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DFID Support to the Control of Neglected Tropical Diseases: The Context

2011 Update

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ACRONYMS AND ABBREVIATIONS

ALB	Albendazole
APOC	African Programme for Onchocerciasis Control
AZI	Azithromycin
BMGF	Bill and Melinda Gates Foundation
CDC	Centers for Disease Control and prevention
CDI	Community-Directed Treatment
BT	Blinding Trachoma
CNTD	Centre for Neglected Tropical Diseases
DALY	Disability Adjusted Life Years
DEC	Diethylcarbamazine
DFID	Department for International Development
EU	European Union
GAELF	Global Alliance to Eliminate Lymphatic Filariasis
GNNTD	Global Network for Neglected Tropical Diseases
GSK	Glaxo Smith Kline
HIV	Human immunodeficiency virus
ITI	International Trachoma Initiative
ITN	Insecticide Treated Bednet
IVM	Ivermectin
J&J	Johnson & Johnson
LEV	Levamisole
LF	Lymphatic Filariasis
LFSC	Lymphatic Filariasis Support Centre
LSTM	Liverpool School of Tropical Medicine
MBD	Mebendazole
MDA	Mass drug administration
MDG	Millennium Development Goal
M&E	Monitoring and Evaluation
MoH	Ministry of Health
MoE	Ministry of Education
NGDO	Non Government Development Organisation
NTD	Neglected Tropical Disease
ONCHO	Onchocerciasis
PC	Preventive Chemotherapy
PYR	Pyrantel
PZQ	Praziquantel
SAFE	Surgery, antibiotics, facial cleanliness, environmental hygiene
SCH	Schistosomiasis
SCI	Schistosomiasis Control Initiative
SSA	Sub-Saharan Africa
STH	Soil-Transmitted Helminthiases
TB	Tuberculosis
TEO	Tetracycline
TRA	Trachoma
USAID	United States Agency for International Development
WASH	Water, Sanitation and Hygiene
WHA	World Health Assembly
WHO	World Health Organization

1. INTRODUCTION

Neglected tropical diseases (NTDs) is the term used for 17 different parasitic and bacterial infections. They include lymphatic filariasis (elephantiasis), onchocerciasis (river blindness), schistosomiasis (bilharzia), leishmaniasis (kala-azar), dracunculiasis (guinea worm), trypanosomiasis (sleeping sickness) and soil transmitted helminthiases (STH).

NTDs have tended to receive little attention because of the once-widespread assumption that people at risk of NTDs experience relatively little morbidity, and that these diseases have low rates of mortality. These views have been comprehensively refuted (WHO 2010a). NTDs have a substantial health and economic burden on poor populations. They cause about 534,000 deaths every year, and share a similar burden of disease to either malaria or tuberculosis (Conteh et al 2010). The best available estimates indicate that some 2 billion people are at risk of contracting an NTD and more than 1 billion people are affected by one or more NTD.[1] In addition, their impact is often underestimated as many of the effects (e.g. anaemia, diarrhoea) are attributed to other causes. Nevertheless, control of NTDs represents some of the best buys in international public health in terms of costs per disability adjusted life year (DALY) averted. In some cases growth and physical defects can be reversed by treatment for helminthiasis. The poor, and other marginalised groups, suffer disproportionately, and although significant progress is being made many trends pose particular challenges – for example climate change, greater urbanisation and migration. Reduction in the health burden related to NTDs should accelerate progress towards MDG 1 (improved nutrition), MDGs 2 and 3 (increased likelihood for school attendance especially for girls who are often more adversely affected by NTDs), as well as the health related MDGs (4, 5 and 6).

In 2008 the UK made a £50 million commitment to support efforts to control NTDs. Two consultants, David Crompton and Mark Pearson, were commissioned to advise DFID on how its support might be best utilised. This report is an updated version of their report (dated October 2008), taking into account recent developments, new data and literature, notably the WHO 2010 report on NTDs. A number of DFID partners and staff were also consulted (Annex 1).

Although there is potential to eliminate some NTDs, there remains considerable uncertainty on how to do this and how rapidly it can be achieved. The need to sustain high levels of coverage in difficult settings poses major challenges. In some cases effective tools are available; in others current tools are inadequate. This report, and DFID's support, focuses on those NTDs for which tools are available.

2. LANDMARKS & POLITICAL COMMITMENT

In recent years there has been a surge of interest in NTDs and recognition that they can and should be addressed. In 2008 the US Government committed $350 million over five years for NTDs. President Obama has included NTDs within his 2010 budget proposals and in his Global Health Initiative. The Bill and Melinda Gates Foundation has played a key role in mobilising support and interest. Strongly supportive statements have also been made by the G8, the European Union, and WHO's Director-General (Box 1).

This increased attention has not been matched by increased funding. Reasons for this include:

- Lower priority at national and international level compared to the 'big three' – HIV, TB and malaria;
- The poorest and most marginalised communities, often living in remote areas and/or fragile states are affected, with no constituency speaking on their behalf;

[1] Salaam-Blyther, 2011, based on various sources.

- NTDs do not spread widely, and so present little threat to high-income countries;
- The diseases are diverse, and are addressed by numerous control initiatives.

Box 1: Key policy statements and developments

2008

- **US/EU Summit Declaration**, Ljubljana, Slovenia, 10 June 2008: "We, the leaders of the United States of America and the European Union ... share a strong interest in supporting global health **...** We will join together to combat **neglected tropical diseases**."

- **US President George W Bush,** Washington DC, 2 July 2008: "We should set a goal to **treat** at least 75% of the people with **neglected tropical diseases** in the most affected countries." [The President had already announced a new global initiative making a total of $350 million over five years to provide integrated treatment of more than 300 million people in Africa, Asia and Latin America.[2]]

- **G8 Meeting, Hokkaido Toyako**, Leaders Declaration, 8 July 2008. 45(f) "To build on our commitments made on neglected tropical diseases at St Petersburg, we will work to support the control or elimination of diseases listed by the WHO through such measures as research, diagnostics and treatment, prevention, awareness-raising and enhancing access to safe water and sanitation. In this regard, by … promoting adequate integrated public health approaches, including through the mass administration of drugs, we will be able to **reach at least 75% of the people affected by certain major neglected tropical diseases** in the most affected countries in Africa, Asia, and Latin America, bearing in mind the WHO Plan. With sustained action for 3-5 years, this would enable a very significant reduction of the current burden with the elimination of some of these diseases."

- **WHO Director-General Dr Chan**, World Health Assembly, 19 May 2008: "I have mentioned at least one 'perfect storm' brewing on the horizon. I believe that control of **neglected tropical disease** represents the opposite: a 'perfect rainbow'. We now see a whole spectrum of opportunities that have converged in a most harmonious way. Safe and powerful drugs are being donated or made available at very low cost. Integrated approaches have been devised for tackling several diseases at once. A strategy of mass preventive chemotherapy, aimed at reaching all at risk, rivals the protective power of immunization **... we are on the brink of eradicating guinea-worm disease ...**"

2009

- **US President Barack Obama**, Accra, Ghana, 11 July 2009: In a speech to the Ghanaian parliament, US President Obama laid out his vision for human rights and democracy in Africa and reiterated his administration's pledge of $63 billion for a new Global Health Initiative, which includes support for NTDs. He stated, "**We will fight neglected tropical disease**."

- The Bill and Melinda Gates Foundation announces a $34 million grant to the Global Network for Neglected Tropical Diseases to attract new sources of funding from the private sector and strengthen WHO AFRO.

- **G8 Leaders Declaration, L'Aquila**, Italy, 8 July 2009: "…We will combine this with actions to: combat TB and malaria; address the spread of n**eglected tropical diseases** and work towards completing the task of polio eradication." (122)

2010

- US President Obama includes NTDs within his 2010 budget proposals and in his six-year Global Health Initiative.

- **G8 Summit, Muskoka, Canada**, June 2010, G8 Muskoka Declaration: "We **continue to support the control or elimination** of high-burden neglected tropical diseases."

[2] For lymphatic filariasis, onchocerciasis, schistosomiasis, soil transmitted helminthiases and trachoma.

- **United Nations, Follow-up to the outcome of the Millennium Summit**, 17 September 2010: MDG 6; 76 (h) "We commit ourselves to accelerating progress in order to achieve MDG 6, including through: ...**Renewing efforts to prevent and treat neglected tropical diseases**" (A/65/L.1).

- **WHO Director-General Dr Chan,** launch of WHO report *Working to overcome the global impact of neglected tropical disease*, 14 October 2010: "Today, instead of waiting for these diseases to gradually vanish, a community of partners is deliberately vanquishing them. Some of the recent progress, viewed against such a long and notorious history, is stunning … For many of the neglected tropical diseases, an end is in sight. … When guinea-worm disease is eradicated, this will be the first disease kicked out of its human host, not by a powerful vaccine, but by health education and behaviour change … These diseases are dreaded by affected populations, and the demand for treatment is growing. The status of these diseases is rising on national and international health agendas. The momentum to accelerate control is growing."

2011

- **WHO Director-General Dr Chan,** address to Executive Board, 128th session, 17 January 2011: "Last year also saw the launch of WHO's first report on the neglected tropical diseases. The striking progress documented in the report is a big blow to some ancient diseases, a big blow to the seemingly endless grip of poverty, and a big triumph for the power of strongly led partnerships … The launch of the report was accompanied by further commitments from the pharmaceutical industry to donate drugs in massive quantities. When the goal is to reach very large numbers of very poor people, no drug price, however low, is affordable. Thanks to these donations, many millions of poor people are receiving the best-quality medicines the world can offer… the [WHO] programme on neglected tropical diseases has been providing this kind of leadership for some time. Again, we see the results."

Although NTDs as a group have become less neglected, some diseases remain more neglected than others. They include leishmaniasis, human African trypanosomiasis, Chagas disease, and Buruli ulcer. Except for Buruli ulcer, all of these can be fatal if left untreated. However they are considered more difficult and costly to control and treat; the available tools are limited and there has been less research devoted to them.

3. CURRENT STATUS OF 'TOOL READY' NTDs

3.1 Overview

Table 1 presents the current understanding on the causes, impact and plans for eliminating or eradicating the key NTDs for which proven and cost-effective tools exist. A further 11 diseases are listed as NTDs (see Annex 2); these include kala-azar and sleeping sickness, for which partially effective tools exist.

Table 1

Disease	**Dracunculiasis/ Guinea worm disease (DRAC)**	**Lymphatic filariasis/ elephantiasis (LF)**	**Onchocerciasis/ river blindness (ONCHO)**	**Schistosomiasis/ Bilharzia (SCH)**	**Soil-transmitted helminthiases (STH)**	**Trachoma/Blinding trachoma (BT)**
Causative agent(s)	*Dracunculus medinensis* (nematode)	*Wuchereria bancrofti, Brugia malayi, B.timori* (nematodes)	*Onchocerca volvulus* (nematode)	Mainly *Schistosoma haematobium* (urinary) and *S.mansoni* (intestinal) – *S.japonicum* and *S.mekongi* to a lesser extent (trematodes)	*Ancylostoma duodenale* and *Necator americanus* (hookworms), *Ascaris lumbricoides* (roundworm), *Trichuris trichiura* (whipworm) – (nematodes)	*Chlamydia trachomatis* (Gram negative micro-organism)
Vector/ intermediate host	Freshwater copepods contaminating drinking water; seasonal transmission leads to annual reinfection of people.	Mosquitoes (breed in fresh and stagnant water)	Blackflies (breed in running fresh water)	Freshwater snails – leads to focal endemicity in countries	None known	None known (house flies as mechanical vectors)
No. countries with endemicity	4 at end of 2010.	81 in 2008	37	74	130 in 2006.	57

Disease	Dracunculiasis/ Guinea worm disease (DRAC)	Lymphatic filariasis/ elephantiasis (LF)	Onchocerciasis/ river blindness (ONCHO)	Schistosomiasis/ Bilharzia (SCH)	Soil-transmitted helminthiases (STH)	Trachoma/Blinding trachoma (BT)
No. people at risk of infection (groups affected)	NA (all ages)	1.3bn (adolescents and adults)	Over 120m	700m (school-aged children, adults)	Over 1bn; often >2 infections per person. (school aged children, women of reproductive age (hookworm only)	300-600 m (children and adults – especially women)
No. people with morbidity	1797 cases in 2010 (1,698 in Sudan, 57 in Mali, 21 in Ethiopia, 10 in Chad, 8 in Ghana, and 3 imported cases in Niger).	Over 120m (mainly adults; men>women); 40m severely incapacitated and disfigured.	37m	Over 207m	Ascariasis: over 1bn; Trichuriasis: 795m; Hookworm disease: 740m. Over 300m with severe morbidity.	84 m (of which 8m visually impaired)
Most affected region	Remaining cases in Africa only.	Sub-Saharan Africa; South and East Asia/Pacific.	Sub-Saharan Africa (30 countries with 99% of cases globally) and Latin America.	Sub-Saharan Africa (85%) and Latin America.	Sub-Saharan Africa; South and East Asia/Pacific; Latin America.	Sub-Saharan Africa; North Africa; Middle East; South and East Asia/Pacific; Latin America.
DALY value ('000)	Not available, but probably now small.	5,941	389	1,707	3,955	1,334
Manifestations	Blister formation, inching, intense pain, bacterial invasion leading to ulcers and abscesses, permanent impairment of joints and reduced mobility;	Impaired lymphatic system, bacterial invasion, pain and fever, adenolymphangitis, gross pathology of limbs (hence elephantiasis),	Skin lesions leading to severe itching (sleep deprivation) and depigmentation; eye lesions from conjunctivitis, visual impairment and blindness. Loss of	Bleeding, liver fibrosis, kidney damage, bladder cancer, female genital lesions accelerating HIV infection; pathology is irreversible;	Mainly children – abdominal pain, nausea, reduced food intake, impaired growth, diminished iron status and anaemia, poor educational	Conjunctivitis with inflammation and scarring, entropin (deviated eye lashes touching the eyeball), corneal opacity, irreversible blindness.

Disease	Dracunculiasis/ Guinea worm disease (DRAC)	Lymphatic filariasis/ elephantiasis (LF)	Onchocerciasis/ river blindness (ONCHO)	Schistosomiasis/ Bilharzia (SCH)	Soil-transmitted helminthiases (STH)	Trachoma/Blinding trachoma (BT)
	seasonality renders people bedfast around harvest time, worker output is reduced and school attendance affected. Other health care affected; e.g. children not taken for immunization.	breasts and genitalia, social stigma, loss of productivity.	productivity as agricultural land is abandoned.	"subtle" morbidity.	performance, school absenteeism: biliary and intestinal obstruction sometimes fatal. Effects on iron status affect maternal health and pregnancy outcomes.	
Public health intervention	Protect people from contact with open water sources, water supply management to prevent contamination, filtration of water to remove infected copepods, water treatment with ABATE® to kill copepods.	IVM+ALB or DEC+ALB Vector control and improved water and sanitation	MDA with IVM Vector control and improved water and sanitation	MDA with PZQ Vector control and improved water and sanitation	MDA with ALB or MBD (LEV and PYR in reserve) Vector control and improved water and sanitation	SAFE strategy (Surgery, Antibiotics, Facial cleanliness, Environmental hygiene) including MDA with azithromycin (antibiotic). Vector control and improved water and sanitation.
Key challenges	Insecurity, limited access to public health control measures in Sudan.	Limited access to essential medicines	Maintaining high treatment coverage where achieved; Post conflict/fragile countries.	Limited availability of/access to essential medicines	Limited availability of/access to essential medicines	Limited access to essential medicines
WHA resolution	WHA 57.9 – to complete eradication of dracunculiasis by	WHA 50.29 – to eliminate lymphatic filariasis as a public	WHA 47.32 – to control onchocerciasis	WHA 54.19 – to reach at least 75% of school-age children	WHA 54.19 – to reach at least 75% of school-age children	WHA 51.11 – global elimination of blinding trachoma by

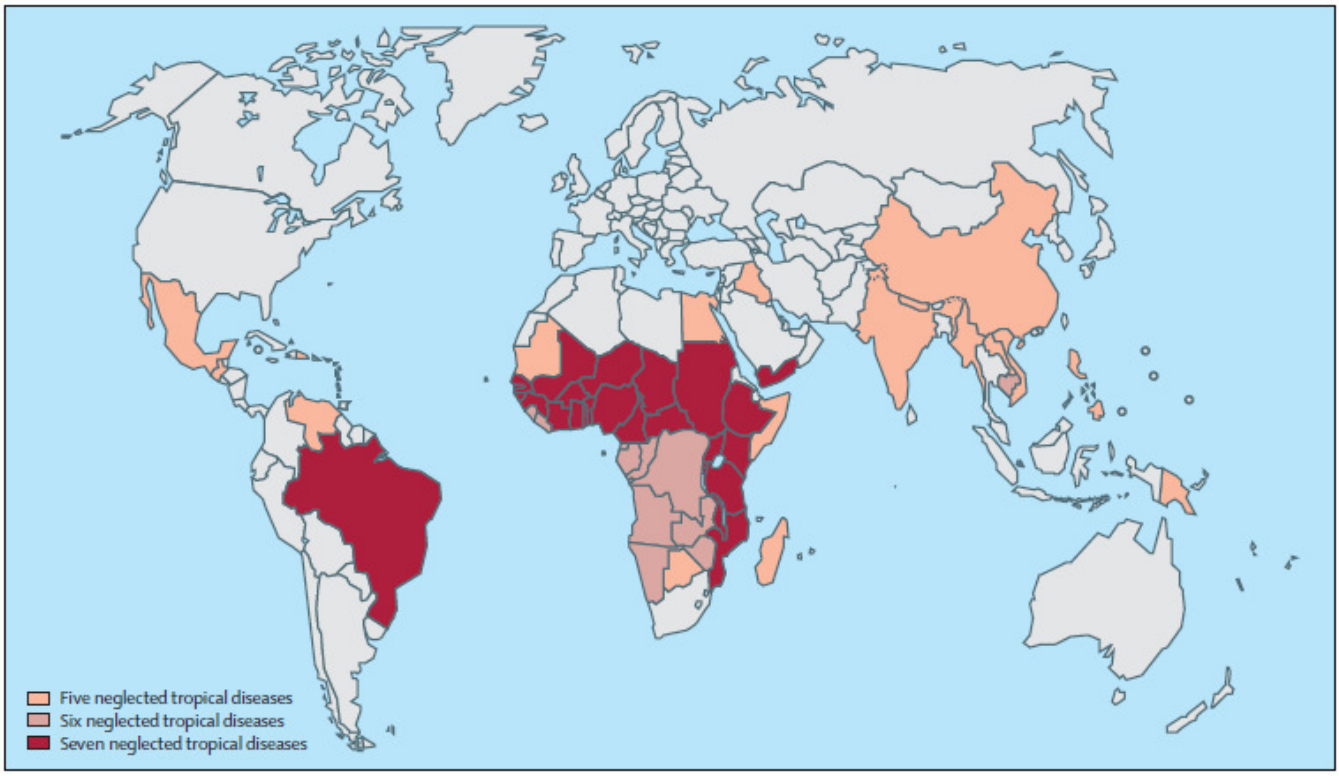
Disease	Dracunculiasis/ Guinea worm disease (DRAC)	Lymphatic filariasis/ elephantiasis (LF)	Onchocerciasis/ river blindness (ONCHO)	Schistosomiasis/ Bilharzia (SCH)	Soil-transmitted helminthiases (STH)	Trachoma/Blinding trachoma (BT)
	2009.	health problem.	through distribution of ivermectin. WHA 59.25 – to prevent avoidable blindness and visual impairment (both onchocerciasis and trachoma).	with anthelminthic treatment by 2010.	with anthelminthic treatment by 2010.	2020 as a public health problem. WHA 59.25 – to prevent avoidable blindness and visual impairment (both onchocerciasis and trachoma).
Elimination/ eradication status *	Elimination probably achievable by 2010 in Ghana, Ethiopia and Mali, almost in line with WHA resolution (2009 eradication target); high country commitment. Sudan is likely to need a few more years.	Elimination date cannot yet be predicted. Probably achievable in smaller countries (in 2009 5 countries no longer required MDA).	Excellent response, with progress in reducing public health significance of the disease in the majority of targeted African countries.	WHA target unattainable mainly due to limited availability of PZQ to date. Achievable in some countries if sufficient PZQ obtained. No prospect of elimination without universal access to safe water supply and effective sanitation.	Many countries will not attain target set by WHA. No prospect of elimination without universal access to safe water supply and effective sanitation.	Possible depending on support and resources to apply the SAFE strategy. Iran, Morocco and Oman have reached elimination targets.

*** Definitions. Elimination**: a reduction to zero of the number of new cases of a specific infection in a defined geographical area, as a result of deliberate efforts. Continued intervention or surveillance measures are required. **Eradication**: a permanent reduction to zero of the world-wide prevalence of infection caused by a specific agent, as a result of deliberate efforts. Continued measures are no longer required. Certification is the responsibility of the World Health Organization.

3.2 Geographic distribution

Approximately 22% of the world population are affected by at least one of the NTDs (WHO 2010a). Africa is the most affected, with an estimated 500 million people infected with one or more parasitic infections, or with organisms which cause one or more NTDs (Fig. 1 and Table 2).

Fig. 1: Geographic overlap and distribution of the seven most common neglected tropical diseases



Source: reproduced from Hotez, 2009.

Table 2. Most prevalent NTDs in Sub-Saharan Africa (SSA)

Diseases	Estimated population infected in SSA	Estimated % global disease burden in SSA	Countries with greatest number of cases
Schistosomiasis	192 – 440 million	>93%	Nigeria, Tanzania, DRC , Ghana, Mozambique
Hookworm	198 million	34%	Nigeria, DRC, Angola, Ethiopia, Cote d'Ivoire
Ascariasis	173 million	21%	Nigeria, Ethiopia, DRC, South Africa
Trichuriasis	162 million	27%	Nigeria, DRC, South Africa, Ethiopia
Lymphatic Filariasis	46-51 million	37-44%	Nigeria, DRC, Tanzania, Ethiopia, Kenya
Onchocerciasis	37 million	>99%	ND
Active Trachoma	30 million	48%	Ethiopia, Sudan, Tanzania, Kenya, Niger

Source: Hotez 2010

These diseases are rooted in extreme poverty. They are found primarily in areas with unsafe water, inadequate sanitation, and where no health services exist, often in fragile states. The three NTDs with the highest burden (schistosomiasis, hookworm and ascariasis, see Table 2) are all associated with inadequate water, sanitation and hygiene.

Because those affected tend to be the most marginalised and hard to access, precise data is difficult to obtain. As a result, commonly used NTD estimates are likely to be very uncertain.

3.2 Key stakeholders in NTD control

An overview of the stakeholders and their main responsibilities is outlined in Table 3.

Table 3: Key stakeholders in NTD control

Type of partner	Key partner	Key roles
Governments	MoH and MoE	Development of integrated national policies, plans, implementation, staff, funding
Lead partners	WHO (UNICEF, WFP, FAO)	Strategic direction, technical assistance, capacity building, procurement of essential drugs, monitoring and evaluation, support for surveillance, resource mobilisation, donor coordination, advocacy, in-country support (e.g. drug importation), multisectoral coordination (e.g. UNICEF/WASH partners).
	Global Network for Neglected Tropical Diseases (GNNTD)	Advocacy and resource mobilisation
	Technical agencies and academia (Centers for Disease Control, Institute of Tropical Medicine, Liverpool School of Tropical Medicine, London School of Hygiene and Tropical Medicine, Imperial College, Centre for Neglected Tropical Diseases, Sabin Vaccine Institute).	Research and knowledge, training (capacity building), evaluation, implementation
	World Bank	Resource mobilisation, donor coordination (for APOC)
Donors and technical partners	Government donor agencies (USAID, DFID)	Funding implementation (grants), advocacy, policy, and technical expertise
	Foundations (Bill and Melinda Gates Foudation, Legatum, Childrens Investment Fund Foundation-CIFF)	Funding (grants), advocacy and technical expertise, strategy development (Gates), development of new tools (Gates)
	Pharmaceutical manufacturers	Sustainable supplies, donations, pharmaco-vigilance, logistics and research
Disease specific initiatives	APOC, GAELF, SCI, Carter Center, RTI, others	Assist national programmes in implementing NTD control: programme design, administrative and operations management, coordination, M&E. Consensus building, advocacy, resource mobilisation, capacity building, community health system strengthening, communication. Setting correct and achievable targets, providing essential accountability for donors, mapping.

	Donation programmes (Mectizan Donation Program, Children Without Worms), International Trachoma Initiative (ITI-coordination).	Drug donation, coordination of donations (ITI)
Non government sector	Many e.g. Geneva Global, Sightsavers etc.	Advocacy, financing, technical and operational support, implementation
	Communities	Implementation, monitoring, data collection, recording and reporting (APOC)

Adapted from WHO 2008 and inputs from consulted partners. The table does not include Water & Sanitation partners.

Many NTDs are addressed by global partnerships. Examples include:

- African Program for Onchocerciasis Control (APOC): governments, donors, international and local NGDOs, a pharmaceutical company (Merck) and communities.
- Guinea Worm Eradication Program: Carter Center, endemic countries, WHO, the US Centers for Disease Control and Prevention, UNICEF, the World Bank, and several NGOs.
- Global Alliance for the Elimination of Lymphatic Filariasis (GAELF): endemic countries, WHO, World Bank, pharmaceutical companies (GSK, Merck and others), donors, NGOs, academia and research.
- International Trachoma Initiative (ITI): created by the Edna McConnell Clark Foundation and Pfizer in 1998 to promote the SAFE strategy and coordinate the distribution of the antibiotic azithromycin (Zithromax), donated by Pfizer.
- Children Without Worms: launched in 2006 by the Task Force for Child Survival and Development and Johnson & Johnson.

Pharmaceutical companies play a key role in several partnerships through drug donations (detailed in Annex 4); in fact NTDs have benefited from the availability of donated drugs to a greater extent than other public health initiatives (Liese 2010). The cooperation between industry and NTDs programmes is a good example of public-private partnership. The APOC external evaluation found that “the Programme … an outstanding public-private partnership for disease control, remains one of the leading health intervention success stories in Africa” (APOC 2010).

4. KEY PUBLIC HEALTH INTERVENTIONS

WHO recommends five strategies for the prevention and control of NTDs:

(i) **Preventive chemotherapy** (see 4.1);
(ii) **Intensified case-management,** i.e. early diagnosis, treatment to reduce infection and morbidity, and management of complications. This is justified as a principal strategy for those NTDs for which there are no medicines available for preventive chemotherapy.
(iii) **Vector control**, as most NTDs involve vector transmission (e.g. insects and snails);
(iv) **Safe water, sanitation and hygiene** (see 4.2); and
(v) **Veterinary public health**, since some NTDs originate in animals.

4.1 Preventive chemotherapy

A subset of five endemic NTDs[3] with high prevalence can be dramatically reduced with mass drug administration (MDA) using a combination of high-quality, safety-tested medicines. Developed by

[3] Lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiases (ascariasis,hookworm infection, trichuriasis), and trachoma.

WHO, preventive chemotherapy is a strategy to target a group of NTDs and at risk-populations rather than specific diseases or infected individuals, as NTDs tend to occur together in the same geographic cluster. Preventive chemotherapy is the main intervention for controlling lymphatic filariasis (LF), onchocerciasis, schistosomiasis and soil-transmitted helminthiases. More than one drug can be given at once to the same person to treat more than one disease (integrated strategy). Preventive chemotherapy can also be used against trachoma, but not as part of the integrated strategy.[4]

The chronic ill health that characterises the four forms of helminthiasis has been demonstrated to be relieved by regular treatment with WHO-recommended oral drugs (WHO, 2004) given once or twice yearly in tablet form according to preventive chemotherapy guidelines (WHO, 2006). In some cases, transmission rates can be reduced. For example, the drug regimen for lymphatic filariasis kills the microfilariae that must be ingested by the vector mosquitoes that sustain and transmit the infection (Ottesen *et al.*1997). Regular treatment of primary school-age children for soil-transmitted helminthiasis is the most cost effective public health measure for a low income country to undertake (World Bank, 1993).

Preventive chemotherapy, even when deployed without other complementary interventions such as improved hygiene and sanitation, surgery, vector control and health promotion, can lead to a significant reduction of morbidity and transmission of helminthic diseases and blinding trachoma. A precondition for success is uninterrupted access to good quality, low cost medicines in order to reach high coverage of populations at risk. Preventive chemotherapy also lends itself to integration with other public health measures (see 4.6).

4.2 Water, sanitation and hygiene

Improved water, sanitation and hygiene (WASH) interventions are critical to the control of several NTDs such as STHs, trachoma, schistosomiasis and guinea worm. The spread of trachoma is strongly related to overcrowding, lack of water for washing the face and hands, and inadequate disposal of human and animal waste. Schistosomiasis results from the unsanitary disposal of human waste and the absence of nearby sources of safe water.

According to Esry (1991)[5], improved WASH can result in a 29% median reduction in illness from *Ascaris* (one of the STH worms), and reduce trachoma by 27%; basic sanitation can reduce schistosomiasis by up to 77%. The date of this evidence however indicates that new research might be needed.

Guinea worm disease is on the verge of being eliminated through innovative health education and the provision of safe drinking water – without drugs or a vaccine. Eliminating or eradicating diseases like schistosomiasis and STHs will not be possible without improved access to safe drinking-water and appropriate sanitation.

Greater focus on WASH interventions can also help limit the potential for drug resistance linked with expanded drug distribution.

4.3 Costs and cost effectiveness of available interventions

Interventions aimed at NTDs are more cost effective than most interventions, and orders of magnitude more cost effective than many of the health interventions currently funded by the donor

[4] The same is true of Visceral Leishmaniasis (kala-azar) requires diagnosis followed by treatment with pentavalent antimony compounds. Dosage and adjustment of treatment need to be made according to patient clinical response. Bone marrow biopsies may be required – none of this lends itself to MDAs or community interventions (see WHO, 2004).

[5] Cited in CDC, 2010, WASH away NTDs.

community. Table 4 (compiled by Conteh et al, 2010) shows the cost-effectiveness of controlling various NTDs, alone or in combination. Almost all interventions considered cost less than $100 per DALY. The example of dengue, however, shows that NTD control may not always be cost effective. (A useful rule of thumb is that an approach is cost effective if it cost less than three times per capita income). More expensive control and treatment estimates are associated with disease for which case management and environmental control are the main interventions.

The five continuing major control or elimination programmes for LF, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis, and trachoma, which use preventive chemotherapy as a key approach, have achieved high levels of coverage and cost-effectiveness (Conteh et al 2010).

Table 4 Cost-effectiveness of controlling NTDs

Disease	Intervention	Cost per DALY[6] averted (US$)
Chagas disease	Vector control	317
Lymphatic filariasis	Where prevalence is greater than 1%, annual mass drug administration to treat the entire at-risk population for 5–7 years: ivermectin and albendazole in Africa, and diethylcarbamazine and albendazole in onchocerciasis-free countries: • to interrupt transmission and achieve elimination of the public-health problem; • to initiate morbidity control, surgery and lymphoedema management; Fortified salt with diethylcarbamazine (China) Vector control	 5–10 35 1–4 59–370
Schistosomiasis	Mass school-based treatment with praziquantel and albendazole combined with schistosomiasis treatment. Mass school-based treatment with praziquantel alone.	10–23 410–844
Trachoma	Trachoma control based on SAFE strategy (Surgery, Antibiotic treatment, Face washing and Environmental control).	5–100
Onchocerciasis	Community-directed treatment programmes with ivermectin.	9
Soil-transmitted helminthiasis (hookworm, roundworm and whipworm)	Mass school-based treatment with albendazole or mebendazole.	2–11
Leprosy	Case-detection and treatment with multidrug therapy using donated drugs. Prevention of disability.	46 1–122
Dengue	Case management. Environmental control.	716–1757 More than 2440

[6] The DALY is a measure of the burden of ill health taking into account reduced life expectancy and quality of life. The number of DALYs lost as a result of a disease is calculated by estimating the number of years lost due to premature death plus equivalent years of ill health.

Leishmaniasis	Case detection and treatment; vector control.	11–22
African Trypanosomiasis	Case finding and treatment: • with melarsopol • with eflornithine	 Less than 12 Less than 24

Source: reproduced from Conteh et al 2010.

Box 2. Low costs of 'rapid impact' packages

The costs of controlling NTDs are small compared with those of responding to HIV, TB and malaria.

Because of the availability of inexpensive drugs (often donated or generically available), it is possible to treat entire communities through mass drug administration (MDA). MDA utilises a 'rapid impact' package of drugs which reduce the prevalence, and in some cases, control or eliminate NTDs for as little as US$0.50 per person per year (Hotez 2010).

Conteh cites a recent study in Laos showing that a school deworming campaign reached a national coverage rate of 95% at a cost of $0.13 per year per child for two rounds of deworming with mebendazole, almost completely eliminating high and moderate intensity infections. Costs included training, health education, drug procurement and distribution, media campaigns, supervision, and monitoring. The largest cost was training teachers in primary schools.[7] This high coverage and low delivery costs have also been reported in Cambodia and Vietnam.[8] A seven-country study assessing costs of mass drug administration to eliminate lymphatic filariasis estimated a financial cost per person treated between $0.07 and $2.67. Economic costs varied between $0.48 and $6.97. Coverage rates varied between 53% and 91%.[9]

These low costs for NTD disease control are driven by four factors: the commitment of pharmaceutical companies to provide free drugs (see Annex 2); the scale of the programmes; the potential synergies in delivery modes to increase efficiency and reduce costs; and the often non-remunerated volunteer contribution of communities and teachers in drug distribution.

Source: Conteh et al, 2010

Conteh argues that DALYs might not adequately indicate the severity of many neglected tropical diseases and the effect on an individual's quality of life and subsequent DALY scores. For example APOC treats only hyper-endemic and meso-endemic communities; hence, the number of infected individuals in hypo-endemic communities (i.e. <40% prevalence of infection), and the burden of eye and skin disease in those areas, is not known. Many populations in the poorest areas are also polyparasitised – a phenomenon not previously assessed in terms of disease-burden calculations.

4.4 Economic benefits of controlling NTDs

Beyond the immediate health benefits of reduced ill health, controlling NTDs can also have broader (and potentially very large) economic and fiscal benefits. A quantifiable dimension to the burden of disease caused by NTDs is the loss of productivity and its impacts on the productivity of individuals, households, communities and nations. Table 5 contains information about the economic impact of selected NTDs based on the latest available data.

[7] Phommasack B, Saklokham K, Chanthavisouk C, et al. Coverage and costs of a school deworming programme in 2007 targeting all primary schools in Lao PDR. *Trans R Soc Trop Med Hyg* 2008; 102: 1201–06.

[8] Sinuon M, Tsuyuoka R, Socheat D, Montresor A, Palmer K. Financial costs of deworming children in all primary schools in Cambodia. *Trans R Soc Trop Med Hyg* 2005; 99: 664–68. Montresor A, Cong DT, Anh TL, et al. Cost containment in school-deworming over 2.7 million children in Vietnam. *Trans R Soc Trop Med Hyg* 2007; 101: 461–64.

[9] Goldman AS, Guisinger VH, Aikins M, et al. National mass drug administration costs for lymphatic filariasis elimination. *PLoS Negl Trop Dis* 2007; 1: e67.

Table 5: Economic costs of selected NTDs

Disease	Setting	Reported productivity loss*
Dengue fever	India	The average total economic burden was estimated at US$ 29.3 million (US$ 27.5–31.1 million). Costs in the private health sector were estimated to be almost 4 times that of public sector expenditures.
Lymphatic filariasis	Various countries	Annual economic burden of LF measured in lost productivity reported in 1998 was about US$ 1.7 billion in 2008, taking into account inflation in countries that are part of the African Programme for Onchocerciasis Control. Economic rates of return are 25% at the end of the investment period in 2019, and 28% over 30 years. The programme breaks even in the tenth year. Lymphatic filariasis causes almost US$ 1.3 billion/year in lost productivity.
Soil-transmitted helminthiases	Kenya	On the basis of the estimated rate of return to education in Kenya, deworming is likely to increase the net present value of wages by more than US$ 40 per treated person. Benefit-to-cost ratio = 100. Deworming may increase adult income by 40%.
Schistomasiasis	Philippines	After a series of computations, of which the disability rate was regarded as the most important, a total of 45.4 days off-work lost per infected person/year was obtained.
Trachoma	Various countries	The economic cost of trachoma in terms of lost productivity is estimated at US$ 2.9 billion annually.

Source: drawn from Conteh et al 2010.
*All costs and losses are inflated from their original year of calculation and converted to their 2008 US$ equivalent with a constant dollar rate.

The indirect costs to people affected by NTDs and their carers, and the economic effect on a household, further compound the costs. An unquantifiable dimension to the burden of NTDs relates to the unpaid work and productivity of millions of women, who tend to be the main caregivers, collect water and fuel, grow vegetables and tend crops, provide meals and maintain the household. This vital work would be easier if they were relieved of NTDs. Several NTDs adversely affect a family's economic potential through their debilitating effects on children, who often are an economic resource. (Hotez 2009, WHO 2010a)

4.5 Social costs

Lymphatic filariasis is estimated by WHO to be the second largest cause of disability in the world. Victims are often subject to severe societal discrimination resulting in poor educational, employment and marriage prospects. The poor are more likely to be affected by NTDs and face more serious consequences. Infections of children with soil-transmitted helminths and schistosomes are associated with reduced education and school performance and attendance, and adverse effects on future earnings and productivity (Hotez 2009).

Brooker et al (2004) found that children, women of reproductive age and pregnant women were far more likely to suffer from hookworm anaemia because of their poor underlying iron status. According to the Disease Control Priorities Project (DCPP), helminths are "intimately associated with poverty, poor sanitation and the lack of clean water" (DCP 2006). De Silva et al (2003) demonstrate the negative correlation between income level and helminths infection. Having said this there have been no benefit incidence studies to assess the extent to which the poor benefit from public subsidies. Nonetheless, it would be reasonable to conclude that efforts to address NTDs are likely to be focused on the poor and vulnerable.

4.6 The importance of integrated approaches (co-implementation)

There is growing consensus based on evidence that integrating activities for a range of NTDs and for other diseases is both feasible and beneficial. In 2006 WHO provided technical guidelines on preventive chemotherapy which advocate for an integrated approach and multi-interventions package for disease control (WHO 2006). Evidence from integrated in-country implementation is also growing.

Molyneux (2005) argued that synergistic gains can be made from linking the control programmes for onchocerciasis, LF, schistosomiasis, STHs, trachoma as well as for other diseases. The mid-term external evaluation of APOC concludes that integrated approaches offer economies of scale, efficiency and cost saving, and maximise benefits for recipients especially among poor, poly-parasitized populations (APOC 2010).

The most compelling evidence for co-implementation to date comes from APOC, which has increasingly used its Community Directed Interventions (CDI) platform to deliver other health commodities and interventions – bednets, lymphatic filariasis treatment, Vitamin A supplementation, control of STHs, primary eye care and immunization. A large-scale country-led NTD control programme supported by APOC Tanzania has also shown that the cost of delivering integrated interventions for five diseases, at $0.08 per person, is less that that of delivering ivermectin alone ($0.28, based on people treated for ivermectin in all APOC countries and total APOC budget spent in 2009).[10]

The Carter Center has found triple drug administration for LF, schistosomiasis, onchocerciasis and STH a safe and more efficient way of delivering treatment, resulting in a 40% reduction in costs.[11] An earlier study from Nigeria on the integration of insecticide-treated bed net (ITN) distribution with mass drug administration also found substantial improvement in ITN ownership and usage, without adversely affecting mass drug administration coverage (Blackburn et al 2006). After integrating MDA campaigns, USAID documented cost-efficiencies of up to 41%, and a 30% reduction in training costs. USAID attributed these savings to streamlining programme management, social mobilisation, drug supply chains, and training.[12]

Box 3: Multiple interventions delivered by APOC

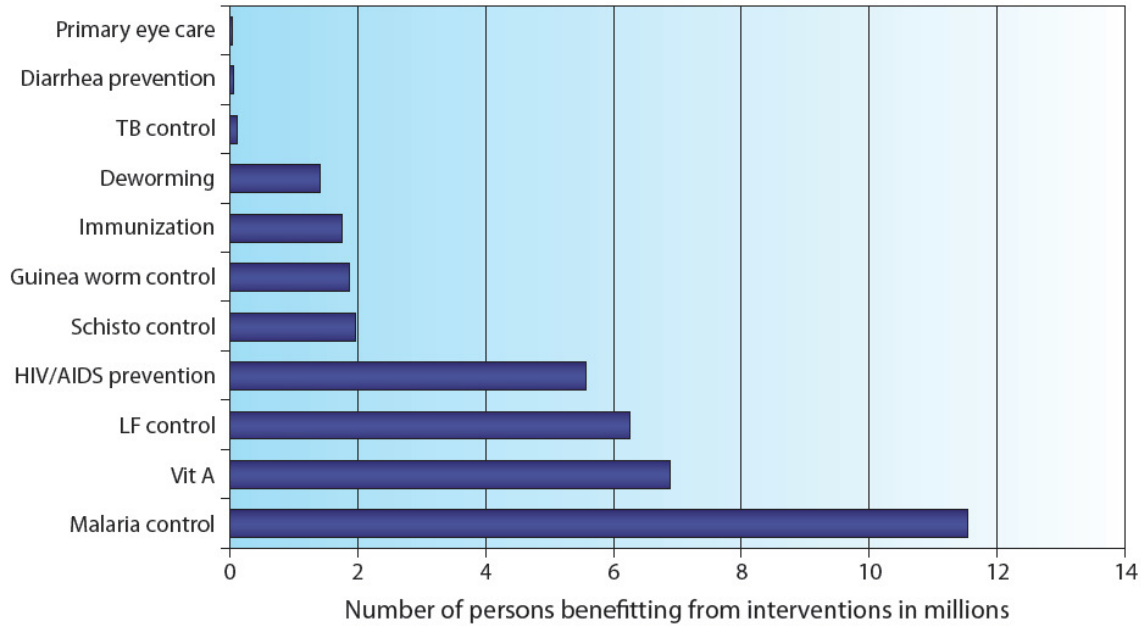
In 2008, APOC's community directed distributors covered around 37.5 million people with additional health interventions (see figure); this is 66.1% of the population treated through CDI in 2008 (56.7 million persons). More than 11.5 million persons benefited from malaria control interventions (home-based treatment of malaria and insecticide treated nets).

Figure 2: additional interventions provided with onchocerciasis control

[10] Communication from APOC, consulted for this report. The five diseases are: onchocerciasis, LF, schistosomiasis, STH and trachoma.

[11] Communication from the Carter Center, consulted for this report.

[12] Quoted in Salaam-Blyther, 2011.



Source: APOC 2010.

APOC experience shows that coordinating resource mobilisation and delivering interventions through a community health system based on the CDI model is feasible and brings significant synergistic benefits (APOC 2010). A multi-country study has also shown that communities managed integrated interventions successfully (WHO/TDR 2008).

In-country implementation of integrated activities is still at an initial stage; in practice there remain several challenges to integrating activities that have different epidemiological goals, different control methods, and different local and international constituencies. There are also differences in key institutional contributors involved – for example the MoE for school-based MDA programmes, the MoH for community-based programmes through district health services – and coordination challenges with disease control units (Liese 2010). Other risks include overburdening of community drug distributors, and setting up an extensive health-care system that is parallel to the existing one (Kolaczinski 2007, cited in Liese 2010).

DFID has consulted key partners on the costs, benefits and challenges of integrated approaches. Regarding the benefits, there is agreement on the cost effectiveness and efficiency of such approaches, with savings in the range of 30%-60%. The potential for leveraging additional government and donor support is seen as an additional benefit of grouping NTDs as a 'package'. On costs, responses cite for example the costs of M&E and training (not only technical but also managerial). There are gaps in support for management training – including change management. Challenges highlighted by partners include:

- M&E: integrated mapping, data collection and reporting for different diseases, and in challenging settings;
- National level: political will, domestic financing, coordination, administrative and managerial difficulties;
- Resistance to change by disease-focused communities (coordinators at national and district level, previously independent programmes, health workers etc.);
- Lack of evidence, best practices and updated guidelines with new data on co-implementation.

The full responses are provided in Annex 3.

4.7 Additional benefits of NTD control

Controlling NTDs brings other benefits (difficult to quantify) such as: alleviation of suffering and stigma, better child care, improved school attendance, elimination of infection-related expenditures and positive effects on savings and income in the long run.

Emerging data suggests that NTDs have a substantial geographical overlap with HIV, TB and malaria, and that controlling NTDs could become a powerful tool against the three diseases (Hotez 2010):

- **Malaria:** Hookworm and malaria co-infections have been shown to produce severe anemia that increases maternal morbidity and mortality, as well as worsened child morbidity and impaired cognition. Ascariasis and other soil-transmitted helminth infections are also associated with increased malaria prevalence.
- **HIV:** There is extensive geographic overlap between HIV and urogenital schistosomiasis (especially in southern and East Africa), the most common form of schistosomiasis in Africa. Three randomized control trials have shown the beneficial impact of deworming in HIV patients, with reductions in viral load and CD4+ cell counts. Helminths also increase the risk of mother-to-child transmission.
- **TB:** evidence from Africa shows that soil-transmitted helminth infections may be one of the risk factors for the development of active pulmonary TB in addition to HIV infection, and possibly diminished therapeutic responses to anti TB chemotherapy.

The drugs used to treat LF also treat intestinal parasites (STHs), onchocerciasis and scabies. The resulting benefits include improved child development and school attendance among children, and reduced anaemia among women, leading to lower maternal and infant deaths.

Some of the drugs used have an effect on more than one NTD (Annex 3). For example ivermectin (used for onchocerciasis and LF) has effects on the prevalence of hookworms, headlice, and scabies. Preventive chemoterapy for LF is also effective against STHs, and brings extensive additional benefits including deworming, reduction of anaemia, enhanced growth, improved nutrition, improved skin condition, better physical performance and reduced school absenteeism.

There are also potential benefits from integrated approaches, as shown by APOC which has delivered other essential health interventions to poor and remote communities (including: health education on HIV/AIDS, malaria drugs and bednets, vitamin A supplementations), as discussed in 4.6.

5. FUNDING

5.1 Global funding needs

Global assessments of NTDs funding requirements and gaps have not been undertaken and the picture remains unclear.[13] Currently the main players are:

- The UK: supporting guinea worm, onchocerciasis; LF, schistosomiasis, and research.
- The US: its programme's goal is to reduce the prevalence of seven of the most prevalent NTDs by at least 50% among 70% of the world's affected populations. The programme currently supports activities in 12 countries (Burkina Faso, DRC, Ghana, Mali, Niger, Sierra Leone, Southern Sudan, Tanzania, Uganda, Bangladesh, Nepal, Haiti).[14]

[13] GNNTD are currently conducting a mapping study of disease burdens, costs and gaps.

[14] At the time of writing this report, the exact US NTDs budget had not yet been determined.

- The Bill and Melinda Gates Foundation: provides grants to programmes, R&D, and funds the GNNTD. Between 1998 and 2009 it contributed over $717 million.[15]

A large number of donor countries and institutions support specific global initiatives. For example, APOC receives support from: African Development Bank, Belgium, Calouste Gulbenkian Foundation, Canada, France, Germany, Kuwait, Luxembourg, Merck, The Netherlands, Norway, OPEC Fund, Poland, Portugal, Saudi Arabia, Slovenia, UNDP, UK, US, World Bank and WHO.

Table 6 shows the estimated funding requirements for a number of NTDs. The data has been provided by partners consulted for this report. In some cases the estimates are rough, with very wide ranges, and should not be considered as conclusive (e.g. for trachoma, and cumulative figures on more than one disease).

Table 6: Estimated funding requirements or gaps for selected NTDs

Disease	**Estimated funding needs (to 2015 or 2020)**	**Notes**
Lymphatic Filariasis	To 2015 **$150 million** per year 2015-2020 **$100 million** per year	*These are funding gaps.* To 2015: funding for all LF endemic countries without loiasis to achieve full geographic coverage. Assuming by 2016 all endemic countries are covered by preventive chemotherapy and transmission control initiatives, the cost of implementation and surveillance starts to decrease.
Onchocerciasis	2012-2015: **$12–16 million** per year To 2020 (and beyond): **over $16 million**	*These are funding requirements – the gap is likely to be small.* Scenarios for funding gap to 2020 under discussion; include all activities to confirm elimination (activities would be beyond 2020).
Guinea Worm	To 2015: **$40 million***	*These are funding gaps* They have been rounded up from $33m to include WHO costs (for 2014 & 2015not available at time of writing). Specific gaps are: FY11 $5.4m (includes WHO); FY12 $7.9m (includes WHO) FY13 $10m (includes WHO) FY14 $8.4m (CC only); FY15 $1m (CC only and Chad mop-up).
Schistosomiasis	To 2020: **$50 million** per year	*These are funding requirements.* Based on 400m people treated 3 times. Drug purchase and delivery.
Trachoma	To 2020: **$700 million**	*These are funding requirements.* Estimates are being revised; the funding gaps are not yet clear; figures based on full SAFE strategy.
7 NTDs STH (3 diseases), LF,	a) To 2015: **$230 million** Increasing to $325m in 2017, then	*These are funding gaps* a) Preliminary data from GNNTD,

[15] Figures from Salaam-Blyther, 2010.

onchocerciasis, schistosomiasis, trachoma.	decreasing. b) 2011-2015: **$2.9 billion** 2016-2010: **$2.9 billion**	assumptions not validated. Based on 1bn people at risk, and treatment of approximately 1/3 of the population (350 m), i.e. gap of approx. 650m people; treatment cost of approx. $0.50/person, and taking into account absorption factor for initiation and scale up of programmes. b) Estimates provided by WHO (estimated breakdown is: drugs: $1.7bn; distribution: $1.2bn).

According to WHO, the key element for scaling up the 'tool ready' diseases will be increasing availability and access to safe medicines (WHO 2010b).

5.2 Global need and cost of medicines

Information on the global need and cost of medicines is more readily available. WHO estimates that about US$1.7 billion is required for covering 100% of target populations with preventive chemotherapy for 2011-2015.[16]

Table 7: Global medicines need

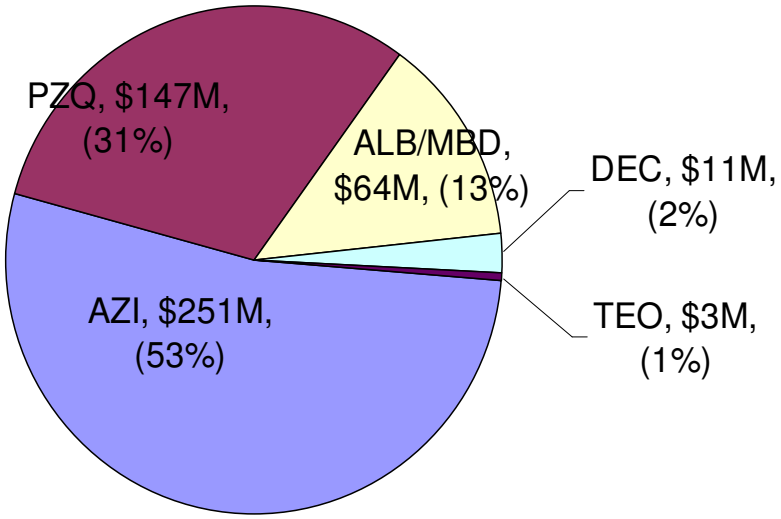
Medicine	Total global need[15]	Projected number of tablets pledged	Share of global need met by donation	Sources
ALB[17]	7,449 million tablets	3,393 million	49%	Donation by GSK
MBD	--	250 million		Donation by J&J
AZI	1,690 million tablets	500 million	30%	Pfizer Inc.
DEC	7,248 million tablets	4,562 million	63%	Direct procurement by Brazil, India and Thailand
IVM	1,967 million tablets	1,967 million	100%	Donation by Merck & Co., Inc.
PZQ	1,942 million tablets	100 million	5%	Donation by Merck KGaA
TEO	19 million tubes	--	--	--

Source: WHO 2010b.
Legend: ALB: albendazole for LF; AZI: Azithromycin for trachoma; MBD: mebendazole for STH; DEC: diethylcarbamazine for LF; IVM: ivermectin; PZQ: praziquantel; TEO: tetracycline eye ointment (TEO) for trachoma.

The total funding gap for medicines is estimated at $476 million (see figure 3 below).

Fig. 3: Estimated funding gaps 2011-2015, by medicine

[16] ;Based on the target populations for preventive chemotherapy against lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis and blinding trachoma for the period of 2011-2015); WHO, 2010b.
[17] GSK donates albendazole for LF to WHO. It is also effective against STH, but not yet donated.



In 2010 GSK, J&J and Pfizer have made additional pledges, which will start to materialise in 2012: GSK has pledged up to 400 million tablets of albendazole (ALB) per year; Johnson & Johnson has pledged 200 million tablets of mebendazole (MBD) per year; and Eisai 300 million tablets of DEC.

These new pledges are expected to change the donations landscape, leaving Praziquantel (PZQ) as the only significant remaining gap. If indeed the needs for AZI, ALB/MBD are met by increased donations, PZQ will constitute 90% of the gap.

A list of major medicine donations by the pharmaceutical industry is in Annex 4.

Annex 1: List of persons consulted (2011)

Uche Amazigo, APOC

Prof. Moses J. Bockarie, Liverpool School of Tropical Medicine

Joan Fahy, Liverpool School of Tropical Medicine

Prof. Alan Fenwick, Imperial College

Danny Haddad, International Trachoma Initiative

Christy Hanson, USAID

Julie Jacobson, Gates Foundation

Nicole Kruse, The Carter Center

Michael Marine, GNNTD

Lorenzo Savioli, WHO

Angela Weaver, USAID

Annex 2: List of all NTDs

1. Dengue/dengue haemorragic fever
2. Rabies
3. Trachoma
4. Buruli ulcer
5. Endemic treponematoses (incl. yaws, endemic syphilis and pinta)
6. Leprosy (Hansen disease)
7. Chagas disease (American trypanosomiasis)
8. Human African trypanosomiasis (sleeping sickness)
9. Leishmaniasis (kala-azar)
10. Cysticercosis
11. Dracunculiasis (guinea-worm disease)
12. Echinococcosis
13. Foodborne trematode infections (incl. clonorchiasis, opisthorchiasis, fascioliasis, and paragonimiasis)
14. Lymphatic filariasis
15. Onchocerciasis (river blindness)
16. Schistosomiasis (bilharziasis)
17. Soil-transmitted helminthiases (incl. ascariasis, trichuriasis, hookworm disease).

Annex 3: Preventive Chemotherapy

The table shows the WHO-recommended anthelminthic medicines for use in preventive chemotherapy.

	Disease	Albendazole	Mebendazole	Diethyl-carbamazine	Ivermectin	Praziquantel	Levamisole[d]	Pyrantel[d]
Target diseases for which a well-defined strategy is available	Ascariasis	√	√	–	(√)	–	√	√
	Hookworm	√	√	–	–	–	√	√
	Lymphatic filariasis	√	–	√	√	–	–	–
	Onchocerciasis	–	–	–	√	–	–	–
	Schistosomiasis			–		√	–	–
	Trichuriasis	√	√	–	(√)	–	(√)[e]	(√)[e]
Target diseases for which a strategy is being developed	Clonorchiasis	–	–	–	–	√	–	–
	Opisthorchiasis	–	–	–	–	√	–	–
	Paragonimiasis	–	–	–	–	√	–	–
	Strongyloidiasis	√	(√)	–	√		–	–
	Taeniasis	–	–	–	–	√ up to 10 mg/kg	–	–
Additional benefits	Cutaneous larva migrants (zoonotic ancylostomiasis)	√	(√)	–	(√)	–	(√)	(√)
	Ectoparasitic infections (scabies and lice)	–	–	–	√	–	–	–
	Enterobiasis	√	√	–	(√)	–	(√)	√
	Intestinal trematodiases	–	–	–	–	√	–	–
	Visceral larva migrants (toxocariasis)	–	–	√	(√)	–	–	–

Notes:
√ indicates medicines recommended by WHO for treatment of the relevant disease;
(√) indicates medicines that are not recommended for treatment but that have a (suboptimal) effect against the disease.
Source: reproduced from WHO 2010a.

Annex 4: Drug Donations

Major donations of medicines for controlling neglected tropical diseases made by the pharmaceutical industry

Medicine	Donation
Albendazole	Unlimited supply from GSK as follows: • For **lymphatic filariasis**: global needs until LF elimination is achieved (all age groups). • For **STH**: all school-age children in Africa at risk. The initial commitment is for 5 years (2012-2016) will then be reviewed. Donation made through WHO
Azithromycin	Unlimited quantity from Pfizer in the context of SAFE
Eflornithine	Unlimited quantity until 2012 from sanofi-aventis for **human African trypanosomiasis**; donation made through WHO
Ivermectin	Unlimited supply for as long as needed donated directly to countries by Merck & Co., Inc., for **lymphatic filariasis** and **onchocerciasis**
Multidrug therapy (rifampicin, clofazimine and dapsone in blister packs) and loose clofazimine	Unlimited supply for as long as needed for **leprosy** and its complications from Novartis; donation made through WHO
Mebendazole	50 million tablets annually from Johnson & Johnson for **soil-transmitted helminthiases** control programmes for children. From 2011, this will increase to 200 million annually
Melarsoprol	Unlimited quantity until 2012 from sanofi-aventis for **human African trypanosomiasis**; donation made through WHO
Nifurtimox	900 000 tablets (120 mg) per year by 2014 from Bayer for treatment of **Chagas disease** and **human African trypanosomiasis**; donation made through WHO
Pentamidine	Unlimited quantity by 2012 from sanofi-aventis for **human African trypanosomiasis**; donation made through WHO
Praziquantel	200 million tablets during 2008–2017 from Merck KGaA for **schistosomiasis**; donation made through WHO
Suramin	Unlimited quantity by 2012 from Bayer for **human African trypanosomiasis**; donation made through WHO
Triclabendazole	From Novartis for **fascioliasis**; donation made through WHO

Source: adapted from WHO 2010a.

Annex 5: Summary of responses to 2011 consultation on integrated approaches

CNTD	**Costs** • Completion of mapping (esp. trachoma); • Training; • Social mobilisation; • Transport; • Delivery • Purchase of PZQ (not covered by donation and grants); • M&E; **Benefits** • Delivery of additional public health interventions; • Stronger recognition of NTDs as a public health problem; • Integrated in-country activities (transport, social mobilisation, training); • Benefits leading to additional government, donor support; • Healthier communities. **Challenges** • Inadequate monitoring of coverage and programme impact; • Costs of carrying out surveys to stop MDA; • Needs for new surveillance tool; • Sustained MoH commitment
APOC	**Costs** • Data from Tanzania (five regions in 39 non-oncho and oncho endemic districts, 2009) shows that comparative cost per person is lower for integrating five interventions (oncho, LF, schisto, STH, trachoma) than for ivermectin delivery (oncho) alone, using the same APOC strategy for co-implementation: • Cost per person – five interventions: 0.08 cents. Estimated costs for ivermectin treatment alone: 0.28 cents (based on the total number of people treated for ivermectin in all APOC countries and total APOC budget spent, 2009). **Benefits** • Integrated mapping; • Cost-effectiveness: e.g. joint training/capacity building of MoH personnel, supervision, logistics; • Improved management of Serious Adverse Events (areas of Loiasis co-endemicity); • Strengthens health system and ensures community empowerment and sustainability. **Challenges** • Timely drug/health commodity procurement; • Cost of non-donated drugs (e.g. PZQ); • Integrated data collection, recording and reporting; • Donors needing immediate results from newly established CDI co-implementation structures (vs setting up CDI as solid foundation of community engagement in, and ownership of MDA for sustained long-term results); • Expansion of integrated mapping esp. in post conflict/fragile or poorly resourced countries; • Health worker behaviour change.
Carter Center	**Costs** • Managerial training (see: challenges) and skills in conflict resolution (between different teams with single disease focus). **Benefits** • Triple drug administration a safe and more efficient way of delivering treatment for LF, schisto, oncho and STH, resulting in a 40% reduction in costs.

	Challenges • Administrative and managerial difficulties of co-implementation: managing funds from multiple donors (many with specific focus) vs sustainable integration. Most MOHs not set up organizationally to manage integrated programs; • Different disease etiologies, different monitoring requirements, different mapping considerations, etc. • Need to address current challenges by national and international technical task forces – but often these only have one or two disease-specific experts able to grapple with real problems; • Earlier WHO guidelines developed by single disease specialist committees; recommendations are not always conducive to integration (e.g. mapping and community assessments).
SCI	**Challenges** • Political will (often mobilised only if there is outside assistance, e.g. a package of drugs and funding) • Coordinating drug donations; • Agreeing strategies; • Bringing together previously independent programmes (vs ambitions of leaders, country/donors and implementers) for the greater benefit of the population. • Coordination of accountability to minimise loss of donated drugs and funding; • M&E; • Duplication of NGO efforts (encouraging mapping of activities by MoE and MoH possible solution).
ITI (Trachoma)	**Benefits** • Increased leverage; • Cost effectiveness; • Broader benefits to various NTDs from larger focus on the prevention side through WASH strategies/ more leverage on larger WASH community to include specific message to have an impact on NTDs. **Challenges** • Coordination at national level – resistance to change form national coordinators for individual diseases suddenly required to collaborate and give up territory; • Ensuring that all coordinators at district level are involved in planning and execution of the programme a challenge in certain countries.
GNNTD	**Costs** • increased needs for training and capacity building at the country management level; • need to develop new tools and performance indicators, and M&E. (None of these costs seem to outweigh the benefits of the investment in integration). **Benefits** • Economies of scale: disease overlaps; leverage of drug donations to treat more than one disease; maximization of social mobilization and engagement of community health workers, opportunity to utilize existing health delivery platforms (e.g. vaccination campaigns). • Increased capacity building within the MoH; • Improvements to the MDA supply and delivery chain. • NTD programming strengthen health systems from the “bottom-up” • Use of existing technical and logistics infrastructure established for the distribution/delivery of drug donations. **Challenges** • Funding gaps for scaled-up distribution, delivery, monitoring and operational research to assess medical, social and economic impacts. • Resistance to change from disease focused communities; • Lack of publicized best practices and case studies from implementers, paucity of

	research into the collateral benefits of integration into the health system, and impact of integrated treatment on other diseases.
USAID	**Benefits** • Grouping diseases as a package has increased the visibility of the programme and led to increased commitment by Ministries. In some cases, countries are supporting up to 30-40% of their NTD programme. • Significant efficiencies compared to vertical programmes, e.g.: o number of MDA treatment reports required at Central level reduced; o number of days of training, use of refresher training reduced; o IEC materials re-used rather than reproduced, and reproduced rather than re-developed; o Number of planning meetings reduced **Challenges** • Need for updated guidelines and policies from WHO (e.g. schistomasiasis) • Need for broader donor base for implementation support.
WHO	**Costs** • Small investments needed in the beginning to ensure appropriate coordination. **Benefits** • Immediate relief to individuals affected from a number of conditions; • Decrease in implementation (drug distribution) costs estimated at minus 30-40%.
Gates Foundation	**Benefits** • Costing work points to 40-60% savings with integration of programmes. • Increased drug coverage for more diseases: integration has been the reason that several programmes (usually trachoma or schisto) have been started in different countries. **Challenges** • Integration adds confusion and coordination issues to programmes especially if they started out as separate programmes. Easier if programmes are started de novo, but this involves the usual start up challenges. • Huge gap in management training and specifically in change management training. • Need for guidelines with the new data on drug co-implementation. • Coordination challenges and support to countries in getting drug donations to programmes to be deployed together.

References

APOC. 2010. Report of the External mid-term Evaluation of the African Programme for Onchocerciasis Control.

Blackburn BG, Eigege A, Gotau H, et al. 2006. Successful integration of insecticide-treated bed net distribution with mass drug administration in Central Nigeria. *Am J Trop Med Hyg* 2006; 75: 650–55.

Brooker, S., J. Bethony, and P. J. Hotez. 2004. "Human Hookworm Infection in the 21st Century." *Advances in Parasitology* 58: 197–288.

CDC, 2010. WASH away NTDs. Preventing neglected tropical diseases and other illnesses with water, sanitation, & hygiene (WASH) interventions. Program in brief.

Conteh, L, Engels, M, Molyneux DH 2010. Socioeconomic aspects of neglected tropical diseases. *Lancet* 2010; 375: 239–47.

de Silva NR, Brooker S, Hotez P, Montresor A, Engels D & Savioli L. 2003. Soil-transmitted helminth infections: updating the global picture. *TRENDS in Parasitology* 19*,* 547 – 551*.*

Disease Control Priorities Project (2006) Disease Control Priorities in Developing Countries (2nd Edition). Chapter 24. Helminth Infections: Soil–Transmitted Helminth Infections and Schistosomiasis.

Esry SA, et al. 1991. Effects of Improved Water Supply and Sanitation on Ascaris, Diarrhea, Dracunculiasis, Hookworm Infection, Schistosomiasis, and Trachoma. *Bulletin of the World Health Organization* 69 (5):609-21.

Gyapong, JO, et al. 2010. Integration of control of neglected tropical diseases into health-care systems: challenges and opportunities. *Lancet* 2010; 375: 160–65.

Hotez, PJ, Fenwick, A, Savioli L, Molyneux DH. 2009. Rescuing the bottom billion through control of neglected tropical diseases. *Lancet* 2009; 373: 1570–75

Hotez, PJ, Kamath, A. 2009. Neglected Tropical Diseases in Sub-Saharan Africa: Review of Their Prevalence, Distribution, and Disease Burden. *PLoS Negl Trop Dis* 3(8): e412

Hotez, PJ. 2010. A White Paper on opportunities for linking NTD control to the control of malaria, HIV/AIDS, and tuberculosis with an emphasis on Sub-Saharan Africa. Paper prepared by GNNTD for DFID.

Kolaczinski JH, et al. 2007. Neglected tropical diseases in Uganda: the prospect and challenge of integrated control. *Trends Parasitol* 2007; 23: 485–93.

Liese, B, Rosenberg, M, Schratz, A. 2010. Programmes, partnerships, and governance for elimination and control of neglected tropical diseases. *Lancet* 2010; 375: 67–76.

Salaam-Blyther, T. 2011. Neglected tropical diseases: background, responses, and issues for Congress. Congressional Research Service.

The Global Health Initiative Project. 2009. The future of global health: Ingredients for a bold and effective US initiative.

WHO. 2010a. Working to overcome the global impact of neglected tropical disease. Geneva: World Health Organization.

WHO. 2010b. Global need for NTD medicines: Scaling up plan for 2011-2015. (Power point presentation by the Department of Control of Neglected Tropical Diseases.)

WHO/TDR. 2008 Community-directed interventions for major health problems in Africa. A multi-country study. Geneva: World Health Organization.

WHO. 2006. Preventive Chemotherapy in Human Helminthiasis. Geneva: World Health Organization.

WHO. 2004. WHO Model Formulary 2004. Geneva: World Health Organization.

World Bank. 1993. World Development Report 1993: Investing in Health. Oxford University Press.