INVESTING TO OVERCOME THE GLOBAL IMPACT OF NEGLECTED TROPICAL DISEASES

Third WHO report on neglected tropical diseases

World Health Organization

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FOREWORD

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"Universal health coverage is one of the most powerful social equalizers among all policy options."

Dr Margaret Chan
Director-General
World Health Organization

FOREWORD BY THE DIRECTOR-GENERAL OF THE WORLD HEALTH ORGANIZATION

This report repositions a group of 17 neglected tropical diseases on the global development agenda at a time of profound transitions in the economies of endemic countries and in thinking about the overarching objectives of development. In doing so, it reinvigorates the drive to prevent, control, eliminate, or eradicate diseases that blind, maim, and disfigure, making life miserable for more than a billion people. Undetected and untreated, several almost invariably kill. The burden of these diseases is further amplified by the fact that many require chronic and costly care, underscoring the economic as well as the health benefits of preventive chemotherapy and early detection and care.

The report brings a new dimension to long-term thinking about the future approach to these diseases. For the first time, it sets out financing needs, options, and targets for meeting WHO Roadmap goals by 2020, but also for reaching universal coverage of all people in need by 2030. The report makes one investment case for cost-effectiveness and a second investment case where equity is the focus. It sets targets for ending catastrophic health expenditures and, as part of the drive to strengthen health systems, for getting services closer to where people live.

As more endemic countries graduate to middle-income status, the report stresses the need for greater investment of domestic resources. It also discusses the pros and cons of using innovative models, such as outcome-based funding, to stimulate more investment. Financing arguments further show how an initiative that progressively builds on its successes can extend its reach in innovative ways that also increase efficiency. As efficiency increases, the impact of investments likewise grows.

In line with new thinking about development in the post-2015 era, the report prioritizes control measures as an integral part of efforts to share the benefits of economic growth more evenly and fairly. Efforts to control neglected tropical diseases provide an entry point for testing a country's determination and ability to do so. Control measures are also put forward as a test case for universal health coverage. By distributing donated medicines to all in need, countries can carve out delivery systems for achieving universal access to other medicines, interventions, and forms of care. Finally, as several of these diseases involve an insect or animal in the transmission cycle, they are highly sensitive to climate variables. Changes in incidence patterns can serve as an early and measurable signal of the health effects of climate change.

Most important, however, is the pro-poor nature of this initiative, on a massive scale, as a contribution to the desired goal of shared prosperity. The poor deserve to be targeted for health care as they have been given so little else in life. With such huge numbers affected, controlling these diseases paves the way for an exodus from poverty. The drive for sustainable results also stimulates environmental improvements in a value-added way, as these diseases flourish in filthy environments created by poor water supplies and sanitation. In a similar way, the need to increase vector control becomes part of the package for sustainable success.

While the emphasis is on long-term financing needs, the report also charts remarkable and accelerating progress. Further momentum comes from the stepped-up commitment of many endemic countries that now see an end in sight and are determined to get there.

Well over 70 countries are implementing or ready to kick-off their master plans for the integrated and accelerated control of these diseases. Verification that lymphatic filariasis has been eliminated has begun in six countries. Sustained efforts by a network of African countries have reduced the incidence of human African trypanosomiasis by 90%. At the end of 2014, 27 countries had already achieved the WHO target of 75% treatment coverage of school-age children to prevent soil-transmitted helminthiases. Since 2006, over 5 billion anti-parasitic treatments have been delivered. During 2012 and 2013, the pharmaceutical industry donated 2.5 billion treatments. Over 800 million people were treated in 2012 alone.

These outstanding results are a tribute to what committed governments, working with equally committed and enthusiastic partners, led by WHO, can do to relieve vast human misery, distribute economic gains more evenly, and free masses of people long trapped in poverty, from one generation to the next. Universal health coverage is one of the most powerful social equalizers among all policy options. Setting this as a future goal for diseases that affect so many can contribute to the social stability and resilience to shocks that our troubled world so visibly and badly needs. In other words, when countries and their partners invest in these diseases, they get a windfall of benefits in return.

Dr Margaret Chan
Director-General
World Health Organization

EXECUTIVE SUMMARY

Introduction

Investing to overcome the global impact of neglected tropical diseases charts new ground in tackling the 17 neglected tropical diseases (NTDs) that affect more than a billion people in 149 countries worldwide. It makes the case for domestic investment to reach the targets of WHO's Roadmap on NTDs by 2020 and sustain enhanced, equitable access to high-quality coverage against these diseases to 2030.

This third WHO report anticipates the investments needed as countries graduate from low-income to middle-income status and as the world's focus expands from the Millennium Development Goals to the Sustainable Development Goals.

Confronting challenges, registering progress

In May 2013, the Sixty-sixth World Health Assembly adopted resolution WHA66.12 on neglected tropical diseases. To ensure that the Resolution has greatest impact, partners, stakeholders and academia are encouraged to generate further momentum for transforming its recommendations into reality.

This report discusses the progress achieved to date. More than 74 countries worldwide are ready to implement national NTD master plans, stimulating increased demand for programme implementation and donated medicines – crucial to reaching the Roadmap's targets. More people than ever received preventive treatment for at least one disease in 2012. Globally, a total of 27 countries have achieved the target of 75% treatment coverage of school-age children for soil-transmitted helminthiases. Sustained efforts over the past 15 years have reduced the number of new cases of human African trypanosomiasis by 90%. In 2013, Colombia became the first country in which WHO verified the elimination of onchocerciasis (river blindness), followed by Ecuador in 2014. Bangladesh is poised to eliminate visceral leishmaniasis as a public-health problem. China has sustained its national schistosomiasis control programme and interrupted transmission in most endemic areas. Since 2006, more than 5 billion anti-parasitic treatments, mostly donated by the pharmaceutical industry, have been delivered to populations in need.

Although support from major donors continues and important progress has been achieved, challenges remain. While this report focuses on the need for enhanced domestic investment, it considers what the universal health coverage (UHC) targets imply for NTD programmes in terms of population coverage with prevention and financial risk-protection against the cost of treatment and care.

Investing towards universal coverage against NTDs

A WHO/World Bank framework for monitoring progress towards universal health coverage at country and global levels calls for two targets to be reached by 2030:

- a minimum of 80% essential health services coverage;
- 100% financial protection from out-of-pocket payments for health services.

The UHC target of 80% essential health services coverage is broadly consistent with coverage targets for the prevention of NTDs. Furthermore, a precondition for reaching the UHC target of 100% financial protection by 2030 is that all NTD cases are financially protected. The report translates these coverage targets into investment targets.

Excluding vector control, the investments required to meet the Roadmap's targets for 2015–2020 total an average of US$ 750 million per year. Maintaining progress beyond 2020 until 2030 will require an additional US$ 460 million per year in investment as interventions are scaled down and diseases are eradicated, eliminated or controlled.

Vector control is expected to assume an increasing share of investment within the NTD portfolio between 2015–2020 as arboviral diseases spread globally with rapid unplanned urbanization, population movement and environmental change. Total investments for this period, including vector control, are estimated at less than US$ 18 billion, or US$ 2.9 billion on average per year. Total investments for the period 2015–2030 amount to US$ 34 billion, excluding donated medicines.

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 10 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. Or as chapter 2 of this report makes clear, universal coverage against NTDs will fail if it fails to mobilize domestic investment.

If the pharmaceutical industry continues to donate medicines, domestic investment in universal coverage against NTDs will be affordable.

The domestic investment target for universal coverage against NTDs represents less than 0.1% (one-tenth of 1%) of domestic expenditure on health expected within the group of low- and middle-income countries for the period 2015–2030. The percentage is highest

for the group of low-income countries, where the domestic investment target for NTDs is nonetheless still well below 1% of domestic expenditure on health. For all income groups, domestic investment targets decrease after 2020 in absolute (dollar) terms, as coverage targets are achieved and NTDs are controlled, eliminated or eradicated.

The report argues that reforms leading to universal health coverage provide an opportunity to bolster public and pooled private financing for universal coverage against NTDs. It foresees, however, that the rebalancing of the financing mix towards less foreign aid and more domestic investment will take time, especially in low-income countries.

Multilateral development banks have a role to play in facilitating the progressive shift in NTD financing from grants to zero-interest loans to low-interest loans to non-concessional loans and domestic revenues. Increasingly, NTD investments are being made through innovative financing mechanisms, with the goal of overcoming some of the perceived problems with traditional mechanisms that have focussed more on inputs and activities than on outputs and outcomes, and may have underemphasized adaptation to local situations.

Key interventions on the path to universal coverage

WHO recommends an integrated approach to overcoming the global impact of NTDs through five interventions: innovative and intensified disease management; preventive chemotherapy; vector ecology and management; veterinary public-health services; and the provision of safe water, sanitation and hygiene.

These interventions are being implemented with variable intensity. Progress in increasing coverage with preventive chemotherapy has resulted in hundreds of millions of people receiving treatment annually. In 2012 alone, more than 800 million people received preventive chemotherapy for at least one disease, a significant advance from 2011 when 729 million people were covered. Global coverage with preventive chemotherapy has expanded significantly over the past few years and is expected to further scale up.

Innovative and intensified disease management is used for the diagnosis and treatment of complex NTDs. This approach lowers the burden of mortality and morbidity of five diseases through early case detection and timely diagnosis. More than 520 000 new cases were treated in 2012, and about 5 million since the start of the century. Continued efforts using existing control methods, including active case-finding and disease-surveillance, have resulted since 2009 in fewer than 10 000 new cases of human African trypanosomiasis reported annually for the first time in 30 years, with 6314 cases in 2013.

Strengthening capacity for vector ecology and management remains a priority. In areas where multiple NTDs are endemic, WHO deploys integrated vector management to control the transmission of pathogens. Pesticides are pivotal to controlling vector populations, and their judicious and sound management in minimizing adverse events on human and animal health and the environment are important tenets of integrated vector management. The WHO Pesticide Evaluation Scheme evaluated and made recommendations on 10 pesticide products during 2012–2013. A further 14 pesticides are undergoing evaluation. Since 2007, more than 20 Member States have received WHO support in preparing regional policies and frameworks for pesticide management and in procuring pesticides for public-health use.

The need to control zoonoses is becoming increasingly urgent. At least four NTDs have prominent zoonotic components. Echinococcosis, foodborne trematodiases, rabies, and taeniasis and (neuro)cysticercosis are neglected zoonotic diseases because they rank far down on the priorities of governments and of the international public-health community. The year 2010 marked a turning point with WHO signing a Tripartite Agreement with the Food and Agriculture Organization of the United Nations and the World Organisation for Animal Health. This agreement calls for intersectoral collaboration covering the three areas of interest involved in the transmission cycle of zoonoses: human health, veterinary health and environmental health. WHO's future plans include working closely with countries that are willing to embark on control and elimination of zoonoses using the most appropriate tools available.

Joint planning, resourcing and delivery of safe water, sanitation and hygiene and control interventions must be prioritized to accelerate progress towards public-health and human development goals. Having achieved important progress in providing access to safe-drinking water, more needs to be done to improve sanitation and hygiene conditions. At the end of 2012, an estimated 2.5 billion people – approximately one-third of the world's population – lacked access to improved sanitation.

Avenues for research and development must be pursued in order to find new approaches and simplified strategies as well as novel diagnostics, medicines, vaccines and vector control methods, as vector-borne diseases continue to spread at an alarming pace and to new geographical areas . Major efforts are needed to control re-emerging threats from dengue and other related arboviruses such as chikungunya and zika. Good-quality research is integral to sustainable control of NTDs. Research must therefore remain an inherent part of the culture of control, even as diseases move towards elimination and eradication.

Neglected tropical diseases: impact on public health

This report discusses the progress achieved for 17 NTDs and presents investments targets for 12.

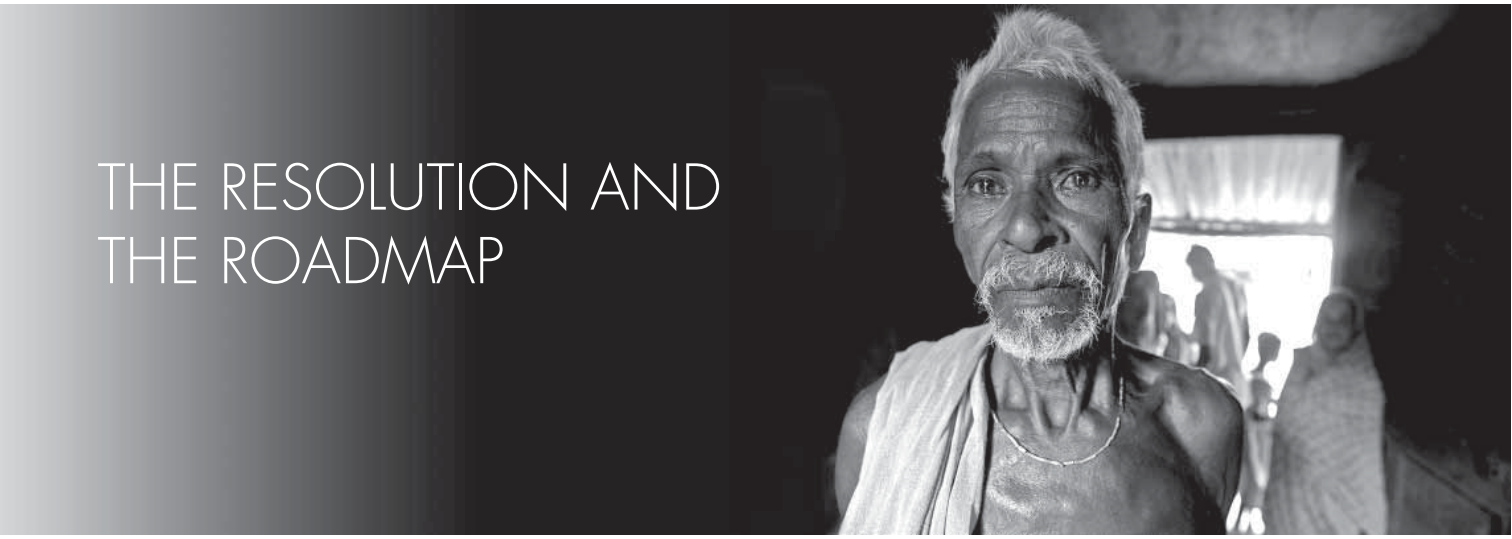
With the advent of the United Nations Sustainable Development Goals, the principle of shared prosperity is framing the global development agenda as never before. Until recently, the highest number of poor people affected by NTDs lived in low-income countries. As their economies continue to improve, these countries are progressively classified into middle-income status. But not everyone has benefitted.

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.

Unpredictable epidemics such as the Ebola virus disease crisis in West Africa and their potential to expand can divert efforts and resources away from NTDs and adversely affect national control programmes.

WHO will continue to assist countries in advancing their investment strategies to achieve universal health coverage against NTDs, the expectation being that enhanced and equitable delivery of interventions to the most marginalized populations will ensure that all peoples affected by NTDs have an opportunity to lead happier, healthier and wealthier lives.

THE RESOLUTION AND THE ROADMAP



THE RESOLUTION AND THE ROADMAP: PROGRESS TOWARDS TARGETS

In May 2013, the Sixty-sixth World Health Assembly adopted resolution WHA66.12, a testimony of the global resolve to prevent, control, eliminate and eradicate neglected tropical diseases through planned interventions.

Introduction

The World Health Organization (WHO) published its second report on neglected tropical diseases in January 2013. *Sustaining the drive to overcome the global impact of neglected tropical diseases* described how renewed momentum had shifted the world closer to eliminating many of these diseases and conditions and largely improved prospects for achieving universal health coverage (UHC).[1] That report called for yet stronger political will, financial and resource planning, and research and development of new diagnostics to implement control programmes at an accelerated rate.

This third report charts new ground.

In May 2013, the Sixty-sixth World Health Assembly adopted resolution WHA66.12 on neglected tropical diseases ("the Resolution"), a testimony of the global resolve to prevent,

[1] The term "universal health coverage" is defined by WHO as "ensuring that all people can use the promotive, preventive, curative, rehabilitative and palliative health services they need, of sufficient quality to be effective, while also ensuring that the use of these services does not expose the user to financial hardship." (http://www.who.int/health_financing/en/). The three dimensions of the so-called "UHC cube" are: (i) extending coverage to individuals who previously were not covered; (ii) extending coverage to services that previously were not covered; or (iii) reducing direct payments needed for each service.

control, eliminate and eradicate these diseases through planned interventions. This landmark resolution on neglected tropical diseases (NTDs) recognizes that increased investments have improved the health and social well-being of populations in many countries.

The Resolution acknowledges, among other things, the need for adequately resourced national programmes working within various ministries as well as with other sectors to provide for an uninterrupted supply and delivery of quality-assured services. To ensure that the Resolution has greatest impact, partners, stakeholders and academia are encouraged to work together to advocate the importance of implementation and to generate further momentum for transforming its recommendations into reality. *Annex 1a* lists the resolutions of the World Health Assembly concerning neglected tropical diseases and *Annex 1b* reproduces the Resolution in full.

Accelerating work to overcome the global impact of neglected tropical diseases: a roadmap for implementation ("the Roadmap") (*1*) was formulated in 2011 by WHO and its Strategic and Technical Advisory Group for Neglected Tropical Diseases and endorsed in 2012 by signatories to the *London Declaration on neglected tropical diseases* ("the London Declaration") (*2*) committed to facilitating its implementation. The Roadmap underpins the Resolution. Two targets are set for the eradication of dracunculiasis (2015) and yaws (2020), six targets for the global elimination of five diseases (2015) and 10 targets for the elimination either globally or in selected geographical areas of nine diseases (2020). *Annex 2* captures the Roadmap's targets "at a glance".

1.1 Building on commitments

Major donors have continued to provide resources beyond the initial commitments announced during the London Declaration meetings in order to sustain and expand disease control programmes. Their support remains crucial to funding the implementation of programmes. Pledges from new partners and philanthropic organizations have added optimism to renewed global momentum against NTDs. These "Cinderella diseases", long ignored and underappreciated, were characterized by WHO in its second report as a "rags to riches" story.

In April 2014, during an event hosted by the Bill & Melinda Gates Foundation to mark the second anniversary of the London Declaration, several additional donors made new commitments amounting to more than US$ 112 million. Partners, donors and the pharmaceutical industry have committed themselves to addressing a large proportion of the "size of the problem". This commitment paves the way for long-term planning and the distribution of quality-assured medicines free of charge to millions more people living in low- and middle-income countries.

The World Bank has committed US$ 120 million from its International Development Association (the fund for the poorest countries) to control and elimination of NTDs in low-income countries in Africa. It is also working to encourage addressing these problems not only

through the health sector but also through smart investments in education, agriculture and other sectors that are key to interrupting transmission.

The pharmaceutical industry donated nearly 1.35 billion[1] treatments in 2013, representing a 35% increase since 2011. To meet the heightened demand for donated medicines and accelerate expansion, monitoring and evaluation of preventive chemotherapy, WHO launched a joint mechanism and tools to support implementation in 2013. A set of forms is available to facilitate application, review and reporting and to improve programme coordination and integration: a Joint Request Form, to assist countries in quantifying the number of tablets required during the year for which medicines are requested; a Joint Reporting Form, to simplify reporting the number of treatments delivered; an annual Workplan, to summarize key activities for implementation; and an Epidemiological Data Reporting form, to collect data.[2] This mechanism puts the Ministry of Health in control by centralizing all country requests for medicines and providing oversight for progressive ownership of control programmes.

Despite the tough financial landscape, funding for projects has increased, broadening prospects for yet improved results in 2015.

1.2 Registering progress

Important progress has been made at regional and country levels. China has sustained the drive to eliminate NTDs, notably schistosomiasis (*Box 1.1*). The Asia Pacific region is addressing diseases of poverty and has achieved remarkable success in tackling NTDs under the leadership of governments in endemic countries and with the support of partners worldwide. Lymphatic filariasis has been eliminated in three countries; a further 10 countries are awaiting verification of elimination or are in the surveillance stage before verification by 2016. WHO's targets for deworming school-age children have been achieved in five countries, and the elimination of trachoma is anticipated in six countries by 2016 (*3*).

As part of country ownership of programmes, more than 74 countries worldwide are poised to implement national NTD master plans, stimulating increased demand for programme implementation and donated medicines. Globally, a total of 27 countries have achieved the Roadmap's target of 75% treatment coverage of school-age children for soil-transmitted helminthiases.

All 47 Member States of the African Region have endorsed a regional plan that includes efforts to eliminate onchocerciasis. Several countries in the Western Pacific Region have progressed towards the Roadmap's elimination targets (*4*). Verification of the elimination of lymphatic filariasis has started in Member States of the South-East Asia (Maldives, Sri Lanka and Thailand) and Western Pacific (Niue, Palau and Vanuatu) regions.

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[1] "Billion" is defined as a thousand million (10^9).

[2] http://www.who.int/neglected_diseases/preventive_chemotherapy/reporting/en/

Box 1.1 Registering progress

Controlling schistosomiasis in China

China has sustained the national schistosomiasis control programme and interrupted transmission in most endemic areas through a comprehensive multi-pronged strategy phased out over several decades. The strategy includes construction of dams, delivery of potable water and providing basic sanitation.[1] WHO is working with the Ministry of Health on a pilot project in Zanzibar on the use and transfer of Chinese expertise through a joint China–Africa–WHO collaboration for schistosomiasis control.

Joining forces to eliminate visceral leishmaniasis in Bangladesh

Bangladesh is poised to eliminate visceral leishmaniasis as a public-health problem and is edging closer to the target of achieving 1 case per 10 000 inhabitants per year in endemic areas at sub-district level by 2015. Through community mobilization, access to improved antileishmanial medicines, a strong national control programme, a robust surveillance system and an integrated vector control programme, more than 15 000 cases were diagnosed and treated during the past 5 years. In 2013, 1284 cases were reported to WHO compared with 4293 cases in 2009. This represents a reduction of more than 70% in the number of new cases reported annually.[2]

[1] China's sustained drive to eliminate neglected tropical diseases. Lancet. 2014;14:881–884. doi:10.1016/S1473-3099(14)70727-3.
[2] http://www.who.int/neglected_diseases/leishmaniasis_Bangladesh_2014/en/

In the Region of the Americas, new levels of political commitment have emerged. During the meeting of the Organization of American States in June 2013, Heads of State endorsed resolution CD49.R19 of the 49th Directing Council on the elimination of neglected diseases and other poverty-related infections. That resolution urged Member States of endemic countries to implement, among other things, treatment strategies in an integrated way and with broad community participation so that these diseases would no longer be considered public-health problems by 2015.

Also in June 2013, the regional meeting of the Council of Ministers of Health of Central America and the Dominican Republic recognized the importance of NTD control and elimination to achieving the Millennium Development Goals (for 2015) and the Sustainable Development Goals (for 2030), including universal health coverage.

Table 1.1 highlights the progress accomplished in WHO's regions.

Table 1.1 Regional highlights

WHO African Region	
March 2014	WHO establishes a network of stakeholders to achieve elimination of human African trypanosomiasis (*Trypanosoma brucei gambiense*) as a public-health problem by 2020. Sustained control has resulted in a reduction of more than 90% in the number of reported cases. In 2013, 6314 new cases were reported to WHO compared with 7216 cases in 2012.
April 2013	The Sixth Conference of African Union Ministers of Health calls on countries to do more to invest in and promote country ownership of NTD programmes and agrees to increase collectively overall support for NTD control and elimination programmes. "Large" (populous) countries such as Ethiopia and Nigeria launch an NTD master plan. During its 63rd session, the WHO Regional Committee for Africa endorses a regional strategy on NTDs[1] and the regional NTD strategic plan (2014–2020).[2]
December 2013	Côte d'Ivoire, Niger and Nigeria are certified free of dracunculiasis transmission.
WHO Region of the Americas	
July 2013	Colombia becomes the first country in the region to be certified free of onchocerciasis and the third country in the region to launch a 5-year integrated national plan to address trachoma and soil-transmitted helminthiases.
August 2013	Guatemala launches a multi-year (2013–2015) integrated national plan on onchocerciasis, soil-transmitted helminthiases, Chagas disease, visceral leishmaniasis, trachoma and leprosy.
September 2014	Ecuador is declared the second onchocerciasis-free country in the region.
WHO Western Pacific Region	
September 2013	Ministers attending an annual meeting in the Philippines sign a Wall of Commitment to end six of the most common NTDs in the country by 2018.[3]
WHO South-East Asia Region	
July 2013	Ministers of Health from the 17 high-burden leprosy countries in all WHO regions, with relevant stakeholders and WHO, sign the Bangkok Declaration towards a leprosy-free world.[4]
September 2013	The Government of India announces that it is working with all stakeholders and the community towards meeting the objectives of WHA66.12 and is committed to sustaining momentum of efforts to tackle NTDs.[5]

[1] http://www.afro.who.int/en/downloads/doc_download/8638-afrrc6310-regional-strategy-on-neglected-tropical-diseases-in-the-who-african-region-20142020-.html

[2] http://www.afro.who.int/en/downloads/doc_download/8637-afrrrc6310add-regional-strategic-plan-for-ntds-in-the-african-region-20142020.html

[3] http://endtheneglect.org/2013/10/the-writings-on-the-wall-philippines-marks-its-commitment-to-end-ntds/?utm_source=rss&utm_medium=rss&utm_campaign=the-writings-on-the-wall-philippines-marks-its-commitment-to-end-ntds

[4] http://www.searo.who.int/entity/global_leprosy_programme/Bangkok_Declaration_24July2013.pdf

[5] http://www.schoolsandhealth.org/Shared%20Documents/Action%20on%20Neglected%20Tropical%20Diseases%20in%20India.pdf

Against this positive outlook, some serious challenges remain.

1.3 Confronting challenges

There is an urgent need to address the shortfall in long-term funding for various programmes. In April 2014, NTD partners published *Delivering on promises and driving progress*, which estimated that an additional US$ 1.4 billion, or US$ 200 million per year, would be needed to meet the 2020 Roadmap targets (*5*). These requirements include implementation costs for some but not all NTD interventions; they do not include, for example, vector control or the broader preventive chemotherapy agenda, such as post preventive chemotherapy surveillance and morbidity management and disability prevention. They also do not cover innovations, new tools or costs associated with improved strategies to achieve the Roadmap's targets for 2020, much less the UHC targets for 2030.

National control programmes must be strengthened, maintained and mandated with clearly defined responsibilities in order to coordinate essential functions such as situation analysis, strategic planning, budgeting, prevention, diagnosis, treatment, surveillance, capacity development, timely distribution of medicines and supervision of operations at all levels of the national system.

Although significant progress has been made against vector-borne diseases, dengue and chikungunya continue to spread at an alarming pace. Challenges also include the shortage of trained health-care personnel, the absence of integrated vector control programmes and the degree of readiness in some countries to implement WHO-recommended integrated programmes comprehensively.

Emerging challenges in Chad and insecurity in Mali and South Sudan have hindered dracunculiasis eradication and may compromise WHO's target of interrupting transmission of the disease by the end of 2015.

Some critical interventions go beyond the scope of health. Unpredictable epidemics such as the current Ebola virus disease crisis in West Africa and their potential to expand can divert resources away from NTDs and adversely affect national control programmes. Long-term political commitment, sustained strengthening of health systems, maintenance of technical capacities, and effective monitoring and evaluation of interventions are crucial to achieving the Roadmap's targets.

More State-level engagement, sustainable and innovative financing and greater coordination are required to bring game-changing treatments and diagnostics to patients. Increased domestic resources, including funding and intersectoral collaboration, must be enhanced to support implementation of programmes to achieve universal coverage against NTDs.[1] The concept of universal coverage against NTDs is more fully developed in *Chapter 2*.

[1] Universal coverage against NTDs (in particular) applies the principles of universal health coverage (in general) to an essential package of interventions for low-income and rural populations, and other disadvantaged groups.

1.4 Supporting innovation

Many pharmaceutical companies are supporting calls for research and development by opening their compound libraries to outside researchers. Major access agreements have been brokered between companies, by the Drugs for Neglected Diseases initiative and through the World Intellectual Property Organization's Re:Search consortium.[1]

Some product development partnerships are advancing the development of new medicines. According to data from the Global Funding of Innovation for Neglected Diseases, or G-Finder, which surveyed global investments into the research and development of products,[2] in 2007 product development partnerships captured US$ 469 million of funding granted by donors to research organizations (*6*).

While existing tools continue to make a substantial impact on the hundreds of millions of people suffering from or at risk of NTDs and for whom innovative and intensified management is typically required, for many diseases, new medicines, diagnostics and innovative technologies are needed to reach the Roadmap's 2020 targets.

1.5 Staying the course

As NTDs are associated with unsafe water and sanitation, their prevention, control and elimination will depend on overall improvements in health-related projects. There must be increased advocacy for and awareness among policy-makers of development projects that foster successful programme implementation. China provides a good example (*Box 1.1*).

The other side of "low-cost" treatment of NTDs is that it results in "market failures". Emerging market economies can play a determining role in shedding the "charity" image of NTDs by doing more to produce new diagnostic tools, shake-up market dynamics, promote investment in research and advocate the development of new medicines.

Lesson should be learnt from high-profile diseases that have attracted global attention through strong advocacy – and the lion's share of global funding.

[1] http://www.wipo.int/research/en/

[2] http://g-finder.policycures.org/gfinder_report/

1.6 NTDs, Sustainable Development Goals and the case for investment

In September 2013, a United Nations panel recommended that measures be accelerated to end extreme poverty by 2030 (*7*). "Neglected tropical diseases" are mentioned in lieu of "other diseases" in recognition of the immense suffering they inflict on poor populations.

The Chairman of the WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases commented in a 2014 correspondence published in the Lancet:

> Access to NTD interventions is an integral part of universal health coverage. Their positive effect in gains for healthy life and reduction in catastrophic health expenditure represent a route out of poverty for households. Access to NTD interventions also reduces financial burden on health systems in almost all countries. Control and elimination of NTDs are sensitive indicators of both poverty alleviation and universal health coverage, and are representative of how developing countries care for the health of the poorest sections of their populations (*8*).

The inclusion of NTDs provides evidence of the growing political will to address these diseases. Their positioning alongside other, better-known global public-health issues is an important milestone for the global health community. Without decisive action to address NTDs, they will remain neglected and continue to pose a barrier to ending extreme poverty.

The task to overcoming the neglected diseases of neglected populations is challenging – requiring a serious investment strategy. *Chapter 2* analyses this case, providing investment targets to match the Roadmap's targets for 2020 and universal coverage against NTDs by 2030.

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INVESTMENT

INVESTING TOWARDS UNIVERSAL COVERAGE AGAINST NEGLECTED TROPICAL DISEASES

Universal coverage against NTDs will be a measure of the success of universal health coverage in reaching the poorest. Domestic investment from within endemic countries will be central to realizing universal coverage against NTDs.

Introduction

This chapter provides targets for the investment needed to achieve the Roadmap's targets by 2020 and universal coverage against NTDs by 2030. It prioritizes domestic investment as a part of efforts under the Sustainable Development Goals to better share the world's prosperity, with less reliance on charity.

2.1 NTDs in the era of the Millennium Development Goals

In the context of the Millennium Development Goals (MDGs), the NTDs were neglected relative to the "big three" diseases (HIV/AIDS, malaria and tuberculosis) in large part because the burden of NTDs tends to be focalized within poor, rural and otherwise marginalized populations. Although the NTDs were not specifically mentioned in the MDGs, their control has contributed to advances in the health and wealth of a significant proportion of the world's population. Since the start of the century, more than 5 billion preventive

treatments have been delivered and an estimated 5 million people have received individual treatment and care. In 2012 alone, more than 800 million people received preventive anti-parasitic treatment for at least one disease. The "rags to riches" story of NTD control[1] was told in *Chapter 1* of this report. This story has played out against the backdrop of dramatic changes in the economic growth of countries and in the distribution of wealth within them.

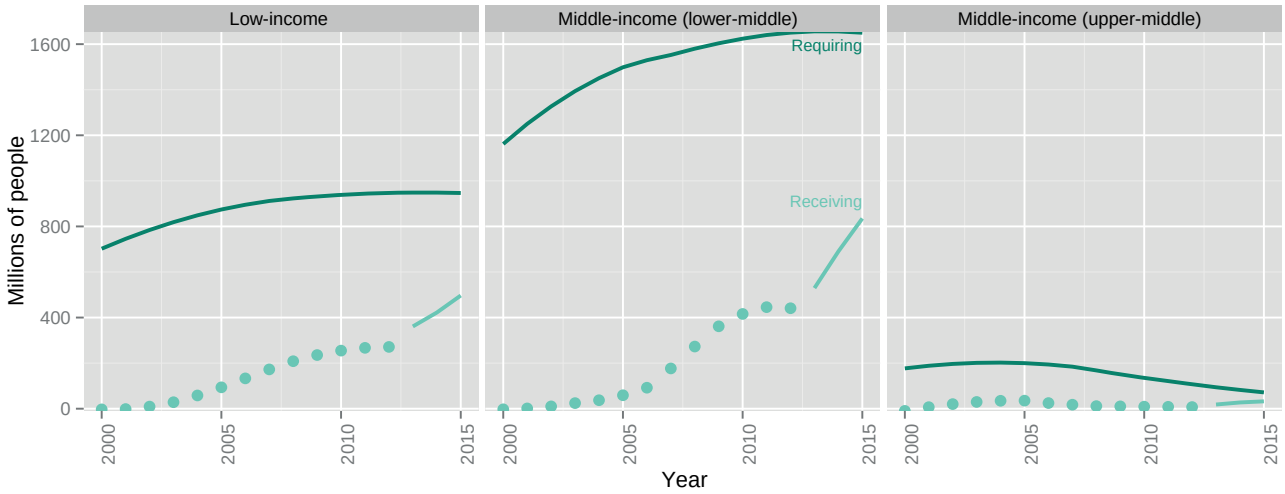
Until relatively recently, the highest number of people affected by NTDs lived in low-income countries.[2] As their economies grew, some were classified as middle-income countries. However, the health and welfare benefits of economic growth have not reached everyone (*1*). Today one billion (about three-quarters) of the world's poor live in the 105 middle-income countries with gross national income (GNI) per capita of between US$ 1045 and US$ 12 746 (*2*). Similarly, most (about 65%) of the people requiring treatment for NTDs live in middle-income countries. Indeed, it is even the case that most of the people requiring but not receiving treatment for NTDs are in middle-income countries. *Fig. 2.1* shows that the gap between the number of people requiring preventive chemotherapy and the number of people receiving preventive chemotherapy is largest for those middle-income countries – specifically lower-middle-income countries.

It is clear that if the 2020 targets of the Roadmap are to be achieved, the coverage gap will have to be closed in both low- and middle-income countries. Recognition of the challenge of inequalities within countries is also implicit in the goals of the World Bank, which has added to its goal to end extreme poverty a new goal to promote shared prosperity (*3*). In measuring progress towards shared prosperity, the World Bank is focusing on the poorest 40% within countries. Evidence revisited later in this chapter points to a high concentration of the burden of NTDs among the poorest 40%. Indeed, the burden of NTDs has already been suggested as a proxy in endemic countries for extreme poverty and for targeting interventions to alleviate it (*4*). This report shifts slightly the focus, towards the burden of NTDs as a proxy for inequitable access to the systems – especially health systems – through which people improve their health and wealth.

[1] In this report, the term "NTD control" refers to NTD control, elimination and eradication.

[2] Among the countries that have moved from low-income to middle-income status between the early 1990s and 2012 are Ghana, India, the Lao People's Democratic Republic, Nigeria, Pakistan, Senegal, Uzbekistan, Viet Nam, Yemen and Zambia.

Fig. 2.1 Number of people requiring and receiving preventive chemotherapy, by country income group, 2000–2015



Notes: World Bank classifications of low-income and middle-income countries are provided in *Annex 5*. The middle-income group includes both lower-middle-income and upper-middle-income countries. Income groups are held constant across the period of analysis. The dark solid line is the number of preventive chemotherapy treatments required for populations at risk of infection and the light dotted line is the number of treatments delivered. The distance between those lines is the coverage gap. The period 2013–2015 (light solid line) is based on an assumption of linear scale-up from actual coverage reported in 2012 towards 2020 targets; these are targets, not forecasts.

2.2 NTDs and the Sustainable Development Goals

At the time of preparation of this report, the post-2015 development agenda was still under discussion. It was already clear, however, that the world's focus has expanded from poverty alleviation to shared prosperity, and from disease-specific goals to universal health coverage (UHC).[1] The Sustainable Development Goals (SDGs) recognize more explicitly than ever before the need to tackle inequity and provide health for all (*5*).

NTDs are listed under proposed SDG 3 to "Ensure healthy lives and promote well-being for all at all ages". The goal has a target to "end the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases and combat hepatitis, water-borne diseases, and other communicable diseases" by the year 2030 (Target 3.3). The inclusion of NTDs is not trivial. The 17 NTDs account for a disease burden of at least 26 million disability-adjusted life years (DALYs), around half the burden of tuberculosis or malaria (*6,7*). Inclusion of other selected neglected diseases and conditions brings the total to about 48 million DALYs, a burden comparable to that of tuberculosis (*7*). Nonetheless, the special role of NTD control to the SDGs is not driven by its impact at the country level, but by its impact on the distribution within populations, especially across socioeconomic groups.

[1] WHO has defined universal health coverage (UHC) as "ensuring that all people can use the promotive, preventive, curative, rehabilitative and palliative health services they need, of sufficient quality to be effective, while also ensuring that the use of these services does not expose the user to financial hardship." There are three dimensions to the so-called "UHC cube": (1) extending coverage to individuals who previously were not covered; (2) extending coverage to services that previously were not covered; or (3) reducing direct payments needed for each service.

This chapter is not intended as a comprehensive review of how NTD control will contribute to the SDGs, much less how the SDGs will contribute to NTD control. However, it is worth mentioning two other SDG targets that provide context for the rest of the chapter:

- Target 3.8. to "achieve universal health coverage, including financial risk protection, access to quality healthcare services, and access to safe, effective, quality, and affordable essential medicines and vaccines for all"; and
- Target 13.3. to "improve education, awareness raising and human and institutional capacity on climate change mitigation, adaptation, impact reduction, and early warning".

These targets provide a framework for investment in universal coverage against NTDs, including disease elimination and eradication, as well as the longer-term investments in vector control that will be required in the context of climate change.

2.2.1 NTD control as a litmus test for universal health coverage

In WHO's second report on NTDs, the Director-General Dr Margaret Chan wrote:

> Overcoming neglected tropical diseases makes sense both for economies and for development. The prospects for success have never been so strong. Many millions of people are being freed from the misery and disability that have kept populations mired in poverty, generation after generation, for centuries. We are moving ahead towards achieving universal health coverage with essential health interventions for neglected tropical diseases, the ultimate expression of fairness.This will be a powerful equalizer that abolishes distinctions between the rich and the poor, the privileged and the marginalized, the young and the old, ethnic groups, and women and men.

This third report is not the first to suggest that the NTDs are a litmus test for UHC. It is, however, the first to attempt to translate existing NTD control coverage targets from the Roadmap into investment targets towards UHC. It describes the process by which coverage could be extended with priority to populations facing the highest burden of NTDs. This is discussed in greater detail at the end of the chapter. Of course, UHC is not only or even primarily about extending the coverage of "vertical" disease programmes – it requires strengthening of "horizontal" health systems.

Indeed, the extension of UHC to those populations with a high burden of NTDs will not be limited to NTD interventions. In areas where NTD control is one of the first health services on offer, it is difficult to separate its benefits from those of health care more generally. Preventive chemotherapy for NTDs has already served as a pathfinder for accelerated and cost–effective delivery of primary care. Nigeria recently launched the first nationwide lymphatic filariasis and malaria co-implementation plan, based on community-

directed distribution of both preventive chemotherapy and long-lasting insecticidal nets. Synergies are also being explored as part of a proposed World Bank project for seasonal malaria chemoprevention in the Sahel subregion of Africa.

2.2.2 NTD control as a canary in the mine for climate-sensitive disease risks

The other major SDG target motivating much of the content of this chapter is that related to climate change mitigation, adaptation, impact reduction, and early warning. Many vector-borne and zoonotic diseases – that is, diseases involving vectors such as blood-feeding insects or animal hosts – exhibit some degree of sensitivity to climate. Climate variability and long-term climate changes in temperature, rainfall and relative humidity are expected to increase the distribution and incidence of at least a subset of these diseases (*8*). Some of these changes are now inevitable. Dengue has already re-emerged in countries in which it had been absent for the greater part of the last century. Its spread is closely related to that of other arbovirus-related diseases, such as chikungunya and Zika, transmitted by the same vectors. Fortunately, public-health interventions can help reduce the health impact of climate change (*9*). More details can be obtained from *Chapters 3* and *4*.

The theme of World Health Day 2014 – "small bite, big threat" – highlighted the importance of vector control for at least five vector-borne NTDs: Chagas disease, dengue, the leishmaniases, lymphatic filariasis, onchocerciasis and schistosomiasis. Investment targets for vector control against another major vector-borne diseases, such as malaria, already exist elsewhere (*10*). This report offers the first investment targets for sustained vector control against Chagas disease and dengue, as well as visceral leishmaniasis in areas that are not co-endemic with malaria. As described later in this chapter, the investments are significant but the cost of doing nothing is larger. Failure to invest in the entomological and other capacities needed to control at least malaria and major vector-borne NTDs would provide a warning that the world is unprepared to manage these and other climate-sensitive disease risks.

Meanwhile, a recent World Bank report has emphasized the interactions between human and livestock health, and their potential consequences for economic security, including food security (*11*). Causal links between changing temperature and rainfall patterns and the incidence of zoonotic disease are yet to be established, although there are many plausible mechanisms through which these could occur (*12,13*). Of the 17 NTDs, at least four have prominent zoonotic characteristics: echinococcosis, foodborne trematodiases, rabies, and taeniasis and (neuro)cysticercosis. Their control demands intersectoral collaboration covering human health, veterinary health and environmental health. Investment targets for the "One Health" approach are beyond the scope of this report, although recent economic evidence is covered in the disease-specific investment cases presented in *Chapter 4*.

2.3 Towards targets for universal coverage against NTDs by 2030

Monitoring of UHC is increasingly focused on two discrete components of health system performance: levels of coverage with health services and financial protection, with a focus on equity (*14*). A joint WHO/World Bank framework for monitoring progress towards UHC (*15*) proposes the following targets:

- By 2030, all populations, independent of household income, expenditure or wealth, place of residence or gender, have at least 80% essential health services coverage; and
- By 2030, everyone has 100% financial protection from out-of-pocket payments for health services.

This section considers what the SDG targets – in particular the UHC targets – imply for NTD programmes in terms of population coverage with *prevention* and financial risk protection against the cost of *treatment and care*. Existing NTD targets are in fact well aligned with UHC targets, and monitoring progress towards the former will assist in monitoring progress toward the latter. Monitoring NTDs can provide some of the detail needed to monitor the equity of UHC progress across population groups.

2.3.1 Prevention of NTDs

A UHC target of 80% essential health services coverage is broadly consistent with coverage targets for the prevention of NTDs. The UHC target could be easily translated into an NTD-specific target such as:

80% coverage of the population requiring prevention of NTDs by 2030.

Coverage targets for preventive chemotherapy, for example, are defined as 100% geographical coverage of endemic districts and between 65% and 85% programme or therapeutic coverage of people requiring treatment within those districts, depending on which diseases are endemic. Coverage targets for integrated preventive chemotherapy will vary among countries, but globally the target is about 80%. Progress towards these targets is reported to WHO. Baseline values for 2012 are provided in *Chapter 3*. Coverage targets for other major interventions for prevention of NTDs, namely vector control, veterinary public-health services and yaws eradication, are reviewed in *Chapter 4*. Specific targets for universal access to improved water and sanitation are expected as part of the SDGs.

It is widely recognized that coverage alone is not sufficient – coverage must be of sufficiently high quality (*16*). High-quality coverage means timely and consistent coverage with the full package of essential interventions. For preventive chemotherapy, low compliance (the percentage of people actually taking the medicine that has been given to them) will undermine efforts to eliminate diseases (*17*). However, if a sufficiently high level of coverage of sufficiently high quality is sustained for a sufficiently long period of time – between 3 and 10 years, depending on the disease – transmission will become less likely or may even be completely interrupted. Interruption is confirmed by surveys. In this sense, the quality of coverage could be assessed at least in part by the achievement of another possible NTD target:

A 90% reduction in the number of people requiring prevention of NTDs by 2030.

What this target means in terms of scale up followed by scale down in the number of people requiring prevention coverage is discussed in *Section 2.4*. Lymphatic filariasis, onchocerciasis and trachoma are targeted for elimination well before 2030, and preventive chemotherapy will only be required, with reduced frequency, in areas with schistosomiasis and soil-transmitted helminthiases. Dracunculiasis and yaws are targeted for eradication by 2015 and 2020 respectively. The scale down of prevention of multiple NTDs will no doubt be facilitated by improved living conditions, including access to improved water and sanitation. Nonetheless, a 90% reduction in populations at risk of climate-sensitive diseases, such as dengue and zoonotic diseases, may not be realistic in all countries. In some, these diseases may require prevention measures beyond 2030.

2.3.2 Treatment and care of NTDs

A necessary condition for the achievement of the UHC target of 100% financial protection by 2030 is that all populations at risk are financially protected against NTDs. That is:

100% of the population at risk protected against out-of-pocket payments due to NTDs by 2030.

Catastrophic health expenditure has been defined as out-of-pocket payments exceeding 10% of annual household spending or, alternatively, 40% of non-subsistence spending. Measurement of NTD-specific catastrophic expenditure is impractical in most countries given that existing survey instruments rarely collect disease-specific out-of-pocket expenditures (*18*). This report therefore focusses on targets related to the adoption of policies to provide an essential package of NTD services free at the point of use.

Section 2.4 provides investment targets for this essential package of services, provided free at the point of use to cases of Buruli ulcer, human African trypanosomiasis, leprosy and the leishmaniases, as well as for hydrocele and lymphoedema due to lymphatic filariasis and trichiasis due to trachoma. As detailed in *Chapters 3* and *4*, these services include diagnosis and treatment, surgery, chronic care, disability prevention and rehabilitation. These targets are not just for NTD programmes; they include investments in the general health services provided by the health system, such as hospital bed days and clinic visits. They include also investments in active case-finding, to keep to a minimum the costs incurred by patients while seeking diagnosis.

Diagnosis and treatment of several of these NTDs are already being provided free of charge in a number of countries. However, as discussed later in this chapter, out-of-pocket payments are not the only source of financial hardship for those affected by NTDs. Even when diagnosis and treatment are provided free of charge, expenses related to transport, accommodation and food can take a heavy toll on households, to say nothing of lost wages. Other disease programmes have already argued for the need to monitor progress "beyond UHC", with indicators of social protection such as paid sick leave and enablers for transport (*19*). The need for such safety nets to complement UHC targets would be mitigated at least in part by the achievement of another possible NTD target:

100% of the population within less than 5-hour travel of free diagnosis, treatment and care for NTDs by 2030.

Travel is only one of many barriers to access, but for the rural populations most affected by Buruli ulcer, Chagas disease, human African trypanosomiasis, leprosy and the leishmaniases, it may be the most obstructive. Increased proximity has been crucial to recent declines in the number of cases of human African trypanosomiasis: 80% of the population at risk for gambiense sleeping sickness now lives within 5-hours travel of a fixed health facility offering diagnosis and treatment for the disease (*20*). However, 5 hours may prove too long and the quality of the services too low as more areas shift from active case-finding to passive surveillance; 5-hour travel is an indicative target that would need to be revised at country level.

Achievement of this target will depend critically on broader investments in the capacity of health systems to deliver services where they are needed, and on the development of diagnostic tools and treatment regimens that can be administered in the field. The example provided in *Chapter 4* of a new rapid diagnostic test for Buruli ulcer illustrates how new tools are needed to bring health systems closer to where NTDs occur. An estimate of the investments required for research and development, from basic research to operational research, were beyond the scope of this report.

2.4 Investment targets for universal coverage against NTDs

This section provides targets for the investments implied by a scale up of current interventions towards the Roadmap's coverage targets for 2020 and universal coverage targets for 2030. Targets for universal coverage against NTDs were translated from UHC targets in *Section 2.3* above.

Investment targets have been developed for interventions to overcome 12 of the 17 NTDs.[1] They combine targets for the number of people requiring interventions against NTDs with benchmarks for the cost per person of delivering those interventions. That is, for any given country and intervention:

investment target = population target × unit cost benchmark.

The global targets presented in this report were built up from intervention-specific population targets and unit cost benchmarks for more than 100 low- and middle-income countries.[2]

Methods are described in detail in a technical appendix.[3] Sources for population targets include publicly available WHO data and documents. Unit costs benchmarks are based on a review and synthesis of cost and cost–effectiveness analyses. For interventions with a sufficient number of studies, benchmarks are inspired by regression models employed by WHO to estimate the unit costs of health-care services (*21*). Unit cost benchmarks for medicines are based on low buyer prices from the International Drug Price Indicator Guide (*22*). Investment targets are presented within a range determined by low and high unit cost benchmarks, because not all of the differences in unit costs across studies could be accounted for.

Specific targets have been developed for domestic investment – that is, investment from sources within endemic countries. These domestic investment targets recognize that most

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[1] Dracunculiasis is targeted for eradication by 2015 and so has not been included in the investment targets of this report. The four neglected zoonotic diseases – echinococcosis, foodborne trematodiases, rabies, and taeniasis and (neuro)cysticercosis – will be covered in future updates. The 12 included diseases account for most of the global burden of disease attributed to NTDs (*6,7*). However, not all interventions have been included for these 12 diseases. For Chagas disease, the targets include investments in vector control in endemic countries but do not (yet) include screening for prevention of transfusional and organ transplantation transmission, or case diagnosis and treatment. Full consideration of these interventions will be given in future analyses considering also affected populations in non-endemic countries, as more data become available. While not 100% comprehensive, the targets laid out in this report are taken to be representative of patterns and trends in investment in universal coverage against NTDs.

[2] Country programmes interested in obtaining investment targets specific to their country should contact WHO.

[3] The technical appendix and related code using the free software R will also be made available via http://www.who.int/neglected_diseases/en/.

of the financing that will be available for the post-2015 development agenda will not be foreign aid (*23*). They are based on the principle that NTD programmes should not be disproportionately dependent on foreign aid relative to other health programmes. In 2011, the domestic share in total expenditure on health was 71% in low-income countries, 98% in lower-middle-income countries and more than 99% in upper-middle-income countries (*24*). These shares are applied to the total investment targets to obtain domestic investment targets, allowing for an upward trend towards 2030 that is in line with recent trajectories in economic growth.

These targets should not be interpreted as forecasts. They are intended to help endemic countries with their plans and budgets for NTD control, not to replace those plans and budgets. Investment targets are perhaps most useful in assessing the affordability to governments and national insurance schemes of universal coverage against NTDs within a longer-term perspective. They may facilitate discussions between ministries of health and other relevant ministries – especially ministries of finance. They may also help in the design of innovative financing mechanisms described in *Section 2.7*. Finally, investment targets may give an idea of the size of the market for innovation. While affordable, universal coverage against NTDs is not so cheap that it does not warrant further investment in new tools and approaches.

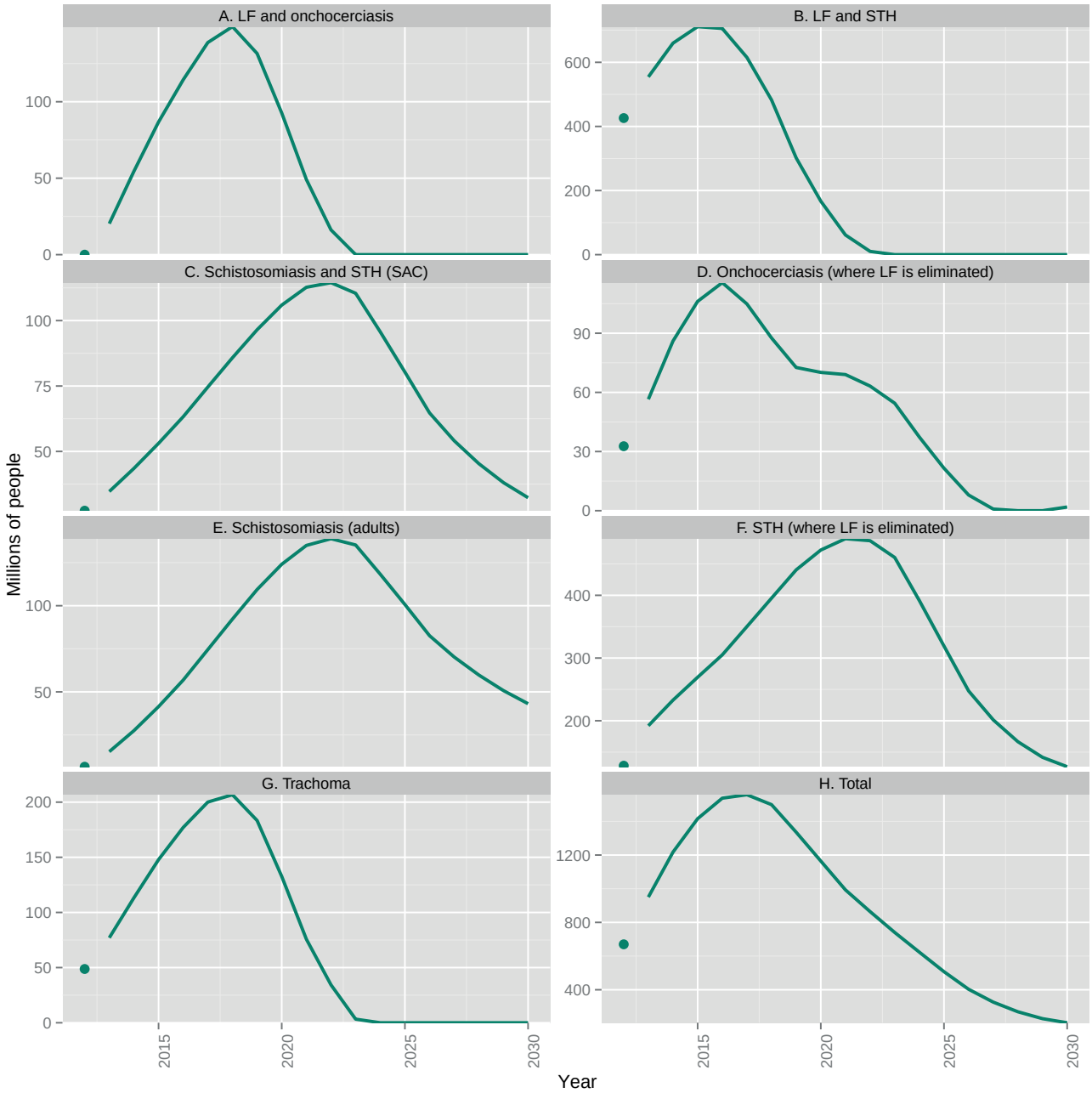
2.4.1 Population and service targets

Populations targeted for coverage with prevention

In the case of preventive chemotherapy for five NTDs, population targets are based on estimates of the population requiring treatment and the Roadmap's targets for treatment coverage and duration. These targets suggest that if a high level of coverage is maintained for a number of consecutive years, populations should no longer require this intervention. *Fig. 2.2* displays the minimum number of people to be targeted. Diseases are grouped based on evidence about co-endemicity and the possibility of integrated delivery of medicines for lymphatic filariasis and onchocerciasis in Africa, schistosomiasis and soil-transmitted helminthiases among school-age children, and lymphatic filariasis and soil-transmitted helminthiases outside Africa. Globally, the total number of people targeted for coverage with preventive chemotherapy for at least one NTD reaches a high of about 1.5 billion in 2017 (*Fig. 2.2, panel H*) and then decreases to 200 million people by 2030.

In the case of vector control for Chagas disease, dengue and visceral leishmaniasis, population targets are based on estimates of the population at risk living in areas eligible for sustained vector control interventions. Targets for Chagas disease imply vector control coverage for an average of 110 million people per year over the period 2015–2030. About 2 billion people are targeted each year for coverage against the dengue vector – a relatively conservative target given recent population-at-risk estimates of between 2 and 4 billion (*25*). For visceral leishmaniasis, long-lasting insecticide-treated nets and indoor residual

Fig. 2.2 Number of people targeted for coverage with integrated preventive chemotherapy, selected NTDs



LF, lymphatic filariasis; SAC, school-age children; STH, soil-transmitted helminthiases.

Notes: The dots indicate the number of people treated in 2012; the solid lines are targets not forecasts. Targets assume integrated delivery of preventive chemotherapy for LF and onchocerciasis in Africa, schistosomiasis and STH among school-age children, and LF and STH outside Africa. Pending further evidence, they do not yet assume further integration of LF and onchocerciasis in Africa with schistosomiasis and STH.

spraying are targeted for areas of South-East Asia in which malaria programmes are not already active – areas with a population of about 35 million people in 2015. This report does not yet include targets for vector control against lymphatic filariasis, although integrated vector management is promoted to support the elimination strategy.

Population targets for surveillance after preventive chemotherapy has been stopped are based on the administration of three surveys within 3–6 years of stopping the intervention for lymphatic filariasis, onchocerciasis or trachoma.

Populations targeted for coverage with treatment and care

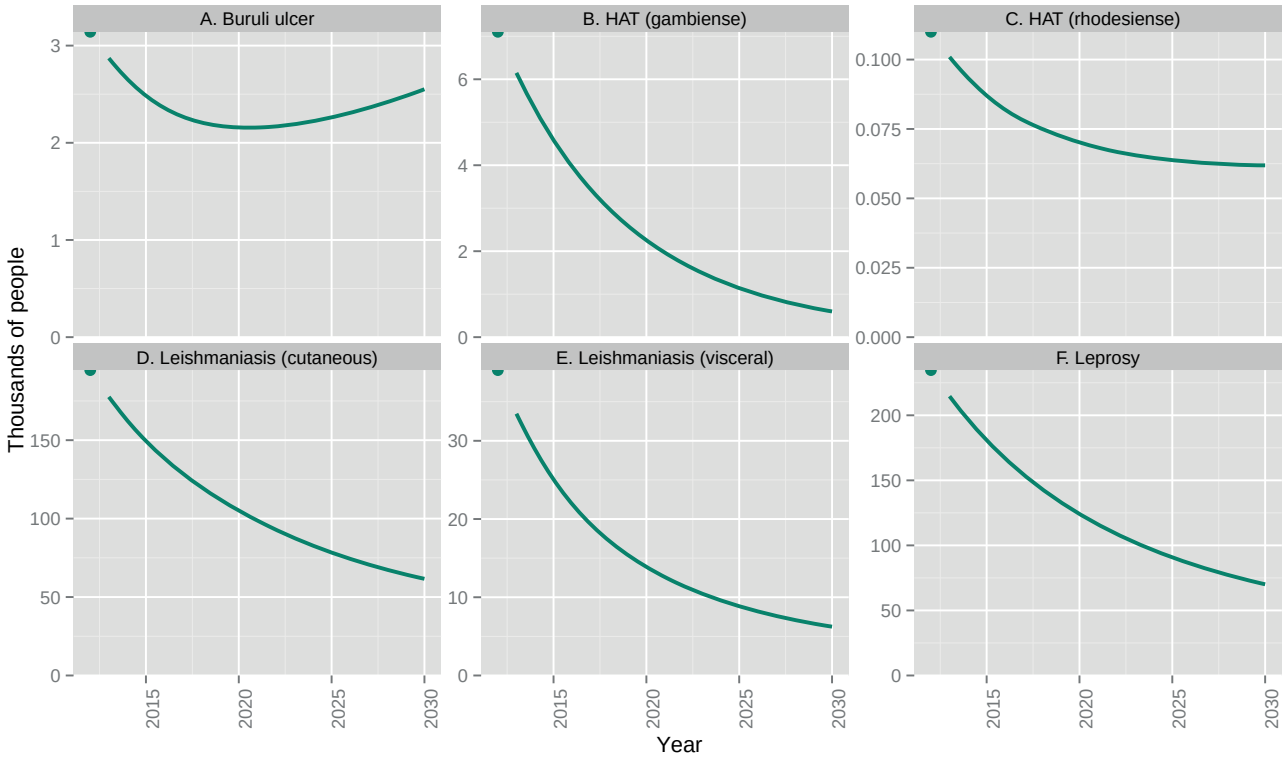
For the purposes of this chapter, population targets for coverage with treatment and care are based on the historic relationship between notification rates and GDP per capita. *Fig. 2.3* displays targets for the number of people targeted for coverage, including financial protection. These targets aim to prevent death and disability as well as indebtedness and impoverishment among the more than 500 000 households still affected by Buruli ulcer, human African trypanosomiasis, the leishmaniases and leprosy each year.

If expressed relative to the total populations within endemic countries, these targets imply that by 2020, incidence would be less than 1 per 10 000 people for leprosy, gambiense human African trypanosomiasis and visceral leishmaniasis. It is difficult to set population targets for Buruli ulcer given the extent of under-reporting and unexplained year-over-year fluctuations in the number of cases reported – the targets displayed in *Fig. 2.3 (panel A)* are effectively flat over time. The number of people targeted for coverage by treatment and care of gambiense human African trypanosomiasis in 2030 exceeds a recently set target for zero incidence, but is consistent with the expectation that coverage will need to be maintained during confirmation of the interruption of transmission.

Population targets for active case-finding for Buruli ulcer and leprosy are based on the population targets for treatment and care and targets for the number of contacts to be traced. Active case-finding for human African trypanosomiasis is based on populations living in high and very high risk areas targeted for annual mobile teams and on moderate risk areas targeted for 3-yearly mobile teams. Camp-based or house-to-house screening for visceral leishmaniasis is limited to parts of Bangladesh and India. Assumptions behind the targets for morbidity management and disability prevention are available from the technical appendix.[1]

[1] The technical appendix and related code using the free software R will also be made available via http://www.who.int/neglected_diseases/en/

Fig. 2.3 Number of people targeted for coverage with treatment and care based on trends in notifications and GDP per capita, selected NTDs



HAT, human African trypanosomiasis.

Notes: The dotted observation is the number of people notified and treated by countries in 2012; the solid lines represent targets based on the historic relationship between notification rates and GDP per capita.

2.4.2 Investment targets towards 2020 and beyond

The total investment targeted for the period 2015–2030 is US$ 34 billion excluding medicines (most of which has been pledged as in-kind donations). *Fig. 2.4* breaks down the total investment target (*panel A*, with or without vector control) by major intervention (*panels B-I*). Investments required for the water and sanitation sector are not estimated in this report, but are available from other sources (*26*).

Towards 2020

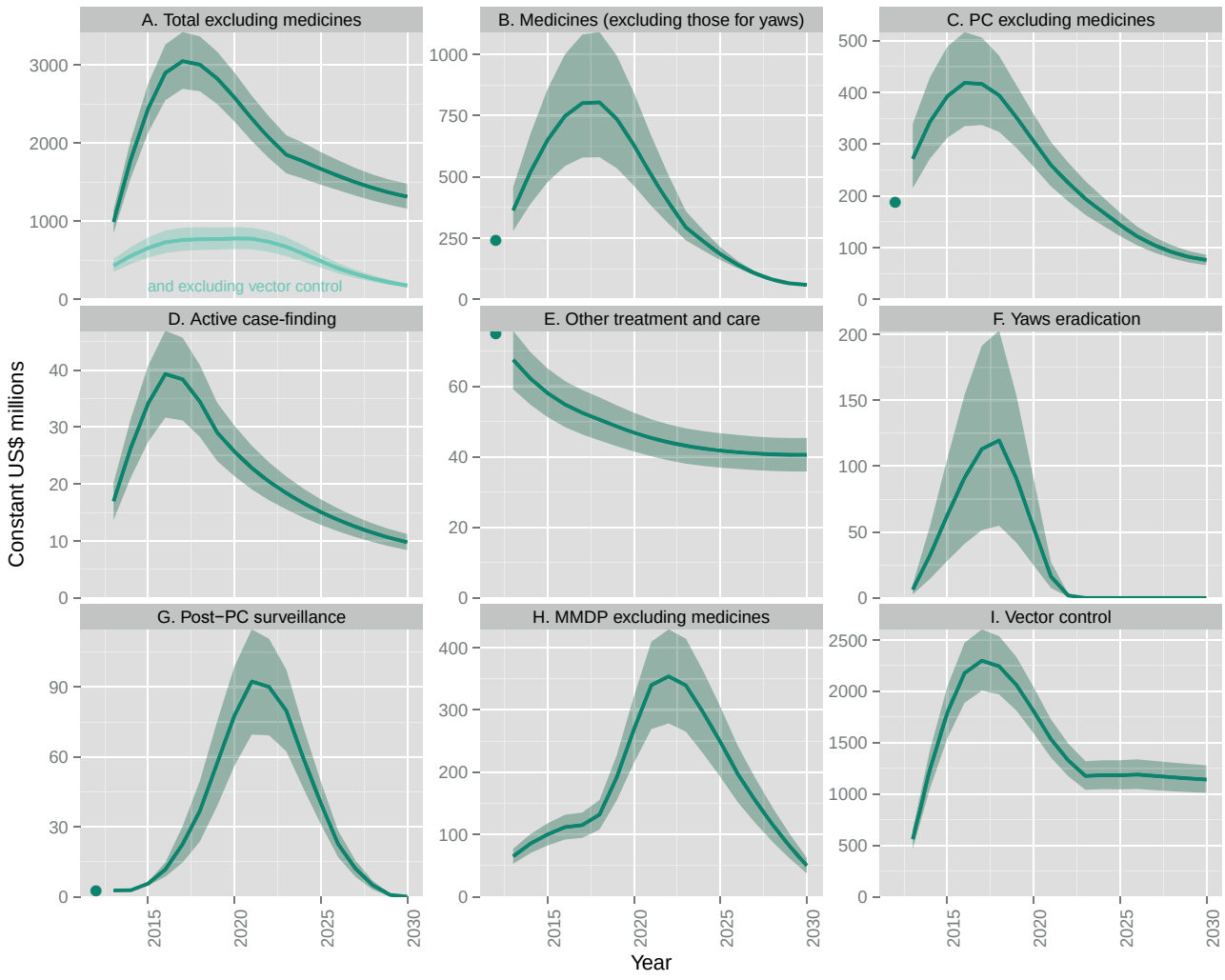
The Roadmap's targets for 2020 remain critical milestones on the path towards universal coverage against NTDs. Excluding medicines, the total investment target for the period 2015–2020 is US$ 18 billion. Excluding investments in vector control, the target for the same period is US$ 4.5 billion, with a peak of US$ 900 million in 2020 (*panel A*). The target for medicines is estimated at about US$ 4.5 billion for the period, peaking at about US$ 810 million in 2017 (*panel B*). Most of this amount has been committed in donations from the pharmaceutical industry. Follow-through on these commitments will be critical to the achievement of 2020 targets. Just as important, however, is the US$ 2.8 billion targeted for delivery of those medicines, through preventive chemotherapy (*panel C*), active case-finding (*panel D*) and individual treatment and care by the general health system (*panel E*). This treatment and care includes costs related to diagnosis, surgery and general health services – namely hospital bed days and clinic visits – for Buruli ulcer, human African trypanosomiasis, leprosy and the leishmaniases. It does not yet include the cost of treatment and care for Chagas disease.

Donations of azithromycin for yaws eradication have not yet been secured and are therefore included in the total for yaws eradication – about US$ 550 million for the period 2015–2020 (*panel F*). A more complete treatment of the investment case for yaws eradication is available in *Chapter 4*.

Preventive chemotherapy will continue to require the biggest investments in delivery of donated medicines. At least US$ 2.3 billion is targeted for 2015–2020. In advocating for this intervention, the NTD community has typically cited values of US$ 0.10 to US$ 0.50 as the delivery cost per person per year. While useful for advocacy, the focus on single numbers risks misrepresenting the complexity of delivering "free" medicines to more than a billion people across the world. For this report, the global average unit cost benchmark is about US$ 0.30 (0.22–0.36) in 2015. Country-specific benchmarks were found to be very sensitive to the scale of implementation and density of the population. Many of the available costing studies are from peri-urban areas rather than from the rural areas in which most of the population requiring treatment is found. In the push towards 2020 targets, future updates to this analysis will need to factor in the cost of the "last mile" of preventive chemotherapy in more diverse settings.

Evidence about co-endemicity suggests that integrating the delivery of preventive chemotherapy for multiple NTDs could lower the total number of deliveries of anthelminthic medicines by 13–24% over the period 2015–2030. The scope for integration varies significantly among countries. Further research is needed to identify the potential costs, especially coordination costs inherent in financing and managing across stakeholder groups. The only published study based on real expenditures rather than projections found overall savings of 16–21% in an integrated programme against lymphatic filariasis, schistosomiasis, soil-transmitted helminthiases and trachoma in Niger (*27*). More such studies are needed. However, integration is not just about integrated delivery of preventive chemotherapy.

Fig. 2.4 Investment targets for universal coverage against NTDs



MMDP, morbidity management and disability prevention; PC, preventive chemotherapy.

Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. The dots in 2012 are actual numbers reported (when available) multiplied by the unit cost benchmarks; these are not actual expenditures, but can be thought of as a benchmark for actual expenditures. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

Integration means also integration of NTD interventions into primary health systems, as well as the systems of the education and water, sanitation and hygiene sectors. A report of the Inter-American Development Bank describes with four case studies the conditions under which "it can be done" (*28*).

In any event, NTD control will not end with the Roadmap in 2020. Approaching 2020, the focus on "quick wins" should not undermine investments in the capacity of endemic countries to sustain the drive to 2030.

Beyond 2020

If the Roadmap's targets are met for eliminating and controlling five of the NTDs, investment in delivery of medicines for preventive chemotherapy can be scaled down over time, from US$ 390 million in 2015 to US$ 74 million by 2030. The period 2021–2030 should see re-investment of these savings into other interventions within the NTD portfolio. US$ 17 billion is targeted for the 10-year period, decreasing from US$ 3.0 billion in 2020 to US$ 1.3 billion by 2030 (*panel A*). This investment will include finishing off the broader preventive chemotherapy agenda, namely surveillance after the intervention has been stopped to prevent recrudescence (*panel G*). Estimates of the backlog of cases requiring surgery for hydrocele and trichiasis are uncertain, but millions are known to be suffering, and investment targets for morbidity management and disability prevention are significant – US$ 3.1 billion over the period 2015–2030 (*panel H*). An investment target for passive infectious disease surveillance has not been included here, but is discussed in *Chapter 4* in the investment case for human African trypanosomiasis.

As targets for preventive chemotherapy are met and transmission of at least three NTDs is interrupted, vector control for Chagas disease, dengue and visceral leishmaniasis will assume an increasingly important share within the NTD portfolio – about US$ 1.2 billion per year or 73% of the total investment targeted for the period 2021–2030 (*panel I*). Although targets imply an ambitious scale up from current levels of coverage, the investment targets are lower than the costs that would be incurred by health systems in the absence of vector control. The economic cost of illness due to vector-borne NTDs is already estimated in billions of dollars each year (*29–32*).

Investments in vector control for Chagas disease may decrease after an initial programme attack phase in 2015–2020, as countries move to a surveillance phase. Investments in vector control for dengue, on the other hand, may continue to increase until 2030, in the context of a changing climate. These investments will contribute also to the control of other arbovirus-related diseases transmitted by the same vectors. Innovative vector control methods under development will hopefully help decrease cost while extending coverage.

In any case, investments in vector control for dengue are expected to be complementary to the eventual introduction of a vaccine against dengue. Although it may be possible to rebalance the investment portfolio – from vector control towards immunization – the cost–effectiveness of any such rebalancing needs to be evaluated. Immunization may be constrained by manufacturing capacity and the lack of vaccines for diseases transmitted by the same vectors. As a result, vector control will continue to play a pivotal role in reducing vector densities and managing outbreaks.

Given the scale of the investment targeted well beyond 2020, universal coverage against NTDs requires a serious investment strategy.

Beyond charity

Excluding medicines, the investment target for universal coverage against NTDs averages US$ 2.1 billion per year over the period 2015–2030. This target approaches the US$ 2.5 billion that was spent on malaria control in 2012, but is less than the US$ 5.1 billion that the malaria control community has estimated is required on average each year (*33,10*). It is aimed at reducing a global burden of disease equivalent to about one half of that for malaria (*6,7*). Investments in universal coverage against NTDs will not be trivial – neither in their scale nor in their impact. The role of foreign donors and community volunteers in the progress made in NTD control to 2015 is highlighted later in this chapter. However, NTD control needs to become an integral part of national health plans and budgets and rely less on charity if it is to achieve universal coverage.

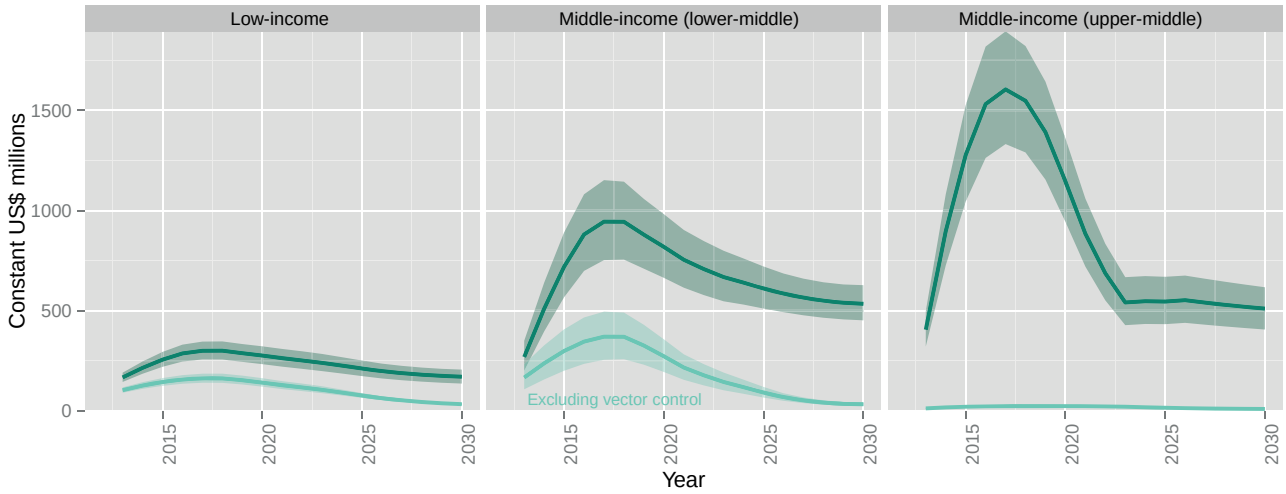
Reliance on foreign donors and community volunteers becomes problematic when it results in fragmented NTD projects that fail to deliver the high levels of sustained coverage that are required to interrupt transmission. The investment target for universal coverage against NTDs is about 10 times the US$ 200–300 million disbursed or committed by foreign donors during 2012–2014 (*34*). It is unlikely that an increase of this order of magnitude can be achieved in the current global health financing climate. Studies of the cost of preventive chemotherapy reviewed for this chapter indicate that unpaid volunteers were used in about 80% of sites. In studies in which the opportunity cost of their time was estimated, it comprises 8–60% of the total. The role of community health workers will continue to play a role in universal coverage against NTDs; but fully-scaled NTD control programmes covering over a billion people cannot expect to recruit and retain sufficient numbers of volunteers if other major disease programmes are offering incentives.

2.4.3 Investment targets for low- and middle-income countries

Where do most of the investments in universal coverage against neglect need to be made? In this section, investment targets are broken down by groups of low- and middle-income countries. Middle-income countries include both lower-middle-income and upper-middle-income countries.

Fig. 2.5 combines investment targets for preventive chemotherapy excluding medicines, surveillance after preventive chemotherapy, yaws eradication and vector control under the heading of "prevention". The investment target for prevention during 2015–2030 is US$ 30 billion. Most of the investment in prevention is required in lower-middle-income countries – US$ 11 billion including vector control or US$ 3.0 billion excluding it. Investment targets decrease as diseases are eradicated, eliminated or controlled such that the frequency of interventions can be scaled down. In upper-middle-income countries, targets for prevention are made up almost entirely of investments in vector control.

Fig. 2.5 Investment targets for prevention, by country income group



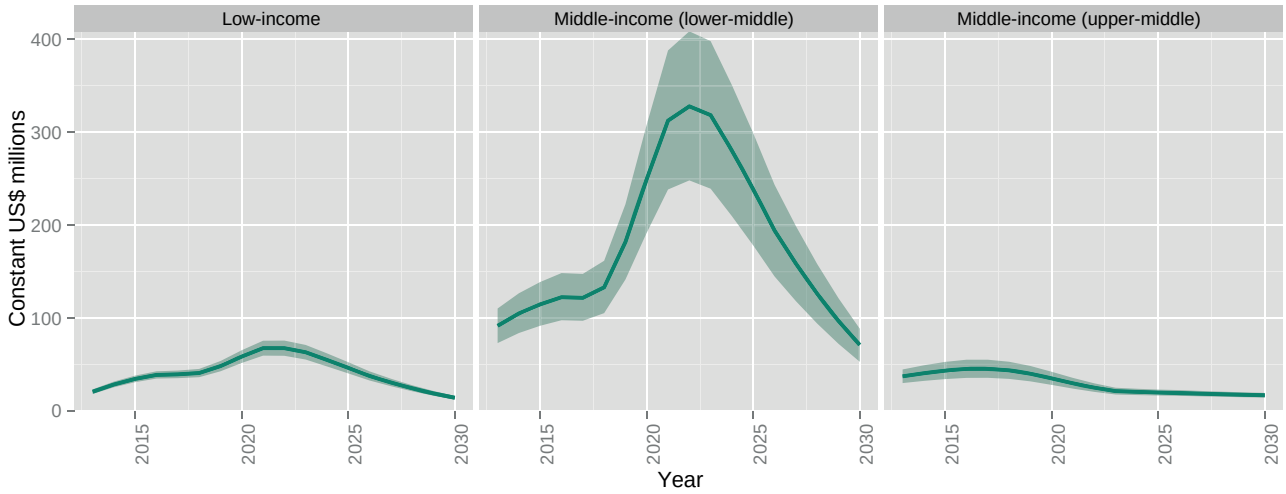
Notes: "Prevention" combines from *Fig. 2.4*: preventive chemotherapy (PC) excluding medicines, post-PC surveillance, yaws eradication, and vector control. Income group status is held constant across the period of analysis. Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

Fig. 2.6 combines active case-finding, morbidity management and disability prevention, and other treatment and care under the heading of "treatment". The investment target for treatment excluding donated medicines is US$ 4.2 billion, or 12% of the total for both prevention and treatment during 2015–2030. At an average of US$ 120 per case found and treated – not including the cost of donated medicines – achievement of the target remains critical to the 36 million people targeted to benefit from coverage. Again, most of the investment is required in lower-middle-income countries – US$ 3.1 billion over the period 2015–2030. Investments do not cover non-medical costs, such as transport to health centres; social protection will have to cover those costs that health systems do not.

2.4.4 Targets for domestic investment

Given that most of the investment targeted is for middle-income-countries, what investment might be raised from sources within endemic countries? In this section, targets are set for domestic investment in universal coverage against NTDs. Unfortunately, most countries do not have good estimates of the share of NTD-related expenditures that are already coming from domestic sources. Fortunately, as described later in this chapter, progress is being made to fill this gap in the data. This report has argued that targets for domestic investment should be set such that the realization of universal coverage against NTDs will not depend disproportionately on foreign aid.

Fig. 2.6 Investment targets for treatment and care, by country income group



Notes: "Treatment and care" combines from *Fig. 2.4*: Morbidity management and disability prevention, active case-finding, and other treatment and care. Income group status is held constant across the period of analysis. Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

Fig. 2.7 displays the targets for domestic investment in universal coverage against NTDs. The domestic investment target for the period 2015–2030 is US$ 33 billion, or 96% of the total investment target. The domestic investment target is greatest for the group of lower-middle-income countries – US$ 14 billion, or 97% of the total investment targeted for this group. As a share of the total investment target, the domestic investment target is lowest among low-income countries – from 82% in 2015 to 92% by 2030. Of course, these averages conceal considerable variation among countries. For some, the domestic investment target represents less than two-thirds of the total for 2015. Nonetheless, if recent trajectories in economic growth are maintained, by 2030 the domestic share could exceed 80% in all of them.

For all income groups, domestic investment targets decrease after 2020 in absolute (dollar) terms, as coverage targets are achieved and NTDs are controlled, eliminated or eradicated. These targets for domestic investment would appear to be affordable on average. The domestic investment target for NTDs represents less than 0.1% (one-tenth of 1%) of domestic expenditure on health expected within the group of low- and middle-income countries during 2015–2030. The percentage is highest for the group of low-income countries, where the domestic investment target for NTDs is nonetheless still well below 1% of domestic expenditure on health.

Fig. 2.7 Targets for domestic investment in universal coverage against NTDs, by country income group

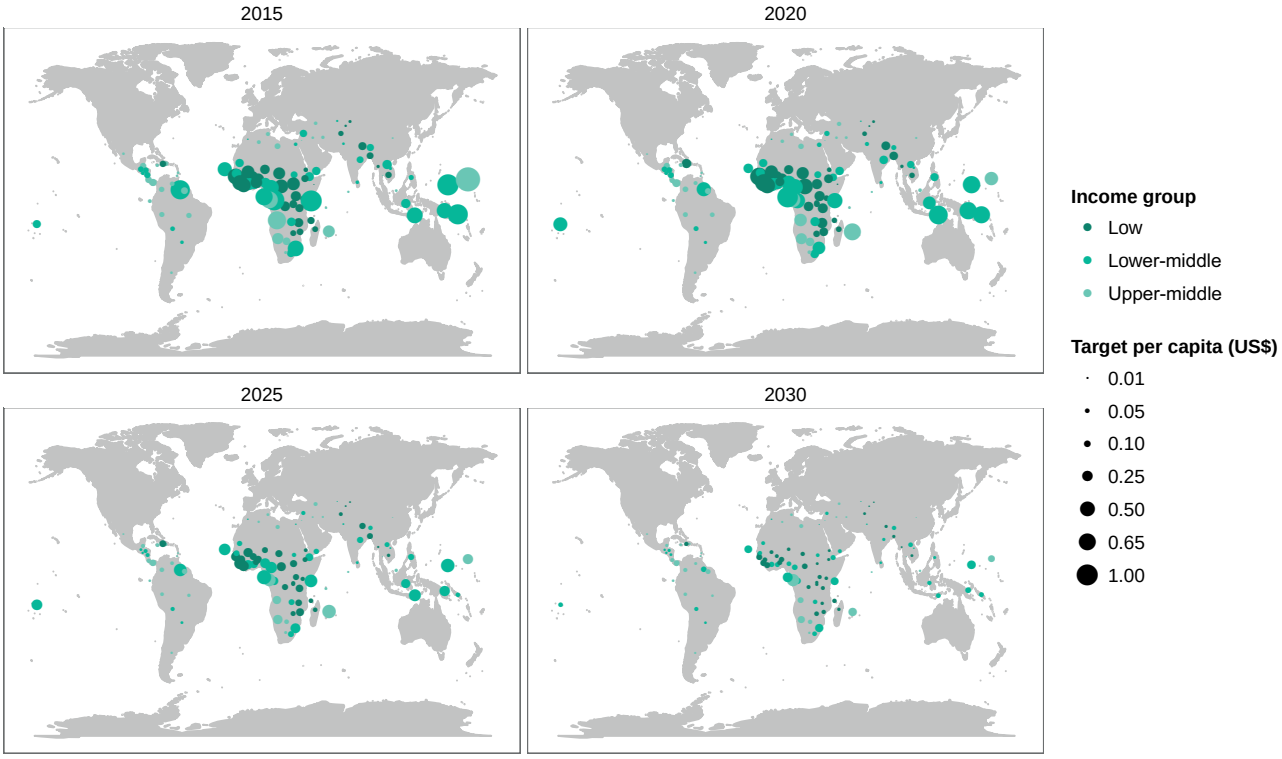
Notes: This is the domestic investment target combining both prevention (*Fig. 2.5*) and treatment and care (*Fig. 2.6*) or all panels of *Fig. 2.4*. Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

Fig. 2.8 illustrates the differences between countries in the relative scale of domestic investments being targeted. The domestic investment target is expressed in per capita terms – that is, a country's target is divided by its total population. Excluding vector control, domestic investment targets are everywhere less than US$ 1.33 per capita in 2015 and everywhere less than US$ 0.35 by 2030. Over the period 2015–2030, the average is US$ 0.10 per capita for the group of low-income countries, US$ 0.11 for lower-middle-income countries and US$ 0.02 for upper-middle-income countries. Targets for vector control are not depicted. Including vector control, domestic investment targets are markedly higher, but remain below US$ 16.50 per capita in 2015 and below US$ 3.25 by 2030. During the period 2015–2030, the average is US$ 0.22 per capita for the group of low-income countries, US$ 0.28 for lower-middle-income countries and US$ 0.33 for upper-middle-income countries.

These targets are low relative to what is already being spent on health from domestic sources, both public and private. In 2011, per capita domestic expenditure on health was US$ 21 in low-income countries, US$ 80 in lower-middle-income countries and US$ 406 in upper-middle-income countries (*24*). The High Level Taskforce on Innovative International Financing for Health Systems estimated that ensuring coverage with a set of essential health services would require US$ 60 per person in low-income countries in 2015.

In theory, domestic investment can be public or private. In practice, however, prevention will likely have to be financed by government, and treatment and care, if not financed by government, will require subsidies for compulsory prepayment into pooled funds such as a health insurance. Government and pooled financing of NTDs is most likely to occur within the context of UHC reform.

Fig. 2.8 Targets for domestic investment in universal coverage against NTDs (excluding vector control) in per capita terms, selected years



Notes: These targets do not replace any existing country plans or budgets. World Bank classifications of low- and middle-income countries are provided in *Annex 5*. Middle-income countries include both lower-middle-income and upper-middle-income countries. Income group status is held constant across the period of analysis. No targets are indicated for small island states for which the World Bank does not provide income groups. Targets exclude vector control to preserve readability of the legend. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

2.5 Towards an investment case for NTDs within universal health coverage

In the context of UHC reform, "countries should primarily first expand coverage for low-income groups, rural populations, and other groups disadvantaged in terms of service coverage, health, or both" (*35*). This "progressive universalism" signals a commitment to include the least well-off from the very beginning of the path towards UHC. WHO has outlined a three-step process:

1) categorize services into priority classes;
2) first expand coverage for high-priority services to everyone; and
3) while doing so, ensure that disadvantaged groups are not left behind.

Evidence-based categorization of services into priority classes (step 1) has typically relied on studies of effectiveness and cost–effectiveness. In the context of priority-setting for UHC, multi-criteria approaches are being advanced that recognize that societies are not interested only in the costs and effects of a given intervention at the country level; they are interested also in the distribution across population groups – in particular socioeconomic groups – of those costs and effects.

2.5.1 The investment case based on cost–effectiveness

The literature on the cost-of-illness, cost–benefit and cost–effectiveness of NTDs and their control is cited in *Chapter 4* of this report. The results, usually specific to a setting, need to be assessed to determine whether they are "generalizable" – meaning that similar results are expected in other settings. Only then can they inform priority-setting at the country, regional or global level. The last major attempt to synthesize the available evidence on cost–effectiveness and prioritize NTD and other infectious disease interventions at the global level was in 2006, in the second edition of the Disease Control Priorities Project. Of note also is the effort in 2012 to bring together the economic evidence in favour of a One Health approach to human and animal health, including the neglected zoonotic diseases (*36*).

Interventions for NTD control were among the most cost–effective interventions assessed by the Disease Control Priorities Project (second edition). Since then, their cost to national health systems has been further decreased by the donation of medicines by the pharmaceutical industry. New tools and strategies, such as vaccine development for dengue and single-dose azithromycin treatment for yaws, warrant an update of the investment case.

With this report, WHO will begin to publish updated cost–effectiveness estimates for NTD interventions at the global or regional level that can be included in priority setting exercises for UHC. This work continues with the third edition of the Disease Control Priorities Project. Country-specific results will be developed with countries upon request, to facilitate country-level priority-setting.

2.5.2 Towards an investment case including equity

WHO's Guidance for Priority Setting in Health Care, or GPS-Health, initiative offers a checklist of equity criteria relevant to the categorization of "priority classes" that should be considered in addition to cost–effectiveness analysis (*37*). These include: criteria related to the disease or condition targeted (severity of disease, capacity to benefit and past health loss); characteristics of social groups (socioeconomic status, area of living, gender, etc.); and non-health consequences of an intervention (financial protection, economic productivity and care for others). Multi-criteria approaches to priority-setting have already been applied in health and are beginning to emerge within the NTD space (*38*). How prepared is the NTD community to provide and use socioeconomic and other non-health evidence to inform the priority-setting process?

A review of the evidence on within-country inequality in the distribution of 10 selected NTDs reveals that most, but not all, evidence points to a higher risk of infection among low socioeconomic groups – the so-called social gradient. Evidence is scarce for some NTDs but more readily available for others and, among the evidence that does exist, the slope of the gradient varies across diseases and countries. In general, however, the prevalence of infection is several times higher in lower compared with higher socioeconomic groups, leading to a high concentration of the burden among the poorest.[1] For example, in Bihar, India, 83% of households in communities with high attack rates of visceral leishmaniasis belonged to the two lowest quintiles (the poorest 40%) of the wealth distribution (*39*). Dengue may be a notable exception within the NTD portfolio, with conflicting evidence on whether risk is associated with socioeconomic status (*40,41*). Nevertheless, the absence of a gradient in the risk of infection does not mean that the economic cost is not heaviest among the poor.

Studies of catastrophic health expenditure[1] or the related concept of indebtedness aim to capture some of the economic cost of disease. Such studies are still relatively few for the NTDs. Catastrophic expenditure and indebtedness have, nonetheless, been documented for treatment and care of Buruli ulcer (*42*), dengue (*43,44*) and human African trypanosomiasis

[1] See Abstract 67 of the 63rd annual meeting of the American Society of Tropical Medicine and Hygiene (New Orleans (LA), USA, 2–6 November 2014): Kulik MC, Houweling TA, Karim-Kos HE, Stolk W, Richardus JH, de Vlas S. Socioeconomic inequalities in the burden of neglected tropical diseases (http://www.astmh.org/AM/Template.cfm?Section=Abstracts_and_Education1&Template=/CM/ContentDisplay.cfm&ContentID=6128; accessed January 2015).

[2] Out-of-pocket payments exceeding 10% of annual household spending or, alternatively, 40% of non-subsistence spending.

(*45*). Evidence is arguably most complete for visceral leishmaniasis, with studies from multiple countries showing that even when diagnosis and medicines are provided free of charge, between 25% and 75% of households of sufferers experience some type of financial catastrophe (*46–50*). At least a few countries have made progress to address this issue. In Nepal, for example, in addition to free diagnosis and treatment, visceral leishmaniasis patients receive cash transfers contingent on completion of treatment, to cover transport and nutrition costs (*51*). Additional evidence on the productivity losses associated with NTDs is presented in *Chapter 4*.

Although some NTDs may already be covered within UHC under inpatient and outpatient service coverage, universal coverage against NTDs requires vigilance that prevention not be neglected within UHC. NTD programmes should demonstrate how progressive (pro-poor) they are in terms of coverage. Income is difficult to measure in low-income settings, and especially difficult to measure in the rural and often informal settings where most NTDs occur. Nonetheless, widely accepted alternatives exist. Reporting routine data broken down by socioeconomic status – including groups based on the ownership of assets, or the education level of the head of the household – would help in identifying remaining barriers to coverage (*52*). Special attention will need to be paid to the diseases of populations so poor that they cannot access even the loans needed to pay for a proper diagnosis – populations so poor that they do not even have the option of incurring financial catastrophe and debt.

The inclusion of an equity focus in policy-making will become more and more important the closer countries get to achieving the targets of the Roadmap. Such a focus will help justify sustained efforts in the remaining number of NTD hot spots where unit costs begin to increase just as the scale of operation begins to decrease. Ultimately, it will be up to countries to define the balance between equity and cost–effectiveness trade-offs in UHC priority-setting (*53*). It is clear, however, that more work can be done by the NTD community to ensure that UHC priority-setting and subsequent monitoring of progress do not neglect the neglected simply for lack of relevant data and tools.

2.6 Financing universal coverage against NTDs

This section provides a broad overview of some of the sources and mechanisms of financing for universal coverage against NTDs in the era of the SDGs (post-2015). It emphasizes the primacy of domestic investment in ensuring that the essential package of health interventions for the poor is not dependent on charity. It invites the NTD community to familiarize itself and engage with sector-wide health financing tools and mechanisms, including newer entries such as "innovative financing" mechanisms.

2.6.1 The role of foreign donors and community volunteers in progress made to 2015

The report of the Uniting to Combat NTDs coalition documents the important role that aid has played, and will continue to play, in the efforts to control NTDs (*34*). As part of its commitment to the London Declaration, the pharmaceutical industry donated 2.5 billion NTD treatments in 2012–2013. The United States Agency for International Development and the United Kingdom Government have been the "stalwarts of NTD funding among traditional donor nations", with support to at least 49 countries. Cash and in-kind aid are estimated in the coalition's report at about US$ 200–300 million a year in 2013 and 2014, excluding the donations of the pharmaceutical industry.

More difficult to quantify is the contribution of community volunteers. In the past, preventive chemotherapy has relied in large part on "an army of volunteers, or community drug distributors (CDDs), to distribute preventative drug packages through community and school-based platforms" (*54*). Volunteers have also been credited with an important role in the early detection and treatment of NTD cases (*55*). The limits of their charity have not gone untested, however. In at least one setting, it was found that the presence of community-based HIV and tuberculosis programmes providing financial incentives discouraged many CDDs from volunteering for free (*56*).

Relative to other major health programmes, NTD programmes have received one of the largest shares of the pharmaceutical industry's donations (*57*). And yet, they are constrained by the smallest number of products on the market and, along with maternal and child health programmes, the smallest number of products in the pipeline. As of 2015, most of these are still in the early stages of development and it will be some time before any of them are on the market. The commitment of foreign donors and community volunteers to NTD control will continue to be important in scaling up access to those products that are available. However, it is unlikely that they can mobilize resources at the scale implied by universal coverage against NTDs. Universal coverage against NTDs will fail if it fails to mobilize domestic investment.

2.6.2 The role of domestic investment in driving progress to 2030

The World Bank has reported that the domestic revenues of low- and middle-income countries amounted to US$ 7.7 trillion in 2012, compared with about US$ 134 billion in official development assistance from traditional donors and US$ 43 billion from emerging donors such as the BRIC countries (Brazil, Russia, India and China) and nongovernmetal organizations (*23*). In other words, governments in low- and middle-income countries already collect more than US$ 40 in domestic revenues for every dollar of foreign aid received. The same World Bank report notes that the citizens of these countries received about US$ 500 billion in officially recorded remittances from a diaspora of 215 million emigrants working abroad. Considering both public and private financing, there is more space than ever before for domestic investment in health. The question is how to realize the potential of domestic investment for universal coverage against NTDs.

Multilateral development banks have a role to play in facilitating the shift in NTD financing from grants to zero-interest loans to low-interest loans to non-concessional loans and domestic revenues. The World Bank's International Development Association (IDA) fund has already contributed to leveraging domestic investment with a mix of grants and loans. These have financed dedicated NTD projects, notably for schistosomiasis control in China, Egypt and Yemen, as well as multisectoral projects, including water resource development in the Senegal River basin. Countries have matched every dollar of IDA funds with about two dollars of domestic revenues. The World Bank recently committed to working with NTD programmes in Africa to access US$ 120 million in IDA funds. Another US$ 75 million project for combining preventive chemotherapy for NTDs with seasonal malaria chemoprevention in the Sahel will leverage domestic funding in Burkina Faso, Mauritania and Niger.

It is with the governments of endemic countries, however, that the ultimate decision lies to make universal coverage against NTDs a domestic policy priority. One of the challenges to the prioritization of NTD control for domestic investment is that it remains largely absent from national health plans and budgets, let alone the plans and budgets of other sectors. WHO and its partners have been providing assistance to countries in the use of the NTD tool for integrated planning and costing, or TIPAC (*58*). WHO will be incorporating an NTD module based on TIPAC within WHO's sector-wide costing tool (*59*). The objective is to present NTDs alongside other diseases within health plans and budgets.

Another challenge is that many endemic countries do not yet have a clear understanding of how much (or little) domestic investment is directed towards NTD programmes relative to foreign aid or relative to other priority disease programmes. WHO is working with countries to track actual expenditures on NTDs through the WHO Health Accounts Country Platform. Health accounts have been completed in 11 countries and at least five low-income, high-burden countries in Africa are now tracking expenditures on NTDs as part of their national statistics. Health accounts are ongoing or will start soon in another

39 countries. Comparisons of domestic funding with domestic investment targets will help inform future WHO reports on progress made towards universal coverage against NTDs.

2.6.3 The role of innovative financing mechanisms in optimizing domestic investments

The rebalancing of the financing mix towards less foreign aid and more domestic investment will take time, especially in low-income countries. But almost nowhere will financing universal coverage against NTDs be business-as-usual. Both foreign and domestic investors will need not only to invest more, but invest more wisely. Wiser investment, in turn, is not only about integrating NTD programmes to lower costs; it is also about strengthening programmes to deliver results. Increasingly, NTD investments are being made through innovative financing mechanisms, with the goal of overcoming some of the perceived problems with traditional mechanisms, which have focussed more on inputs and activities than on outputs and outcomes and may have underemphasized adaptation. This section considers the recent arrival of "development impact bonds" within the NTD space.

Development impact bonds, or DIBs, are a form of "payment by results" (PbR) in which private investment is leveraged against commitments from governments and donors to pay for certain outcomes (*60*). DIBs bring these "outcome funders" together with private investors and their service providers or "delivery partners". Private investors provide upfront funding to their delivery partners, who work towards measured outcomes. If results are delivered, the private investors are paid back by the outcome funders, with an agreed financial return. If interventions fail, private investors lose some or all of their investment. The outcome funders do not specify or fund inputs. They pay if, and only if, independently verified outcomes are achieved. At first, the most likely investors will be philanthropic foundations and the emerging class of impact investors that are motivated by social as well as financial returns. DIBs are not a replacement for public provision of public goods but one available model for engagement with the private sector in areas in which it may have a comparative advantage. Indeed, in the spirit of universal coverage against NTDs, the group of outcome funders should be led by the governments of endemic countries.

The UK Department for International Development (DFID) has recently announced support for DIBs (*61*). Importantly, the first DIB piloted by DFID will target control of rhodesiense human African trypanosomiasis with veterinary public-health interventions in Uganda. DFID will also support the development of other such partnerships by bringing together investors, governments and aid agencies to design new investments. Groups behind the initial development of the DIB for human African trypanosomiasis are looking at the feasibility of DIBs for dengue and rabies control. Initiatives such as these will help to identify the necessary conditions under which DIBs might be expected to improve the performance of health systems in controlling these and other NTDs. Further experience is

needed to determine whether the approach could be extended to other NTDs with targets for elimination or eradication. Indeed, a more solid evidence base is required on PbR more generally, in its application to NTDs.

After all, not all PbR for NTDs will come in the form of a DIB. Results-based financing or pay-for-performance, for example, centres on payments from governments or donors directly to service providers or patients. A full review of PbR is beyond the scope of this report, but the 2010 World Health Report on *Health systems financing: the path to universal coverage* cautioned that pay-for-performance schemes will not lead automatically to improved performance (*62*). At a minimum, such schemes will require "a clear statement of the rules of the game and what is expected from each participant", based on measurable as well as attributable outcomes. Even if they have an impact on results, their impact on costs will need to be considered, including any unintended consequences for the public sector (*63*). In fact, much of the PbR discourse has focussed in the past on results-based aid or cash-on-delivery aid, thereby limiting itself to payments from donors to governments. Although it offers some promise, PbR for universal coverage against NTDs should be aligned with broader health financing policy and put domestic investment back at its core.

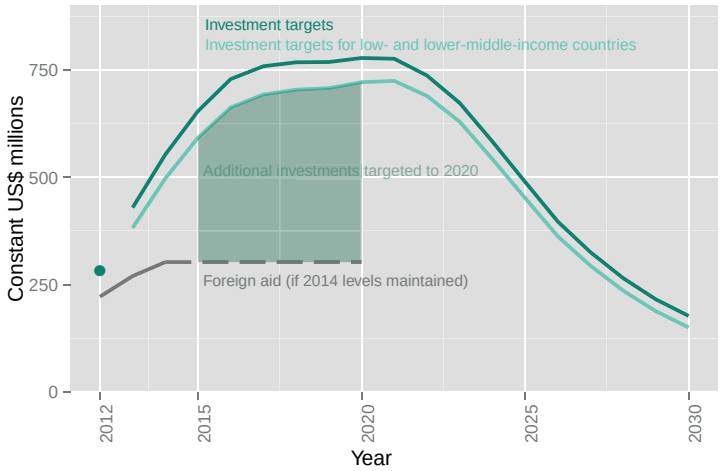
Furthermore, not all innovative financing for NTDs will come in the form of PbR. The term "innovative financing" has applied also to solidarity levies on a range of products and services, such as airline tickets or mobile phone calls, taxes on financial market transactions and tobacco or alcohol. These mechanisms increase the flow of payments without (necessarily) linking them to results. The advent of PbR receives special consideration in this section of the report because, within the context of health financing reform, it is both an opportunity and a threat to universal coverage against NTDs. It is an opportunity to the extent that it may increase and diversify the pool of investors and, under some conditions, may also improve service delivery and enhance results. It is a threat if rewards for NTDs are set independently of those for diseases that are already better known and understood by providers or investors, such that perceptions of the risk–return trade-off remain unfavourable to NTDs. In this case, the poorest populations most heavily burdened by NTDs will continue to be left behind.

2.7 Moving forward with country programmes

In summary, the investment targeted by this report is about US$ 750 million on average per year during the period 2015–2020, not counting investments in vector control. This target represents an increase of about 130% over (more than double) the benchmark cost of interventions delivered in 2012, based on reported coverage data. *Fig. 2.9* gives a sense of the magnitude of the scale-up required to 2020. If targets are met by 2020, investments in preventive chemotherapy and treatment and care may decrease to about US$ 460 million on average per year during 2021–2030.

The Uniting to Combat NTDs coalition has reported that foreign aid in support of the London Declaration amounted to about US$ 300 million in 2014, not counting vector control (*34*). Commitments for the period 2015–2020 are currently projected at less than US$ 200 million per year. Some aid is destined for regional or global coordination, making direct comparison with the investment targets difficult. Nonetheless, *Fig. 2.9* suggests that even if aid remains at 2014 levels until 2020 and all of it goes to countries, most of the investment will still have to come from other sources, increasingly from within endemic countries.

Fig. 2.9 Foreign aid (2012–2014) and investment targets under the Roadmap (to 2020) and universal coverage against NTDs (to 2030), excluding vector control



Notes: Foreign aid is reported by the Uniting to Combat NTDs coalition; it excludes the cost of medicines donated by the pharmaceutical industry and vector control. Two investment targets are presented: one for all endemic countries, the other for all countries excluding upper-middle-income countries where programmes are expected to be almost fully funded from domestic sources. The dot in 2012 is based on reported coverage numbers multiplied by unit cost benchmarks; it can be thought of as a benchmark for expenditures in 2012. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

Indeed, the investment targets outlined in this report imply additional investments of about US$ 450 million on average per year during 2015–2020 for preventive chemotherapy and treatment and care, of which about US$ 390 million will have to be invested on average per year in low- and lower-middle-income countries. It is important to emphasize that these numbers do not include investments in vector control. When vector control is included, additional investment in universal coverage against NTDs will likely have to exceed US$ 1 billion per year until 2030.

Again, many endemic countries do not yet have a clear understanding of how much (or little) domestic investment is currently directed towards universal coverage against NTDs. Part of the reason is that public investments in health systems are harder to attribute to individual diseases or interventions than are vertical foreign aid projects. As discussed earlier in this chapter, WHO is working with countries to track actual expenditures on NTDs through the WHO Health Accounts Country Platform. At the time of publication, about US$ 100 million in NTD expenditures were being tracked in five endemic countries; many more countries are expected in the coming years.

In the meantime, an important first step is ensuring that the NTD interventions outlined in this report – both prevention and treatment and care – are given high priority in the context of UHC reform. Their inclusion within UHC benefit packages will be affordable and fair. It is hoped that the analyses undertaken for this report will help country programmes to identify opportunities for domestic investment in universal coverage against NTDs. Clearly, however, there is still scope for refinement and adaptation.

WHO will continue to provide technical assistance to countries for developing investment targets that meet their needs. Country-specific investment targets may facilitate discussion between ministries of health and ministries of finance in developing health sector plans and budgets, particularly within the context of UHC reform. They may also inform innovative financing mechanisms, by helping governments, development partners, impact investors and delivery partners to agree on the scale and scope of the investment required and, as appropriate, a reasonable return for the results that are delivered.

WHO can further assist countries in moving forward with their investment strategies with cost-effectiveness and multi-criteria approaches to priority-setting for UHC; planning, budgeting and resource-tracking; monitoring innovative financing mechanisms; and programme evaluation, not least in terms of the socioeconomic impact of progress made towards universal coverage against NTDs.

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KEY INTERVENTIONS

KEY INTERVENTIONS: SITUATION REPORT

WHO recommends five public-health interventions to accelerate the prevention, control, elimination and eradication of NTDs.

Introduction

WHO recommends five public-health interventions to accelerate the prevention, control, elimination and eradication of NTDs: innovative and intensified disease management;[1] preventive chemotherapy;[2] vector ecology and management;[3] veterinary public-health services;[4] and the provision of safe water, sanitation and hygiene.[5] Although one approach may predominate for the control of a specific NTD or group of NTDs, more effective control results when these approaches are combined and delivered locally. Research underpins all five interventions.[6] Avenues for research and development must be pursued in order to find new approaches and simplified strategies as well as novel diagnostics, medicines, vaccines and vector control methods to enhance interventions and advance progress towards the Roadmap's targets.

[1] http://www.who.int/neglected_diseases/disease_management/en/

[2] http://www.who.int/neglected_diseases/preventive_chemotherapy/en/

[3] http://www.who.int/neglected_diseases/vector_ecology/en/

[4] http://www.who.int/neglected_diseases/zoonoses/en/

[5] http://www.who.int/water_sanitation_health/en/

[6] http://www.who.int/tdr/en/

3.1 Innovative and intensified disease management

The concept of innovative and intensified disease management (IDM) was first devised a decade ago as a way of accelerating efforts to eliminate diseases that are proving difficult to eliminate despite the availability of effective tools.

The underlying principle of IDM is the need to ensure that obstacles to control are being confronted with the most appropriate combination of strategies and tools available, given the multiplicity of factors underpinning perpetuation of a disease. These factors include:

- the current epidemiological status of the disease;
- the availability and efficacy of available medicines, vaccines and diagnostic tools;
- the level of awareness about the disease in the population at risk;
- the strength or weakness of the health systems and resources available in the affected country;
- the degree of technical training given to health workers; and
- the efficacy of vector control strategies.

An innovative approach would first define the obstacles to control and then consider whether and in what way to change the existing combination of strategies and tools and whether new tools should be introduced in order to overcome the obstacles. The new, innovative combination will be tested for its efficacy and may in time have to be replaced by a subsequent innovative configuration of disease control tools and approaches.

3.1.1 Innovation

To reduce disease prevalence to near elimination, the routine management measures in place are unlikely to achieve this aim. A new strategy specifically focused on elimination is required. Such a strategy may demand, as a first step, a major scaling up of detection, treatment, monitoring and surveillance.

3.1.2 Intensification

WHO has adopted the IDM approach in its efforts to lower the burden of mortality and morbidity of five diseases: Buruli ulcer, Chagas disease, human African trypanosomiasis, leishmaniases cutaneous and visceral and yaws.

3.1.3 IDM at work

Buruli ulcer

Until 2004, control of Buruli ulcer consisted mainly of surgery to remove infected tissue. The procedure was done at a late stage in the course of the disease, when severe lesions are common. Surgery usually involved multiple operations and hospitalization of about 3 months, if and where an adequately equipped hospital was available. As Buruli ulcer is caused by a mycobacterium of the same family as the causative agents of tuberculosis and leprosy, in 2004 the possibility was mooted that it might respond to treatment with the existing antibiotics that had proven effective against the two related mycobacterial infections. This possibility was confirmed and opened the door to a completely new control strategy, making treatment of patients feasible at an early stage of the disease before mutilating lesions developed that could only be managed by surgery.

Early treatment, however, calls for early diagnosis. For want of simple diagnostic tools, diagnosis was traditionally based on clinical examination. Confirmation of diagnosis required laboratory resources that are often absent in the resource-poor areas where the disease prevails. The search is now on for a field-friendly diagnostic test that is based on detection of the toxin itself and that will enhance the overall effectiveness of the new strategy.

Chagas disease

Chagas disease has traditionally been thought to be endemic only in Latin America, hence its name, American trypanosomiasis. In 2007, following the deaths of a few transfusion or organ graft recipients in Europe, WHO surveys found many cases of the disease among Latin American immigrants to Europe. This finding prompted WHO to launch a Non-Endemic Countries Initiative aimed at assessing the prevalence and possible transmission of *Trypanosoma cruzi* infection in countries where vectorial transmission had never been reported. The findings of surveys carried out by the Initiative convinced many countries, including Australia, Canada, Japan, the United States of America and several European countries, to set up surveillance systems to track the disease.

Today, a worldwide Chagas disease surveillance system is in place. It focuses mainly on transmission of the infection via blood transfusion and organ transplantation but also on congenital transmission. A recent development is the finding in many countries, especially in Asia, of Chagas disease vectors capable of transmitting the infection and thereby raising the risk of establishing vector transmission in these countries. According to surveillance findings, about 7 million people are infected worldwide, mostly in the endemic areas of 21 Latin American countries. A study published in 2011 reported an estimated 68 000–123 000 cases in nine European countries: Belgium, France, Germany, Italy, the Netherlands, Portugal, Spain, Switzerland and the United Kingdom (*1*).

Cutaneous leishmaniasis

Until 2007, control of cutaneous leishmaniasis was not achieving the desired results. That year, WHO set up a network aimed at intensifying surveillance and control activities. This promising initiative, however, faced a major difficulty: the lack of skilled personnel to implement the intensified control activities. In response, WHO in collaboration with the Open University of Catalonia, Spain, devised a comprehensive 3-month training course for health personnel working in cutaneous leishmaniasis control programmes. Participants can access the course online and receive guidance from trainers through two-way internet communication technology (e.g. Skype). Participants sit an examination on completion of the course.

Visceral leishmaniasis (kala-azar)

The medicines traditionally used to treat patients with visceral leishmaniasis have proven too costly, too toxic and of limited efficacy. Ten years ago, clinical trials confirmed the efficacy of a new medicine – liposomal amphotericin B (AmBisome) – but treatment regimens have tended to be too prolonged and too costly, and they also require administration by multiple injections. In 2012, a study supported by WHO showed that a single injection was as effective as the multiple-injection regimens. WHO has encouraged countries affected by the disease to incorporate the new regimen in their kala-azar control strategies. Bangladesh was the first country to comply. Thanks to a WHO-brokered donation of AmBisome by the manufacturer, more countries, notably Bhutan, Ethiopia, Nepal, Sudan, South Sudan and, most recently, India, have decided to incorporate it in their control strategies.

Human African trypanosomiasis (sleeping sickness)

By 1964, mass screening and treatment campaigns in West and Central Africa had reduced the prevalence of human African trypanosomiasis to a record 4500 cases. Over the next four decades, however, the disease resurged to an estimated prevalence of more than 300 000 cases.

From 2000, WHO intensified control measures by deploying mobile teams to screen entire populations in vast areas of the continent believed to harbour the disease. This strategy reduced the prevalence to fewer than 7000 cases.

Several hurdles hampered continued control efforts. The mobile teams had to systematically screen all populations at risk in order to detect the infection at an early stage, before the causative parasite reached the brain. Early detection also made it possible to treat patients with pentamidine, a much safer medicine than melarsoprol and as effective, but only for those patients with early infection.

Melarsopol, once the only medicine available to treat late-stage disease, is complex to administer, highly toxic and kills about 5–10% of patients. In 2001, eflornithine, a less toxic medicine, became available free of charge but proved too difficult to administer by unskilled

health personnel working under field conditions. In 2006, WHO partially solved the problem by designing a medical kit containing all the materials that a health worker would need. It also provided training in the use of these kits to all health personnel charged with administering eflornithine. Deployment of eflornithine, however, was complicated by the possibility of drug resistance and the difficulty of its administration in remote health centres. In 2009, a combination of two medicines – eflornithine and nifurtimox – was devised. Combination therapy not only reduces the risk of drug resistance developing but also halves the duration of treatment compared with eflornithine alone.

Fexinidazole, a recently developed medicine currently in Phase III clinical trials, is administered orally over a 10-day period. It could facilitate treatment of both stages of sleeping sickness. A novel oxaborole compound is also under development for administration as a single, oral dose. Its availability could be an important element in searches for sustainable elimination of the disease.

Research is ongoing to devise new diagnostic tools that are easier to use in non-specialized health services for the disease. This research is facilitated by a human African trypanosomiasis specimen bank created by WHO and hosted by the Institut Pasteur in Paris, France. To date, the bank contains nearly 50 000 samples of plasma, sera, cerebrospinal fluid, saliva and urine from patients infected with trypanosome parasite and controls. About 3000 samples have already been distributed to 10 international research teams (*2*).

The new tools for diagnosis and treatment under development could make integrated control and surveillance in primary health-care services possible and allow sustainable elimination of human African trypanosomiasis.

WHO provides coordination of the different partners working to eliminate human African trypanosomiasis through the network for HAT elimination.

Yaws

From 1952 to 1964, WHO and the United Nations Children's Fund led mass treatment campaigns that administered injectable benzathine penicillin to some 300 million people in 46 countries. Despite a major shortcoming of this therapy, notably the need for a painful injection that deterred many young patients, the campaign reduced the prevalence of yaws by 95% – from 50 million cases at the start of the campaign to 2.5 million at its close.

Yaws has resurged during the past decade, particularly in parts of Africa, South-East Asia and the Pacific Islands. Clearly, a new strategy was needed, especially as WHO in 2011 had added yaws to its list of diseases targeted for eradication. In the following year, a study carried out in a Papua New Guinea island where yaws is endemic showed that a single dose of an antibiotic (azithromycin) is as effective in curing children of yaws as benzathine penicillin given by injection. The major asset of azithromycin is that it is administered orally and thus painlessly. It has therefore become the mainstay of WHO's Morges Strategy for eradication of yaws by 2020.

3.2 Preventive chemotherapy

Preventive chemotherapy is defined as the large-scale delivery of safe, single-administration, quality-assured medicines, either alone or in combination, at regular intervals, to entire population groups (*3*).WHO recommends preventive chemotherapy against the four main helminth diseases: lymphatic filariasis, onchocerciasis, schistosomiasis and soil-transmitted helminthiases. This intervention is also a component of the SAFE strategy for trachoma (Surgery, Antibiotics, Facial cleanliness and Environmental improvements), and is recommended for controlling morbidity due to foodborne trematodiases.

In line with WHO recommendations and because of their proven safety record, medicines can be distributed to target population groups by non-medical personnel after a short training session. Schools, community networks and other social platforms can be used as outreach points to maximize coverage.

Preventive chemotherapy is expected to be implemented in conjunction with complementary public-health interventions, such as providing management for chronic cases and people with disabilities, controlling vectors and their intermediate hosts, providing veterinary public-health services, and providing safe drinking-water, sanitation and hygiene services. Such measures enhance the impact of the intervention both in terms of controlling morbidity and in decreasing transmission.

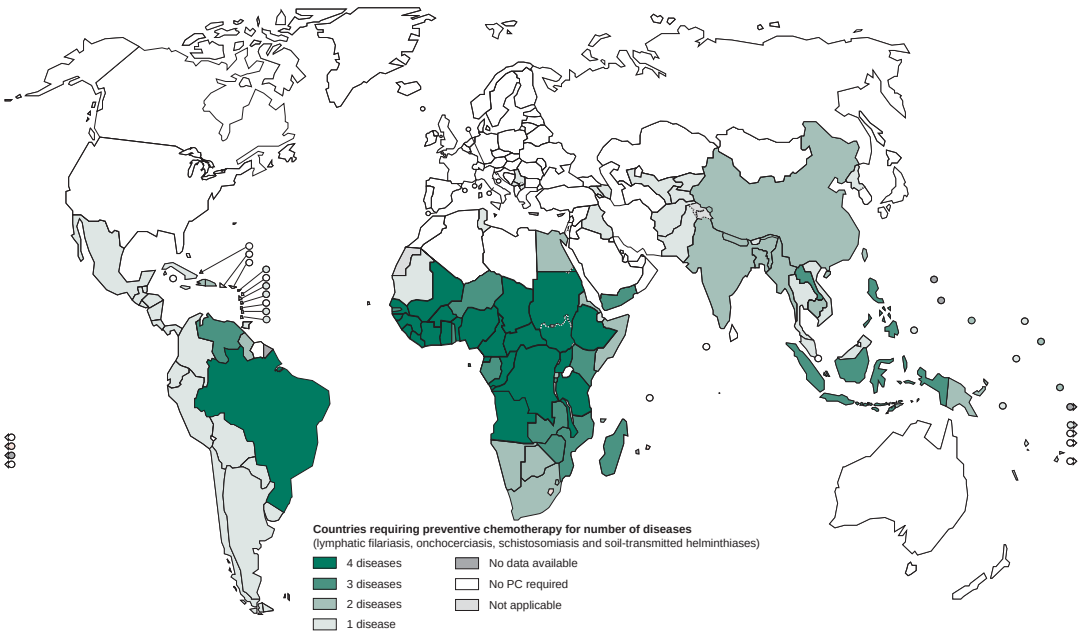
Today, the implementation of preventive chemotherapy interventions is possible thanks to the large-scale donations of medicines by partners in the pharmaceutical industry either through WHO or directly to countries; this has enabled a major reduction in the overall costs of NTD programmes. Albendazole, azithromycin, diethylcarbamazine, ivermectin, mebendazole and praziquantel are all readily made available to Ministries of Health of endemic countries upon application. Scaling up preventive chemotherapy and attaining high coverage among eligible population groups is therefore feasible, and this should enable the Roadmap's targets to be achieved.

In areas where preventive chemotherapy is recommended for treatment of more than one disease, integrating and coordinating activities for all relevant diseases, including safe co-administration of medicines and strategic and operational planning, are key to success. Integrated activities have been shown to result in increased cost–effectiveness, enhanced health impact, political advantages, improved logistical convenience and better timing.

3.2.1 Scaling up is the priority

In 2012, 1.892 million people in 122 countries were estimated to require preventive chemotherapy for at least one disease, 34% of whom required treatment for three or more diseases and 20% for two diseases owing to overlapping geographical distribution (*Fig. 3.2.1*). Overall, 25 countries required treatment for the four helminths diseases; with the exception of Brazil and Sudan, all of them are in the African Region (*4*).

Fig. 3.2.1 Countries requiring preventive chemotherapy for at least one NTD (lymphatic filariasis, onchocerciasis, schistosomiasis or soil-transmitted helminthiases) and number of those diseases in each country, 2012



Since 2010,WHO has published operational guidelines to assist Member States and their partners in developing national plans to combat NTDs. Programmatic tools to facilitate integrated planning for, and reporting on, the delivery of preventive chemotherapy – such as the joint request form for selected medicines, the joint reporting form, the annual workplan and the epidemiological data reporting form – were introduced in all WHO regions in 2013. Training modules have been developed, and regional and subregional workshops have been organized to help programme managers build their capacity to adapt global strategies to their countries, design and implement interventions, and monitor and evaluate outcomes.

Estimates of the number of people who require preventive chemotherapy are regularly updated for each disease, based on the most recent epidemiological data generated by monitoring and evaluation activities of programmes, and on demographic information reflecting population growth rates. Analyses have been carried out to determine the geographical overlap of the different diseases targeted by preventive chemotherapy. *Table 3.2.1* shows the number of countries eligible for preventive chemotherapy, the types of infections transmitted in each country and the number of people requiring at least one intervention.

Although preventive chemotherapy is required in 122 countries, most of the population in need of treatment is concentrated in a few high-burden countries. Some 10 countries host approximately 70% of the global population requiring preventive chemotherapy (listed in order of the number of people requiring treatment): India, Indonesia, Nigeria, Bangladesh, the Democratic Republic of the Congo, Ethiopia, the United Republic of Tanzania, the Philippines, Myanmar and Pakistan.

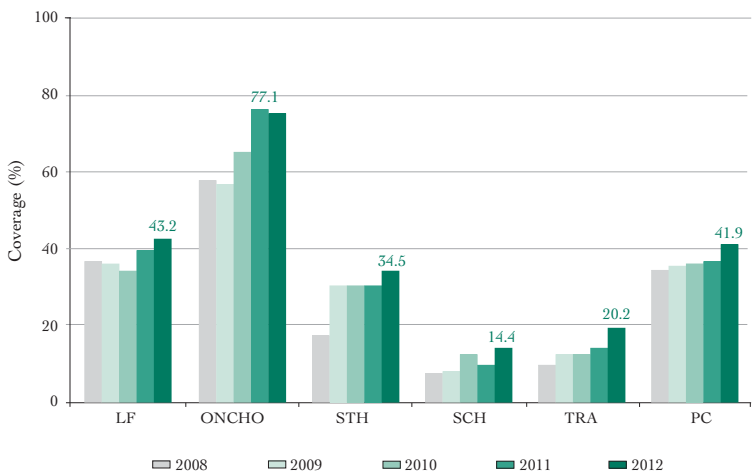
3.2.2 Implementation status

In 2012, approximately 807.6 million people received preventive chemotherapy for at least one disease, a significant advance from 2011 when 729.4 million people were covered by this intervention for at least one disease. Data for 2012 show that 596 million people received preventive chemotherapy for lymphatic filariasis, 338.1 million for soil-transmitted helminthiases, 99.5 million for onchocerciasis and 42.1 million for schistosomiasis (*Fig. 3.2.2* and *Table 3.2.1*). Data reported on treatment for trachoma show that 48.8 million people received antibiotics in 2012.

The number of people treated for schistosomiasis increased sharply between 2005 and 2012, mainly because of scaling up in the African Region: coverage achieved in 2012 was the highest ever, representing a 40% increase from the previous year. Similarly, the coverage for soil-transmitted helminthiases increased significantly between 2005 and 2012, reaching 34.5% in 2012. By the end of 2012, mass drug administration (MDA) for lymphatic filariasis had been implemented in 56 countries; 13/56 had implemented five or more rounds of preventive chemotherapy and achieved the target threshold of infection levels nationwide, allowing them to stop treatment and transition to post-MDA surveillance of elimination. Overall, onchocerciasis control programmes achieved 76% coverage in 2012.

High-burden countries are scaling up rapidly: of the 807.6 million people reached with preventive chemotherapy in 2012, 62% (501 million) were treated in the top three countries with the highest burden (India, Indonesia and Nigeria) and 74% in the top 10 countries. Overall, India was the single country reaching most individuals, in excess of 421 million. Of note is that some countries, such as Brazil and India, completely covered the cost of distributing the donated medicines using their own resources.

Fig. 3.3.2 Trends in coverage of preventive chemotherapy, 2008–2015



LF, lymphatic filariasis; ONCHO, onchocerciasis; STH, soil-transmitted helminthiases; SCH, schistosomiasis; TRA, trachoma; PC, preventive chemotherapy.

Table 3.2.1 Estimated number of people requiring and receiving preventive chemotherapy by disease, and total number of people requiring and receiving preventive chemotherapy for at least one disease, by WHO region in 2012

Status of implementation		LF	ONCHO	STH	SCH	PC
African	No. of countries requiring PC[a]	33	24	42	40	44
	No. of people requiring PC (million)	464.1	124.2	300.6	232.0	633.2
	No. of countries reported[b]	14	22	27	23	33
	No. of people treated (million)[c]	105.9	96.7	87.0	35.6	201.4
	Coverage (%)[d]	22.8	77.9	25.3	13.6	31.7
Americas	No. of countries requiring PC[a]	3	3	9	5	10
	No. of people requiring PC (million)	22.1	6.2	80.6	15.3	107.1
	No. of countries reported[b]	0	3	2	3	5
	No. of people treated (million)[c]	ND	2.7	6.1	2.7	10.4
	Coverage (%)[d]	0	43.6	6.9	13.3	9.5
Eastern Mediterranean	No. of countries requiring PC[a]	4	2	30	2	30
	No. of people requiring PC (million)	13.4	0.132	49.3	1.6	59.1
	No. of countries reported[b]	3	2	14	2	14
	No. of people treated (million)[c]	8.4	0.1	27.0	0.027	31.3
	Coverage (%)[d]	62.7	75.8	33.1	1.7	37.3
European	No. of countries requiring PC[a]	NA	NA	8	NA	8
	No. of people requiring PC (million)	NA	NA	1.8	NA	1.8
	No. of countries reported[b]	NA	NA	3	NA	3
	No. of people treated (million)[c]	NA	NA	3.1	NA	3.1
	Coverage (%)[d]	NA	NA	42.9	NA	42.9
South-East Asia	No. of countries requiring PC[a]	7	NA	8	1	9
	No. of people requiring PC (million)	843.2	NA	368.9	0.003	989.7
	No. of countries reported[b]	5	NA	7	0	7
	No. of people treated (million)[c]	462.5	NA	200.2	ND	530.6
	Coverage (%)[d]	54.9	NA	51.2	0	53.3
Western Pacific	No. of countries requiring PC[a]	13	NA	15	4	21
	No. of people requiring PC (million)	37.5	NA	74.7	0.635	100.9
	No. of countries reported[b]	6	NA	12	3	13
	No. of people treated (million)[c]	19.1	NA	14.7	3.8	30.8
	Coverage (%)[d]	51.0	NA	19.6	36.0	30.5
Global	No. of countries requiring PC[a]	60	29	112	52	122
	No. of people requiring PC (million)	1 380.4	130.5	875.9	249.4	1 891.7
	No. of countries reported[b]	28	27	65	31	75
	No. of people treated (million)[c]	596	99.5	338.1	42.1	807.6
	Coverage (%)[d]	43.2	76.2	34.5	14.4	41.9

NA, not applicable; ND, no data available. LF, lymphatic filariasis; ONCHO, onchocerciasis; PC, preventive chemotherapy; SCH, schistosomiasis; STH, soil-transmitted helminthiases

[a] Number of endemic countries moving to post-PC surveillance stage are not included in the total.

[b] Number of countries reporting data on PC implementation; countries submitting blank reports are not included in the total.

[c] Estimated number of people covered by PC calculated based on the disease-specific reports from countries; it may also include the number of people treated in areas where PC is not required.

[d] Coverage is calculated as the number of people treated in need of PC out of the population requiring PC. The numerator does not include the number of people treated in areas where PC is not required.

3.2.3 A positive outlook

Global coverage with preventive chemotherapy has expanded significantly over the past few years and is expected to further scale up as result of: (i) the increasing quantities of medicines made available by the pharmaceutical industry and other partners to countries; (ii) the preparation of national action plans and other tools facilitating implementation and resulting in increased coordination of activities at country level; and (iii) the commitments to strengthen efforts to overcome NTDs made by national governments and supported by growing interest from donor agencies.

In 2012, of the 122 countries requiring preventive chemotherapy, 75 reported treatment data for at least one disease. That same year, 56 countries submitted requests for donated medicines. One year later, there were 70 applicant countries. The trend is positive as it reflects a progressive expansion of preventive chemotherapy interventions. Despite the progress made, efforts must be further intensified to consolidate gains and enable countries to meet the targets set in the Roadmap and by the World Health Assembly in its various resolutions (*Annex 1a*).

3.3 Vector ecology and management

WHO promotes integrated vector management (IVM) for the prevention and control of vector-borne diseases and the judicious use of insecticides.[1] IVM, defined as a rational decision-making process to optimize the use of resources for vector control, aims to reduce transmission of vector-borne diseases in order to achieve the global targets, while promoting the application of sound ecological principles, evidence-based interventions, and collaboration within and outside the health sector. An increasing number of Member States are now implementing vector control through the IVM approach.

3.3.1 VEM in action

Integrated vector management

In areas where multiple NTDs are endemic, IVM is deployed to control transmission of the causative pathogens of lymphatic filariasis, dengue, loiasis and malaria, and to eliminate lymphatic filariasis in areas where *Loa loa* is co-endemic. Because ivermectin or diethylcarbamazine can cause serious adverse events in people infected with *Loa loa* (African eye worm), an endemic disease in a large part of central Africa, and in order to meet the Roadmap's 2020 target, an alternative strategy for interrupting transmission of lymphatic filariasis must be implemented that could potentially include both medication and vector control. WHO

[1] http://www.who.int/neglected_diseases/vector_ecology/information/en/

advocates implementation of cost–effective and sustainable vector control activities based on the principles of IVM and through strong multi-stakeholder and multi-sectoral approaches.

WHO Pesticide Evaluation Scheme

The WHO Pesticide Evaluation Scheme (WHOPES) has coordinated the testing and evaluation of pesticides for vector-borne disease control since 1960.[1] The Scheme also evaluates application methods that are safe and cost–effective, develops and promotes policies, strategies and guidelines for application of public-health pesticides, and assists and monitors their implementation by Member States. WHOPES acts as the focal point within WHO for public-health pesticide management and global partnerships on public-health pesticide development. It also operates a joint collaboration programme with the Food and Agriculture Organization of the United Nations (FAO) on pesticide management, including the development of guidelines and quality standards. During 2012–2013, WHOPES evaluated and made recommendations on 10 pesticide products; a further 14 pesticides are undergoing evaluation.[2]

Pesticides are pivotal to controlling populations of disease vectors. Their sound management and appropriate use in minimizing adverse events on human and animal health and the environment are important considerations in IVM. Many disease-endemic countries, however, lack capacity to manage public-health pesticides throughout their life-cycles.

A WHOPES-administered project on reducing health risks through sound pesticide management, completed in 2013, aimed to facilitate the establishment of national pesticide regulatory frameworks, optimize registration procedures, strengthen capacity for pesticide management and reduce trade of substandard pesticide products. The major achievements of this project (2007–2013) include the creation of a global evidence base on the management and use of public-health pesticides as a reference for future work; publishing peer reviewed guidelines, norms and standards on pesticide registration and management; and providing technical support and training to priority countries in the sound management of pesticides.[3] Life-cycle management of pesticides also demands a multisectoral approach at national and international levels to ensure effective legislation.

International Code of Conduct on Pesticide Management

WHO in collaboration with FAO and the United Nations Environment Programme has developed an International Code of Conduct on Pesticide Management as a voluntary framework for the management of public-health and agricultural pesticides.[4] FAO and WHO have jointly published guidelines on data requirements for registration of pesticides and WHO specifications for eight pesticide products. Improved collaboration between WHO and FAO has

[1] http://www.who.int/whopes/en/

[2] http://www.who.int/whopes/recommendations/en/

[3] http://www.who.int/iris/bitstream/10665/90546/1/9789241506106_eng.pdf

[4] http://www.who.int/whopes/recommendations/International_Code_of_Conduct_on_Pesticide_Management_Y2014.pdf

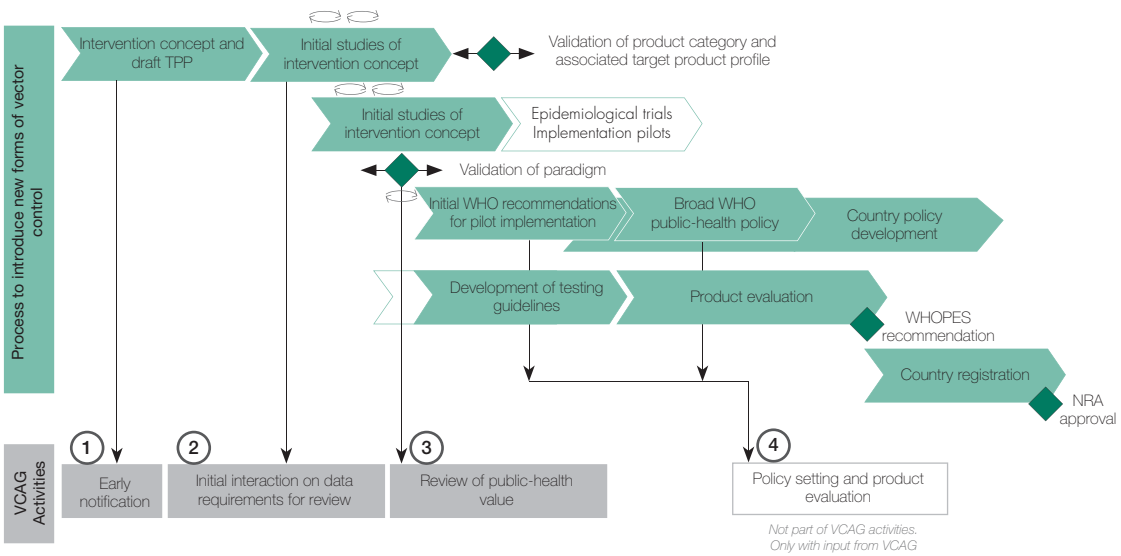
provided unified, coordinated and consistent support to Member States and other stakeholders on the sound management of pesticides.

Since 2007, WHOPES has supported more than 20 Member States (six of them during 2012–2013) in conducting situation analyses and needs assessments for the use of pesticides, and has assisted four WHO regions (African, Americas, Eastern Mediterranean and South-East Asia) in preparing regional policies and frameworks for pesticide management. It has published peer-reviewed guidelines on procuring pesticides for public-health use, which is a tool being used by international and national pesticide procurement agencies.

Vector Control Advisory Group

In 2013, WHO constituted the Vector Control Advisory Group (VCAG) to provide strategic advice to the Malaria Policy Advisory Group of the Global Malaria Programme and the Strategic and Technical Advisory Group for Neglected Tropical Diseases on the public-health value of new forms of vector control (paradigms, tools, technologies and approaches) within the context of IVM in multi-disease settings.[1] Assessments are based on evidence derived from studies with clear entomological and epidemiological end-points. VCAG invites submissions from any interested parties (manufacturers, academia, donors, innovators) in a specified dossier with relevant supporting evidence on the public-health value of such tools, technologies or approaches. *Fig. 3.3.1* shows the three steps of the evaluation process.

Fig. 3.3.1 Three steps of a Vector Control Advisory Group (VCAG) evaluation



NRA, national regulatory authority; TPP, target product profile; WHOPES, WHO Pesticide Evaluation Scheme

[1] http://www.who.int/neglected_diseases/vector_ecology/VCAG/en/

The first meeting (July 2013) standardized the operational procedures and submission dossier. All meetings consist of an open session (with all stakeholders) and a closed session (of VCAG members and the Secretariat). The second meeting (February 2014) reviewed the first batch of submissions from innovators, namely eight items belonging to the five different paradigms:

- combination nets for use in areas of pyrethroid resistance (2 submissions);
- microbial control of human pathogens in adult vectors (1 submission);
- spatial repellents (1 submission);
- lethal house lures (1 submission); and
- vector traps for disease management (3 submissions).

By strengthening WHO's capacity to assess the public-health value of new forms of vector control and develop appropriate technical recommendations, VCAG supports national and global efforts to control and eliminate vector-borne diseases worldwide.

Global Collaboration for the Development of Pesticides for Public Health

WHO established the Global Collaboration for the Development of Pesticides for Public Health (GCDPP), a public–private partnership, in 1997 in response to the need to stimulate the development of alternative insecticides and application technologies.[1] GCDPP meetings bring together major stakeholders in pesticide product development and the sound management of pesticides, including from industry, national and government agencies and programmes, funding organizations and academic researchers, to discuss and strengthen collaboration on critical vector control issues. Recent meetings have discussed emerging and re-emerging vector-borne diseases, dengue surveillance and vector management. The 9th biennial meeting (September 2014) reviewed insecticide resistance and its monitoring and management.

Capacity strengthening

WHO supports Member States in strengthening their capacity to implement IVM and pesticide management through training programmes. In 2012–2013, regional IVM courses were held in India and Malaysia, and capacity strengthening workshops were organized to devise a national IVM plan in Sudan. To assist vector control programmes in developing and adopting IVM strategies, WHO has published a handbook on IVM (*5*), guidance on IVM policy-making (*6*), training curricula (*7*) and indicators for monitoring and evaluation (*8*). Training workshops were organized in China and India for pesticide regulatory personnel on the preparation of pesticide specifications as quality standards, which have been published as training manuals in collaboration with FAO (*9*).

[1] http://www.who.int/whopes/gcdpp/en/

WHOPES has contributed to strengthening the capacity of several research institutions through the use of its standard guidelines and procedures for evaluating vector control products. The Scheme publishes efficacy testing and risk assessment guidelines for various applications. In 2013, it issued guidelines on the evaluation of long-lasting insecticidal nets. Other guidelines published during 2010–2013 include those for monitoring the durability of long-lasting insecticide-treated nets, testing the efficacy of spatial repellents and of insecticide products used in aircrafts, and risk assessment models for different uses of pesticides.[1]

Technical collaboration

WHO enjoys strong technical collaboration for IVM among its departments and regional offices as well as with major stakeholders, namely research and scientific institutions, national programmes, international financial institutions, industry, nongovernmental organizations and United Nations agencies.

To ensure that the full potential of IVM is deployed to control transmission of vector-borne diseases, countries must strengthen their capacities in public-health entomology, entomological surveillance and operational research. The lack of a career path for entomologists has nurtured a migration towards academic research and away from public-health entomology. This trend must be reversed. Countries considering the development of human capacity must pay attention to the skills required for effective programme management, including financing, logistics and promotional activities. WHO will continue to play a key role in developing appropriate training tools and courses in vector control and pesticide management.

3.4 Veterinary public-health services

At least four of the 17 diseases included in the Roadmap for lowering the public-health burden of NTDs are zoonotic because their life-cycles entail animals. echinococcosis, foodborne trematodiases, rabies, and taeniasis and (neuro)cysticercosis are neglected zoonotic diseases because they rank far down on the priorities of governments and the international public-health community. Yet today, there are more than 200 zoonoses and nearly two-thirds of all human pathogens are zoonotic, according to WHO estimates. The burden these diseases lay collectively on neglected, poverty-stricken communities is far from negligible. Not only are they detrimental to human health but they also threaten the viability of livestock on which these communities depend for their survival.

[1] http://www.who.int/whopes/resources/en/

Clearly, the need to control the zoonoses is becoming increasingly urgent. Population growth in developing countries is fuelling an escalating demand for animal protein. Meat production in these countries is likely to rise by 73% of current levels by 2050, according to FAO estimates, and dairy consumption by 58% (*10*). Moreover, much of the future demand for livestock production will require a vast scaling up of animal-rearing activities, particularly in the burgeoning urban populations of the world. "The threat of animal diseases, some of which may directly threaten human health, will have to be carefully managed as livestock production is ramped up," the FAO warns. One concern is the environmental impact of such ramping up of livestock production, which is likely to increase groundwater pollution and greenhouse gas emissions and could, in turn, increase the risk of animal and human disease. A second concern, linked to the scaling up of agricultural production, is the increase in the number of animals kept in crowded conditions or transported in cramped trucks over increasingly long distances. A third concern is the growing spread of zoonotic pathogens resistant to currently available antimicrobial agents.

The need to control neglected zoonotic diseases is urgent, but the task is not simple. It requires interventions that break the human–animal–environmental cycle of transmission. This objective calls for intersectoral collaboration covering the three areas of interest involved in the cycle: human health, veterinary health and environmental health. The need for such collaboration prompted the launching in 2008 of a global One Health concept that aims to foster intersectoral, interdisciplinary collaboration across these three health sectors (*11*).

In 2010, efforts to achieve collaboration gained momentum through the establishment of a Tripartite Concept agreement between WHO, FAO and the World Organisation for Animal Health (OIE) (*12*). The objective of this agreement was to bring about, through multisectoral cooperation and strong partnerships, "a world capable of preventing, detecting, containing, eliminating, and responding to animal and public-health risks attributable to zoonoses and animal diseases".

Coordination is often lacking within and among countries in many parts of the world. Communication between ministries of health and of agriculture is often weak or absent. Well-coordinated action is needed to prevent and respond to both the endemic and the epidemic zoonotic diseases by linking efforts targeting people, animals, food and the environment. Surveillance data on zoonoses and public awareness of the threat to public health of zoonoses are often lacking. There are, moreover, clear benefits associated with intersectoral collaboration, such as avoiding duplication of effort (*13*). Collaboration also facilitates the adaptability of strategies to the prevention and control of the various zoonoses.

A number of general obstacles are hampering the prevention and control of zoonoses in many resource-poor areas. These include:

- A misconception that the burden of these diseases is low, with the result that funding of control efforts is hard to come by.
- The difficulty of bringing together the normally separate roles and interests of different sectors, such as human health and veterinary services and environmental concerns, and focussing them on problems that can only be solved through collaboration among these sectors.
- Weak surveillance and reporting systems.
- Inertia to changing traditional behaviours and invested interests that must be changed to lower the burden of zoonotic diseases.
- Limited resources and skills for laboratory diagnosis of endemic or emerging zoonoses and for deployment of the tools required to control zoonoses.
- The complexity of the life-cycles of zoonotic diseases.
- The diversity of potential parasite hosts: human and animal, vertebrate and non-vertebrate, domestic and wild.
- Informal slaughter practices and poor meat inspection.
- Unhygienic cooking practices and eating habits that carry risks of foodborne zoonoses.

Future plans include working closely with countries that are willing to embark on control and elimination of zoonoses and that look to WHO and its partners for support in implementing these programmes using the most appropriate tools that are currently available in their settings. *Table 3.4.1* presents for the four NTDs with prominent zoonotic aspects the main obstacles to control, the objectives for control and the results expected from interventions.

Table. 3.4.1 Control of four NTDs with prominent zoonotic characteristics: interventions, obstacles and ultimate objectives

Disease	Disease-specific obstacle	Ultimate objective	Expected result
ECHINOCOCCOSIS			
A validated control strategy implemented in selected countries through pilot projects (2015)	Lack of tools in peripheral health centres for early diagnosis	Greater diagnostic capacity and wider availability of tools in health-care settings	Decreased prevalence in humans
	Weak political commitment and veterinary sector involvement; inadequate availability or absence of case detection tools, vaccines and medicines	Where feasible, integration of control activities with those for dog-borne diseases such as rabies and leishmaniases or sheep-borne diseases such as brucellosissis	Incidence of human cases progressively reduced
A validated control strategy and scaled-up interventions implemented in selected countries (2020)	The long-term commitment needed to measure the impact of interventions		
FOODBORNE TREMATODIASES			
Inclusion of foodborne trematodiasesin a mainstream preventive chemotherapy strategy	Inadequate availability of medicines to treat clonorchiasis and opisthorchiasis	Availability of triclabendazole for fascioliasis	Morbidity reduced and associated mortality prevented
		Preventive chemotherapy integrated with that used for the prevention of schistosomiasis and soil-transmitted helminthiases	
75% of the population at risk covered by preventive chemotherapy and transmission control (2020)	The difficulty of establishing links with the veterinary sector	Greater support from the veterinary sector	Morbidity reduced and associated mortality prevented
		Improved aquaculture practices	
RABIES			
Elimination of human dog-mediated rabies in Latin America (2015)	Maintaining support for elimination programmes where elimination is imminent	Greater community awareness about rabies	Zero deaths attributed to rabies
	Weak surveillance, especially where disease prevalence is declining	Strengthened surveillance through regional laboratory networks	Zero deaths attributed to rabies
Elimination of human rabies transmitted by dogs in the South-East Asia and Western Pacific regions (2015)	Scaling up dog-bite prevention and administering timely post-exposure treatment (with or without immunoglobulin)	Improved access to and availability of safe and affordable human vaccine	Transmission of disease interrupted
	Covering > 70% of dogs targeted by vaccination programmes aimed at reducing and subsequently halting transmission of the infection to humanss	Improved access to and availability of dog vaccine	
TAENIASIS AND (NEURO)CYSTICERCOSIS			
A validated strategy for control and elimination of *Taenia solium* taeniasis and (neuro)cysticercosis (2015)	Lack of ready-to-use tools, including diagnostic tools. Poor sanitary conditions and roaming pigs	Integrated use of available improved tools to reduce tapeworm infection in people and cysticercosis in people and pigs	Improved understanding through monitoring and evaluation of impact of strategy on infection in humans and pigs
Interventions Scaled up in selected countries for control and elimination of *T. solium* taeniasis and (neuro)cysticercosis (2020)	The difficulty of preventing recrudescence of infection following elimination		Accelerated reduction of *T. solium* taeniasis and (neuro)cysticercosis

3.5 Water, sanitation and hygiene

The burden of NTDs is disproportionately influenced by environmental determinants of health, especially water, sanitation and hygiene (WASH). The growing political will to tackle the water and sanitation global crisis has not been harnessed to address NTDs, even while health concerns – notably reduction of diarrhoeal disease – have been a central driver of action. In this context, the NTDs remain truly neglected, including by the WASH community and public-health professionals promoting primary prevention.

Questions remain as to the exact nature of the processes influencing the interface between WASH and specific public-health issues in different settings. In a complex picture of cause, effect and different interventions, relative attribution remains a challenge. This challenge explains why proven medical interventions are emphasized within disease-control programmes while primary prevention remains relatively under-prioritized.

In addition, NTD-related chronic conditions can also be exacerbated by lack of sufficient water for hygiene purposes. Those suffering from conditions caused by lymphatic filariasis, such as lymphoedema or elephantiasis, require large amounts of water to be able to wash affected limbs in order to reduce the severity of the disease and associated disability. The stigmatization and financial hardship experienced by sufferers means also that they are more likely to be excluded from access to water and sanitation services.

3.5.1 Global access to drinking-water and sanitation – a mixed picture

The threshold for reaching the MDG drinking-water target (to halve the proportion of people without sustainable access to safe drinking-water) was crossed in 2010; if trends continue, the number of people deprived of access to improved sources will have been reduced to 547 million by the end of 2015. Yet the 2014 report of the WHO/UNICEF Joint Monitoring Programme for Water Supply and Sanitation indicates that by the end of 2012, globally an estimated 748 million people still lacked access to improved sources of drinking-water. Broken down by region, important disparities emerge from the global picture. Progress has been greatest in East Asia, while countries in Africa are seriously lagging behind; similarly, there are disparities between urban and rural areas, with 90% of the 748 million without access living in rural areas. Quintile Gap Analysis shows a range of patterns in different countries, but the general picture is that of continued inequality: the rich have benefited more from progress made than the poor. Of the 748 million people without access to improved sources of drinking-water, some 350 million live in Africa.

Sanitation has long been a neglected area not only in broader development policy and programming but within the water sector itself. Despite increasing recognition of the importance of sanitation, there is still a long way to go to redress the many years of political and financial neglect. Perhaps not surprisingly, progress towards meeting the MDG sanitation target is slowest compared with that for all other targets. At the end of 2012, an estimated 2.5 billion people – approximately one-third of the world's population – lacked access to

improved sanitation facilities; of these, 784 million used shared or public facilities, 732 million used facilities that did not meet basic standards of hygiene and the remaining 1 billion people practised open defecation on a daily basis.

3.5.2 Implications of the current situation on achieving progress on NTDs

The existence of water and sanitation infrastructure tells only a partial story. Access, availability and reliability all play a role in whether people are able to use existing services and to gain the expected benefits to health and well-being. For example, people in rural and peri-urban areas will collect water from wells for storage at home; people with unreliable piped water supplies in cities will also store water in their homes. Water storage facilities that are not mosquito-proof will, collectively and cumulatively, add importantly to the breeding potential for the *Aedes* vector of dengue. Furthermore, access, availability and reliability of water also affects whether people have sufficient quantities of water to practise adequate household and personal hygiene. Hygiene-promotion interventions that are delivered without addressing access to water may therefore have a limited public-health impact. *Annex 4* summarizes the linkages between WASH and NTDs.

Open defecation is a particularly important risk factor for the transmission of many of the NTDs, and progress towards the elimination of this practice should lead to a reduction in the incidence of NTDs. The practice is not just a result of poverty – wealth quintile analysis shows that in some countries open defecation is also practised by people from the wealthiest fifth of the population. Eliminating open defecation alone will not solve the problem altogether; ineffective management of the sanitation chain (i.e. what happens to faecal matter beyond the latrine) contributes significantly to persistent contamination of the environment with human excreta.

Case detection and drug treatment have been successful in reducing mortality rates and, to some extent, morbidity. Yet, short-term achievements become short-lived if there is no support for transmission risk reduction to sustain them, through environmental management and lasting behavioural change, and through services that improve community development overall to enable communities to sustain change. WASH plays a crucial role also in the latter.

3.5.3 Moving towards collaboration for elimination

A greater emphasis on joint planning, resourcing and delivery of WASH and disease control interventions will yield important dividends for NTD control as well as other public-health and human development goals.

The international policy framework for bringing together the WASH and public-health spheres has evolved rapidly over the past 5 years. In 2010, the United Nations, through resolutions of the General Assembly and of the United Nations Human Rights Council, acknowledged access to safe drinking-water and sanitation as a human right, closely associated

with the human right to health. In 2011, resolution WHA64/24 on drinking-water, sanitation and health called for the formulation of a new, integrated WHO strategy, including a specific focus on water quality and monitoring issues, and on promotion of sanitation and hygiene behaviour. Resolution WHA66/12 on NTDs urged Member States to "improve coordination for reducing transmission and strengthening control of neglected tropical diseases taking into account social determinants of health, through provision of safe drinking-water, basic sanitation, health promotion and education, vector control and veterinary public health".

Efforts are under way to define the drinking-water and sanitation targets under a dedicated Water Goal as part of the SDGs, which will set the agenda for development and sustainability starting in 2015. Furthermore, efforts are being made to ensure that other SDGs, for example those on health and nutrition, include targets and/or indicators on WASH as determinants of health and nutrition.

3.6 Priority areas for NTD research

New approaches and simplified strategies are urgently needed to control NTDs. Research is critical to this objective, from basic research to finding new ways to deploy existing tools and strategies where they are needed most.

To ensure that country needs are being addressed, the identification of research priorities should be embedded at the national level. The 2013 World Health Report on research for universal health coverage called for all nations to be producers as well as consumers of research. WHO is encouraging national governments and international donors to invest in research and support mechanisms for sharing information and data, and in strengthening research training and institutions.

Although basic research and improved methods can be assisted by northern institutions, research on implementing these new and improved tools must be done in country, and the capacity to do so must be built.

3.6.1 Generating basic knowledge

For many NTDs, there is a pressing need to go back to the drawing board using state-of-the-art tools of genomics or molecular biology to understand the pathogenesis of the disease. This could help to identify new avenues for research and development.

For example, understanding the pathogenic process of Chagas disease as an auto-immune process would obviate the need to further develop the current treatment of chemotherapy focused on the parasite. Sequencing the *T. brucei* genome for human African trypanosomiasis or improving the understanding of cell–parasite interactions in leishmaniases has key implications for drug development.

At the other end of the spectrum, basic health policy or social research can clarify issues such as obstacles to improving access to treatment, seeking behaviour and adherence to treatment.

3.6.2 Developing new methods

New medicines, vaccines, diagnostics and vector control methods are usually developed in close collaboration with industry. There have been some notable successes through public–private partnership activities. Public and private sector incentives must be set up to encourage NTD research and development using appropriate collaborative measures that can allow exchange of expertise and scientific knowledge through:

- procurement and provision of long-term funding for NTDs;
- industry-wide disease-focused research that is based on need and not solely market-driven;
- corporate responsibility schemes and platforms such as the Uniting to Combat NTDs coalition, to encourage innovative incentives;
- funding sources and opportunities such as those provided by Horizon 2020, to promote sustainable research; and
- provsion of opportunities to emerging economies such as Brazil, China and India, to make a greater contribution to research.

Vaccine research faces formidable scientific and technical obstacles and is in its early days for parasitic diseases. There is growing interest in the development of new diagnostics and vector control tools, such as improved pesticides. A key challenge involves translating basic academic research into new medicines, vaccines, diagnostics and insecticides.

The treatment of many NTDs depends on medicines that are old – some as old as 50 years. Of the 1556 new medicines developed between 1975 and 2004, only 21 – representing about 1% – were for tropical diseases (including tuberculosis) (*14*).

Effective tools exist for some NTDs but their geographical coverage is often limited due to complex diagnostic and treatment protocols. Simplified control of NTDs that can be managed by local health services with minimal support from specialized staff is called for; this will require refining existing methods, as well as devising new ones. Examples for improved methods are research on a uniform multidrug therapy regimen for all types of leprosy patients that would facilitate the further integration of control in routine health services; studies on the efficacy of increased praziquantel dosage for treatment of schistosomiasis; and short-dose pentamidine for treatment of human African trypanosomiasis. Fixed-dose combinations of existing drugs are other research avenues that would lead to simplified treatment delivery, reduced risk of parasite resistance as well as simplified logistics.

Research on new methods includes research into techniques and procedures that would improve the effectiveness of disease control. An example for lymphatic filariasis is simple foot

care for lymphoedema patients, which has proven an effective intervention that significantly improves quality of life. For dengue, research is ongoing to develop new entomological sampling methods for more cost–effective vector control. Research on rapid assessment methods to determine the geographical distribution of the prevalence and intensity of infection has produced new methods that have proven of great practical importance for onchocerciasis and lymphatic filariasis control in Africa.

Often, the mere proof of efficacy of new tools and methods is not enough. Their effectiveness must be demonstrated in field conditions. This may require large-scale field trials, which tend to be expensive but are essential to convincing health decision-makers to make a new tool or method available through routine health services.

3.6.3 Devising new and improved strategies

Research is also crucial to ensure the greatest reach of the product with optimal impact. This is particularly important in reducing the risk of transmission within a community. Field research can determine the impact of the intervention on transmission, and epidemiological modelling can predict the long-term impact of alternative control strategies. Such research is ongoing for lymphatic filariasis, for which effective microfilaricides are available. Key questions such as the duration of treatment and minimal treatment coverage rates to interrupt transmission must be answered to provide critical information for the global elimination programme.

Implementation research helps to identify obstacles from a health service perspective and improve treatment coverage. Objective scientific evidence is needed on what works and what does not, and why, in order to develop and test more effective implementation strategies that are appropriate for the socio-economic environment in which they are needed. An example is the development of community-directed treatment for onchocerciasis. Among the new research initiatives are strategies for MDA for NTDs in urban areas and implementation of miltefosine treatment for visceral leishmaniasis. Funds for implementation research remain limited and more research is needed to improve implementation and ensure that health products reach those who need them.

3.6.4 Setting priorities

Research is a continuum from basic research through to implementation research.

Good-quality research is integral to making a sustainable impact on NTD control. Research must therefore remain an inherent part of the culture of control, even as diseases move towards elimination and eradication, to address continuously evolving circumstances, and new scientific and operational questions.

An iterative dialogue and balance must be developed and sustained. A systematic and dynamic prioritization process involving disease-focused and needs-driven research can underpin such a process.

A critical element in moving projects forward, and to ensure their relevance, is that they are embedded as early as possible in and linked to developing countries' needs and activities. Building and using this research capacity, and providing opportunities for ideas to be developed just as effectively whether they originate from the South or the North, is crucial to long-term sustainability.

As WHO moves to address research and development objectives that become increasingly significant, there is a continuous need to scale up and coordinate large-scale activities (e.g. medicine and vaccine development projects; multi-site effectiveness studies). With increased needs and expectations, many new initiatives have developed. These must in turn be linked to a broader international dialogue that has a common understanding of major goals, priorities, policies and strategies. It is from this type of interaction that effective research will be converted into effective policy that is sustainably managed and owned by the affected populations.

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DISEASES

IMPACT ON PUBLIC HEALTH OF THE 17 NEGLECTED TROPICAL DISEASES

This third report presents the investment case for NTDs in the context of the post-2015 development agenda of the United Nations; that is, in the context of the Millennium Development Goals and the Sustainable Development Goals. This Chapter discusses the investments needed to achieve the Roadmaps' targets.

Introduction

The NTDs result from a variety of causative pathogens: viruses (dengue and rabies); bacteria (Buruli ulcer, leprosy, trachoma and yaws); protozoa (Chagas disease, human African trypanosomiasis and the leishmaniases); and helminths (taeniasis and (neuro) cysticercosis), dracunculiasis, echinococcosis, foodborne trematodiases, lymphatic filariasis, onchocerciasis, schistosomiasis and soil-transmitted helminthiases). This chapter presents for selected NTDs the investment needed to achieve the Roadmap's targets.

4.1 Buruli ulcer

Introduction

Buruli ulcer is a chronic necrotizing skin disease caused by infection with *Mycobacterium ulcerans*. Historically, the disease has been reported from 33 countries, 15 of which continue to report cases to WHO annually (*1*). Globally, there is no clear pattern in the distribution of cases, but an increasing trend has recently been found in Australia (*2*), Gabon (*3*) and Ghana (*4*).

Although in areas without ready access to reference laboratories, diagnosis by experienced clinicians may suffice to initiate treatment, increasingly countries are expected to ensure that at least 70% of reported cases are laboratory-confirmed. In 2014, WHO published a manual on the laboratory diagnosis of Buruli ulcer to guide health workers in the field (*5*).

WHO recommends combined antibiotic treatment using rifampicin and streptomycin, with or without surgery and physiotherapy, depending on the stage, location and extent of the disease (*6*). Since the publication of WHO treatment guidelines in 2004, more than 50 000 people have benefited from combination antibiotic therapy, almost halving the need for surgery, the mainstay of treatment in the past.

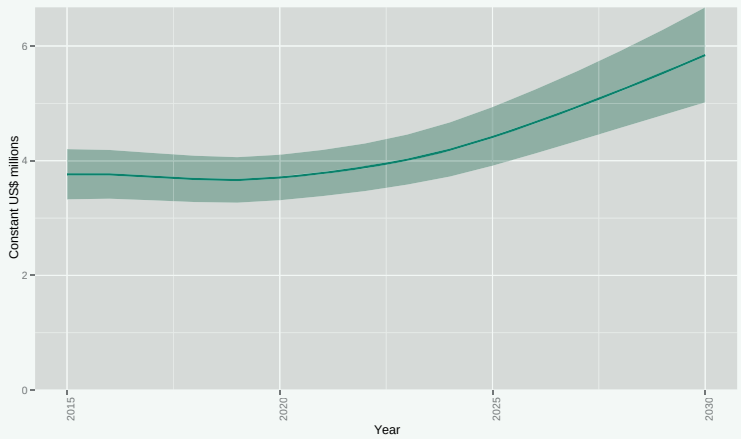
The main challenges associated with management of the disease are the long periods needed for healing, a process that includes hospitalization, and the contractures resulting from late healing, especially when lesions cross joints and treatment is inadequate. At least 25% of healed cases have some degree of disability. Death in patients is related to sepsis and tetanus. Coinfection with HIV is an emerging issue for which optimal clinical management has yet to be defined. Provisional guidance has been published until more data are accumulated (*7*).

The Global Buruli Ulcer Initiative comprises academic and research institutions, donor agencies, nongovernmental organizations, Member States and WHO. Its aims are to raise awareness of the disease, improve access to early diagnosis and treatment, and promote the development of better tools for treatment and prevention. The strategy, which is based on the Cotonou Declaration adopted in Benin in 2009 (*8*), is designed to minimize morbidity and prevent disability through early detection and treatment. Opportunities to implement control measures for Buruli ulcer together with other public-health programmes should be seized.

Investment case

The socioeconomic impact of Buruli ulcer is high. A study conducted in Ghana in 2012 showed the high burden on household costs of out-patient treatment despite its availability free of charge.[1] Medical costs made up less than 4% of total direct costs. The largest cost (81% of direct costs) was transportation. More difficult to quantify financially was the cost of lost productivity (more than 8 days per patient), school absenteeism (19 days per child) and social isolation (self-reported by 84% of children). In Central Cameroon, the cost of hospitalization has been estimated at 25% of household annual earnings, again despite treatment being available free of charge.[2]

Investment targets for active case-finding, treatment and care of Buruli ulcer (excluding medicines), 2015–2030



Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

Buruli ulcer is known to be severely underreported.[3,4] Prevention of disability will require increased public investment in early case detection. To prevent catastrophic expenditure of those cases that are found, public investment in treatment and care is also needed. If targets of coverage and value for money are met, about US$ 4.3 million (US$ 3.8–4.8 million) per year may be required during 2015–2030 for active case-finding, diagnosis, treatment and care, including medicines and surgery when necessary. This covers only the direct medical costs, not the cost of transportation.

The development of a new rapid diagnostic test offers new investment opportunities. Currently, clinical diagnosis relies on well-trained, experienced health professionals; laboratory confirmation by polymerase chain reaction (PCR) can be done only in reference laboratories. Fluoroscent thin-layer chromatography has potential as an important new

tool for field workers, resulting in higher and faster rates of detection. Studies of the cost–effectiveness of PCR should be undertaken to determine whether a new active case-finding strategy is warranted, to detect cases earlier, thereby achieving better treatment outcomes.

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[3] Mavinga Phanzu D, Suykerbuyk P, Saunderson P, Ngwala Lukanu P, Masamba Minuku JB, Imposo DB et al. Burden of *Mycobacterium ulcerans* disease (Buruli ulcer) and the underreporting ratio in the territory of Songololo, Democratic Republic of Congo. PLoS Negl Trop Dis. 2013;7:e2563. doi:10.1371/journal.pntd.0002563. eCollection 2013.

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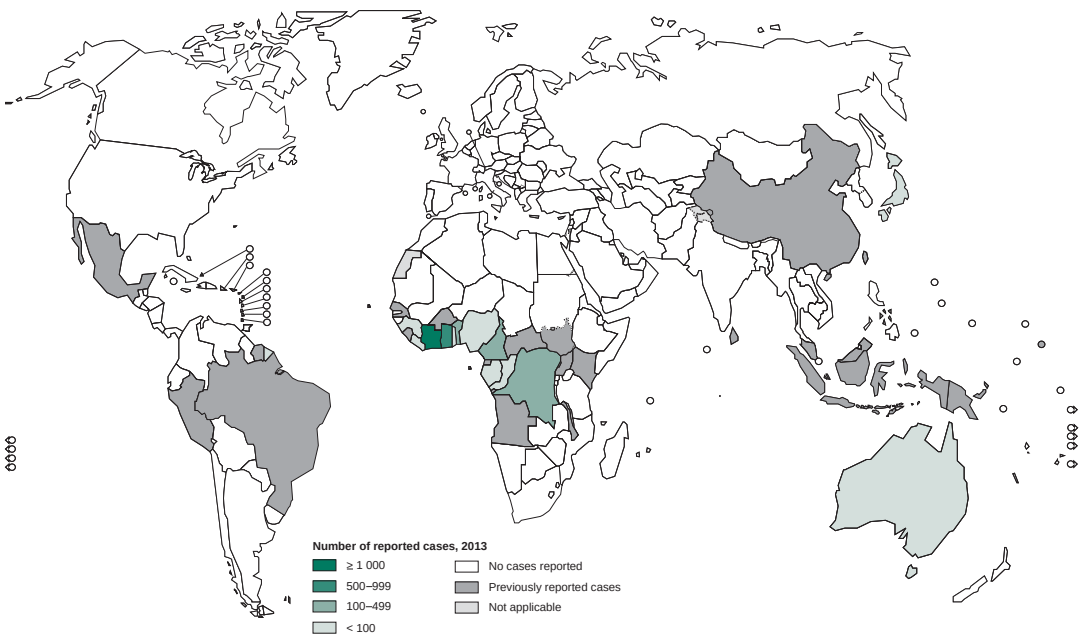
Burden and distribution

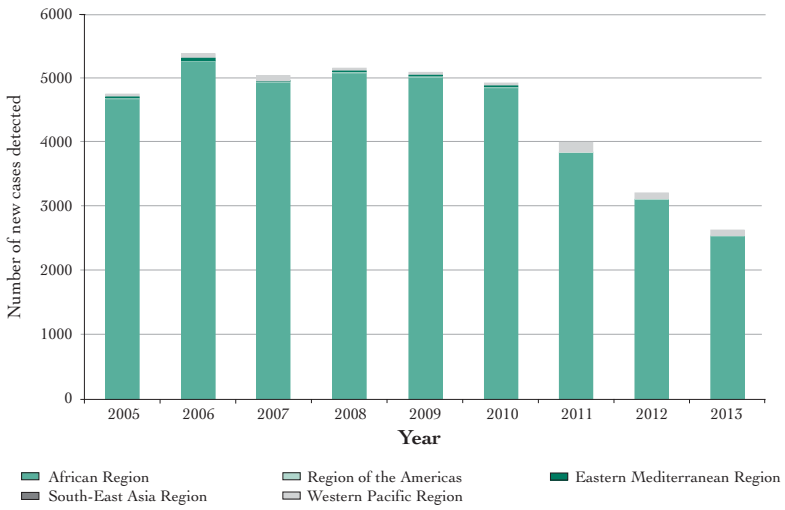
The 33 countries in which Buruli ulcer has been detected have mainly tropical and subtropical climates (*Fig. 4.1.1*). About 5000 cases annually are reported from 15 of those countries, but this number is considered low. Since 2010, the number of reported cases has declined gradually,

Fig. 4.1.1 Distribution of Buruli ulcer, worldwide, 2013



possibly as a result of less intensive case-finding activities (*Fig. 4.1.2*). The incidence in endemic regions of Ghana has been estimated at 150 cases per 100 000 population. Japan has reported 46 cases since 1980. Australia reported 695 cases between 2002 and 2013, where an increasing trend is evident. The number of cases has also increased in Gabon. The number of cases has been decreasing in Benin (since 2007) and in Côte d'Ivoire (since 2010).

Fig. 4.1.2 Number of Buruli ulcer cases reported to WHO, by region, 2005–2013



The data available to WHO are limited because (i) control activities within endemic countries have a restricted geographical scope and data may not reflect the national burden; (ii) in some areas there are few or no case-detection activities and the extent of the disease is therefore unknown; (iii) underreporting may result from insufficient knowledge of the disease and its occurrence mainly among poor people in rural communities.

Progress towards Roadmap targets

The Roadmap's first target for achieving intensified control of Buruli ulcer requires completion by 2015 of a clinical trial of oral antibiotic therapy (using rifampicin and clarithromycin). The study started in Benin and Ghana in 2013; completion is expected in 2016 instead of 2015 because of the slow recruitment rate. The use of an oral antibiotic regimen would ensure that more people have access to treatment, enabling achievement of the Roadmap's second target: to cure 70% of cases in endemic countries by 2020.

Research priorities

The priority for research is to develop a rapid point-of-care diagnostic test. In November 2013, WHO and FIND [the Foundation for Innovative New Diagnostics] convened a meeting of experts to review and prioritize diagnostic technologies under development (*9*). One innovation – the direct detection of toxin (mycolactone) in human tissues – may offer a simpler and faster way to confirm suspected cases of Buruli ulcer than current diagnostic methods (*10*).

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4.2 Chagas disease

Introduction

Chagas disease, also known as American trypanosomiasis, is caused by infection with the protozoan parasite *Trypanosoma cruzi*. The infection originally found in rural areas of the Americas, mostly in the 20th century, changed its epidemiological pattern with increased prevalence, urbanization and spread to other continents (*1*).

Human transmission usually occurs through the faeces/urine of infected vector insects (haematophagous triatomines). These bugs typically live in the cracks of poorly constructed homes in rural or suburban areas. Normally they become active at night, feeding on mammal blood, including humans, biting exposed skin such as the face, and defecating close to the bite. The parasites enter the body when the person instinctively smears the bugs' faeces/urine into the bite or any other skin break, or the eye or oral membranes. The ingestion of food contaminated by faeces/urine of infected insects is another important route of transmission, especially in hot and humid climates.

Transmission can also occur through transfusion of infected blood, congenital transmission and, less frequently, organ transplantation or laboratory accidents. In areas with intradomiciliary vectorial transmission, children aged under 5 years are more often found to be infected; in areas without such transmission, the infection is detected in older children and is associated with activities that provide greater exposure to peridomestic and sylvatic vectors.

Diagnosis during the initial acute phase or early chronic phase provides a critical but time-limited opportunity to detect and successfully treat patients with antiparasitic medicines. Early diagnosis can prevent the potentially catastrophic expenditures associated with underdiagnosis or misdiagnosis leading to a high morbidity burden, consequent mortality and possible co-infections and co-morbidities in the chronic phase (*2,3*).

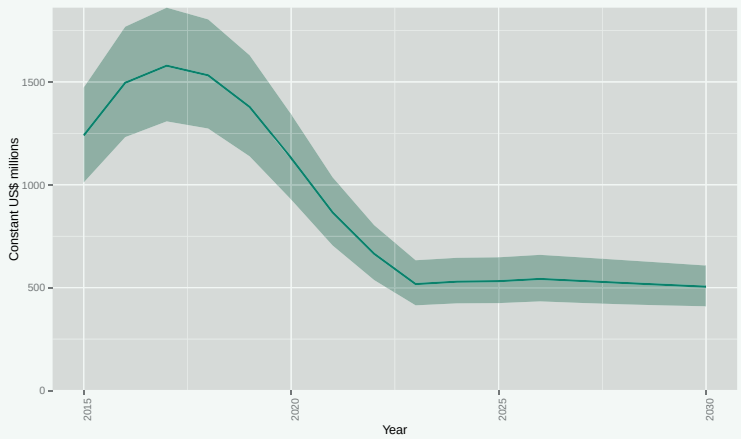
Besides the biomedical approach, psychosocial approaches are crucial to change defective perceptions of a silent and silenced disease as well as health-seeking behaviours (*4–6*).

Two medicines are available to treat *T. cruzi* infection: benznidazole, the first-line treatment in most countries, and nifurtimox. During 2011–2012, WHO managed a global shortage of benznidazole and consequent impairment of detection and treatment. In 2013–2014, both medicines were made available, WHO updated its List of Essential Medicines for Children, three paediatric presentations were offered for distribution globally and a WHO information system on drug distribution was revised (*7*).

Investment case

The cost of Chagas disease was estimated in 2013 at more than US$ 7 (4–11) billion per year, including lost productivity.[1] Cost-of-illness studies including productivity losses must be interpreted with caution, especially when comparing them with those for other diseases, as they are often highly sensitive to methodological assumptions. Nonetheless, health-care costs alone were estimated at US$ 0.6 (0.2–1.6) billion per year. Of note is that almost one-fifth of health-care costs are estimated to have been incurred outside the endemic countries. The cost of treatment ranges from less than US$ 200 to more than US$ 30 000 per person per year in endemic countries, and exceeds US$ 40 000 in the USA (forthcoming review of the literature). In Mexico, the cost – including diagnosis, treatment and productivity losses – may increase more than 20-fold from an acute case to a chronic case.[2] In Brazil, the cost of hospitalization for chagasic cardiomyopathy with heart failure has been estimated at an average of US$ 467 per day – higher than for non-chagasic admissions with heart failure.[3]

Investment targets for vector control against Chagas disease (attack phase and sustained surveillance), 2015–2030



Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

A better understanding of the costs and effects of prevention may help create incentives for increased collaboration between endemic and non-endemic countries, including for both prevention of infection (primary prevention) and early detection of infection (secondary prevention). This report addresses primary prevention through vector control strategies in endemic countries, given the available evidence of its cost-effectiveness. In 2006, the second edition of the Disease Control Priorities Project put the cost per DALY averted by vector control at less than US$ 300 based on a study from Brazil. More recent economic evaluations put the cost of the most cost–effective vector control interventions at less than US$ 200 per household per year and less than US$ 200 per case averted in Argentina.[4]

Evidence on the cost–effectiveness of screening strategies has been strengthened since 2006, namely on screening of blood banks and mothers and children of positive mothers.[5,6]

Investment targets for sustained vector control amount to about US$ 720 million (US$ 620–820 million) per year during 2015–2020. In the period to 2020, this includes countries pursuing a vertical attack phase as well as those having already progressed to sustained surveillance. Areas with ongoing transmission require "attack" with a systematic assessment and vector control of all houses and dwellings. After 2 years of attack (targeted for completion in all eligible communities by 2020), almost all areas should be experiencing only sporadic transmission and can then shift to sustained surveillance with rapid response to reports of vector presence and acute cases. As countries move from the attack phase to sustained surveillance, investments may decrease to about US$ 450 million (US$ 390–520 million) per year during 2021–2030. This range does not fully reflect uncertainty about the size and distribution of the population at risk and it does not include passive surveillance, which will be required in a third and definitive phase.

This report does not provide investment targets for blood screening related to transfusional and organ transplantation routes of transmission, early case detection and treatment. These will be added in future analyses considering also people affected in non-endemic countries as a result of population movements.

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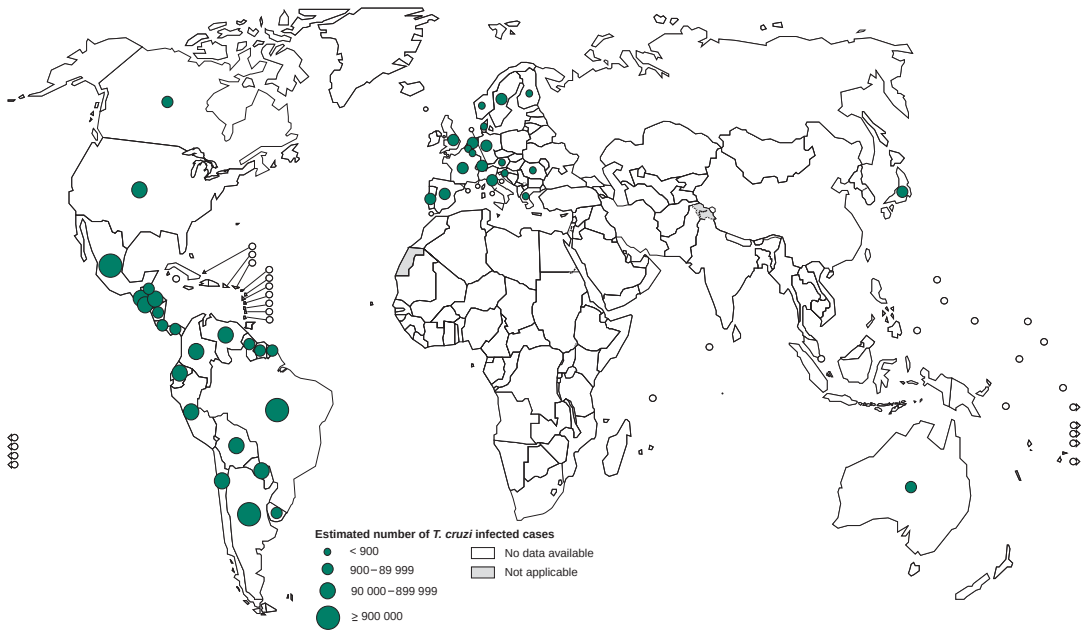
Burden and distribution

An estimated 7 million people are infected with *T. cruzi* worldwide, mostly in 21 continental Latin American countries: Argentina, Belize, the Bolivarian Republic of Venezuela, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, French Guyana, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, the Plurinational State of Bolivia, Suriname and Uruguay (*Fig. 4.2.1*).

Fig. 4.2.1 Distribution of Chagas disease cases reported to WHO, worldwide, 2010–2013



Chagas disease remains one of the biggest public-health problems in Latin America, where it causes more than 7000 deaths per year as well as life-long morbidity and disability without early and successful antiparasitic treatment; over 25 million people are at risk for the infection. The presence of the disease outside Latin America mainly results from population exchange between Latin America and other world territories (*8*). WHO has advocated three principal areas of work for overcoming the disease: (i) interrupting intradomiciliary, vectorial and blood transfusional transmission (since the 1990s); (ii) implementing the two-pillar strategy for the interruption of all transmission routes, and increased detection and care of affected populations (since 2007); and (iii) raising awareness of the disease in endemic and non-endemic countries (since 2007).

The changing epidemiological pattern of *T. cruzi* combined with the spread of HIV has led to coinfection and comorbidity. These two chronic infections met in the 1980s following urbanization and population movements (*9*). Despite frequent under-diagnosis of coinfections, several countries – including Argentina, the Bolivarian Republic of Venezuela, Brazil, Chile, Colombia, Italy, Mexico, Paraguay, Spain, the United States of America and Uruguay – have reported cases of coinfection; the highest prevalences are detected in the south of South America and in southern Europe (*10)*.

National and multinational initiatives technically supported by PAHO/WHO (the Southern cone, Central American, Andean Pact and Amazonian Intergovernmental initiatives) have contributed to substantial reductions in transmission by the principal intradomiciliary vectors and the risk of transmission by blood transfusion (since the 1990s).

The launch by WHO in 2007 of the Non-Endemic Countries initiative continued to stimulate political impetus for control and elimination of the disease and marked a historic signal for action in both disease-endemic and non-endemic countries. Launched during the Third WHO meeting of the Non-Endemic Countries Initiative (June 2013), the "tricycle strategy" is based on two power wheels (interrupting transmission and providing care in affected populations) and a steering wheel (an information and surveillance system). The building of this system has important additional value: to raise awareness of Chagas disease, especially by facilitating access to interactive data, disease statistics, maps and diagrams.

The switch from a two-pillar to a tricycle strategy had three objectives: (i) to raise the third (information and surveillance) component to the level of the other two areas; (ii) to promote an active strategy (of diagnosis, treatment and interruption of transmission); and (iii) to increase visualization of the disease, improving and expanding access to disease statistics and maps.

Progress towards Roadmap targets

The two targets selected for the Roadmap are related to two (out of the six) routes of transmission: (i) to interrupt transmission through blood transfusion in the Americas, European and Western Pacific regions (2015); and (ii) to interrupt intradomiciliary vectorial transmission in Latin America (2020). Countries have made major progress towards achieving these targets. WHO has established a surveillance system and is working with countries to advance in all areas with remaining vectorial house infestation and to improve screening of blood donors.

The following prevention and control tools are used depending on the geographical areas affected: spraying homes and surrounding areas with residual insecticides; improving the walls and roofs of dwellings (e.g. by plastering cracks) and enhancing domestic hygiene to prevent vectorial infestation; implementing personal control measures (such as using bednets); and practising good hygiene when preparing, transporting, storing and consuming food.

Screening blood from donors, organ donors, cell donors and their recipients is a fundamental method for interrupting transmission. The risk of transmission by blood transfusion has been substantially reduced throughout Latin America: 20/21 countries have achieved 100% screening of blood.

These achievements were made possible thanks to the commitment of endemic countries, the strength of their research and control organizations, and support from many international partners. Challenges include the implementation of a systematic quality control and verification of the interruption of transmission in all countries with Chagas disease.

Research priorities

There is no vaccine against Chagas disease. The priorities for research include: improved understanding of the diversity of the disease in different geographical settings and in relation to the different performance of diagnostic tests, clinical manifestations, therapeutic responses and effectiveness of control measures; assessment of new tools for vectorial control; production and assessment of screening and diagnostic tools, including rapid diagnostic tests and confirmatory tests; investigating markers of therapeutic response; optimizing dosage according to age and different therapeutic responses in different geographical areas, and in relation to new antiparasitic medicines and new drug combinations (*11–13*).

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4.3 Dengue

Introduction

Dengue is a mosquito-borne viral disease of public-health significance that has affected all regions of WHO since 2010. The flavivirus is transmitted by female mosquitoes mainly of the species *Aedes aegypti* and, to a lesser extent, *Ae. albopictus*.

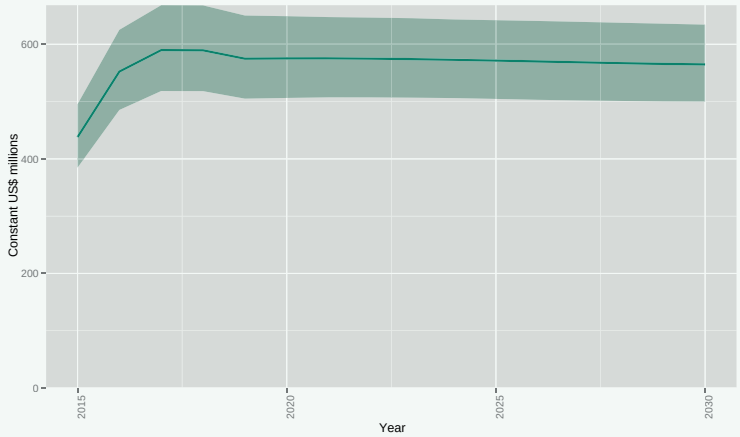
Investment case

Dengue, a rapidly spreading vector-borne disease, is endemic in more than 100 countries and affects travellers and local communities worldwide. Today, hundreds of thousands of severe dengue cases arise every year, including about 3000 deaths. The cost of ambulatory care and hospitalization is unaffordable for poor people. In Cambodia and Viet Nam, between half and two-thirds of affected households have incurred debt as a result of treatment.[1,2] The economic burden of the disease is already measured in the billions of dollars annually.[3,4,5] Environmental change and urbanization are conspiring to elevate the cost even further beyond the reach of health systems and households. Fortunately, outbreaks are preventable if detected and managed early. In 2006, the second edition of the Disease Control Priorities Project put the cost per DALY averted by sustained vector control at less than US$ 3500 using environmental management and less than US$ 2000 using insecticides. More recent evidence suggests the number might be even lower.[6] (See the Technical Appendix for further references on cost and cost–effectiveness of vector control interventions.)

The investment target for sustained vector control is US$ 510 million (US$ 440–580 million) per year during 2015–2030. This range does not fully reflect uncertainty about the size and distribution of the population at risk, especially in Africa. It probably underestimates the cost of sustained vector control for all populations at risk. Nonetheless, these conservative estimates indicate that vector control will be of increasing importance within the NTD portfolio. The investments are significant, but less than the costs of the alternatives. A review of the literature suggests that the cost of sustained vector control is lower than that of outbreak response.[7]

The introduction of a highly effective vaccine against dengue may re-programme some of the investments in vector control towards immunization but is unlikely to obviate the need for it. The available models suggests that vector control will remain cost–effective in the presence of a vaccine.[8,9,10] Vector control may enhance the cost–effectiveness of a medium-efficacy vaccine, or a vaccine that is highly effective but only against one of the four dengue

Investment targets for vector control against dengue, 2015–2030



Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

serotypes. It may allow for lower levels of coverage by immunization programmes, especially when and where vaccine production is constrained. Investments in vector control should therefore be seen as complementary to the development and implementation of a future dengue prevention and control strategy. As the disease continues to expand to newer areas, vector control alone can prevent and reduce outbreaks.

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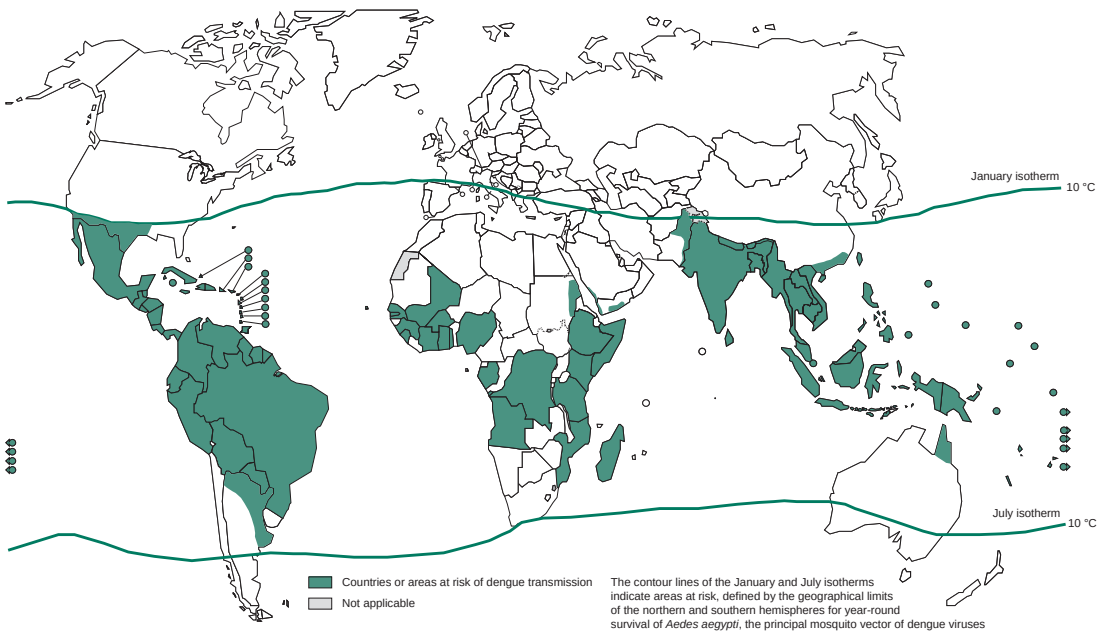
Burden and distribution

Dengue is widespread throughout the tropics, with local spatial variations in risk influenced strongly by rainfall, temperature and the degree of urbanization. The actual numbers of cases are underreported and many cases are misclassified. One recent estimate indicates 390 million dengue infections per year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease) (*1*). Another study, of the prevalence of dengue, estimates that 3900 million people, in 128 countries, are at risk of infection with dengue viruses (*2*). Member States in three WHO regions regularly report the annual number of cases to the Secretariat; in 2013, nearly 3 million cases were so reported. Although the full global burden of the disease is uncertain, its epidemiological patterns are alarming for both human health and the global economy (*Fig. 4.3.1*) (*3*).

Fig. 4.3.1 Distribution of countries or areas at risk of dengue transmission, worldwide, 2014



The principal vectors of dengue have continued to silently expand their distribution globally and are now present in more than 150 countries. Movement of goods (used tyres and plants with axils) containing dried mosquito eggs have facilitated the vectors' spread. Both the main vectors transmit not only dengue virus but also other closely related arboviruses such as chikungunya and Zika viruses.

Although the burden of dengue in the African Region is still unknown, outbreaks have been reported from 22 countries. The presence of the disease and the high prevalence of antibodies to dengue viruses in serological surveys suggest that dengue virus infection is endemic in many parts of Africa. Dengue continues to be underreported in Africa owing to a lack of awareness among health-care providers, the presence of other febrile illnesses (especially malaria), and insufficient clinical diagnosis, laboratory testing and case reporting that hinders systematic surveillance. Since 2013, dengue outbreaks have been reported in Angola, Mauritius (*4*), Mozambique and the United Republic of Tanzania.

Dengue is considered an emerging disease in the Eastern Mediterranean Region because laboratory-confirmed cases have been reported for only two decades. Generally, cases have been detected along the coasts of countries bordering the Red Sea and the Arabian Sea. Dengue is emerging as a major public-health problem in Pakistan, Saudi Arabia and Yemen, with repeated outbreaks in urban centres and spread of the disease to rural areas (in Pakistan and Yemen). Outbreaks are becoming more frequent in Djibouti, Somalia and Sudan, where multiple virus serotypes co-circulate and where the disease is probably expanding its geographical reach. Oman has reported imported cases.

Transmission of dengue viruses was interrupted in much of the Region of the Americas in the 1970s following the campaign to eradicate *Ae. aegypti*. As vector surveillance was not sustained, however, mosquitoes thrived and dengue outbreaks recurred in the Caribbean and in Central and South America (*5*). These regions are now in a hyperendemic state, with indigenous transmission in almost all countries. A regional initiative that uses an integrated management strategy for prevention offers the most promising approach for control (*6*). The initiation of activities to record all dengue cases and improve surveillance partly explains the sharp increase in the number of cases reported in recent years.

Dengue is endemic in the South-East Asia Region, although the incidence varies significantly among countries and within each country. Asia Pacific countries bear the heaviest burden, where more than 1.8 billion people are estimated to be at risk for the disease. The epidemiology of dengue is rapidly evolving as outbreaks occur with increasing frequency and expand to new, previously unaffected geographical areas. Mortality is highest during the initial period of the outbreak or epidemic. Children are at highest risk of mortality owing to complications with, and lack of access to, prompt diagnosis and treatment. The progressive worsening of the dengue situation in the region is attributed to unplanned urban development, poor water storage practices and unsatisfactory sanitary conditions, all of which contribute to the proliferation of the main vector, the *Ae. aegypti* mosquito.

In the European Region, *Ae. albopictus* has rapidly spred to more than 25 countries, mainly through the global trade in used tyres and lucky bamboo. The threat of dengue outbreaks therefore exists in Europe. Local transmission of the virus was reported for the first time in Croatia and in France (2010); imported cases were detected in several other European countries. An outbreak in Madeira island of Portugal (2012) resulted in more than 2200 cases and importation of cases into 17 other European countries.

The Western Pacific Region reported 348 452 dengue cases in 2012, including 1199 deaths (case-fatality rate, 0.30%). The incidence was highest in the Philippines, Cambodia and Malaysia and also in Australia in the Pacific. Island nations are susceptible to epidemics;

during 2013–2014, the DEN-3 virus serotype was recorded in Fiji and in several other islands, inflating the number of reported cases. Malaysia and Singapore indicated sustained epidemic activity during the same period. Since late 2013, a few countries in the Pacific have reported concurrent outbreaks of dengue, chikungunya and Zika viruses (*Box 4.3.1*). Diagnosis and management remain a challenge, with all efforts now focused on vector control with active community involvement.

Fig. 4.3.2 shows the global number of dengue cases reported to WHO and *Fig. 4.3.3* the trend in the number of deaths.

Box 4.3.1 Chikungunya

Chikungunya virus has caused large epidemics of chikungunya fever since 2004, with considerable morbidity and suffering. The virus is transmitted by the same vectors as those responsible for dengue. After initially affecting the African and Asian regions, the virus has spread to the Region of the Americas.

As of October 2014, more than 776 000 suspected cases of chikungunya (including 152 deaths) had been recorded in the Caribbean islands, Latin American countries and some South American countries. Mexico and the United States of America have also recorded imported cases. On 21 October 2014, France confirmed four cases of locally-acquired chikungunya infection (in Montpellier).

Fig. 4.3.2 Number of dengue cases reported to WHO, by region, 1995–2013

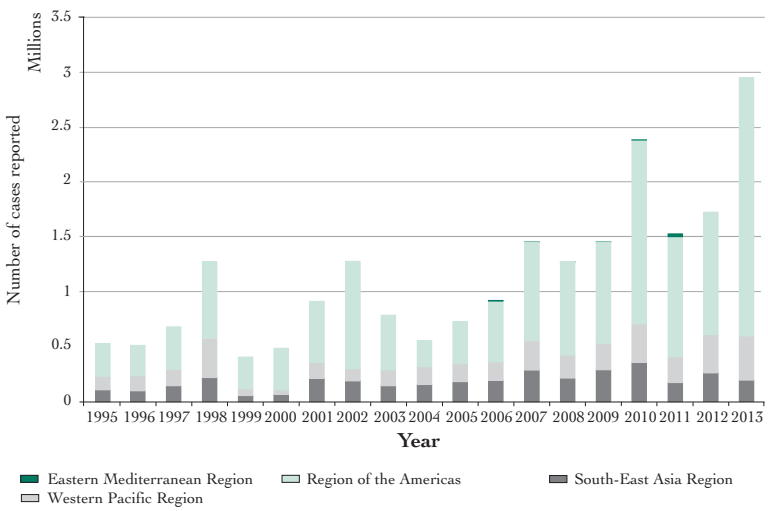
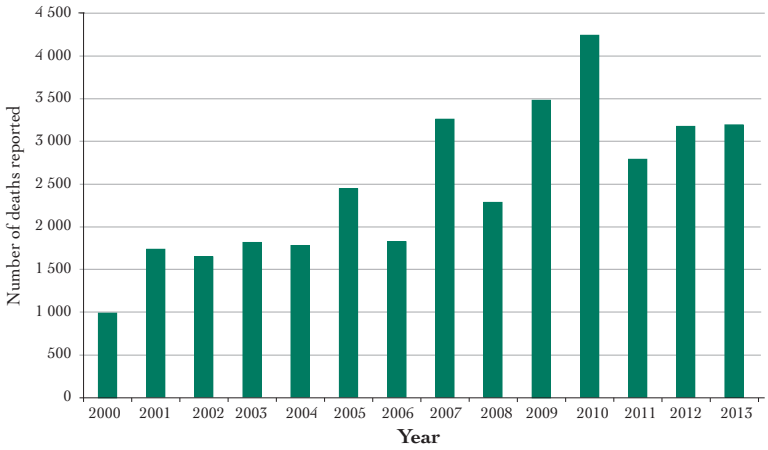


Fig. 4.3.3 Number of dengue deaths reported to WHO, worldwide, 2000–2013



Progress towards Roadmap targets

The Roadmap's targets for intensified control can be achieved by implementing the global strategy in full (see below). Trends indicate declining mortality, but morbidity has continued to increase, due partly to better reporting systems. Estimates of the burden of the disease are under way in selected countries.

After extensive consultations with experts, country programme managers and regions, WHO published the *Global Strategy for dengue prevention and control (2012–2020)* in 2012 (*7*). Its goal is to reduce the burden of dengue worldwide, with specific objectives to reduce mortality by 50% (2020), reduce morbidity by 25% (2020) and estimate the true burden of the disease (2015). The strategy relies on five technical elements: diagnosis and case management; integrated surveillance and outbreak preparedness; sustainable vector control; future vaccine implementation; and research. Regions and Member countries are encouraged to adopt the strategy and work towards its objectives.

As with prevention and control of other vector-borne diseases, effective surveillance, prevention and outbreak response as well as tools (vector control) must continue to complement each other in reducing the burden of dengue. The scientific community, donors, vaccine producers and all stakeholders have concluded that there is a need to integrate any new vaccines (as and when available) with existing vector control activities; all prevention activities can control infection rates and systematic targeted vaccine introduction can raise herd immunity over time. Sustained vector control against *Aedes* also helps to control dengue outbreaks and other arboviral diseases such as chikungunya and Zika, in accordance with the Global Strategy.

The impact of dengue outbreaks on health systems and the associated costs to other sectors (diverting resources to other ministries) and the community at large are hard to predict. Dengue has been identified as a disease of the future owing to increased urbanization, scarce

water supplies (resulting in storage practices) and, possibly, environmental and climate change. Control of dengue is technically feasible with coordinated international technical and financial support for national programmes, and has proven effective in reducing the global burden of malaria.

Research priorities

WHO needs to further coordinate activities, including quality assurance of dengue diagnostics; strengthen capacity for case management and vector control; develop an evidence base for integration of preventive strategies such as vaccination (when available) and sustained vector control; and enhance integrated surveillance. Dengue in the African Region is of serious concern and must be included in existing surveillance systems in order to map the distribution of the disease and its vectors, and to develop policy at country level. WHO has received a grant from the Bill & Melinda Gates Foundation to estimate the burden of dengue in selected countries and to design a methodology and guidelines for adoption by Member States.

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4.4 Dracunculiasis (guinea-worm disease)

Introduction

With 148 cases reported in 2013 (*1*), the lowest ever recorded, dracunculiasis is poised for eradication as targeted in the Roadmap. The disease results from infection with the nematode *Dracunculus medinensis*, commonly known as the guinea worm. People become infected by drinking water containing infected copepods (Crustacea). Once eradicated, dracunculiasis will be the first parasitic disease to be eradicated, that too without any medicine or vaccine.

Investment case

Disease eradication is the ultimate example of universal health coverage. Eradicating dracunculiasis will ensure that all peoples are forever spared the agony and often permanent disability that results from the guinea worm. There will also be long-term economic benefits. A seminal study in Nigeria in 1987 found that farmers were incapacitated by the disease for an average of 5 weeks.[1,2] In countries where the disease is no longer endemic, for every US$ 1 invested, agricultural earnings have increased about US$ 1.30.[3]

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Burden and distribution

During the 1980s, dracunculiasis was endemic in 20 countries in WHO's African, Eastern Mediterranean and South-East Asia regions. In 1989, a total of 892 055 cases in 13 682 villages were reported from the 15 countries that submitted reports from village-based case searches (*2*). In 2013, a total of 148 cases were reported from 103 villages: 113 cases in 79 villages (South Sudan); 14 cases in 10 villages (Chad); 11 cases in 8 villages (Mali); 7 cases in 5 villages (Ethiopia); and 3 cases in 1 village (Sudan) in areas bordering South Sudan (*1*). From January to August 2014, a total of 82 cases were reported from 50 villages: 70 cases in 38 villages (South Sudan); 9 cases in 9 villages (Chad); 1 case in 1 village (Mali); and 2 cases in 2 villages (Ethiopia) (*1*) (*Fig. 4.4.1*).

Fig. 4.4.2 shows the steady decline in the number of cases reported monthly. The overall increase observed during July–August 2014 resulted from the recorded increase in the number of cases reported in South Sudan during those months compared with the same period in 2013.

Fig. 4.4.1 Distribution of villages reporting dracunculiasis cases to WHO, 2013 and 2014 (January–August)

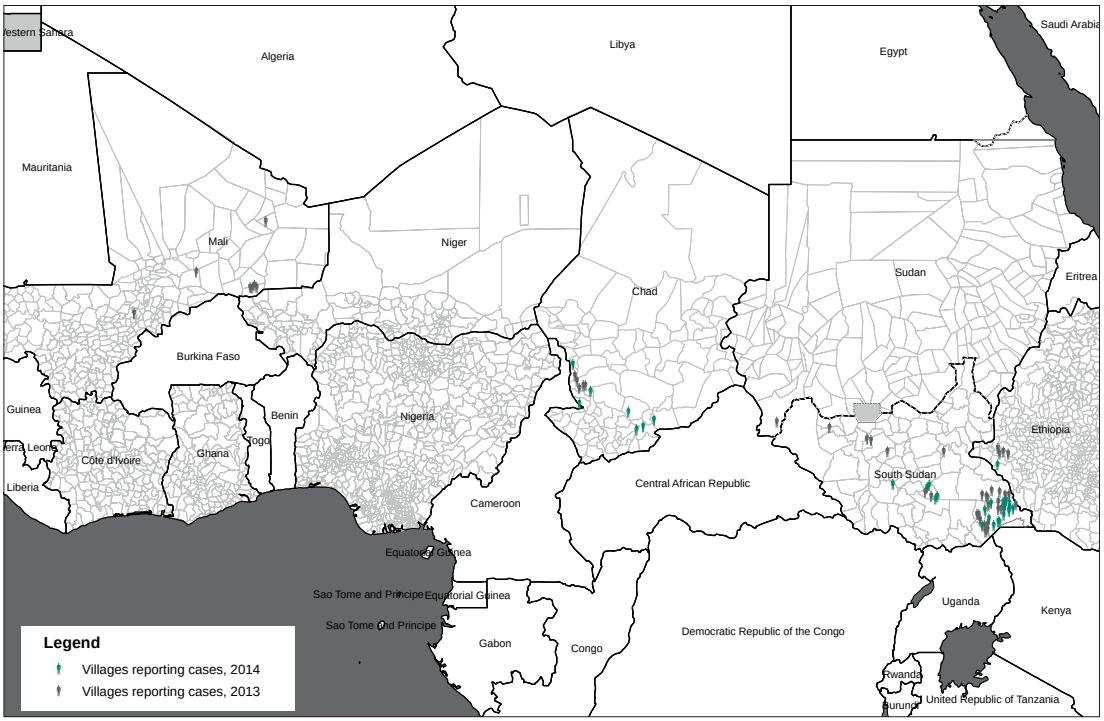
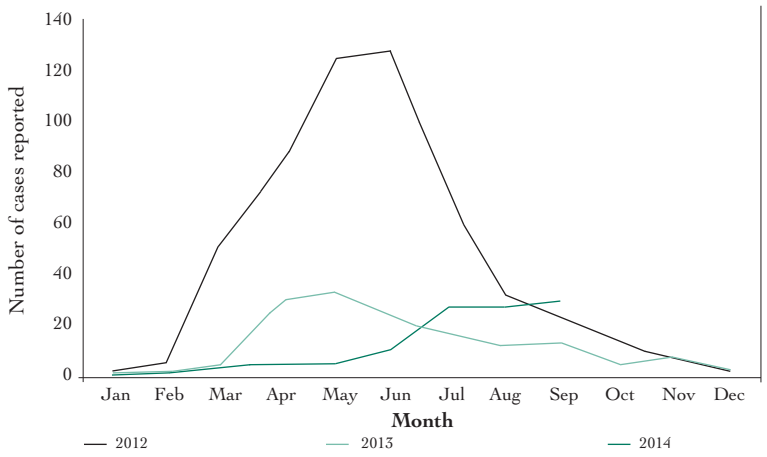


Fig. 4.4.2 Number of dracunculiasis cases reported to WHO, by month, 2012–2014



*Data for 2014 are provisional up to September.

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
2012	2	5	55	82	125	128	71	32	22	14	4	2
2013	1	2	4	29	33	23	17	12	13	5	7	2
2014	1	1	4	5	5	11	25	22	26			

Progress towards Roadmap targets

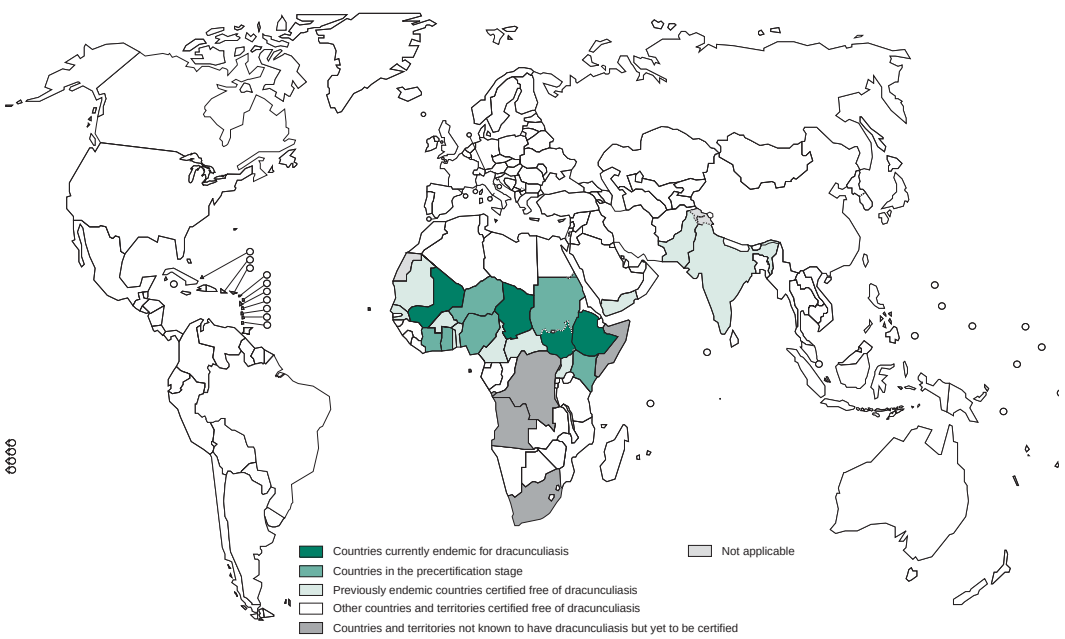
The eradication strategy recommended by WHO and adopted by all national programmes combines the following approaches: (i) heightened surveillance, through a combination of strategies, including active village-based surveillance in at-risk villages, nationwide passive surveillance, through the Integrated Disease Surveillance and Response system, supplemented by a cash reward for voluntary reporting of cases, house-to house case searches during national immunization days and other mass contact health programmes; (ii) intensified case-containment measures; (iii) vector control, by treating potential sources of unsafe water with temephos (Abate) and distributing filters to strain water; (iv) advocacy for increased access to improved drinking-water sources; and (v) behavioural change and awareness, by providing information and education.

The Roadmap targets the interruption of transmission in all countries by the end of 2015, implying zero cases reported from 2016 henceforth. Once a country claims to have interrupted transmission, it becomes eligible for certification of eradication after completing a 3-year precertification period. An intensive process of assessment is carried out as recommended by the International Commission for the Certification of Dracunculiasis Eradication, or ICCDE (*3*).

Historic opportunity

Progress towards global eradication continues to be substantive. In 2013, a record decline (73%) in the annual number of cases (148) was registered compared with the 542 cases reported in 2012. This decrease was largely driven by the 78% decline in the number of cases in South Sudan, from 521 cases in 2012 to 113 cases in 2013. While Chad, Ethiopia, Mali and Sudan reported a slight increase in the number of cases in 2013 compared with 2012, the total number of cases reported from these four remaining endemic countries (35 cases) was limited to a few foci (*Fig. 4.4.1*).

Fig. 4.4.3 Status of global certification of dracunculiasis eradication, 2014



In 2014, all endemic countries and those in the precertification stage implemented monetary reward schemes for voluntary reporting of cases. In 2013, surveys indicated that the level of awareness among the population of the reward varied between 56% and 83% in endemic districts and between 16% and 90% in non-endemic districts. The ICCDE has recommended that at least 50% of the general population should be aware of the reward and its exact amount.

With the certification of five additional countries in 2013, WHO has certified a total of 197 countries, territories and areas belonging to 185 Member States as dracunculiasis-free. *Fig. 4.4.3* shows the status of all countries by endemicity and certification stage.

New challenges

The insecurity resulting from conflicts in Mali and South Sudan is of concern to their national eradication efforts. The conflict that erupted in South Sudan (December 2013) spared much of the region where the majority of cases and the height of transmission occur, but has the potential to jeopardize achievements if access to areas of insecurity continues to be difficult. Security concerns in the north of Mali interrupted the national eradication programme in 2012, although United Nations bodies involved in humanitarian support have facilitated intermittent surveillance. With improvement in security in 2013, surveillance is being strengthened in three of the four endemic regions (Gao, Timbuktu and Mopti), but in Kidal region security remains a concern and interventions could not be implemented regularly. Furthermore, conflicts lead to population displacements both within and outside the borders of the countries, posing additional challenges to surveillance. Surveillance has been intensified in the Malian refugee camps in Burkina Faso, Mauritania and Niger in an effort to prevent the spread of infection and disease. The Ethiopian dracunculiasis eradication programme is likewise reinforcing surveillance in areas bordering South Sudan.

In 2012, Chad was re-designated as an endemic country after transmission continued for 3 consecutive years following the outbreak detected in 2010, more than 10 years after the last known case had occured in 2000. Investigation revealed an unusual occurrence of large numbers of cases among dogs during 2012–2013 (*4*), a phenomenon noted in contrast to the few infections in animals previously recorded in other countries. In addition to the known method of transmission, scientists have hypothesized the role of fish or other aquatic animals as paratenic hosts in channeling the infection to both dogs and humans through ingestion of partially or uncooked fish or its entrails (*5*). Since the Cyclops continues to be the intermediate host, the ICCDE has recommended the implementation of an effective vector control strategy as well as community education about the importance of eating properly cooked fish and disposing of fish entrails appropriately.

Steadfast resolve

In accordance with resolution WHA64.16, WHO has monitored its implementation and reported progress on the eradication of dracunculiasis to the World Health Assembly every year since 2012. Each year, the Health Assembly holds an informal meeting of the ministers of health of affected countries. The meeting held during the Sixty-seventh Health Assembly in 2014 was attended by 15 country delegations and eight Ministers of Health as well as interested partners. The Regional Director of the WHO African Region chaired the meeting, which was addressed by the Director-General in person and by former President Jimmy Carter through a video message. All the ministers and their representatives reiterated their resolve to interrupting transmission by 2015 as per the Roadmap's target (*Table 4.4.1*).

Table 4.4.1 Milestones for eradicating dracunculiasis

Milestone	2013	2014	2015
Additional countries where transmission has been interrupted		Ethiopia	Chad, Mali, South Sudan
Total number of countries targeted for certification	183 Member States	183 Member States	190 Member States
Total number of countries certified	185 Member States	185 Member States	

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4.5 Echinococcosis

Introduction

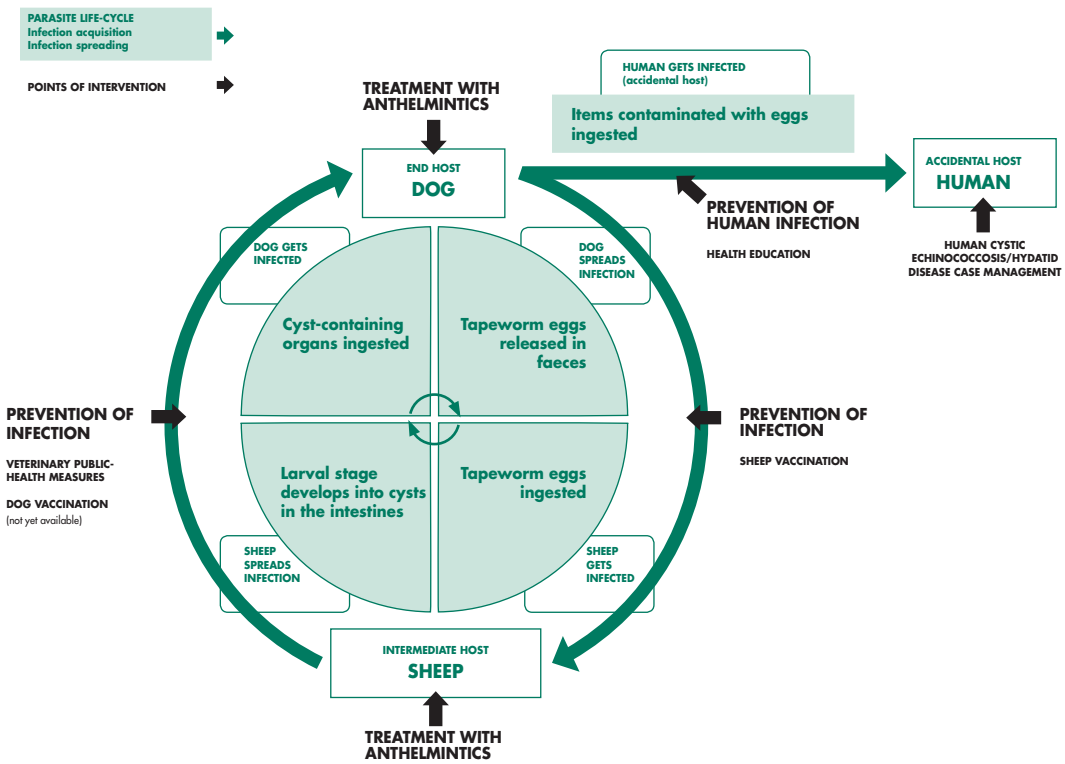
Echinococcosis is a parasitic zoonosis caused by infection with species of *Echinococcus*. Two diseases result: cystic echinococcosis (hydatidosis), due to *E. granulosus* infection, and alveolar echinococcosis, due to *E. multilocularis* infection. Both organisms are tapeworms and their definitive hosts (domestic and wild carnivores) harbour the adult parasite in their intestines. The intermediate hosts (a number of farm animals and wild ungulates for *E. granulosus* and rodents and other small mammals for *E. multilocularis*) harbour the larval stages. Humans are accidental intermediate hosts.

Humans become infected by ingesting *Echinococcus* eggs:

- *E. granulosus* infection leads to the development of one or several fluid-filled cysts (so-called hydatid cysts) that are surrounded by a capsule of host origin; these are located mainly in the liver and lungs and, less frequently, in other parts of the body including the central nervous system, bones, kidneys, spleen, muscles and behind the eye. The incubation period can last many years; symptoms depend on the location of the cyst(s) and the pressure exerted on the surrounding tissues and organs. Clinical management depends on the medical infrastructure and human resources available. Cystic echinococcosis is 100% preventable because it involves domesticated animal species as definitive and intermediate hosts. Periodic treatments of dogs with praziquantel, ensuring control measures in the slaughter of livestock with safe destruction of contaminated offal, and engaging in public education have been found to lower transmission and to prevent disease. Echinococcosis control benefits from strengthened veterinary systems and cross-sectoral strategy development and implementation (*1*).
- *E. multilocularis* infection leads to the formation of a multi-vesiculated tumour, mainly in the liver. Alveolar echinococcosis is characterized by an asymptomatic incubation period over 5 years. Larval metastases may form in organs adjacent to the liver or in distant locations following dissemination of the parasite by the haematogenous or lymphatic routes. Early diagnosis in humans, with staging of the parasitic lesion, is key. Radical surgery can be performed on confined lesions followed by anti-infective prophylaxis with albendazole. Advanced lesions that are deemed inoperable can be treated with albendazole to offer stabilization (*2*). Liver transplantation remains a final option.

Prevention and control of alveolar echinococcosis are more complex because the parasite's life-cycle involves wild animal species as definitive and intermediate hosts (*Fig. 4.5.1*). Regular anthelminthic treatment of domestic carnivores that have access to wild rodents should help to reduce the risk of infection to humans. Anthelminthic treatment of wild and stray definitive hosts using baits has drastically reduced the prevalence in Europe (*3*) and Japan (*4*).

Fig. 4.5.1 *Echinococcus* transmission cycle and possible intervention points



Investment case

Echinococcosis imposes an economic burden in developing countries estimated at US$ 2 billion in livestock losses.[1] Human echinococcosis can be life-threatening if undiagnosed and untreated. Treatment often includes costly surgery. The Roadmap seeks to provide proof of concept for effective control strategies against cystic echinococcosis in selected countries. Ideally, this would include integrated control packages for major dog-related zoonoses such as rabies and echinococcosis. The investments required by the public sector would appear to be affordable. The cost of implementing these pilot projects in three countries over a 5-year period has been estimated at about US$ 10 million, or less than US$ 0.20 per year per person at risk.[2]

Investment targets for these veterinary public-health interventions may be included in updates to the analyses contained in *Chapter 2* of this report.

[1] People, pathogens and our planet : the economics of one health. Washington (DC): The World Bank (Report number 69145-GLB; http://documents.worldbank.org/curated/en/2012/06/16360943/people-pathogens-planet-economics-one-health; accessed October 2014).

[2] The interagency meeting on planning the prevention and control of neglected zoonotic diseases (NZDs). Geneva: World Health Organization; 2011 (WHO/HTM/NTD/NZD/2011.3).

Burden and distribution

The lack of data on echinococcosis arises from the absence of systematic programmes to generate these data, which remain fragmented. As a result, the global distribution of cystic echinococcosis has changed little since 2010 (*Fig. 4.5.2*). Highly endemic areas are mostly found in the eastern part of the Mediterranean region, northern Africa, southern and eastern Europe, at the southern tip of South America, and in Central Asia, Siberia and western China.

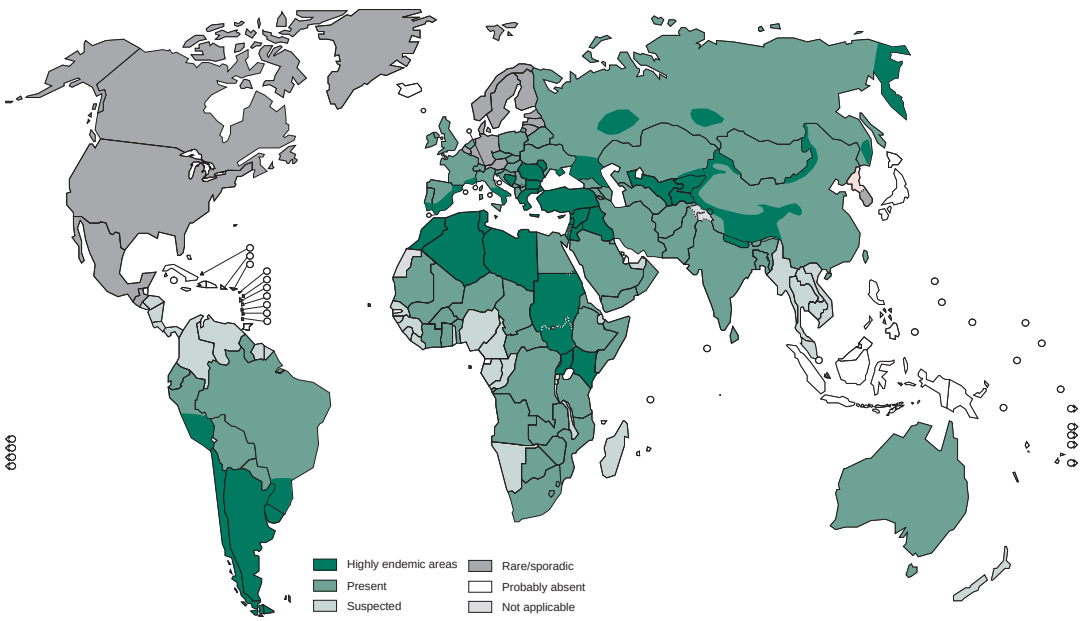
In regions where cystic echinococcosis is endemic the incidence in humans can exceed 30/100 000 person-years; prevalences as high as 5–10% may occur in parts of South America, Central Asia, China and Africa (*5,6*). The postoperative death rate for surgical patients is 2.2%; 6.5% of cases relapse after intervention and require prolonged recovery time (*7*). In certain communities on the Tibetan Plateau of China, as many as 5–10% of the population may be infected with *E. multilocularis*, and the annual incidence of cases of alveolar echinococcosis possibly exceeds 16 000 in this region (*8*).

In livestock, the rate of cystic echinococcosis found in slaughterhouses in hyperendemic areas of Latin America varies from 20% to 95% of slaughtered animals. The highest rates have been found in rural areas where older animals are slaughtered (*9*). In Sardinia, Italy, during 2005–2010 in the absence of specific control measures, the prevalence of cystic echinococcosis in sheep was 65%; about 14% of sheep harboured at least one fertile cyst (*10*). Livestock production losses attributable to cystic echinococcosis include the liver and lungs being condemned as unfit for consumption, a reduction in the weight of carcasses, a decrease in the value of the animal's hide, a decrease in milk production and reduced fecundity (*11*).

As with the other dog-transmitted NTDs, management of waste has a direct impact on roaming dog populations and therefore the source of the disease. The involvement of other sectors – including the veterinary as well as the water, sanitation and hygiene sectors – is critical.

Alveolar echinococcosis is confined to the northern hemisphere, in particular to regions of China, Central Asia, the Russian Federation and countries in continental Europe, and in North America. The parasite is endemic, but human cases are not observed. Both diseases are considered to be underreported; however, data indicate that echinococcosis is re-emerging as an important public-health problem. More than 1 million people worldwide are affected by these diseases at any one time (*8*).

Fig. 4.5.2 Distribution of *Echinococcus granulosus* and cystic echinococcosis, worldwide, 2012



Research priorities

2015 target: pilot projects to validate effective echinococcosis control strategies implemented in selected countries where the disease is a public-health problem.

2020 target: validated control strategy available and scaled up.

Morocco, with support from the Italian Ministry of Health, is piloting a project aimed at decentralizing diagnostic and therapeutic techniques and promoting the PAIR (puncture, aspiration, injection, re-aspiration) strategy in rural and hyperendemic areas.

Mongolia has recognized the importance of echinococcosis as a public-health problem and at the request of the Ministry of Health, in 2013 WHO conducted an initial situation analysis. The analysis focused on implementing early diagnosis and building a basic surveillance system covering humans and animals to understand the actual burden of the disease. No significant investment for echinococcosis has been made and programmatic progress has therefore stalled.

Research priorities

Early detection of *E. granulosus* and *E. multilocularis* infections especially in low-resource settings is still needed in addition to evaluation of clinical treatment options. Further assessment and potential commercialization of a vaccine for *E. granulosus* recombinant oncosphere antigen (EG95) is being trialled in sheep to impede *E. granulosus* infection of lambs (*11*). This could supplement control measures such as the treatment of dogs and culling of older sheep.

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4.6 Endemic treponematoses

Introduction

Endemic treponematoses, comprising yaws, endemic syphilis (bejel) and pinta, result from infection with bacteria of the genus *Treponema* (*1*). Yaws is the most widespread of the three diseases. Mass treatment campaigns led by WHO and UNICEF during 1952–1964 reduced the prevalence of treponematoses from 50 million to 2.5 million (*2,3*). Progress was not sustained, however, and endemic treponematoses resurged in the 1970s, prompting the World Health Assembly to adopt resolution WHA31.58 in 1978 for their control (*Annex 1a*). Yaws is not a fatal disease. Nonetheless, there are social, economic, humanitarian and ethical considerations that justify the intensification of efforts to eradicate it.

Children aged 2–14 years are those worst affected and serve as the main reservoir of infection for yaws and endemic syphilis. For yaws, cases peak among those aged 2–10 years (*4*). For pinta, the age range is 10–30 years. Yaws affects boys more often than girls; there is no difference between males and females in the numbers affected by endemic syphilis and pinta. In its late stages, yaws can cause disfiguring, crippling disabilities and deformities that prevent children from going to school and adults from doing physical labour. Ulcers that become infected may lead to severe secondary bacterial infection, including tetanus. Long-term complications of yaws (arising 5 or more years after the onset of infection) occur in 10% of untreated cases, causing disfigurement of the face and legs.

Diagnosis is often made on a clinical basis, but recent reports show that ulcers caused by *Haemophilus ducreyi* coexist in areas endemic for yaws and may be a confounder in yaws diagnosis (*5*). A new rapid dual non-treponemal and treponemal point-of-care syphilis test has been evaluated against the standard serological tests in yaws (*6*). The results are promising (sensitivity 95% and specificity 97%); the rapid test can therefore be used in yaws eradication efforts. Molecular techniques such as polymerase chain reaction can also be used to confirm yaws and monitor resistance to available treatment (*7,8*). Effective and inexpensive treatment is available against the treponematoses, which can now be accomplished with a single oral dose of azithromycin or, in instances where azithromycin is not available or appropriate, a single injection of long-acting benzathine benzylpenicillin.

Investment case

Yaws is a disabling and disfiguring disease that "begins where the road ends" – among the poorest and most isolated communities. It is targeted by WHO for eradication by 2020 but the global campaign is not yet financed.

It has been estimated that a global yaws eradication campaign could be established with new investments of as little as US$ 100 million in the 12 known endemic countries, provided that the necessary medicines are donated.[1] The full economic cost including medicines (yet to be donated) and existing Ministry of Health staff and assets would be higher (as depicted in *Chapter 2, Fig. 2.4*). Even with these economic costs, however, eradication would cost only US$ 26 (4.2–78) for each additional year of life lived without disability or disfigurement due to yaws.

The cost of the "end game" of any eradication effort is uncertain, with the emergence of complexities requiring some local adaptation of global strategies. Much of the uncertainty will be resolved as endemic countries implement the programme. In any case, under most reasonable assumptions, a global eradication campaign will be highly cost–effective. Importantly, from the perspective of universal health coverage, it will benefit some of the world's least well off citizens. Eradication of this neglected disease of poverty can be seen as complementary to universal health coverage and shared prosperity on the post-2015 development agenda.

There is less evidence to estimate investments for the control of bejel or pinta. Investment targets for these diseases may be added in future updates to the analyses of this report.

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Burden and distribution

The global burden of endemic treponematoses is not known accurately. *Fig. 4.6.1* and *Fig. 4.6.2* show the most recent (2013) data, based on routine surveillance and surveys from some countries. Since reporting of yaws is not mandatory, these figures are only indicative of the distribution of the disease. However, with the eradication of yaws by 2020 in mind, it will be essential to make its reporting mandatory.

Fig. 4.6.1 Distribution of yaws, worldwide, 2013

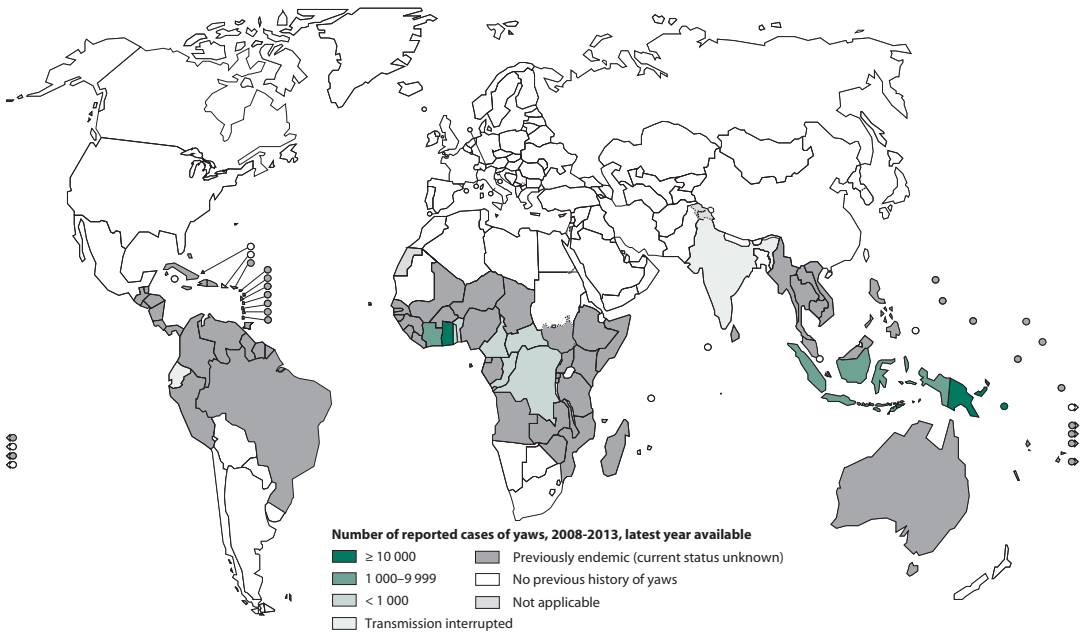
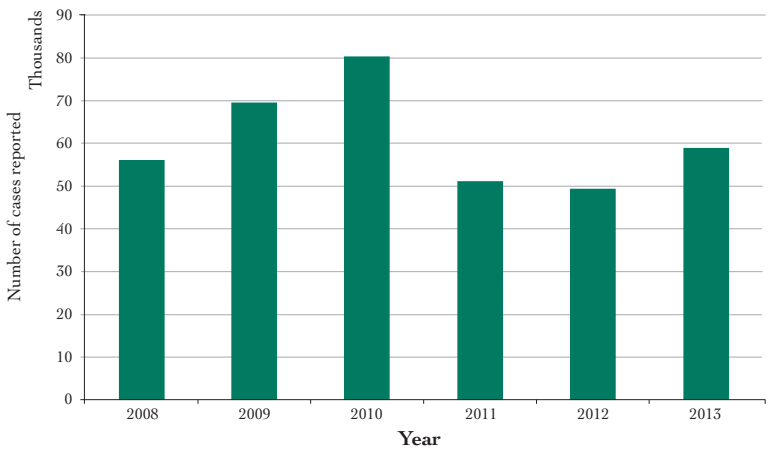


Fig. 4.6.2 Number of yaws cases reported to WHO, 2008–2013



	2008	2009	2010	2011	2012	2013
Global	56 223	69 467	80 226	51 101	49 375	58 915

Progress towards Roadmap targets

In 2012, WHO developed the Morges Strategy for yaws eradication by 2020, which relies on the use of oral azithromycin as the main intervention (*9*). Two new treatment policies replace those developed in the 1950s: (i) delivering mass treatment to entire endemic communities irrespective of the number of active clinical cases, followed by regular surveillance until clinical cases are no longer identified; and (ii) delivering targeted treatment to all active clinical cases and their contacts (household, school and playmates), an approach that requires support from available health-care services.

Oral azithromycin used in mass treatment can interrupt transmission within 6–12 months, as demonstrated in the Nsukka district of Nigeria (*10*). The Morges Strategy was piloted accordingly during 2012–2013 in selected districts in the Congo, Ghana, Papua New Guinea and Vanuatu (*11*). About 90 000 people have been treated, with coverage exceeding 90%. The experience gained from these pilot interventions will be used to guide implementation in endemic countries and inform timelines for scaling up eradication efforts according to the Roadmap's targets and milestones (*Table 4.6.1*).

Table 4.6.1 Targets and milestones for eradicating yaws

Year	Milestone
2017	50% of endemic countries report zero cases
2020	100% of endemic countries report zero cases

Epidemiological assessments in various countries are in progress to help plan implementation of eradication activities towards the eradication objective.

Research priorities

The third WHO consultation on yaws eradication (March 2014) identified the following priorities for research:

- Develop a non-treponemal luminex assay as part of a multiplex assay for NTDs in general and as a more refined tool to determine baseline and impact measures of mass treatment.
- Continue to type *T. pallidum* subsp. *pertenue* strains from different geographical areas.
- Attempt culture of *H. ducreyi* from leg ulcerations of children and determine antimicrobial susceptibilities.
- Attempt to determine the etiology of non-yaws/*H. ducreyi* lesions using advanced molecular techniques.

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4.7 Foodborne trematodiases

Introduction

Foodborne trematodiases are a group of helminth infections acquired by ingesting food contaminated with metacercariae, the larval stages of each relevant worm. The diseases associated with the highest public-health burden are clonorchiasis (caused by infection with *Clonorchis sinensis*), opisthorchiasis (infection with *Opisthorchis viverrini* or *O. felineus*), fascioliasis (infection with *Fasciola hepatica* or *F. gigantica*) and paragonimiasis (infection with *Paragonimus* spp.). All such diseases have complex life-cycles entailing intermediate and reservoir hosts (*Table 4.7.1*).

Table 4.7.1 Epidemiological characteristics of the most common foodborne trematodiases

Disease	Infectious agent	Acquired through consumption of	Natural final host	Primary organ affected
Clonorchiasis	*Clonorchis sinensis*	Fish	Dogs and other fish-eating carnivores	Liver
Opisthorchiasis	*Opisthorchis viverrini; O. felineus*	Fish	Cats and other fish-eating carnivores	Liver
Fascioliasis	*Fasciola hepatica; F. gigantica*	Vegetables	Sheep, cattle and other herbivores	Liver
Paragonimiasis	*Paragonimus* spp.	Crustacea (crabs and crayfish)	Cats, dogs and other crustacean-eating carnivores	Lungs

Investment case

Information on the economic burden of foodborne trematodiases is scarce. Livestock and aquaculture industries are clearly affected, with losses in animal production and trade. Although estimates are not currently available, the cost of these losses is expected to be significant.

Investment targets for veterinary public-health interventions may be included in updates to the analyses contained in *Chapter 2* of this report.

Burden and distribution

Although cases of foodborne trematodiases have been reported from more than 70 countries worldwide, countries in Asia and Latin America are those worst affected. The burden of disease associated with these infections is still unclear. For example, paragonimiasis is known to be transmitted in the central and western parts of Africa, yet information on its epidemiological status is limited. Estimates referring to a selected group of 17 countries indicate that in 2005 more than 56 million individuals were infected with foodborne trematodes: 7.9 million had severe sequelae and more than 7000 died (*1*) (*Fig. 4.7.1–4.7.4*).

Morbidity due to foodborne trematode infections is both acute and chronic, and both systemic and organ-specific; it becomes more severe as the number of worms increases through subsequent rounds of infection. Chronic infections with *C. sinensis* and *O. viverrini* are strongly associated with cholangiocarcinoma, a fatal form of bile duct cancer. Both parasites are classified by the International Agency for Research on Cancer as carcinogenic to humans (*2*).

Fig. 4.7.1 Distribution of clonorchiasis, worldwide, latest year available

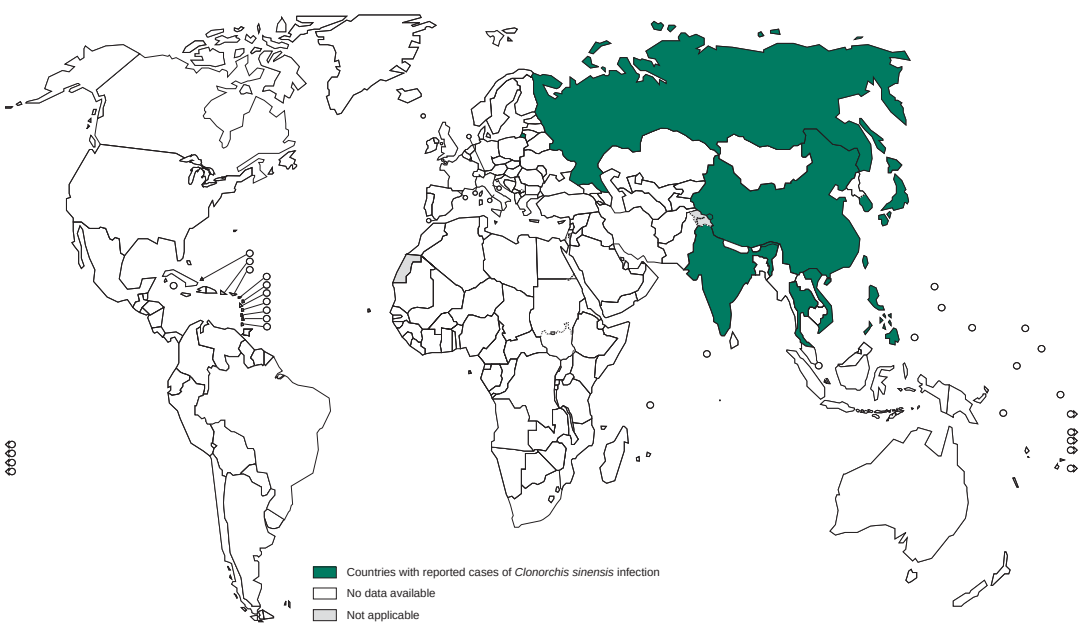


Fig. 4.7.2 Distribution of opisthorchiasis, worldwide, latest year available

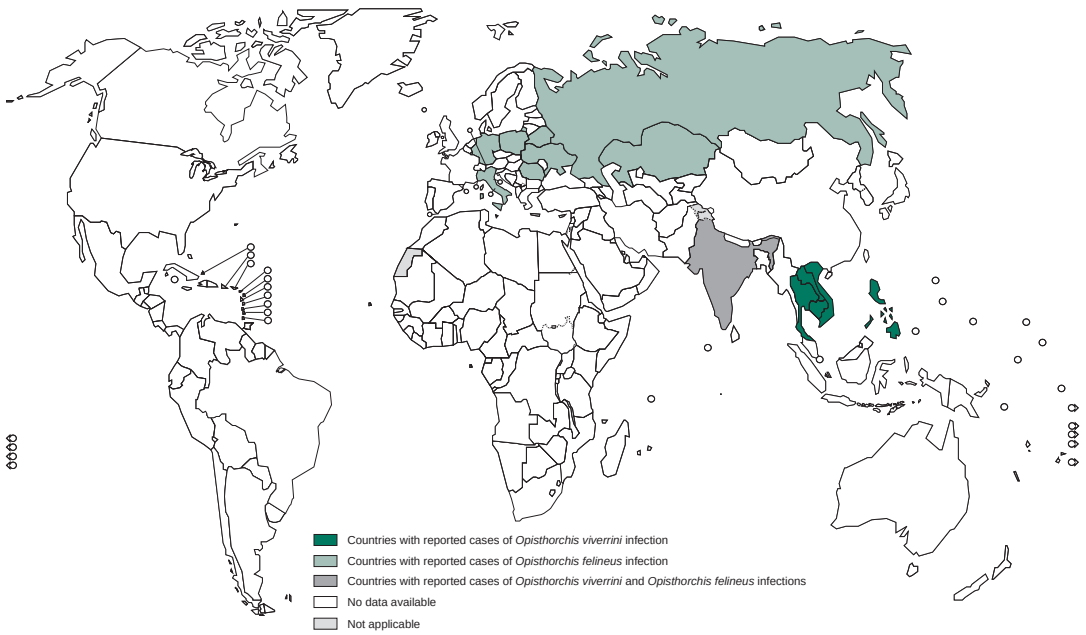


Fig. 4.7.3 Distribution of fascioliasis, worldwide, latest year available

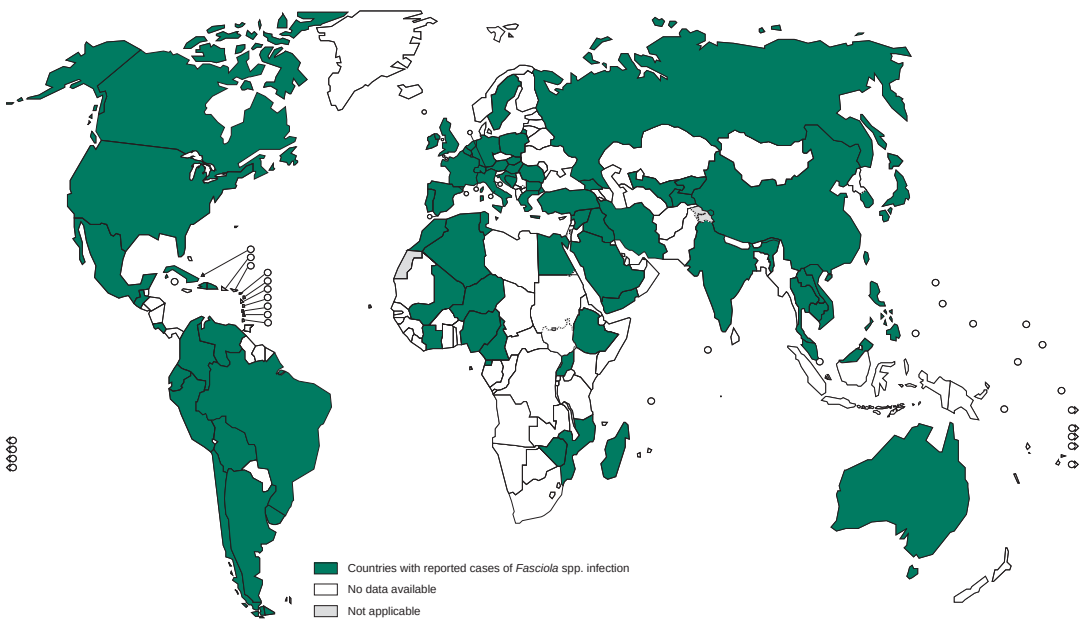
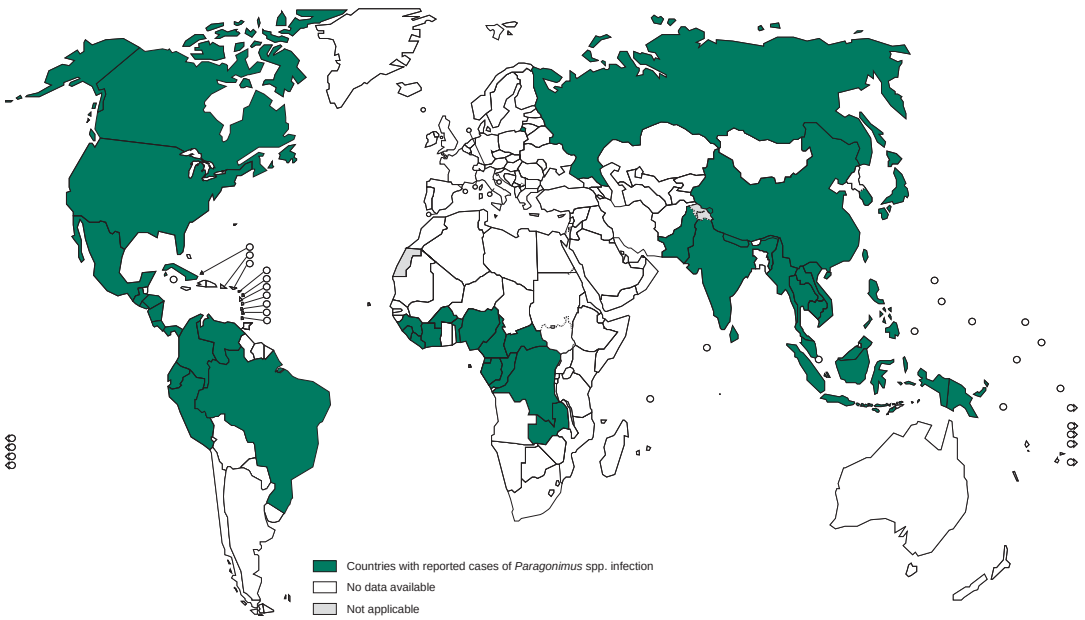


Fig. 4.7.4 Distribution of paragonimiasis, worldwide, latest year available



Progress towards Roadmap targets

The Roadmap sets two implementation milestones for foodborne trematodiases by 2015: (i) to ensure that norms and standards supporting preventive chemotherapy as the main public-health approach against foodborne trematodiases are fully delineated, thus consolidating the current WHO-recommended strategy developed in 2009–2011 (*3*); and (ii) to ensure that control interventions are implemented in the most endemic countries in order to control morbidity associated with these diseases in such priority, high-burden settings.

The target for 2020 is to ensure that at least 75% of the global population requiring preventive chemotherapy against foodborne trematodiases has been reached so that morbidity is controlled in all endemic countries.

Availability of medicines to national control programmes is key to achieving these targets. Triclabendazole is recommended against fascioliasis and paragonimiasis, while praziquantel is the treatment of choice for clonorchiasis, opisthorchiasis and paragonimiasis. Triclabendazole is donated through WHO, and several countries have taken advantage of this opportunity. On the contrary, access to praziquantel has not yet been secured.

A number of countries are scaling up coverage of treatment against foodborne trematodiases, thus contributing to achievement of the 2015 milestones.

In the Plurinational State of Bolivia, more than 155 000 people were treated for fascioliasis in 2013. Since 2008, more than 680 000 doses of triclabendazole have been administered. Surveys carried out in 2013 show a 90% decrease in the prevalence of infection with *F. hepatica* from pre-intervention levels.

Peru is also scaling up its control programme by providing preventive chemotherapy in high-priority areas in the Andes mountain range: 17 000 people were treated in 2012 and 7000 in 2013.

In Egypt, 553 children and adults infected with fascioliasis were identified and treated with triclabendazole in 2011; their number decreased to 245 in 2012 and to 195 in 2013.

In the Lao People's Democratic Republic, almost 400 000 adults and children were treated for opisthorchiasis in 2012, while in 2013 the implementation of treatment interventions was delayed by the occurrence of severe adverse events following treatment.

In Viet Nam, more than 128 000 people were treated for clonorchiasis in 2011. While no large-scale intervention was implemented in 2012, approximately 108 000 people were treated in 2013. Mapping was carried out in northern Viet Nam in 2014 to assess the local burden of disease.

In Cambodia, where mapping is also ongoing, treatment was offered to 67 000 individuals in 2012 and to 23 000 individuals in 2013.

Research priorities

The most important knowledge gaps on foodborne trematodiases are related to:

- The delineation of endemic areas and the definition of the global burden attributable to foodborne trematodiases.
- The development and standardization of serological and molecular diagnostic tools, allowing a better identification of affected individuals.
- The operationalization of a strategic approach complementing preventive chemotherapy with other interventions (veterinary public-health services and environmental management).

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4.8 Human African trypanosomiasis (sleeping sickness)

Introduction

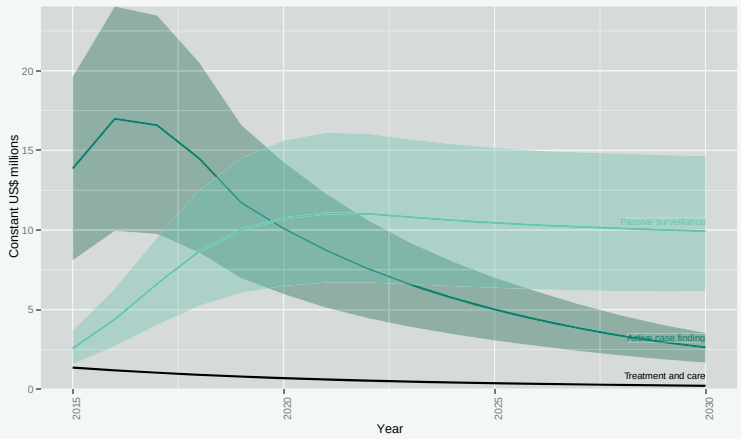
Human African trypanosomiasis, or sleeping sickness, is caused by infection with protozoan parasites of the genus *Trypanosoma*. The disease is vector-borne; parasites enter the body through the bites of tsetse flies (*Glossina* spp.). Without prompt diagnosis and treatment, the disease is usually fatal as the parasites multiply in the body, cross the blood–brain barrier and invade the central nervous system.

Investment case

As a result of successful control efforts, the number of reported cases of human African trypanosomiasis is now small. But the socioeconomic impact on patients, households and communities remains large. Non-medical and indirect costs related to, for example, transport and income losses have persisted as a barrier to accessing diagnosis and treatment even where national control programmes provide these services free of charge.[1] The cost to affected households in a rural community in the highest burden country (the Democratic Republic of the Congo) has been estimated at more than 40% of annual household income, mostly from lost productivity.[2] The shift to melarsoprol-free treatment has increased the average cost to treat one patient with second-stage gambiense sleeping sickness from US$ 30 in 2001 to US$ 440 in 2010. This change requires sustained health system investment in finding cases early, treating patients free of charge and, as required, other social protection to cover transport and other non-medical and indirect costs.

This report estimates that active case-finding and treatment and care may require investments of about US$ 13.5 million (US$ 9.8–17.1 million) per year during 2015–2030. This benchmark does not include critical investments in passive surveillance. While relatively small in the aggregate, these public investments required are significant for existing programmes, especially for the Democratic Republic of the Congo, where more than 80% of cases are reported. Investments in active case-finding and treatment and care may decrease over time, from about US$ 32 million in 2015 to US$ 4 million by 2030, as very high, high and moderate risk areas are contained and active case detection is scaled down in favour of more sustainable alternatives. While populations eligible for active case-finding are assumed to decrease, interrupting transmission by 2030 will require adequately resourced health systems to assure passive surveillance. As progress is made towards the

Investment targets for human African trypanosomiasis treatment and care, active case-finding and passive surveillance, 2015–2030



Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

interruption of transmission, current budgets for active case-finding may be reprogrammed towards passive surveillance.

The total investment in passive surveillance attributable to human African trypanosomiasis will depend on the country and on the scope for integrated surveillance of multiple diseases. Integrated infectious disease surveillance has been estimated to cost between US$ 0.02 and US$ 0.16 per capita per year (2002 prices) in three low-income countries in Africa.[3] Making adjustments to these prices in countries (including upper middle income countries such as Angola), it is estimated that about US$ 11 million (US$ 7–17 million) would ensure coverage of the population at risk for human African trypanosomiasis with passive surveillance by the general health system. Sometime after 2020, it is expected that most of the investment targeted for human African trypanosomiasis will be for passive surveillance. A lean but sufficiently well-resourced sleeping sickness programme will guide the efforts of the general health system through to interruption of transmission.

Interestingly, one of the first pilots of a development impact bond seeks to control the disease (rhodesiense) in humans by reducing the infection in cattle. *Chapter 2* provides more details on this and other innovative financing mechanisms.[4]

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1 Boelaert M, Meheus F, Robays J, Lutumba P. Socio-economic aspects of neglected diseases: sleeping sickness and visceral leishmaniasis. Ann Trop Med Parasitol. 2010;104:535–42. doi:10.1179/136485910X12786389891641.

2 Lutumba P, Makieya E, Shaw A, Meheus F, Boelaert M. Human African trypanosomiasis in a rural community, Democratic Republic of Congo. Emerg Infect Dis. 2007;13:248–54.

3 Somda ZC, Meltzer MI, Perry HN, Messonnier NE, Abdulmumini U, Mebrahtu G et al. Cost analysis of an integrated disease surveillance and response system: case of Burkina Faso, Eritrea, and Mali. Cost Eff Resour Alloc. 2009;7:1. doi:10.1186/1478-7547-7-1.

4 Investing in social outcomes: development impact bonds. London (UK): The Center for Global Development and Social Finance; 2013 (http://international.cgdev.org/publication/investing-social-outcomes-development-impact-bonds; accessed October 2014).

Burden and distribution

Since 2009, fewer than 10 000 new cases have been reported annually for the first time in 30 years, with 6314 new cases in 2013. This trend represents a decrease of 76% since 2000. The number of cases reported annually is considered to be a fraction of the real burden. According to the latest (2011) estimates (*1*), the incidence could be around 20 000 cases a year.

Human African trypanosomiasis affects impoverished rural areas of sub-Saharan Africa, where it coexists with animal trypanosomiasis. The presence of human and animal trypanosomiasis impedes development in these communities and traps people in a cycle of poverty.

Approximately 70 million people distributed over an area of 1.55 million km^2 are at risk (*2*). Advances in controlling the disease made during the past decade have achieved an important decrease in its burden, but control and research efforts must continue and be based on sustainable public-health objectives, not only on the actual burden of the disease. *Fig. 4.8.1* shows the decline in the numbers of new cases reported globally from 1990 to 2013.

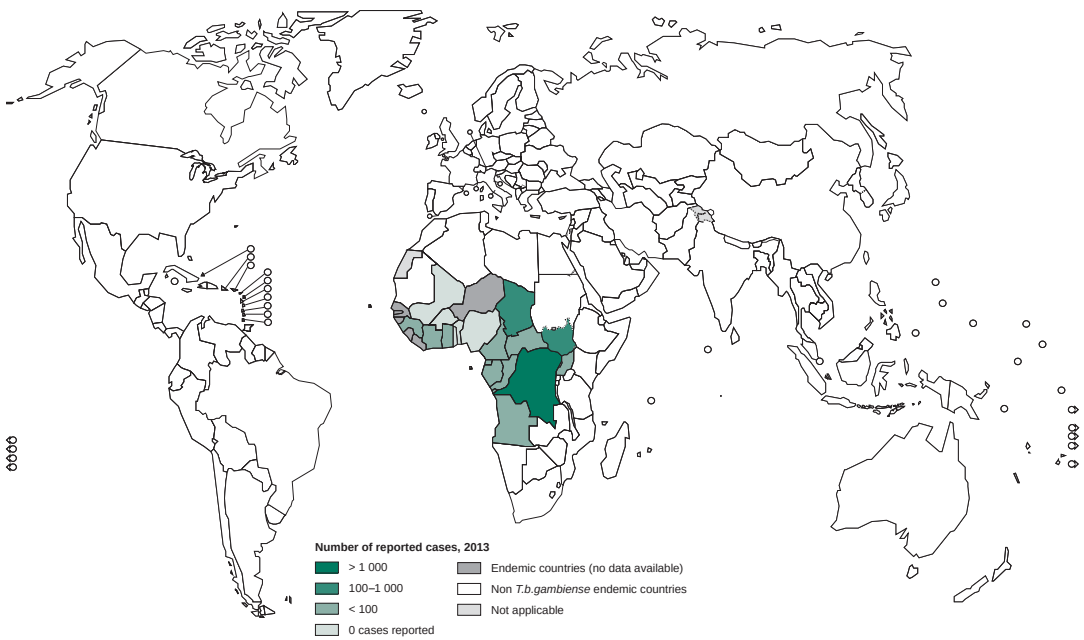
Fig. 4.8.1 Number of human African trypanosomiasis cases reported to WHO,1990–2013

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
T.b. gambiense	12 756	10 987	14 088	16 607	23 266	23 671	28 736	36 585	37 385	27 862	25 865	26 117
T.b. rhodesiense	1933	1219	1147	831	711	935	591	592	606	619	709	755

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
T.b. gambiense	23 836	19 963	17 130	15 644	11 382	10 473	10 388	9 685	6 978	6 637	7 106	6 228
T.b. rhodesiense	617	536	552	710	453	305	259	190	156	113	110	86

The chronic form of human African trypanosomiasis, caused by infection with *Trypanosoma brucei gambiense*, is endemic in 24 countries and represents 98% of reported cases (*Fig. 4.8.2*).

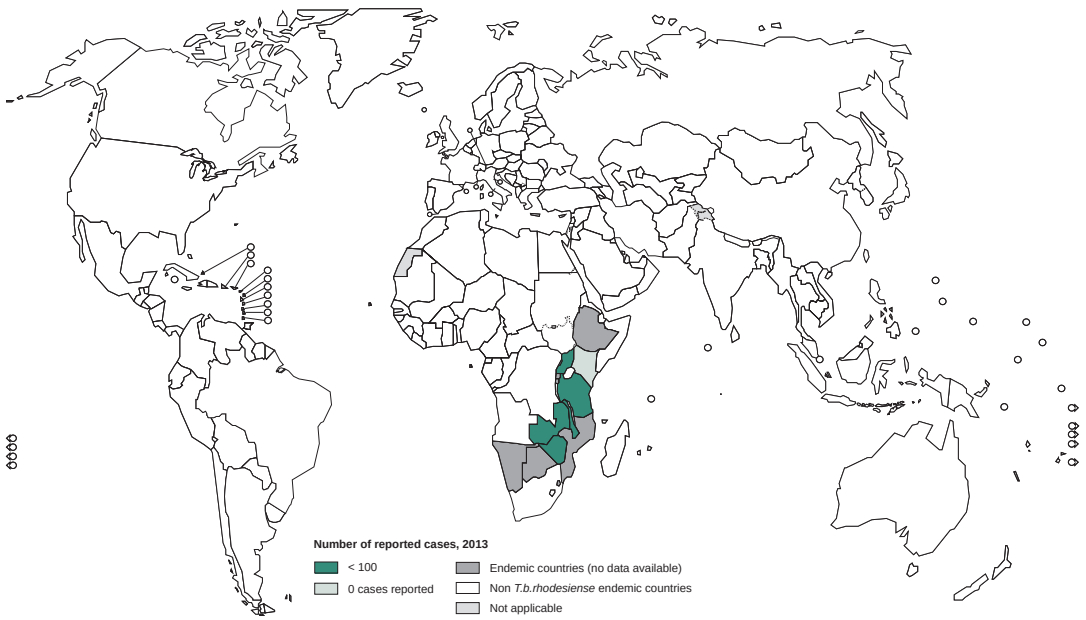
Fig. 4.8.2 Distribution of human African trypanosomiasis (*T.b. gambiense*), worldwide, 2013



During 2011, 2012 and 2013, Benin, Burkina Faso, Mali and Togo continued reporting zero cases. No cases have been reported in the past 30 years in the Gambia, Guinea-Bissau, Liberia, Niger, Senegal and Sierra Leone, although no specific control activities have been conducted; field assessment is needed to verify the epidemiological status in these countries. Cameroon, the Congo, Côte d'Ivoire, Equatorial Guinea, Gabon, Ghana, Guinea, Nigeria and Uganda reported fewer than 100 new cases annually; Angola, the Central African Republic, Chad and South Sudan reported between 100 and 500 new cases annually. The Democratic Republic of the Congo is the only country reporting more than 500 new cases annually; it accounts for 89% of the cases reported in 2013. All reported cases of sleeping sickness occur in WHO's African Region.

The acute form of human African trypanosomiasis, caused by infection with *Trypanosoma brucei rhodesiense*, is endemic in 13 countries and represents 2% of all cases of the disease reported during 2011–2013 (*Fig. 4.8.3*). Botswana, Namibia and Swaziland, considered to be endemic, have not reported any cases in the past 20 years; the vector appears to be no longer present in these countries. Data are not available from Burundi, Ethiopia, Mozambique and Rwanda; field studies are needed to clarify the epidemiological status. Kenya and Zimbabwe have reported sporadic cases; Malawi, the United Republic of Tanzania, Uganda and Zambia have reported fewer than 100 new cases annually.

Fig. 4.8.3 Distribution of human African trypanosomiasis (*T.b. rhodesiense*), worldwide, 2013



More detailed information about the distribution of both forms of the disease is available in WHO's Atlas of human African trypanosomiasis (*3*).

The distribution of medicines to treat cases is under the full responsibility and control of WHO, permitting the establishment of a surveillance system of the disease diagnosed in travellers and migrants in non-endemic countries (*4*).

Progress towards Roadmap targets

Achieving the Roadmap's targets for elimination will depend on increasing access to early, accurate diagnosis; delivering safer and more effective treatment; and continuing surveillance. *Table 4.8.1* shows the crucial stages for achieving the targets.

In 2012, WHO convened a meeting of national disease control coordinators of endemic countries and WHO collaborating centres at which criteria for the elimination of gambiense human African trypanosomiasis were defined and accepted (*5*).

In 2013, A WHO Expert Committee on the control and surveillance of human African trypanosomiasis met to consider information about new diagnostic approaches, new therapeutic regimens and improved understanding of the distribution of the disease provided by mapping. The Committee reviewed and updated control and surveillance methods and prepared a strategy towards the objective of eliminating the disease as set out in the Roadmap.

During 2012–2013, an inventory of fixed health facilities involved in diagnosis and treatment of human African trypanosomiasis was performed: 622 facilities are involved in any sort of diagnosis in almost all transmission areas; 495 facilities are involved in treatment; and although fewer facilities are offering treatment, they are distributed in almost the same areas.

The final result of the study – combining the distribution of identified fixed health facilities, the distribution of people at risk and the African "friction" layer of cost-time to travel from one pixel to another – indicated that 40–80% of people at high or very high risk of infection are potentially covered by a centre offering diagnosis at 1 or 5 hours' travel time respectively.

Table 4.8.1 Indicators and milestones for eliminating human African trypanosomiasis

Indicators and milestones for disease elimination	Year								
	2012	2013	2014	2015	2016	2017	2018	2019	2020
Define elimination criteria	√								
Establish Expert Committee on control and surveillance		√							
Provide annual update of number of people at risk covered by surveillance or treatment	√	√	√	√	√	√	√	√	√
Provide biennial update of disease distribution	√		√		√		√		√
Provide biennial update of number of people at risk	√		√		√		√		√
Convene biennial stakeholders meeting			√		V		√		√
Convene annual country report meeting	√	√	√	√	√	V	√	√	√
Targets for global number of cases reported annually	6000	5500	5000	4500	4000	3500	3000	2500	< 2000
Proportion of foci eliminated (< 1 case/10 000 population)				10%	30%	40%	60%	80%	> 90%

Treatment results showed that 87% of people at high risk of the disease lived within 5 hours' travel time to access the first stage of treatment. However, for the second stage, which requires complex administration of treatment by skilled staff, access within 5 hours' travel time is 74% for people at high risk (*6*).

In 2014, WHO convened its first meeting of stakeholders on the elimination of gambiense human African trypanosomiasis (g-HAT) attended by national sleeping sickness control programmes, groups developing new tools to fight the disease, international and nongovernmental organizations, and donors. The meeting agreed to establish a WHO-led network to ensure a coordinated, strengthened and sustained effort to eliminate g-HAT (*7*).

The first available indicator of progress towards elimination of g-HAT is the global number of cases reported annually. In 2012, the observed gap of 1106 more reported cases than expected, a deviation of 18% (7106/6000), was mainly due to cumulative cases from preceding years. These cases were detected in 2012 in Orientale province (Democratic Republic of the Congo) and Ouham foci (Central African Republic) when improved security facilitated access to areas not visited for some years and the detection of cumulated cases for 2–3 years. In 2013, the indicator was improved and the gap observed was of 728 more reported cases than expected, a deviation of 13% (6228/5500).

The second indicator, the proportion of foci eliminated, will be calculated as for 2015. In collaboration with FAO, under the framework of the Programme Against African Trypanosomiasis, WHO has completed the Atlas of human African trypanosomiasis for the period 2000–2012. The Atlas maps control activities and cases reported at village level. The 36 endemic countries have completed their mapping, including 196 667 cases and 30 321 geographical sites (*8*). The Atlas is a powerful tool that can help endemic countries prepare control strategies, implement interventions, monitor their impact and sustain progress through surveillance. Using the data in the Atlas and population layers, a methodology has been developed to calculate secondary indicators to assess the quality and extent of activities and elimination programmes. These indicators include the proportion of the population at risk that is covered by control and surveillance activities, the geographical extent of the disease and the population at different levels of risk (*9*).

Research priorities

The current rapid test for screening populations at risk of *T.b. gambiense* is based on native antigen with limited production. The development of a new-generation test using recombinant antigens is needed to improve costs and overcome the restrictions of native antigen. Blood or urine tests for stage determination will still require the feared lumbar puncture.

A specimen bank set up by WHO in 2009 is available to researchers to facilitate the development of new and affordable diagnostic tools. The bank contains samples of blood, serum, cerebrospinal fluid, saliva and urine from patients infected with both forms of the disease

as well as samples from uninfected people from areas where the disease is endemic. Overall, samples have been obtained from 1798 participants in six countries (*10*). The specimen bank has contributed to the development of the new individual screening test recently introduced for control and surveillance, and can contribute to the new requirements.

Safe, if possible oral, medicines that are active against both forms of the disease and are easy to use are required to facilitate the integration of treatment at all levels of the health system.

As the number of new cases declines, operational research aimed at integrating human African trypanosomiasis into existing health systems, and optimizing passive case detection, surveillance and management of the disease in these systems, are required. New cost-effective approaches to integrate control and surveillance for the disease into health-care systems have been developed and are being tested in different epidemiological settings. At the same time, the epidemiological role of both parasitologically non-confirmed human suspects and animals as reservoirs of *T.b. gambiense* needs to be investigated. In this context, uncertainties concerning the proportion of undetected cases need also to be addressed.

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4.9 Leishmaniases

Introduction

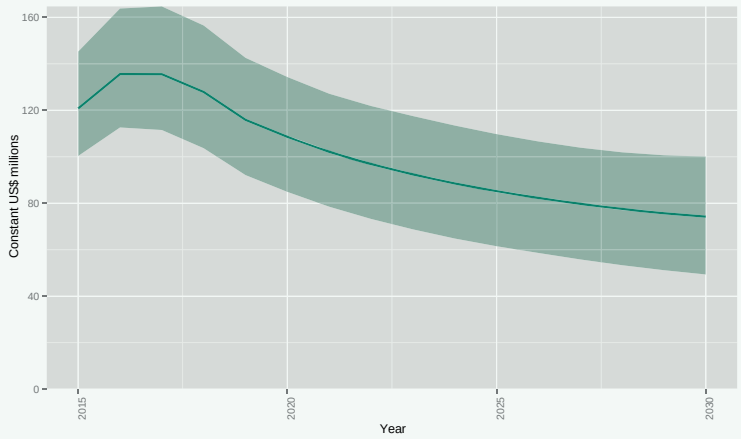
The leishmaniases are a range of diseases caused by protozoan parasites transmitted through the bites of infected female sandflies. Visceral leishmaniasis, also known as kala-azar, is usually fatal within 2 years if left untreated. After treatment, visceral leishmaniasis sometimes evolves into a cutaneous form, known as post-kala-azar dermal leishmaniasis, cases of which may serve as sources of infection for sandflies and thus maintain transmission (*1*). Cutaneous leishmaniasis is the most prevalent form, causing ulcers that heal spontaneously. Mucocutaneous leishmaniasis invades the mucous membranes of the upper respiratory tract, causing gross mutilation by destroying tissues in the nose, mouth and throat.

Investment case

Visceral leishmaniasis tends to be highly focalized among the lowest socioeconomic groups. In Bihar, India, 83% of households in communities with high attack rates belonged to the two lowest quintiles (the poorest 40%) of the wealth distribution.[1] Studies from several of the highest burden countries show that even when diagnosis and medicines are provided free of charge, 25–75% of affected households experience some type of financial catastrophe.[2,3,4,5,6] Other studies are summarized in a review of the burden of visceral leishmaniasis in South Asia.[7] Free diagnosis and treatment (at point of care) is a minimum requirement to avoid catastrophic health expenditure, but other forms of social protection will also be required to prevent impoverishment. In Nepal, in addition to free diagnosis and treatment, kala-azar patients receive cash transfers contingent upon completion of treatment, to cover transport and nutrition costs.[8]

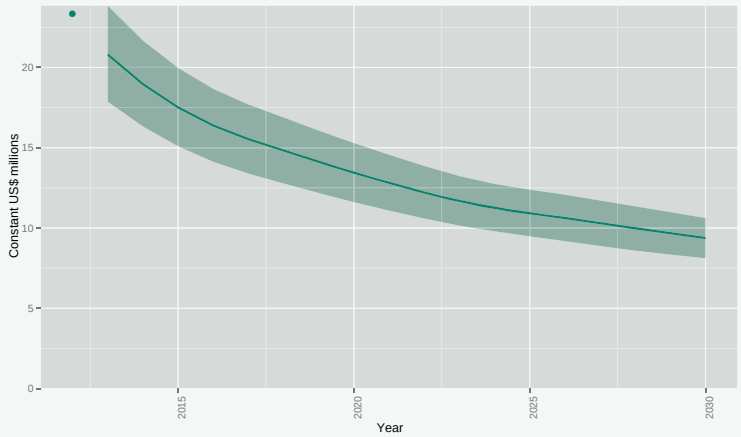
Cutaneous leishmaniasis has been less studied from an economic perspective despite the oft-cited link between poverty and disease.[9] The cost-effectiveness of interventions was not specifically discussed in the second edition of the Disease Control Priorities Project in 2006. The difficulty with assessing the cost-effectiveness is that this form of the disease is not fatal and disability weights may not fully reflect the social stigmatization associated with disfigurement. Nonetheless, a few economic evaluations have emerged since 2006, suggesting that interventions for early diagnosis and treatment could be highly cost-effective but that (late) diagnosis and treatment in complex emergency settings may not

Investment targets for active case-finding, vector control, and treatment and care of visceral leishmaniasis (including medicines), 2015–2030



Notes: Grey lines represent uncertainty bands (5th and 95th centiles). The light blue section represents the transition period from actual coverage reported in 2012; coverage data are not currently available for active case finding or vector control.

Investment targets for treatment and care of cutaneous leishmaniasis (including medicines), 2015–2030



Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. The dots in 2012 are actual numbers reported (when available) multiplied by the unit cost benchmarks; these are not actual expenditures, but can be thought of as a benchmark for actual expenditures. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

be.[10,11] The financial impact of cutaneous leishmaniasis to the health system is considerable. Medical and non-medical costs associated with an outbreak exceeded US$ 385 000 for the treatment of 1524 patients in a single hospital, excluding indirect costs incurred by those patients (e.g. travel costs or loss of salaried work-time).[12] These costs would dramatically decrease if a topical treatment based on paromomycin cream is proven as a convenient tool for large-scale treatment of the most prevalent disease forms.[13,14]

An effective vaccine is needed, but the difficulties in the standardization of crude *Leishmania* vaccines or the lack of an appropriate adjuvant make it realistically not feasible in the short and mid-term.[15,16]

Active case-finding plus treatment and care for visceral leishmaniasis will require investments of about US$ 100 million (US$ 80–130 million) per year during 2015–2030. If current trends continue, investments may decrease over time, from US$ 150 million in 2015 to US$ 75 million by 2030. Most of this total can be attributed to the need for dedicated vector control interventions in those areas of South-East Asia where malaria is not co-endemic. About 4% of the total can be attributed to the cost of active case-finding. An analysis of "yields, feasibility and costs" suggests the use of a camp approach in high endemic settings and an index approach in high to moderate endemic settings.[17] About 3% of the total investment can be attributed to the cost of medicines (including the market value of donations), and another 3% to the cost of general health system services (inpatient and outpatient care during diagnosis and treatment).

Treatment and care of cutaneous leishmaniasis is estimated to require investments of US$ 13 million (US$ 11–14 million) per year during 2015–2030, from US$ 17 million in 2015 to US$ 9 million by 2030. Medicines account for about 17% of the total.

As work continues on the third edition of the Disease Control Priorities Project, WHO is analysing the cost-effectiveness of eliminating visceral leishmaniasis, including vector controls.

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Burden and distribution

The leishmaniases are prevalent in 98 countries and three territories on five continents (*Fig. 4.9.1–4.9.2*). Approximately 1.3 million new cases occur annually: 300 000 are visceral (90% in Bangladesh, Brazil, Ethiopia, India, Nepal, South Sudan and Sudan); and 1 million are cutaneous (mainly in Afghanistan, Algeria, Brazil, Colombia, the Islamic Republic of Iran, Pakistan, Peru, Saudi Arabia, the Syrian Arab Republic and Tunisia) or mucocutaneous (mainly in Brazil, Peru and the Plurinational State of Bolivia). The estimated number of deaths from visceral leishmaniasis ranges from 20 000 to 50 000 annually (*2,3*).

The distribution of the leishmaniases has expanded during the past two decades and the number of reported cases has increased exponentially. As reporting is mandatory in only 34% of the endemic countries, the exact burden of the disease remains unknown. Risk factors facilitating its spread include poor socioeconomic conditions, malnutrition, climatic and environmental changes, increased population movement, conflicts, immunosuppressive conditions such as HIV coinfection and, in some areas, rapid urbanization or establishment of new settlements (*4,5*).

In East Africa, particularly in South Sudan and Sudan, epidemics of visceral disease with high mortality rates are frequent. The epidemic in South Sudan (2009–2012) resulted in more than 28 000 new cases and 850 deaths (*6*). The rapid response from WHO, Médecins Sans Frontières and other partners in collaboration with the Government kept the mortality rate to below 5% compared with 35% in the epidemic of the 1990s.

Coinfection with *Leishmania* and HIV increases susceptibility to visceral disease and affects its epidemiology. As of 2013, 35 countries endemic for the disease had reported cases of coinfection with HIV. A significant, increasing trend of HIV–visceral leishmaniasis coinfection

Fig. 4.9.1 Distribution of visceral leishmaniasis, worldwide, 2012

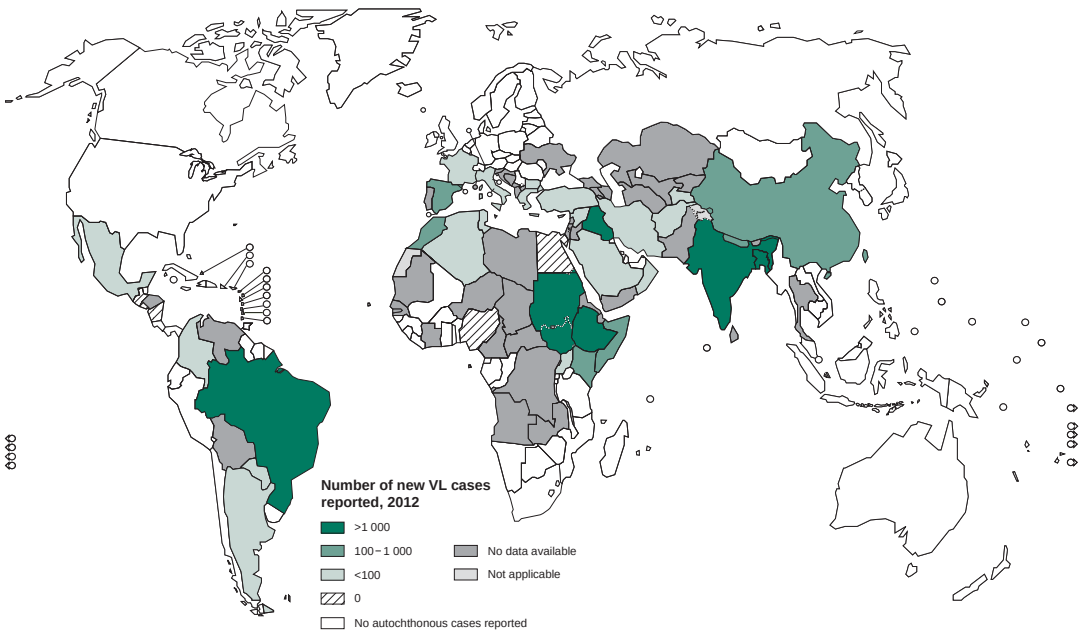
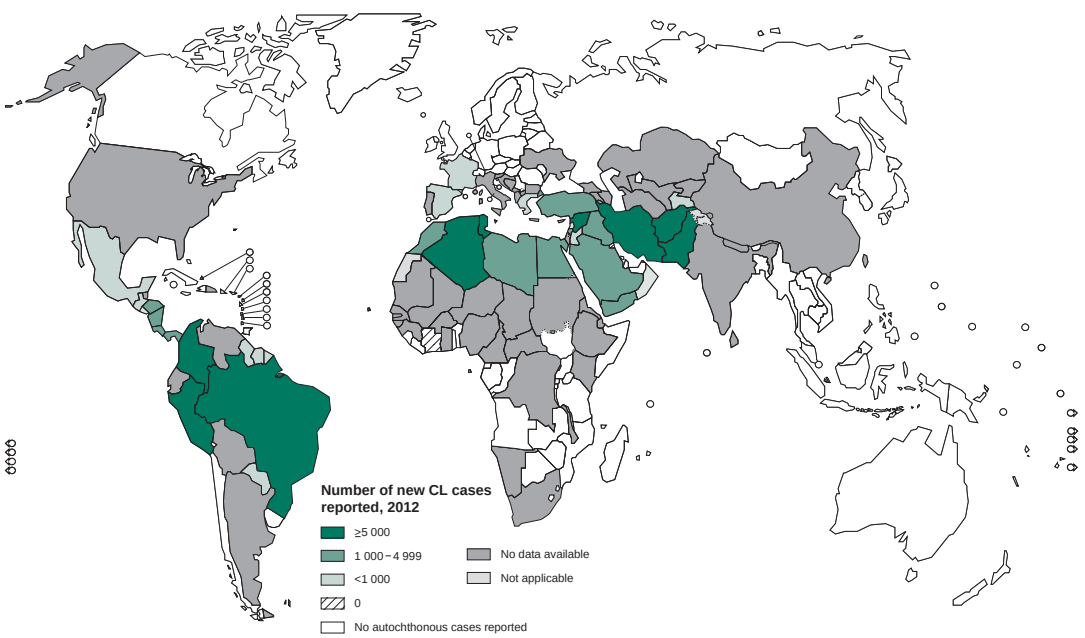


Fig. 4.9.2 Distribution of cutaneous leishmaniasis, worldwide, 2012



rates has been reported from Brazil and Ethiopia. In Brazil, the coinfection rate increased from around 2.5% (2005) to 6.6% (2011), and in northern Ethiopia from 19% (1998–1999) to 34% (2006–2007). The introduction and expanded implementation of antiretroviral treatment, however, has helped to reduce the incidence of visceral disease, delay relapses and increase survival of coinfected patients in many countries.

Epidemics of cutaneous leishmaniasis in Afghanistan and the Syrian Arab Republic, where war and civil unrest prevail, have hampered control (*7*). Outbreaks in other major endemic countries, such as Algeria and Morocco, have been managed and the number of cases reduced significantly. Algeria reported over 30 000 cases in 2005 but only 6428 in 2013. Morocco reported 6700 cases of zoonotic cutaneous leishmaniasis in 2010 but only 537 in 2013.

Progress towards Roadmap targets

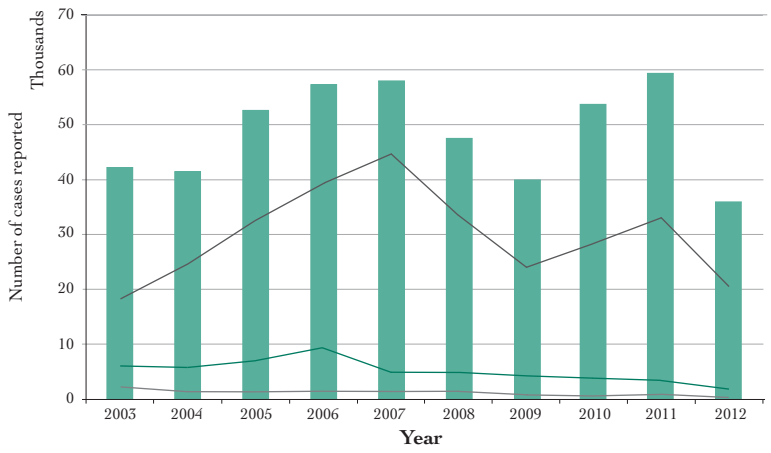
The World Health Assembly adopted resolution WHA60.13 on the control of leishmaniasis in May 2007, reinvigorating WHO's mandate to lead the expansion of control programmes (*Annex 1a*). Following this major milestone, WHO convened an Expert Committee on the control of the leishmaniases that resulted in the publication of the technical report series in March 2010 (*8*). Since then, WHO has updated information on global epidemiology and access to medicines. The epidemiological update identified gaps in knowledge about the actual burden of the disease and its incidence in most endemic countries, and the need to develop robust surveillance systems. Mapping of the distribution of the disease has been updated and made available in the WHO Global Health Observatory; a new leishmaniases country profile is in progress. WHO has also published two manuals on the control of post kala-azar dermal leishmaniasis and a health workers' atlas for distribution to the endemic countries.

The Roadmap targets the elimination of visceral leishmaniasis as a public-health problem from the South-East Asia Region by 2020 and a significant reduction in its morbidity and mortality in other endemic regions. Following the agreement in 2011 between WHO and Gilead Sciences for the donation of 445 000 vials of liposomal amphotericin B to treat visceral leishmaniasis, the medicines were distributed to all the beneficiary countries in 2013. The UK Government through DFID is providing substantial financial support to WHO and other stakeholders to strengthen the fight against this disease. Particularly in the South-East Asia Region, the DFID fund provides an important opportunity to achieve the target set by the kala-azar elimination programme of reducing the incidence of the disease to less than 1 case per 10 000 population at subdistrict level. Such financial assistance has contributed significantly to reinvigorating the coordination and implementation capacity of the ministries of health of the beneficiary countries; strengthening the capacity of the health-care system in the most endemic areas to deliver better services; and improving case management, disease surveillance and vector control.

A review of progress of the elimination programme in Bangladesh, India and Nepal indicated a declining trend in the incidence of the disease and a significant increase in the number of subdistricts that have achieved the elimination target (< 1 case per 10 000 population) (*9*). The Government of Bangladesh has adapted a new treatment policy guideline applying the use of single-dose AmBisome and has started rolling out its implementation in various health facilities.

The incidence of reported cases in Bangladesh, India and Nepal decreased respectively in 2013 by around 37%, 33% and 50% from 2012 (*Fig. 4.9.3*). Coverage with indoor residual insecticides in villages endemic for visceral leishmaniasis has improved, but its quality has many gaps. Implementation of active case searches has also improved in the endemic areas using community structures. Capacity-building activities have been intensified by training a large number of health professionals.

Fig. 4.9.3 Top six high-burden countries for visceral leishmaniasis, 2003–2012



	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Bangladesh	6 113	5 920	6 892	9 379	4 932	4 840	4 293	3 800	3 376	1 902
Brazil	2 971	3 580	3 597	3 651	3 604	3 852	3 693	3 716	3 840	3 118
Ethiopia	NA	1 403	2 585	2 375	1 579	1 356	1 083	1 936	2 032	2 500
India	18 214	24 479	32 803	39 173	44 533	33 598	24 213	28 382	33 155	20 571
South Sudan	7 722	3 777	3 141	1 117	758	582	1 907	9 166	11 862	5 012
Sudan	704	2 619	3 713	1 827	2 788	3 310	4 880	6 957	5 226	3 165
Top 6 HBC	42 324	41 778	52 731	57 522	58 194	47 538	40 069	53 957	59 491	36 268

Most endemic countries in East Africa have revised their national guidelines and initiated combination treatment for visceral leishmaniasis (sodium stibogluconate and paromomycin). Combination therapy has reduced the duration and cost of treatment, improved compliance with treatment and is expected to delay or even prevent drug resistance.

In order to control cutaneous leishmaniasis in the Eastern Mediterranean Region, which has the highest burden of the disease, WHO has published a 5-year strategic framework for action (2014–2018) and a case-management manual (*10*). The European Region has likewise prepared a strategic framework for control (2014–2020). These frameworks aim to build country capacities, enhance surveillance, case management, and vector and reservoir control, and strengthen outbreak preparedness and response (*11*). The Region of the Americas has also instituted regional surveillance for visceral and cutaneous leishmaniasis and has mapped their distribution at subnational level. Moreover, guidelines for the treatment of the leishmaniases, including a self-directed online learning course (*12*), have helped many health workers to receive training without leaving their workplaces.

In the Syrian Arab Republic and in the neighbouring countries receiving Syrian refugees, WHO has supported various partners to treat cases of cutaneous leishmaniasis by providing supplies, guidance and technical assistance. In areas where the conflict is ongoing, control has been hampered significantly. In general, controlling vectors and their reservoir hosts is important for controlling the leishmaniases. Countries should therefore regularly monitor and assess the effectiveness of the various strategies being deployed for vector control, including indoor residual spraying with insecticides and the use of insecticide-treated bednets.

Research priorities

The priorities for research are to address the major gaps in the epidemiological and transmission patterns of the disease as well as the diagnostic, treatment and prevention aspects of all three major forms of the leishmaniases (*13*). A concerted effort is needed to accurately define the population at risk and the global burden of the disease and to determine the role of asymptomatic infections and post kala-azar dermal leishmaniasis in transmission.

Other research needs include improved rapid diagnostic tests for detecting visceral leishmaniasis and post kala-azar dermal leishmaniasis; diagnostic tools for monitoring drug resistance and test of cure; new therapeutics (short course, efficacious and safer) to improve case management and prevent drug resistance for visceral leishmaniasis and post kala-azar dermal leishmaniasis; easy to apply treatments for cutaneous leishmaniasis; better treatment for mucocutaneous leishmaniasis as well as diffuse and other complicated forms; and vaccines against *Leishmania* infection and disease as well as vaccines to prevent transmission of *Leishmania*.

Studies are needed to incriminate vectors in foci where they are unknown and in new foci as they arise. Vector population characteristics, new vector control tools and technologies are also needed; and insecticide resistance patterns require continual monitoring.

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4.10 Leprosy

Introduction

Leprosy is a complex ancient disease caused by infection with *Mycobacterium leprae*. The course and pathology of the disease depend on the response of the person's immune system to the infection. Most control programmes use clinical criteria for classifying and selecting the appropriate treatment regimen for individual patients, particularly when skin-smear services are unavailable. The clinical system of classification uses the number of skin lesions and nerves involved to group patients into categories of either multibacillary leprosy or paucibacillary leprosy.

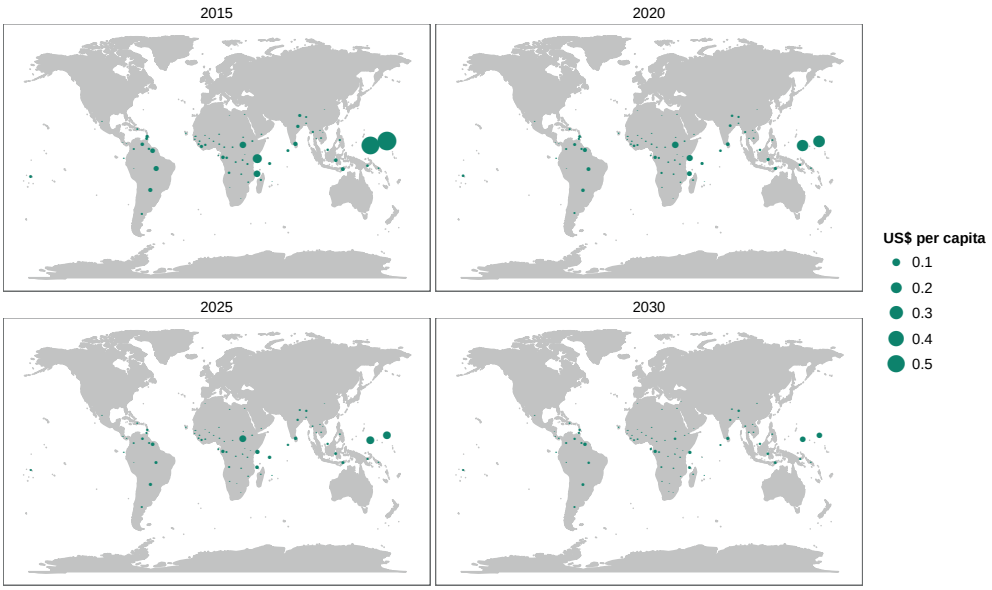
Early detection of cases and treatment with multidrug therapy (MDT) remain the key strategies in reducing the burden of disease due to leprosy. MDT also shortens the duration of infectivity and thereby reduces the risk of further transmission to healthy individuals in the community. Three decades ago, large numbers of cases requiring MDT were reported from more than 122 countries and over these years some 16 million patients were cured. MDT has been made available free of charge to all in need through WHO for the past 20 years, thanks to the creation of global MDT funds by Mr Sasakawa and the Nippon Foundation (1995–2000) followed by the donation of MDT by Novartis and the Novartis Foundation for Sustainable Development (since 2000).

WHO has twice updated the global leprosy strategy since 2006, focusing on strategies to further reduce the burden of the disease in consultation with national programmes of Member States, partner organizations and donor agencies. Detection of all cases in a community and completion of prescribed treatment using MDT are the basic tenets of the enhanced global strategy.

Investment case

Leprosy remains one of the most stigmatized of the diseases of the poor.[1] Recent evidence from the Islamic Republic of Iran confirms the persistence of the gap between rich and poor and of social stigmatization.[2] In at least one part of Brazil, a higher relative risk of leprosy has been associated with higher levels of inequality[3] In 2006, the second edition of the Disease Control Priorities Project put the cost per DALY averted by case detection and treatment at less than US$ 50. The pharmaceutical industry has committed an unlimited number of treatments to overcome the disease. From the health system perspective, therefore, treatment is more cost-effective than ever. The economic evaluation of leprosy

Investment targets for active case-finding and treatment and care of leprosy (including medicines), per capita, 2015–2030



Notes: These targets do not replace any existing country plans or budgets. The investment target is divided by total population within a given country. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

elimination programmes focusses primarily on the cost-effectiveness of interventions to detect and treat more cases earlier.[4,5] The challenge is to deliver those treatments early enough to prevent further transmission.

This report targets an investment of about US$ 37 million (US$ 32–42 million) on average each year during 2015–2030 for contact tracing, treatment and care. Investment targets decrease slowly over time, from US$ 52 million (US$ 45–58 million) in 2015 to US$ 30 million (US$ 25–34 million) by 2030. Of the total, only about 7% is accounted for by the market value of donated medicines. About 13% may be required for contact tracing. Most of the investment required (about 80%) is for general health services, including surgery and rehabilitation.

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Burden and distribution

By the beginning of 2014, 102 countries (in five regions) had submitted reports on leprosy to WHO (*1*). The data were from 20 countries (African Region), 25 countries (Region of the Americas), 11 countries (South-East Asia Region), 14 countries (Eastern Mediterranean Region) and 32 countries (Western Pacific Region). The European Region did not submit reports. Mid-year population estimates for 2013 were derived from data published by the United Nations Department of Economic and Social Affairs/Population Division (*2*). *Fig. 4.10.1* summarizes the global situation of leprosy at the beginning of 2014.

Fig. 4.10.2 shows the regional distribution of leprosy at the beginning of 2014. The total number of new cases detected in 2013 and reported by 102 countries was 215 656. Globally, the number of cases registered at the beginning of 2014 was 180 618.

The number of new cases detected annually continues to decrease in all regions, except in the African Region (*Fig. 4.10.3*). The apparent increase in the African Region is due to the transfer of South Sudan from the Eastern Mediterranean Region to the African Region.

Fig. 4.10.1 New case-detection rates for leprosy, data reported to WHO as of January 2014

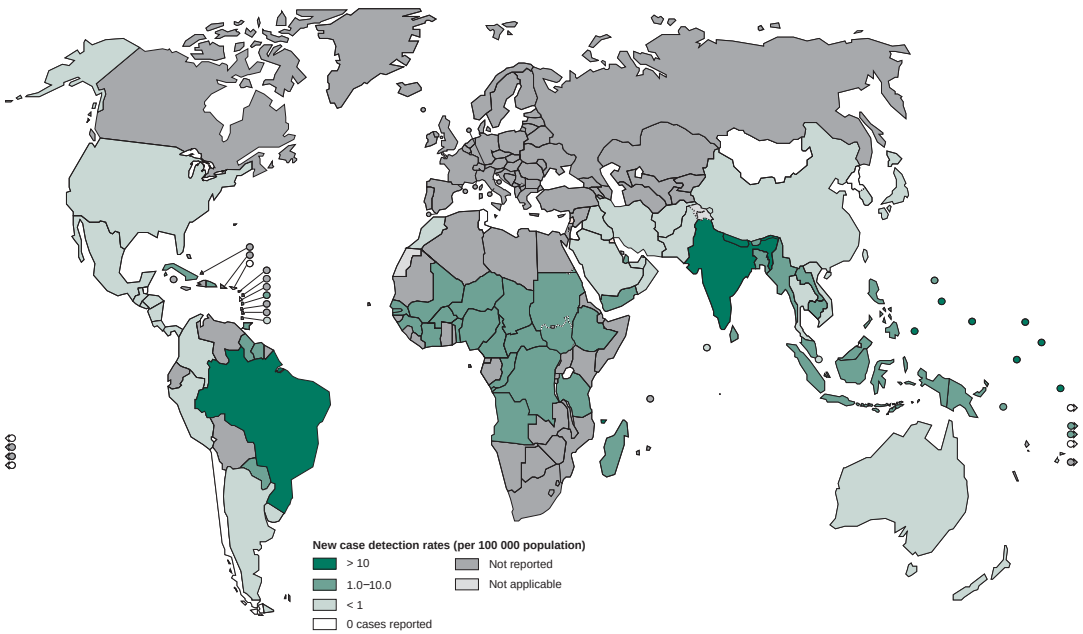
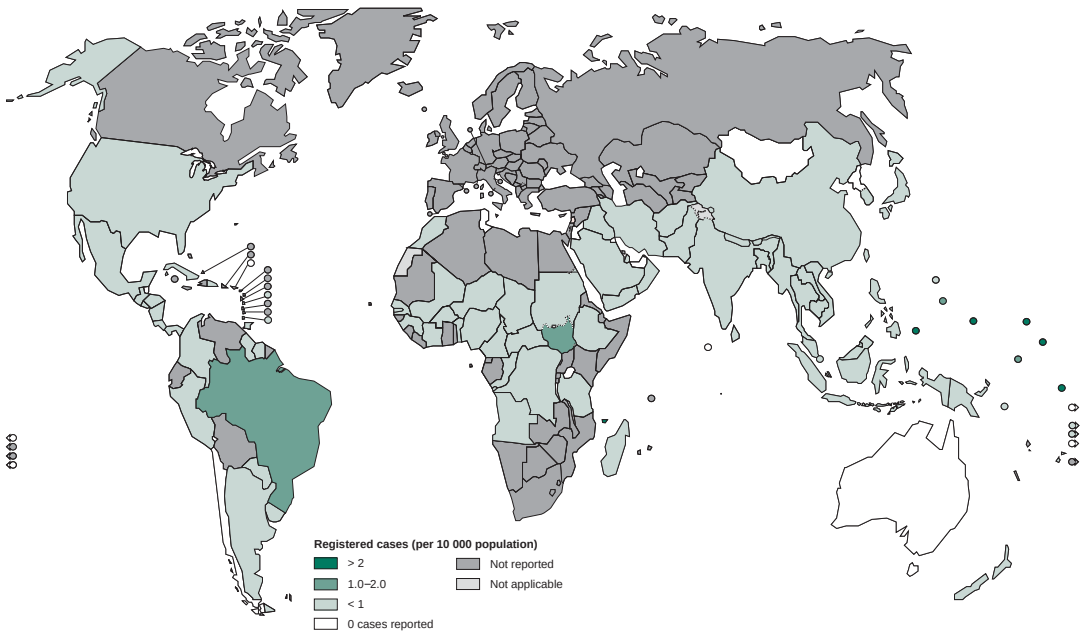
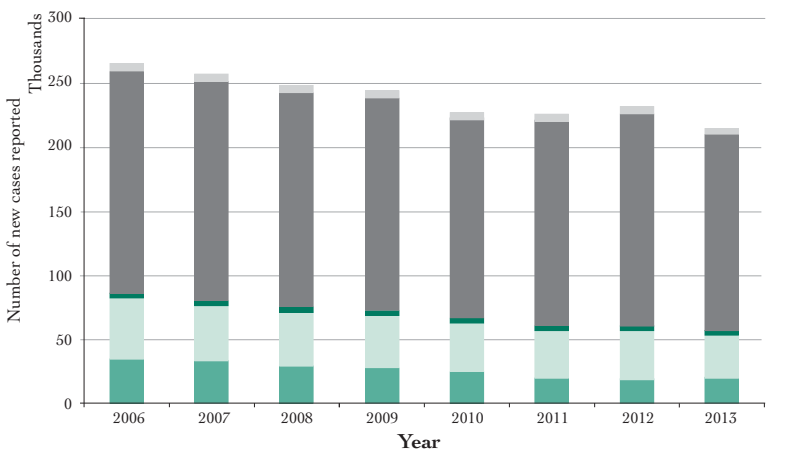


Fig. 4.10.2 Registered cases of leprosy, data reported to WHO as of January 2014



Number of new leprosy cases reported to WHO, by region, 2006–2013



	2006	2007	2008	2009	2010	2011	2012	2013
AFR	34 480	34 468	29 814	28 935	25 345	20 213	20 599	20 911
AMR	47 612	42 135	41 891	40 474	37 740	36 832	36 178	33 084
EMR	3 261	4 091	3 938	4 029	4 080	4 357	4 235	1 680
SEAR	174 118	171 576	167 505	166 115	156 254	160 132	166 445	155 385
WPR	6 190	5 863	5 859	5 243	5 055	5 092	5 400	4 596
Total	265 661	258 133	249 007	244 796	228 474	226 626	232 857	215 656

AFR–African Region / AMR–Region of the Americas / EMR–Eastern Mediterranean Region / SEAR–South-East Asia Region / WPR–Western Pacific Region

Table 4.10.1 shows the number of new cases detected during 2013 in the 14 countries previously reporting 1000 or more new cases and the number of new cases detected annually since 2006 in the countries reporting 1000 or more new cases in 2013. The 14 countries that reported 1000 or more new cases during 2006–2013 account for 96% of the new cases detected worldwide in 2013; six of these countries are in the African Region.

Table 4.10.1 Number of new leprosy cases detected in countries previously reporting more than 1000 new cases in 2013 and number of new cases detected annually, 2006–2013

Country	Number of new cases detected							
	2006	2007	2008	2009	2010	2011	2012	2013
Bangladesh	6 280	5 357	5 249	5 239	3 848	3 970	3 688	3 141
Brazil	44 436	39 125	38 914	37 610	34 894	33 955	33 303	31 044
Côte d'Ivoire	976	1 204	998	884	NR	770	1 030	1 169
Democratic Republic of the Congo	8 257	8 820	6 114	5 062	5 049	3 949	3 607	3 744
Ethiopia	4 092	4 187	4 170	4 417	4 430	NR	3 776	4 374
India	139 252	137 685	134 184	133 717	126 800	127 295	134 752	126 913
Indonesia	17 682	17 723	17 441	17 260	17 012	20 023	18 994	16 856
Madagascar	1 536	1 644	1 763	1 572	1 520	1 577	1 474	1 569
Myanmar	3 721	3 637	3 365	3 147	2 936	3 082	3 013	2 950
Nepal	4 235	4 436	4 708	4 394	3 118	3 184	3 492	3 225
Nigeria	3 544	4 665	4 899	4 219	3 913	3 623	3 805	3 385
Philippines	2 517	2 514	2 373	1 795	2 041	1 818	2 150	1 729
Sri Lanka	1 993	2 024	1 979	1 875	2 027	2 178	2 191	1 990
United Republic of Tanzania	3 450	3 105	3 276	2 654	2 349	2 288	2 528	2 005
Total (%)	241 971 (91%)	236 126 (91%)	229 433 (92%)	223 845 (91%)	209 937 (92%)	217 803 (94%)	216 773 (93%)	204 094 (95%)
Global Total	265 661	258 133	249 007	244 796	228 474	226 626	232 857	215 656

NR, Not reported.

Table 4.10.2 shows the data on multibacillary leprosy, the proportion of cases among women and children, and those with grade-2 disabilities. The proportion of cases with multibacillary leprosy among new leprosy cases in the African Region ranged from 93.6% (Nigeria) to 24.1% (Kiribati); in the Region of the Americas from 81.9% (Cuba) to 62.8% (United States of America); in the South-East Asia Region from 83.4% (Indonesia) to 43.9% (Bangladesh); in the Eastern Mediterranean Region from 80.7% (Pakistan) to 56% (Yemen); and in the Western Pacific Region from 92.7% (Philippines) to 24.1% (Kiribati).

Table 4.10.2 Countries with highest and lowest proportions of newly detected cases of leprosy in countries reporting more than 100 new cases, by type of case and WHO region, 2013

WHO region[a]	% cases of multibacillary leprosy among new cases[b]	% of females among new leprosy cases[b]	% of children among new leprosy cases[b]	% of new leprosy cases with grade-2 disabilities[b]
African	Nigeria, 93.6% Comoros, 50.4%	South Sudan, 56.4% Madagascar, 24.2%	Comoros, 29.0% Niger, 0.9%	Burkina Faso, 33.2% Comoros, 2.1%
Americas	Cuba, 81.9% United States of America, 62.8%	Cuba, 47.8% Argentina, 28.5%	Dominican Republic, 9.4% Argentina and Mexico, 0.6%	Columbia and Paraguay, 12.3% Mexico, 5.2%
Eastern Mediterranean	Pakistan, 80.7% Yemen, 56.4%	Sudan, 30.3% Pakistan, 0.5%	Yemen, 12.3% Sudan, 2.1%	Sudan, 16.2% Yemen, 7.3%
South-East Asia	Indonesia, 83.4% Bangladesh, 43.9%	Sri Lanka, 40.8% Timor-Leste, 16.7%	Indonesia, 11.9% Nepal, 4.1%	Myanmar, 14.3% Nepal, 2.7%
Western Pacific	Philippines, 92.7% Kiribati, 24.1%	Kiribati, 52.6% Malaysia, 28.4%	Micronesia, 39.5% China, 1.5%	China, 20.3% Micronesia, 0.5%

[a] The European Region did not submit reports; [b] By countries with highest and lowest proportions, and for each region.

The proportion of females among new cases in countries reporting 100 or more cases ranged in the African Region from 56.4% (South Sudan) to 24.2% (Madagascar); in the Region of the Americas from 47.8% (Cuba) to 28.5% (Argentina); in the South-East Asia Region from 40.8% (Sri Lanka) to 16.7% (Timor-Leste); in the Eastern Mediterranean Region from 30.3% (Sudan) to 0.5% (Pakistan); and in the Western Pacific Region from 52.6% (Kiribati) to 28.4% (Malaysia).

The proportion of children among new cases in countries reporting 100 or more cases ranged in the African Region from 29.0% (Comoros) to 0.9% (Niger); in the Region of the Americas from 9.4% (Dominican Republic) to 0.6% (Argentina and Mexico); in the South-East Asia Region from 11.9% (Indonesia) to 4.1% (Nepal); in the Eastern Mediterranean Region from 12.3% (Yemen) to 2.1% (Sudan); and in the Western Pacific Region from 39.5% (Federated States of Micronesia) to 1.5% (China).

The proportion of new cases with grade-2 (visible) disabilities ranged in the African Region from 33.2% (Burkina Faso) to 2.1% (Comoros); in the Region of the Americas from 12.3% (Colombia and Paraguay) to 5.2% (Mexico); in the South-East Asia Region from 14.3% (Myanmar) to 2.7% (Nepal); in the Eastern Mediterranean Region from 16.2% (Sudan) to 7.3% (Yemen); and in the Western Pacific Region from 20.3% (China) to 0.55% (Federated States of Micronesia).

Table 4.10.3 shows the trends in the number of new leprosy cases with grade-2 disabilities and rates per 100 000 population from 2007 to 2013. In 2013, the global rate was 0.23. The rate of disabilities and numbers in the Eastern Mediterranean showed a significant reduction from 700 (0.12) to 191 (0.05) in 2013. Also during 2013, a total of 13 289 new cases with grade-2 disabilities were detected, a slight reduction compared with 2010 (13 275 cases). In 2013, this rate ranged from 0.02 (Western Pacific Region) to 0.43 (African and South-East Asia regions).

Table 4.10.3 Number of cases of leprosy (rate/100 000 population) with grade-2 disabilities detected among new leprosy cases, by WHO region, 2006–2013

WHO region[a]	Year[b]						
	2007	2008	2009	2010	2011	2012	2013
African	3 570 (0.51)	3 458 (0.51)	3 146 (0.41)	2 685 (0.40)	2 300 (0.26)	2 709 (0.40)	2 552 (0.43)
Americas	3 431 (0.42)	2 512 (0.29)	2 645 (0.30)	2 423 (0.27)	2 382 (0.27)	2 420 (0.28)	2 168 (0.25)
Eastern Mediterranean	466 (0.10)	687 (0.14)	608 (0.11)	729 (0.12)	753 (0.12)	700 (0.12)	191 (0.05)
South-East Asia	6 332 (0.37)	6 891 (0.39)	7 286 (0.41)	6 912 (0.39)	7 095 (0.39)	8 012 (0.43)	7 964 (0.43)
Western Pacific	604 (0.03)	592 (0.03)	635 (0.04)	526 (0.03)	549 (0.03)	568 (0.03)	386 (0.02)
Total	14 403 (0.26)	14 140 (0.25)	14 320 (0.25)	13 275 (0.23)	13 079 (0.22)	14 409 (0.25)	13 289 (0.23)

[a] The European Region did not submit reports; [b] Values are numbers (rate/100 000 population).

Table 4.10.4 shows the trends in the number of relapsed cases reported globally from 2006 to 2013. Of note is the increased rate of relapse in Sri Lanka, from 11 cases in 2012 to 59 in 2013. The number of relapsed cases reported in 2013 (3196) exceeded that reported in 2010 (2113).

Table 4.10.4 Number of relapsed cases of leprosy reported worldwide, 2006–2013

Year	No. of countries reporting	No. of relapses
2006	41	2270
2007	43	2466
2008	49	2985
2009	122	3120
2010	117	2113
2011	100	3004
2012	105	3427
2013	96	3196

Progress towards Roadmap targets

Plans to eliminate leprosy worldwide as a public-health problem by 2020 have been prepared and their implementation is progressing. National programmes in endemic countries are implementing the *Enhanced global strategy for further reducing the disease burden due to leprosy (plan period: 2011–2015)* (*3*). This strategy aims to reduce the global rate of new cases with grade-2 disabilities per 1 million population by at least 35% by the end of 2015; the baseline for comparison is the end of 2010. The approach underlines the importance of early case detection, provision of timely multidrug therapy and ensuring a high standard of care in a setting of integrated services. Whether the elimination target is achieved will depend on the following five components of the strategy:

1. Implementing the WHO strategy in all endemic countries.
2. Reducing the burden of the disease at subnational levels by 2015 (at least 50% of new cases and at least 35% of new cases with disabilities). This will be achieved by (i) implementing advocacy and awareness campaigns in countries reporting more than 1000 new cases annually, and (ii) improving the specificity of diagnosis by using clinical or other investigations.
3. Strengthening capacity to intensify and sustain leprosy-control activities. This will be achieved by (i) establishing or strengthening institutions that conduct regular courses on leprosy diagnosis and treatment and organizing training workshops at the subnational level, and (ii) convening annual intercountry and regional meetings of national programme managers to review programmes' performance and share experiences.
4. Reducing stigmatization and discrimination. Countries have agreed to implement the principles of the United Nations resolution on the elimination of discrimination against persons affected by leprosy and their family members (*4*). This will be achieved by encouraging collaboration among relevant ministries, including social services, education and justice, as well as with other partners to expand welfare and development programmes for people affected by leprosy, by engaging in regular advocacy and encouraging the goodwill ambassador for leprosy elimination to regularly visit affected countries.
5. Intensifying research by investing in the development of diagnostics and treatment, and working to prevent neuritis. Additionally, coordinating operational research should help to increase early diagnosis and the quality of leprosy services.

Brazil has demonstrated the feasibility of implementing innovative, integrated approaches to leprosy case-finding (*Box 4.10.1*).

Box 4.10.3 Brazil: Implementing innovative approaches to leprosy case-finding

Leprosy remains a significant public-health problem in Brazil, where new case detection is high in endemic clusters throughout the country. More than 50% of cases are reported in areas where 17.5% of the population lives. Highly endemic areas for leprosy continue to persist despite large-scale national efforts to control the disease; high urban migration levels have been identified as one factor, as migrants move between endemic and non-endemic areas and often experience overcrowded conditions, poor sanitation and low levels of social development.

In 2013, the Brazilian Ministry of Health decided to combine school-based deworming with leprosy case-finding campaigns, targeting more than 9 million children aged 5–14 years. The magnitude of this public-health intervention was vast, involving 800 municipalities of 27 states with financial support from the Brazilian Ministry of Health.

Schoolchildren received an appropriate dose of the deworming medicine albendazole, donated through WHO. The objective of the campaign was to reduce the parasitic burden of soil-transmitted helminthiases in schoolchildren and at the same time to identify suspected cases of leprosy through a survey that involves mapping of suspect lesions. Any suspected leprosy cases were referred to a primary care centre for diagnostic confirmation and treatment with mutidrug therapy.

The campaign formed part of Brazil's integrated Strategic Action Plan for the Elimination of Neglected Diseases and other Poverty-Related Infections. The approach allows for the early detection of leprosy cases and reduced morbidity caused by soil-transmitted helminthiases, as these parasites cause a high impact on the growth and development of children aged under 15 years. It is for this reason that deworming has focused mainly on this age group.

This is the first time that the Ministry of Health has implemented a massive, nationwide deworming campaign. Integration with active case searches for leprosy and with different partners, such as state and municipal health secretariats and the education sector, in addition to active community participation, has demonstrated the feasibility of implementing integrated strategies.

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4.11 Lymphatic filariasis

Introduction

Lymphatic filariasis is caused by infection with one of three species of filarial nematode (*Wuchereria bancrofti, Brugia malayi* or *B. timori*) that are transmitted by mosquitoes. Adult worms live almost exclusively in humans and lodge in the lymphatic system. The infection is commonly acquired during childhood but usually manifests during adulthood as hydrocele, lymphoedema and elephantiasis.

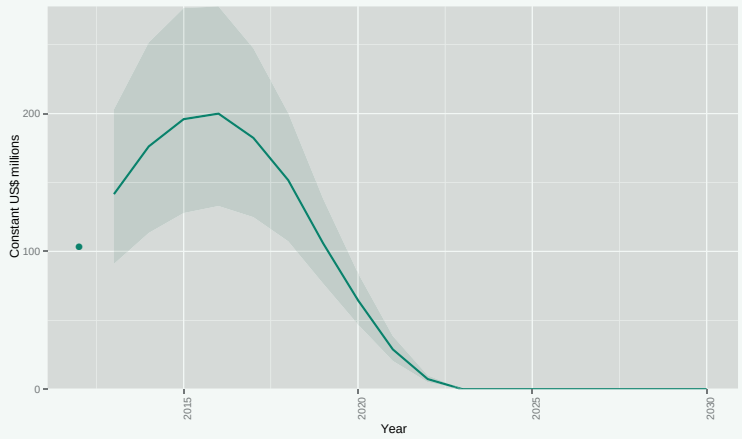
Investment case

Elimination of lymphatic filariasis provides both health and economic benefits. The first decade of the Global Programme to Eliminate Lymphatic Filariasis is estimated to have yielded economic benefits exceeding US$ 24 billion.[1] Cost-of-illness studies must be interpreted with caution, especially when comparing them with those for other diseases, as they are often highly sensitive to methodological assumptions. But it is plausible that people suffering from hydrocele or lymphoedema could experience productivity losses of up to 30%.[2] These losses are ill-afforded, as the burden of the disease is concentrated among the poorest.[3] In 2006, the second edition of the Disease Control Priorities Project put the cost per DALY averted of mass drug administration for LF at less than US$ 30. Since then, the pharmaceutical industry has pledged to donate the necessary medicines.

This report provides targets for the investment needed to deliver those medicines. Projections are based on scale up towards the coverage targets for 2016 using the latest data available on populations requiring treatment and current levels of implementation. These costs cover co-administration of medicines in areas co-endemic with soil-transmitted helminthiases or onchocerciasis. Once 65% coverage is achieved and maintained for a minimum of 5 years, the available evidence suggests that mass treatment can be stopped. The investment target for preventive chemotherapy (delivery excluding medicines) during 2015–2020 is about US$ 154 million (US$ 105–208 million) per year, falling to US$ 0 during 2021–2030. *Chapter 2* discusses the need for investments in surveillance after preventive chemotherapy.

Interventions are also required for those people for whom preventive chemotherapy arrived too late. Given the potentially very large number of cases of hydrocele and lymphoedema, health systems must be prepared to find and deliver curative, surgical and rehabilitative

Investment targets for preventive chemotherapy against lymphatic filariasis (delivery excluding medicines), 2015–2030



Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. The dots in 2012 are actual numbers reported (when available) multiplied by the unit cost benchmarks; these are not actual expenditures, but can be thought of as a benchmark for actual expenditures. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

interventions. A single hydrocele surgery is not particularly expensive (estimated in this report at US$ 80–360). The cost of interventions to prevent and manage lymphoedema is even smaller. Estimates of the backlog of cases requiring care are uncertain but high. Millions are thought to be suffering and the total cost will therefore be significant. *Chapter 2* provides more details.

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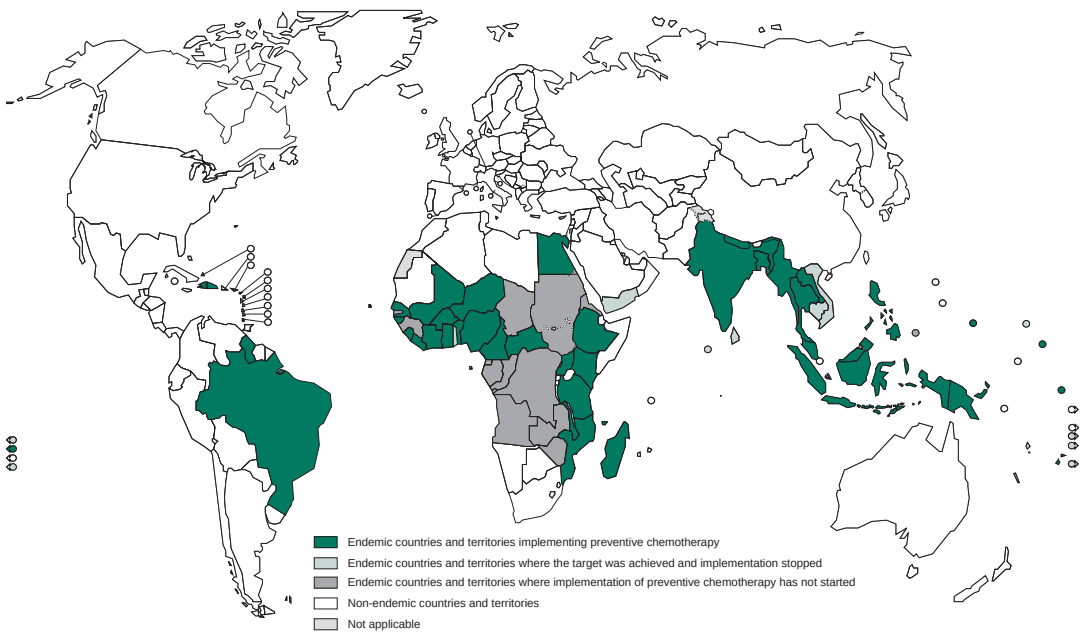
Burden and distribution

Globally, 1.38 billion people are living in areas where lymphatic filariasis is considered endemic. Approximately 80% live in 10 of the 73 endemic countries where the disease is targeted for elimination (*Table 4.11.1*). Regionally as of 2012, 843 million people in 7 countries (South-East Asia Region), 464 million in 33 countries (African Region), 37.5 million in 13 countries (Western Pacific Region), 13.4 million in 4 countries (Region of the Americas) and 22.1 million in 3 countries (Eastern Mediterranean Region) are living in areas that require interventions to eliminate lymphatic filariasis (*1*) (*Fig. 4 11.1*).

Table 4.11.1 Status of lymphatic filariasis (LF) elimination programmes in 10 heaviest burden countries (highest population living in LF-endemic areas), 2012

Country	Total population in LF-endemic areas	Mapping	MDA	Surveillance
India	594 042 240	Completed	Full geographical coverage achieved	Partial
Indonesia	113 283 453	Completed	Partial	Partial
Nigeria	108 526 381	Partial	Partial	Partial
Bangladesh	77 230 000	Completed	Partial	Partial
Democratic Republic of the Congo	49 140 000	Partial	Not started	Not started
United Republic of Tanzania	45 173 251	Completed	Partial	Partial
Myanmar	41 666 403	Completed	Partial	Not started
Ethiopia	30 000 000	Partial	Partial	Not started
Philippines	29 383 286	Completed	Full geographical coverage achieved	Partial
Nepal	15 755 990	Completed	Partial	Partial

Fig. 4.11.1 Distribution and status of delivering preventive chemotherapy for lymphatic filariasis, worldwide, 2012



At least 120 million people are infected with filarial parasites, including 40 million people with clinical manifestations of lymphatic filariasis (*2*). Infection is often asymptomatic, leading to hidden damage of the lymphatic system. Chronic disease manifests as lymphoedema, acute dermatolymphangioadenitis, elephantiasis of limbs and hydrocele. These complications limit occupational activities, educational and employment opportunities, and mobility. Those suffering with physical disfigurement of limbs and genitals often experience stigmatization and discrimination.

Progress towards Roadmap targets

In 2000, WHO launched the Global Programme to Eliminate Lymphatic Filariasis with the goal of eliminating the disease by 2020 (*3*). The programme has two strategic and parallel goals: (i) to reduce by a strategy of preventive chemotherapy the proportion of the population infected to a threshold below which transmission of the infection is no longer sustainable and people are no longer threatened by the disease; and (ii) to provide access to a basic package of care to every affected person in endemic areas to manage morbidity and prevent disability. The Roadmap's target is to achieve global elimination of lymphatic filariasis as a public-health problem by 2020.

WHO recommends preventive chemotherapy to ensure that all diagnosed and undiagnosed infected persons can be treated to reduce the number of parasites in the blood and prevent mosquitoes from transmitting infection. The medicines albendazole plus diethylcarbamazine, or in countries where onchocerciasis is endemic, albendazole plus ivermectin, are delivered annually. Simple hygiene measures can reduce the frequency of acute dermatolymphangioadenitis and improve lymphoedema, thus reducing progression to more advanced stages (elephantiasis). Common antibiotics can also treat acute attacks of dermatolymphangioadenitis. Surgery is recommended for hydrocele and is offered in an increasing number of communities in endemic areas (*2*). This basic package of care has the potential to alleviate suffering in all those affected by the disease.

WHO recommends the following strategy to guide countries towards achieving elimination :

(i) mapping of the geographical distribution of the disease to determine where interventions are required;

(ii) providing preventive chemotherapy to the total population living in endemic areas annually for 5 years;

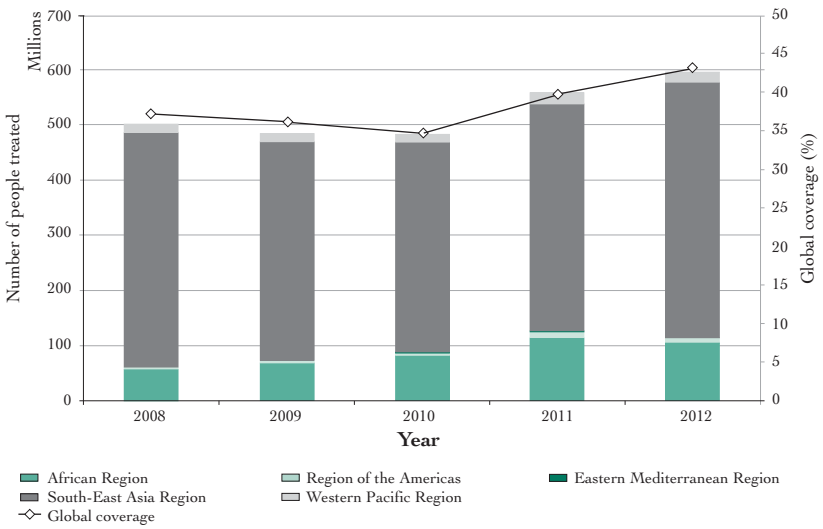
(iii) ensuring access to the basic package of care to manage morbidity and prevent disability;

(iv) conducting surveillance after preventive chemotherapy has been discontinued; and

(v) validating that elimination has been achieved (*4*).

Major accomplishments have been achieved since the initiation of the global programme. A total of 4.4 billion treatments of preventive chemotherapy have been delivered according to the elimination strategy (*Fig. 4.11.2*). To achieve the Roadmap's target, all 73 endemic countries must have stopped preventive chemotherapy and have ensured access to the basic package of care by 2020. Much work must therefore be done in the next 6 years. By 2012, 13 countries (18%) had stopped preventive chemotherapy and were conducting surveillance. Currently, 43 countries are delivering preventive chemotherapy but only 20 countries are covering all endemic areas fully (100% geographical coverage). In order to be eligible to achieve the Roadmap's target, the 23 countries that have started preventive chemotherapy partially and the 17 countries that have yet to start will need to scale up this intervention fully by 2015 under the current strategies.

Fig. 4.11.2 Number of people treated and global coverage of preventive chemotherapy for lymphatic filariasis, by WHO region, 2008–2012



Only about one-third of national programmes have reported activities to manage morbidity and prevent disability in people suffering from lymphatic filariasis. Within the next 6 years, all 73 countries should prioritize building the basic package of care within their national health system. In order to facilitate scale-up of this strategy, in 2013 WHO published an aide-memoire for national programme managers, which provides general guidance in starting with situation analysis and planning to implementation, monitoring and evaluation of activities in all areas where cases are present. to achieve full coverage (*2*). A toolkit to assist national programmes in conducting situation analyses and planning activities is being drafted with partners.

Table 4.11.2 summarizes the progress as of 2012 towards meeting the milestones of the global programmes. Clearly, scaling up preventive chemotherapy to reach all endemic areas and ensuring access to morbidity management and disability prevention are the priorities. Other

Table 4.11.2 Status of milestones for the Global Programme to Eliminate Lymphatic Filariasis, 2011–2020

Year	Milestone	Progress summary
2011	Revised WHO guidelines on interrupting transmission and conducting post-intervention surveillance completed and available	Completed: Monitoring and epidemiological assessment of mass drug administration: a manual for national elimination programmes published
	WHO guidelines and criteria for verifying the absence of transmission completed and available	Ongoing: Development of a common platform to document when NTD elimination targets have been achieved
	WHO guidelines and training modules for morbidity management completed and available	Completed: Managing morbidity and preventing disability: an aide-memoire for national programme managers published; training modules for morbidity management under development
2012	Mapping completed in all countries	Ongoing: mapping initiated in 72/73 endemic countries and ongoing in 14 countries
	MDA started in all countries without co-endemic loiasis	Ongoing: 53/63 countries not endemic for loiasis have started MDA
	Provisional strategy for interrupting transmission in loiasis-endemic countries developed and circulated	Completed: Provisional strategy for interrupting lymphatic filariasis transmission in loiasis-endemic countries published; provisional guidelines presented during meetings of country programme managers
	25% of endemic countries have met the criteria for stopping interventions and entered post-intervention surveillance phase	Ongoing: 18% (13/73) of endemic countries have stopped MDA and entered the surveillance phase
2013	Revised strategy for interrupting transmission implemented in all loiasis-endemic countries	Ongoing: Limited areas in 2/10 loiasis-endemic countries are implementing the provisional strategy
	Metrics for annual reporting on morbidity management programmes developed by WHO and disseminated	Ongoing: Indicators for morbidity management and disability prevention are included in the new PC Epidemiological Data Reporting Form; additional metrics are being defined and will be disseminated through a toolkit for programme managers
2014	20% of endemic countries verified free of transmission	Ongoing: 14% of endemic countries are preparing their dossiers documenting the achievement of the elimination targets
	All endemic countries collecting and reporting data on morbidity management to WHO	Ongoing: 39% of endemic countries provided morbidity management information in annual reports
2015	Full geographical coverage with MDA or other interventions, or both, achieved in all endemic urban areas	Unknown: 72% of all endemic countries have stared MDA including some urban areas but the proportion of those areas covered is unknown
	Full geographical coverage with MDA or other interventions, or both, achieved in all countries where loiasis is not endemic	Ongoing: 81% of countries where loiasis is not endemic have initiated MDA
	Progress, global impact and remaining challenges assessed mid-plan	Ongoing: Publication of a sub-national, country-by-country progress analysis is in preparation to determine the direction and needs at this time-point 5 years away from 2020
2016	Full geographical coverage with MDA or other interventions, or both, achieved in countries with heaviest burden	Ongoing: MDA in 9/10 heaviest burden countries started and partial coverage achieved; full geographical coverage achieved in India and the Philippines
	Full geographical coverage with MDA or other interventions, or both, achieved in all countries with co-endemic loiasis	Ongoing: 2/10 countries with co-endemic loiasis are implementing interventions
	70% of endemic countries have met the criteria for stopping interventions and entered into post-intervention surveillance phase	Ongoing: MDA stopped in 18% (13/73) of endemic countries and surveillance phase entered into
2020	70% of countries verified as free of lymphatic filariasis and 30% under post-intervention surveillance	Ongoing: Common platform to be devised for process and criteria to document achievement of elimination target and measure progress towards milestones
	Full geographical coverage and access to basic care for lymphoedema (and hydrocele in areas of bancroftian filariasis) offered in all countries	Ongoing: 39% of endemic countries have reported implementing morbidity management and disability prevention activities

MDA, mass drug administration; PC, preventive chemotherapy

challenges remain in those countries that have implemented MDA successfully. Sustained resources for evaluating impact and implementing surveillance are needed.

In 2013,WHO and partners developed training modules to assist national programmes in applying the WHO guidelines on evaluating the interruption of transmission and conducting surveillance through implementation of transmission assessment surveys (*4,5*). Additionally, the national programme managers responsible for elimination of lymphatic filariasis in those countries that are fast approaching the elimination targets have been trained for the surveys in the WHO regional training workshops held during 2012–2013. Since then, 25 countries have implemented transmission assessment surveys in at least some areas.

Research priorities

Current operational research initiatives are addressing the barriers to progress as they arise and guiding the future direction of the global programme. The main priorities for operational research are those that will help countries to meet the elimination target faster than current strategies; this is especially important for those countries not yet at scale with preventive chemotherapy. Additionally, sensitive surveillance methodologies that are feasible for applying at scale are needed to ensure interruption of transmission.

Enhanced vector control as a supporting strategy to preventive chemotherapy can provide additional impact towards elimination (*6,7*). In 2013, WHO published an entomology handbook for national programmes that encourages the development of practical vector control plans tailored to local epidemiology (*6*). New vector control strategies in areas where *Culex* is the major vector mosquito are specifically needed.

Scaling up preventive chemotherapy has been a major challenge for countries in which *Loa loa* is co-endemic. WHO has published a dual strategy that recommends single-drug preventive chemotherapy with albendazole twice per year combined with integrated vector management approaches to eliminate lymphatic filariasis (*7,8*). Additional research is needed to determine how long this strategy must be implemented to achieve the elimination targets.

Given the alignment of strategies and endemicity, integrating onchocerciasis and lymphatic filariasis elimination programmes in Africa offers potential for synergy in scaling up preventive chemotherapy (*9*). Treatment twice per year is perhaps faster than once per year in interrupting transmission of onchocerciasis (*10*). The impact of more frequent delivery of preventive chemotherapy should be established for lymphatic filariasis in programmatic settings (*11*).

New medicines and new combinations of existing medicines effective at killing or sterilizing adult worms are vital for immediate transitioning to programmes upon availability. Additional research on drug therapy to reverse or halt the development of early-stage lymphoedema is warranted (*12*). Continued coordinated effort and commitment to operational research are needed to overcome the dynamic challenges faced by the programme. Yet, only when current and new strategies are implemented fully will elimination of lymphatic filariasis be achieved.

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4.12 Onchocerciasis (river blindness)

Introduction

Onchocerciasis, or river blindness, is caused by infection with a filarial nematode (*Onchocerca volvulus*) transmitted by infected blackflies (*Simulium* spp.) that breed in fast-flowing rivers and streams. The adult worms produce embryonic microfilariae that migrate to the skin, eyes and other organs. Microfilariae cause severe itching, disfiguring skin disease and may enter the eye, causing visual loss and blindness over time.

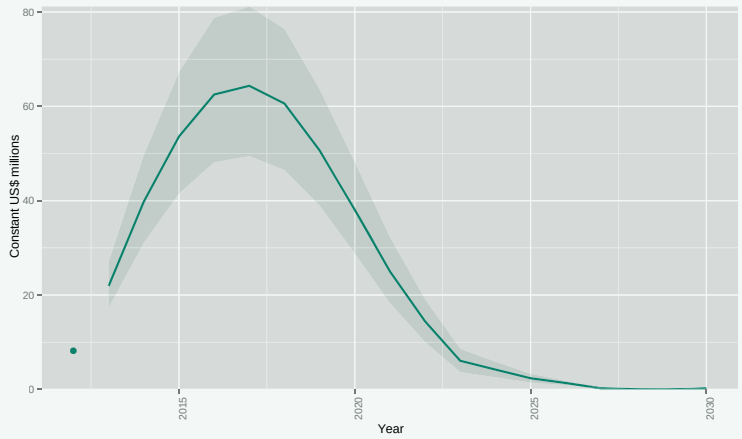
Investment case

In the 1990s, the investment case for onchocerciasis control was based largely on findings that the cost of control was far less than the cost of the disease in terms of lost productivity and earnings. These early cost–benefit analyses have been reviewed elsewhere.[1] In 2006, the second edition of the Disease Control Priorities Project put the cost per DALY averted by mass drug administration for onchocerciasis at less than US$ 10 – one of the most cost-effective interventions on offer. Since then, it has been estimated that by 2015 the African Programme for Onchocerciasis Control (APOC) will have averted about 19 million DALYs at a nominal cost of less than US$ 500 million.[2,3]

Integrated delivery of donated medicines for both onchocerciasis and lymphatic filariasis should strengthen the cost–effectiveness of preventive chemotherapy by reducing the number of deliveries required and by sharing fixed costs and good practices. The pharmaceutical industry has pledged to donate the medicines necessary to achieve elimination.

This report provides targets for the investment needed to deliver those medicines. Estimates do not yet include investments needed for collaboration of cross-border issues, reinforcement for post-conflict and other difficult settings, and verification of the interruption of transmission, among other regional-level investments. Projections are based on scale up towards the coverage targets, using the latest data available on populations requiring treatment and current levels of implementation. If adequate coverage is maintained for 5 years for lymphatic filariasis and 10–14 years for onchocerciasis, the

Investment targets for preventive chemotherapy against onchocerciasis and lymphatic filariasis in Africa (delivery excluding medicines), 2015–2030



Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. The dots in 2012 are actual numbers reported (when available) multiplied by the unit cost benchmarks; these are not actual expenditures, but can be thought of as a benchmark for actual expenditures. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

available evidence suggests that mass treatment can be stopped. The investment target for the delivery of preventive chemotherapy (excluding medicines) during 2015–2020 is about US$ 58 million (US$ 45–73 million) per year, falling to US$ 4.1 million (US$ 2.7–5.6 million) per year during 2021–2030.

Chapter 2 discusses the need for post-preventive chemotherapy surveillance and management of morbidity and disability prevention.

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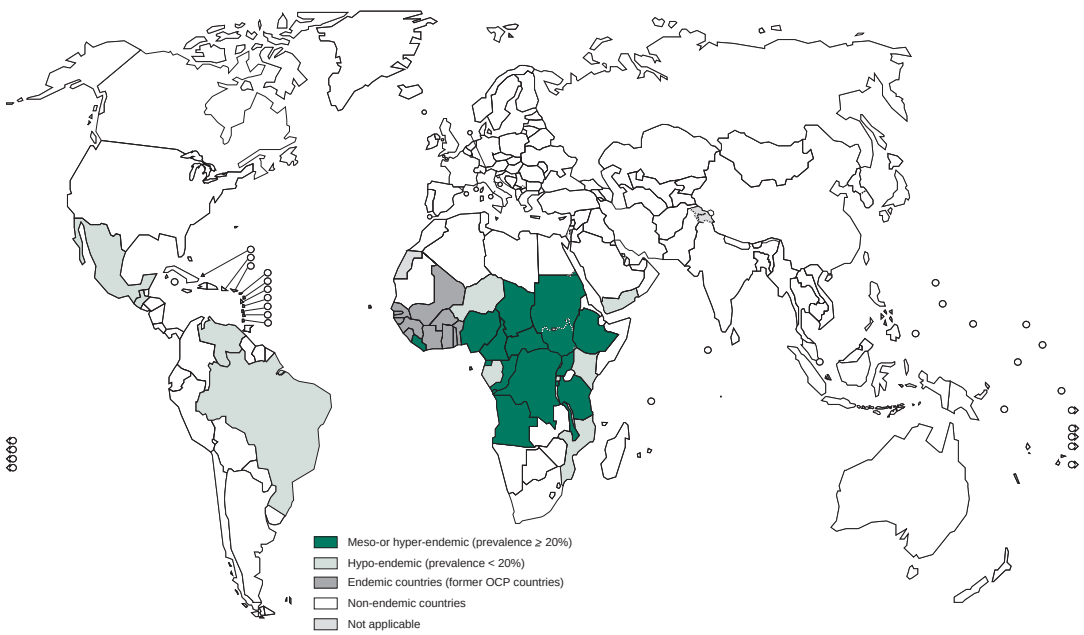
[3] Coffeng LE, Stolk WA, Zouré HGM, Veerman JL, Agblewonu KB, Murdoch ME et al. African programme for onchocerciasis control 1995–2015: updated health impact estimates based on new disability weights. PLoS Negl Trop Dis. 2014;8:e2759. doi:10.1371/journal.pntd.0002759.

Burden and distribution

More than 99% of the about 37 million people infected with *O. volvulus* live in 31 sub-Saharan African countries (Angola, Benin, Burkina Faso, Burundi, Cameroon, the Central African Republic, Chad, Congo, Côte d'Ivoire, the Democratic Republic of the Congo, Equatorial Guinea, Ethiopia, Gabon, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Malawi, Mali, Mozambique, Niger, Nigeria, Rwanda, Sierra Leone, Senegal, Sudan, South Sudan, Togo, Uganda and the United Republic of Tanzania), representing about 120 million people at risk in 2012. The infection also occurs in Yemen and in four out of six original endemic countries in Latin America (the Bolivarian Republic of Venezuela, Brazil, Guatemala and Mexico). *Fig. 4.12.1* shows the global distribution of onchocerciasis in 2014.

Fig. 4.12.1 Distribution of onchocerciasis, worldwide, 2014



Progress towards Roadmap targets

The Onchocerciasis Elimination Program in the Americas (OEPA) was launched in 1992 with the goal of interrupting onchocerciasis transmission in six endemic countries in Latin America by 2015, in accordance with resolutions CD48.R12 and CD49.R19 of the Pan American Health Organization Directing Council. In 2013, Colombia became the first country in Latin America verified by WHO as having achieved elimination of onchocerciasis (*1*). Verification was successfully conducted by an international verification team in Ecuador in May 2014; WHO announced in September 2014 that Ecuador had become the second country in Latin America to have eliminated onchocerciasis (*2*). During its last meeting in 2014, the OEPA Programme Coordinating Committee concluded that Mexico and Guatemala have successfully completed post-treatment surveillance. Both countries are now compiling national dossiers and are expected to file formal applications to WHO for independent verification in 2015. Ministers of health from the Bolivarian Republic of Venezuela and Brazil signed on 20 May 2014 a new bilateral agreement aimed at enhancing coordinated cross-border health interventions required to interrupt transmission in the Yanomami area shared by the two countries (*3*).

The African Programme for Onchocerciasis Control (APOC) started in 1995 and targets endemic countries that were not covered by the former Onchocerciasis Control Programme (OCP). Its mandate was later expanded to cover also some ex-OCP countries where transmission was still ongoing. During 2012, about 100 million people were treated with ivermectin in 24 African countries where community-directed treatment with ivermectin is being implemented, representing 76% therapeutic coverage (*4*). Although national interruption of transmission has not been recorded in any country in Africa to date, mass distribution of ivermectin has been halted in some areas, including nine districts in Uganda (Bududa, Bushenyi, Kabarole, Kyenjojo, Manafwa, Maracha, Mbale, Mitooma and Siromko), two districts in Mali (Bougouni and Yanfolila) and one district in Sudan (Abu Hamed) (*5*–*9*).

By 2020, 12 countries are expected to have eliminated onchocerciasis successively (Niger, Senegal, Malawi, Burundi, Chad, Kenya, Mali, Benin, Guinea, Guinea-Bissau, Sierra Leone and Togo). Despite these achievements and expectations, some challenges persist in Africa, notably in sustaining high coverage, particularly in conflict and post-conflict zones as well as in areas where loiasis is co-endemic, and in preventing cross-border transmission among endemic countries.

According to the national action plan for onchocerciasis elimination in Yemen, which was prepared and adopted in June 2013, mass drug administration and vector control interventions will be launched in due course. In the interim, clinical cases have been treated for the past two decades. In 2012, a total of 51 505 patients were treated with ivermectin. Government commitment and enhanced support from partners will facilitate achieving elimination of onchocerciasis in Yemen by 2020 instead of the initial (2015) target.

Research priorities

Despite the enormous progress made in eliminating river blindness during the past decades, the need remains for new diagnostic tools to refine mapping and for improved evaluation and surveillance activities. Research priorities should focus also on better understanding the epidemiology of the disease and in developing more effective interventions to address the challenges in areas where loiasis is co-endemic and in conflict and post-conflict zones (*10*).

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4.13 Rabies

Introduction

Rabies is an infectious viral disease that is almost always fatal following the onset of clinical signs. In more than 99% of human cases, the rabies virus is transmitted by domestic dogs (*1*). Human rabies is 100% preventable through timely administration of post-exposure prophylaxis to victims who have been exposed through the bite of a rabid animal. Elimination at source is feasible through mass vaccination of domestic dog populations (*1*).

Prevention of human rabies and control of canine rabies have been successful in North America, Western Europe and a number of Asian and Latin American countries (*1*). The Resolution recognizes human rabies of canine origin and supports the Roadmap's targets for elimination in Latin America (2015) and in South-East Asia (2020) discussed below.

WHO, the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE) and the Global Alliance for Rabies Control are collaborating to eliminate human rabies of canine origin (*2*). In 2013, FAO, OIE and WHO announced their unified aims of eliminating human rabies and controlling the disease in animals (*3*); together, the tripartite is raising awareness of and commitment to overcoming this persistent zoonosis.

As with other NTDs, community engagement is critical to achieve and sustain effective delivery of rabies interventions. Those interventions that hamper community engagement, notably indiscriminate culling of dogs, are not only ineffective at controlling rabies but also generate antagonism and suspicion among communities and compromise dog vaccination efforts. Where control programmes have been successfully implemented, investments and effort have been made to ensure community engagement; for example, by creating community-based rabies action groups (KwaZulu-Natal, South Africa) and mobilizing community volunteers on a large scale to implement dog vaccination campaigns (Philippines).

Investment case

The high cost of rabies is attributed to mortality and lost productivity, both direct and indirect costs of post-exposure prophylaxis and dog vaccination, surveillance and livestock losses. Fortunately, government-led strategies to eliminate canine rabies have succeeded in many countries worldwide. In the long term, dog vaccination is more cost-effective than human post-exposure treatment.[1] Dog vaccination will drive down not only the deaths attributable to rabies but also the need for post-exposure prophylaxis as a part of dog-bite patient care. While human deaths are entirely preventable through post-exposure prophylaxis and pre-exposure vaccination, these interventions will not eliminate the disease and costs will therefore continue to escalate over time if rabies is not controlled at its canine source.[2,3] Unfortunately, investment in dog vaccination to eliminate rabies from endemic countries in Africa and most of Asia has been minimal to date.

Three large-scale projects are under way in the Philippines, South Africa and the United Republic of Tanzania. The project in KwaZulu-Natal has reduced the prevalence of rabies, facilitating a shift towards rapid outbreak response. As a result, it is being expanded within South Africa to the Eastern Cape and across the country's borders to Lesotho, Mozambique and Swaziland. Vaccination costs across the three sites are between US$ 1.18 and US$ 11.27 per dog. In these endemic regions, the substantial costs associated with human intervention could be avoided if elimination was achieved. In areas where the cost per dog vaccinated is very high, however, efforts will be needed to reduce costs to levels that are more affordable in order to maintain and sustain high coverage vaccination campaigns needed to eliminate the disease. For example, integration with existing platforms for control of other NTDs and access to health is being considered as a way of increasing the reach, cost-effectiveness and sustainability of rabies control programmes in Africa.

As work continues on the third edition of the Disease Control Priorities Project, WHO is analysing the cost-effectiveness of elimination of dog-mediated human rabies.

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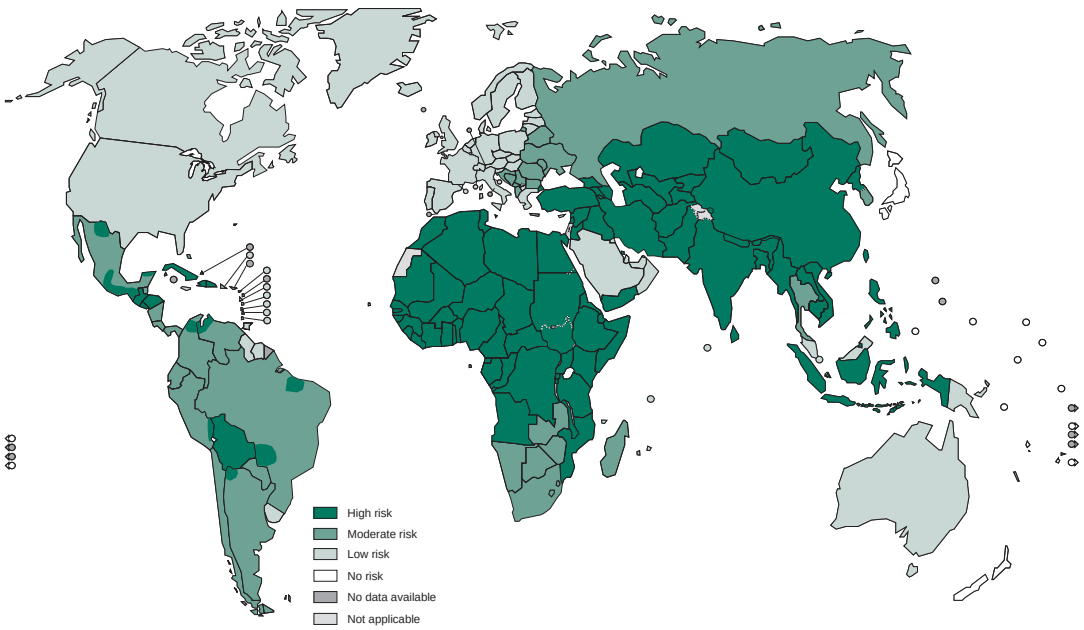
Burden and distribution

Rabies causes tens of thousands of deaths annually worldwide. Its global distribution has changed little since 2011, with more than 90% of rabies deaths occurring in Africa and Asia (*Fig. 4.13.1*).

Fig. 4.13.1 Distribution of risk to humans of contracting rabies, worldwide, 2013



Official reporting of rabies incidence in animals and of human exposure to the virus remains inadequate, making it difficult to accurately determine the global burden of the disease. It is increasingly accepted that the available data underestimate the true incidence (*4,5*). Methods have been developed to improve estimates of mortality attributable to rabies. A predictive approach that uses a probability decision-tree method has been introduced to establish the likelihood of developing rabies following a bite from a dog suspected of being rabid. This approach has been used to estimate mortality in Africa and Asia, and to determine country-specific mortality estimates in Bhutan and Cambodia. Most recently, it has been adapted to estimate the global burden of endemic canine rabies (*6*).

As with the other dog-transmitted NTDs, management of waste has a direct impact on roaming dog populations. The involvement of other sectors – including the veterinary but also water, sanitation and hygiene sectors – is therefore critical.

Progress towards Roadmap targets

2015 target: regional elimination (Latin America)

By 2015, human rabies transmitted by dogs should have been eliminated and dog-to-dog transmission interrupted in all Latin American countries. Canine rabies and human rabies transmitted by dogs have been eliminated in many Latin American countries, including Chile, Costa Rica, Panama, Uruguay, and most of Argentina, the states of São Paulo and Rio de Janeiro in Brazil, and large parts of Mexico and Peru. During 2010–2012, human rabies transmitted by dogs was reported in Brazil, the Dominican Republic, Guatemala, Haiti, Honduras, Peru and the Plurinational State of Bolivia; 40% of all reported human rabies cases transmitted by dogs during this period occurred in Haiti (*7*).

Human rabies transmitted by vampire bats is a public-health issue of increasing importance in Latin America, particularly in remote areas of the Amazon region of Brazil, Colombia, Ecuador and Peru where access to appropriate medical treatment is limited.

2020 target: regional elimination (South-East Asia and Western Pacific regions)

Rabies has been eliminated for decades in Japan and Malaysia. Many countries in the South-East Region have embarked on elimination campaigns in line with the target of regional elimination by 2020. Bangladesh launched an elimination programme in 2010 and through management of dog bites, mass dog vaccination and increased availability of vaccines free of charge, human rabies deaths decreased by 50% during 2010–2013. The Ministry of Health in Bangladesh has provided funding for the mass dog vaccination programme.

A regional Association of Southeast Asian Nations framework on prevention and control of rabies was developed in 2009 and endorsed by the working group on livestock in 2010. The South Asian Association for Regional Cooperation countries has identified rabies as a regional priority and adopted a resolution for prevention and control with an elimination target of 2020 (*8*).

Improvements in control have also been reported from areas of the Philippines where a project is under way as part of a Bill & Melinda Gates Foundation project led by WHO. This collaboration has resulted in two of the nine islands in the Visayas being declared rabies-free in 2013 in line with WHO and OIE recommendations (*9*). The number of human deaths from rabies in the Visayas decreased from 51 in 2008 to 4 in 2013 (*Table 4.13.1*).

Table 4.13.1 Human rabies deaths by project region, Philippines, 2008–2013

Region	2008	2009	2010	2011	2012	2013
Western Visayas	14	14	15	8	3	1
Central Visayas	14	12	13	10	7	2
Eastern Visayas	23	17	12	11	6	1
Total	51	43	40	29	16	4

Cross-border cooperation is essential to control the disease regionally and globally. Elimination requires consistent sustained commitment, close collaboration between health and veterinary sectors, investment in mass dog vaccination and effective surveillance to monitor the impacts of disease control efforts.

Research priorities

Programmatic interventions would be aided by innovations in developing thermostable dog and human vaccine, easy-to-use diagnostic tests and pursuing production of monoclonal antibodies in response to the current global shortage, and in reducing costs for rabies immunoglobulin. Engineered rabies virus neutralizing monoclonal antibodies have been generated in transgenic tobacco plants (*Nicotiana tabacum*), which could open new, low-cost sources of rabies immunoglobulin for post-exposure prophylaxis in humans. Antivirals are being devised for use in humans that would be efficacious as a therapeutic against rabies.

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4.14 Schistosomiasis

Introduction

Schistosomiasis is a parasitic disease caused by blood flukes of the genus *Schistosoma* (*1*). Six species of schistosomes are responsible for infection in humans: *Schistosoma guineensis, S. haematobium, S. intercalatum, S. japonicum, S. mansoni* and *S. mekongi; S. haematobium* and *S. mansoni* are predominant causes of disease.

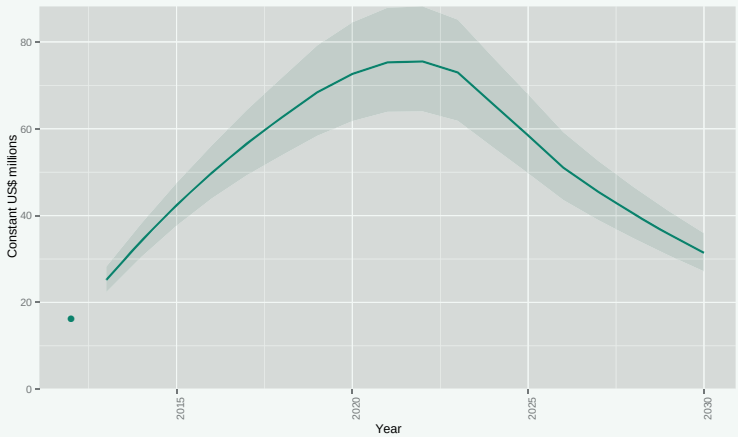
Human schistosomiasis manifests as intestinal and urogenital disease. Transmission begins when human excreta containing parasite eggs reaches fresh water bodies and hatched larvae infect susceptible snail hosts. Parasites undergo asexual multiplication in snails and another larval stage, infective to humans, is released into water. People become infected during domestic, occupational and recreational contact with water.

Investment case

The distribution of the burden of schistosomiasis remains highly unequal. In the south western part of Nigeria for example – a middle-income country with the highest burden of schistosomiasis according to estimates of total DALYs – the prevalence of *Schistosoma haematobium* infection increases from 1.5% for annual household incomes above US$ 1600 to 72.8% for annual household incomes below US$ 600.[1] Similar findings have been found for *S. mansoni* infection.[2] After recent revisions, GDP per capita in Nigeria is now estimated at more than US$ 3000 per annum. Investment in schistosomiasis control is largely a question of equity, but it yields financial returns too. Mass administration of praziquantel may be more cost-effective in reducing HIV infections in sub-Saharan Africa than other interventions currently being implemented with the same aim.[3] This case is particularly compelling from the health system perspective, since NTD partners including the pharmaceutical industry have pledged to donate a significant share of the required medicines.

This report provides targets for the investment needed to deliver those medicines to the people that need them. Using the latest data available on populations known or thought to be at risk and levels of coverage, this report estimates the investment required to meet the coverage targets of the Roadmap and the Strategic Plan for Schistosomiasis Control. About half of these (the school-age children) will, in fact, be treated for both schistosomiasis and soil-transmitted helminthiases. If 75% coverage is attained by 2020 and maintained for long enough, it is expected that the frequency of preventive chemotherapy rounds

Investment targets for in preventive chemotherapy against schistosomiasis (delivery excluding medicines), 2015–2030



Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. The dots in 2012 are actual numbers reported (when available) multiplied by the unit cost benchmarks; these are not actual expenditures, but can be thought of as a benchmark for actual expenditures. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

can be reduced. The investment target for preventive chemotherapy (delivery excluding medicines) during 2015–2020 is about US$ 59 million (US$ 51–67 million) per year. The investment target falls to US$ 55 million (US$ 47–64 million) per year during 2021–2030, or US$ 31 million (US$ 27–36 million) by 2030.

As work continues on the third edition of the Disease Control Priorities Project, WHO is working also on an analysis of the cost-effectiveness of integrated preventive chemotherapy for helminth elimination and control.

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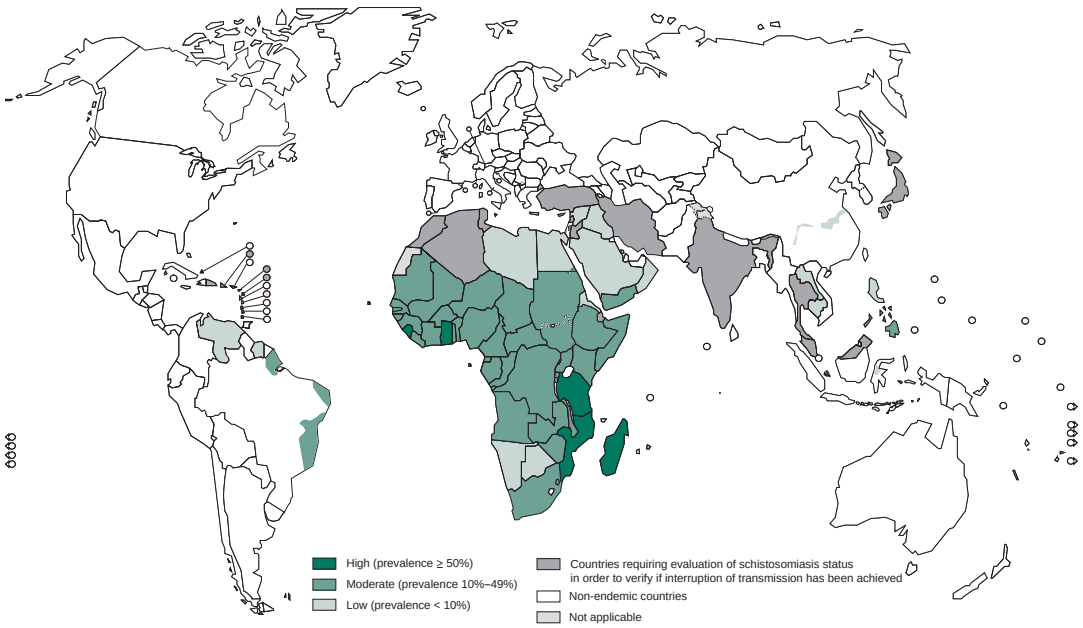
Burden and distribution

The distribution of schistosomiasis is focal, since transmission depends on specific snail hosts and infective human activities (*Fig. 4.14.1*). Endemicity changes with the environment, water development schemes, migration, control interventions and snail host distribution (*2*).

Fig. 4.14.1 Distribution of schistosomiasis, worldwide, 2012



Morbidity due to schistosomiasis was discussed in the second WHO report on NTDs. There is acceptance of the plausibility that genital schistosomiasis is a risk factor for HIV and contributes to progression to AIDS, and of the need to advocate inclusion of schistosomiasis treatment in HIV preventive interventions. In addition to school-age children and adults, pre-school children are also a risk group for schistosomiasis.

An estimated 249 million people required preventive chemotherapy for schistosomiasis in 2012, 93% of them in sub-Saharan Africa (*3*). Scale up of treatment is still slow in the 10 highest burden African countries where 70% of affected people live (*Table 4.14.1*).

Control of morbidity should focus on 52 countries with moderate and high transmission. The status of transmission in 26 additional countries will be determined in order to implement elimination programmes or verify the interruption of transmission.

In the Region of the Americas, transmission has probably stopped in some countries and could be interrupted by enhanced efforts where it is low.

Table 4.14.1 Number of people requiring preventive chemotherapy for schistosomiasis and number treated in 2012 in the 10 highest-burden countries in the African Region

Country	Number of people requiring preventive chemotherapy (PC)	Number of people treated	Coverage* (%)
Nigeria	60 622 091	3 247 696	5.36
Ethiopia	22 092 015	0	0
Democratic Republic of the Congo	18 026 622	0	0
Mozambique	13 456 367	1 314 383	9.77
Kenya	11 762 213	0	0
United Republic of Tanzania	10 135 069	3 134 150	30.92
Cameroon	9 922 513	2 149 500	21.66
Uganda	8 624 509	1 604 434	18.6
Malawi	6 782 369	3 161 535	43.10
Ghana	6 632 462	1 975 117	29.78
Total	168 056 230	16 586 815	

* Coverage is calculated as the number of people treated in need of PC out of the population requiring PC. The numerator does not include the number of people treated in areas where PC is not required.

In the Eastern Mediterranean Region, control has been successful. Transmission is high in Somalia and Sudan and in Yemen where a robust national control programme is implemented.

Transmission could be interrupted in the focus in Indonesia, the only endemic country in the South-East Asia Region, with enhanced interventions, including water, sanitation and hygiene (WASH), and snail control.

In the Western Pacific Region, *S. japonicum* infection has been successfully controlled in China but remains highly prevalent in the Philippines. Morbidity associated with *S. mekongi* has been controlled in Cambodia but highly endemic foci persist in the Lao People's Democratic Republic (*4*).

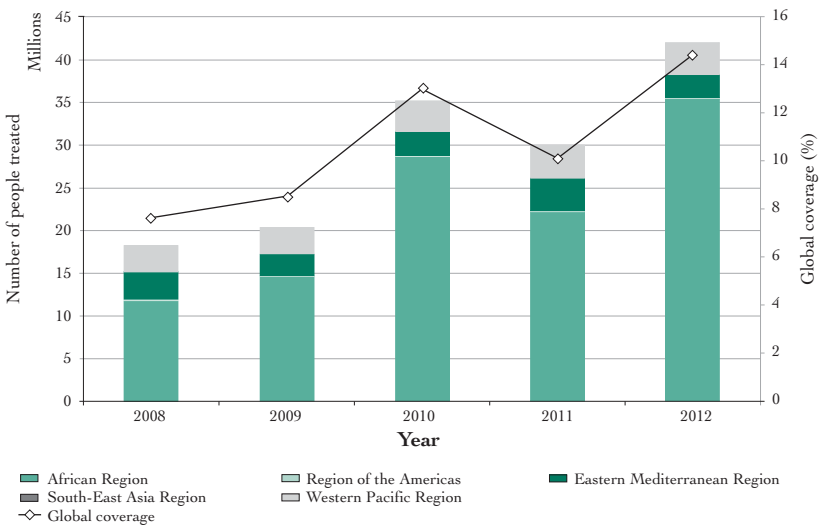
Progress towards Roadmap targets

Regional elimination in the Eastern Mediterranean Region is unlikely to be achieved in 2015 as scale up of schistosomiasis control still has to be sustained in Sudan and Yemen. In the Lao People's Democratic Republic and the Philippines, efforts to interrupt transmission are compromised by reservoir hosts and little investment in WASH interventions. Elimination in the Americas by 2020 is a feasible goal provided political will and resources are available to meet the target. The status of schistosomiasis in Algeria and Mauritius has yet to be determined as outlined in the Strategic Plan for NTDs in the African Region (2014–2020).

WHO recommended control of morbidity 30 years ago as a "feasible objective" for countries without resources to implement comprehensive control programmes (*5*). Praziquantel, the only medicine available against schistosomiasis, continues to be effective at 40 mg/kg body weight (*6*). Oxamniquine, effective only against *S. mansoni*, can be modified for other schistosome species (*7*).

Preventive chemotherapy is the only strategy routinely reported on to WHO (*Fig. 4.14.2*). In 2012, reports were received from 31 (60%) of 52 countries where 42.1 million people were treated (3). This represented 14.4% of those to be treated, a 40% increase from 2011 when 25 countries reported. The African Region accounted for 84.5% of the global number of people treated, a 60% increase from 2011.

Fig. 4.14.1 Number of people treated and global coverage with preventive chemotherapy for schistosomiasis, by WHO region, 2008–2012



Children of school age accounted for 70% of all those treated, representing 26% of the global coverage for this age group requiring preventive chemotherapy. In the African Region, treatment is targeted at children of school age, and 81% of those treated were in this age group. Only in six of 31 reporting countries was the target of reaching at least 75% of school children achieved.

Access to praziquantel remains an issue for treating those at risk of morbidity, but it was not a limiting factor for the number of people treated in 2012. More tablets were shipped than were used; it is likely that management issues and limited resources hampered implementation. Low national coverage in the 10 highest burden countries confirms this observation (*Table 4.14.1*).

The proportion of countries implementing schistosomiasis control in 2012 (60%) is in line with the milestone set in the *Strategic plan 2012–2020* for 2012 (*8*).

The STAG-NTD Working Group on Access to Quality Assured Medicines coordinates the supply of donated praziquantel through WHO and harmonizes partner activities. In 2012 and 2013, it supplied 125 million and 181 million tablets respectively to countries. Donated praziquantel is expected to increase to 250 million tablets per year by 2016, an amount sufficient to treat 100 million schoolchildren. Partners, who pledged 305 million tablets for 2014, should continue to supply praziquantel to meet requirements for other age groups.

As treatments are scaled up, the efficacy of praziquantel should be monitored using the standard operating procedures published by WHO in 2013 (*9*) and in use in Brazil, Cameroon, Mali, the Philippines and the United Republic of Tanzania.

To ensure implementation, 75% of countries requiring preventive chemotherapy for schistosomiasis have national control plans (i.e. 39 of 52 countries). Capacity-building for national programme managers at central and decentralized levels is ongoing in many countries. In 2014, WHO supported country-level training (Ethiopia and Nigeria) and regional-level training (Eastern Mediterranean Region).

Resolution WHA65.21 on the elimination of schistomasiasis, adopted by the Sixty-fifth World Health Assembly in 2012, encouraged "Member States and the international community to make available the necessary and sufficient means and resources, particularly medicines, and water, sanitation, and hygiene interventions, to intensify control programmes in most disease-endemic countries and initiate elimination campaigns, where appropriate". This requires a paradigm shift from morbidity control to a comprehensive approach that ensures all those infected are treated every year. Delineation of endemic foci is required. The WHO African Region is leading mapping in sub-Saharan Africa: 51% of countries are fully mapped and completion is expected by the end of 2015.

Inclusion of WASH will require collaboration with sectors responsible for infrastructure and social development. For snail control, training is essential because experience is limited. The priority is to ensure that molluscicides are available; only niclosamide (Bayluscide) has WHOPES specifications. Guidelines for evaluating molluscicide efficacy are under review, and those for snail control will be updated in 2015.

Resolution WHA65.21 called on WHO to prepare guidance for Member States on initiating elimination campaigns and on procedures for verifying the interruption of transmission. Procedures for elimination are being aligned with the WHO Guidelines Review Committee. As few countries have eliminated schistosomiasis, the evidence base is small; procedures will therefore be based initially on expert opinion. The discussion by the World Health Assembly was requested by a Member State with documented interruption of transmission. Another country requested assessment to determine elimination but has yet to compile a dossier on the evolution of the control programme.

Completion of mapping and scale up of interventions require strengthened monitoring and evaluation to ensure that progress is aligned with the Strategic Plan. Advocacy should ensure that the necessary resources are available to implement comprehensive control interventions, including snail control and WASH.

In 2015, preparations will be made for the mid-term review of the Strategic Plan.

Research priorities

That 14.4% of people requiring treatment for schistomasiasis were reached in 2012 highlights the limited resources and tools available. Priorities for research have been outlined, but the new sciences have had limited impact on control (*10,11*). Control strategies depend on limited epidemiological surveys. Sensitive and specific diagnostic tests would better define endemic areas, targeting treatment and accurate monitoring. Antigen tests are more sensitive than the Kato–Katz technique for intestinal schistosomiasis; their utility and cost-effectiveness await assessment (*12*). Detection of schistosome DNA in definitive and intermediate hosts has been evaluated but tests are not available (*13,14*).

Praziquantel remains efficacious and the mainstay of schistosomiasis control, but its use in integrated helminthiasis control is limited. New medicines are required, as are models for testing them and their cost-effectiveness.

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4.15 Soil-transmitted helminthiases

Introduction

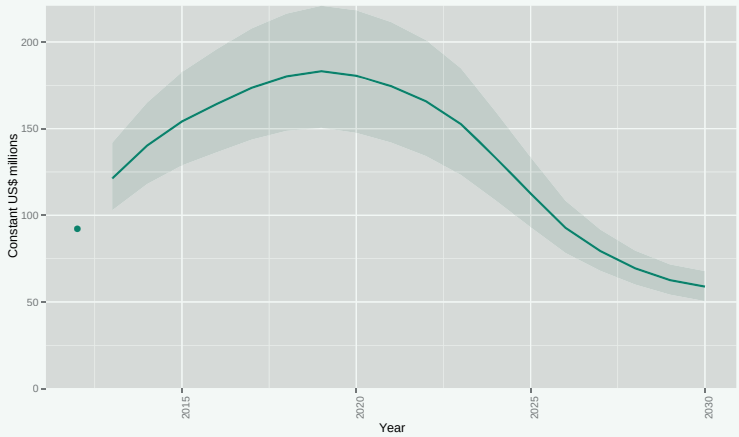
Soil-transmitted helminthiases are a group of diseases caused by infection with four intestinal parasites: *Ascaris lumbricoides, Trichuris trichiura, Necator americanus and Ancylostoma duodenale* (*1,2*). Morbidity can be controlled by the widespread delivery of quality-assured, single-dose medicines (preventive chemotherapy) (*3*). Elimination and eradication of the causative parasites will not be achieved until affected populations have access to effective sanitation.

Investment case

The investment case for control of soil-transmitted helminthiases is perhaps best made in human development rather than strictly health terms. The cost per additional year of school participation has been found to be less than that of other methods of increasing schooling; economic analyses of long-term benefits have concluded that deworming at school age enhances earnings in adulthood.[1,2,3] This is important for global targets to reduce poverty and inequality. The burden of the disease is known to be highly concentrated among the poorest socioeconomic groups. In Brazil and Malaysia, for example, about three-quarters of infected children belonged to households living below the national poverty line or earning less than the minimum wage.[4,5] A survey of a rural area of Côte d'Ivoire found that the prevalence of infection with hookworm and *Trichuris trichiura* was higher in poorer households.[6]

Using the latest data available on populations known or thought to be at risk and levels of coverage, this report provides targets for the investment required to meet the coverage targets laid out in the Roadmap and the Strategic Plan for STH Control. Most of these people will, in fact, be treated for both lymphatic filariasis and soil-transmitted helminthiases; a smaller proportion will also be treated for schistosomiasis. If 75% coverage is maintained, it is expected that the frequency of preventive chemotherapy rounds can be gradually reduced (about 50% every 5 years). The investment target for preventive chemotherapy (delivery excluding medicines) during 2015–2020 is about US$ 174 million (US$ 144–207 million) per year, falling to US$ 109 million (US$ 91–131 million) per year during 2021–2030, or US$ 57 million (US$ 49–66 million) by 2030.

Investment targets for preventive chemotherapy against soil-transmitted helminthiases (delivery excluding medicines), 2015–2030



Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. The dots in 2012 are actual numbers reported (when available) multiplied by the unit cost benchmarks; these are not actual expenditures, but can be thought of as a benchmark for actual expenditures. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

As work continues on the third edition of the Disease Control Priorities Project, WHO is working also on an analysis of the cost-effectiveness of integrated preventive chemotherapy for helminth elimination and control.

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Burden and distribution

WHO estimates that about 875 million children require annual treatment with preventive chemotherapy (*4*). *Fig. 4.15.1* shows the global distribution of soil-transmitted helminthiases and the proportion of all children needing regular preventive chemotherapy. *Fig. 4.15.2* shows the number of preschool-age children treated during 2008–2012.

Fig. 4.15.1 Distribution of soil-transmitted helminthiases and proportion of children (aged 1–14 years) in each endemic country requiring preventive chemotherapy for the diseases, worldwide, 2012

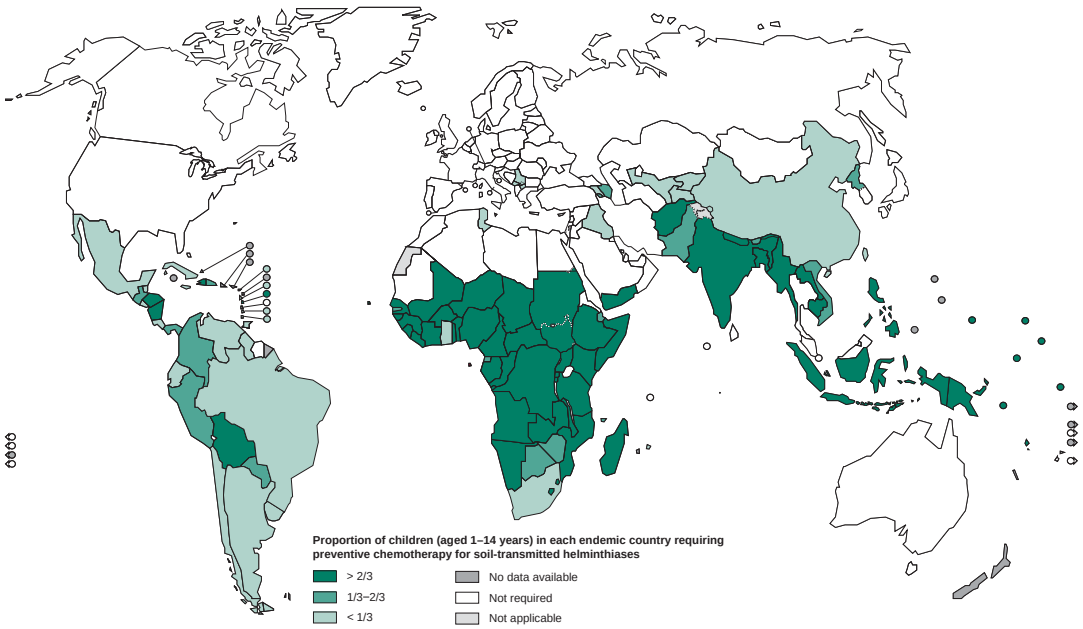


Fig. 4.15.2 Number of preschool-aged children (1–14 years) treated and global coverage of preventive chemotherapy for soil-transmitted helminthiases, by WHO region, 2008–2012

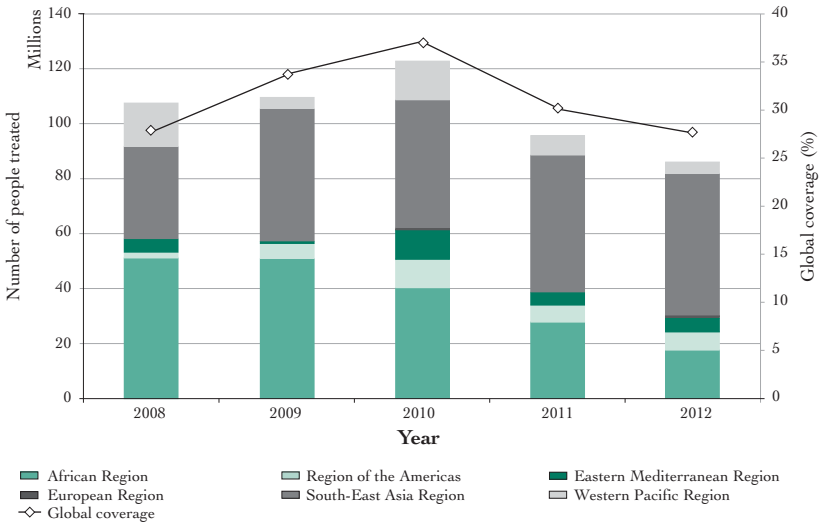
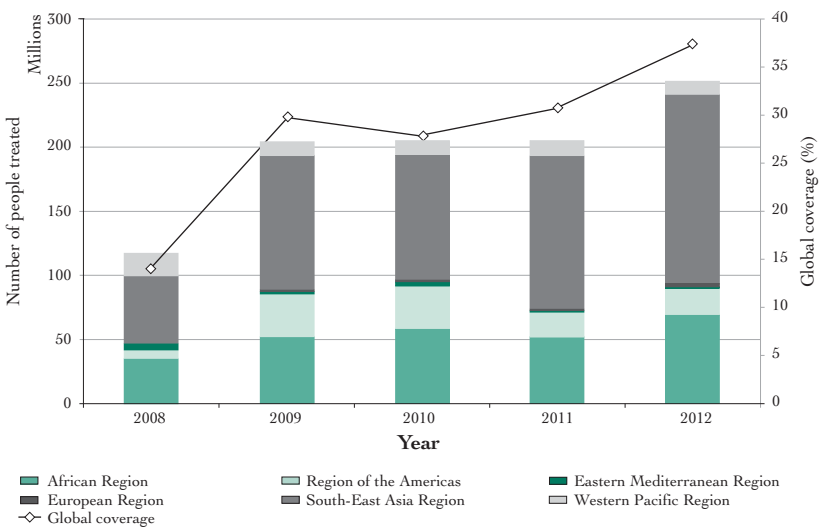


Fig. 4.15.3 Number of school-age children (5–12 years) treated and global coverage of preventive chemotherapy for soil-transmitted helminthiases in this age group, by WHO region, 2008–2012



Progress towards Roadmap targets

WHO recommends the regular administration of preventive chemotherapy with albendazole or mebendazole as the main intervention for controlling soil-transmitted helminthiases. The coverage of this intervention is the main indicator for success. Based on expanded coverage in recent years and increasing requests for donated medicines, the Roadmap's target of 50% coverage of school-age children by 2015 is feasible. Furthermore, most of the endemic countries have prepared an integrated plan of action for NTD control that includes plans and budget estimates in accordance with the 2015 milestones (*Table 4.15.1*).

Global coverage of preventive chemotherapy increased significantly during 2009, reaching more than 273 million children or roughly 30% of those in need. In 2010, this number remained constant (*4*). The main coverage increase was in school-age children, the age group for which donated medicines are available (*Fig. 4.15.3*). Coverage in preschool-age children decreased slightly; discussions to obtain donated, quality-assured medicines for this age group are under way.

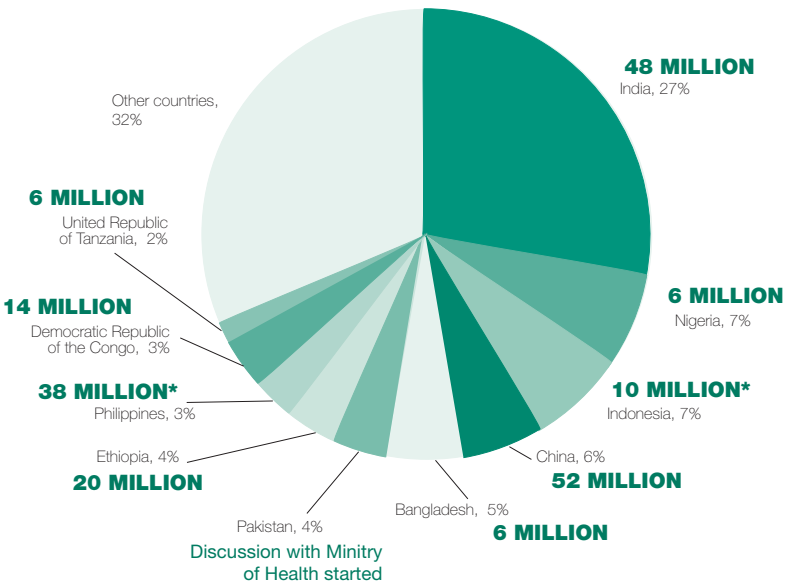
In order to achieve the 75% coverage target by 2020, WHO is focussing efforts on implementing preventive chemotherapy programmes against soil-transmitted helminthiases in the 10 most populous countries where more than 65% of the children needing treatment reside (*Fig. 4.15.4*). Programmes at different scale are implemented in eight countries (Bangladesh, the Democratic Republic of the Congo, China, Ethiopia, India, Nigeria, Indonesia and the United Republic of Tanzania).

Table 4.15.1 Milestones for eliminating soil-transmitted helminthiases as a public-health problem in children (status as of 2014)

Year	Milestone
2013	National plans of action for NTD control developed by 75% of countries requiring preventive chemotherapy for STH (achieved)
	National policies for STH control involving intersectoral collaboration (for example, in education and water and sanitation sectors) exist in 75% of countries requiring preventive chemotherapy for STH (achieved)
	Manuals for control of STH in all at-risk groups produced and disseminated (2 manuals produced and 1 manual drafted)
	Mapping to identify areas requiring preventive chemotherapy completed in all countries where STH are endemic (in progress)
2015	National plans of action for NTD control developed by 100% of countries requiring preventive chemotherapy for STH
	National policies for STH control involving intersectoral collaboration (for example, in education and water and sanitation sectors) available in 100% of countries requiring preventive chemotherapy for STH
	50% of countries requiring preventive chemotherapy for STH have achieved 75% national coverage of SAC and pre-SAC, and 50% of SAC and pre-SAC needing treatment worldwide have been treated
2020	100% of countries requiring preventive chemotherapy for STH have achieved 75% national coverage of SAC and pre-SAC
	100% of countries requiring preventive chemotherapy for STH regularly assess intensity of the infections in sentinel sites
	Less than 1% of countries requiring preventive chemotherapy for STH have infection of high or moderate intensity
	75–100% of children (SAC and pre-SAC) needing preventive chemotherapy worldwide have been treated

NTD, neglected tropical disease; pre-SAC, preschool-age children; SAC, school-age children; STH, soil-transmitted helminthiases

Fig. 4.15.4 Anthelminthic medicines donated for controlling soil-transmitted helminthiases in 10 priority countries, status as of 2014[a]



A total of 194 million tablets were sent (or locally procured*) for school programmes conducted in 2014

[a] Adapted from reference (*5*)

From 2010, 600 million tablets of donated albendazole or mebendazole became available annually to treat school-age children in endemic countries. In 2012, these countries requested more than 200 million tablets. Although complete coverage data for 2013 and 2014 are not yet available, endemic countries have requested an additional 50 million tablets annually in anticipation of an increasing trend in coverage.

In 2013, WHO published three manuals to support scaling up of helminthiasis control in children (*6*–*8*). In 2014, a manual on assessing the epidemiology of soil-transmitted helminths during a transmission assessment survey was published (*9*); a publication addressing control in women of reproductive age has been drafted and shared with collaborating institutions for review (*10*). Application of this guidance should help national programme managers to achieve the milestones set by WHO in the Roadmap.

Research priorities

Experience from the veterinary field has highlighted the risk of drug resistance developing when benzimidazoles are administered at large scale for several years. To date in 2014 alone, more than 1 billion tablets of benzimidazoles have been donated for preventive chemotherapy against lymphatic filariasis and soil-transmitted helminthiases, and the risk of drug resistance emerging is therefore high.

The research priority for WHO is to identify strategies that would delay the emergence of drug resistance, for example by alternating the mebendazole or albendazole rounds with second-line drugs (or drug combinations) every 3 or 4 years. WHO is working with three collaborating centres to address this priority.

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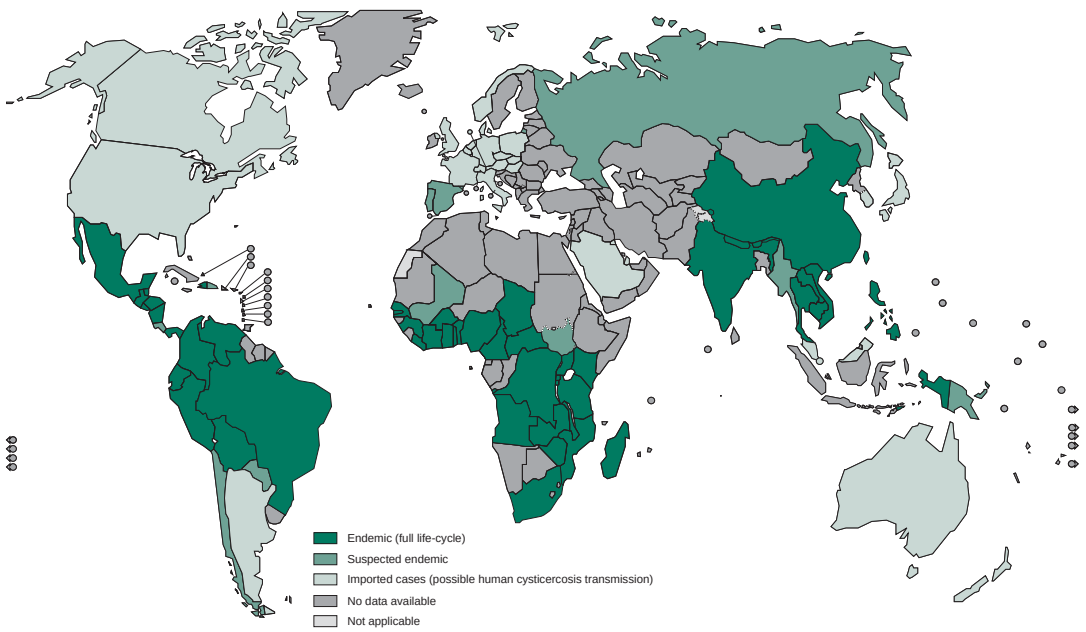
4.16 Taeniasis and (neuro)cysticercosis

Introduction

Taeniasis is a parasitic zoonosis caused by the tapeworm *Taenia solium*. Humans acquire the infection by eating raw or undercooked pork. Millions of tapeworm eggs (invisible to the naked eye) are excreted into the environment through infected people's stool. Pigs become infected by eating human stool containing eggs or by ingesting eggs from the environment. Eggs develop into small cysts throughout the pig's body (porcine cysticercosis).

Humans can also become infected with *T. solium* eggs by ingesting contaminated food or water (human cysticercosis) or as a result of poor hygiene. Tapeworm larvae (cysticerci) develop in the muscles, skin, eyes and the central nervous system. When cysts develop in the brain, neurocysticercosis may result. Symptoms include epilepsy, severe headache and blindness, and can be fatal. Neurocysticercosis is the most frequent preventable cause of epilepsy worldwide.

Fig. 4.16.1 Countries and areas at risk of cysticercosis, 2012



Investment case

In Peru, symptoms of neurocysticercosis have been estimated to cause to the average sufferer a loss of 44.5 hours of productive activity per month. Such symptoms cause two-thirds of wage-earners to lose their jobs, and only 61% are able to re-engage in wage-earning activities.[1] Annual losses due to porcine cysticercosis have been estimated at about US$ 25 million for 10 West and Central African countries in 2002,[2] and US$ 5 million for the Eastern Cape Province of South Africa in 2004.[3] Porcine cysticercosis has a serious impact on pig-producing communities, leading to poor-quality pork, falling pork prices or pork being condemned as unfit for human consumption, thereby reducing income and rendering an important source of protein unsafe to eat.

Investment targets for veterinary public-health interventions may be included in updates to the analyses contained in *Chapter 2* of this report.[4]

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Burden and distribution

The lack of data on this zoonotic disease results from the absence of any systematic programme to generate them; the data therefore remain fragmented. There are indications, however, that the burden of cysticercosis may be emerging in South Africa due to value and trade patterns in pig production. *T. solium* cysticercosis is especially common where humans live in close proximity with their pigs, with low levels of sanitation and poor understanding of porcine management. Cysticercosis has been a serious public-health problem in Latin America for decades (*1*). The disease is endemic in South and South-East Asia (*2*) and is emerging in large areas of sub-Saharan Africa (*Fig. 4.16.1; Table 4.16.1*). New reports of neurocysticercosis cases are re-emerging in the developed world, with recent reports in Europe (*3*) and the United States of America (*4*).

WHO estimates that at least 50 million people worldwide have epilepsy. Neurocysticercosis is responsible for about 30% of epilepsy cases in endemic countries (*6*) and around 3% globally (*7*). The *Global burden of disease* (2010) study estimated that neurocysticercosis was responsible for around 0.5 million DALYs per year. In low- and middle-income countries where pork is consumed, the burden of epilepsy is almost 6.8 million DALYs per year (*8*). Where access to health services is limited, mortality due to neurocysticercosis is about 3–6 times higher in these disadvantaged populations than in the general population.

Table 4.16.1 Prevalence of cysticercosis in sub-Saharan Africa[a]

Country	Porcine prevalence % (95% CI)	Human prevalence % (95% CI)
Angola	0–6.8	ND
Benin	ND	0.13 (0.9–1.9)
Burkina Faso	0–48.2	0-10.3
Burundi	ND	26.1 (23.2–28.9)
Cameroon	26.6 (15.6–31.0)	0.4-3
Central African Republic	ND	2.9 (0.5–5.31)
Chad	40.8 (32.2–49.4)	ND
Democratic Republic of the Congo	38.4–41.2	21.6 (18.3–25.0)
Côte d'Ivoire	2.5	Reported
Equatorial Guinea	ND	Reported
Gabon	ND	Reported
Gambia	4.8 (3.4–6.5)	1.74 (0.72–2.8)
Ghana	11.7 (3.57–19.83)	Reported
Kenya	32.8 (26.8–39.2)	Reported
Madagascar	Reported	18
Mozambique	34.90 (22.1–66.7)	12.1 (9.2–15)
Nigeria	14.4 (8.1–20.7)	ND
Rwanda	10-30	7
Senegal	6.4–13.2	11.9 (8.9–15.4)
South Africa	56.7 (40.6–76.3)	5.5 (4.3–6.7)
Togo	17	3.8 (2.8–4.8)
Uganda	8.5 (6–11)	ND
United Republic of Tanzania	17.40 (12.5–22.3)	16.3 (13.2–19.4)
Zambia	16.9–30.0	5.8 (4.1–7.5)
Zimbabwe	28.6	Reported

ND, no data.
[a] Source: reference (*5*)

Neurocysticercosis is reported as a cause of death in Brazil (*9*), Cameroon (*10*), Mexico (*11*) and the United States of America (*12*). The annual proportion of deaths caused by epilepsy associated with neurocysticercosis has been estimated to be 6.9% of incident cases in Cameroon (*10*) and 0.5% in Mexico (*11*).

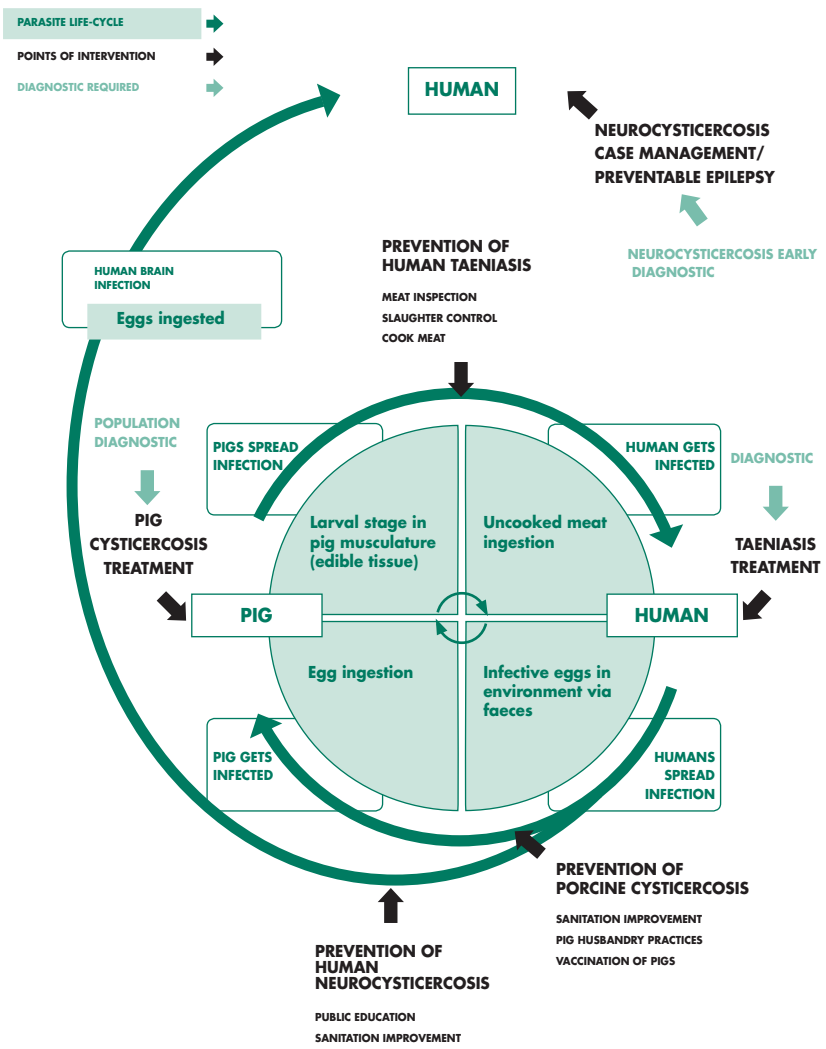
Progress towards Roadmap targets

The Roadmap seeks to pilot a strategy for controlling *T. solium* taeniasis and (neuro) cysticercosis (by 2015) and scaling it up in selected endemic countries (by 2020).

A combination of tools – such as cysticercosis vaccine and oxfendazole treatment for pigs – has been shown to eliminate transmission of *T. solium* to pigs (*13*). Vaccine for pigs (*14*) is undergoing registration, with regulatory approval expected in India in 2016. Oxfendazole treatment is now commercially available for treatment of porcine cysticercosis in Africa.

WHO and its partners have taken the first steps towards identifying the "best-fit" strategy with countries to interrupt transmission of *T. solium* and improve case detection and management of neurocysticercosis using the tools currently available (*Fig. 4.16.2*). Results of the landscape

Fig. 4.16.2 *Taenia solium* transmission cycle and possible intervention points



analysis reinforce that a single intervention to control diseases caused by *T. solium* is insufficient (*15*). Working with the veterinary and food safety authorities as well as with other sectors will be necessary to attain the long-term outcomes of reducing the burden of disease and safeguarding the food value chain.

Research priorities

Simple, cost-effective and rapid diagnostic tools are needed for use in field conditions to detect *T. solium* carriers as well as human and porcine cysticercosis cases, and to direct programme planning and monitoring.

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4.17 Trachoma

Introduction

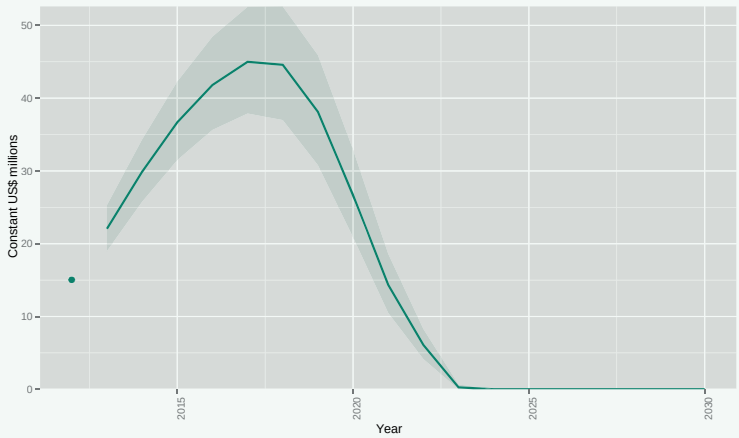
Trachoma, caused by infection with *Chlamydia trachomatis*, accounts for about 3% of all cases of blindness worldwide (*1*). Repeated episodes of inflammation and resolution (precipitated by ocular *C. trachomatis* infection and occurring over years to decades) generate conjunctival scar that can misdirect the eyelashes to rub on the surface of the eye and damage the cornea.

Investment case

The global economic cost of trachoma from lost productivity has been estimated at up to US$ 5 billion annually.[1] Such cost-of-illness estimates must be interpreted with caution, especially when compared with those for other diseases, as they are highly sensitive to methodological assumptions. Clearly, however, trichiasis surgery remains one of the most cost-effective interventions to combat loss of vision.[2,3] At about US$ 40 per surgery, it is also very affordable. An early estimate of the backlog of cases (almost 5 million cases) suggested that US$ 200 million might be needed between 2011 and 2020.[4] This is a conservative estimate of the backlog, relative to more recent regional estimates. Updated country-specific estimates are expected in 2015. Thanks in part to a large donation of azithromycin, preventive chemotherapy is also cost-effective. The pharmaceutical industry has pledged to donate the medicines necessary to achieve elimination.

Using the latest data available on populations known or thought to be at risk, this report updates estimates of the cost of delivering those medicines to the people who need them. Once 80% coverage is achieved (at the latest by 2017) and maintained for a minimum of 3 years (a minimum of 5 years where baseline prevalence of active trachoma exceeds 30%), mass treatment may be able to be stopped, although stopping decisions may need to be made on a district-by-district basis. The investment target for preventive chemotherapy (delivery excluding medicines) during 2015–2020 is about US$ 39 million (US$ 32–46 million) per year. The total amount for this period is slightly higher than an earlier estimate

Investment targets for preventive chemotherapy against trachoma (delivery excluding medicines), 2015–2030



Notes: Shaded areas reflect the range determined by low and high values of the unit cost benchmarks; they do not reflect uncertainty about future rates of scale-up and scale-down of interventions. The dots in 2012 are actual numbers reported (when available) multiplied by the unit cost benchmarks; these are not actual expenditures, but can be thought of as a benchmark for actual expenditures. All numbers expressed in US$ are constant (real) US$, adjusted to reflect purchasing power in the United States of America in 2015.

of about US$ 180 million that assumed, based on 2011 data, that only 50% of districts suspected of having endemic active trachoma would be confirmed as having active trachoma prevalences exceeding the mass treatment threshold.[4] The investment target drops to US$ 1.9 million (US$ 1.3–2.5 million) per year during 2021–2030.

Chapter 2 discusses the need for surveillance after preventive chemotherapy has been stopped.

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1 Frick KD, Hanson CL, Jacobson GA. Global burden of trachoma and economics of the disease. Am J Trop Med Hyg. 2003;69(5 Suppl):1–10.

2 Baltussen RMPM, Sylla M, Frick KD, Mariotti SP. Cost-effectiveness of trachoma control in seven world regions. Ophthalmic Epidemiol. 2005;12:91–101. doi:10.1080/09286580590932761.

3 Baltussen R, Smith A. Cost effectiveness of strategies to combat vision and hearing loss in sub-Saharan Africa and South East Asia: mathematical modelling study. BMJ. 2012;344:e615. doi:10.1136/bmj.e615.

4 The end in sight: 2020 INSight. International Coalition for Trachoma Control; 2011 (http://trachoma.org/sites/default/files/guidesandmanuals/2020INSight_EnglishLR.pdf; accessed October 2014).

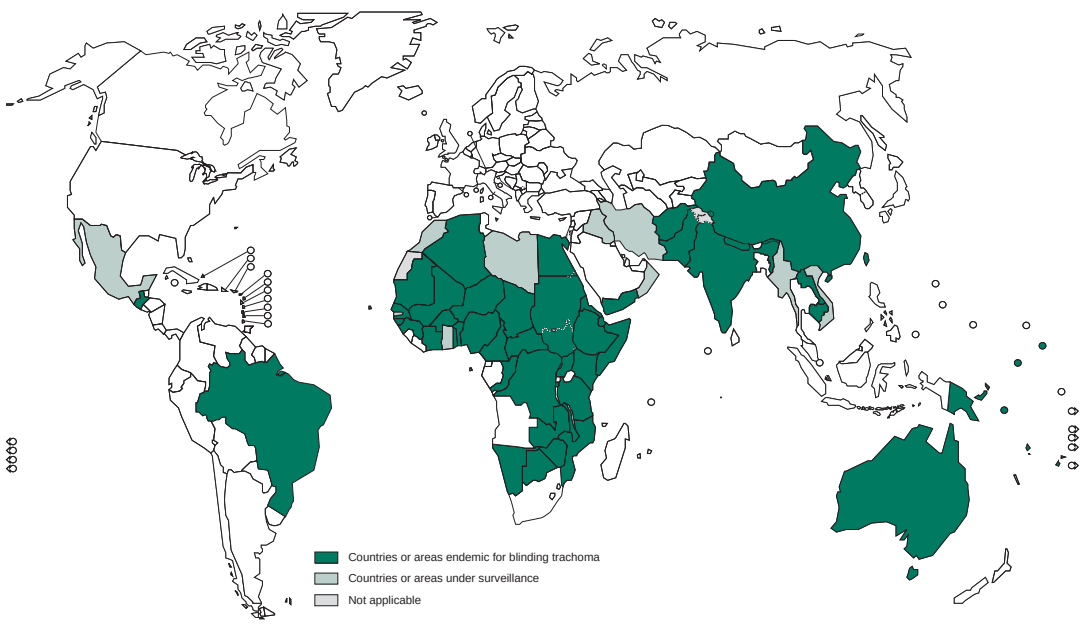
Burden and distribution

An estimated 232 million people live in areas where trachoma is endemic: more than 21 million have active trachoma, 7.2 million require surgery for in-drawn eyelashes (trichiasis) and 1.2 million are irreversibly blind (*2,3*).

Blinding trachoma is endemic in many of the poorest and most remote areas of 53 countries in Africa, Asia, Central and South America, Australia and the Middle East (*Fig. 4.17.1*) (*3*). Africa is the worst affected continent: 18 million cases of active trachoma (85% of all cases globally) and 3.2 million cases of trichiasis (44% of all cases globally) are thought to exist in 29 of the 47 countries in WHO's African Region (*2*). Ethiopia and South Sudan have the highest prevalences of active trachoma: in some areas of these countries, active disease is present in more than 50% of children aged 1–9 years and trichiasis affects more than 10% of adults. The risk of blinding trachoma is greater in women than in men.

In addition to blindness, trichiasis causes pain every time a person blinks. Women with trichiasis have severe difficulties carrying out their daily activities even if they do not have visual impairment or blindness (*4*).

Fig. 4.17.1 Distribution of trachoma, worldwide, 2012



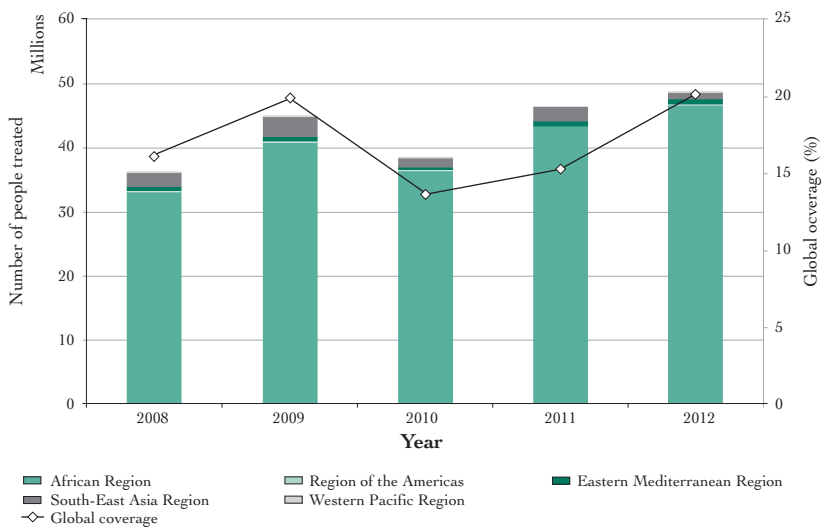
Progress towards Roadmap targets

In 1998, the World Health Assembly resolved to eliminate blinding trachoma as a public-health problem by 2020. Elimination as a public-health problem is defined as a reduction in the prevalence of trichiasis "unknown to the health system" to less than 1 case per 1000 total population ("known" cases are those in whom trichiasis has recurred after surgery, those who refuse surgery, or those yet to undergo surgery whose surgical date is set) (*5*); and a reduction in the prevalence of the active trachoma sign "TF" in children aged 1–9 years to less than 5%.

Elimination of blinding trachoma is technically feasible through implementation of the SAFE strategy, comprising Surgery for individuals with trichiasis; Antibiotics to reduce the reservoir of ocular chlamydial infection; and Facial cleanliness and Environmental improvement to reduce transmission.

Significant progress has recently been made in generating data for programme planning purposes, thanks to strong partnerships anong ministries of health, nongovernmental organizations and research institutions within the Global Trachoma Mapping Project. This ambitious project aims to complete baseline mapping of the global distribution of trachoma in 2015 by completing population-based prevalence surveys in all districts in which trachoma is suspected but where prevalence data are unavailable (*6*). As of April 2014, 1033 districts in 19 countries had been mapped through this project, providing data for an underlying population of 124 million people. Most countries endemic for trachoma have now set target dates for eliminating blinding trachoma (*3*) and have agreed with partners to accelerate implementation of the SAFE strategy. In 2012, 169 121 patients had surgery for trichiasis and nearly 48 million people received antibiotics for trachoma (*3*) (*Fig. 4.17.2*).

Fig. 4.17.2 Number of people treated and global coverage of azithromycin for trachoma, by WHO region, 2008–2012



Alongside rapid scale-up elsewhere, the Gambia, Ghana, the Islamic Republic of Iran, Morocco, Myanmar, Oman and Viet Nam are thought to have reached the elimination targets. In 2012, Oman became the first country to be verified as having achieved national elimination of trachoma (*3*).

Research priorities

Research is needed urgently to: determine the place of alternative diagnostic strategies (to supplement or replace clinical diagnosis) at impact assessment and in trachoma surveillance; to test decision algorithms for discontinuing mass antibiotic treatment; to investigate the efficacy and safety of co-administering azithromycin with other preventive chemotherapy agents; to design strategies for accurately estimating antibiotic coverage; to identify methods for detecting trichiasis cases and encouraging them to seek surgery; and to establish how to most effectively and cost-effectively implement the facial cleanliness and environmental improvement components of the SAFE strategy.

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ANNEXES

Annex 1a. **Resolutions of the World Health Assembly concerning neglected tropical diseases, 1948–2013**

Subject area	Resolution	Title	Year
Neglected tropical diseases	WHA66.12	Neglected tropical diseases	2013
Schistosomiasis	WHA65.21	Elimination of schistosomiasis	2012
Dracunculiasis	WHA64.16	Eradication of dracunculiasis	2011
Chagas disease	WHA63.20	Chagas disease: control and elimination	2010
WHOPES	WHA63.26	Improvement of health through sound management of obsolete pesticides and other obsolete chemicals	2010
Avoidable blindness (for both onchocerciasis and trachoma)	WHA62.1	Prevention of avoidable blindness and visual impairment	2009
Leishmaniases	WHA60.13	Control of leishmaniasis	2007
Avoidable blindness (for both onchocerciasis and trachoma)	WHA59.25	Prevention of avoidable blindness and visual impairment	2006
Buruli ulcer	WHA57.1	Surveillance and control of *Mycobacterium ulcerans* disease (Buruli ulcer)	2004
Human African trypanosomiasis	WHA57.2	Control of human African trypanosomiasis	2004
Dracunculiasis	WHA57.9	Eradication of dracunculiasis	2004
Human African trypanosomiasis	WHA56.7	Pan African tsetse and trypanosomiasis eradication campaign	2003
Avoidable blindness (for both onchocerciasis and trachoma)	WHA56.26	Elimination of avoidable blindness	2003
Dengue and dengue haemorrhagic fever	WHA55.17	Prevention and control of dengue fever and dengue haemorrhagic fever	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
Vector-borne disease	WHA50.13	Promotion of chemical safety, with special attention to persistent organic pollutants	1997
Lymphatic filariasis	WHA50.29	Elimination of lymphatic filariasis as a public health problem	1997
Dracunculiasis	WHA50.35	Eradication of dracunculiasis	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
Dracunculiasis	WHA44.5	Eradication of dracunculiasis	1991
Leprosy	WHA44.9	Leprosy	1991
Research	WHA43.18	Tropical disease research	1990
Dracunculiasis	WHA42.25	International Drinking Water Supply and Sanitation Decade	1989
Dracunculiasis	WHA42.29	Elimination of dracunculiasis	1989
Vector-borne disease	WHA42.31	Control of disease vectors and pests	1989
Leprosy	WHA40.35	Towards the elimination of leprosy	1987
Dracunculiasis	WHA39.21	Elimination of dracunculiasis	1986
Human African trypanosomiasis	WHA36.31	African human trypanosomiasis	1983
Dracunculiasis	WHA34.25	International Drinking Water Supply and Sanitation Decade	1981

Annex 1a (cont'd). Resolutions of the World Health Assembly concerning neglected tropical diseases, 1948–2013

Subject area	Resolution	Title	Year
Leprosy	WHA32.39	Leprosy	1979
Zoonoses	WHA31.48	Prevention and control of zoonoses and foodborne diseases due to animal products	1978
Endemic treponematoses	WHA31.58	Control of endemic treponematoses	1978
Leprosy	WHA30.36	Leprosy control	1977
Research	WHA30.42	Special Programme for Research and Training in Tropical Diseases	1977
Schistosomiasis	WHA29.58	Schistosomiasis	1976
Leprosy	WHA29.70	Leprosy control	1976
Schistosomiasis	WHA28.53	Schistosomiasis	1975
Avoidable blindness (for both onchocerciasis and trachoma)	WHA28.54	Prevention of blindness	1975
Leprosy	WHA28.56	Leprosy control	1975
Research	WHA28.71	WHO's role in the development and coordination of research in tropical diseases	1975
Research	WHA27.52	Intensification of research on tropical parasitic diseases	1974
Leprosy	WHA27.58	Coordination and strengthening of leprosy control	1974
Vector-borne disease	WHA23.33	Research on alternative methods of vector control	1970
Vector-borne disease	WHA22.40	Research on methods of vector control	1969
Vector-borne disease	WHA13.54	Vector-borne diseases and malaria eradication	1960
Leprosy	WHA9.45	Inter-regional conference on leprosy control, 1958	1956
Leprosy	WHA6.19	Expert Committee on Leprosy: first report	1953
Leprosy	WHA5.28	Leprosy	1952
Vector-borne disease	WHA5.29	Supply and requirements of insecticides: world position	1952
Trachoma	WHA4.29	Trachoma	1951
Vector-borne disease	WHA4.30	Supply of insecticides	1951
Rabies	WHA3.20	Rabies	1950
Trachoma	WHA3.22	Trachoma	1950
Hydatidosis	WHA3.23	Hydatidosis	1950
Schistosomiasis and soil-transmitted helminthiases	WHA3.26	Bilharziasis	1950
Vector-borne disease	WHA3.43	Labelling and distribution of insecticides	1950
Vector-borne disease	WHA2.18	Expert Committee on insecticides: report on the first session	1949
Endemic treponematoses	WHA2.36	Bejel and other treponematoses	1949
Leprosy	WHA2.43	Leprosy	1949
Vector-borne disease	WHA1.12	Vector biology and control	1948

Annex 1b. **Resolution WHA66.12 on neglected tropical diseases, 2013**

SIXTY-SIXTH WORLD HEALTH ASSEMBLY **WHA66.12**

Agenda item 16.2 **27 May 2013**

Neglected tropical diseases

The Sixty-sixth World Health Assembly,

Having considered the report on neglected tropical diseases,[1] and recalling the previous World Health Assembly resolutions listed therein;

Recognizing that increased national and international investments in prevention and control of neglected tropical diseases have succeeded in improving health and social well-being in many countries;

Recognizing also the importance of the Global Plan to Combat Neglected Tropical Diseases 2008–2015;

Noting WHO's roadmap to accelerate the work to overcome the global impact of neglected tropical diseases;[1]

Acknowledging the linkages between, and mutual supportiveness of, control and elimination of neglected tropical diseases and the global strategy and plan of action on public health, innovation and intellectual property;

Acknowledging also that expansion of activities to prevent and control neglected tropical diseases will need adequately resourced national programmes functioning within effective health, education and other sectors in order to provide for an uninterrupted supply and delivery of quality-assured commodities and services;

Realizing that current approaches to the prevention and control of neglected tropical diseases, when implemented in an integrated manner and across all relevant sectors, are highly effective and contribute to stronger health systems and the achievement of the health-related Millennium Development Goals, but that there are still many challenges;

Appreciating the generous contribution of pharmaceutical companies in donating sufficient quantities of quality-assured essential medicines for the prevention and treatment of neglected tropical diseases, while acknowledging the need to ensure their continuous availability and affordability;

Recognizing the contribution of bodies in the United Nations system, intergovernmental and nongovernmental organizations, academic institutions and civil society;

[1] Document A66/20.

WHA66.12

Recognizing also the diversity of neglected tropical diseases, their causative agents and relevant vectors and intermediate hosts, their epidemic potential (such as for dengue, Chagas disease, human rabies of canine origin and leishmaniasis), and their morbidity, mortality and associated stigmatization,

1. URGES Member States:

(1) to ensure continued country ownership of programmes for neglected tropical disease prevention, control, elimination and eradication;

(2) to further strengthen the disease surveillance system especially on neglected tropical diseases targeted for eradication;

(3) to expand and implement, as appropriate, interventions against neglected tropical diseases in order to reach the targets agreed in the Global Plan to Combat Neglected Tropical Diseases 2008–2015, as set out in WHO's roadmap for accelerating work to overcome the global impact of neglected tropical diseases and noting the London Declaration on Neglected Tropical Diseases by;

(a) ensuring that resources match national requirements and flow in a sustainable manner as a result of thorough planning and costing of prevention and control activities and detailed analysis of associated expenditures;

(b) enabling improvement of the management of the supply chain, in particular through forecasting, timely procurement of quality-assured goods, improved stock-management systems, and facilitating importation and customs clearance;

(c) integrating neglected tropical diseases control programmes into primary health care services and vaccination campaigns, or into existing programmes where feasible, in order to achieve greater coverage and reduce operational costs;

(d) ensuring appropriate programme management and implementation through the development, sustenance and supervision of a cadre of skilled staff (including other sectors than health) at national, district and community levels;

(4) to advocate predictable, long-term, international financing for the control of neglected tropical diseases;

(5) to enhance and sustain national financial commitments, including resource mobilization from sectors other than health;

(6) to strengthen capacity for prevention and control of neglected tropical diseases, strengthening research, in order to accelerate implementation of the policies and strategies designed to achieve the targets set by the Health Assembly in various resolutions related to specific neglected tropical diseases as well as in the roadmap and the London Declaration;

(7) to strengthen national capacity for monitoring and evaluation of the impact of interventions against neglected tropical diseases;

WHA66.12

(8) to devise plans for achieving and maintaining universal access to and coverage with interventions against neglected tropical diseases, notably:

(a) to provide prompt diagnostic testing of all suspected cases of neglected tropical diseases and effective treatment with appropriate therapy of patients in both the public and private sectors at all levels of the health system including the community level;

(b) to implement and sustain coverage with preventive chemotherapy[1] of at least 75% of the populations in need, as a prerequisite for achieving goals of disease control or elimination;

(c) to improve coordination for reducing transmission and strengthening control of neglected tropical diseases taking into account social determinants of health, through provision of safe drinking-water, basic sanitation, health promotion and education, vector control and veterinary public health, taking into consideration One Health;

2. CALLS upon WHO's international partners, including intergovernmental, international and nongovernmental organizations, financing bodies, academic and research institutions, civil society and the private sector:

(1) to support Member States, as appropriate:

(a) to provide sufficient and predictable funding to enable the targets for 2015 and 2020 to be met and efforts to control neglected tropical diseases to be sustained;

(b) to harmonize the provision of support to countries for implementing a national plan based on WHO-recommended policies and strategies and using commodities that meet international quality standards;

(c) to promote universal access to preventive chemotherapy, and diagnostics, case management, and vector control and other prevention measures, as well as effective surveillance systems;

(2) to encourage initiatives for the research and development of new diagnostics, medicines, vaccines, and pesticides and biocides, improved tools and technologies and other innovative instruments for vector control and infection prevention and to support operational research to increase the efficiency and cost–effectiveness of interventions, taking into account the global strategy and plan of action on public health, innovation and intellectual property;

(3) to collaborate with WHO in order to provide support to Member States in measuring progress towards, and in accomplishing, their goals of elimination and eradication of selected neglected tropical diseases;

[1] Preventive chemotherapy means large-scale preventive treatment against helminthiases and trachoma with safe, single-dose, quality-assured medicines.

3. REQUESTS the Director-General:

(1) to sustain WHO's leadership in the drive to overcome neglected tropical diseases;

(2) to support the development and updating of evidence-based norms, standards, policies, guidelines and strategies and research for prevention, control and elimination of neglected tropical diseases in order to chart a course for reaching the related targets set in resolutions of the Health Assembly;

(3) to monitor progress in achieving the targets for neglected tropical diseases set in WHO's roadmap for accelerating work to overcome the global impact of neglected tropical diseases, and to provide support to Member States in their efforts to collect, validate and analyse data from national surveillance systems;

(4) to provide support to Member States to strengthen human resource capacity for prevention, diagnosis and control of neglected tropical diseases, including vector control and veterinary public health;

(5) to encourage and support initiatives to discover and obtain new diagnostic tools, medicines and vector control measures, and to support operational research to increase the efficacy and cost–effectiveness of interventions;

(6) to report, through the Executive Board, to the Sixty-eighth World Health Assembly on progress towards the elimination and eradication of targeted diseases.

Ninth plenary meeting, 27 May 2013
A66/VR/9

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Annex 2. **Roadmap targets for eradicating and eliminating neglected tropical diseases, at a glance***

Disease	2015				2020			
	Eradication	Global elimination	Regional elimination	Country elimination	Eradication	Global elimination	Regional elimination	Country elimination
Rabies			√ Latin America				√ Latin America	
Blinding trachoma						√		
Endemic treponematoses (yaws)					√			
Leprosy						√		
Chagas disease			√ Transmission through blood transfusion interrupted				√ Intra-domiciliary transmission interrupted in the Region of the Americas	
Human African trypanosomiasis				√ In 80% of foci		√		
Visceral leishmanisis							√ Indian subcontinent	
Dracunculiasis	√							
Lymphatic filariasis						√		
Onchocerciasis			√ Latin America					√ Selectd countries in Africa
Schistosomiasis			√ Eastern Mediterranean Region, Caribbean, Indonesia and the Mekong River basin				√ Region of the Americas and Western Pacific Region	√ Selected countries in Africa

*Adapted from *Accelerating work to overcome the global impact of neglected tropical diseases: a roadmap for implementation.* Geneva: World Health Organization; 2012 (WHO/HTM/NTD/2012.1).

Annex 3. **Classification of countries by income status***

Income status	Countries
Low-income	Countries with GNI per capita, calculated using the World Bank Atlas method, of US$ 1045 or less in 2013. This group includes: Afghanistan, Bangladesh, Benin, Burkina Faso, Burundi, Cambodia, Central African Republic, Chad, Comoros, Democratic People's Republic of Korea, Democratic Republic of the Congo, Eritrea, Ethiopia, Gambia, Guinea, Guinea-Bissau, Haiti, Kenya, Kyrgyzstan, Liberia, Madagascar, Malawi, Mali, Mozambique, Myanmar, Nepal, Niger, Rwanda, Sierra Leone, Somalia, South Sudan, Tajikistan, Togo, Uganda, United Republic of Tanzania and Zimbabwe.
Middle-income	Countries with GNI per capita, calculated using the World Bank Atlas method, of more than US$ 1045 but less than US$ 12 746. This group includes both lower-middle and upper-middle-income countries. See lower-middle-income and upper-middle-income for lists of countries.
Lower-middle-income	Countries with GNI per capita, calculated using the World Bank Atlas method, of more than US$ 1045 but less than US$ 4125. This group includes: Armenia, Bhutan, Bolivia (Plurinational State of), Cape Verde, Cameroon, Congo, Côte d'Ivoire, Djibouti, Egypt, El Salvador, Georgia, Ghana, Guatemala, Guyana, Honduras, India, Indonesia, Kiribati, Lao People's Democratic Republic, Lesotho, Mauritania, Micronesia (Federated States of), Mongolia, Morocco, Nicaragua, Nigeria, Pakistan, Papua New Guinea, Paraguay, Philippines, Republic of Moldova, Samoa, Sao Tome and Principe, Senegal, Solomon Islands, Sri Lanka, Sudan, Swaziland, Syrian Arab Republic, Timor-Leste, Ukraine, Uzbekistan, Vanuatu, Viet Nam, Yemen and Zambia.
Upper-middle-income	Countries with GNI per capita, calculated using the World Bank Atlas method, of more than US$ 4125 but less than US$ 12 746. This group includes: Albania, Algeria, Angola, Argentina, Azerbaijan, Belarus, Belize, Bosnia and Herzegovina, Botswana, Brazil, Bulgaria, China, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, Fiji, Gabon, Grenada, Hungary, Iran (Islamic Republic of), Iraq, Jamaica, Jordan, Kazakhstan, Lebanon, Libya, Malaysia, Maldives, Marshall Islands, Mauritius, Mexico, Montenegro, Namibia, Palau, Panama, Peru, Romania, Saint Lucia, Saint Vincent and the Grenadines, Serbia, Seychelles, South Africa, Suriname, Thailand, The Former Yugoslav Republic of Macedonia, Tonga, Tunisia, Turkey, Turkmenistan, Tuvalu and Venezuela (Bolivarian Republic of).

GNI, gross national income.

* Source: World Bank country and lending groups (http://data.worldbank.org/about/country-and-lending-groups).

Annex 4. **Linkages between neglected tropical diseases and water, sanitation and hygiene**

Neglected Tropical Disease (NTD)	Linkage with water, sanitation and hygiene (WASH)
Dengue	Drinking-water storage in and around the household can create breeding places for the vector mosquitoes. Access (for example: remote wells), availability (for example: rainwater harvesting to bridge brief periods of drought) and reliability (for example: where piped water services are not guaranteed 24/7) are determining factors for household water storage. Safe storage requires adequate containers as well as practices such as closing containers and regular cleaning.
Dracunculiasis (guinea-worm disease)	Worms are transmitted through ingestion of water fleas in contaminated water. WASH control measures include water source protection, treatment of contaminated water sources with insecticide (temephos) and water filtration. Success towards eliminating this disease over the past 25 years includes how a focus on drinking-water quality can make a major contribution to an integrated public-health programme. Where the infection has been seen to rebound, mostly in areas of humanitarian crises where the delivery of health services is interrupted, reliance on water filtering practices has provided a certain level of resilience.
Foodborne trematodiases	The eggs of liver, lung and intestinal flukes are released with faeces into open water and are ingested by aquatic snails. Human infection occurs when secondary intermediate hosts (fish, crustaceans, molluscs or aquatic plants) are eaten raw. Required interventions are prevention of faecal contamination of freshwater bodies due to lack of sanitation or poor hygiene behaviour, and improving cooking habits.
Lymphatic filariasis	**Transmission:** The *Culex* vectors prefer breeding in organically polluted water as well as in faecal matter found in poorly-constructed pit latrines. Necessary interventions include construction, maintenance and management (including pit emptying and disposal) of improved latrines, maintaining sewers, phasing out open sewerage systems, infrastructure upgrading and mosquito proofing of existing systems for wastewater management. **Morbidity management**: access to sufficient clean water is needed to practise hygiene behaviours such as limb-washing in order to reduce the severity of disease symptoms.
Schistosomiasis	Infection via eggs of worms in human faeces and urine deposited in water where emerging larvae enter freshwater snails. After development in snail, larvae forms emerge in water and penetrate skin during contact with infested water. Control measures include snail control, improved sanitation and health education and reduced contact with surface water. This is probably the most researched disease in terms of environmental management interventions, including the provision of sanitation facilities to prevent contamination of open waters, hydraulic infrastructures and water management to eliminate snail intermediate hosts, and the provision of safe recreational waters such as swimming pools, and efforts to induce behavioural change both in terms of proper use of sanitation and avoiding contact with contaminated water. The lessons learned indicate that none of these measures by itself will lead to sustained success – just like case detection and treatment programmes will remain without an end-point as long as the environment and social risk factors are not tackled. Dealing with the environmental factors effectively is often economically not feasible, while lasting behavioural change has proved hard to achieve. Yet, applying a combination of measures in an intersectoral context has shown to produce lasting results in specific settings.
Soil-transmitted helminthiases (ascariasis, hookworm, trichuriasis)	Eggs ingested through contaminated vegetables or water, or directly bychildren placing soil in mouth; hookworm larvae penetrate skin when walking barefoot on contaminated soil (no direct person-to-person transmission). Prevention requires improved sanitation and hygiene (hand-washing). Of all the NTDs, this group of infections will benefit the most from the elimination of open defecation and safe management of excreta, and reduced transmission risks will translate into improved nutritional status, increased productivity, enhanced learning capacity and reduced costs for the health sector. The other area where WASH can contribute to the reduction of helminthiases is in the promotion of safe use of wastewater in agriculture and aquaculture. An increasingly important practice around urban centres in water-scarce parts of the world, WHO guidance on safe use practices aims to protect agricultural workers, peri-urban communities involved in wastewater-supported agriculture and the consumers of their produce.2
Trachoma	Transmission occurs between infected persons through flies. Full implementation of the SAFE strategy for trachoma control (Surgery, Antibiotics, Facial cleanliness and Environmental improvement) is required to achieve elimination. The SAFE strategy offers the most comprehensive WASH-NTDs framework and firmly embeds the need for environmental and promotive health measures alongside medical interventions. WASH interventions are crucial for the delivery of the F and E aspects of the SAFE strategy, through improved sanitation in order to reduce fly numbers and transmission of infection from person to person; and through hygiene by promoting washing of children's faces as well as improving overall personal hygiene (such as laundry). All hygiene behaviours require increased access to a reliable and sufficient supply of water and soap.

Annex 5. **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

Annex 6. **Methods used to prepare maps and charts**

Population

The total population of each country is taken from *World population prospects: the 2012 revision* (*1*). In some cases, the population of children aged 1–4 years and 5–14 years is also given since these are the age groups specifically targeted for anthelminthic treatments.

Preventive chemotherapy data

Unless otherwise specified, data on preventive chemotherapy are as provided by national authorities to WHO through reporting processes in country and regional offices using standardized templates. Maps and charts for lymphatic filariasis, soil-transmitted helminthiases, schistosomiasis, onchocerciasis and trachoma were prepared using data reported to WHO annually. Information from the Preventive Chemotherapy and Transmission Control (PCT) databank was used to compile sections of this report, and is accessible online (*2*).

The main definitions of data used to describe preventive chemotherapy are as follows:

- **population requiring preventive chemotherapy** – the total population living in all endemic areas that requires preventive chemotherapy;
- **geographical coverage** – the proportion (%) of endemic districts covered by preventive chemotherapy;
- **programme coverage** – the proportion (%) of individuals who were treated according to the programme's target;
- **national disease-specific coverage** – the proportion (%) of individuals in the population requiring preventive chemotherapy for the specific disease that was treated.

Dracunculiasis data are reported weekly to WHO by national authorities that provide updates on the status of the eradication initiative at the country level as well as related epidemiological information.

Foodborne trematodiases data are based on information obtained from peer-reviewed publications, and supplemented by the opinions of international experts.

Innovative and intensified disease-management data

Data for neglected tropical diseases in which the large-scale use of existing tools is limited have been obtained by various non-integrated methods that depend on the particulars of the disease-control programme. Details of the data sources are given below.

- **Buruli ulcer** data are reported to WHO annually by national authorities using a standardized template;
- **Chagas disease** data are reported to WHO as official estimates and endorsed through a consultative process among national authorities and international experts;
- **Endemic treponematoses** data are reported to WHO annually by national authorities using a standardized template;
- **Human African trypanosomiasis** data are reported to WHO annually by national authorities using a standardized template;
- **Leishmaniases** data are reported to WHO annually by national authorities using a standardized template;
- **Leprosy** data are reported to WHO annually by national authorities using a standardized template.

Vector ecology and management data

- **Dengue** data are reported to WHO annually by national authorities using a standardized template.

Veterinary public health data

- **Cysticercosis** data are based on information obtained from peer-reviewed publications, and supplemented by the opinions of international experts;
- **Echinococcosis** data are based on information obtained from peer-reviewed publications and the opinions of international experts;
- **Rabies** data are based on information obtained from peer-reviewed publications, and supplemented by the opinions of international experts.

Sources of information for figures and chapters

Sources of information are mostly indicated in each figure and specific chapter. All reasonable precautions have been taken to verify and confirm the accuracy of the information contained in this publication.

REFERENCES

[1] World population prospects: the 2012 revision. New York (NY): United Nations Population Division; 2013 (http://esa.un.org/wpp/index.htm; accessed October 2014).

[2] PCT databank. Geneva: World Health Organization; 2014 (http://www.who.int/neglected_diseases/preventive_chemotherapy/databank/en/; accessed October 2014).

WHO REGIONAL OFFICES

Regional Office for Africa
Cité du Djoué, P.O. Box 06
Brazzaville, Republic of the Congo
Telephone: +47 241 39100 / +47 242 770 02 02
Fax: +47 241 39503
E-mail: postmaster@afro.who.int

Regional Office for the Americas
525, 23rd Street, N.W.
Washington, DC 20037, USA
Telephone: +1 202 974 3000
Facsimile: +1 202 974 3663
E-mail: postmaster@paho.org

Regional Office for South-East Asia
World Health House
Indraprastha Estate
Mahatma Gandhi Marg
New Delhi 110 002, India
Telephone: +91 11 2337 0804 / 2337 0809-11
Facsimile: +91 11 2337 0197 / 2337 9395 / 2337 9507
E-mail: postmaster@searo.who.int

Regional Office for Europe
Regional Office for Europe
UN City, Marmorvej 51
2100 Copenhagen Ø, Denmark
Telephone: +45 45 33 7000
Facsimile: +45 45 33 7001
E-mail: postmaster@euro.who.int

Regional Office for the Eastern Mediterranean
Monazamet El Seha El Alamia Street
Extension of Abdel Razak El Sanhouri Street
P.O. Box 7608, Nasr City
Cairo 11371, Egypt
Telephone: +20 2 2276 5000
Fax: +20 2 2670 2492 / +20 2 2670 2494
E-mail: postmaster@emro.who.int

Regional Office for the Western Pacific
P.O. Box 2932
1000 Manila, Philippines
Telephone: +63 2 528 8001
Fax: +63 2 521 1036 / 526 0279
E-mail: postmaster@wpro.who.int

The presence, or absence, of neglected tropical diseases (NTDs) can be seen as a proxy for poverty and for the success of interventions aimed at reducing poverty. Today, coverage of the public-health interventions recommended by the World Health Organization (WHO) against NTDs may be interpreted as a proxy for universal health coverage and shared prosperity – in short, a proxy for coverage against neglect.

As the world's focus shifts from development to sustainable development, from poverty eradication to shared prosperity, and from disease-specific goals to universal health coverage, control of NTDs will assume an important role towards the target of achieving universal health coverage, including individual financial risk protection. Success in overcoming NTDs is a "litmus test" for universal health coverage against NTDs in endemic countries.

The first WHO report on NTDs (2010) set the scene by presenting the evidence for how these interventions had produced results. The second report (2013) assessed the progress made in deploying them and detailed the obstacles to their implementation. This third report analyses for the first time the investments needed to achieve the scale up of implementation required to achieve the targets of the WHO Roadmap on NTDs and universal coverage against NTDs.

INVESTING TO OVERCOME THE GLOBAL IMPACT OF NEGLECTED TROPICAL DISEASES presents an investment strategy for NTDs and analyses the specific investment case for prevention, control, elimination and eradication of 12 of the 17 NTDs. Such an analysis is justified following the adoption by the Sixty-sixth World Health Assembly in 2013 of resolution WHA6612 on neglected tropical diseases, which called for sufficient and predictable funding to achieve the Roadmap's targets and sustain control efforts.

The report cautions, however, that it is wise investment and not investment alone that will yield success.

The report registers progress and challenges and signals those that lie ahead. Climate change is expected to increase the spread of several vector-borne NTDs, notably dengue, transmission of which is directly influenced by temperature, rainfall, relative humidity and climate variability primarily through their effects on the vector. Investments in vector-borne diseases will avoid the potentially catastrophic expenditures associated with their control. The presence of NTDs will thereby signal an early warning system for climate-sensitive diseases.

The ultimate goal is to deliver enhanced and equitable interventions to the most marginalized populations in the context of a changing public-health and investment landscape to ensure that all peoples affected by NTDs have an opportunity to lead healthier and wealthier lives.

Department of Control of Neglected Tropical Diseases

http://www.who.int/neglected_diseases

World Health Organization

20, Avenue Appia
CH-1211 Geneva 27
Tel: +41 22 791 2111
Fax: +41 22 791 3111
Visit WHO at www.who.int

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