Neglected Tropical Diseases

John O. Gyapong
Boakye A. Boatin *Editors*

Neglected Tropical Diseases - Sub-Saharan Africa

Second Edition

Springer

Neglected Tropical Diseases

Series Editor
Peter J. Hotez, National School of Tropical Medicine, Baylor College of Medicine and Texas Children's Hospital, Houston, USA

This book series publishes contributions from individuals engaged in any of the fields related to neglected tropical diseases clearly connected with their exceptional status as neglected. Specific focus of each title lies on the discussion of relevant issues in particular geographic areas of the world. Each volume of the series deals with the unique situation of one region and is built up by a team of authors lead by an expert for the geographic area discussed. This series provides a forum for wealthy discussion on the topic of neglected infectious diseases with a clear focus on basic scientific topics, clinically relevant issues as well as policy issues associated with the area. Topics to be covered: detection, diagnosis, monitoring, vaccine and drug development, new treatments, translational research (link basic research and health system research), clinical aspects, epidemiology, development of new surveillance and control strategies, public health/health policy issues.

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This book on Neglected Tropical Disease in Sub-Saharan Africa is dedicated to the memory of:
Dr Likezo Mubila for her dedication to the control of NTDs
Dr Dominque Kyelem for his steadfast drive to research in lymphatic filariasis
Dr Ricardo Thompson for his leadership and commitment as a research scientist in NTDs.
Dr Mwele Malecela for her vision and leadership in the efforts toward the research, control, elimination, and eradication of the neglected tropical diseases

Foreword to the Second Edition

I congratulate Professors Gyapong and Boatin on their second edition of *Neglected Tropical Diseases—Sub-Saharan Africa*. Africa remains the epicenter of the world's neglected tropical diseases (NTDs), generally considered the most common afflictions of people who live in extreme poverty. In parallel, there also remains no shortage of poverty on the African continent. According to the World Bank, Africa's population accounts for roughly two-thirds of our global citizens living in destitution. Poverty and disease go hand in glove, especially for the NTDs—the NTDs overwhelmingly thrive among the poor, and in turn the NTDs promote poverty because of their long-term or chronic deleterious effects including disfigurement, blindness, growth failures, cognitive delays, and adverse reproductive outcomes.

In specific regard to the NTDs, what does it mean that approximately 460 million Africans live at or below World Bank extreme poverty levels? From my perspective, this translates to a stark reality that probably all these individuals likely suffer from at least one NTD, including hookworm infection or other soil-transmitted helminthiases, schistosomiasis, lymphatic filariasis, onchocerciasis, scabies, yaws, and many others. Thus, while great progress has been made in terms of mass drug administration and preventive treatments to reduce the prevalence or transmission of Africa's major NTDs, these conditions remain highly prevalent. But poverty is not the sole driver—Africa is undergoing sweeping changes due to other social and physical determinants. Among the former is progressive urbanization with more and more people living in large African cities, which are gradually becoming megacities of more than 10 million people. We are also starting to see shifts with some soil-transmitted helminth infections and schistosomiasis now occurring in urban and peri-urban locations. Political instability is also a driver especially in some of Africa's fragile nation states where it is difficult to implement control and elimination programs for the NTDs. And then, climate change and its associated higher temperatures and higher rainfall patterns appear to be shifting the geographic ranges of several NTDs including schistosomiasis and hookworm infection, among others.

Therefore, it is important to recognize that the NTDs are not static and as Africa's population begins coalescing into megacities such as Kinsasha, Lagos, or Dar, we should expect shifts in the epidemiology and biodiversity of their NTD pathogens. Solving Africa's NTD problem will require a multi-pronged approach including social scientists to design culturally sensitive interventions. We must expand mass treatments, especially for diseases such as schistosomiasis, a disease for which only

about 10–15% of children have access to praziquantel, together with case detection and treatment for NTDs such as HAT and leishmaniasis. Mass treatment needs to be accompanied by intersectoral approaches that embrace sanitation, clean water, and other environmental measures. In parallel, vector control will be needed for leishmaniasis, HAT, and other NTDs. The good news is that through these approaches we are beginning to see declines in the number of cases of lymphatic filariasis, onchocerciasis, and HAT, so it is now possible to realistically discuss the potential for eliminating these NTDs. For others, we need to enlarge programs of research and development, which must include capacity enhancement for African scientists.

I am excited that Professors Gyapong and Boatin have embarked on a new edition. Regular updates will be needed to keep up with these dramatic Anthropocene shifts. The fight to combat NTDs on the African continent continues.

Houston, TX, USA Peter Hotez

Preface

The second edition of this book has been necessitated by some advances in the field of neglected tropical diseases (NTDs) since 2016 when the first edition was published. Inasmuch as NTDs occur in neglected populations across the world, we focus on the major challenges of sub-Saharan Africa (SSA). In the first edition, 12 of the major NTDs in Africa were presented. They included Buruli ulcer, Guinea worm, human African trypanosomiasis, leishmaniasis, leprosy, Loa loa and lymphatic filariasis, onchocerciasis, podoconiosis, schistosomiasis, soil-transmitted helminths, trachoma, and yaws. In this edition, all these have been revised at varying detail based on new knowledge that has become available in the last 5–6 years. Leishmaniasis is presented as two separate sections within the chapter. Scabies has been added. Additionally, we have dedicated a chapter to the elimination of onchocerciasis in view of the new knowledge and dynamics supporting a paradigm change from control to elimination. The areas which transcend all the NTDs in sub-Saharan Africa such as health systems and their role in NTDs, the social and economic impact, and the role of vector control in NTDs have also been revised and best read together with the specific diseases. The issue of female genital schistosomiasis (FGS) is given prominence in the chapter on "Social and economic impact of NTDs," and a new chapter on "Drug donations" has been included.

The structure and the common theme for all the chapters were retained. However, important variations on the theme given new available knowledge are evident in the sections within the chapters. The new chapter on "Drug donations" provides additional detailed information and cross-references to the donated medicines that are used in the management of virtually all the diseases presented in the book. Discussion on diagnostics—new and or improved—especially for those diseases that are targeted for elimination is a common thread in the chapters. Future control tools including drugs as well as critical research needed to help overcome the challenges that have been identified for each disease are highlighted again.

Cross-cutting challenges that continue to persist for the control/elimination of the diseases have been reemphasized to maintain the need to try and overcome them. Additionally, new specific challenges, for example, the presence of Guinea worm in dogs just as one approached the "end game" in its eradication, are presented. With these in mind, the section on the expected situation for each disease in the next decade where appropriate is highlighted for each of the chapters.

We have been fortunate to be able to maintain most of the original authors—almost entirely all African research scientists—to undertake the revision of their chapters. Several new authors have also been brought in. As before, they also have experience in the ministries of health in the control of the diseases, have research experience in tropical medicine, and have had practical experiences in managing NTDs in their countries. It is regretted that some of the authors of the first edition were unable to take part in preparing this second edition, but we are grateful for their support and advice.

The revision for this edition of the book took far longer than one expected, the challenge being mostly in obtaining fresh and current data as well as relevant information through time. Despite this, the authors stayed the course as a team and in close collaboration with each other. Their contributions, as well as that of the many people who are not listed in the book but helped in diverse ways, are greatly acknowledged.

The hope remains the same: that this second edition of the book will provide some basic information on the specific NTDs and the special ways that NTDs present in SSA and will be a useful resource read for all who are interested in doing something about NTDs in SSA. It is also our wish that the wide range of references on NTDs will be useful to readers.

Ho, Ghana — John O. Gyapong
Accra, Ghana — Boakye A. Boatin

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We acknowledge our colleagues who were part of the first edition but for various reasons were unable to participate in the second edition. They include Dr Dieudonne P. Sankara, Dr Andrew S. Kokor, Dr Junerlyn Agua-Agum, and Dr Daniel Argaw. We thank them for their original concept and contribution.

The first edition of this work was partly supported by a grant (Grant Number: G1001337) from the UK Medical Research Council (MRC) and the UK Department for International Development (DFID) under the MRC/DFID Concordat agreement, through the Liverpool School of Tropical Medicine Council and managed by the School of Public Health, University of Ghana.

This second edition was done while Professor John Gyapong was on sabbatical leave at the Global Health Program of the Graduate School of Arts and Sciences, Georgetown University, Washington DC, USA.

About the Book

This book provides an overview of the major neglected tropical diseases (NTDs) occurring in sub-Saharan Africa, such as leishmaniasis, Buruli ulcer, and schistosomiasis. In well-structured chapters, the epidemiology and biology of these parasitic diseases will be discussed in detail. Further, diagnostics and therapeutic approaches as well as prevention strategies will be reviewed. The book will be of interest to basic researchers and clinicians engaged in infectious disease, tropical medicine, and parasitology and a must-have for scientists specialized in the characteristics of the sub-Saharan region.

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About the Editors

John O. Gyapong is Public Health Physician and Epidemiologist. He studied Medicine at the Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, and later studied Public Health (MSc) and Epidemiology (PhD) at the London School of Hygiene and Tropical Medicine of the University of London. His main area of research is infectious diseases epidemiology, especially lymphatic filariasis and other neglected tropical diseases and malaria. He established and managed the Ghana Filariasis Elimination Programme for eight (8) years where he was also in charge of the Onchocerciasis Control. For twelve (12) years, he was Director for Research and Development of the Ghana Health Service where he was responsible for health systems and implementation research.

He served as Vice-Chancellor of the University of Health and Allied Sciences, Ho, from 2016 to 2022. From 2011 to 2016, Professor Gyapong was the Pro-Vice-Chancellor of the University of Ghana responsible for Research, Innovation and Development. He was the Vice-Dean and Professor of Epidemiology and Disease Control at the School of Public Health of the University of Ghana and Adjunct Professor of International Health at the Georgetown University in Washington DC, USA. He serves on several international research review committees and boards and has over 150 publications in peer-reviewed journals.

Boakye A. Boatin is Public Health Physician and Epidemiologist with degrees in medicine, international public health, and epidemiology. He studied medicine in Ghana and undertook postgraduate studies in the Liverpool School of Tropical Medicine (Community Health), University of Liverpool, and epidemiology at the London School of Tropical Medicine and Hygiene (LSTMH) of the University of London. His research focuses on infectious diseases epidemiology, particularly onchocerciasis, schistosomiasis, and human African trypanosomiasis. Until his retirement from the World Health Organization (WHO), he led research in integrated community-based interventions and lymphatic filariasis at the Special Programme for Tropical Diseases (TDR) and had a short stint as the head of the Aids Medicines and Diagnostics (AMDS) Unit at the World Health Organization.

He worked at the Onchocerciasis Control Programme in West Africa (WHO) for 15 years, first as Chief Epidemiologist and then as Head of Planning Evaluation and Transfer and later as Director of the Programme until its closure. He is currently Adjunct Professor in Tropical Health at the Institute of Parasitology, McGill University, Canada, and Senior Scientific Advisor to the Lymphatic Filariasis Support Center for Africa, Ghana. He served for a long period on the Mectizan Expert Committee and several review committees. He has authored chapters on onchocerciasis in several books, has many publications in peer review journals, and has co-edited a book on *Neglected Tropical Diseases in Sub-Saharan Africa*.

An Overview of Neglected Tropical Diseases in Sub-Saharan Africa

John O. Gyapong

Contents

Abstract

Neglected tropical diseases (NTDs) affect many neglected and marginalized 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. To scale up interventions to achieve control, elimination, or eradication of NTDs, programs must be integrated into the regular health system of endemic countries. Efforts to expand

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global coverage and targeting of NTDs must therefore involve national and international harmonization 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 programs. The positioning of NTDs within the Universal Health Coverage (UHC) agenda and the Strategic Development Goals (SDGs) could galvanize stakeholder support for these NTDs. Ultimately, we need to address the social structures in which NTDs flourish and invest in research and development for new diagnostics and drugs.

Introduction

Neglected tropical diseases (NTDs) are a diverse group of diseases that prevail in tropical and subtropical conditions in developing countries. They affect more than one billion people and cost developing economies billions of dollars every year. Populations living in poverty, with inadequate sanitation, and in close contact with infectious vectors and domestic animals and livestock are those worst affected. Thus, they 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, have improper ways of disposing of human waste, and therefore live in unsanitary environments tend to have a high burden of NTDs (Hotez et al. 2006; WHO 2010, 2013).

The World Health Organization has prioritized 20 of these NTDs in 149 endemic countries for focused global attention (Table 1). 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 2020).

NTDs cost developing communities billions of dollars each year in direct health costs, loss of productivity, and reduced socioeconomic and educational attainment

Table 1 The 20 WHO prioritized neglected tropical diseases for action

Helminth	*Protozoa*
Cysticercosis/taeniasis	Chagas disease
Dracunculiasis (Guinea-worm disease)	Human African trypanosomiasis (sleeping sickness)
Echinococcosis	Leishmaniases
Foodborne trematodiases	*Bacteria*
Lymphatic filariasis	Buruli ulcer
Onchocerciasis (river blindness)	Leprosy (Hansen disease)
Schistosomiasis	Trachoma
Soil-transmitted helminthiases	Yaws
Virus	*Others*
Dengue and chikungunya	Mycetoma
Rabies	Scabies
	Snakebite envenoming

(WHO 2012a). 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, 2020). In addition, these diseases place considerable financial constrain on patients and their families. Human African trypanosomiasis in the Democratic Republic of the Congo costs affected households in a typical rural community more than 40% of their annual household income (Lutumba et al. 2007), and up to 75% of households affected by visceral leishmaniasis in Bangladesh (Anoopa et al. 2006, Ozaki et al. 2011), India (Sundar. 2010), Nepal (Uranw et al. 2013), and Sudan (Meheus et al. 2013) experience some financial catastrophe in obtaining diagnosis and treatment, even when tests and medicines are free of charge.

The German government under GTZ (now GIZ) played an important role in the NTD movement by co-sponsoring with the World Health Organization (WHO) two key meetings of leading stakeholders in 2003 and 2005 in Berlin. These meetings achieved two important outcomes: (1) unified support for an integrated approach in addressing NTD control and elimination efforts, and (2) the brand "neglected tropical diseases" was coined and has since become part of the global health nomenclature (WHO 2004, 2006). This progress reflects the continuity of initiatives and long-standing support and dedication of the global NTD community, from the first meeting of NTD global partners convened by WHO in 2007 to bring together various disease initiatives under the umbrella of the NTD "brand," to the pledges made in the 2012 London Declaration on Neglected Tropical Diseases and the 2017 meeting of global partners. They demonstrate the immense potential that can be unlocked by working in partnership to ensure that NTDs have a prominent position on the global health agenda (WHO 2020).

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

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 program activities; to strengthen local programs 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 diagnosis disease management, and data management in order to improve clinical, epidemiological, and operational activities directed toward eliminating lymphatic filariasis as a public health problem; and to mobilize support of all relevant sectors, affected communities, and nongovernmental organizations for the elimination of the disease (WHA50.29).

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
Leishmaniases	WHA60.13	Control of leishmaniasis	2007
Buruli ulcer	WHA57.1	Surveillance and control of *Mycobacterium ulcerans* disease (Buruli ulcer)	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 feve	2002
Schistosomiasis and soil-transmitted helminthiases	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

The Assembly also invited other specialized agencies of the United Nations system, bilateral development agencies, nongovernmental organizations, and other groups concerned to increase cooperation in the elimination of lymphatic filariasis through the support of national and international programs relevant to the prevention and elimination of lymphatic filariasis. Finally, they urged the Director-General of the WHO to inform various specialized agencies, United Nations organizations, bilateral development agencies, nongovernmental organizations, and other concerned groups about the imperative for enhanced cooperation in eradicating lymphatic filariasis as a public health problem. Their aim is to garner support for both global and national elimination activities (WHA50.29).

This is probably the most comprehensive global commitment one could get for a disease elimination program. However, by the year 2005, only 8 out of the 38 endemic countries in Africa had active lymphatic filariasis elimination programs, and of these, only Burkina Faso, Ghana, Togo, and Zanzibar were treating their

entire national populations at risk. Clearly, targeting 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 roadmap 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).

In the last decade, there has been significant progress in fighting these diseases, with new interventions and tools, increased donor support, and increased country commitment. The establishment of public–private partnerships has vastly facilitated progress toward the elimination and control of NTDs: pharmaceutical companies have donated nearly three billion tablets of safe, quality-assured medicines annually to support the control and elimination of NTDs in countries where they are endemic (WHO 2020).

More recent data show that the burden of disease is going down though not significantly in Africa as a result of many interventions, strategies, and buy-in from many stakeholders. In 2021, 1.65 billion people were reported to require mass or individual treatment and care for NTDs, down from 2.19 billion in 2010, a reduction of 25%; however, over the same period the reduction in Africa was only 5% (Fig. 1; WER 2021; WHO 2023). The majority of these individuals continued to require mass treatment for diseases amenable to preventive chemotherapy, while the numbers requiring other NTD services such as individual disease management or care were much smaller, approximating a few million.

Global progress in reducing the number of people requiring interventions against NTDs, which is one of the road map's overarching indicators, as well as Sustainable Development Goal indicator 3.3.5, was driven by three main factors: first, a number of countries have eliminated at least one NTD; second, although not yet certified, verified, or validated, several countries have reached the post-intervention surveillance phase for at least one NTD; third, remapping for a number of NTDs has led to the reclassification from endemic to nonendemic status of several geographical areas within a few countries. Improved livelihoods and living conditions may have also contributed, although in uneven and varying ways, as several countries endemic for NTDs are affected by social instability entailing destruction and population displacement (Bangert et al. 2017; WHO 2020, 2023).

In spite of the above, at the end of 2022, WHO's South-East Asia Region still has the largest number of people requiring interventions against NTDs at 857 million (51.8% of the global total), followed by the African Region (584 million, 35.3%). The remaining four regions account for 212 million people requiring interventions, or 12.9% of the global total.

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

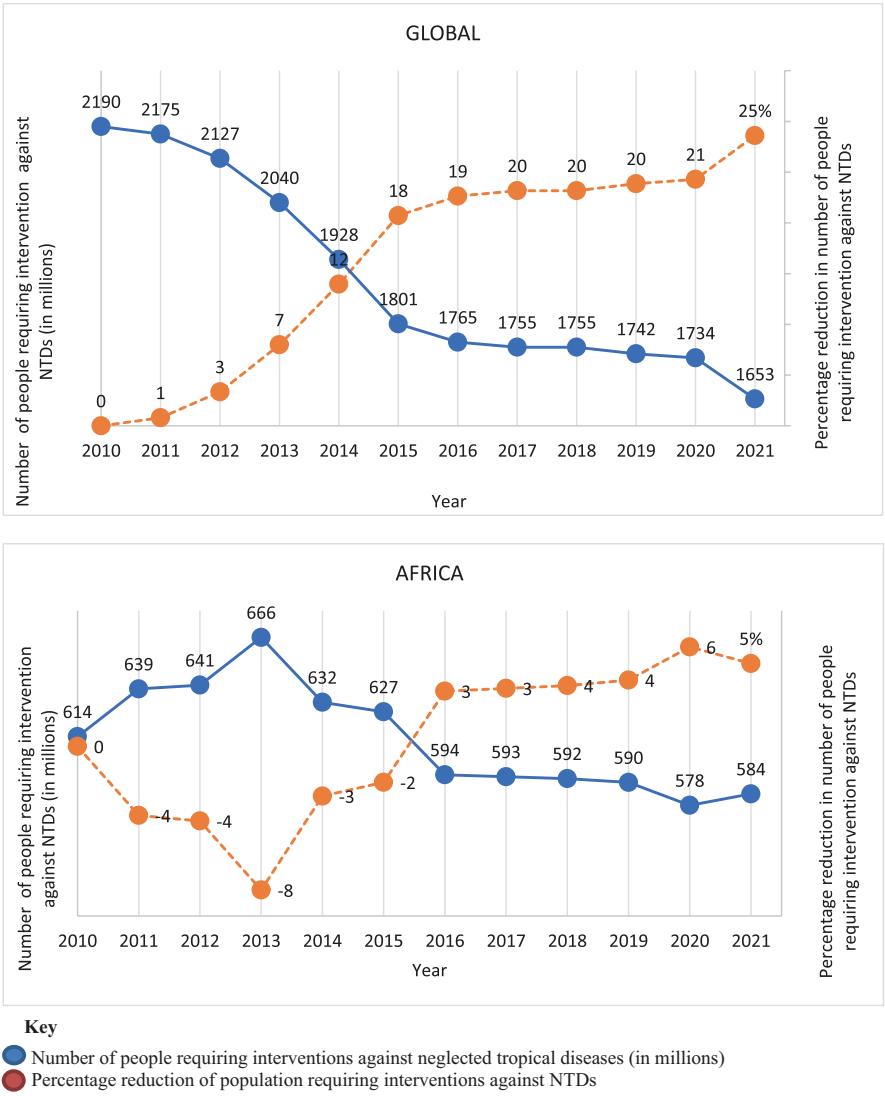

Fig. 1 Number of people requiring interventions against NTDs and associated percentage reduction globally and regionally, 2010–2021 (Adapted from WHO 2023)

- 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 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 program creation. As a result, we have a better understanding of the

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

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.
- 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 do 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 programs effectively if we can mobilize the necessary economic, social, and political capital (Fig. 2).

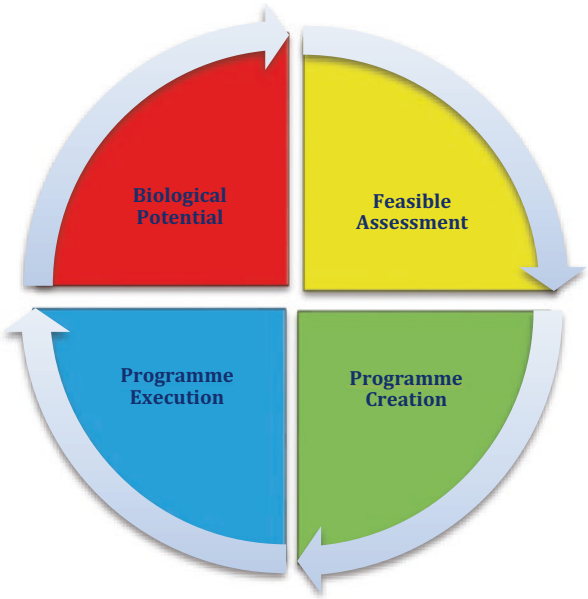

Fig. 2 Control program planning process

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

Figure 4 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), foodborne 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).

One of the issues of concern with the PCT strategy is the potential for drug resistance to appear with long-term use of these medicines in the communities. Even though some cases of non-response have been reported for ivermectin treatment for onchocerciasis in some communities in Ghana, there is no evidence of drug resistance (Osei-Atweneboana et al. 2007). There are some who think it is only a matter

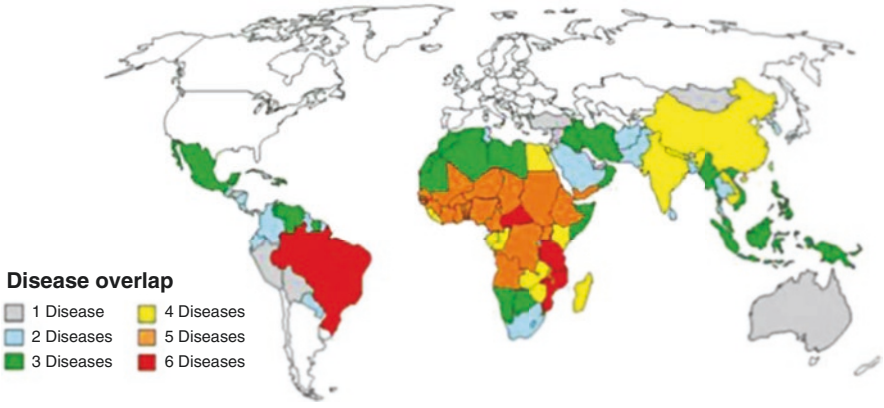

Fig. 3 Extent of disease overlap

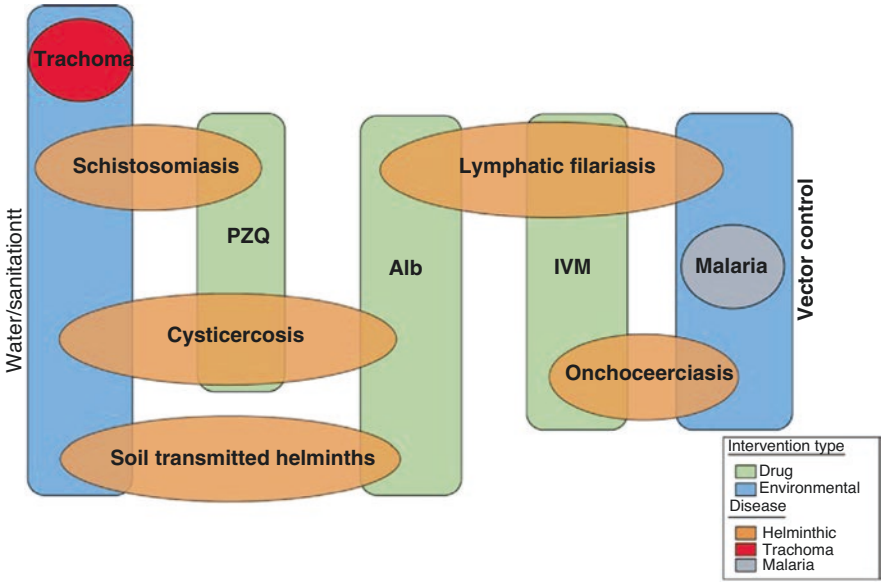

Fig. 4 Some strategies, tools, and interventions for NTD control

of time for drug resistance to occur, as has been reported with many parasites and chemotherapeutic agents. Research for new drug discoveries, repurposing of drugs, and multiple drug therapy is therefore encouraged (King et al. 2020; Jacobson 2022).

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 prioritized NTDs for control, having mapped their distribution and 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. To improve access, there is the need to engage other cadres 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 the community to

deliver interventions, has 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 populations even when standard operating procedures are adhered to. This requires putting in place 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 Steven Johnson syndrome occurs. How strong is our pharmacovigilance infrastructure to pick up these occasional mishaps? (Gyapong et al. 2003).

Integrated approaches to NTDs should be mainstreamed within various components of national health systems; for example, planning should be incorporated into overall national health planning and budgeting, data management should be included in health management information systems at all levels, and delivery of medicines should be coordinated through national medicines supply and logistics systems. Diligent monitoring for the safe administration of treatment for NTDs and reporting and responding to adverse events align with the objectives of national pharmacovigilance programs and demonstrate a core element of universal health coverage and high-quality people-centered care. Integrated NTD interventions, from prevention to diagnosis, treatment, care, and rehabilitation, can and should be delivered through community or primary- or secondary-care facilities in the national health system. Efforts to expand global coverage and targeting of NTDs must involve national and international harmonization. We need coordination of the activities of partnerships devoted to the control or elimination of these diseases. Programs 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. To scale up neglected tropical disease (NTD) interventions to achieve complete eradication, programs must be integrated into the regular health system of countries with the principles of the following:

- Where things fit well; do them together.
- Where things don't, do them separately.
- Look for ways of coordinating efforts to deliver in 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 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 has garnered political and social support, especially when there is an indication that these interventions will not jeopardize existing health systems but rather offer opportunities for synergies with health system activities (Molyneux 2008; Seddoh et al. 2013).

Although the resources for NTDs are often not commensurate with the vast need, NTD interventions are one of the best buys in global public health. The end of NTDs is expected to result in an estimated net benefit to affected individuals of about US$ 25 for every US$ 1 invested in preventive chemotherapy, representing a 30% annualized rate of return, and to contribute significantly toward universal health coverage and social protection for the least well-off (Fitzpatrick et al. 2017). In 2015, it was estimated that 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 could 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 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 (WHO 2015). Thus, with the concept of Universal Health Coverage (UHC) high on the agenda, tackling NTDs supports UHC, which means that all individuals and communities receive the health services they need without suffering financial hardship (WHO 2019). Actions against NTDs and their monitoring and evaluation reinforce each other. NTD interventions reach some of the world's most remote communities and can thus improve the potential for equitable access to health care services for these populations. Investment in NTDs can have important benefits for both health and economies (Fitzpatrick and Engels 2016; Seddoh et al. 2013).

NTDs and the Sustainable Development Goals (SDGs)

Sustainable Development Goal 3 (SDG3) aims to ensure healthy lives and ensure well-being for all at all ages, with the third sub-objective focusing on ending epidemics and NTDs by 2030. Ambitious as this may be, it galvanizes stakeholder actions to achieve these objectives. Thus, the SDGs can be achieved only if the NTD goals are met. Successful interventions against NTDs contribute to meeting other SDGs, such as alleviating poverty (SDG1) and hunger (SDG2), enabling people to

pursue an education (SDG4) and lead productive working lives (SDG8) and promoting equality, for example, regarding gender (SDG5 & SDG10). Progress toward other Goals can accelerate the achievement of NTD goals. For example, wider provision of clean water, sanitation, and hygiene (WASH) (SDG6) is believed to help eliminate or control NTDs; the availability of resilient infrastructure (SDG9) should facilitate delivery of medicines and outreach to remote communities; the goals of sustainable cities (SDG11) and climate action (SDG13) can support the environmental management necessary for control of disease vectors. Attaining all SDGs and NTD goals is founded on strong global partnerships (SDG17). The interlinkages with the 2030 Agenda for Sustainable development are expected to encourage the NTD community to think differently about the impact of interventions and to work proactively across sectors and disciplines to ensure progress toward sustainable development. Ending the epidemic of NTDs could therefore have an impact on and improve prospects for attaining the SDGs (Bangert et al. 2017; WHO 2020).

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. First, 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 emphasize since it has long been recognized 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. Second, 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 programs and must be mobilized at all costs. Broad social perception of the importance of the disease is essential; without it, there is no program! Polio, guinea worm disease, and lymphatic filariasis elimination/eradication were 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 mobilization by Rotary International, their network of volunteers, and the overwhelming support of civil society groups has been the lifeblood of the program. Chinese President Zemin, South African President Mandela, and US

President Clinton have heightened the program's visibility and through that raised lots of resources for the program. 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.

Advocacy and funding provide countries with the necessary support for delivering NTD interventions. Considerable progress has been made both globally and domestically. For example, Brazil, India, and Indonesia contribute significant funding for leprosy and other NTD programs. In some countries, there have been some increases in overall funding available for integrated NTD programs. In view of the growing commitment of the global community to attaining the SDGs and universal health coverage, particularly in the decade of action for the SDGs, this roadmap builds on the experiences and lessons learned and the momentum of the past decade, resulting in increased geographical and population coverage (WHO 2015).

Neglected Tropical Diseases (NTDs) as a brand on the other hand had not had that much visibility with heads of states until President Bush committed USD 350 million to their control. The NTD forum in London and the follow-up in Paris convened by the Gates Foundation has raised the profile of NTD elimination even more. Total commitments at this forum were way more than 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 immunization 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).

Drug Donations and Supply Chain

In this edition, there is a new chapter on drug donations for the NTD program; what is presented here, however, is a brief overview of this issue. 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. Once 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 programs 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 these medicines to the global program for as long as they are needed as part of corporate social responsibility. Diethylcarbamazine (DEC), for instance, is not a donated product in Southeast Asia, so it must be procured at production cost. Table 3 shows a list of pharmaceutical companies that contribute to the NTD portfolio of medicines.

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

Company	Medicine	Quantity donated	Disease	Commitment	Coordinator
Bayer	Nifurtimox	7,750,000 tablets total	Chagas disease	2021–2025	WHO
	Nifurtimox (120 mg)	300,000 tablets annually	Human African trypanosomiasis	2021–2025	WHO
	Nifurtimox (30 mg)	20,000 tablets annually	Human African trypanosomiasis	2021–2025	WHO
	Suramin	10,000 vials annually	Human African trypanosomiasis	2021–2025	WHO
	Niclosamide (400 mg)	2,800,000 tablets total	Taeniasis/cysticercosis	2020–2024	WHO
	Praziquantel (600 mg)	1,339,000 tablets total	Taeniasis/cysticercosis	2020–2024	WHO
Chemo Ibérica S.A.	Benznidazole (12.5 mg)	3000 tablets total	Chagas disease	2020–2022	WHO
(Fundación Mundo Sano)	Benznidazole (100 mg)	105,000 tablets total	Chagas disease	2020–2022	WHO
Eisai	Diethylcarbamazine citrate	2,200,000,000 tablets total	Lymphatic filariasis	Until elimination	WHO
Gilead Sciences	Liposomal amphotericin B	380,000 vials total	Visceral leishmaniasis	2016–2021	WHO
Sanofi	Eflornithine	Unlimited	Human African trypanosomiasis	Until 2025	WHO
	Melarsoprol	Unlimited	Human African trypanosomiasis	Until 2025	WHO
	Pentamidine	Unlimited	Human African trypanosomiasis	Until 2025	WHO
	Fexinidazole	Unlimited	Human African trypanosomiasis	Until 2025	WHO
Novartis	Multidrug therapy[1]	Unlimited	Leprosy	2021–2025	WHO
	Clofazimine	Unlimited	Severe erythema nodosum leprosum reactions	2021–2025	WHO
	Triclabendazole	600,000 tablets total	Fascioliasis	2016–2022	WHO
EMS	Azithromycin	Up to 153,000,000 tablets	Yaws	2021–2025	WHO
Pfizer	Azithromycin	Unlimited	Trachoma	1998–2025	International Trachoma Initiative
Johnson & Johnson	Mebendazole	200,000,000 tablets annually	Soil-transmitted helminthiases (SAC)[2]	Until 2025	WHO