EDCTP

European & Developing Countries Clinical Trials Partnership

AFRICA MAPPING

CURRENT STATE OF HEALTH RESEARCH ON POVERTY-RELATED AND NEGLECTED INFECTIOUS DISEASES IN SUB-SAHARAN AFRICA

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The European & Developing Countries Clinical Trials Partnership (EDCTP) was created in 2003 as a European response to the global health crisis caused by the three main poverty-related diseases of HIV/AIDS, tuberculosis and malaria. Its aim is to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics for these diseases, with a focus on phase II and III clinical trials.

RAND Europe is an independent not-for-profit policy research organisation that aims to improve policy and decision making in the public interest, through research and analysis. RAND Europe's clients include European governments, institutions, NGOs and firms with a need for rigorous, independent, multidisciplinary analysis.

Baird's CMC provides high-level strategic solutions to governments, corporations and social sector organisations. Baird's CMC has a global team of experts whose diverse expertise and on-the-ground knowledge is deployed across a wide range of projects in different locations.

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Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
CANTAM	Central African Network for TB, HIV/AIDS and Malaria
CSA	Coordination and Support Action
CRO	Contract Research Organisation
DAC	Development Assistance Committee
DoD	Department of Defense
DRC	Democratic Republic of Congo
DFID	UK Department for International Development
EC	European Commission
EDCTP	European & Developing Countries Clinical Trials Partnership
OECD	Organisation for Economic Co-operation and Development (OECD)
EU	European Union
FP7	Seventh Framework Programme
HIV	Human Immunodeficiency Virus
LF	Lymphatic Filariasis
MDGs	Millennium Development Goals
MRC	Medical Research Council
MRC CTU	Medical Research Council Clinical Trials Unit
MVI	Malaria Vaccine Initiative (PATH)
NCDs	Non-Communicable Diseases
NCE	New Chemical Entities
NIDs	Neglected Infectious Diseases
NIH	National Institutes for Health
PATH	Program for Appropriate Technology in Health
PDP	Product Development Partnership
PD-PPP	Product Development – Public Private Partnerships
PEPFAR	President's Emergency Plan For Aids Relief
PMTCT	Prevention of Mother-to-Child Transmission
PRD	Poverty-related disease
PRNIDs	Poverty-related and Neglected Infectious Diseases
RCT	Randomised Clinical Trial
R&D	Research and Development
STH	Soil-transmitted Helminths
TB	Tuberculosis
TDR	Special Programme for Research and Training in Tropical Diseases
US	United States
USAID	US Agency for International Development
WHO	World Health Organization

1. Executive Summary

With the establishment of the Millennium Development Goals (MDGs) in 2000, the volume of global research and development (R&D) investments for poverty-related and neglected infectious diseases (PRNIDs) has shown a marked increase. Not only have the MDGs attracted funding from new sources, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, and Stop TB, but also increased funding from existing donors, such as those countries belonging to the Development Assistance Committee (DAC) of the Organisation for Economic Co-operation and Development (OECD). Many sub-Saharan African countries are, however, still heavily dependent on external funding for research and international development assistance for health services. In 2012, the European & Developing Countries Clinical Trials Partnership (EDCTP) commissioned a study to conduct a landscape analysis of health research and national funding commitments for PRNIDs in sub-Saharan Africa. The overall aim of this exercise was to review the current state of sub-Saharan African health research, the funding landscape and research capacity in the field of HIV/AIDS, tuberculosis (TB), malaria, neglected infectious diseases (NIDs), and health systems/operational research. The study also aimed to identify how these research activities and capacities relate to the mission of EDCTP.

The study comprised a combination of desk-based research and fieldwork. RAND Europe conducted a literature review on health research and funding for PRNIDs in sub-Saharan Africa. Key search terms were defined and a web-based literature search of major databases was conducted using a combination of terms capturing diseases, research themes, policy areas and regions/countries of interest. Relevant papers identified were subjected to an abstract review, of which 100 papers (i.e. 50 health research and 50 funding papers) were selected for a full text review.

The abstract review highlighted that the majority of the health research papers (n=501) and funding papers (n=265) focused on South Africa (16%), followed by Kenya, Uganda, Malawi and Tanzania, cumulatively accounting for 23% of all country references. A relatively high number of the health research publications focused on HIV/AIDS compared to other PRNIDs, with HIV/AIDS (40%) accounting for more than double the number of papers on malaria (20%), followed by TB (10%) and NIDs. Among the NIDs, schistosomiasis (6%), onchocerciasis (4%) and soil-transmitted helminths (STH) (2%) infections were the most often covered. Of the funding papers that specifically mentioned a funder (29%), international/regional funding bodies such as the World Health Organization (WHO), the Bill & Melinda Gates Foundation, the European Union (EU) and pharmaceutical companies were referred to most frequently (20%), followed by national governmental sources (9%) (i.e. European and Unites States governmental agencies, plus a very small minority of local sub-Saharan African sources). Key funding issues identified in the full review of the health research funding papers included a need for: 1) alignment of funding bodies and pooling of resources for increased donor coordination and more effective allocation of funds through a global policy agenda; 2) funding of the implementation phase of previously proven treatments to assure uptake; 3) better financial assessment of research budget needs, including direct and indirect costs; 4) pharmaceutical industry to take on an important role in PRNIDs research through the creation of Product Development-Public Private Partnerships to advance the pipeline of PRNIDs, and 5) investments in product development in combination with training of African scientists, to meet the demand for research on the increasing pool of new chemical entities (NCE), as well as collaboration and knowledge transfer between Africa and the developed world.

The fieldwork component was conducted by Baird's CMC through in-depth interviews with key stakeholders in sub-Saharan African governments, research institutions and international organisations using a semi-structured questionnaire and reporting process. The fieldwork was conducted between March and November 2013, with a total of 303 interviews conducted across 46 sub-Saharan African countries. Analysis of the interviews, supplemented with the desk review, showed that the majority of clinical research in all 46 countries was funded by international donors, although researchers' level of awareness of programmes taking place in other regions or disease areas varied considerably from country to country. Where government funding was available, respondents were frequently unable to quantify the levels of support. The main findings of the fieldwork were:

- In almost all countries, respondents considered HIV/AIDS, TB and malaria to be the main priority for clinical research. The importance of non-communicable diseases (NCDs) was also discussed, especially in countries such as Kenya and Nigeria. Amongst NIDs, leishmaniasis and STH infections were commonly mentioned
- All countries had some kind of government policy in place for the control of HIV/AIDS, TB, malaria and NIDs and most respondents were aware of these policies
- The respondents' knowledge of published government policy(ies) to support clinical research related to HIV/AIDS, TB, malaria and NIDs was almost evenly split across all countries. Some respondents stated that no such policy(ies) existed while others, though unclear on details, indicated that such policies must exist without being able to refer to a specific policy document
- Most respondents pointed out that local research structures are in place and most mentioned that national research programmes are being conducted to support clinical research on PRNIDs
- Most respondents were unsure about the existence of large-scale training programmes in the areas of clinical research and in areas related to clinical research, such as laboratory capacity, regulatory strengthening and pharmacovigilance, mentioning local training programmes conducted by universities and research institutions instead, especially those focusing on the ethical aspects of clinical research
- In most countries, government funding appears to be limited to indirect (i.e. in-kind) support such as staff salaries, infrastructure and provision of subsidised equipment rather than funding health research programmes. A notable exception to this finding was South Africa, where government support outweighs donor funding
- The great majority of respondents mentioned links to other African research institutions and to academic collaborators in Western Europe or North America. Several respondents mentioned EDCTP and its funding for projects. Most respondents were aware of EDCTP and its objectives, though there were a few notable exceptions.

Respondents were asked to rank four barriers to the development of clinical research in their country. A narrow majority of respondents (n=120, 40%) considered lack of funding to be the main barrier, but almost as many (n=116, 38%) cited lack of policymakers' understanding of the importance and benefits of research, which was ranked the second largest barrier, above lack of human resources and lack of infrastructure.

This study showed significant regional differences in the volume of R&D in health research and funding across sub-Saharan Africa. Furthermore, both the desk research and the fieldwork indicate high relative coverage of HIV/AIDS, in terms of research conducted

and funding allocated, followed by malaria, TB and NIDs. The majority of respondents mentioned that a lack of funding is the main barrier to the development of clinical research capacity in Africa, closely followed by the lack of policymakers' understanding of the benefits and importance of research. Ultimately, with the political will and contribution of African governments to fund R&D for PRNIDs, more resources can be leveraged to move forward the development of new and improved products for these diseases, while simultaneously creating a sustainable research environment in sub-Saharan Africa.

2. Background

Introduction

Substantial progress has been made in reducing the burden of poverty-related and neglected infectious diseases (PRNIDs) across the world over the last few decades.(1) The establishment of the Millennium Development Goals (MDGs) in 2000 has led to a concerted effort by the international community to increase investments in developing new diagnostics, treatments and preventive interventions for major PRNIDs. However, human immunodeficiency virus (HIV), tuberculosis (TB) and malaria remain major health issues for sub-Saharan Africa. Despite the region only accounting for 10% of the world's population, the region has 90% of the world's malaria-related deaths, 66% of the HIV infected population and over 30% of all TB sufferers.(2) In addition, neglected infectious diseases (NIDs), such as schistosomiasis, lymphatic filariasis (LF), soil-transmitted helminth (STH) infections, trachoma and onchocerciasis affect more than 500 million people in sub-Saharan Africa.(3)

In recent years the importance of health research and efforts to strengthen health research capacity have been emphasised as crucial to improving healthcare in sub-Saharan Africa and contributing to the fight against PRNIDs. Several international funders of health research and development (R&D) such as the World Health Organization (WHO), the Special Programme for Research and Training in Tropical Diseases (TDR), the European Union (EU), the Bill & Melinda Gates Foundation and the Wellcome Trust, as well as institutions supported by government funding from the United States have all embarked on initiatives to help improve the research environment, support individuals and provide institutional support across the region.(4) The implementation of successful and sustainable systems for health innovation 'requires collaborative activity not only at a national level but between countries and increasingly at a regional African level'.(5)

As a response to the global health crisis caused by HIV/AIDS, TB and malaria, the European Union, 14 Member States, and Norway created in 2003 the European & Developing Countries Clinical Trials Partnership (EDCTP). The aim of EDCTP is to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics for these diseases, with a focus on phase II and III clinical trials in sub-Saharan Africa. EDCTP funds projects that combine clinical trials, capacity building and networking, and involves institutions in both sub-Saharan Africa and Europe. Since its establishment, EDCTP has launched 65 Calls for Proposals and has supported 246 grants for a total amount of US$518.9 million (€382.7 million) (EU plus cofunding). This represents a substantial investment to tackle HIV/AIDS, TB and malaria in sub-Saharan Africa.

In preparation for its second programme, EDCTP commissioned in 2012 a study to conduct a landscape analysis of health research and national funding commitments for PRNIDs in sub-Saharan Africa. The overall aim of the project was to review the current state of sub-Saharan African health research activity funding landscape and capacity in the field of HIV/AIDS, TB, malaria, NIDs, and health systems/operational research. The project also aimed to identify how these activities and capacities relate to the mission of EDCTP. This study was commissioned to RAND Europe and Baird's CMC and consisted of a literature review of publications focusing on health research and funding to PRNIDs and fieldwork in sub-Saharan Africa.

Health funding for PRNIDs

Out of the three major disease areas (HIV/AIDS, TB, malaria), HIV/AIDS has received the largest share of overall investment over the past decade. International donor funding for HIV/AIDS to curb the epidemic, including funding assistance for HIV prevention, care, treatment and support activities, has increased over 25-fold from 1996 to 2012, from US$300 million to US$7.86 billion(6) globally, and it is expected to increase year-on-year.(7) Malaria funding over the past decade has also increased substantially with a 66-fold increase between 2002 and 2008 in annual investments from US$9.8 million to US$651.7 million.(8) By 2010, total funding for malaria control had exceeded US$2.55 billion.(9) International donor funding for TB care and control increased in the last decade from US$0.2 billion in 2006 to almost US$0.5 billion in 2013, but remains far lower than funding for malaria and HIV/AIDS.(10) International donors for TB control programmes represent a significant proportion of the overall funding, accounting for almost 60% of total funding for 35 low income countries.(10) Despite the increases in funding across these three disease areas, between 2007 and 2011, the overall share of global neglected disease R&D funding has fallen from 76.6% in 2007 to 69.4% in 2011, as a result of increased investment in other NIDs, such as dengue, kinetoplastids and helminth infections, which increased their share from 16.2% to 24.1%, across the same time period.(11)

Most of the countries in sub-Saharan Africa rely on the international donor community for investments in health for PRNIDs.(12) On average, external resources for health account for approximately 25% of total expenditure on health across sub-Saharan Africa.(12) However, as shown in Figure 1, in six sub-Saharan African countries (i.e. Eritrea, Ethiopia, Gambia, Liberia, Malawi, and Mozambique) over 50% of the total national expenditure on health comes from international donors.(12) Hence, any decrease in the level of global funding for health may have a significant and immediate impact in these countries. In ten countries, including Angola, Botswana, Cameroon, Equatorial Guinea, Gabon, Seychelles, Mauritania, Mauritius, Nigeria, and South Africa, external resources account for less than 10% of the total government expenditure on health.(12)

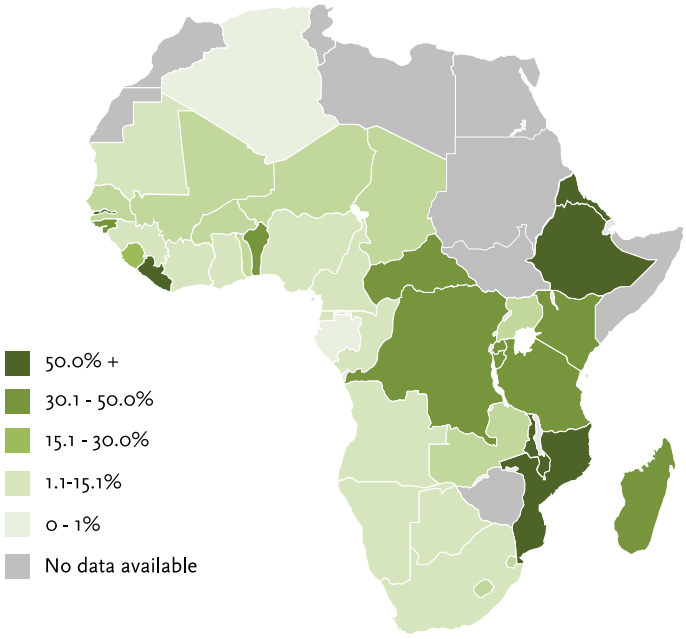

Figure 1. External resources for health as percentage (%) of total expenditure on health by national governments in sub-Saharan Africa, 2011(12)

R&D in PRNIDs

Although investment into HIV/AIDS, TB and malaria in sub-Saharan Africa has increased substantially over the last decade, funding is dominated by international support (Figure 1) and focused on control programmes rather than R&D. The lack of systematic data

collection on funding for health R&D in sub-Saharan Africa, as well as the difficulties in comparing any data currently available has left a significant information gap for funders who focus specifically on health research for PRNIDs.

In order to address this gap, The George Institute for International Health was commissioned by the Bill & Melinda Gates Foundation to construct a comprehensive database of R&D funding data for PRNIDs, known as G-FINDER.(13) In short, annual data on global investment into R&D of new pharmaceutical products to prevent, manage, or cure diseases of the developing world are collected through an online survey.(13) In 2012, the survey comprised 504 funders in 52 countries. These include public, private and philanthropic funders in high-income countries; public funders in Argentina, Brazil, Chile, Colombia, Ghana, Guatemala, Honduras, India, Iran, Malaysia, Mozambique, Nicaragua, Nigeria, Papua New Guinea, Senegal, South Africa, Tanzania, Thailand, and Uganda, and private sector funders in Brazil, India, Indonesia and Thailand.(11) Furthermore, "G-FINDER also surveyed a wide range of funding intermediaries, product development partnerships (PDPs) and researchers and developers who received funding". G-FINDER quantifies neglected disease investments in the following R&D areas: basic research, product discovery and preclinical development, product clinical development, phase IV/pharmacovigilance studies of new products, and baseline epidemiology in preparation for product trials. G-FINDER does not include data on "advocacy, implementation research, community education and general capacity building, or investment into non-pharmaceutical tools".(11)

Disease area	Total Amount Invested (US$)	% of total funding allocated
HIV/AIDS	5,488,168,543	43.5%
Malaria	2,709,915,003	21.5%
TB	2,508,349,300	19.9%
Dengue	781,191,533	6.2%
Kinetoplastids*	706,168,846	5.6%
Helminths (Worms & Flukes)	352,659,673	2.8%
Leprosy	42,627,803	0.3%
Trachoma	19,653,909	0.2%
Buruli Ulcer	17,429,734	0.1%
Grand Total	**12,626,164,344**	**100%**

Table 1. Total global R&D investments by disease (2007–2011)(14)

* Including Chagas disease, African trypanosomiasis and leishmaniasis

As shown in Table 1 and Figure 2, a large proportion of global R&D for PRNIDs is invested in HIV/AIDS, accounting for approximately 44% of the total investments of the diseases listed[i], followed by malaria and TB. Additionally, a large proportion of R&D funding is directed towards vaccine and drug development in all diseases, with R&D investments into HIV/AIDS vaccines alone larger than total investments into malaria or TB. For most diseases listed, prophylactic vaccines and drug development receive the largest share of investments, followed by basic research. Investments in diagnostics have been significantly less for all diseases.

Table 2 highlights the top twelve funders between 2007 and 2011 by amounts invested, as reported by G-FINDER.(14) The data show that global health R&D on PRNIDs is heavily dependent on a relatively small number of

i G-FINDER also includes information on bacterial pneumonia & meningitis, diarrhoeal diseases, rheumatic fever typhoid and paratyphoid fever and salmonella infections.

funders, with the majority of the total investments being made by two funders.(14) The United States government invested the highest amount through the National Institutes of Health (NIH). This was followed by the Bill & Melinda Gates Foundation, which represents the largest private foundation contributing to R&D into PRNIDs. Although there are substantial investments of the private sector, through pharmaceutical and biotechnology companies, the vast majority of funding is still reliant on public and philanthropic donors.(14)

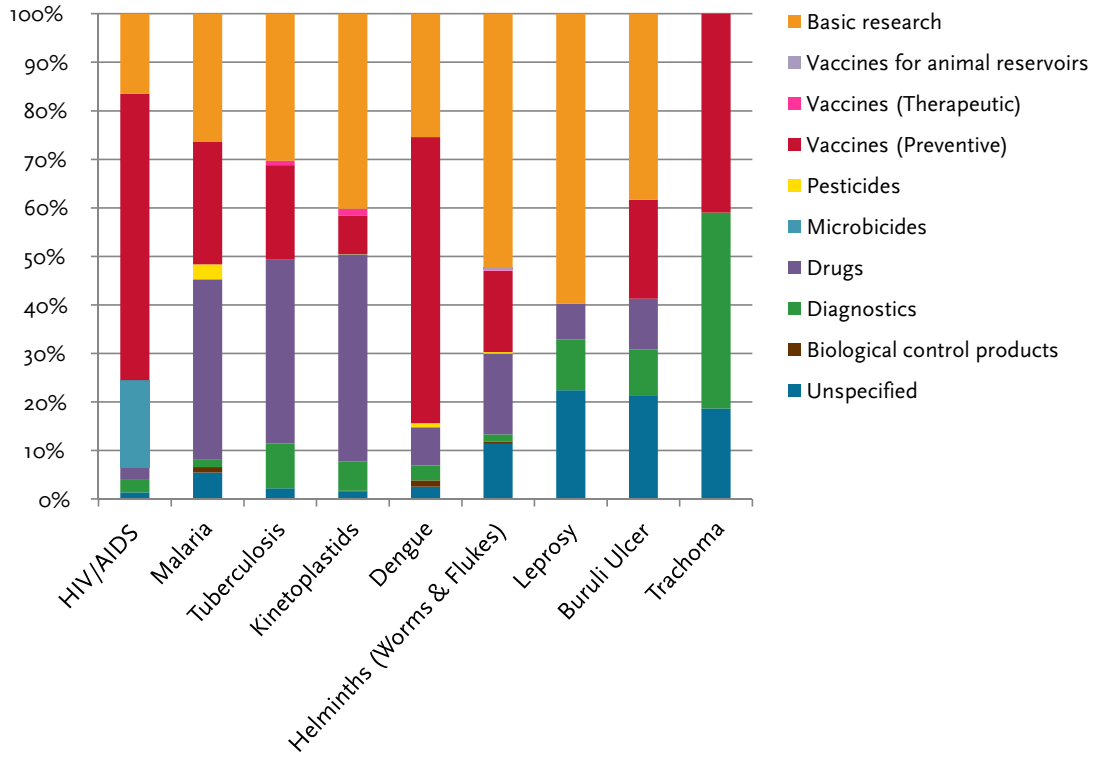

Figure 2. Share of R&D funded by disease (2007–2011)(14)

Name of funder	Type of funder	Total Amount Invested (US$)
US National Institutes of Health (NIH)	Government	5,795,734,228
Bill & Melinda Gates Foundation	Private foundation	2,530,342,885
Aggregate Pharmaceutical and Biotechnology Company Respondents	Private	2,037,077,360
European Commission: Directorate-General for Research and Innovation*	Government	567,311,143
United States Agency for International Development (USAID)	Government	416,278,263
US Department of Defense (DOD) including DOD Defense Advanced Research Projects Agency (DARPA)	Government	403,029,646
The Wellcome Trust	Charity	361,225,501
UK Department for International Development (DFID)	Government	348,154,635
UK Medical Research Council (MRC)	Government	270,742,509
Institut Pasteur	Private foundation	161,012,834
Dutch Directorate General of International Cooperation	Government	128,593,178
Australian National Health and Medical Research Council	Government	100,613,706
Grand total		**13,120,115,888**

Table 2. Top twelve funders of R&D into PRNIDs (2007–2011)(14)

* This does not include funding provided by EDCTP

3. Methodology

Literature review

RAND Europe conducted a literature review on health research and funding of PRNIDs (i.e. HIV, TB, malaria and NIDs) in sub-Saharan Africa using both peer-reviewed and grey literature sources (i.e. non peer-reviewed published written material). Searches focused on the PubMed, Embase, and Scopus databases. Search key words included a combination of terms capturing diseases, research themes, policy areas and countries or regions of interest (Annex 1). Databases were searched individually and results were collected into a single EndNote library. Searches included publications in English, French and Portuguese, to cover the major languages of academic publications in sub-Saharan Africa. However, all abstracts found in non-English journals were translated into English. Health research papers were examined for the time period 2003-2012 and papers on research funding for the time period 2007-2012. The latter narrower time frame was chosen due to the lack of systematic data collected on health research funding in sub-Saharan Africa prior to 2007.

Figure 3 shows the methodology followed for the literature review. Papers included in the initial sample were deemed not relevant to the study if they did not focus on the diseases of interest and/or had a geographical focus outside sub-Saharan Africa. After applying these exclusion criteria and removing any papers without abstract and duplicates, the remaining papers in the sample were categorised according to the following information available in the abstract: geographic focus; disease area; type of study (e.g., empirical, review, case study) (Annex 2) and, research theme (e.g., broad aspect of the health policy debate). A sample of 100 papers was then selected for a full review including 50 research papers and 50 funding papers.

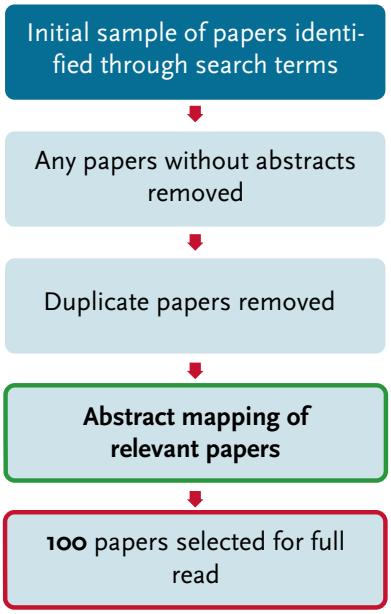

Figure 3. Literature review methodology

To select the 50 research papers for a full review, the relevant publications were classified into one of five groups: 1) three-way overlap (i.e. papers that appear in all three databases); 2) two-way overlap (papers that appear in two out of the three databases); 3) Embase only; 4) PubMed only; 5) Scopus only. From the three-way overlap papers, the project team randomly extracted 50 papers on health research. A full review of these papers enabled an in-depth examination of current debates in particular areas and provided observations on what authors of the selected papers identified as gaps in their specific research areas.

Abstracts in the health research funding sample covered a wide range of topics. As a result, it was decided not to randomly draw papers for a full review but, instead, select 25 relevant peer-reviewed journal articles and supplement these with 25 reports from the grey literature. These 50 articles aimed to provide detail on trends and gaps in investment for health research in the disease areas of interest.

To facilitate the analysis of the full text review a detailed qualitative template was used to summarise the key points of each article. These were then grouped to identify common themes discussed in the literature. From this, a subset of gaps that were discussed in the literature was found. In addition, based on the information reviewed and prior knowledge from other projects, gaps were identified where issues were not discussed. Once the fieldwork had been conducted the findings from both the fieldwork and literature review were compared to understand the areas of agreement and divergence in the findings.

Fieldwork

To understand what research is being supported and conducted, but not fully captured in the literature, qualitative research methods were applied with trained consultants interviewing key informants (mostly in person). For all countries in sub-Saharan Africa (n=46), interviewees were selected based on a list of respondents developed and agreed between Baird's CMC, RAND Europe and EDCTP. It was agreed that for each country the list of interviewees would comprise a mix of researchers, civil servants, employees of multilateral organisations (e.g., WHO, UNICEF), and other individuals familiar with the health research and policy landscape of the various countries. To conduct the face to face interviews, consultants were recruited and trained by the project team. Most interviews were conducted by nationals of the country concerned with the exception of the Gambia, Seychelles and Senegal. In these countries non-nationals were recruited, but they had lived and worked in those countries for several years. All interviewers had a strong background in public health, journalism or both. Interviews in Central and Eastern Africa[ii] were conducted between March and June 2013, and interviews in Western and Southern Africa[iii] between July and November 2013.[iv]

Interviewers followed a detailed discussion guide with key questions developed based on the scope and remit of the project. Respondents spoke to each interviewee in the language of their choice. Interviews were transcribed and notes were then translated into English by a native English speaker familiar with the subject matter, briefed on the objectives of the enquiry and proficient in French, Portuguese or Spanish. Proper names, acronyms and references to legislation or announcements were checked by the project team and, where needed, any inconsistencies were resolved through discussion with the interviewer and, where necessary, through a follow-up discussion with the interviewee. All interviews were summarised in a standardised format. From these, summaries were written for each country giving an overview of all interviewees' responses, together with relevant epidemiological data and a brief discussion of political and economic factors likely to influence policy. Each country report was then checked for internal consistency and quality.

ii Angola, Burundi, Cameroon, Chad, Democratic Republic of the Congo, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Kenya, Republic of the Congo, Rwanda, São Tomé and Príncipe, Somalia, Southern Sudan, Tanzania, Uganda

iii Benin, Botswana, Burkina Faso, Cabo Verde, Comoros, Côte d'Ivoire, Central African Republic, Gambia, Ghana, Guinea, Guinea-Bissau, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Senegal, Seychelles, Sierra Leone, South Africa, Swaziland, Togo, Zambia, Zimbabwe

iv Central African Republic was not included in the fieldwork due to armed conflict and very limited government capacity. Sudan was not included in the fieldwork because under UN classifications it is considered part of North Africa

4. Results

Literature review

As shown in Figure 4 the literature searches yielded 868 relevant publications on health research and 365 publications on health research funding. After removing papers with no abstract, duplicates and applying the exclusion criteria (i.e. disease scope and geography) the final sample included 501 health research and 265 funding papers, respectively.

Health research papers

The 501 abstracts on PRNIDs health research in sub-Saharan Africa mentioned 577 countries or groups of countries using whole counting[v]. As shown in Figure 5A, South Africa accounted for 90 (15.6%) of all country references, followed by Kenya, Uganda, Tanzania and Malawi, together accounting for 131 (22.7%) of country references. The distribution of the geographical focus was heavily skewed, with the top five (mentioned above) and the top 10 countries accounting for 38.3% and 50.4% of references, respectively.

The distribution of abstracts by disease (Figure 5B) was also heavily skewed, with over 40% (N=230) focusing on HIV/AIDS followed by malaria (n=114, 20%), and TB (n=58, 10%) with NIDs trailing behind. Among the NIDs peer-reviewed health literature, schistosomiasis (n=33, 6%), onchocerciasis (n=23, 4%) and STH (n=14, 2%) had the highest coverage compared to other NIDs. Among the 501 abstracts, empirical papers (n=202, 40%)[vi] and case studies (n=106, 21%)[vii], which broadly describe individual treatments and interventions, were most prevalent (61%) followed by reviews (n=69, 14%) and articles specifically on clinical trials (n=21, 4%) (Figure 5C).

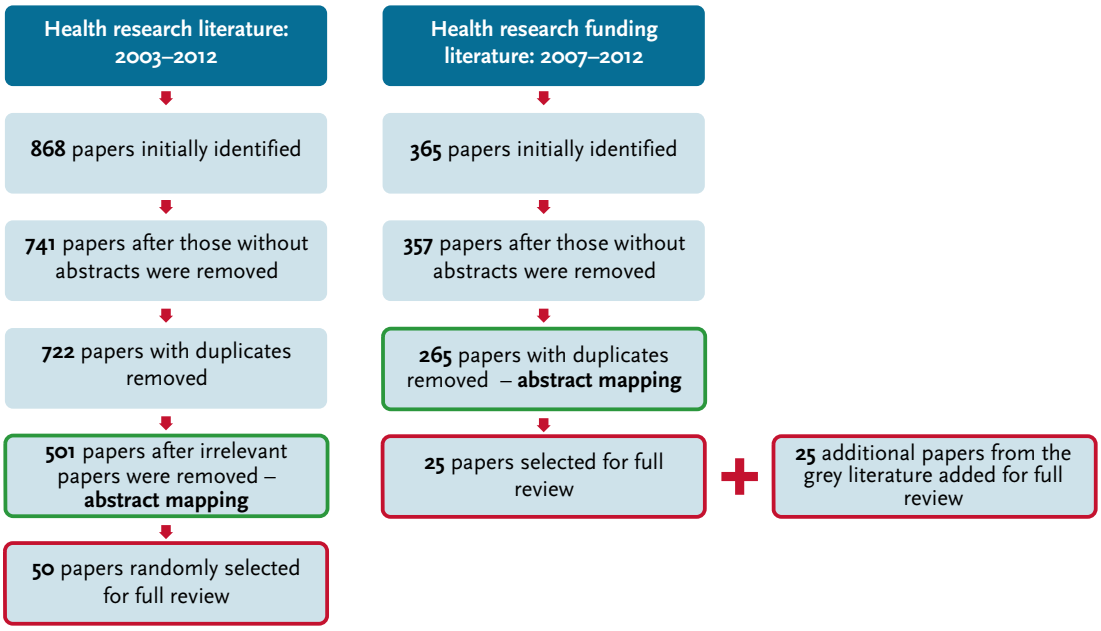

Figure 4. Flowchart of literature review sample

v Whole counting means that a country gets credit of '1' for each paper in which it is mentioned, even if several countries were mentioned in a single paper. A country was counted if research was conducted in that country or if the data used for the publication originated from that particular country

vi Papers where primary or secondary data is used to describe a population or draw qualitative/quantitative inferences about an intervention or delivery mechanism

vii Papers in which a particular intervention or programme forms the basis of the study

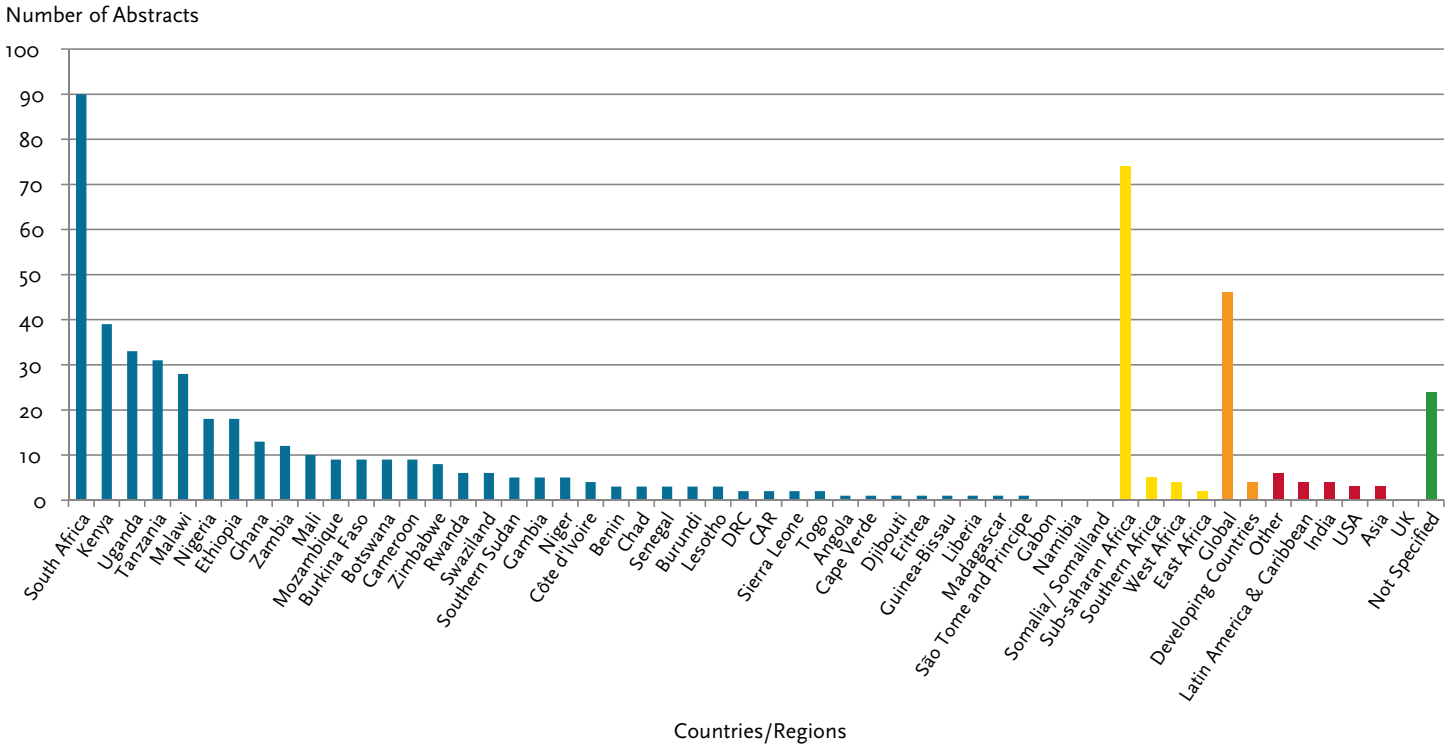

Figure 5A. Health research papers: abstracts by country or region

Note: Individual countries are shown in blue, regional groupings in yellow, non-Africa specific/global groupings in orange and non-African countries in red. Some abstracts may be double counted for example if a paper compares more than one country or region. Individual countries are not included in the regional count.

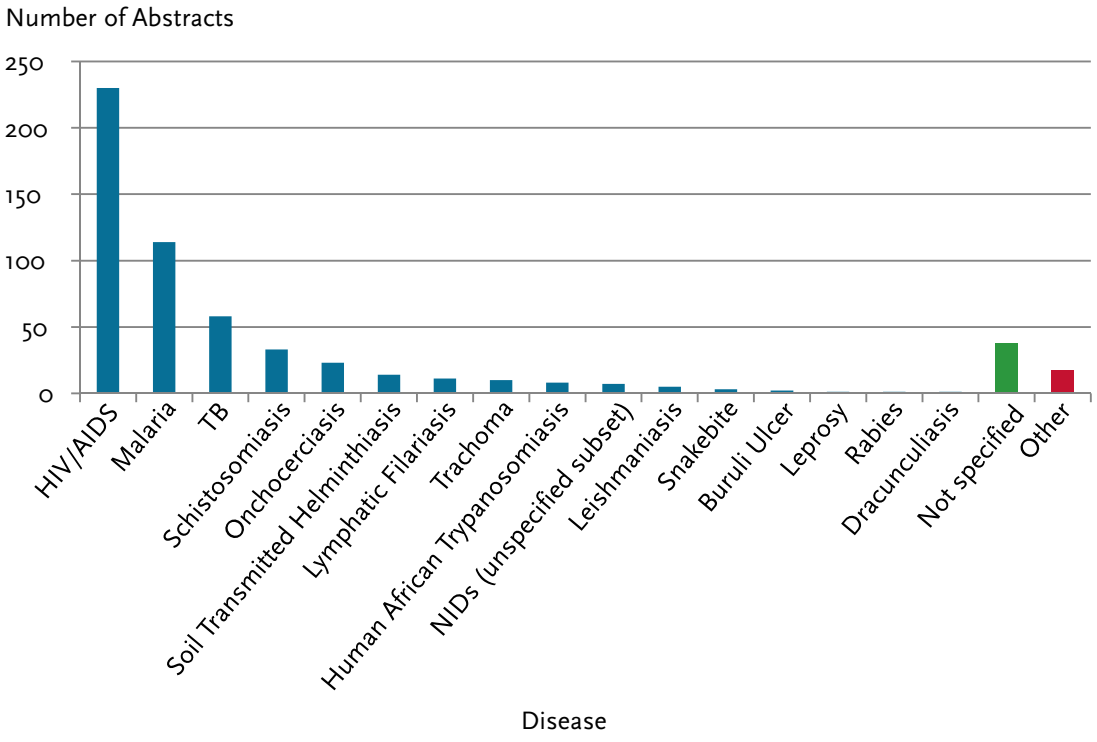

Figure 5B. Health research papers: abstracts by disease

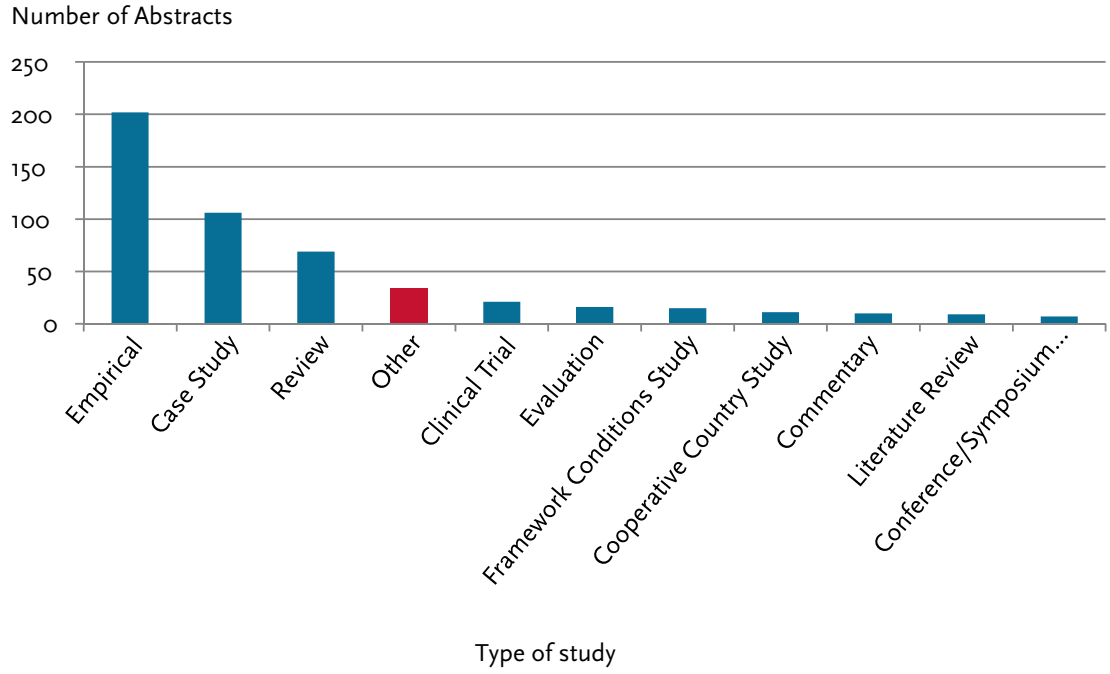

Figure 5C. Health research papers: abstracts by type of paper

When exploring the content of the 501 health research paper abstracts according to research theme, papers discussing the health impact of particular programmes/policies, those discussing health services (including design of services, human resources issues and barriers to service delivery), and those discussing health systems (including the design of health systems) were the most widely observed. Among papers focused on HIV/AIDS, studies tended to be on the health impact of particular programmes/policies, followed by health services and health systems. For malaria, the top categories were health impact of particular programmes/policies, followed by health services and disease monitoring/surveillance studies. However, in the case of TB, there were more papers focusing on health services and health policy.

Health research funding papers

Using whole counting, the 265 abstracts mentioned 31 sub-Saharan countries and seven groups of countries[viii]. As shown in Figure 6A, funding papers focused on South Africa made up a significant proportion of the analysis, accounting for 18% (n=48) of all country references. Uganda, Kenya, and Malawi together also accounted for 18% (n=48) of country references. The distribution of the geographical focus was heavily skewed, with the top five and the top ten countries accounting for 59% and 80% of references, respectively. Additionally, a large number of papers were non-country specific and tended to focus more generally on regions or global funding trends.

Similar to the results from the review of health research papers, the distribution of the funding abstracts by disease (n=249) was also heavily skewed, with over 57% (n=142) focusing on HIV/AIDS followed by malaria (n=46, 18%), TB (n=31, 12%), and non-communicable diseases (NCDs), including heart disease, liver, cancer (n=13, 5%) (Figure 6B). Twelve percent (n=30) of the funding papers focused on NIDs.

viii Whole counting means that a country gets credit of '1' for each paper in which it is mentioned, even if several countries were mentioned in a single paper. A country was counted if research was conducted in that country or if the data used for the publication originated from that particular country

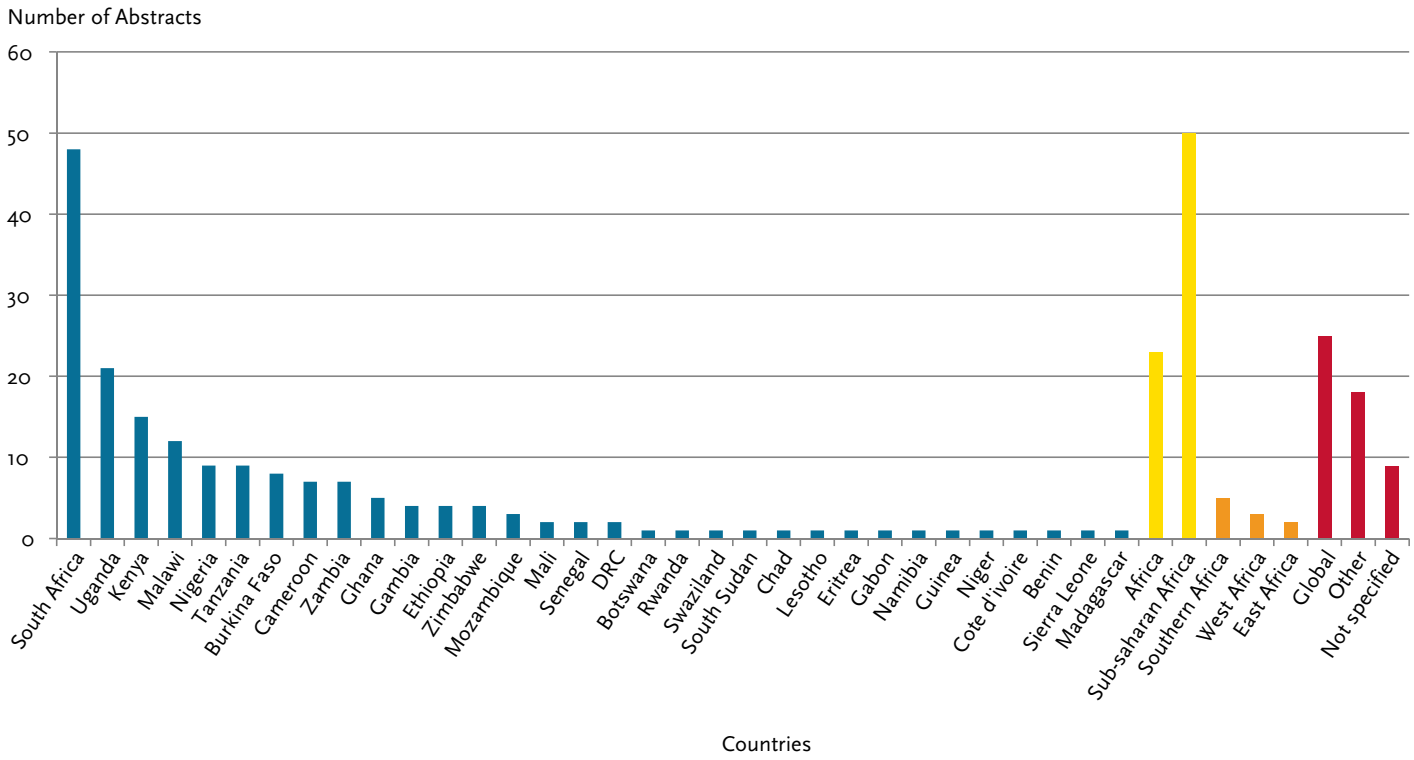

Figure 6A. Health research funding papers: abstracts by country

Note: Individual countries are shown in blue, regional groupings in yellow, non-Africa specific/global groupings in orange and non-African countries in red. Some abstracts may be double counted for example if a paper compares more than one country or region.

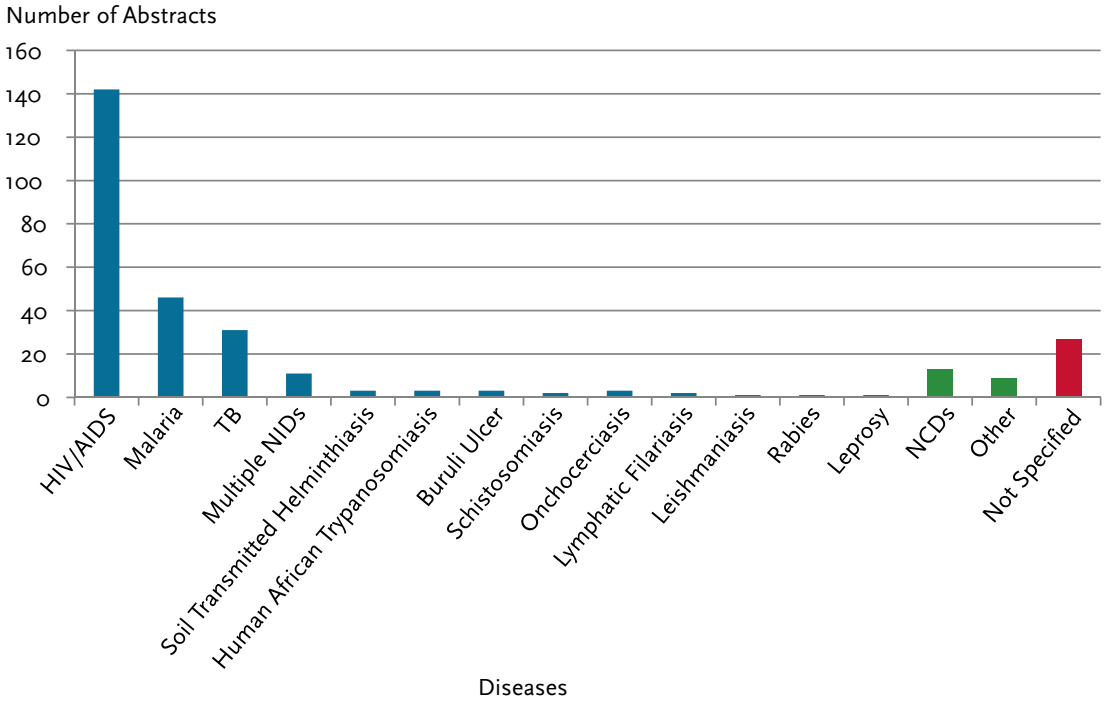

Figure 6B. Health research funding papers: abstracts by disease

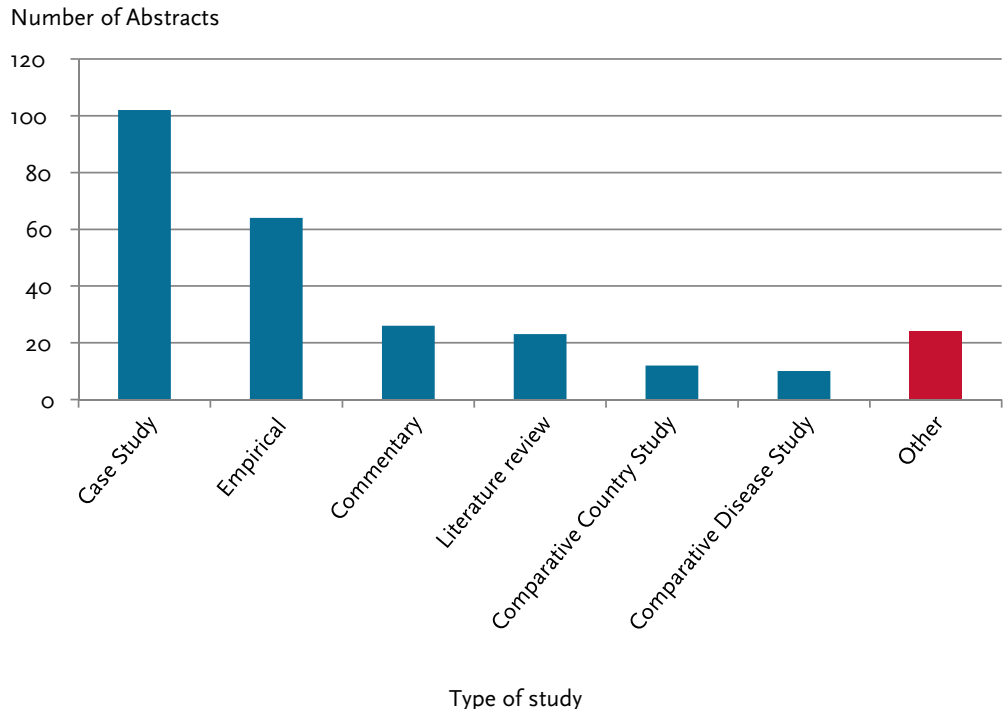

Figure 6C. Health research funding papers: abstracts by type of paper

Case studies (n=103, 39%) and empirical studies (n=64, 25%) were the most prevalent amongst the papers focusing on funding, followed by commentaries (n=26, 10%) and literature reviews (n=23, 9%) (Figure 6C). The distribution of funding papers by research theme showed that papers discussing the health impact of particular programmes/policies, those discussing health systems (including the design of health systems) and those discussing health services (including design of services, human resources and barriers to service delivery) were the most widely observed. However, across these themes, very few papers (n=11, 4%) dealt specifically with the funding of health research. Of the papers that mentioned a funder[ix], (n=77, 29%), international/regional funding bodies such as WHO, the EU, the Bill & Melinda Gates Foundation, and pharmaceutical companies, were referred to most frequently (n=54, 20%), followed by national governmental sources (n=23, 9%) (i.e. European, US governmental agencies, and a very small minority of local sources).

Analysis of full text reviews

The main disease specific gaps identified by the authors in the sample of 50 health research papers are described below.

HIV

Scientific studies on the complex relationships/interactions between HIV and other common infectious diseases are needed as there is a need to understand how HIV may interact with other communicable diseases, which may be co-endemic in a region. This is particularly important in light of increased survival rates for persons living with HIV/AIDS. Furthermore, the need for effectiveness and cost-effectiveness studies of interventions on large scales was identified.(15–17) Studies on interaction of behavioural/psychological influences and health systems/interventions showed that cohort and cross sectional studies have demonstrated important correlations between aspects of the social environment, psychological factors and likelihood of treatment uptake and adherence. Nevertheless, important gaps remain as to the causal mechanism. (18,19) More research into the interactions of

ix Mention of the funder either in the content of the publication or in the acknowledgment section of the publication

how HIV affects individuals' and communities' food security, health status and behaviour, and access to public health interventions also needs to be undertaken.(20)

TB

The main gap discussed was the need for scientific studies to underpin the development of an effective, affordable diagnostic test.(24) The need for evaluation of diagnostics in young children was also mentioned.(25)

Malaria

More research is needed on (i) scientific studies into the interaction of uncomplicated malaria with other variants of the disease;(21) (ii) creation of epidemiological databases, for research into trends of infection and of the impact on vulnerable groups;(22) and (iii) mappings of bed net distribution systems, with estimations of the importance of different channels (local public sector, local private sector, donor) for coverage levels.(23)

NIDs

Research suggests the importance of epidemiological and surveillance mappings, which would allow for more nuanced understanding and tracking of the temporal and geographical spread of NIDs and the impact on vulnerable groups(26,27). Furthermore, scientific studies are necessary to better understand and begin identifying new targets for diseases or disease variants(28): this was flagged particularly with respect to human African trypanosomiasis (for which existing therapies have poor safety profiles) and schistosomiasis (for which a single therapeutic tool is in use). In addition, environmental and social risk factors influencing spread and evolution of the diseases vary from region to region, and are often not considered fully in the design of integrated control programmes.(29)

Health research funding papers

Key findings identified through the review of the 50 publications on funding for health research that are relevant to the research and sub-Saharan African are: 1) The proliferation of private funding sources has led to increases in overall donor contributions to PRNIDs but has, at the same time, made tracking and synthesis of funding data more complex. Creation and maintenance of an international funding database would facilitate donor coordination and more effective allocation of funds across countries; 2) Donors may follow general funding trends by disease or region. Such actions may be beneficial where large-scale, short-term investments in health infrastructure or control programmes are necessary, and therefore the emergence of a global policy agenda may be required. However, this may also expose recipient countries to any volatility in the donor community, if donors move as a group, short-term inflows and outflows of funds may be exaggerated (30); 3) Research funding needs are often underestimated in low and middle income countries, and there is a need to calculate indirect and direct costs for funding agencies more accurately; 4) There is a gap between funding new potential tools and treatments and implementation of previously proven treatments. In this sense, it is important to fund the implementation that follows to ensure uptake(31); 5) The pharmaceutical industry can play an important role in the creation of Product Development-Public Private Partnerships (PD-PPPs) using their R&D knowledge and experience. The success of PD-PPPs in the area of vaccines for NIDs has stimulated further pharmaceutical engagement in this area, with Novartis and Merck & Co. establishing spin-off enterprises in Siena, Italy; Delhi, India(32) and Singapore; 6) PDPs themselves receive funding from a variety of sources such as government donations and private sector although they heavily rely on philanthropic donations. Philanthropic funding

of PDPs reached US$212 million in April 2005, which accounted for 78.5% of funding for these initiatives – a significant amount came from the Bill & Melinda Gates Foundation. (33) Investments since then have increased dramatically, with over US$2 billion invested during 2007–2010 from a variety of sources and over US$451 million invested in PD-PPPs in 2011 alone (14), and 7) The expense and cost of conducting clinical trials in sub-Saharan Africa should not be underestimated. There is already insufficient funding to conduct clinical trials on new chemical entities (NCEs) in development.(33) As the pool of NCEs continues to grow, this problem may be exacerbated.(33) To address this challenge, investments in product development in combination with training African scientists will be important as well as collaboration and knowledge transfer between Africa and the developed world.

Fieldwork

A total of 303 key informant interviews were conducted across the 46 countries. Of these, 75% were conducted face-to-face and 25% by phone or, in three cases, by email. The total number of interviews varied between two and 18 per country, with the weighting based on size and perceived position of the country in clinical research development. Larger countries with robust systems and active research institutions in place were assigned more interviews. Figure 7A and 7B show the categorisation of respondents that were interviewed.

Interviewees highlighted that the overwhelming majority of clinical research in all 46 countries is based on funding from external donors. In the majority of cases, clinical research typically appears to be conducted in vertical 'silos', with African researchers working closely with their donors and European and US academic partners, while local governments are taking a peripheral role. Where government funding was available, respondents were often unable to quantify levels of support. Where it was quantifiable, it was often for relatively small amounts, and sometimes varying strongly from year to year. Nearly all respondents from countries where clinical research was conducted said that there was some indirect government funding, primarily in-kind. Some governments, such as Kenya, Mozambique and Senegal offered more direct provision such as funding training programmes, particularly in ethics of clinical trials and for improving the quality of laboratory services. Researchers in different countries displayed varying levels of awareness of programmes taking place in regions or disease areas other than their own. The results of the fieldwork showed that that there were variable responses to questions about government policies for control and support of clinical research on PRNIDs.

In terms of research priorities, HIV/AIDS, TB and malaria were mentioned, almost without exception, in all countries. However, in some countries, prominence was given to NCDs, primarily cancer, cardiovascular disease and diabetes[x]. Amongst NIDs, leishmaniasis and STH infections were commonly mentioned. Diseases such as schistosomiasis, trypanosomiasis, onchocerciasis and leprosy were also mentioned, and NIDs were overall seen as a priority, especially in Benin, Cabo Verde, Democratic Republic of Congo (DRC), Republic of the Congo, Ethiopia, Nigeria, São Tomé and Príncipe, Sierra Leone, Swaziland, Zambia and Zimbabwe.

x Respondents did not specify type 1 or type 2 diabetes, but International Diabetes Federation data suggest the overwhelming burden of disease is in type 2. See http://www.idf.org/diabetesatlas/5e/africa

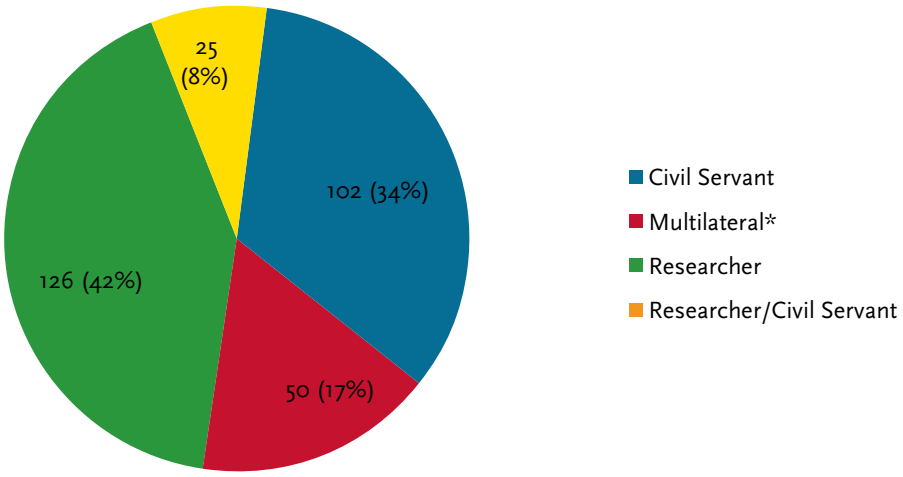

Figure 7A Categorisation of the 303 respondents*

*Multilateral includes international agencies such as WHO, UNICEF

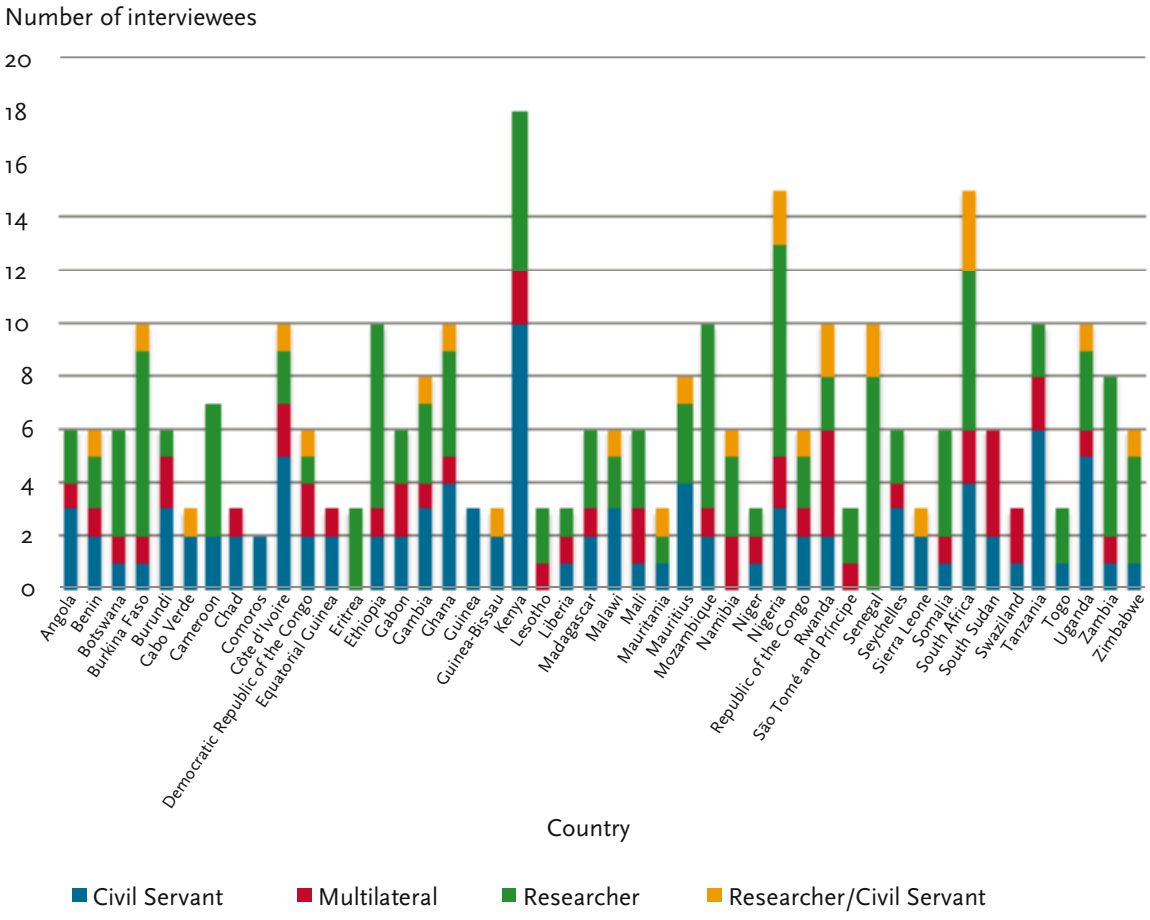

Figure 7B Categorisation of interviewees by country

All countries had some government policy in place for the control of HIV/AIDS, TB, malaria and NIDs. The respondents' knowledge on published government policies to support clinical research related to HIV/AIDS, TB, malaria and NIDs was almost evenly split across all countries. Some stated that no such policy(ies) existed while others explained that such policy(ies) exist. Of note, larger countries, with a stronger research tradition (e.g., South Africa, Kenya, Tanzania) seem to have such government policies in place. As for national programmes to support clinical research, most interviewees explained that there are research structures in place and mentioned programmes being conducted to support clinical research. However, not all the programmes mentioned were national and not all were related to clinical research.

The great majority of respondents mentioned links to other African research institutions and to academic collaborators in Western Europe or North America, although some respondents mentioned specific linkages to Asian countries such as Japan, Taiwan and China. Several respondents mentioned EDCTP and its funding for projects such as the Central African Network for TB, HIV/AIDS and Malaria (CANTAM).

In regards to capacity building, most respondents mentioned local training programmes conducted by universities and research institutions, especially on the ethical aspects of clinical research. Respondents had several comments on how to improve clinical trial capacity, including: making research a part of the educational curriculum, upgrading facilities, providing greater financial resources, supporting capacity building at a regional level, facilitating the publishing of work of local researchers in peer-reviewed journals, developing a research database, and conducting gap analyses at clinical research institutions to identify unmet need.

Respondents were asked to rank four barriers that may impact on the development of clinical research capacity in African countries and make any other comments regarding obstacles to research in their countries. The four barriers were:

- Levels/sustainability of funding
- Policymakers' understanding of the importance of research
- Infrastructure in research institutions
- Human resources available for research.

While a majority said that a lack of funding was the main barrier to the development of clinical research capacity in Africa, there was an almost similar number identifying a lack of policymaker understanding of the benefits of research; in 18 out of 47 countries, half or more of the respondents considered that this was the most important factor (Figure 9).

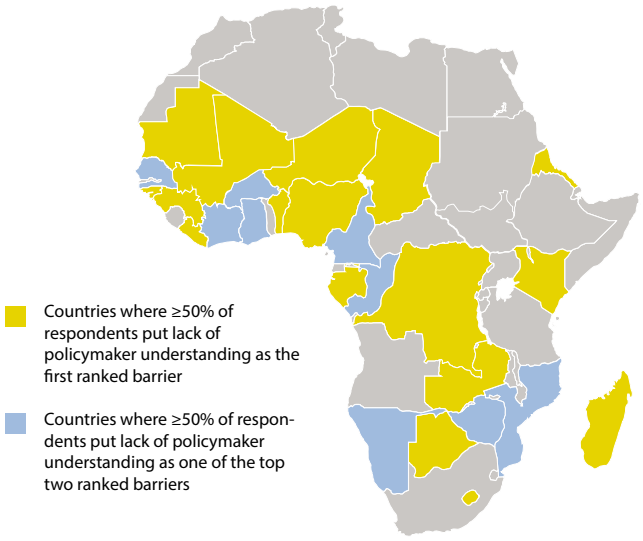

Figure 9. Overview of lack of policymaker understanding as an important barrier to clinical research capacity in 46 sub-Saharan African countries

Out of the 303 respondents interviewed, 120 ranked lack of funding as the most important barrier to the development of clinical research capacity in Africa, while 116 ranked lack of policymaker understanding of the importance of research as the most important barrier. 50 respondents ranked the availability of human resources as the most important barrier and only 17 respondents ranked infrastructure as the most important barrier (Figure 10).

Respondents suggested several other barriers that may impact on the development of clinical research capacity in African countries, including poor research coordination, lack of long-term collaboration between institutions, lack of national and regional health information systems, and a paucity of local publication opportunities.

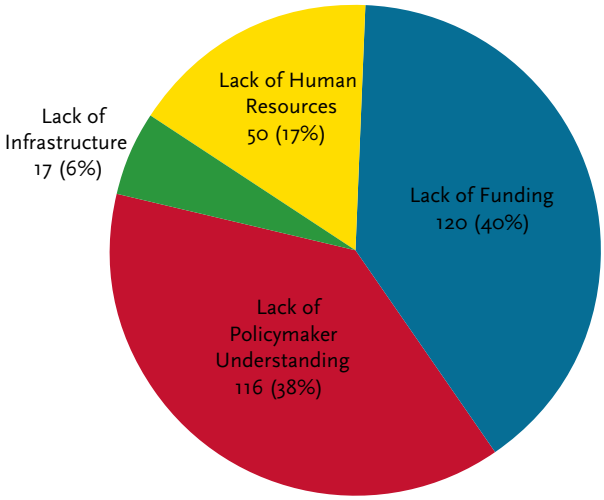

Figure 10. Barriers ranked as the most significant by respondents (N=303)

5. Discussion

Synthesis of findings

The health and funding literature showed clear regional differences with a geographical distribution of health research and funding papers heavily skewed towards South Africa and East Africa. Both the literature review and fieldwork indicate high relative coverage of HIV/AIDS, in terms of research conducted and funding allocated. HIV/AIDS is covered more than double that of malaria. TB is third-most covered, with NIDs trailing behind. Peer-reviewed health literature indicates, however, that the top three NIDs (schistosomiasis, onchocerciasis and STH), have high coverage relative to other NIDs. In the fieldwork, HIV/AIDS, TB and malaria were mentioned as priorities almost without exception for clinical research and its associated funding in all countries.

Both the literature and fieldwork showed that a lack of funding is the main barrier to the development of clinical research in sub-Saharan Africa. However, a surprising number of interviewees cited lack of policymaker understanding of the importance of research, which was ranked second, above lack of human resources and lack of infrastructure. This lack of understanding at the policymaker level may lead to funds to support clinical research being either unallocated or not spent. A number of limitations were also noted as gaps in the information available from the literature. For example, lack of information on capacity building in certain geographical regions and the absence of national policy documents appeared as significant factors in the literature searches and in the documents referred to in the interviews. These limitations were also observed in the fieldwork, where many respondents were unable to quantify levels of national investment and only countries with a more established research culture and more sophisticated trials infrastructure could cite the existence of published government policy.

The peer-reviewed literature showed that there is also an absence of information regarding the systems of research funding. Only in recent years and partly as a result of the Paris Declaration on Aid Effectiveness (2005) (34), which aimed to enhance mutual accountability and transparency in regard to the delivery of international development assistance, has information about funding started to become available. Other contributing factors to this shift include increasing reporting requirements by funders, journals and publishers.

Reflections on future issues around R&D for PRNIDs

The fieldwork found that lack of funding for research remained the major barrier to the development of clinical research capacity, but political, economic or socio-cultural factors affecting countries and institutions should also be taken into account. In this respect, countries in sub-Saharan Africa could be categorised according to the following criteria:

- State-of-the-art and established countries – countries with reputable and internationally recognised research centres, which financially support the development of research. For example, Cameroon, the Gambia, Kenya, South Africa, Tanzania and Uganda
- Countries where capacity strengthening is needed - countries with existing research capacity but with less advanced research infrastructure – including, Botswana, Ethiopia, Ghana, Mozambique, Rwanda and São Tomé and Príncipe
- Countries that would greatly benefit from capacity development - countries with no existent or basic research infrastructure. These countries also have major health problems and large populations at risk (and where therefore would be easier to recruit a large trial cohort), and often cite lack of

political will as the major barrier – including Angola, the Democratic Republic of Congo and South Sudan.

This categorisation is elaborated in Figure 11, based on the findings of the fieldwork. While this approximate categorisation is only based on a sample of 303 respondents and the wider knowledge and experience of the project team, and therefore may not address the diversity of research capacity within a given region or country, it highlights locations where funders may leverage existing capacity (state-of-the-art and established countries), provide additional support for substantial progress and advocate for additional funding for clinical research (countries where capacity strengthening and development is needed).

The literature review and the fieldwork both confirmed that clinical research in sub-Saharan Africa relies heavily on international funding. Respondents noted that vertical silos in which African researchers work closely with donors and European/US academic partners are commonplace, with national institutions or governments taking more of a peripheral role. This is also reflected in the lack of national sub-Saharan African funding sources in the literature review and the inability of many respondents to cite specific government policies related to research funding. The fieldwork shows that there is little or no sustained government funded research in sub-Saharan Africa, with the exception of South Africa and Equatorial Guinea. This despite the 2001 Abuja declaration on HIV/AIDS, TB and other infectious diseases, which states that 2% of government budgets is to be devoted to research. (35) The impact that external donations have on levels of internal funding for research is largely unknown. What should be elucidated is whether there are instances where the presence of external funding removes the impetus for (i) national funding and (ii) sustainable national decision making structures to emerge. Overall, it would be important to explore if increased international funding will lead to more domestic funding over the longer term.

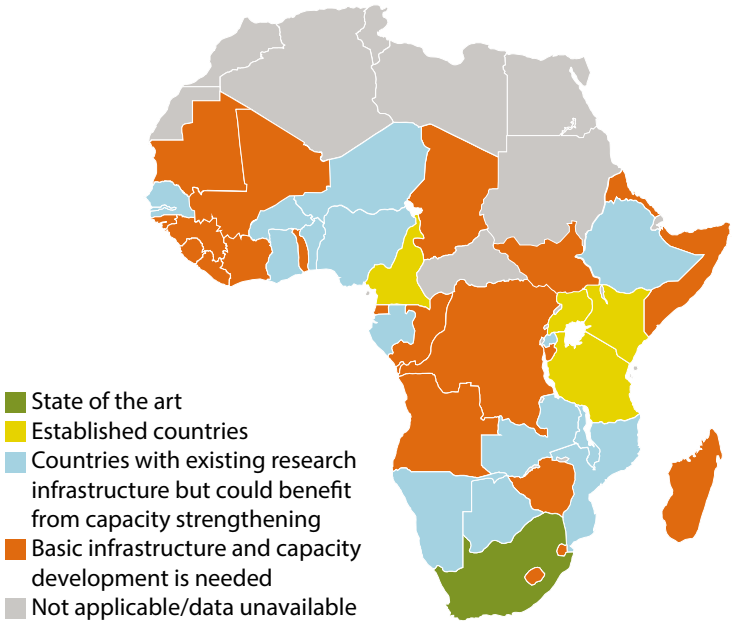

Figure 11 Categorisation of countries into research capacity for PRNIDs tiers

Many funders currently provide restricted funding, often disease specific, location specific and/or donor driven. This can enforce the silo effect observed in the fieldwork. The principles of the Paris Declaration on Aid Effectiveness,(34) offer a useful framework for achieving greater coherence between external funds and domestic structures and between donors themselves. More could be done to further implement recommendations.

The literature review and the fieldwork both indicated that sub-Saharan Africa is facing an increasing burden of NCDs, especially in those countries with greater economic development or higher urbanisation such as Kenya and Uganda. Frequently cited NCDs include cancer, diabetes and cardiovascular disease. Additionally, the fieldwork also found that NCDs were gaining prominence in

other countries such as Ethiopia, Cameroon, Eritrea, Gabon and Rwanda, although this was not reflected in the literature. This may be a product of the lag in publishing and it could be expected that in five years' time more of the literature will be devoted to these issues.

In contrast to the areas experiencing an increased burden of NCDs, respondents reporting NIDs as priority diseases were either from poorer countries, such as DRC, or from countries with higher rural populations. The urban-rural divide between NCDs and NIDs was also found in the literature review, and this division between NCDs and NIDs may have implications for the funding of NIDs going forward. It is also important to look at the connections between the two disease types. Many NCDs (e.g., diabetes) cause those affected to be immunocompromised and, therefore, at more risk of infectious disease.

Throughout the literature review and fieldwork, the discussion on the role of the private industry is limited. Where pharmaceutical companies are engaged, this is often in initiatives led by philanthropic organisations, such as the Bill & Melinda Gates Foundation or public-private partnerships such as the Program for Appropriate Technology in Health (PATH). In the last decade, South to South networks in health research have been emerging across the world, and countries such as Brazil, China, India and South Africa have begun to develop capacity in clinical research. South-South collaboration has enabled these countries to strengthen their own health systems while building capacity in partner countries. The rationale behind increased South-South collaboration builds upon the idea that developing countries share similar health needs, creating economies of scale when working together in procuring expensive research equipment and ensuring the translation of both specialised and indigenous knowledge on health research.(36) Collaboration with non-European research institutes was cited in the fieldwork with some respondents mentioning collaborations with researchers in China, India and Vietnam. EDCTP has also engaged non-African partners from other developing regions in some of its projects, such as Cambodia and Malaysia. By jointly expanding networks and incorporating institutions from other developing regions, there is the opportunity to accelerate the development of clinical research and knowledge translation of PRNIDs, while reflecting national priorities and shared development contexts.(37)

In addition to broadening the geographic scope of South-South collaborations, funders should also strive to ensure a range of stakeholders, including the pharmaceutical industry, local governments and policy/decision makers. This should ensure the sustainability of networks through informing policies, product development and improving health practices and interventions.(38)

Lastly, networked models aimed at developing capacity can be particularly difficult to evaluate, as capacity building is often seen as a subjective attribute and is highly context-specific. Therefore, another important consideration for funders of networked models of research capacity building efforts, whereby institutions are encouraged to collaborate across geographies, is in how to measure or evaluate the utility of a network.(39)

6. Conclusion

This report demonstrates significant regional differences in the volume of R&D in health research across sub-Saharan Africa. South Africa is the country of focus in over twice as many papers as any other country. The next most prevalent countries are Kenya, Uganda, Tanzania and Malawi. This trend is also observed in the funding literature.

Overall, global funding for the three main poverty-related diseases (HIV/AIDS, TB and malaria) has increased in the last decade, with a proliferation of funding streams emerging. Both literature searches and the fieldwork indicate high relative coverage of HIV/AIDS, in terms of research conducted and funding allocated, followed by malaria, TB and NIDs. The majority of respondents indicated that a lack of funding is the main barrier to the development of clinical research capacity in Africa, closely followed by the lack of policymakers' understanding of the benefits and importance of research. Lack of human resources and infrastructure were considered of less importance among the respondent interviewed as part of this study.

7. Recommendations for future research and opportunities

In providing insight into the current situation, the findings of this study point to additional questions, while highlighting the need for on-going research in the field. Opportunities and specific recommendations for future research by the donor community and health policy researchers are:

- More research with policymakers and policy influencers should be undertaken to explore why understanding, support and funding for research are lacking in sub-Saharan African countries where these were identified as the key barriers
- More in-depth and sophisticated research techniques should be employed to establish how scientists, officials and policymakers in sub-Saharan African countries contribute to and develop research priorities
- More research should be undertaken to get a better understanding of training needs and how they could be met cost-effectively. For example, low interest loans or other collaborative funding schemes were mentioned by a few respondents
- The findings of this study raise the question of whether there is a paradoxical effect of externally funded research, meaning that there could be instances in which external funding removes the impetus for national funding and sustainable national decision making structures to emerge. This could be examined by looking at comparisons and by using in-depth research techniques to explore opinions in countries where this was and was not highlighted as a concern
- There may be more opportunities for public-private partnerships in health research. Participants rarely mentioned the private sector. When they did (e.g., research on the candidate malaria vaccine RTS,S), the research is usually seen as being led by not for profit or government actors (e.g., Bill & Melinda Gates Foundation; PATH) and not the private sector actor themselves.

Acknowledgements

The project team is grateful that many expert respondents in Africa were very generous with their knowledge and insights. It is particularly impressive that so many found time to discuss these issues in countries with severe constraints on resources and manpower and with many pressing demands for the attention of health policy makers. This could be taken as an indication of the sentiment expressed by many interviewees that clinical research is vital to accomplishing the goal of better health for Africa.

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Annex 1: RAND Literature Review Search Terms

Peer-reviewed health literature

RAND Europe carried out a search of the literature using a combination of terms capturing diseases, research themes, policy areas and region/countries of interest. The terms were therefore composed of four sets of 'tags':

Disease tags were provided by EDCTP, derived from those used in an independent bibliometric study it had commissioned

AND

Research theme tags were:

"health research capacity building"[Title/Abstract] OR ("health research" [Title/Abstract] AND "capacity building" [Title/Abstract]) OR "health policy research"[Title/Abstract] OR (("health system"[Title/Abstract] OR "health systems"[Title/Abstract]) AND research[Title/Abstract]) OR "health services research"[Title/Abstract)] OR "phase II trials"[Title/Abstract] OR "phase III trials"[Title/Abstract] OR "trial site capacity"[Title/Abstract] OR (("clinical trials"[Title/Abstract] OR "clinical trial"[Title/Abstract]) AND (approval[Title/Abstract] OR approvals[Title/Abstract])) OR "Clinical Trials, Phase III as Topic"[Mesh] OR "Clinical Trials, Phase II as Topic"[Mesh]

OR "clinical trials" [Title/Abstract] OR "clinical approval" [Title/Abstract] OR "regulatory approval" [Title/Abstract] OR "drug development" [Title/Abstract] OR "drug discovery" [Title/Abstract] OR "drug registration" [Title/Abstract] OR ("product development"[Title/Abstract] AND partnership[Title/Abstract]) OR (health[Title/Abstract] AND "research and development"[Title/Abstract]) OR ("public private partnership"[Title/Abstract] AND health[Title/Abstract]) OR (mapping[Title/Abstract] AND "health system"[Title/Abstract]) OR (health[Title/Abstract] AND delivery[Title/Abstract]) OR "phase I trials"[Title/Abstract] OR "phase IV trials"[Title/Abstract] OR "donor funding"[Title/Abstract] OR "development funding"[Title/Abstract] OR "neglected tropical diseases"[Title/Abstract] OR NTD[Title/Abstract] OR (("clinical trials"[Title/Abstract] OR "clinical trial"[Title/Abstract]) AND recruitment[Title/Abstract]) OR (("clinical trials"[Title/Abstract] OR "clinical trial"[Title/Abstract]) AND "community engagement"[Title/Abstract]) OR (("clinical trials"[Title/Abstract] OR "clinical trial"[Title/Abstract]) AND patients[Title/Abstract]) OR "Clinical Trials, Phase I as Topic"[Mesh] OR "Clinical Trials, Phase IV as Topic"[Mesh] OR "Field Study"[Title/Abstract]

AND

Policy tags were:

"published government policy"[Title/Abstract] OR "government policy"[Title/Abstract] OR "ministry of health"[Title/Abstract] OR "ministries of health"[Title/Abstract] OR (minist*[Title/Abstract] AND health [Title/Abstract]) OR "national programmes"[Title/Abstract] OR "national programs"[Title/Abstract] OR policy[MeSH] OR health policy[MeSH] OR "department of health"[Title/Abstract] OR "health sector"[Title/Abstract] OR "medical services"[Title/Abstract] OR "Ministry of Public Health"[Title/Abstract] OR "public health"[Title/Abstract] OR "ministry of science"[Title/Abstract] OR "ministry of higher education" [Title/Abstract] OR "ministry of research"[Title/Abstract] OR "national control programmes"[Title/Abstract] OR "national control programs"[Title/Abstract] OR "national health policy"[Title/Abstract] OR "national health guidelines"[Title/Abstract] OR "health policy recommendations"[Title/Abstract] OR "treatment programme"[Title/Abstract] OR "treatment program"[Title/Abstract]

AND

Region/Country tags were:

("subsaharan africa"[Title/Abstract] OR "sub-saharan africa"[Title/Abstract] OR "sub saharan africa"[Title/Abstract] OR Africa South of the Sahara[MeSH])

OR

Africa[Title/abstract] OR Africa[MeSH]

Peer-reviewed funding literature

RAND Europe carried out a search of the literature using a combination of terms capturing regions/countries of interest, funding, clinical research, policy areas and diseases of interest. The terms were therefore composed of five sets of 'tags':

Region/Country tags were:

"subsaharan africa"[Title/Abstract] OR "sub-saharan africa"[Title/Abstract] OR "sub saharan africa"[Title/Abstract] OR Africa South of the Sahara[MeSH]) OR Africa[Title/abstract] OR Africa[MeSH]

AND

Funding tags were:

"research funding"[Title/Abstract] OR (funding[Title/Abstract] AND research[Title/Abstract]) OR (research[Title/Abstract] AND financ*[Title/Abstract]) OR (investment[Title/Abstract] AND health[Title/Abstract] AND research[Title/Abstract]) OR (financial[Title/Abstract] AND investment[Title/Abstract] AND research[Title/Abstract]) OR (monetary[Title/Abstract] AND commitment[Title/Abstract] AND research[Title/Abstract])

AND

Research tags were:

("Clinical Trials, Phase I as Topic"[Mesh] OR "Clinical Trials, Phase III as Topic"[Mesh] OR "Clinical Trials, Phase II as Topic"[Mesh] OR "Clinical Trials, Phase IV as Topic"[Mesh] OR "phase I trials"[Title/Abstract] OR "phase I trial"[Title/Abstract] OR "phase IV trials"[Title/Abstract] OR "phase II trial"[Title/Abstract] OR "phase II trials"[Title/Abstract] OR "phase III trials"[Title/Abstract] OR "phase II trial"[Title/Abstract] OR "phase III trial"[Title/Abstract] OR (("trial site"[Title/Abstract] AND "capacity building"[Title/Abstract]) OR ("trial site capacity"[Title/Abstract] AND building[Title/Abstract])) OR ("clinical trials" [Title/Abstract] AND (ethnic* AND approval[Title/Abstract]) OR ("clinical trials" [Title/Abstract] AND ("regulatory approval"[Title/Abstract]) OR (("health system"[Title/Abstract] OR "health systems"[Title/Abstract]) OR "health policy research"[Title/Abstract] OR AND research[Title/Abstract]) OR "regulatory approval" [Title/Abstract] OR epidemiology [Title/Abstract] OR "operational research"[Title/Abstract] OR "drug development" [Title/Abstract] OR "drug discovery" [Title/Abstract] OR "drug registration" [Title/Abstract] OR ("health services research" AND development[Title/Abstract]) OR (("product development"[Title/Abstract] AND partnership[Title/Abstract]) AND health[Title/Abstract]) OR ("public private partnership"[Title/Abstract] AND health[Title/Abstract]) OR (mapping[Title/Abstract] AND "health system"[Title/Abstract]) OR (health[Title/Abstract] AND delivery[Title/Abstract])

OR

Policy tags were:

"published government policy"[Title/Abstract] OR "government policy"[Title/Abstract] OR "national programmes"[Title/Abstract] OR "national programs"[Title/Abstract] OR "ministry of health" OR "ministries of health" OR

"Ministry of Public Health" OR "Ministries of Public Health" OR "department of health" OR "health sector"[Title/Abstract])

AND

Disease tags were:

HIV: "human immunodeficiency virus" [Title/Abstract] OR "human immuno-deficiency virus" [Title/Abstract] OR hiv[Title/Abstract] OR "acquired immunodeficiency syndrome" [Title/Abstract] OR "acquired immuno-deficiency syndrome" [Title/Abstract] OR "acquired immunodeficiency syndrome"[MeSH] OR "HIV infections"[MeSH]

NOT feline OR simian OR siv

OR

MALARIA: Malaria[Title/Abstract] OR plasmodium[Title/Abstract] OR anopheles[Title/Abstract] OR "black water fever"[Title/Abstract]

NOT physarum

TB: Tuberculosis[Title/Abstract] OR tuberculosis[MeSH] OR "tubercle bacillus"[Title/Abstract] OR tuberculin[Title/Abstract]

POVERTY: "neglected tropical disease"[Title/Abstract] OR "neglected tropical diseases"[Title/Abstract] OR NTD[Title/Abstract] OR "neglected infectious disease"[Title/Abstract] OR "neglected infectious diseases" [Title/Abstract] OR NID OR "protozoan infection" OR (Poverty[MeSH] AND "communicable diseases"[MeSH]) OR (disease*[Title/Abstract] AND poor*[Title/Abstract])

NOT chagas

BURULI ULCER: "buruli ulcer"[Title/Abstract] OR (buruli*[Title/Abstract] AND ulcer*[Title/Abstract]) OR "mycobacterium ulcerans" [Title/Abstract]

CYSTICEROCOSIS: Cysticercosis [Title/Abstract] OR "taenia solium" [Title/Abstract]

Dengue: Dengue[Title/Abstract] OR "aedes aegypti" [Title/Abstract]

Dracunculiasis: (("guinea-worm"[Title/Abstract] OR "guinea worm"[Title/Abstract]) AND disease*[Title/Abstract]) OR "dracunculus medinensis" [Title/Abstract] OR dracunculiasis[Title/Abstract]

Echinococcosis: Echinococcosis[Title/Abstract] OR "hydatid disease"[Title/Abstract] OR echinococcus[Title/Abstract]

Fascioliasis: Fasciolosis[Title/Abstract] OR fascioliasis[Title/Abstract] OR distomatosis[Title/Abstract] OR "fasciola hepatica" [Title/Abstract] OR "fasciola gigantica" [Title/Abstract]

Human African Trypanosom: (trypanosom*[Title/Abstract] AND Africa*[Title/Abstract] OR "sleeping sickness"[Title/Abstract] OR (trypanosom*[Title/Abstract] AND teste[Title/Abstract]) OR (trypanosom*[Title/Abstract] AND human[Title/Abstract])

Leishmaniasis:"sand fly"[Title/Abstract] OR sandfly[Title/Abstract] OR sandflies[Title/Abstract] OR "sand flies"[Title/Abstract] OR Leishmaniasis[Title/Abstract] OR Leishmania[Title/Abstract] OR phlebotomine[Title/Abstract] OR psychodidae[Title/Abstract] OR kalaazar[Title/Abstract] OR "kala-azar" [Title/Abstract] OR "kala azar" [Title/Abstract]

Lymphatic Filariasis: (lymphatic[Title/Abstract] AND filariasis[Title/Abstract]) OR elephantiasis[Title/Abstract] OR wuchereria[Title/Abstract] OR "brugia malayi" [Title/Abstract] OR Elephantiasis, Filarial[MeSH Terms]

Leprosy: Leprosy[Title/Abstract] OR Leprosy[MeSH] OR (Hansen*[Title/Abstract] AND disease*[Title/Abstract]) OR "mycobacterium leprae"[Title/Abstract]

Onchocerciasis: Onchocerciasis[Title/Abstract] OR Onchoceriasis[MeSH] OR "river blindness"[Title/Abstract]

Rabies: Rabies[Title/Abstract] OR Rabies[MeSH]

Schistosomiasis: Schistosomiasis[Title/Abstract] OR Schistosomiasis[MeSH] OR bilharzia*[Title/Abstract] OR "schistosoma mansoni"[Title/Abstract] OR "schistosoma haematobium"[Title/Abstract] OR "schistosoma intercalatum"[Title/Abstract] OR "schistosoma japonicum"[Title/Abstract] OR "schistosoma mekongi"[Title/Abstract]

Soil Transmitted Helminths: Helminths[MeSH] OR helminth*[Title/Abstract] OR hookworm*[Title/Abstract] OR "hook-worm"[Title/Abstract] OR "hook-worms"[Title/Abstract] OR "hook worms"[Title/Abstract] OR "hook worm"[Title/Abstract] OR "ascaris lumbricides"[Title/Abstract] OR "trichuris trichiura"[Title/Abstract] OR geohelminth[Title/Abstract] OR "necator-americanus"[Title/Abstract] OR "necator americanus"[Title/Abstract] OR "ancylostoma-duodenale"[Title/Abstract] OR "ancylostma duodenale"[Title/Abstract]

Trachoma: Trachoma[Title/Abstract] OR Trachoma[MeSH]

Yaws: Yaws[Title/Abstract] OR Yaws[MeSH] OR treponematos*[Title/Abstract]

Annex 2 Definitions of study types

Type of studies identified in the literature

Type of study	Description for the purposes of this report	Example
Empirical Study	Papers where primary or secondary data is used to describe a population or draw qualitative/quantitative inferences about an intervention or delivery mechanism	O'Meara, W. P., Smith, N., Ekal, E., Cole, D., & Ndege, S. (2011). "Spatial distribution of bednet coverage under routine distribution through the public health sector in a rural district in Kenya." *PloS One* 6(10): e25949.
Case Study	Papers in which a particular intervention or programme forms the basis of the study	Worley, S., Didiza, Z., Nomatshila, S., Porter, S., Makwedini, N., Macharia, D., & Hoos, D. (2009). "Wellness programmes for persons living with HIV/AIDS: experiences from Eastern Cape province, South Africa." *Global Public Health* 4(4): 367–385.
Review	Reviews analysing general material on a subject, including the establishment and operation of specific government health policies and disease programmes	Amazigo, U. (2008). "The African programme for onchocerciasis control (APOC)." *Annals of Tropical Medicine and Parasitology*, 102(Suppl. 1): 19–22.
Literature Review	Specific types of reviews incorporating systematic or rapid analysis of peer-reviewed work and/or grey literature in a field, where the aim is to understand the state of the evidence base in a particular subject area. This category also includes meta-analysis	Bethony, J. M., Cole, R. N., Guo, X., Kamhawi, S., Lightowlers, M. W., Loukas, A.,& Hotez, P. J. (2011). "Vaccines to combat the neglected tropical diseases." *Immunological Reviews*, 239(1): 237–270.
Commentary	'Commentary' pieces provide opinions on a given topic	Schrecker, T., & Labonte, R. (2004). "Taming the brain drain: a challenge for public health systems in Southern Africa." *International Journal of Occupational and Environmental Health*, 10(4): 409–415.
Framework conditions	Framework conditions' papers explore the wider contextual factors influencing health research, including variables affecting drug development, delivery and programme implementation	Quentin, W., König, H. H., Schmidt, J. O., & Kalk, A. (2008). "Recurrent costs of HIV/AIDS-related health services in Rwanda: implications for financing." *Tropical Medicine & International Health*, 13(10): 1245–1256.
Clinical trial	Randomised clinical trial or clinical study	Ndiaye, J. L., Randrianarivelojosia, M., Sagara, I., Brasseur, P., Ndiaye, I., Faye, B., & Gaye, O. (2009). "Randomized, multicentre assessment of the efficacy and safety of ASAQ–a fixed-dose artesunate-amodiaquine combination therapy in the treatment of uncomplicated Plasmodium falciparum malaria." *Malaria Journal* 8 (1): 125.

Evaluation/Impact assessment	Papers aimed at specifically evaluating a particular programme or intervention	Peltzer, K., & Henda, N. (2008). "Traditional birth attendants, HIV/AIDS and safe delivery in the Eastern Cape, South Africa-evaluation of a training programme." *South African Journal of Obstetrics and Gynaecology* 12(3): 140-145.
Conference review	An article summarising research presented at a particular conference or series of conferences	Kort, R. (2010). "5th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention: summary of key research and implications for policy and practice–Operations research." *Journal of the International AIDS Society* 13 Suppl. 1: S5.
Comparative country study	Papers which compare two or more countries in relation to areas such as the impact or burden of a disease, levels of funding, treatments and outcomes	Ojikutu, B., Makadzange, A. T., & Gaolathe, T. (2008). "Scaling up ART treatment capacity: lessons learned from South Africa, Zimbabwe, and Botswana." Current HIV/AIDS Reports, 5 (2): 94–98.
Comparative disease study	Papers which compare two or more diseases in relation to areas such as the impact or burden of a disease, levels of funding, treatments and outcomes	Tadesse, Z., Hailemariam, A., & Kolaczinski, J. H. (2008). "Potential for integrated control of neglected tropical diseases in Ethiopia." *Transactions of the Royal Society of Tropical Medicine and Hygiene* 102(3): 213–214.

Colophon

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