



Delivery of neglected tropical disease control interventions

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Question

What is the evidence, from academic or other sources, comparing integrated versus disease-specific NTD control programmes and what are the key evidence gaps in this area?

Contents

1. Overview
2. Efforts to control NTDs
3. Delivery of disease-specific and integrated NTD programmes
4. Integrating NTD control with WASH
5. Integrating NTDs into global health and development
6. Key evidence gaps
7. References

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1. Overview

Delivery of integrated neglected tropical disease (NTD) control programmes with similar strategic approaches, geographical overlap and prevalence can minimise costs and expand intervention coverage. This has been evidenced through mass drug administration (MDA) of preventive chemotherapy for lymphatic filariasis, onchocerciasis, schistosomiasis, three soil-transmitted helminth infections and trachoma. Where programmes lack a common, simplistic approach and NTD co-endemicity, integration of delivery of NTD control programmes is not necessarily warranted. However, integration of NTD programmes with other disease-specific programmes with operational synergies, with vector control efforts, with other sectors e.g. with WASH to break transmission of NTDs, and within the broader health system will be needed to prevent, control, eliminate and eradicate NTDs and this will demand increased collaboration. Research needs to increase in scope to develop better evidence on the effect of NTDs on mental health in patients and caregivers, to include equity analysis and to address social determinants such as stigmatisation.

Key findings in the delivery of NTD interventions are as follows:

- Progress made towards achieving the World Health Organization's (WHO) 2020 Roadmap targets can be ascribed to the implementation of WHO's five key interventions but primarily through MDA of preventive chemotherapy which has been well resourced and effective (WHO, 2017).
- Experience and lessons learned of integrating disease-specific programmes targeting seven NTDs through MDA for preventive chemotherapy at national scale have cumulated in a "roll-out package" - a strategy and supporting tools for initiating and sustaining effective and efficient integrated NTD country programmes. Sustaining high rates of treatment coverage over many years will require health education adapted to local settings, particularly in remaining pockets of high transmission.
- Combining the delivery of multiple NTD programmes (within preventive chemotherapy and within disease management) with similar strategic approaches, geographical overlap and prevalence can be highly cost-effective and expand intervention coverage.
- Some NTDs do not geographically overlap (as mapped at the start of programmes or where treatment is no longer required as elimination of some diseases moves quicker than for others), have regional rather than global distribution, have programmes that do not have a common approach, or require specialist treatment and management knowledge. Under these circumstances integrated delivery of disease-specific programmes may not be suitable.
- As programmes move into the post-transmission era and approach elimination there will be a greater emphasis on intensified surveillance to rapidly detect recrudescence or ongoing transmission and target interventions to focus on these remaining pockets of disease. This will drive a trend towards greater integration among programmes, especially with vector ecology and management.
- Integration of NTD programmes and water, sanitation and hygiene (WASH) strategies will be needed to prevent transmission and reinfection and ultimately eliminate some NTDs. WASH strategies have been shown to be effective for reducing rates of trachoma, with

collateral benefits for other NTDs. However, more rigorous evidence about which WASH interventions are effective at mitigating exposure and reinfection, and how WASH interventions act together with MDA is needed for all relevant NTDs.

- Some targets of the Roadmap will not be met as NTD programmes continue to struggle with limited financial resources, inadequate capacity (including capacity to implement effective surveillance), disruptive conflicts, and important barriers to accessing needed health services that range from poverty to stigmatisation. Failings can be linked to the geopolitics of the NTDs and to closing coverage gaps and providing universal access.
- Progress demonstrated by delivery of NTD programmes has led to the development of capacities and the accumulation of experiences that have the potential to accelerate progress towards universal health coverage (UHC). Community-directed distribution of MDA for preventive chemotherapy has empowered communities, reached geographically isolated communities and had ancillary benefits on local health systems. Even if all NTD elimination targets are attained by 2030, millions of people living with chronic debilitating, disabling and disfiguring conditions because of NTD infection will continue to require innovative and intensified disease management, ranging from medicines to surgery. A key objective going forward will be finding optimal ways to integrate management of these diseases into broader health systems.
- Continued efforts and research is required to ensure treatments are implemented efficiently, monitoring and surveillance tools are improved, alternative medicines are sought in the event of a loss of efficacy or the development of resistance, reporting systems are effective, and optimal levels of coverage are maintained.
- Further work is needed to document the benefits derived from the economies of scope and scale. For example, research is needed to explore the point at which programmes grow too large and are no longer economic. Threshold analysis can help to inform decision makers when it is cost effective to switch interventions, delivery strategies, or first-line drugs if resistance develops, to step up vector control measures, or to target subgroups instead of the general population.
- Researchers should develop studies to generate more evidence to inform policy frameworks and related guidelines for gender mainstreaming within national NTD programmes.

2. Efforts to control NTDs

NTDs disproportionately affect people in extreme poverty in countries at all levels of income but primarily affect impoverished populations in the developing world (WHO, 2017). WHO currently classifies 17 diseases as NTDs but acknowledges that there are still many tropical, poverty-related diseases that affect the same populations and share many features with NTDs. These diseases are considered “neglected” as mostly affect the poorest populations, living in remote, rural areas, urban slums or conflict zones. Reaching these communities involves extending the concept of value for money beyond cost-effectiveness to maximising impact. NTDs are frequently clustered together geographically and individuals are often afflicted with more than one parasite or infection. Children are the most vulnerable to these diseases, which kill, impair or permanently disable often resulting in life-long physical pain and social stigmatisation.

In 2005 there was a paradigm shift from delivery of disease-specific NTD control programmes to integrated delivery of NTD control programmes. The newly formed WHO's Department of Control of NTDs developed a strategic framework for tackling these diseases in a coordinated and integrated way. Implementation of five interconnected public health key interventions were recommended:

1. preventive chemotherapy
2. innovative and intensified disease management
3. vector ecology and management
4. veterinary public health services
5. provision of safe water, sanitation and hygiene (WASH)

In 2012, the WHO published a Roadmap for implementation with targets set for 2015 and 2020. The aim was to accelerate the prevention, control, elimination or eradication of the commonest NTDs (WHO, 2012). This was quickly endorsed by a community of partners in the 2012 London Declaration on NTDs (Uniting to Combat NTDs, 2012) which led to a boost in large-scale donations of drugs for preventive chemotherapy by pharmaceutical companies creating huge leverage; 1.8 billion treatments were donated by the pharmaceutical industry in 2016 (Uniting to Combat NTDs, 2017) at an annual value of USD2-3 billion (Molyneux, Savioli, & Engels, 2017). Whilst progress has been made towards these targets, challenges have emerged that could delay further progress (Molyneux, 2017) and Hotez highlights gaps which remain in NTD control by listing 10 failings in global NTD control grouped into failings linked to the geopolitics of the NTDs and failings linked to closing coverage gaps and providing universal access (P. J. Hotez, 2017).

Each year WHO produces a report on progress towards the 2020 Roadmap targets (WHO, 2017) and The Uniting to Combat NTDs organisation provides information on where countries are now with respect to reaching these targets, where we can get with existing tools and strategies, and new tools and strategies (Uniting to Combat NTDs, 2017). During 2015, nearly one billion people received protection through preventive chemotherapy for at least one of seven diseases (described below) that are being targeted through integrated preventive chemotherapy. Progress made over the past decade can be ascribed to the implementation of the five key interventions listed above (WHO, 2017), but primarily through MDA of preventive chemotherapy. This is because this intervention is relatively simple, most of the medicines used are tablets, so they are relatively easy to administer and safe for use, and adverse reactions are generally mild and self-limiting, especially when the medicine is given as a single dose (World Health Organization, 2011a). This means that delivery systems can be set up using people in the community who do not have medical qualifications, such as school teachers, traditional healers and community volunteers, and who will require only basic training and supervision to become effective distributors of preventive chemotherapy (community-directed distribution). This has led to the development of capacities and the accumulation of experience, immensely important in contexts in which the public health system lacks resources as is the case in many countries where NTDs are endemic. Preventive chemotherapy has also had a profound impact on the prevalence of infection. Consequently, this intervention has received considerable support.

MDA for preventive chemotherapy of NTDs, such as lymphatic filariasis, is being scaled back in some countries as progress is made in interrupting or significantly reducing transmission. As some NTD programmes move into the post-transmission era and approach elimination, priorities will shift

by putting greater emphasis on intensified surveillance to rapidly detect recrudescence or ongoing transmission and target interventions to focus on these remaining pockets of disease. Focusing on specific locations or populations may ensure the best use of limited resources (WHO, 2017).

Categorising NTDs into preventive chemotherapy programmes may though have inadvertently caused neglect of the other key interventions which are also vital in advancing the NTD agenda (Rosenberg, Utzinger, & Addiss, 2016). For example, putting lymphatic filariasis into the preventive chemotherapy category has diminished the importance and led to neglect of the careful case management required for millions of people who already have filariasis-associated lymphedema. The authors suggest that this categorisation may now need to be rethought because of these unintended consequences and to reflect new tools and approaches that may require some diseases to be reclassified. All five key interventions must be supported to achieve the 2020 Roadmap and the 2030 SDGs (WHO, 2017).

3. Delivery of disease-specific and integrated NTD programmes

Preventive chemotherapy

Combining the delivery of multiple NTD programmes has the potential to minimise costs and expand intervention coverage. Seven NTDs have similar strategies to address their control, namely, single doses of preventive chemotherapy given once or twice a year to broad segments of the population in disease-endemic areas through MDA. These diseases are lymphatic filariasis, onchocerciasis, schistosomiasis, three soil-transmitted helminth infections and trachoma. There is also considerable geographical overlap of these NTDs. The treatment and diagnostic tools currently available for this group of diseases are sufficiently effective for these NTDs to be targeted either for elimination or for reduction to such low levels that they no longer constitute a significant public health problem. Most of the drugs used in these single-dose, once- or twice a year treatment regimen are donated through large public-private partnerships that bring together public health implementers, public-sector and private-sector donors, and the major pharmaceutical firms producing these drugs. Praziquantel, albendazole, mebendazole and ivermectin or diethylcarbamazine are donated and distributed to control these diseases. Importantly, co-administration of the drugs used for treatment has been shown to be safe.

In 2006, USAID established the Neglected Tropical Diseases Program to support national governments in developing successful, cost-efficient NTD programmes that integrate disease-specific programmes targeting elimination or control of lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis and trachoma, into coordinated national initiatives, in accordance with the WHO recommendations. By the end of year 3, 12 countries were supported by this programme, 98 million persons had received 222 million treatments with donated drugs valued at more than USD1.4 billion, and more than 220,000 persons had been trained to implement the programmes (Linehan et al., 2011). The experience of this programme has demonstrated that an integrated approach to control these five NTDs can be effective at full national scale (Linehan et al., 2011).

One of the principal aims of the Neglected Tropical Diseases Program was to identify empirically the most effective and efficient strategies that could later be used to inform other programmes also seeking to integrate their NTD activities. Hanson et al capture the early experiences of countries introducing and/or scaling up integrated NTD activities during the first four years. They summarise

the key lessons learned from these early experiences and identify practices that are now appreciated as successful strategic approaches (or best practices) for developing and rolling out integrated NTD control programmes at full national scale (Hanson et al., 2012). The 3-stage “roll-out package”, a strategy and supporting tools for initiating and sustaining effective and efficient integrated NTD country programmes, was developed in partnership with WHO’s NTD Control Department (Box 1 Roll-out package elements) and subsequently endorsed by WHO’s Strategic and Technical Advisory Group (STAG) for global use (World Health Organization, 2011b).

Box 1
Roll-out package elements

<p>Lay the groundwork</p> <ul style="list-style-type: none">Ensuring government commitmentPerforming a situation analysisCreating a POA (Plan of Action)Analyzing the funding gap <p>Roll out program</p> <ul style="list-style-type: none">Convening stakeholder meetingsDeveloping a work planMapping disease distributionDefining an M&E strategy <p>Establish management</p> <ul style="list-style-type: none">Agreeing on roles and responsibilitiesOrganizing a central coordinating mechanism
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Ref: Hanson et al 2012 (Hanson et al., 2012)

Stage 1 lays the groundwork. A key element of this stage is getting and maintaining commitment by the national government for the short and long-term success of the programme. Ideally, a country’s comprehensive integrated NTD control programme would begin its roll out (stage 2) after all preliminary groundwork is completed. In reality many groundwork and roll-out activities are carried out simultaneously. Either way meetings of national stakeholders, annual work plan development, disease mapping and monitoring and evaluation are key for the successful roll out of any NTD national programme (Hanson et al., 2012). For example, identification of all possible existing service delivery platforms (e.g. schools, child health days) on which the programme could be based, can yield efficiencies for scale up by not requiring costly new infrastructure or networks. Such inclusive consultation can stimulate the willingness of partners to expand their activities, such as adding delivery of an additional drug to a previously single-disease project, to support the national scale up of an integrated approach. Establishing clear roles and responsibilities within government and among partners is essential (stage 3). The roll-out strategy represents a strong focus on host-country government ownership and leadership. A symposium article also outlines key challenges and solutions to assist countries in establishing efficient integrated MDA delivery programmes by sharing experiences from Uganda, Tanzania, Southern Sudan and Mozambique (Kabatereine et al., 2010).

Innovative and intensified disease management

Innovative and intensified disease management uses interventions ranging from medicine to surgery to vector control to manage persons already infected with a NTD. Six NTDs are targeted

with this intervention: three distinct vector borne diseases that are caused by related kinetoplastid protozoan pathogens (Chagas disease, cutaneous and visceral leishmaniasis, and human African trypanosomiasis); those caused by bacteria (Buruli ulcer, leprosy and yaws); and mycetoma, which is caused by bacteria and fungi groups (WHO, 2017). Geographical distribution can differ e.g. the kinetoplastid diseases and some have received less attention by the global community because they are not globally distributed albeit important regional e.g. Buruli ulcer in West Africa.

Several NTDs exhibit significant cutaneous manifestations that are associated with long-term disfigurement and disability. These include Buruli ulcer, cutaneous leishmaniasis, leprosy, mycetoma, yaws, onchocerciasis and lymphoedema. These diseases require similar detection, skin examination offers an opportunity to screen people in the communities or children in schools to identify multiple conditions in a single visit, and case-management approaches which offer opportunities for integration to increase cost effectiveness and expand coverage (Mitja et al., 2017).

The disabling effects of both lymphatic filariasis and leprosy can be managed through self-care and the supportive effects of self-help groups. In Nepal, a network of self-help groups exists for people affected by leprosy in four districts in Nepal's Central Development region, but no such service exists for people with lymphatic filariasis. Pryce et al 2018 assessed the feasibility of integrating lymphatic filariasis affected people into existing leprosy self-help groups in this area (Pryce et al., 2018). They found that despite stigma being a potential barrier, attitudes towards integration were positive and that integrated self-help groups may be a good platform on which people with lymphatic filariasis could start self-care.

Cost-effectiveness of programme delivery

Preventive chemotherapy programmes targeting multiple NTDs with similar strategic approaches can be more cost-effective when drugs are co-administered through a single integrated delivery system rather than separate systems. In 2005, integrating control of seven major NTDs in Africa was estimated to be achieved at the minimal cost of about USD0.40 per person per year (Fenwick, Molyneux, & Nantulya, 2005). In 2006, Brady et al estimated the potential cost savings of 26-47% of integrating programmes for five NTDs that share a similar strategy of preventive chemotherapy – lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis and trachoma – at a cost of USD58-81 million versus USD110 million for vertical preventive chemotherapy programmes in sub-Saharan Africa in 2006 (Brady, Hooper, & Ottesen, 2006). More recently, Leslie et al showed integrated preventive chemotherapy treatment to control trachoma, schistosomiasis, lymphatic filariasis and soil-transmitted helminthiasis in Niger had savings of 16% and 21% in programmes costs in 2008 and 2009, respectively compared with vertical programmes (Leslie et al., 2013). The low cost of NTD control is driven by four factors: the commitment of pharmaceutical companies to provide free drugs; the scale of programmes; the opportunities for synergising delivery modes and the non-remunerated volunteer contribution of communities and teachers in drug distribution (Conteh, Engels, & Molyneux, 2010).

Coverage of programme delivery

A prerequisite for efficiency gains in co-administration of drugs is sufficient geographical overlap of the targeted diseases. Distribution and prevalence of major NTDs can vary between and within a country. This was illustrated in a survey conducted in three States of South Sudan which found marked spatial variation of NTD endemicity between and within the States, highlighting the importance in identifying (co)-endemic areas for evidence-based targeting of treatments (Finn et

al., 2012). Integrated survey designs inevitably involve balancing the costs of surveys against accuracy of classifying areas for treatment. This requires an understanding of the main cost drivers and of how operating procedures may affect both cost and accuracy of surveys. Analysis of costs of the first integrated NTD survey round in South Sudan found that key cost drivers were survey consumables and personnel, both of which are recurrent costs, and that these inputs could be reduced or put to more efficient use by modifying sampling for lymphatic filariasis (Kolaczinski et al., 2010). The authors provide detailed cost data and guidance on how to replicate this work to enable comparable cost estimates and identification of key cost drivers in other settings and which may help budget for integrated and single NTDs surveys elsewhere. Where the targeted diseases are co-endemic, integrating and coordinating programmatic activities for all relevant diseases increases cost effectiveness, enhances the impact on health and supports national health-sector strategic plans (WHO, 2017).

4. Integrating NTD control with WASH

The prevention, control and elimination of many NTDs including schistosomiasis and trachoma depends on the availability of improved WASH in endemic communities (WaterAid & (NNN)). Treatment of NTDs alone will not break the cycle of transmission and reinfection of these diseases will remain a problem if behaviours and the environment remain unchanged. The importance of this is recognised by the WHO in its 2020 Roadmap which includes the provision of safe WASH as one of its five key NTD interventions (see section 2). No targets have been set though and there is no strategy for integration of WASH and MDA (WHO, 2012).

Control of trachoma includes the SAFE strategy which consists of surgery (S) to correct advanced stages of the disease; antibiotics (A) to treat active infection; facial cleanliness (F) to reduce disease transmission; and environmental change (E) to increase access to clean water and improved sanitation to eliminate the disease altogether. This strategy includes two specific components for transmission control (the F and E) (Emerson, Kollmann, MacArthur, Bush, & Haddad, 2012). WASH strategies have been shown to be effective for reducing rates of trachoma and research also highlights collateral benefits of these improvements on other NTDs (King et al., 2013).

There is no such strategy for soil-transmitted helminthiasis and there is limited evidence linking specific WASH access or practices to infection rates. In 2014, a systematic review and meta-analysis found that overall people with access to WASH strategies or practices were about half as likely to be infected with any soil-transmitted helminthiasis infections (Strunz et al., 2014). Despite the low quality of studies included and some evidence for publication bias, the findings confirmed that WASH access and practices provide an effective control measure. A Cochrane review is now being conducted to explore the rigorous evidence of the impact of WASH improvements on soil-transmitted helminthiasis infection and to assess the effectiveness and cost-effectiveness of these interventions (Matthew C. Freeman, Strunz, Utzinger, & Addiss, 2016).

The NTD and WASH sectors need to work together (integrate) to address the link between WASH and NTDs, as few organisations that are highly experienced in NTD programming have a similar level of expertise in WASH. Although the definition of 'integration' differs between the two sectors, within the NTD literature integration often refers to the delivery of multiple drugs for the treatment of several NTDs at the same time (preventive chemotherapy), whilst within the WASH sector the definition of integration often refers to the delivery of a range of interventions through coordination across a variety of sectors and with participation of all relevant stakeholder to achieve a common

goal, both approaches provide opportunities for integration and can operate alongside one another manifesting in a programme to prevent and control NTDs (WaterAid & (NNN)).

In December 2012, WASH and NTD control experts convened for a two-day roundtable discussion in Seattle to discuss opportunities to foster collaboration and partnership between these two sectors. The resulting Policy Platform article presents the background and current evidence for overlap between the WASH and NTD sectors, identifies priorities for collaboration and proposes a common vision for specific collaborations between the two sectors arising from these priorities (M. C. Freeman et al., 2013). Challenges for collaboration are outlined and strategic opportunities proposed. Four key areas of collaboration were identified (i) advocacy, policy and communication, (ii) capacity building and communication, (iii) mapping, data collection and monitoring, and (iv) research.

5. Integrating NTDs into global health and development

Integrating NTD programmes with other non-NTD disease programmes

The geographic overlap between HIV-AIDS, tuberculosis and malaria and NTDs, together with increasing evidence that NTD infections might increase transmission or worsen the course of the “big three”, argue for integrating control and elimination efforts and consideration of the potential operational synergies (P. J. Hotez, Mistry, Rubinstein, & Sachs, 2011). Girls that receive frequent and periodic praziquantel treatments are less likely to acquire HIV, pregnant women who receive anthelmintic drugs are less likely to pass the virus to their foetus, and preventive chemotherapy for all the helminth infections may reduce HIV transmissions among children and young adults by reducing viral load (Kjetland et al., 2006; Walson, Herrin, & John-Stewart, 2009). Downs et al found that women in rural Tanzania who had schistosome infections had a 2.8-fold increased risk of becoming HIV-infected compared to women without schistosome infections (Downs et al., 2017). No evidence of increased HIV acquisition in men with schistosome infections was found. In addition, the concentrations of HIV in the blood shortly after people became HIV-infected was higher in those who had schistosome infections than in those who did not have schistosome infections. This study demonstrates the effect of schistosome infection on HIV-1 susceptibility and viral control, and differential effects by gender. Validation studies are now needed at additional sites. In 2015, Nigeria launched its first nationwide plan to address both lymphatic filariasis and malaria, based on community-directed distribution of both preventive chemotherapy and long-lasting insecticide-treated nets.

Many NTDs are transmitted by insects and other disease vectors that flourish in impoverished settings. Global integration of vector control efforts is a core aim of the newly published Global vector control response strategy for 2017-2030 (WHO, 2017). This strategy aims to strengthen inter- and intra-sectoral action and collaboration, and the expansion and integration of vector-control tools and approaches.

A paper published by Cunningham et al. 2018 shows the value of cross disease communication and collaboration and indicates cost-effective resource use (Cunningham et al., 2018). The study, conducted in Ghana on 448 faecal samples, demonstrates the suitability of using the Global Polio Laboratory Network (GPLN), a well-developed network of laboratories critical to the success of the polio programme, as a diagnostic platform to screen for two of the NTDs, soil transmitted helminthiasis and schistosomiasis. The study showed that it is possible to identify alternative

pathogens to polio in the samples collected by the GPLN and to introduce new diagnostic assays to their laboratories. Moreover, the diagnostic methods used were also able to identify *S. stercoralis* infection, difficult to identify using parasitological methods, suggesting that the GPLN could be used for the surveillance of a wider range of diseases which would both benefit the efforts to control the NTDs and increase the scope of the GPLN as a diagnostic platform.

Integrating NTD control programmes with other health control strategies

Reaching out to communities that are geographically isolated is integral to many NTD interventions. Community-directed distribution of MDA for preventive chemotherapy has empowered communities and has had ancillary benefits on local health systems. A study found that using community-directed treatment with ivermectin, efficiently provided integrated delivery of at least three additional health interventions, achieving significantly higher coverage for vitamin A supplementation, insecticide-treated nets and home management of malaria (C. D. I. Study Group, 2010).

The strategies, programmes and interventions used to address NTDs are closely aligned with the goals for achieving universal health coverage (UHC). These include delivering essential high-quality interventions across the full spectrum of services, increasing the coverage of services to ensure that they reach all who need them and ensuring financial protection that minimises out-of-pocket payments and financial hardship (WHO, 2017). The progress demonstrated by NTD programmes during the past decade, notably through MDA of preventive chemotherapy, has led to the development of capacities and the accumulation of experience that have the potential to accelerate progress towards UHC while advancing the broader 2030 SDGs (WHO, 2017).

6. Key evidence gaps

Since the London Declaration in 2012, advances and innovations in research have empowered national programmes to treat more people faster and more intelligently. For example, confirmatory mapping for lymphatic filariasis has given programmes a clearer picture of lymphatic filariasis infection than previous methods and prevents needless MDA. The supervisor's coverage tool has been designed to help programme managers assess the coverage of MDA while it is being implemented, identifying treatment gaps and improving coverage. In 2015, WHO published guidelines to help programme staff understand how lymphatic filariasis treatment affects soil-transmitted helminthiasis infections, so staff could decide whether MDA should be continued to control intestinal worms. Yet despite progress made, it is starting to become clear that not all of the 2020 Roadmap targets will not be met and new tools, resources and approaches are required (Uniting to Combat NTDs, 2017).

Unlike diseases amenable to preventive chemotherapy, sleeping sickness, Buruli ulcer, Chagas disease, and leishmaniasis have been identified by WHO as requiring innovative and intensified disease management. These diseases have poorly understood burdens, lack optimal control tools, receive insufficient R&D investment, and affect the poorest of the poor. This situation is starting to change with the advent of new technical tools, supported by an increasing number of public-private partnerships for product development (WHO, 2017).

Opportunities are being missed to integrate NTD control programmes with HIV and malaria control and to promote NTD control and elimination beyond MDA, such as vector control to drive down

transmission, increasing human capacity with a knowledge base on NTDs, and clinical management of patients who continue to suffer from the long-term consequences of infection, neglected to date as attention has focussed on the targets for MDA (P.J. Hotez, Fenwick, Ray, Hay, & Molyneux, 2018).

Research priorities for NTDs have been published (TDR, 2010) and a review by Molyneux et al 2017 defines research priorities (Molyneux et al., 2017). A consensus has been reached that new drugs, insecticides and diagnostics are required, which will offer improved and cost-effective therapies, vector-control tools and diagnostics. Research to improve delivery of existing products and evaluate efficacy of existing therapeutics is required as well as exploration of combinations of products known to be effective. Research linked to implementation of programmes and challenges that programmes face as they mature require social science involvement to improve coverage and adherence. Communication about the rationale for MDA with target populations is instrumental for continued uptake e.g. to address why people with no visible symptoms should take tablets and the confusion around why many of those with symptoms take the tablets but seem not to be cured (Allen & Parker, 2012).

The impact of NTDs on mental health has only recently been recognised as a problem with considerable additional burden (Molyneux et al., 2017). A study in 2015 estimated that 50% of those suffering from filariasis had an overall prevalence of depression with a further burden of associated depression amongst caregivers, although the authors suggest that these are conservative estimates (Ton, Mackenzie, & Molyneux, 2015). The burden of mental illness of other NTDs on patients and caregivers needs to be undertaken and reported as a contributor to the global burden of disease (Ton et al., 2015).

To date, there has been little attention paid to gender analysis in efforts to control NTDs (Theobald et al., 2017). Frameworks to promote and implement gender mainstreaming exist but have not been applied to NTDs. Theobald et al 2017 distil five key lessons learnt from gender mainstreaming in approaches in health for promoting gender equity in NTD programmes and explore this through the specific case study of MDA (Theobald et al., 2017). The authors acknowledge that this may increase costs in the short term, but eventually could lead to more effective allocation of resources to those most affected. It is important to consider gender analysis in both patients and caregivers. Martindale et al found a disproportionate gender balance in females more commonly caring for patients with lymphatic filariasis patients at home in Malawi than males (Martindale S et al., 2017). Although the numbers in the study are small, it highlights the burden on caregivers, and specifically on females who may be missing out on an education or employment opportunities. Equity analysis must ensure that interventions are reaching the most vulnerable groups and target those with the greatest need.

There is a paucity of rigorous experimental evidence of the impacts of WASH improvement on NTDs control. This makes it difficult to draw conclusive inferences and quantify the precise impact of WASH interventions on transmission and control of NTDs in general, and in specific contexts, or to recommend which interventions should be prioritised or have greatest effect on disease control (M. C. Freeman et al., 2013). More specific information is needed about which WASH interventions are effective at mitigating exposure and reinfection and how WASH interventions act in concert with MDA (M. C. Freeman et al., 2013).

Further work is needed to document the benefits derived from the economies of scope and scale. For example, research is needed to explore the point at which programmes grow too large and are no longer economic. Threshold analysis can help to inform decision makers when it is cost effective

to switch interventions, delivery strategies, or first-line drugs if resistance develops, to step up vector control measures, or to target subgroups instead of the general population. With implementation programmes operating on a large scale and integrated strategies expanding within and outside of NTD programmes, economic studies should adopt common core protocols and strong cross-country collaborations to generate methodologically comparable data within and across countries (Conteh et al., 2010).

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Key websites

- Uniting to Combat Neglected Tropical Diseases: <http://unitingtocombatntds.org/>
- WHO Neglected Tropical Diseases Department:
http://www.who.int/neglected_diseases/en/

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