Current status of the field

The WHO distinguishes two groups of NIDs: NIDs requiring "preventive chemotherapy and transmission control" and NIDs requiring "innovative and intensified disease management". R&D needs are higher for the latter category. For VISCERAL LEISHMANIASIS (VL), HUMAN AFRICAN TRYPANOSOMIASIS (HAT) and BURULI ULCER (BU) in Sub-Saharan Africa, case detection and treatment are the cornerstone of disease control strategies. Rapid tests are now available for screening of HAT and diagnosis of VL (although with limited sensitivity). BU diagnosis relies on PCR. Simplification of diagnostic procedures for VL & HAT & BU is still needed in order to better diagnoses relapses (VL) and to improve case-finding in remote and insecure settings (HAT, BU). Treatments are too lengthy (VL, HAT, BU) and injections are poorly adapted to the settings where diseases thrive (active HAT foci are now typically in insecure remote settings; many communities affected by VL are mobile – nomadic, displaced). Short oral treatments are needed. Of note is that a very safe and short treatment which would be effective for both stages of HAT would also change completely the disease control strategy as it could be given to all those who screened positive, regardless of confirmation of infection and determination of stage. Tailoring treatment to patients co-infected with HIV is also a major challenge (VL & BU).

Future Directions

Recent investments in pre-clinical research for NIDs by DNDi and others are now paying off. There are promising new chemical entities in the pipeline for HAT and VL. A WHO-sponsored multicentric RCT with an oral treatment for BU is about to start. The BU antibiotic pipeline needs to be strengthened with the discovery of new compounds active against m. ulcerans: there are good candidates among drugs known to have some mycobacterial activity. Diagnostic research is also improving (new rapid tests for VL and HAT with new antigens, use of simplified DNA amplification assays for HAT and BU, biomarker research for HAT and BU) and new tools will be ready for testing in the next few years.

The role of EDCTP

EDCTP can contribute by providing support to the set-up of clinical trials. As some of the NIDs are very focal, there may be a need to strengthen local capacity to set up research projects in compliance with GCP principles. DNDi has started doing this for HAT&VL. EDCTP also needs to take into consideration access issues before late stage clinical research projects are implemented. Will the diagnostics and drugs be accessible (once they have finalised clinical trials)? How to guarantee access, considering that there is little programmatic support to control these diseases? EDCTP's experience in TB/HIV/malaria may help, but the market dynamics behind tools for NIDs are different.

Prof Meba Banla

CHU Campus - Université de Lomé Togo

Current status of the field

The main challenge in the battle against onchocersiasis in west Africa is the lack of patient data (demographics, prevalence...) this limits our ability to efficiently control this disease.

Future Directions

The most appropriate step to take at this point is to make efforts to obtain a complete knowledge of the prevalence of onchocerciasis in our region. Then, we would start thinking about eradicating the disease.

The role of EDCTP

The best that EDCTP can do is to maintain good relationships with local physicians and research teams to find out the best ways to target the diseases in question.



Dr Emmanuel Baron

Epicentre MSF France

Current status of the field

Define and describe as much as possible the real burden of those NDs in terms of both morbidity and mortality

One of the key challenge is implementation of controls in conflict or unstable areas in fragile states

The general question of the ability to properly diagnose the concerned NDs with viability and accuracy

Treatments are not always developed with the underlying objective to address the various stages of a disease

Future Directions

Significant advances will rely on diagnostic means and drugs developed with appropriate target product profiles

This may imply to have this done by non profit organisations such as PDDs

Strengthening of clinical research platforms is also an area of progress

Fields dedicated to research should be selected according to burden and in synergy with other funding bodies

The role of EDCTP

Invests on research platforms

Include researchers and physicians and civil society representatives to participate to the selection of projects

Promote access to the products of the research proposal as a condition of funding Secure funding according to innovative mechanisms

Dr Blayney Benedict

Sanofi France

Current status of the field

Adequate medical infrastructure re-notably trained, regularly paid ,and correctly equipped health workers

Good coordination between all the vertical disease based initiatives, whether at national or international level, to optimise efficacy of field based medical personnel

Support from political leaders and Ministry of finance for NTD prevention and control (the above applies across all diseases)

Future Directions

HAT

Development of a recombinant antigen based diagnostic test

Development of an oral treatment

LF

Development of a macrofilaricide

Visceral leishmaniasis

Development of an oral treatment

Chagas disease

Development of an oral treatment

The role of EDCTP

Support DNDi development of HAT drugs, and trialling of new diagnostic tests.

Support VL drug research through funding of clinical trials and training

Ensure that EDCTP shares projects and plans with other large funders (notably Gates Foundation, but also TDR, DFID, Pharma Industry, DNDi, and others), so that plans dovetail rather than overlap.



Prof Moses Bockarie

Centre for Neglected Tropical Diseases United Kingdom

Current status of the field

The key challenges to scaling mass drug administration for the elimination of lymphatic filariasis, onchocerciasis and schistosomiasis are 1) completing the mapping of diseases to identify implementation units and 2) strengthening in-country technical capacity for scaling up treatment.

Future Directions

Availability of improved diagnostics will facilitate mapping and impact assessment. A new RDT for lymphatic filariasis that is more sensitive and stable was described in May 2013 and is now ready for further field testing.

The role of EDCTP

Through providing support for operational research that addresses the critical challenges to achieving the 2020 target for eliminating lymphatic filariasis and onchocerciasis. These include the implementation of mass drug administration in urban settings and investigating the impact of malaria vector control on filariasis transmission in areas where both diseases are transmitted by the same mosquito species.

Dr Marleen Boelaert

Institute Tropical Medicine Belgium

Current status of the field

1. A key issue in the control of sleeping sickness and leishmaniasis is that these are povertyrelated diseases and therefore occur in regions with very poor health systems. Any control program needs to take the socio-economic dimension of these diseases and correlated health systems deficiencies into account. E.g. in sleeping sickness the weakness of the primary care centres prevents an effective integration of screening and treatment in the regular routine care package. But the answer to this should not necessarily be to take shortcuts and to bypass those primary care facilities. With the current technology, new rapid tests, better and oral drugs, it is possible to put together packages of care that is appropriate to these contexts. The R&D for new diagnostics and drugs in these domains should take this socio-economic context into account, because better safer oral drugs and diagnostics are definitely needed. 2. Several of the NIDs, and definitely tryapnosomiasis, Chagas disease and leishmaniasis are vectorborne diseases. Innovation in vector control tools is highly needed, and should be encouraged at the prototype development level as well as at the level of effectiveness evaluation through large scale cluster randomized trials. Because of the emergence of resistance to insecticides worldwide, this field should not be abandoned, and a stimulus for R&D in this domain is needed.

3. in several of these diseases, the WHO is promoting elimination. But as the tryponomatids cause a number of latent infection (also in sleeping sickness!), for all of them the importance of these latent carriers can be questioned at individual (prognosis?) as well as public health (transmission?) level. Working out better markers of infection and tools to monitor exposure (as antibody tests to vector saliva) is also a must to prepare for large -scale intervention trials of vaccines and vector control tools

Future Directions

PROMISING TOOLS

IN HUMAN AFRICAN TRYPANOSOMIASIS

fexinidazole as on oral drug for sleeping sickness (pivotal trial ongoing) but more evidence needed

Rapid diagnostic tests for sleeping sickness (two protypes were developed, but need evaluation of clinical benefit and

More remote: vaccines

IN VISCERAL LEISHMANIASIS

Combination regimens for VL and single -dose Ambisome have shown efficacy in Phase-3 trials but need more evidence in large-scale pragmatic trials



Systemic insecticide treatment for cattle (fipronil/ivermectine) is being evaluated now at prototype level and could become a valuable intervention if safety is proven **The role of EDCTP**

To encourage innovation by funding prototype development, clinical testing and effectiveness evaluation of products to prevent and control NID

More specifically this should include:

- 1. Drugs and diagnostics
- 2. Vector control tools
- 3. Vaccines.

Dr Michel Boussinesq

Institut de Recherche pour le Développement France

Current status of the field

- Onchocerciasis and lymphatic filariasis (LF)
- lack of macrofilaricidal drugs usable in mass treatment
- possible emergence of ivermectin resistance
- risk of post-ivermectin serious adverse events (SAEs) in persons highly coinfected with Loa
- unreliable mapping of LF in Africa
- attrition of community distributors
- difficulties to launch control programmes in post-conflict countries
- integration and coimplementation of control activities for co-endemic NIDs

Future Directions

- development of macrofilaricidal drugs applicable in the field, preferably with no microfilaricidal effect on Loa loa

- development of markers to detect ivermectin resistance in O. volvulus
- development of tests to identify individuals at risk for post ivermectin SAEs

The role of EDCTP

- development of macrofilaricidal drugs applicable in the field, preferably with no microfilaricidal effect on Loa loa
- development of markers to detect ivermectin resistance in O. volvulus
- development of tests to identify individuals at risk for post ivermectin SAEs

Mr Paul Chinnock

United Kingdom

Current status of the field

Identifying priority NIDs for research, and prioritising the types of research needed in each case. This will be hard, as the incidence/prevalence of most of the NIDs is not reliably known. Epidemiological studies to improve knowledge on this matter will be necessary.

Co-infection (one or more NIDs plus one or more of the 'big three' infections) is a key issue requiring attention,

Future Directions

I have no up-to-date information on potential new products.

The role of EDCTP

Recent years have seen a rise in interest in NIDs and a number of organisations/institutions are now active in this area. ECTP must forge links with others in this area, in order to proceed in its usual spirit of partnership. EDCTP must identify the gaps which exist and support research in key areas not yet attracting attention. The trial sites already developed by EDCTP offer opportunities for NID studies.



Mrs Song Ding

EuroVacc Foundation The Netherlands

Current status of the field

The specific interest of our group is in the co-infection between helminth and HIV, TB and malaria. To date, there is still very limited understanding of the impact by worm infections on HIV-, TB- and malaria-specific immune responses and their clinical outcome.

Future Directions

Obtaining clear understanding of the immunological interplay between helminths infection and PRD, could lead to clear international guidelines in terms of whether de-worming programmes are beneficial for the health of communities with high burden of worms and PRD, as well as better designs of vaccines.

The role of EDCTP

EDCTP will be instrumental in supporting this very important research and will put European-African research in a leading role in the international research community

Prof Jean-Claude Dujardin

Institute of Tropical Medicine Belgium

Current status of the field

Lack of knowledge on natural history of several NIDs. For instance in Kala-Azar (which I know better), (i) what is the role of asymptomatics in transmission (vs PKDL), (ii) what is the biology of the vector, (iii) is there an animal reservoir....the answer to these questions could have an impact on control strategies. Chemotherapy is also a major issue: lack of drugs, risk of resistance. Absence of coordinated surveillance.

Future Directions

1. Surveillance of the infection/the disease (the tools are available)

2. Monitoring of treatment outcome and drug resistance (the tools are available)

3. Combination therapy to protect existing drugs (but coupled with surveillance, as resistance can emerge quickly also against combos)

4. Developing new drugs or recycling other ones: in the frame of our Kaladrug project (FP7) in India/Nepal, we identified two drugs commonly used for other medical applications with a potential impact on Kala-Azar (Imipramine and Quercetine)

5. Improving vector control strategies

The role of EDCTP

- Not restrict activities to clinical trials (drugs), but also consider surveillance and vector control

- making links with other regions: I understand that the current focus is on Africa, but there is no need to reinvent the wheel...for instance the experience acquired in Indian subcontinent could be very useful to avoid making the same mistakes...thus involving partners from other regions

- what about extending EDCTP in the future to other regions where NIDs are endemic and where the same problems are encountered

Prof Alison Elliott

MRC/UVRI Uganda Research Unit on AIDS; London School of Hygiene & Tropical Medicine Uganda

Current status of the field

Referring to worm infections, especially schistosomiasis

1. Lack of prioritisation of worm control and sanitation by affected communities due to acceptance of existing practices, poverty, lack of health education and awareness, variable levels of training and motivation among providers especially at village level

2. For some settings, challenges remain regarding the construction of suitable latrines given high water table, sandy soil etc.



3. Logistical and financial difficulties in maintaining provision of treatment in the long term, especially among hard-to-reach, heavily affected communities

4. Neglect of provision of mass treatment to certain key groups due to persistence of outdated policies – e.g. continuing exclusion of pregnant and breast-feeding women and preschool children. Focus on school children fails to eliminate reservoir in other age groups 5. Lack of effective vaccines – and significant challenges as to how feasible it may be to develop them, given the characteristics of natural immunity (or lack of it)

6. Potential for the development of resistance to the small number of available drugs

7. Lack of paediatric formulation for praziquantel

8. Lack of conclusive data on benefits of mass anthelminthic treatment for many outcomes. Much advocacy is based on studies reporting observational associations between worms and anaemia, growth, cognitive performance, but there are few studies on the impact of mass treatment on these outcomes. Almost nothing is known about the potential beneficial or detrimental effects of mass anthelminthic treatment on response to immunisation, susceptibility to unrelated infections, allergy-related and inflammatory disease outcomes 9. Lack of both implementation and research capacity in endemic countries

Future Directions

1. Key opportunities in endemic countries for understanding the human immune system in its "normal" state – i.e. in symbiosis with chronic infections. Opportunities for this are likely to diminish over the coming ten-year period. Incorporation of relevant basic science studies within programmes designed to control infectious diseases offers potential benefits for both endemic countries and countries (such as European countries) where these infections are increasingly uncommon

2. New, rapid diagnostic tests, e.g. urine CCA for schistosomiasis

The role of EDCTP

1. Support research on the development of suitable latrines for difficult environments

2. Support operational studies on the implementation of interventions known to be effective against worms, including approaches to the use of new diagnostic tests

3. Support research – perhaps nested within trials of different operational approaches to worm control – to evaluate, rigorously, the benefits of the interventions; thus allowing both improved advocacy, and realistic prediction of the likely outcomes of intervention

4. Clinical trials of intervention in groups for whom doubt remains regarding risk versus benefit (e.g. pregnant women). Again, allowing greater confidence in recommendations, and more effective advocacy

5. Support basic research designed to understand human immunity to worm infections, and mechanisms by which worm infections may modulate immunity to themselves and to unrelated antigens

6. Support career pathways for scientists from endemic countries for research in these fields:

a. consistent provision of opportunities at Masters, PhD and post-doc levels are required to support development of research leaders

b. technical training opportunities required for laboratory and field staff

c. management and administration training for programme managers

d. opportunities to apply for research and equipment grants for current and emerging research leaders in endemic countries

Dr Huub Gelderblom

International Trachoma Initiative, Emory University United States

Current status of the field

Trachoma: Key issues:

- Tools needed for impact evaluation, to guide program decisions, tools needed for surveillance
- Integration and coordination of trachoma program with other NTD programs
- Country capacity to absorb programs
- Countries sharing experiences, hit the ground running



Challenges:

- Integrated programs seem simple but bring in increased number of stakeholder, leading to complexity

- Country capacity to absorb may be limited in numbers and overburdened
- Coordination between external partners, sometimes pulling in different directions

Future Directions

Trachoma:

- On track to eliminate blinding trachoma by 2020, but significant scale up needed
- Integration of aspects trachoma program with other programs if appropriate
- Coordination and integration may be example for other programs

- Capacity built by trachoma program can be directed towards other public health programs after end of trachoma campaigns

The role of EDCTP

- Help build clinical research capacity
- Stimulate North-South and South-South collaboration and sharing
- Coordinate exchange and sharing between HIV/AIDS, TB, malaria and NTD silos
- Coordinate and stimulate laboratory (research) capacity
- Focus on diagnostics (evaluation research, regulation, lower prices).

Dr Thomas Kariuki

Institute of Primate Research, Nairobi

Kenya

Current status of the field

For all 17 diseases (as listed by WHO): we broadly define them in tow categories; those for which we have some good tools, mostly drugs, for prevention and control and can therefore move towards mass chemotherapy; and those which we lack tools and need to invest in discovery R&D. For schistotomiasis we have only one drug, so we need to support development of new drugs to guard against emerging resistance; poor diagnostics (microscopy) is a hindrance to point of care diagnosis, proof of cure, disease surveillance etc-we need better diagnostics. Another key challenge is co-infections which complicates treatment, vaccination and diagnosis.

Future Directions

We can make significant advances by:

1. a strong push on implementation of existing strategies backed by consistent implementation research.

2. focused investment in development of new tools using global collaborative mechanisms with a strong input of African scientists.

3. Strong investment in capacity building to support PhD training programs in infectious diseases in Africa , post-doctoral programs and centers of excellence with state-of the-art facilities.

The role of EDCTP

In addition to what is outlined above, EDCTP should identify Networks of NTD scientists that can be avenues for achieving specific outcomes including research and mentor ship programs. Support African leaders who already have a good track record of NTD research in Africa.

Dr Mohammed Lamorde

Makerere University

Uganda

Current status of the field

Neglected infectious diseases contribute to a great health burden in sub-Saharan Africa. However, there are limited data on the pharmacology of these drugs as well as their interactions with coadministered drugs for other endemic diseases including HIV/AIDS, tuberculosis and malaria.

Future Directions



Optimization of clinical pharmacokinetic studies with in vitro in vivo extrapolation is a potentially promising approach to bridge the information gap for a wide range of drugs using relatively smaller sample sizes than are required for clinical pharmacokinetic studies.

The role of EDCTP

Providing specific calls to address funding requirements for pharmacology studies on drugs for NIDs. Ensuring capacity building initiatives to develop expertise in this field.

Prof Odile Leroy

European Vaccine Initiative Germany

Current status of the field

For Leihmaniosis, shistosomiasis, and helminths infections : key issues:

Mapping

Burden of diseases

Public health importance

Analysis/modeling of vaccination impact in global context for disease control

Future Directions

For vaccines:

Feasibility of vaccine: need of investing in

1. Antigen discovery based on system biology approach

2.Production development: development of cheap process for stable vaccines, new route of administration, new system delivery/adjuvants

3.Clinical development : strengthen the clinical trial capacity in endemic region (ideally in already existing centres working on other PRDs)

The role of EDCTP

Conduct research on pathogen biology and pathogen-host interactions

Develop standardised assays and reagents...

Identify and validate correlates of protection...

Develop systematic criteria for prioritising and down-selecting

Standardise clinical trial end points to enable comparison among trials

Develop robust, accessible process development capacity

Mr Yves Leurguin

Takeda Switzerland Current status of the field The burden of disease due Dengue and Norovirus are not well defined. Surveillance systems for these diseases are not established. **Future Directions** Vaccines against Dengue and Norovirus are in development. The role of EDCTP

Resource support for the establishment of the burden of disease and the evaluation of these vaccines.

Prof David Mabey

LSHTM

United Kingdom

Current status of the field

Elimination targets are being approached for several NIDs in some parts of Africa (eq trachoma, onchocerciasis, lymphatic filariasis and guinea worm). Except in the case of guinea worm, we lack diagnostic tools that are sufficiently sensitive and specific to enable us to decide when interventions such as mass drug administration can be discontinued, and to set up surveillance systems to ensure they are not reintroduced. **Future Directions**



Thanks to generous drug donation programmes, we are making real progress in the struggle to eliminate trachoma, onchocerciasis and LF in Africa. We need better diagnostics, preferably on an integrated platform that can diagnose several NIDs, to guide elimination programmes and to monitor for drug resistance

The role of EDCTP

EDCTP can support the development of new diagnostics, and implementation research to evaluate their utility in elimination programmes. This has to be a multi-country operation, as NIDs do not respect international borders, and EDCTP is well placed to deliver this kind of research programme

Dr Enock Matovu

Makerere University

Uganda

Current status of the field

Human African Trypanosomiasis has hitherto relied on old, lengthy, complicated treatments and diagnostic techniques. Of late new and easier to use interventions have been formulated **Future Directions**

New treatment combination that reduces hospitalisation is now available in rural health centres, safe oral treatments are in the pipeline. Also novel ultrasensitive diagnostics to support treatment and follow-up are under evaluation

The role of EDCTP

Research into new drugs and or combinations themselves (clinical trials) and feasibility of application in rural resource poor settings should be given priority

Dr Concepta Merry

Trinity College Dublin Ireland

Current status of the field

There are no data on the interactions between drugs used to treat NIDs and other common infections eg HIV/ TB/ malaria as summarised in the below paper we published in AIDS. Drug-drug interactions between antiretrovirals and drugs used in the management of neglected tropical diseases: important considerations in the WHO 2020 Roadmap and London Declaration on Neglected Tropical Diseases. Seden K, Khoo S, Back D, Prevatt N, Lamorde M, Byakika-Kibwika P, Mayito J, Ryan M, Merry C. AIDS. 2013 Mar 13;27(5):675-86. doi: 10.1097/QAD.0b013e32835ca9b4.

The role of EDCTP

Consideration of funding to study the pharmacokinetics of drugs used to prevent and treat NIDs with drugs used to treat HIV/TB/malaria.

Alhaji Musa Muhibi

Lautech Teaching Hospital Osogbo

Nigeria

Current status of the field

Modern diagnostic tools and skills are the factors affecting progress in the prevention of viral hemorrhagic diseases(Lassa and dengue viruses)

Future Directions

Appropriate diagnostic tools.

The role of EDCTP

Training for scientists and health administrators on appropriate skills and policies for laboratory diagnosis.



Dr Godwin Nchinda

CIRCB - Cameroon Cameroon

Current status of the field

There is no systematic differential diagnosis between Dengue and Malaria even though the two diseases overlap. There are no coherent measures for eliminating lymphatic filariasis. No information on the impact of schistomiasis, dengue and filaria on HIV-1 disease progression.

Future Directions

With the right funding Dengue incidence and prevalence could be mapped in sub Saharan Africa. The introduction of a Dengue vaccine in Africa could dramatically change the story. There is need for molecular biology methods at point of care to diagnose filaria, schistosomiasis and dengue.

The role of EDCTP

Funding for point of care strategies to diagnosis these diseases. Fund for the development of new vaccines and also integrative approach in managing these diseases

Prof Joseph Ndungu

FIND Diagnostics Switzerland

Current status of the field

Sleeping sickness: (a) Implementation of appropriate tools for surveillance, (b) inadequate capacity at the level of implementation, (c) Sustainable funding, (d) commitment by governments of endemic countries

Future Directions

1) NECT, a new drug combination implemented recently, has made treatment a lot easier, safer and cheaper. The challenge now is to identify cases and put them on treatment. 2) A Rapid Diagnostic Test has been launched, which will make it a much easier to screen people, actively and passively.

3) Two new methods for confirming disease have also been launched (one an LED fluorescence microscope and the other is LAMP, a simple molecular method for detecting parasite DNA).

The role of EDCTP

Since surveillance and control of sleeping sickness requires that more than one test is used to make a diagnosis, the best and cost-effective ways to use the new tools in diagnostic algorithms in regions with different levels of endemicity have not been determined. EDCTP could sponsor multi-centre and multi-country implementation trials under different scenarios.

Dr Albert Picado

Barcelona Centre for International Health Research (CRESIB) Spain Current status of the field

Visibility, basic science knowledge (e.g. vectors) and political commitment

Future Directions

Integrated control strategies

The role of EDCTP

clinical trials to develop new tools (e.g. drugs, diagnostic tests) and training of local scientists. Expand the EDCTP activities to other areas (e.g. South America, South East Asia, Pacific)

Dr Raymond Pierce

Institut Pasteur de Lille

France

Current status of the field

In the case of schistosomiasis, in the absence of an effective vaccine, the current approach to treatment and control of the disease relies on the use of the only available drug, praziguantel (pzq). Although pzq is safe and effective its massive use, particularly in sub-Saharan Africa, for example in the context of the Schistosomiasis Control Initiative, raises justified concerns about



the future development of resistance to pzq in the parasite population. For this reason the development of new drugs is a priority. However, the new drugs will have to match pzq in terms of safety and efficacy, and be cheap to produce. This means that a variety of strategies and leads have to be followed in order to have a chance of developing a new drug that can be used in the field.

Future Directions

Three vaccine candidates are currently in clinical trials, but no information is available about efficacy. A variety of approaches to drug development are being pursued, including the exploitation of natural products, the use of existing drugs for other pathologies such as anti-malarials, and strategies to develop novel chemotherapeutic agents, such as ours. For instance, during the SEtTReND FP7 project, we showed that selective inhibitors of Schistosoma mansoni histone deacetylase 8 could be developed, and that these were effective against the parasite in vitro and in vivo. However, further bioguided optimisation, pharmacokinetic and toxicological studies are necessary to convert the current leads into candidate drugs that could be tested in clinical trials. Testing in the field remains a long way off.

The role of EDCTP

The funding of clinical trials in the field is a valuable contribution. However, the main problem that we are rapidly approaching is a funding gap between the basic research (characterization of lead compounds and basic ADMET) and the steps that are necessary before clinical trials can be envisaged. These include formulation development and regulatory toxicity studies. Although funding mechanisms exist at a national level, this may prove a barrier in the case of drugs for neglected infectious diseases

Dr Gabrielle Pohlig

Swiss TPH Switzerland

Current status of the field

HAT: Funding needed for evaluation and use of new drugs in T.b. rhodesiense and for drug continuation in children; also continuous funding is necessary to complete the clinical development of fexinidazole and the oxaboroles.

Worms: Complete lack of adequate funding for clinical trials hampers progress

Future Directions

HAT: Two new drugs may be ready for registration: Phase 3-b/Phase IV testing under real field conditions, assessment of effectiveness will be key for success and for evaluating their impact on disease elimination/eradication.

Worms: Jointly, the worm infections will have a major impact on disease burden in the future. A handful of molecules are in the pipeline and need a push to their development.

The role of EDCTP

EDCTP funding will provide a key push towards the new tools. It may fill a widening gap – donor fatigue is a serious difficulty in this complex and slowly advancing field of work.

Prof John Reeder

The Special Programme for Research and Training in Tropical Diseases (TDR) Switzerland

Current status of the field

There are major limitations in the capacity of many disease endemic countries to perform the research necessary for the effective implementation of interventions. This stretches from basic operational questions needed by disease control programmes to implement their work efficiently, through to use of locally generated evidence to form health policy. It also encompasses lack of capacity in regulatory mechanisms to introduce new drugs and vaccines. This limitation spans a whole spectrum of NIDs.

Future Directions

Undoubtedly new drugs and vaccines are needed, but as has been shown in the great gains made in malaria, aggressive effective evidence-based implementation has been the key to gains in many NIDs. This has been greatly enhanced by greater accessibility to treatment, promoted by donation and pricing initiatives.



The role of EDCTP

To think beyond the production and trial of new therapies and also consider their uptake and effective deployment in disease endemic countries.

Dr Morven Roberts

Medical Research Council United Kingdom

Current status of the field

Requirement for development of cost effective interventions (prevention and treatment). Evaluation of both products and delivery systems, Persuasive evidence to influence policy and practice.

Future Directions

Need to engage with key partners to understand products and delivery systems in various pipe lines. May also require development of more rapid and sensitive diagnostics.

The role of EDCTP

Capacity strengthening, clear mechanism for pull through of pipeline products, partnerships, support for definitive, large scale generalisable trials that will provide robust data.

Dr Syamal Roy

Indian Institute of Chemical Biology

India

Current status of the field

Leishmaniasis is not only a problem in Africa but also Indian sub-continent. Drug resistance is a big problem. There is a genuine need for newer, affordable, orally active drug against leishmaniasis.

Future Directions

New use of old drugs. Tricyclic antidepressant, imipramine is highly active against antimony sensitive and antimony resistant Leishmania donovani in the animal models. The drug is orally active and thus there is a great prospect to use this drug for the treatment of kala azar.

The role of EDCTP

By providing necessary funds and training.

Dr Jutta Reinhard-Rupp

Merck Serono Switzerland

Current status of the field

Referring to schistosomiasis, we do not have a pipeline of new drugs and we do not have many success examples of elimination. Not only the drug pipeline is important, but also other factors (vector control, sanitation, improved diagnostic tools) need to be developed or improved in parallel. In addition, we do not have sufficient data about the current treatment (with praziquantel) in younger children or with respect to drug-drug interactions. Baseline data missing, no clear aligned strategy for elimination, fragmented donor activities, no integration with other programs

Future Directions

Improved diagnostics, new products (as backup to praziquantel), integrated programs (health, education, water, nutrition) per country.

The role of EDCTP

We have a huge gap between early discovery and clinical development in schistosomiasis. No funding mechanism exists today to move preclinical candidates into clinical development. Also, training and education of scientists and MDs in endemic countries to work on helminth-related diseases is missing. Advance product developments from preclinical into clinical phase, including diagnostics/



Dr Moussa Sacko

National Institute for Research in Public Health Mali

Current status of the field

Schistosomiasis and STH: Mapping is not completed in all endemic countries in Sub-Saharan Africa; Low chemotherapy coverage rate; Poor integration of control activities into health system; Poor Capacity in many countries regarding program management; Insufficient Monitoring and evaluation activities; Partnership not well coordinated; Drug delivery system Operational research/implementation research; Sustainability of control activities questionable **Future Directions**

Intensify PCT scaling up; Strengthening capacity building; Improve drug delivery system; Development of new approach for Integration control activities into health system; Development of new diagnostic technique more sensitive for surveillance and elimination Facilitate Implementation research to improve control strategy.

The role of EDCTP

Strengthening capacity building: training of African scientists (MSc PhD level); Support development of new diagnostic techniques ; Support operational/implementation research Support monitoring and surveillance; Setting strong of partnership and sustainability.

Dr Gustavi Simo

University of Dschang Cameroon

Current status of the field

The key issues and challenges in the control of human african trypanosomiasis is that the case detection and treatment will not lead to the elimination of this disease because the animal reservoir and the infected flies remaining in the disease focus after medical surveys could maintain the disease and the resurgence can occurs at any time. Currently, the disease prevalence is very low in most foci and demotivations are observed: technicians demotivation (few patients detected after examining thousands of people), population demotivation (several medical surveys with sometime no patient), donor demotivation (thousand dollars spent with very few patients). This will lead to the reduction of the awareness of the disease that will lead to the resurgence in most foci as was observed in the last century.

Future Directions

Use the concept of one health to develop control measures targeting animal trypanosomiasis with the ultimate goal of achieving the elimination of human and animal trypanosomiasis as well as sustainable economic development in rural areas

The role of EDCTP

EDCTP can contribute to this research field by promoting ideas that will use available tools to develop approaches enabling to control human and animal trypanosomiasis in order to achieve the elimination goal of both diseases

Prof Prof Peter Sobsoslay

University of Tuebingen

Germany

Current status of the field Elimination of Filariasis/Onchocerciasis

Control of Intestinal Helminth Infections

Control of Schistosomiasis

Development and Application of new drug (combinations)

Prevention and reduction of helminth infection- associated morbidity/pathology

Anti-Helminth Vaccine development

Future Directions

Comprehensive drug-based control of helminth infection associated morbidity Long-term follow up of clinical manifestations in helminthiases patients post Intervention



Helminth-specific rapid-test development and application to improved field based surveillance Drug-facilitated immune Intervention

The role of EDCTP

Support comprehensive helminth control activities, Clinical long-term follow-up of patients New diagnostic Tools

Combined Treatment approaches

Development of Immunotherapy approached

Prof Mamadou Souncalo Traore

National Institute for Research in Public Health Mali

Current status of the field

Country leadership; Coordination of all actors; Strengthening the capacity of health services for real integration. For all diseases especially the those of MDA; Schisto, STH, Trachoma, LF and Oncho.

Future Directions

Any change will come after strong country leadership. RD of new drugs for schisto and Oncho (growing fear of resistance for ivermectine and praziguantel) New drug? moxidectiin?

The role of EDCTP

Institutional Strengthening and networking.

Dr Nathalie Strub Wourgaft

DNDi

Switzerland

Current status of the field

• In the field of Visceral Leishmaniaisis, more safe and effective treatments need to be developed for (East) Africa - additionally, there may be a need to develop treatment for asymptomatic carriers if they are proven to represent a meaningful reservoir for the disease -Post Kala Azar Dermal Leishmaniasis is a significant consequence of VL in Sudan with currently no safe, effective affordable treatment - a treatment will be needed for patients who don't spontaneously cure and develop a severe form - they most probably also contribute to the transmission of the disease and therefore may all need to receive adequate treatment which is vet missing - HIV-VL co-infection bears a significant morbidity / mortality weight and requires additional research too. For Sleeping sickness (African trypanosomiasis), research is ongoing and a promising new treatment should enter in a pivotal trial in 2014. Onchocerciasis with Loa Loa case management is challenging in some areas and will require new approaches - a macrofilaricidal drug would be of great advantage and could also be used to complement the current MDA approach. Finally there are other NIDs that are still requiring new tools and where EDCTP funding could be of great support - Another area is support to large

pharmacovigilance/effectiveness studies: once tools have been developed it is crucial to verify their suitability in real life field conditions as well as to further establish their safety in the field or contribute to risk management plan studies and later facilitate the promotion of passive pharmacovigilance by the doctors. In some instances, this is the only way a new tool can be reliably added to a program's guidelines. EC and NRA's approvals to run clinical trials are sometimes very long, often unpredictable, sometimes duplicated ... Lastly we know that laboratory ranges used in most clinical trials usually are based on international norms that are not fit to the African population: there is a real need to advance research in that area

Future Directions

As mentioned above, a potential new treatment is currently in phase 1 and should enter phase 2/3 for stage 2 (and 1) sleeping sickness in 2014. There are some products currently in the DNDi pipeline for VL that could help answering some of the highlighted needs and the same for a macrofilaricidal drug -

The role of EDCTP

1. funding clinical research (including first in man) in all these Aeras - up until field pharmacovigilance studies.-



2. facilitating CTAs ... by funding/supporting joint reviews mechanisms and working on a framework for these

3. possibly initiating a consortium project on laboratory (and ECG) normal ranges project for Africa

Prof David Taylor

University of Edinburgh United Kingdom

Current status of the field

Control of river blindness (onchocerciasis) in Africa. Over optimistic expectation of feasibility of using ivermectin alone to eliminate infection. This cannot be achieved in areas of high endemicity but notion is promulgated by some charities. Ivermectin is not given to children under 5 and thus these remain at risk of developing disease and contribute to continued transmission.

It should be noted that the WHO Roadmap to elimination of NTDs appears to be predicated on use of a single drug for all identified diseases. Again, this raises expectation that cannot be realised.

Future Directions

Elimination of onchocercias as a public health problem in sub-Saharan Africa could be achievable through wider use of doxycyline (community-directed treament programmes) and introduction of a vaccine.

EU funded research has identified 4 vaccine candidates that are ready to take to phase I firstin-human safety trials. If started tomorrow, and assuming there are no safety issues, Phase II efficacy trials could begin by 2020. Such vaccines would target pre-school children but may also have therapeutic application to reduce microfilarial loads that would reduce pathology in adults and help block transmission.

The role of EDCTP

Funding of production of vaccine to GMP and support for regulatory processes. Assuming safety concerns are not apparent, the cost of phase II efficacy trials needs to be covered. In parallel with such work it will be necessary to support investigation of immune responses of neonates and pre-school children. Entomological studies and assessment of prevalence in study cohorts will be required throughout any trial.

Dr Wendy Van de Sande

ErasmusMC The Netherlands

Current status of the field

- currently it is not known what the prevalence of mycetoma is in the endemic area. Better prevalence data will result in establishing help centers were needed

- the identification of the causative agent of mycetoma is still troublesome. Long culture times, many misidentification result in delay in treatment. Better diagnostic tools need to be developed which can be used in the endemic area

- currently fungal mycetoma is usually treated with high doses of antifungal agents and surgery with only limited success rates. Amputation is still necessary in many patients. Development of new drugs, or access to newer drugs available in the west could help the patients a lot

Future Directions

- new diagnostic tools are currently developed but their merit in the endemic area should be determined in clinical trials.

- in vitro, we know that voriconazole, ravuconazole and posaconazole are more potent in inhibiting the growth of the most common causative agents. The therapeutic efficacy of these drugs is only known from case reports in the west. Large clinical trials are needed to determine if these newer drugs will have a higher successrate in mycetoma treatment than the currently used ketoconazole. Furthermore, due to the better safety profiles of these azoles compared to



ketoconazole, it is expected that discontinuation of the therapy due to toxic side effects will be much lower.

The role of EDCTP

- for these large clinical trials funding is needed. So-far mycetoma has been neglected among the neglected diseases although current prevalence estimations are comparable to other neglected infections and the burden for the patient is much higher than in other infections. By opening funding programms also for mycetoma, a big leap forward can be made for the mycetoma patient.

Dr Johan Van Griensven

ITM

Belgium

Current status of the field

With regards to visceral leishmaniasis: coinfection with HIV is common in certain parts, with clear clinical and public health impact, but this is under-researched in East Africa. Diagnostic tools are insufficient, treatment options limited.

Future Directions

novel RDTs, molecular POC tests; combination therapy; preventive strategies

The role of EDCTP

Building capacity in laboratory, clinical and operational research

Dr Remko van Leeuwen

AIGHD

The Netherlands

Current status of the field

We believe that there is a lack of funding to overcome technical and organisational hurdles toward effective vaccine development and implementation for NTDs. While this picture has certainly been improved over the last decades for several other poverty related diseases, such as for tuberculosis and malaria, research efforts into effective vaccines for the group of neglected infectious diseases – which includes hookworm – are insufficient.

Future Directions

The vaccine candidate in HOOKVAC is the currently the only vaccine being developed to confer preventive immunity against human hookworm disease. HOOKVAC may play a crucial role in advancing the development of the hookworm vaccine toward large-scale efficacy studies in African endemic areas. HOOKVAC can be a possible step-up towards a future multivalent anthelminthic vaccine for hookworm infection and schistosomiasis, which would represent an important new tool for combating disease and poverty, as hookworm infection and schistosomiasis are two of the world's most important human parasitic infections.

The role of EDCTP

EDCTP can provide access to validated research infrastructure (build through research capacities funded by the EDCTP) and expertise for testing in target countries in an ethically sound way.

Also EDCTP should contribute financially towards projects to perform clinical trials with the vaccine, as well as scale up and optimize production of both antigens to allow affordable production processes transferable to manufacturers in endemic regions.

Dr Jorge Varanda

University Coimbra; Instituto de Higiene e Medicina Tropical (CDMT) Portugal

Current status of the field

Human African Trypanosomiasis

- Difficult Diagnosis to determining infection to use in the field (bush/hinterland areas)
- Difficult Diagnosis particularly to determine the infection stage 1 or 2
- Old drug for stage 1 and toxic drugs with little hope for arsenic resistant patients
- Long follow-up (up to 18months)
- Little or no work on community level (patients follow-up; and more importantly vector



knowledge/control)

- Little or No attention to local views on the treatment (before, during and follow-up); as well as perceptions on the vector and disease itself.

- Technical staff leaving the field for new job opportunities due to the decrease on the number of patients.

- Little or No information on the animal reservoirs

Future Directions

Human African Trypanosomiasis

Help developing New Diagnosis kits particularly easy tools for determining stage 1 or stage 2
Help developing new Medical Drugs (easy to use in rural African settings) for both stages (less toxic and easier to apply)

- New measures so that for follow-up (currently up to 18months) is considerably shorten or that is carried out thoroughly by patients.

- New focus on procedures for community engagement (patients follow-up; but more importantly vector knowledge and control)

- Design of studies (to include more social sciences - views of the peoples treatment; before, during and after; as well as perceptions on the vector and disease)

- Push forward for new design of research studies that include more social sciences - views of the peoples treatment; before, during and after; as well as perceptions on the vector and disease , i.e. identify cultural, social, structural obstacles)

- Study the burden on the patients' families (called the end of the road communities, poorest of the poor) of treatment, hospitalisation and follow-up.

- Consider new ways of maintaining highly specialized teams - lab technicians and nurses among others- that work on this ailment.

- Put forward more epidemiological knowledge of historical foci

- Fund Geo information systems studies, that is the informatisation of national health servicestraining and maintenance of these highly specialised teams.

- Fund studies on the impact of the climate change and globalisation a; structural changes related to agricultural shifts occurring in Africa as well as population movements.

- Rethink a horizontalization of these campaigns and its yearly actions, in order to avoid new surges on the number of patients.

- insert it in Verbal Autopsy diseases to be tracked down.

- More research on animal reservoirs and the burden of disease in terms of cattle as well as local livelihoods, and the possible increase of numbers of Europeans affected due to tourism to pristine - tsetse infected- areas.

The role of EDCTP

Human African Trypanosomiasis

Work with other institutions: African Union, Drugs for Neglected Diseases Initiative (DNDi), Foundation for Innovative Diagnosis (FIND); PATTEC, as well as local governments.
Critically (Re)evaluate the information brought forward Northern studies publish in big biomedical journals that show little or no details/awareness of the difficulties putting together/applying vertical campaigns like this one.

Dr Monique Wasunna

Kenya Medical Research Institute

Kenya

Current status of the field

Leishmaniasis: Lack of resources, remoteness of the areas where the disease occurs, no adequate data on the epidemiology of the disease in East Africa. No efficacious and safe oral treatments. Diagnosis still invasive and requires skilled manpower.

Future Directions

Mapping of Leishmaniasis in the region

Improved diagnosis preferably rapid antigen kits

improved treatment preferably oral- DNDi working on this but has limited funding



Capacity strengthening for clinical trials integrated control measures for NTDs

The role of EDCTP

EDCTP major role - Funding and coordinating efforts in NTD research .Identify groups working on NTDs and strengthen their capacities and improve funding mechanisms. LEAP in Eastern Africa is such a group as it involves 4 East African countries working on Leish and has capacity to work on any NTDs endemic in the region. Involve endemic areas more when planning research or interventions. Encourage south- south- north collaborations. Equal partnerships to be fostered.

Dr Dawit Wolday

Medical Biotech Laboratory Ethiopia

Current status of the field

Sub-Saharan Africa bears disproportionate share of the world's infectious disease burden and NIDs contribute to a major public-health problems in the region. They contribute to significant mortality & morbidity. Major challenges and gaps include:

- lack of appropriate diagnostic tools
- lack of and/or very few drugs available to prevent or treat NIDs
- lack of effective vaccines to prevent NIDs
- limitation with access to available drugs for some of the NIDs
- problems related with implementation and scale-up of already available intervention
- programs due to problems related with integration of other programs.

Future Directions

There are several opportunities for making significant advances in the future, because of the involvement of several partners including PDPs, bilateral and international organizations, including Bill Gates Foundation, EDCTP, etc...

Several point-of-care diagnostic tools are being tested in the field currently that can offer a cost-effective way of diagnosing NIDs, such as the one being developed by groups at FIND for TAH. Moreover, promising vaccines for Hook worm, schistosomiasis and leishmaniasis are under trial. In addition, MSF is working in Africa in collaboration with PDPs in testing newer drug regimens or combination of existing one for leishmania with or without HIV-co-infection. The impact of co-infection with STHs on potentially efficacious vaccines for other diseases (especially HIV, TB and malaria) need to be investigated thoroughly., Moreover, there is a need to undertake systems research to understand how best to integrate programs for NIDs with that of HIV/TB/Malaria.

The role of EDCTP

The fact that EDCTP has made significant investment during its first phase by establishing several capacities for research on the major infectious diseases (HIV/TB/Malaria) in Africa puts it in unique position to contribute to the field by providing further funding in the prospective areas mentioned above and by partnering with PDPs and others interested initiatives. One such mechanism is development of joint program activities.

Dr Alex Yaw Debrah

Kwame Nkrumah University of Science and Technology Ghana

Current status of the field

Lymphatic filariasis which (leads to elephantiasis of the legs and genitals) and onchocerciasis (which causes blindness) affect about 140 million people and about 1 billion people are at risk of being infected. The current drug of choice kill only the baby worms (microfilariae) but has no effect on the adult worms so the inhabitants in endemic areas have to take it several years in the form of mass drug dministration (MDA). The long treatment duration brings about fatigue and put the success of the program in jeopardy.



Future Directions

The future direction is that already registered drug candidates that have anti-wolabachia and macrofilaricidal effects and therefore has used to treat onchocerciasis and lymphatic filariasis should be exploited. Many drug candidates have been identified and these should be exploited. **The role of EDCTP**

EDCTP can facilitate the trials of anti-wolbachia drugs such as flubendazole, minocycline, etc for the treatment of lymphatic filariasis and onchocerciasis. EDCTP can identify some centres of excellence such as KCCR in Kumasi, Ghana and others in Africa for testing of some of these repurposive drugs.

Prof. Maria Yazdanbakhsh

Leiden University Medical Center

The Netherlands

Current status of the field

National and international funding for pre-clinical and clinical studies in schistosomiasis (in general and female genital schisto in particular), filariasis and soil transmitted helminth both in terms of single infections and co infections.

Funding, Trained and skilled people who have the freedom to work in their area of expertise Area: parasitic infections

Future Directions

Vaccine development; New drugs; commitment; Diagnostics; Multi-faceted control **The role of EDCTP**

Development of talent and career path for scientists from endemic regions Lobby for funding not only from governments but also from (inter)national companies South-South collaborations eg S E Asia and Africa exchange of expertise Identify clusters of research groups to invest in and identify north south and south south sustainable collaborations