

# Rescuing the bottom billion through control of neglected tropical diseases

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People in the bottom billion are the poorest in the world; they are often subsistence farmers, who essentially live on no money and are stuck in a poverty trap of disease, conflict, and no education.<sup>1,2</sup> One of the most potent reinforcements of the poverty trap is the neglected tropical diseases (panel 1).<sup>3</sup> Almost everyone in the bottom billion has at least one of these diseases. Several diseases coexist in 56 of 58 countries that are home to the people in the bottom billion.<sup>3</sup> Here we outline low-cost opportunities to control the neglected tropical diseases through preventive chemotherapy, and propose financial innovations to provide poor individuals with essential drugs.

13 parasitic (helminthic and protozoan) and bacterial tropical infections, and dengue are the highest-burden neglected tropical diseases; another 20 include fungal, viral, and ectoparasitic infections (panel 2).<sup>3,4</sup> Seven diseases are noteworthy because of their high prevalence and amenability to control. These are the soil-transmitted helminth infections (hookworm, ascariasis, and trichuriasis); lymphatic filariasis; schistosomiasis; and diseases that cause blindness—trachoma and onchocerciasis (river blindness; table 1). About 600–800 million people, mostly children, have the soil-transmitted helminth infections.<sup>3</sup> Of these, hookworm infection, which causes childhood and maternal anaemia, results in the greatest disability, and is the highest-burden neglected tropical disease.<sup>3,4</sup> Among 200 million people with schistosomiasis, adolescents and young adults (15–25 years) have the highest infection intensities, as measured by numbers of eggs in stool or urine, and the most severe adverse effects—anaemia, wasting, and pain.<sup>9</sup> Another 120 million people have lymphatic

filariasis; most are adults and have lymphoedema, hydrocele, and disfiguring elephantiasis.<sup>3</sup> Trachoma and onchocerciasis arise in about 84 million and 37 million people, respectively.<sup>3</sup> In addition to these seven diseases, the vector-borne arboviral and protozoan diseases, including dengue, leishmaniasis, Chagas disease, and human African trypanosomiasis, can result in high mortality in some disadvantaged areas.

The seven main diseases often cluster in the same rural geographic regions (figure 1), where commonly one person is concurrently infected with several of the seven neglected tropical diseases.<sup>3,4</sup> Infections can last for decades and cause severe disability and disfigurement, with profound economic, social, and political consequences.<sup>3,11,12</sup> The core group of 13 neglected tropical diseases results in roughly 57 million disability-adjusted life years lost, which are greater than those for malaria and tuberculosis.<sup>4</sup> More than 90% of this disease burden results from the seven major diseases.<sup>4</sup> Three features of these diseases have brought them to international attention: they lead to poverty; low-cost and highly cost-effective control approaches might eliminate some of the diseases and create universal access to essential medicines; and control of these diseases would have simultaneous and sustainable effects on poverty reduction.

The economic effects of disease control have been shown around the world since the early 20th century.<sup>13</sup> Investment in disease control could rescue the people in the bottom billion through its effect on four key elements of the poverty trap: health (especially maternal and child), agriculture, education, and infrastructure.<sup>2</sup>

Several major neglected tropical diseases adversely affect a family's economic potential through their debilitating effect on the health of children. The soil-transmitted helminth infections and schistosomiasis impair children's growth, development, and physical fitness.<sup>3,4</sup> Hookworm infection and schistosomiasis also reduce child survival by causing severe anaemia during pregnancy, which leads to low birthweight and increased infant and maternal mortality.<sup>14</sup> In Africa, anaemia caused by hookworm infection can exacerbate the clinical course of falciparum malaria, especially in children and women.<sup>15</sup> For diseases, such as leishmaniasis, the treatment can easily cost a family's income for the year and lead to sale of assets (eg, land and livestock).<sup>16</sup>

Because they arise mainly in rural areas where families depend on subsistence agriculture, the neglected tropical diseases impair agricultural productivity.

## Panel 1: Poverty-promoting features of neglected tropical diseases

### Reduced child survival

Hookworm infection; ascariasis; trichuriasis; schistosomiasis

### Costs of treatments and seeking inappropriate or ineffective health care

Leishmaniasis; lymphatic filariasis; onchocerciasis; human African trypanosomiasis

### Reduced agricultural productivity

Lymphatic filariasis; onchocerciasis; trachoma; hookworm infection; schistosomiasis; dracunculiasis

### Educational effects

Hookworm infection; trichuriasis; ascariasis; schistosomiasis; onchocerciasis

**Panel 2: Neglected tropical diseases****Helminth infections**

Ascariasis;\* trichuriasis;\* hookworm infection;\* strongyloidiasis; toxocariasis and larva migrans; lymphatic filariasis;\* onchocerciasis;\* loiasis; dracunculiasis;\* schistosomiasis;\* food-borne trematodiasis; taeniasis cysticercosis; echinococcosis

**Protozoan infections**

Leishmaniasis;\* Chagas disease;\* human African trypanosomiasis;\* amoebiasis; giardiasis; balantidiasis

**Bacterial infections**

Bartonellosis; bovine tuberculosis; buruli ulcer;\* leprosy;\* leptospirosis; relapsing fever; rheumatic fever; trachoma;\* treponematoses

**Viral infections**

Dengue fever; yellow fever; Japanese encephalitis; rabies; haemorrhagic fevers

**Fungal infections**

Mycetoma; paracoccidiomycosis

**Ectoparasitic infections**

Scabies; myiasis; tungiasis

\*13 core neglected tropical diseases.

Agricultural activity is reduced directly from impaired worker productivity and hence reduced harvests, or indirectly by reduction of food security when farmers are forced to flee fertile areas because of high rates of endemic diseases. The seven main diseases have a particularly devastating effect on agricultural labour. Workers with lymphatic filariasis and chronic, irreversible lymphoedema of the lower limbs, and hydrocele have substantially reduced agricultural productivity or, in some cases, they are forced to stop working altogether.<sup>12,17</sup> Similarly, blindness, resulting from trachoma or onchocerciasis,<sup>18,19</sup> and anaemia, which might arise in adults because of hookworm disease and schistosomiasis,<sup>4,15</sup> have pronounced effects on agricultural worker productivity. Furthermore, when neglected tropical diseases become pervasive, subsistence farmers are often forced to migrate, even if the new locations have poor-quality soil and climate.<sup>20</sup> When rates of river blindness reach 10% in an agricultural community, the land is often abandoned.<sup>20</sup> But the return of arable land from onchocerciasis control results in an economic rate of return of up to 18%.<sup>18,20</sup>

Paediatric infections with soil-transmitted helminths and schistosomes are associated with a reduction in education and school performance and attendance, and adverse effects on future earnings.<sup>13,21–24</sup> These effects result, in part, from impairments in cognition and memory, as has been shown for chronic hookworm infection,<sup>13,22</sup> trichuriasis,<sup>23</sup> and schistosomiasis.<sup>24</sup> But

deworming programmes have shown that intervention against neglected tropical diseases in childhood is a highly cost-effective approach to improvement of education.<sup>21,25</sup>

**An investment of US\$3·50 per child on disease control could result in the gain of an extra school year.<sup>25</sup>**

Because these diseases prevent the achievement of the first six Millennium Development Goals,<sup>3</sup> their control with low-cost and cost-effective interventions could start long-term economic growth and development. Reduction of disease burden or interference with transmission of neglected tropical diseases through population-based chemotherapy was introduced in the 1920s. Examples of success since then include mass drug administration with diethylcarbamazine, and selective treatment or administration of diethylcarbamazine-medicated salt to interrupt the transmission of lymphatic filariasis.<sup>26</sup> Similarly, vector control followed by mass treatment with ivermectin led to the control of onchocerciasis in ten west African countries,<sup>20</sup> whereas azithromycin treatment and the SAFE (surgery, antibiotics, face cleanliness, and environmental improvement) strategy have eliminated trachoma that causes blindness in Morocco, Oman, and Iran, as reported to WHO,<sup>27</sup> and multidrug treatment has eliminated leprosy as a public health problem in more than 93 countries.<sup>28</sup> The efficacy of mass treatment was confirmed in a systematic review of randomised controlled trials.<sup>29</sup> Because the major multinational pharmaceutical companies provide many of the drugs used for mass treatment free of charge (whereas other drugs are available as low-cost generics), this approach is one of the most cost-effective global public health control measures.<sup>3</sup> Mass drug administration for neglected tropical diseases also provides some of the highest rates of economic return in any public health programmes, often from 15–30%, and addresses fundamental human-rights issues.<sup>3,11,28,30</sup> Public-private partnerships working with WHO, the World Bank, and other UN agencies are providing mass drug administration to millions of people every year, leading to control and, in some cases, elimination of neglected tropical diseases.<sup>3,31</sup> In sub-Saharan Africa, the network of more than 162 000 community-based drug distributors that provide mass treatment has strengthened health services by adding interventions such as vitamin A distribution, childhood vaccinations, and antimalarial bednets; improving national surveillance and monitoring systems; and strengthening operational research and laboratory services.<sup>3,20,28</sup>

Figure 2 shows the estimated current coverage of the main diseases with mass drug administration. Efficiency and effectiveness of mass treatment could be increased through the integration of several vertical disease control programmes.<sup>3,4,28,31</sup> In 2005–06, a low-cost rapid effect package of four drugs—albendazole or mebendazole, and praziquantel, ivermectin or diethylcarbamazine, and azithromycin—was developed to simultaneously target the seven major neglected tropical diseases.<sup>3–5,31</sup>

For more on neglected tropical diseases see <http://www.plosntds.org> and <http://www.globalnetwork.org>

Integration provides cost savings of almost 50%.<sup>31</sup> To further increase efficiencies, several public–private partnerships created an alliance, the Global Network for Neglected Tropical Diseases, to begin a global campaign for integrated control in 56 countries where at least five major diseases are coendemic.<sup>3</sup> WHO has published preventive chemotherapy guidelines for countries with the highest disease burden,<sup>5</sup> and a Bill & Melinda Gates

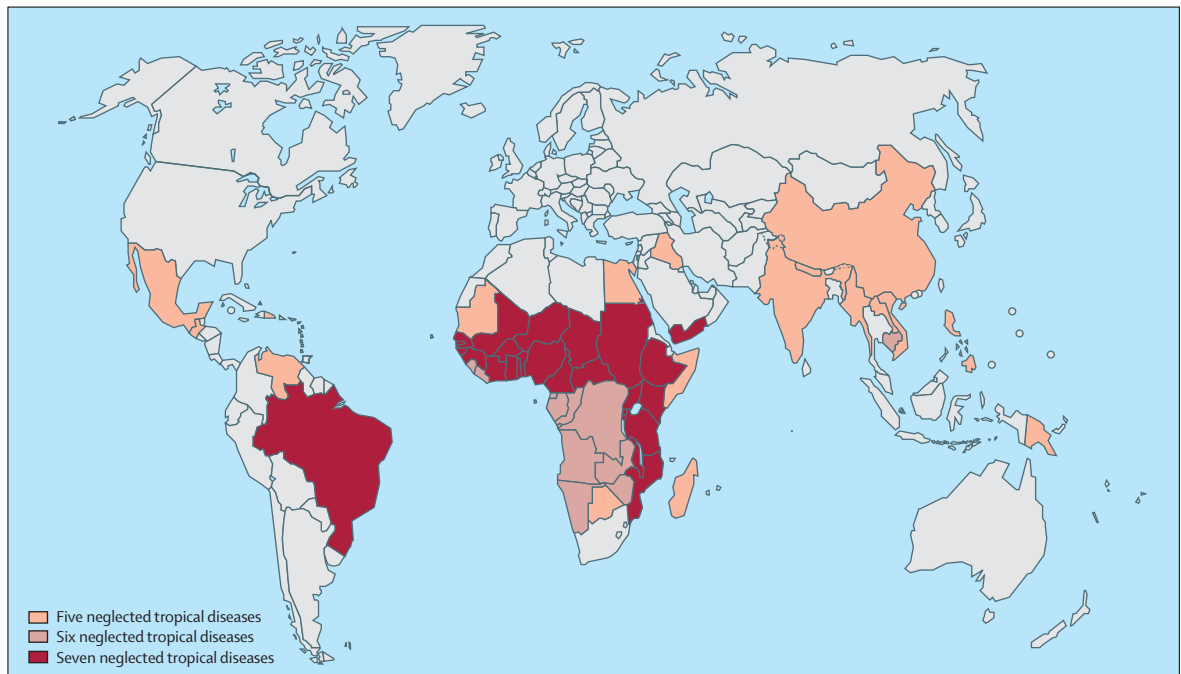
Foundation programme of implementation research will assess the public health and economic efficiencies of integration.

The control of high-burden neglected tropical diseases in low-income countries will depend on sustainable, although not indefinite, external financial assistance.<sup>33</sup> On the basis of estimates that \$0.40–0.50 per person per year is needed for integrated control, about

	Disability-adjusted life years	Deaths	Approximate global prevalence	Approaches to control
High-prevalence diseases	14.9–52.1 million	24 000–415 000	1.0–1.2 billion	MDA with rapid effect package
Hookworm infection	1.8–22.1 million	3000–65 000	600 million	MDA with rapid effect package or albendazole
Ascariasis	1.2–10.5 million	3000–60 000	800 million	MDA with rapid effect package or albendazole or mebendazole
Trichuriasis	1.6–6.4 million	3000–10 000	600 million	MDA with rapid effect package or albendazole or mebendazole
Lymphatic filariasis	5.8 million	<500	120 million	MDA with rapid effect package or diethylcarbamazine+albendazole or ivermectin+albendazole
Schistosomiasis	1.7–4.5 million	15 000–280 000	200 million	MDA with rapid effect package or praziquantel
Trachoma	2.3 million	<500	84 million	SAFE strategy with azithromycin
Onchocerciasis	0.5 million	<500	37 million	MDA with rapid effect package or ivermectin
Vector-borne protozoan and viral diseases	5.0 million	132 000	70 million	Integrated vector management or case detection and management or both
Dengue fever	0.7 million	19 000	50 million	Integrated vector management
Leishmaniasis	2.1 million	51 000	12 million	Case detection and management, and integrated vector management
Chagas disease	0.7 million	14 000	8–9 million	Integrated vector management
Human African trypanosomiasis	1.5 million	48 000	<0.1 million	Case detection and management, and tsetse control

Data from Hotez and colleagues,<sup>34</sup> WHO,<sup>3,7</sup> and Bethony and colleagues.<sup>8</sup> MDA=mass drug administration. SAFE=surgery, antibiotics, face cleanliness, and environmental improvement.

**Table 1: High-prevalence and other vector-borne neglected tropical diseases**

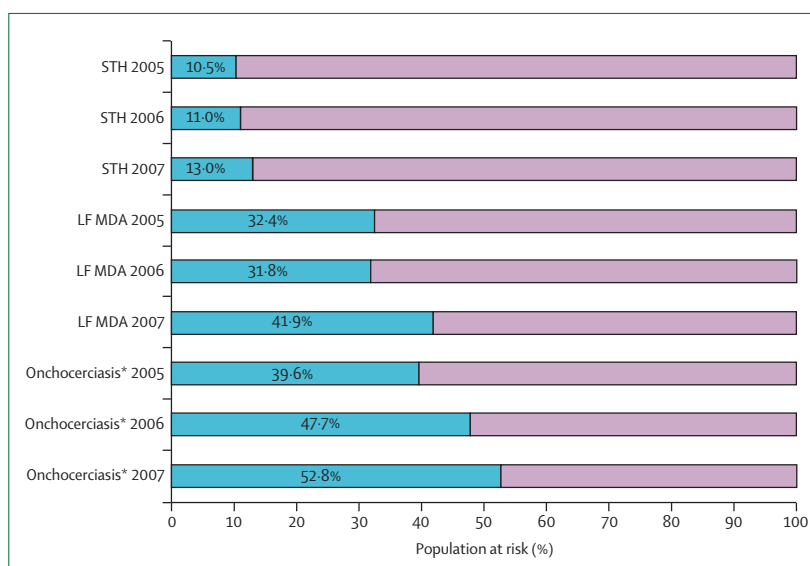


**Figure 1: Map showing geographic overlap and distribution of the seven most common neglected tropical diseases**  
Reproduced with permission from Hotez.<sup>10</sup>

\$2–3 billion will be needed over the next 5–7 years to effect a sustained global assault on the seven major diseases affecting the people in the bottom billion.<sup>3</sup> This amount includes funds for monitoring, assessment, and parallel operational research, and for strengthening health systems. A long-term strategy also requires additional funds for new drugs, diagnostic materials, insecticides, and vaccines.<sup>3</sup> Control of neglected tropical diseases remains mainly a responsibility for the public sector.<sup>33</sup> In 2008, the UK Department for International Development committed £50 million and the US Government committed \$350 million for disease control within the next 5 years. However, the US commitment must still be authorised and appropriated by the US Congress. Additional funds are needed to complete elimination efforts for guinea worm, leprosy, and other neglected tropical diseases.

Global financing mechanisms for neglected tropical diseases should take into consideration several principles. First, disease-control programmes must be nationally owned, embedded in national health plans, and backed by political commitment.<sup>33</sup> The central role of WHO and the national health ministries in the countries with endemic diseases must also be recognised, besides the work of the partners of the Global Network for Neglected Tropical Diseases, the Carter Center, and other major non-governmental development organisations, and the affected communities. Up till now, community-directed interventions, especially those done through the African Programme for Onchocerciasis Control have been highly successful, even in some fragile nations where few other health programmes exist.<sup>20</sup> This community involvement needs to be maintained and become part of the overall health services. Improvements in health resource tracking would help monitor governance performance measures and provide better accountability for national ownership and the partners.<sup>34</sup> An initial meeting of the global partners for neglected tropical diseases was convened by WHO in 2007, and a regular meeting must be established under the auspices of the UN.<sup>33</sup>

Even with adequate funding, there are many challenges to global disease control. Some of the most fragile countries are characterised by poor governance, authoritarian regimes, suppression of human rights, conflict, and marginalisation of particular ethnic groups; their neglected populations will continue to be denied access to essential medicines and basic services.<sup>11,28</sup> Disenfranchised populations, including refugees, migrants, and ethnic minorities in conflict with central governments, are particularly vulnerable to these tropical diseases.<sup>3,4,11,28</sup> Civil conflict or unrest and health service collapse are intimately related to neglected tropical diseases. A few well reported examples include lymphatic filariasis in Myanmar, leishmaniasis and Chagas disease in Colombia and Mexico, dracunculiasis in Ghana and Sudan, and onchocerciasis and human



**Figure 2: Epidemiological coverage of the five major neglected tropical diseases**

Epidemiological coverage shown is the proportion of the population at risk in the country that has been treated with preventive chemotherapy. Population at risk is the total population living in all the endemic areas in a country and needing preventive chemotherapy. For soil-transmitted helminths (STH) target population is children aged from 1 year to 15 years. Modified from WHO.<sup>33</sup> LF=lymphatic filariasis. MDA=mass drug administration. \*Data for sub-Saharan Africa only.

	Total number of tablets	Share of global need	Sources
Albendazole	3.39 billion	49%	Donation by GlaxoSmithKline
Mebendazole	0.25 billion	49%	Donation by Johnson & Johnson as substitute for albendazole
Diethylcarbamazine	4.56 billion	63%	Procurement by Brazil, India, Thailand, and WHO
Praziquantel	0.10 billion	5%	Donation by Merck KGaA and MedPharm
Ivermectin	1.97 billion	100%	Donation by Merck & Co
Azithromycin	500 million	30%	Donation by Pfizer

Reproduced with permission from WHO.<sup>35</sup> 100% albendazole is donated by GlaxoSmithKline for lymphatic filariasis programme.

**Table 2: Total amount of medicines for neglected tropical diseases provided by donation and direct procurement**

African trypanosomiasis in Angola, Democratic Republic of the Congo, and Sudan.<sup>3,11,28</sup>

More drugs, provided at no cost, are required to scale up preventive chemotherapy.<sup>33</sup> However, multinational pharmaceutical companies that donate drugs for neglected tropical diseases might not have the capacity to scale up at the rate needed for immediate global control. Moreover, increased demand for these drugs could reduce the availability of raw materials used in manufacture.<sup>33</sup> A WHO business plan to procure essential medicines for the expansion of preventive chemotherapy showed that less than 5% of the praziquantel estimated to be needed between 2008 and 2012 is being donated, and only half the necessary albendazole, mebendazole, and diethylcarbamazine (table 2).<sup>35</sup> Global financing of disease control should

take into consideration the ability of pharmaceutical manufacturers to produce the drugs at a scale commensurate with need.

Funds should be earmarked for monitoring and evaluation, and for operational aspects of integration of control of neglected tropical diseases as a routine activity of national health systems at all levels. Large-scale drug distribution for the seven major diseases has the risk of drug resistance, just as it does for malaria, tuberculosis, and HIV/AIDS.<sup>3</sup> The possibility of resistance must be anticipated; therefore global financing mechanisms should take into consideration investments for new anthelmintic drugs and vaccines, especially for hookworm infection and other neglected tropical diseases.<sup>3,4</sup> Additional support must be considered for the control (including case detection and management, and intensified vector management) of the selected vector-borne diseases other than the seven major neglected tropical diseases (table 1). Global financing for neglected tropical diseases should also support research and development for new diagnostic agents, drugs, insecticides, and vaccines.

Over the next few years the funds so far committed by the G8 nations will probably represent only a small fraction of those needed for the global control of the seven major diseases. No other major commitments exist for the control of other important vector-borne neglected tropical diseases or for research. Global financing for these diseases must be created to encourage additional private investments like those secured by the Global Network for Neglected Tropical Diseases and non-governmental development organisations. New and catalytic funding by the Bill & Melinda Gates Foundation in 2009 is expected to leverage investments in disease control and to help harmonise existing partnerships. The Global Philanthropy Forum, Clinton Global Initiative, and World Economic Forum are possible venues to link donors with the neglected-tropical-disease partnerships and WHO, procure essential medicines, and expand preventive chemotherapy. An important goal would be to reach 100% coverage in endemic countries with high-quality medicines free of charge by 2012.<sup>33</sup> Control efforts have largely been focused on Africa. However, fund allocation must optimise flexibility, because control of neglected tropical diseases in Latin America, Asia, and the Middle East have ecologies, infections, and health systems that differ from the mechanisms delineated for Africa.

We live in an almost \$100 trillion economy;<sup>2</sup> therefore \$2–3 billion committed as innovative, flexible, responsive, transparent, and accountable funds for comprehensive disease control should be considered a modest yet highly cost-effective mechanism for alleviating the poverty of people in the bottom billion. Such low costs and efficiencies will be especially welcomed in these new times of economic difficulties.

With the track record of high return rates on investments in neglected tropical diseases,<sup>28</sup> and recognition that these diseases represent an important challenge to global security<sup>11</sup> and fundamental human rights,<sup>3</sup> this amount is especially small and will address a major development problem and bring hope to the most disenfranchised populations.

#### Contributors

PJH, AF, LS, and DM contributed to the writing of the paper and to subsequent revisions.

#### Conflicts of interest

PJH, AF, LS, and DM are cofounders of the Global Network for Neglected Tropical Diseases.

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