

# An Overview of Neglected Tropical Diseases in Sub-Saharan Africa

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**Abstract** Neglected tropical diseases (NTDs) affect many neglected and marginalised populations worldwide, but the burden in sub-Saharan Africa is rather overwhelming. Many of the endemic communities are of very low socioeconomic status with very limited access to health services. Investing to overcome the global impact of NTDs will yield a very high economic rate of return and impact significantly on the quality of life of these populations. In order to scale up interventions to achieve control, elimination or eradication of NTDs, programmes must be integrated into the regular health system of endemic countries. Efforts to expand global coverage and targeting of NTDs must therefore involve national and international harmonisation with coordination of the activities of partnerships devoted to control of these diseases. The continued support of major donors beyond the initial commitments announced during the London Declaration meetings remains crucial to funding the implementation of programmes. Ultimately, we need to address the social structures in which NTDs flourish and invest in research and development for new diagnostics and drugs.

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## Introduction

Neglected tropical diseases (NTDs) are a diverse group of diseases with distinct characteristics that thrive mainly among the poorest and deprived populations. Most NTDs are found primarily in low- and middle-income countries of Africa, Asia and Latin America. Within these countries, the affected populations are in themselves very neglected in many ways and are usually in the lowest socioeconomic status. Populations, where people have little access to clean water, improper ways of disposing human waste and therefore live in unsanitary environments, tend to have a high burden of NTDs (Hotez et al 2006, WHO 2013).

The World Health Organization has prioritised 17 of these NTDs in 149 endemic countries for focused global attention (Table 1). These affect more than 1.4 billion people, costing developing economies billions of dollars every year. This list is by no means exhaustive since there are some other diseases in neglected populations that are not on this list; however, this list represents the biggest disease burden they face (WHO 2010).

The burden of these diseases is extremely high in sub-Saharan Africa (SSA). For example, approximately 40 % of the global burden of lymphatic filariasis (LF) is found in SSA, while all the remaining cases of guinea worm disease (GWD) are also found in the same region (WHO 2010).

The German government under GTZ (now GIZ) played an important role in the NTD movement by cosponsoring with the World Health Organization (WHO) two key meetings of leading stakeholders in 2003 and 2005 in Berlin. These meetings achieved two important outcomes: (i) a unified support for an integrated approach in addressing NTD control and elimination efforts and (ii) the brand “neglected tropical diseases” was coined and has since become part of the global health nomenclature (WHO 2004, 2006).

Prior to the Berlin meetings, several global directives in the form of World Health Assembly resolutions had been passed to mobilise political and social capital to address these diseases individually, and many more have been passed since then (Table 2) (WHO 2015).

**Table 1** WHO prioritised neglected tropical diseases for control

Helminth	Protozoa
Cysticercosis/taeniasis	Chagas disease
Dracunculiasis (guinea worm disease)	Human African trypanosomiasis (sleeping sickness)
Echinococcosis	Leishmaniases
Food-borne trematodiasis	Bacteria
Lymphatic filariasis	Buruli ulcer
Onchocerciasis (river blindness)	Leprosy (Hansen’s disease)
Schistosomiasis	Trachoma
Soil-transmitted helminthiasis	Yaws
Virus	
Dengue and chikungunya	
Rabies	

**Table 2** Selected resolutions of the World Health Assembly concerning neglected tropical diseases

Subject area	Resolution	Title	Year
Neglected tropical diseases	WHA66.12	Neglected tropical diseases	2013
Schistosomiasis	WHA65.21	Elimination of schistosomiasis	2012
Chagas disease	WHA63.20	Chagas disease: control and elimination	2010
Leishmaniasis	WHA60.13	Control of leishmaniasis	2007
Buruli ulcer	WHA57.1	Surveillance and control of <i>Mycobacterium ulcerans</i> disease	2004
Dracunculiasis	WHA57.9	Eradication of dracunculiasis	2004
Human African trypanosomiasis	WHA56.7	Pan-African tsetse and trypanosomiasis eradication campaign	2003
Dengue and dengue haemorrhagic fever	WHA55.17	Prevention and control of dengue fever and dengue haemorrhagic fever	2002
Schistosomiasis and soil-transmitted helminthiasis	WHA54.19	Schistosomiasis and soil-transmitted helminth infections	2001
Trachoma	WHA51.11	Global elimination of blinding trachoma	1998
Chagas disease	WHA51.14	Elimination of transmission of Chagas disease	1998
Leprosy	WHA51.15	Elimination of leprosy as a public health problem	1998
Lymphatic filariasis	WHA50.29	Elimination of lymphatic filariasis as a public health problem	1997
Human African trypanosomiasis	WHA50.36	African trypanosomiasis	1997
Onchocerciasis	WHA47.32	Onchocerciasis control through ivermectin distribution	1994
Dengue and dengue haemorrhagic fever	WHA46.31	Dengue prevention and control	1993
Endemic treponematoses	WHA31.58	Control of endemic treponematoses	1978
Leprosy	WHA30.36	Leprosy control	1977

These resolutions were all very comprehensive, for example, the 50th World Health Assembly held in Geneva in May 1997 called on Member States to take advantage of recent advances in the understanding of lymphatic filariasis and the new opportunities for its elimination by developing national plans leading to its elimination, as well as for the monitoring and evaluation of programme activities; to strengthen local programmes and their integration with the control of other diseases, particularly at the community level, in order to implement simple, affordable, acceptable and sustainable activities based on community-wide treatment strategies, but supplemented where feasible by vector control and improved sanitation; to strengthen capabilities for training, research, laboratory diagnostic, disease management and data management in order to improve clinical, epidemiological and operational activities directed towards eliminating lymphatic filariasis as a public health

problem; and to mobilise support of all relevant sectors, affected communities and non-governmental organisations for the elimination of the disease (WHA50.29).

The Assembly also invited other specialised agencies of the United Nations system, bilateral development agencies, non-governmental organisations and other groups concerned, to increase cooperation in the elimination of lymphatic filariasis through support of national and international programmes relevant to the prevention and elimination of lymphatic filariasis. Finally, they requested the Director General of WHO to bring to the attention of the other specialised agencies and organisations of the United Nations system, bilateral development agencies, non-governmental organisations and other groups concerned the need for closer collaboration in the elimination of lymphatic filariasis as a public health problem, to mobilise support for global and national elimination activities (WHA50.29).

This is probably the most comprehensive global commitment one could get for a disease elimination programme. However, by the year 2005, only 8 out of the 38 endemic countries in Africa had active lymphatic filariasis elimination programmes, and of these only Burkina Faso, Ghana, Togo and Zanzibar were treating their entire national populations at risk. Clearly, targeting the individual diseases was not the most efficient way of dealing with the huge burden of NTDs; hence, in 2013, a more encompassing resolution WHA66.12 called for monitoring progress in achieving the targets for NTDs set in WHO's road map for accelerating work to overcome the global impact of NTDs and intensified, integrated measures and planned investments to improve the health and social well-being of the affected populations (WHA66.12).

There are many factors that have contributed to the belief that something can really be done about these diseases which hitherto were perceived to have no remedies. As a result, these World Health Assembly resolutions have managed to draw attention by mobilising resources and political capital to support these initiatives. These factors include among others:

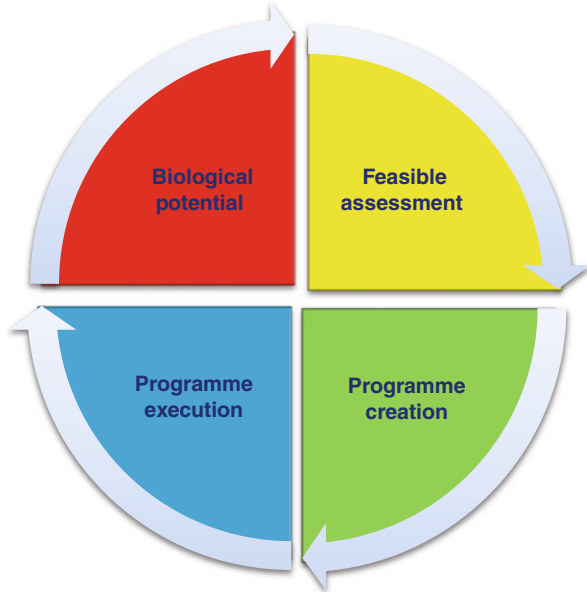
- Better understanding of the diseases
- Improved delivery mechanisms including opportunities for integration
- Investment case including cost-benefit evaluation, funding and economic considerations
- Moral, political and social determinants
- Drug donations

## **Better Understanding of the Diseases**

Research over many years has played a critical role in providing the necessary information to understand these diseases and the subsequent development of interventions and programme creation. As a result, we have a better understanding of the:

- Epidemiology of these diseases
- Transmission dynamics and vector biology
- Socioeconomic factors

**Fig. 1** Control programme planning process



These have also led to:

- Development of drugs and diagnostics
- Testing of new interventions
- Operational delivery of interventions
- Development of monitoring and evaluation tools to assess the impact of these interventions
- The development of better surveillance tools

Thus, knowledge generated in recent years has demonstrated aptly that the biological potential of controlling, eliminating and even eradicating these NTDs does exist, and ample diagnostic tools and strategies are available to assess the burden and distribution of these diseases and that it is possible to create and execute control programmes effectively if we can mobilise the necessary economic, social and political capital (Fig. 1).

### **Improved Delivery Mechanisms and Opportunities for Integration**

Various mapping studies and other available anecdotal information suggest that most countries in SSA have more than three of these diseases (Fig. 2). Strategies, tools and interventions available for combating these diseases can be used for more than one disease. Therefore, the integration and co-implementation of these

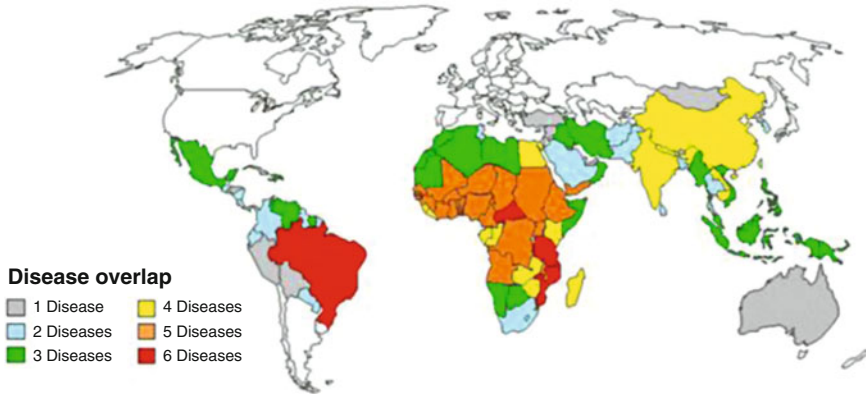


Fig. 2 Extent of disease overlap

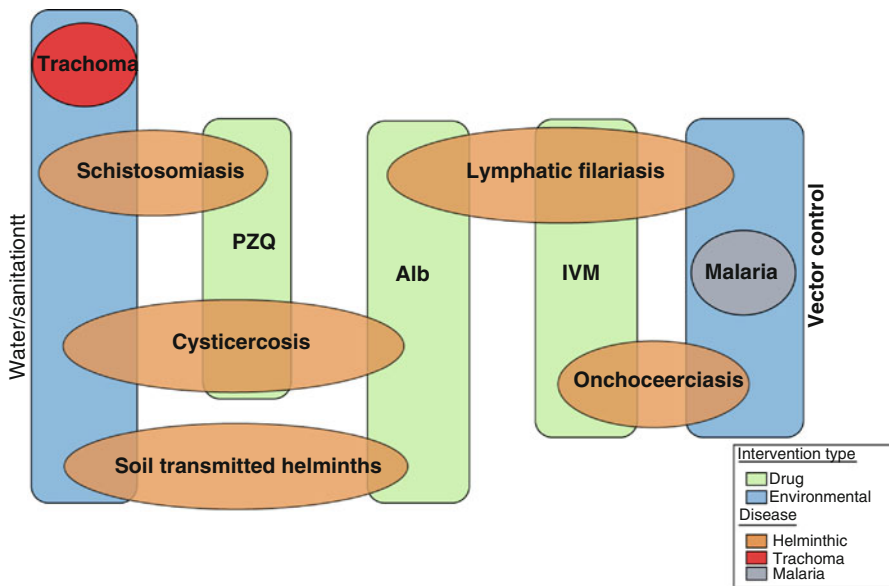


Fig. 3 Some strategies, tools and interventions for NTD control

strategies, tools and interventions is the key to the control/elimination of the diseases (Gyapong et al. 2010; Molyneux et al. 2005).

Figure 3 illustrates how improved water and sanitation, drugs (praziquantel, albendazole and ivermectin) and vector control could be delivered as an intervention package to fight several NTDs and malaria. As a result, the World Health Organization (WHO) recommends two main strategies for NTD control: preventive chemotherapy and transmission control (PCT) and innovative intensified disease management (IDM) (WHO 2010, 2015).

PCT focuses on diseases for which a strategy exists as well as on tools and the availability of safe and effective drugs that make it feasible to implement large-scale preventive chemotherapy. The diseases amenable to the PCT strategy include cysticercosis, dracunculiasis (guinea worm disease), food-borne trematode infections, lymphatic filariasis, onchocerciasis, schistosomiasis and soil-transmitted helminthiasis. Blinding trachoma control through the SAFE strategy – combining drug treatment with hygiene and environmental management – can be linked to helminth control interventions to improve the overall health of affected communities (WHO 2010, 2015).

IDM focuses on diseases for which cost-effective control tools do not exist and where large-scale use of existing tools is limited. The diseases include Buruli ulcer, Chagas disease, human African trypanosomiasis and leishmaniasis and share the following characteristics:

- Difficult and costly to manage in terms of diagnosis, treatment and follow-up.
- Burden is poorly understood.
- Lack of appropriate control tools.
- Relatively lower investment in research and development.
- People affected often live in remote rural areas with limited access to diagnosis and treatment (WHO 2010, 2015).

Having prioritised NTDs for control, having mapped their distribution and being armed with interventions that work, the biggest challenge has been to deliver these interventions through a health system in the midst of severe human resource constraints and other health system challenges (Gyapong et al. 2010). The health worker/population ratio is extremely high in Africa with some areas not served at all. In order to improve access, there is the need to engage other cadre of staff for the delivery of these interventions and explore other delivery mechanisms such as school-based and community-based distribution. The community-directed treatment approach, which provides opportunities for health services to work closely with, and the community to deliver interventions have been shown to be highly feasible (Amazigo et al. 2007; Gyapong et al. 2000; WHO 2008). These studies have found community volunteers to be capable, motivated and reliable; however, they need to be provided with incentives. With this approach, the community decides the timing of the distribution and selects distributors to be trained by health workers. The distribution is done at the convenience of community, and the health worker helps with monitoring and supervision.

Such large-scale community-based treatments could be associated with inadvertent exposure of some population even when standard operating procedures are adhered to. This requires putting in place an efficient community education, monitoring and evaluation systems. The challenge of dealing with serious adverse events in any mass drug distribution exercise can be daunting particularly if an adverse reaction like Stevens-Johnson syndrome occurs. How strong is our pharmacovigilance infrastructure to pick up these occasional mishaps? (Gyapong et al. 2003)

Efforts to expand global coverage and targeting of NTDs must involve national and international harmonisation. We need coordination of the activities of partnerships devoted to the control or elimination of these diseases. Programmes with similar delivery strategies and interventions such as those for lymphatic filariasis,

onchocerciasis and soil-transmitted helminthiasis could be managed on the same platform and together. In order to scale up neglected tropical disease (NTD) interventions to achieve complete eradication, programmes must be integrated into the regular health system of countries with the principles of:

- Where things fit well, do them together.
- Where things do not, do them separately.
- Look for ways of coordinating efforts to deliver a more cost-effective way.
- Make integration an “attitude”, not a strategy.

## Investment Case

Investment case (IC) for the control, elimination or eradication of these diseases has been done in various forms including the traditional cost-benefit evaluation of proposed interventions. The “critical elements” of an IC include the proposed investment, the rationale for the investment, the management and the governance. The final product is practical in nature, going beyond a description of what to do, by describing how to do it with respect to some core methodological issues. A reasonable projected cost based on an investment case have garnered political and social support especially when there is indication that these interventions will not jeopardise existing health systems but rather offer opportunities for synergies with health system activities (Molyneux 2008, Cochi and Dowdle 2011).

Investing to overcome the global impact of neglected tropical diseases makes the case that the elimination and control of NTDs will be a “litmus test” for universal health coverage. Endemic countries can contribute by increasing domestic investments and scaling up interventions. Large middle-income economies can also play an important role in developing new diagnostics and medicines and in influencing market dynamics. The recent report of the Uniting to Combat NTDs coalition estimates cash and in kind aid at about US\$ 300 million in 2014, excluding donated medicines. Investing to overcome the global impact of neglected tropical diseases sets investment targets for universal coverage against NTDs that are more than double current levels of foreign aid – as much as ten times when including investments in vector control. It is unlikely that an increase in aid of this magnitude can be achieved in the current global health financing climate. NTD control must become an integral part of national health plans and budgets if it is to achieve the scale of universal coverage (Cochi and Dowdle 2011, WHO 2015).

## Moral, Political and Social Determinants

The “duty to rescue” is a moral one! The potential of getting rid of a disease forever or controlling it to insignificant levels will protect future generations from its scourge, but beyond all, the notion of disease control/eradication as a public good is one that cannot be overlooked. Firstly, an ethical analysis presents a dimension of the



investment case for control/eradication. This can be called the “moral investment” that is seldom discussed in the literature. This is an important dimension to emphasise since it has long been recognised that social and political commitment is essential for the successful control/eradication of a disease. Social and political commitment involves moral motivation, or the ethical reasons to act. It is thus important to understand those reasons and how they are relevant in decisions involving large-scale public health interventions. Secondly, as moral beings, members of the global community have a fundamental interest in identifying what ethical obligations they have to one another. In the context of disease control/eradication, such obligations can impact the lives of millions of people and reflect choices about the kind of world in which we want to live: one where all are free from the burden of disease or one where inequity exists and only some have that luxury of good health (Hotez et al. 2006).

Political and societal support is therefore crucial for initiating and delivering these programmes and must be mobilised at all costs. Broad social perception of the importance of the disease is essential, and without it, there is no programme! Polio, guinea worm disease and lymphatic filariasis elimination/eradication was launched with the high-level political and technical consensus inherent in World Health Assembly resolutions. Polio eradication from the onset had tremendous societal and political support because of the awareness of the disease in developed and endemic countries. Resource mobilisation by Rotary International, their network of volunteers and the overwhelming support of civil society groups have been the lifeblood of the programme. Chinese President Zemin, South African President Mandela and US President Clinton have heightened the programme’s visibility and through that raised lots of resources for the programme. The guinea worm eradication initiative has also relied heavily on political advocacy, benefiting tremendously from the support of former heads of state such as US President Carter.

Neglected tropical diseases (NTDs) as a brand on the other hand had not had that much visibility with heads of states until recently when President Bush committed USD 350 million to their control. The recent NTD forum in London and the follow-up in Paris convened by the Gates foundation have raised the profile of NTD elimination even the more. Total commitments at these fora were way in excess of USD 800 million. The challenge is to maintain the commitment of central-level authorities for a campaign that targets a very small proportion of the national morbidity burden in the poorest communities. Sustaining societal-level support is complicated by the logistic difficulties of routinely supplying, supervising and ensuring surveillance in remote rural areas and the fatigue of multiple years of national immunisation days. A lot more advocacy is therefore required especially at the local level to maintain the required steam (Hotez et al. 2006; Molyneux et al. 2005; Gyapong et al. 2010).

## **Drug Donations**

Investing in drug/vaccine development for interventions targeted for elimination is a critical part of the equation. This is where big pharmaceutical industry comes in. Once these products are developed, they need to be tested for their applicability in the field. When they are proven to be efficacious, access to these medicines at

reasonable costs becomes an issue. Given that these diseases occur mainly in the poorest communities, most affected individuals would be unable to afford these essential drugs. The decision by many of the pharmaceutical companies to donate or supply at production cost to the programmes is therefore highly commendable and a good example of appropriate corporate social responsibility. In the case of LF elimination GlaxoSmithKline and Merck decided to donate Albendazole and Ivermectin to the global programme for as long as they are needed as part of the corporate social responsibility. Diethylcarbamazine (DEC), for instance, is not a donated product in Southeast Asia, so it has to be procured at production cost. Table 3 shows a list of pharmaceutical companies that contribute to the NTD portfolio of medicines.

The pharmaceutical industry donated nearly 1.35 billion treatments in 2013, representing a 35 % increase since 2011. A set of forms is available to facilitate application, review and reporting and to improve programme coordination and integration. This puts the Ministry of Health in control by centralising all country requests for medicines and providing oversight for progressive ownership of control programmes (WHO 2015).

Beyond the drug donation, some of the pharmaceutical companies such as GlaxoSmithKline and Merck have in addition made substantial investments in support for programme delivery at the global and country level, operational research and capacity building in endemic areas and in many other areas. These investments have been critical and timely for success of the programme.

## Control, Eliminate or Eradicate?

Disease control, elimination and subsequent eradication are a desirable goal that many health systems hope to achieve. It represents the ultimate in global equity and the definitive outcome of good public health practice. The elimination of smallpox over three decades ago demonstrated that disease eradication could bring lasting benefits to society. As a result today, several diseases have been identified as potentially eradicable with massive investments by several stakeholders. In 1997, the Dahlem conference on eradication of infectious diseases provided some working definition for disease elimination and eradication. These definitions have since been revised based on better understanding of epidemiology and control of infectious diseases. The recent Ernst Strüngmann Forum helped to build consensus around these working definitions (Cochi and Dowdle 2011; Dowdle 1999).

*Control* refers to “reduction of disease incidence, prevalence, morbidity, and/or mortality to a locally acceptable level as a result of deliberate efforts; continued intervention measures are required to maintain the reduction”.

*Elimination of transmission* (interruption of transmission) means “reduction to zero of the incidence of infection caused by a specific pathogen in a defined geographical area, with minimal risk of reintroduction, as a result of deliberate efforts; continued actions to prevent re-establishment of transmission may be required”.

The process of documenting elimination of transmission is called “verification”.

**Table 3** Medicines for controlling neglected tropical diseases donated by the pharmaceutical industry

Pharmaceutical company	Medicine	Donation
Bayer	Nifurtimox	Up to 300,000 tablets of 120 mg and 20,000 tablets of 30 mg per year during 2014–2019 for human African trypanosomiasis; donation made through WHO
	Nifurtimox	Up to 1 million tablets of 120 mg including paediatric formulations in 30 mg tablets during 2012–2017 for second-line treatment of Chagas disease; donation made through WHO
	Suramin	Up to 10,000 1 g vials per year until November 2017 for human African trypanosomiasis; donation made through WHO
Eisai	Diethylcarbamazine	Up to 2.2 billion tablets until 2020 for lymphatic filariasis; donation made through WHO
Gilead sciences	AmBisome	Up to 445,000 vials during 2012–2016 for visceral leishmaniasis in South East Asia and East Africa; donation made through WHO
GlaxoSmithKline	Albendazole	Unlimited supply for as long as needed for lymphatic filariasis and up to 400 million tablets during 2012–2016 for soil-transmitted helminthiases; donation made through WHO
Johnson & Johnson	Mebendazole	Up to 200 million tablets per year during 2012–2016 for soil-transmitted helminthiases control programmes for school-age children; donation made through WHO
Merck & Co., Inc	Ivermectin	Unlimited supply for as long as needed; donation made directly to countries for lymphatic filariasis and onchocerciasis
Merck KGaA	Praziquantel	Up to 250 million tablets per year for an unlimited period for schistosomiasis; donation made through WHO
Novartis	Multidrug therapy (rifampicin, clofazimine and dapsone in blister packs) and loose capsules of clofazimine	Unlimited supply for as long as needed for leprosy and its complications; donation made through WHO
	Triclabendazole	Unlimited supply for fascioliasis and paragonimiasis; donation made through WHO
Pfizer	Azithromycin	Unlimited quantity for blinding trachoma until at least 2020
Sanofi	Eflornithine	Unlimited quantity until 2020 for human African trypanosomiasis; donation made through WHO
	Melarsoprol	Unlimited quantity until 2020 for human African trypanosomiasis; donation made through WHO
	Pentamidine	Unlimited quantity until 2020 for human African trypanosomiasis; donation made through WHO

Source: WHO (2015)

*Eradication* means “permanent reduction to zero of a specific pathogen, as a result of deliberate efforts, with no more risk of reintroduction”. The process of documenting eradication is called “certification”.

Current global eradication initiatives are poliomyelitis and guinea worm. In the short term, measles and rubella could get onto the list. Potentially cysticercosis and lymphatic filariasis may be included in the list in the long term. Onchocerciasis and yaws are not on the list of International Task Force for Disease Eradication but have received considerable attention in recent times.

## **The Role of Research**

Research has been very key to this whole process. Basic research to understand the biology and transmission dynamics of these diseases continues to open opportunities to the development of diagnostic tools and drugs. Several clinical trials are ongoing to help optimise these tools for field use. The importance of research in identifying solutions and options for overcoming implementation obstacles in health systems and programmes has been pursued vigorously. Such implementation research has helped to resolve many operational challenges in a multidisciplinary approach. This form of research addresses implementation bottlenecks, identifies optimal approaches for a particular setting and promotes the uptake of research findings: ultimately, it leads to improved health care and its delivery. There are however many disease-specific research questions that need answers, which are discussed in subsequent chapters.

## **Conclusion**

The control of neglected tropical disease is definitely a good public health investment with potentially high economic return. The political platform provided by World Health Assembly resolutions coupled with drug donations by pharmaceutical companies and financial support from the international community sets the scene for success. The remaining chapters in this book address some of these NTDs that are prevalent in sub-Saharan Africa, focusing on:

1. *Epidemiology of the disease*: distribution, burden and public health impact of disease in sub-Saharan Africa
2. *Basic biology*: life cycle, mode of transmission, disease presentation and diagnosis of the infection/disease
3. *Diagnostic tools*: what is available? Are they adequate? Are their use supported by evidence? How cost-effective is their application? Are they operationally feasible?

4. *Treatment and control strategies*: what are the available options? Are currently available strategies effective? Are they evidence-based? Is their application sustainable/cost-effective?
5. *Chemotherapy-based strategies*: is the choice of first-line treatment evidence-based? What are the gaps in knowledge, for example, dose and regimen, geographic/regional variation in effect, their implications on treatment and control etc.? Was there any hosts' variation in efficacy, for example, between children and adults and implications for control? Were there opportunities for combination therapies and would they improve therapeutic efficacy and/or slow resistance development? How reliable are the data used over the years for policy recommendations?
6. *Challenges of programme implementation*
7. *Further research for policy and control*
8. *Outlook for the next decade*

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