



More medicines alone cannot ensure the treatment of neglected tropical diseases

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Neglected tropical diseases afflict more than 1 billion of the world's poorest people. Pharmaceutical donations of preventive chemotherapy for neglected tropical diseases enable the largest en masse treatment campaigns globally with respect to the number of people targeted for treatment. However, the blanket distribution of medicines at no cost to individuals in need of treatment does not guarantee that those individuals are treated. In this Personal View, we aim to examine the next steps that need to be taken towards ensuring equitable treatment access, including health system integration and the role of endemic countries in ensuring medicines are delivered to patients. We argue that the expansion of medicine donation programmes and the development of new medicines are not the primary solutions to sustaining and expanding the growth of neglected tropical disease programmes. Treatment is often not verified by a medical professional, independent surveyor, or national programme officer. Additionally, access to medicines might not be equitable across at-risk populations, and treatment targets for disease control remain largely unmet within many endemic countries. To enable equitable access and efficient use of existing medicines, research is needed now on how best to integrate the treatment of neglected tropical diseases into local health systems. A comprehensive approach should be used, which combines mass drug administration with on-demand access to treatment. Increased commitment by endemic countries, when possible, around the ownership of treatment campaigns is essential to improve access to medicines for neglected tropical diseases.

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Mass drug administration: reconceptualising treatment from clinics to campaigns

Affliction with a neglected tropical disease (NTD) is generally a direct indicator of extreme poverty, signalling financial deprivation and social marginalisation.^{1,2} Though infrequent, NTDs are also observed in non-endemic areas in immigrants and travellers.³ The most prevalent NTDs, causing greatest morbidity and mortality, include schistosomiasis, lymphatic filariasis, onchocerciasis, trachoma, and soil-transmitted helminths; these chronic infections affect at least 1 billion individuals with many more individuals at risk of infection (table).⁴ An estimated 6.35 million disability adjusted life-years (DALYs) were caused by these NTDs in 2017.⁵ For example, if left untreated, intestinal schistosomiasis can cause hepatosplenomegaly, liver fibrosis, portal hypertension, anaemia, and diarrhoea.⁷ The populations at risk of NTDs have inadequate access to safe sanitation, potable water, or government health centres, and in many cases such destitution is further exacerbated by conflict.^{8,9} Within these endemic poor communities, individuals with the greatest morbidity attributable to NTDs are of the lowest socio-economic status, stigmatised, and on the periphery of social networks.^{8,10-14}

The concept and scale of treatment for NTDs is unique. To accommodate the number of at-risk individuals and resource constraints within endemic countries, public health approaches for chronic parasitic infections were reconceptualised in the 1970s. Treatment approaches for these non-vaccine treatable pathogens with high reinfection rates were changed from diagnose-and-treat strategies within clinics to diagnosis-free medicine distribution campaigns within at-risk communities. Vastly different diseases,¹ which vary by pathogen, vector or intermediate host, transmission dynamics, lifecycle,

morbidity caused, and medicines used, are targeted with a single vertical treatment approach—mass drug administration (MDA). MDA is the mainstay of treatment for schistosomiasis, lymphatic filariasis, onchocerciasis, trachoma, and soil-transmitted helminths.¹⁵ These diseases are commonly referred to as preventive chemotherapy (PC)-NTDs because they are amenable to MDA using PC. The aim of MDA is to deliver oral, single-dose PC to all at-risk individuals irrespective of infection status. Volunteer lay health workers, village members, and schoolteachers are trained to administer treatments. MDA is a vertical approach in that donated drugs are not available to local health centres, but instead are administered through scheduled campaigns. These blanket treatment programmes have shown remarkable success in making available treatment for diseases that are otherwise of low priority in national health systems.¹

Several possible reasons have been proposed as to why PC-NTDs are of low priority within health systems of endemic countries. First, PC-NTDs cause morbidities

	Number of individuals infected (in millions) ⁴	Disability adjusted life-years (in millions) ⁵	Number of countries requiring PC ⁶	Number of people requiring PC (in millions) ⁵	Reported number of individuals receiving PC (in millions) ⁶
Schistosomiasis	142.79	1.43	52	212.70	96.70
Lymphatic filariasis	64.62	1.36	52	888.90	465.10
Onchocerciasis	20.94	1.34	31	205.20	136.50
Trachoma	3.82	0.30	40	165.10	83.50
Soil-transmitted helminths	894.92	1.92	101	856.10	489.20

PC=preventive chemotherapy. *114 countries in total.

Table: Estimated prevalence and number of treatments (in millions) for neglected tropical diseases in 2017

attributable to many diseases that manifest over long time periods.¹⁶ The chronic differentiated nature of PC-NTDs might result in both policy makers and patients discounting the clinical consequences of PC-NTDs, most detrimentally by underestimating or dismissing potential DALYs and deaths. Second, PC-NTDs predominantly affect the poorest individuals who might have few political freedoms and insufficient access to government health care to report on the need for treatment.¹ Third, the massive scale of pharmaceutical medicine donations and international aid for MDA might reduce within-country incentives to invest in NTDs amenable to PC.

More than 1 billion people were reported to receive treatment through MDA in 2017 (table).⁶ The largest medicine donation programmes worldwide were established to enable MDA.¹⁷ Pharmaceutical companies, including but not limited to Eisai, Johnson & Johnson, GlaxoSmithKline, Merck KGaA, Merck Sharp & Dohme, and Pfizer manufacture and donate billions of tablets, capsules, and liquid form PC at no cost to WHO.¹⁸ Endemic countries apply to WHO¹⁹ or work with non-profit organisations to procure dose forms for a diversity of treatments delivered during MDA. Coupled with implementation support from non-profit organisations (eg, Bill & Melinda Gates Foundation, The END Fund, Children's Investment Fund Foundation, and the Kuwait Fund) and high-income country governments (predominantly the UK and USA), the value of these philanthropic contributions is unprecedented. In April, 2017, the Guinness Book of World Records confirmed that this donation was the largest public health donation ever made²⁰ and to celebrate 5 years of MDA achievements since the donations were consolidated by the London Declaration,¹⁷ pharmaceutical companies and donors additionally pledged around £613 million (\$US 812 million) for medicine donations and implementation support.²¹ These pledges were led by the UK Department for International Development, which committed £360 million (>\$476 million) over 5 years in MDA implementation support.²² All received and pledged medicine donations for NTDs and MDA have been valued at around £13 billion (\$17 billion),²¹ although it is not transparent how medicine costs were estimated.

Two-thirds of the way: translating large-scale medicine donations into equitable treatment

MDA is at the heart of the WHO's access strategy for PC-NTDs.¹⁵ Donated medicines and blanket treatment campaigns have proven crucial for increasing advocacy, establishing initial treatment regimens, and substantially controlling or progressing towards eliminating the most prevalent NTDs. However, these steps are insufficient to ensure equitable access to treatment. In the figure, we propose a conceptual framework, which is split into five steps, for the sustainable treatment of NTDs. Medicine donations and rapid-impact treatment strategies constitute

essential early steps towards delivering medicines in a sustainable manner to at-risk individuals. These early steps brought MDA 70% (3·5 of five steps) of the way along the crucial path to equitable treatment access. In the 1970s, substantial progress for disease prioritisation (step 1), treatment design (step 2), and market availability (step 3) for NTDs was observed. First generation en masse treatment programmes were formed.^{23–25} The Onchocerciasis Control Programme was set up in 1974. In 1995, treatment for onchocerciasis rapidly expanded within west Africa due to unlimited donations of ivermectin by Merck Sharp & Dohme for the establishment of the African Programme for Onchocerciasis Control.²⁶ The reach of MDA quickly increased under this programme, serving as a paradigm for additional PC-NTD programmes. In the early 2000s, increased advocacy for schistosomiasis, lymphatic filariasis, trachoma, and soil-transmitted helminths enabled further expansion of MDA.^{15,23,27,28} This advocacy²⁷ garnered essential resources to provide treatment for multiple NTDs in endemic countries (half of step 4) and improved the market availability of medicines (step 3).¹⁸

Currently, the major focus for equitable access to treatment remains on market availability (step 3).²⁹ Increased medicine donations are prioritised and medicine development is incentivised.^{17,30} In this Personal View we aim to examine the last steps (steps 4–5) to equitable treatment access—ie, health system integration and the role of endemic countries in ensuring medicines are delivered. We argue that a new approach, which is data-driven and focused on increased verification and accountability of local governments is needed for MDA.

How do we know if someone was treated?

The blanket treatment strategy of MDA does not require knowledge of individual infection status; however, there remains a need to verify if an individual received and complied with treatment. WHO guidelines for morbidity control or elimination depend on the percentage of the target population treated.³¹ In a clinical setting, a nurse or doctor, in theory, administers and observes treatment. In a MDA campaign, national programmes rely on a chain of individuals to report where medicines were distributed.³² The information reported takes one of two forms: medicine distribution inventories or during or post-MDA surveys.³³ Medicine distribution inventories trace the number of medicines delivered to an administrative unit, whereas surveys use accounts from the lay medicine distributors (most common) or independent surveyors who collect information on treatment delivery directly from recipients at primary schools or within communities. Both methods exhibit problems of over reporting of treatments administered, incomplete data, inaccurately aggregated data, and little information on individual treatment rates when compared with aggregated treatment rates.^{8,33–35} Observations from independent surveyors are used as the benchmark of true population treatment rates. These

validation surveys will be inaccurate when sentinel sites or sampling groups are not representative of the whole target population and patient recall is low.

Concerning patient compliance, directly observed therapy (DOT)³⁶ is recommended for MDA. With DOT for MDA, patients ingest medicines in the presence of lay medicine distributors. Information is needed concerning how many countries provide DOT training to lay medicine distributors during annual MDA activities. For countries that provide DOT training for MDA, DOT in practice is not verified. Any methods to verify DOT would require providing disaggregated data by patient or medicine distributor. One potential method of verifying DOT might be to establish report cards for patients to self-report or monitor compliance. For tuberculosis, this method has been shown to be just as effective in increasing compliance with treatment when compared with a strict form of DOT in which patients were observed in a clinical setting.³⁶

Treatment verification is challenging when medicine delivery indicators are poorly defined for MDA. WHO guidelines for treatment coverage focus on medicine ingestion.³² Yet, medicine delivery cannot be equated with medicine ingestion.¹⁰ Factors that predict whether an at-risk individual is likely to be offered medicines (delivery) differ from the determinants of medicine ingestion.^{8,10,11} A focus on ingestion leads to the downstream blaming of recipients of MDA, which in turn results in intensified health education campaigns to convince individuals to participate in MDA.³⁷ However, the recognition of MDA as a two-step process—first medicine delivery (supply) then ingestion (demand)—can help reveal detailed issues (step 5, figure) that explain differences in reported and validated treatment coverage. Inappropriately timed MDA implementation or social biases of medicine distributors might cause marginalised individuals to be systematically missed, thus not providing them the option to decide to participate in MDA.³⁸ The NTD community should use standard terminology to distinguish delivery from the ingestion of medicines.³⁴ This distinction is needed for endemic countries to distinguish between contexts that require alternative modes of medicine delivery or intensified health education.³⁹

The detailed data required to verify treatment and distinguish medicine delivery from ingestion pose challenges to local health systems. Capacity is needed to

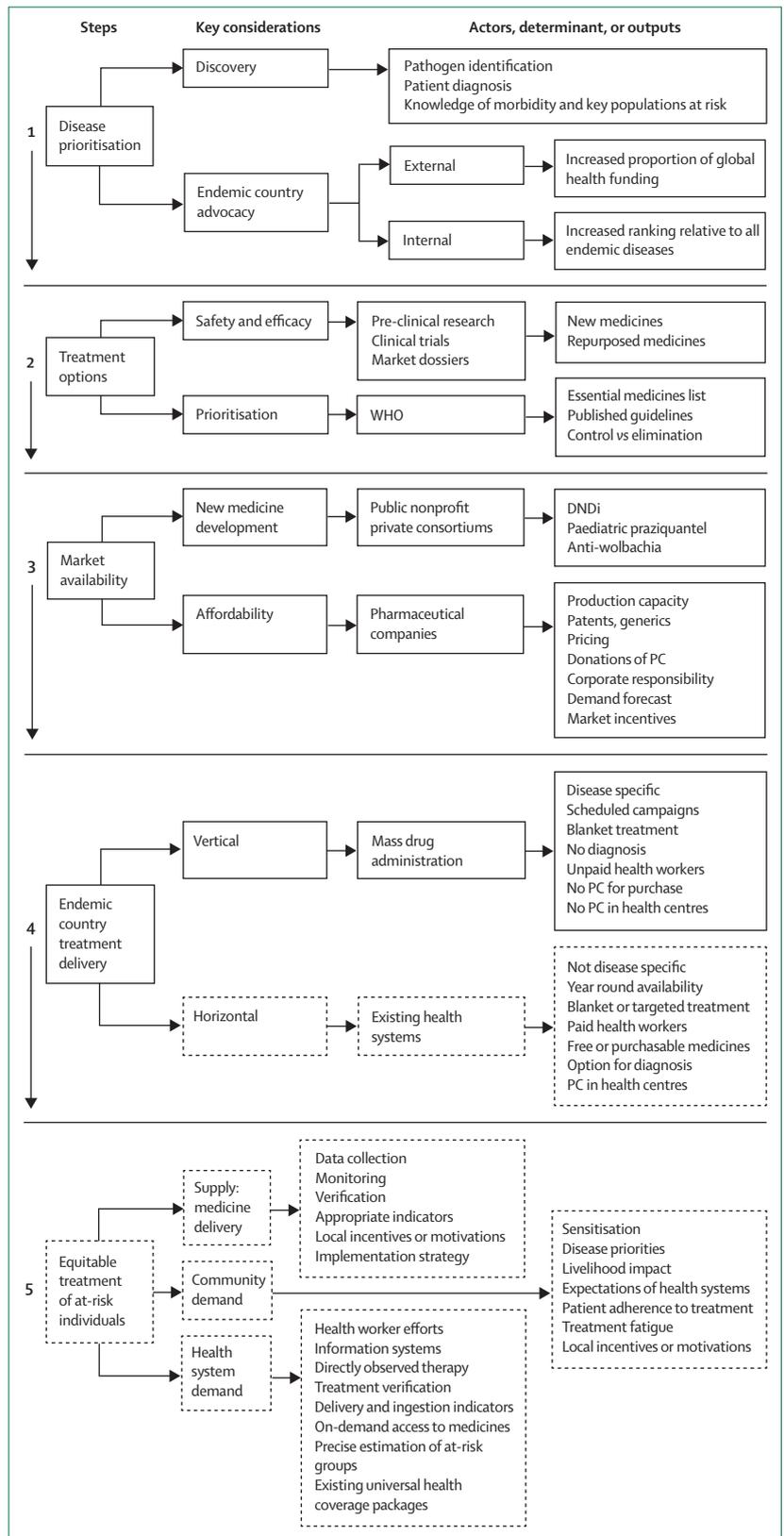


Figure: A comprehensive approach for the sustainable treatment of NTDs
A conceptual framework is proposed for understanding progression towards equitable access to treatment for NTDs and the integration of NTDs into local health systems. Dash-lined boxes represent priority areas requiring additional research to support the growth of NTD programmes and facilitate the inclusion of the treatment of NTDs in universal health coverage delivery packages. The steps shown are not mutually exclusive. Feedback loops and co-dependencies between the different steps exist. NTDs=neglected tropical diseases. DNDi=Drugs for Neglected Diseases initiative. PC=preventive chemotherapy.

analyse individual-level data in nearly real-time, to respond to unusual patterns or inaccuracies in reporting, and to frequently visit endemic communities for monitoring. At present, the WHO PCT databank⁴⁰ contains government-reported treatment rates at the national level. This reported information is sparse, does not necessarily accord with post-MDA validated surveys, and provides no information on the verification measures (if any) used for data retrieved from endemic areas.⁴¹ Progress is being made by the Expanded Special Project for Elimination of NTDs in sub-Saharan Africa to provide technical support for a more complete, subnational tracking of MDA.⁴² With the project, local NTD officers will be better placed to train workers within local health systems.

Donated medicines do not equal access to treatment for everyone

Medicine donation programmes, despite their scale, do not address all steps needed for equitable access to treatment for NTDs (figure).⁶ One reason is that medicine donations are not necessarily based on infection epidemiology and therefore, do not reach all individuals in need of treatment. Albendazole is not donated to treat adults with hookworm infections, although these individuals have been shown to have the heaviest infection intensities thereby acting as parasite reservoirs and predisposing children typically aged 5–14 years who receive donated medicines to infection.^{12,43,44} For middle-income to high-income countries, there are no medicine donations for PC-NTDs.⁴⁵ There is an assumption that individuals, for whom medicines are not donated, will receive treatment through existing health systems. Yet, as previously noted, PCs are not available from hospitals or health centres. To revise medicine donation regimens or to establish procurement models beyond donations, new treatment guidelines for all individuals currently at high risk of PC-NTDs are required from WHO.^{46,47}

In 2017, many countries did not meet WHO treatment targets for MDA, which are set at 65–75% of at-risk individuals across all PC-NTDs.⁶ This failure is indicative of poor medicine delivery.⁴¹ For example, in Mayuge District, Uganda, individuals most heavily infected with schistosomes or hookworm are less likely to be offered medicines despite provision of a sufficient number of PCs to lay medicine distributors.^{8,10,11} Medicines are also wasted by national MDA programmes. Imprecise mapping of infection prevalence results in overestimations of the number of individuals requiring treatment.⁴⁸ Suboptimal medicine delivery and wastages could undermine pharmaceutical company commitments to increase or continue donations.⁴⁹ If donations are reduced or temporarily stopped then MDA will be disrupted in endemic areas, thereby halting the access to PCs for at-risk individuals. Consequently, without access to treatment within local health centres, a relapse to baseline prevalence or intensity, in particular for schistosomiasis or soil-transmitted helminths, will ensue.⁵⁰

For more equitable access to and efficient use of existing medicines, recommendations are needed from WHO to integrate treatment for NTDs into universal health coverage (UHC) delivery packages (expansion of step 2, figure). UHC is a priority objective of WHO.⁵¹ In 2017, WHO along with the World Bank and other international organisations affirmed that country-led UHC is technically and financially feasible. Yet, there is little guidance for implementation research from WHO that would facilitate the integration of PC-NTDs into local health systems. Instead, the benefits of existing vertical MDA are emphasised in either addressing the goals of UHC or serving as a proxy indicator for progress towards UHC.^{47,52}

Increased medicine options do not equal increased treatment rates

A greater diversity of treatment options for PC-NTDs does not necessarily lead to improved access to treatment. WHO's approval of PCs (ie, the inclusion of PCs on the WHO Model List of Essential Medicines⁵³) neither represents the variety or the number of medicines individuals can access nor the affordability of WHO-approved medicines.⁵⁴ New combinations of existing PCs are being used within MDA to establish more effective treatment regimens for lymphatic filariasis. Triple medicine therapy—ivermectin plus diethylcarbamazine plus albendazole (IDA)—better reduces microfilarial loads when compared with the standard two-medicine regimen of diethylcarbamazine plus albendazole.^{55,56} Both regimens are similar in their reductions of macrofilarial loads. To provide benefits beyond the standard regimen, the triple medicine therapy relies on achieving currently unrealised high rates of treatment delivery and compliance.^{6,57} The new regimen also nearly doubles the number of pills or tablets provided to patients per single-dose treatment.

Concerning new medicines, incentive schemes for the pharmaceutical industry to invest in tropical medicine such as the United States' Priority Review Vouchers have no requirement that these new medicines are delivered to at-risk or infected individuals.^{30,58,59} NTD not-for-profit consortiums^{60–62} are in place to develop new medicines for onchocerciasis, lymphatic filariasis, and schistosomiasis. Yet, at least for the treatment of schistosomiasis in children aged less than 5 years, there is no commitment to donate the new medicines.^{63,64} An access strategy for PC-NTDs that moves away from donated medicines and blanket treatment requires a better understanding of data-driven, computational approaches to guide treatments to the right individuals in the right place at the right time.^{65,66} Notably, the evaluation of the need for new medicines is difficult in areas with poor medicine delivery rates. In such areas, there is the challenge of untangling problems of high pathogen transmission, pharmacological resistance, and limited medicine efficacy from poor medicine delivery that limits the

access to PC for at-risk individuals. For example, pharmacological resistance and limited medicine efficacy warrant the development of better diagnostics and new medicines, whereas poor medicine delivery requires revised government implementation, monitoring, and accounting strategies. Confounding these issues diverts essential funding and research away from helping the individuals afflicted with NTDs. Only precise tracking and verification of treatment will be able to identify which issue should be pursued.

The way forward—a more comprehensive view of treatment for PC-NTDs

The exceptional scale of medicine donations from the pharmaceutical industry has led to unprecedented levels of MDA for PC-NTDs, which has improved disease control for more than 1 billion people.^{1,67} However, the continued expansion of medicine donation programmes is not the only method of increasing or sustaining the treatment of PC-NTDs. The quantity of PC donations now exceeds the capacity of endemic countries to deliver PCs.⁶⁸ Instead, embracing a more comprehensive view of treatment (figure) will result in the more efficient use of existing medicines. There is a need to better target at-risk populations, improve treatment verification, and overturn the view that treatment is synonymous with the availability of PCs.

For MDA, test-and-treat strategies, which require improved rapid diagnostics, might reduce implementation costs in low transmission areas or increase treatment rates of non-compliant populations. More detailed spatial mapping based on disease ecology, especially for focal diseases such as schistosomiasis,⁶⁸ might improve prevalence mapping not only for MDA but also for selecting local health centres to administer PCs. In addition to more efficiently directing PCs to individuals in need of treatment, more accurate maps might reduce the quantity of donated PCs required. These methods to improve the targeting of at-risk populations also might increase patient safety in communities where *Loa loa* is endemic and PC (ivermectin) cannot be administered en masse.⁶⁹

To directly confirm that a patient was present during treatment, existing tools such as DOT and sentinel site surveys should be combined with emerging technologies. Examples include mobile phone reports for either tracking supply chains in real-time or receiving confirmations directly from patients, and biometric tools for iris scanning and digital fingerprinting.^{70,71} Using biometric tools is feasible in low-income countries with ongoing MDA. Currently, the Geshiaro project in Ethiopia, which is led by the London Centre for NTDs and funded by the Children's Investment Fund, is tracking medicine delivery during MDA with digital fingerprinting. These emerging verification methods could increase the accountability of MDA programmes by reducing data misrepresentation, errors, and

incompleteness while also making data immediately available for analysis in local health systems. Disease control can also depend on vector control and water, sanitation, and hygiene.^{72,73} Without these complementary interventions, MDA might be undermined by high reinfection rates and, in turn, unnecessarily prolonged.

A comprehensive approach is needed now that combines MDA with on-demand access to treatment within local health systems, when appropriate, as well as enhanced accountability and country ownership. Future research should examine how large-scale medicine donation programmes affect the way that national health systems respond to PC-NTDs. This work would provide insight into the barriers, if any, of integrating the treatment of PC-NTDs into UHC delivery packages. With WHO 2020 goals⁷⁴ fast approaching and pharmaceutical commitments heavily aligned with these goals, medicine donation programmes might be curtailed in the near future. Alternative strategies for sustaining the growth of NTD programmes are needed that do not rely on more medicines.

Contributors

All authors reviewed the manuscript and are in agreement with regard to the contents.

Declaration of interests

We declare no competing interests.

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References

- Molyneux DH, Savioli L, Engels D. Neglected tropical diseases: progress towards addressing the chronic pandemic. *Lancet* 2017; **389**: 312–25.
- Fitzpatrick C, Nwankwo U, Lenk E, Vlas Sd, Bundy D. An investment case for ending neglected tropical diseases. In: Homes KK, Bertozzi S, Bloom BR, Jha P, eds. *Disease control priorities*. 3rd edn. Washington, DC: The World Bank and Oxford University Press, 2017: 411–32.
- Norman FF, Pérez de Ayala A, Pérez-Molina J-A, Monge-Maillo B, Zamarrón P, López-Vélez R. Neglected tropical diseases outside the tropics. *PLoS Negl Trop Dis* 2010; **4**: e762.
- James SL, Abate D, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392**: 1789–858.
- Kyu HH, Abate D, Abate KH, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392**: 1859–922.
- WHO. Summary of global update on provision of preventive chemotherapy in 2017 and progress towards ensuring timely supplies and management. *Wkly Epidemiol Rec* 2018; **93**: 508–20.
- Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. *Lancet* 2014; **383**: 2253–64.
- Chami GF, Kontoleon AA, Bulte E, et al. Profiling nonrecipients of mass drug administration for schistosomiasis and hookworm infections: a comprehensive analysis of praziquantel and albendazole coverage in community-directed treatment in Uganda. *Clin Infect Dis*. 2016; **62**: 200–07.

- 9 Jacobson J, Bush S. Neglected tropical diseases, neglected communities, and conflict: how do we leave no one behind? *Trends Parasitol* 2018; **34**: 175–77.
- 10 Chami GF, Kontoleon AA, Bulte E, et al. Community-directed mass drug administration is undermined by status seeking in friendship networks and inadequate trust in health advice networks. *Soc Sci Med* 2017; **183**: 37–47.
- 11 Chami GF, Kontoleon AA, Bulte E, et al. Diffusion of treatment in social networks and mass drug administration. *Nat Commun* 2017; **8**: 1929.
- 12 Chami GF, Fenwick A, Bulte E, et al. Influence of *Schistosoma mansoni* and hookworm infection intensities on anaemia in Ugandan villages. *PLoS Negl Trop Dis* 2015; **9**: e0004193.
- 13 Person B, Bartholomew LK, Gyaopong M, Addiss DG, van den Borne B. Health-related stigma among women with lymphatic filariasis from the Dominican Republic and Ghana. *Soc Sci Med* 2009; **68**: 30–38.
- 14 Bundy DAP, Silva Nd, Horton S, et al. Investment in child and adolescent health and development: key messages from Disease Control Priorities, 3rd edition. *Lancet* 2018; **391**: 687–99.
- 15 WHO. Preventive chemotherapy in human helminthiasis, coordinated use of anthelmintic drugs in control interventions: a manual for health professionals and programme managers, 2006. https://www.who.int/neglected_diseases/preventive_chemotherapy/pct_manual/en/ (accessed April 25, 2019).
- 16 King CH, Dickman K, Tisch DJ. Regauging the cost of chronic helminth infection: meta-analysis of disability-related outcomes in endemic schistosomiasis. *Lancet* 2005; **365**: 1561–69.
- 17 London Declaration on Neglected Tropical Diseases. London, 2012. https://www.who.int/neglected_diseases/London_Declaration_NTDs.pdf (accessed April 25, 2019).
- 18 Table of Commitments, London Declaration 2012. London: Uniting to Combat Neglected Tropical Diseases, 2012. https://www.who.int/neglected_diseases/NTD_London_Event_Table_Commitments.pdf (accessed April 25, 2019).
- 19 US Agency for International Development, Systems for Improved Access to Pharmaceuticals and Services. Supply chain management manual for health managers of neglected tropical diseases. Geneva: World Health Organization, 2015. <http://apps.who.int/medicinedocs/en/m/abstract/j/s22013en/> (accessed April 25, 2019).
- 20 Stephenson K. Uniting to Combat NTDs program tackles infectious diseases with new world record. Geneva: Guinness World Records; 2017.
- 21 Uniting to Combat NTDs. Ending neglected tropical diseases: A gateway to universal health coverage: Uniting to Combat Neglected Tropical Diseases, 2017. <https://unitingtocombatntds.org/reports/5th-report/> (accessed April 25, 2019).
- 22 Department for International Development. UK to protect 200 million people from tropical diseases. London; 2017. <https://www.gov.uk/government/news/uk-to-protect-200-million-people-from-tropical-diseases> (accessed April 25, 2019).
- 23 Webster JP, Molyneux DH, Hotez PJ, Fenwick A. The contribution of mass drug administration to global health: past, present and future. *Philos Trans R Soc Lond B Biol Sci* 2014; **369**: 20130434.
- 24 Keating C. Kenneth Warren and the Great Neglected Diseases of Mankind Programme: Springer International Publishing; New York, 2017.
- 25 Warren K, Bundy D, Anderson R, et al. Helminth infection: public health significance of helminth infection strategies for control of helminth infection chemoprophylaxis as a primary strategy. In: Mosley W, Jamison D, Measham A, Bobadilla J, eds. 1st edn. Washington, DC: World Bank; 1993: 131–60.
- 26 Molyneux DH. Onchocerciasis control in West Africa: current status and future of the onchocerciasis control programme. *Parasitol Today* 1995; **11**: 399–402.
- 27 Molyneux DH, Hotez PJ, Fenwick A. “Rapid-impact interventions”: how a policy of integrated control for Africa’s neglected tropical diseases could benefit the poor. *PLoS Med* 2005; **2**: e336.
- 28 Fenwick A, Webster JP, Bosque-Oliva E, et al. The Schistosomiasis Control Initiative (SCI): rationale, development and implementation from 2002–2008. *Parasitology* 2009; **136**: 1719–30.
- 29 Lin WM, Addiss DG. Sustainable access to deworming drugs in a changing landscape. *Lancet Infect Dis* 2018; **18**: PE395–98.
- 30 Ridley DB, Grabowski HG, Moe JL. Developing drugs for developing countries. *Health Aff* 2006; **25**: 313–24.
- 31 Hollingsworth TD. Counting down the 2020 Goals for 9 Neglected Tropical Diseases: what have we learned from quantitative analysis and transmission modeling? *Clin Infect Dis* 2018; **66**: S237–44.
- 32 WHO. Monitoring drug coverage for preventive chemotherapy. Geneva: World Health Organization. 2010. https://www.who.int/neglected_diseases/preventive_chemotherapy/monitoring_evaluation_manual/en/, (accessed April 25, 2019).
- 33 Cromwell EA, Ngondi J, McFarland D, King JD, Emerson PM. Methods for estimating population coverage of mass distribution programmes: a review of practices in relation to trachoma control. *Trans R Soc Trop Med Hyg* 2012; **106**: 588–95.
- 34 Shuford KV, Turner HC, Anderson RM. Compliance with anthelmintic treatment in the neglected tropical diseases control programmes: a systematic review. *Parasit Vectors* 2016; **9**: 29.
- 35 Cohen JP, Silva L, Cohen A, Awatin J, Sturgeon R. Progress report on neglected tropical disease drug donation programs. *Clin Ther* 2016; **38**: 1193–204.
- 36 Zwarenstein M, Schoeman JH, Vundule C, Lombard CJ, Taitley M. Randomised controlled trial of self-supervised and directly observed treatment of tuberculosis. *Lancet* 1998; **352**: 1340–43.
- 37 Krentel A, Fischer PU, Weil GJ. A review of factors that influence individual compliance with mass drug administration for elimination of lymphatic filariasis. *PLoS Negl Trop Dis* 2013; **7**: e2447.
- 38 Krentel A, Gyaopong M, Ogundahunsi O, Amuyunzu-Nyamongo M, McFarland DA. Ensuring no one is left behind: urgent action required to address implementation challenges for NTD control and elimination. *PLoS Negl Trop Dis* 2018; **12**: e0006426.
- 39 Kappagoda S, Ioannidis JPA. Prevention and control of neglected tropical diseases: overview of randomized trials, systematic reviews and meta-analyses. *Bull World Health Organ* 2014; **92**: 356–66C.
- 40 WHO. Neglected tropical diseases: PCT databank. Geneva: World Health Organization. https://www.who.int/neglected_diseases/preventive_chemotherapy/lf/en/ (accessed April 25, 2019).
- 41 Chowdhury D, Krotki K, Courtney LP, et al. Effective sampling methodology for program evaluation in developing countries. *Proc Am Stat Assoc* 2010; 4584–92.
- 42 WHO. Framework for the establishment of the expanded special project for elimination of neglected tropical diseases. Geneva: World Health Organization: Regional Office for Africa NTD Programme. 2015. <https://www.infondt.org/resource/framework-establishment-expanded-special-project-elimination-neglected-tropical-diseases> (accessed Feb 9, 2019).
- 43 Turner H, Truscott J, Hollingsworth TD, Bettis A, Brooker S, Anderson R. Cost and cost-effectiveness of soil-transmitted helminth treatment programmes: systematic review and research needs. *Parasit Vectors* 2015; **8**: 1–23.
- 44 Turner HC, Truscott JE, Bettis AA, et al. An economic evaluation of expanding hookworm control strategies to target the whole community. *Parasit Vectors* 2015; **8**: 570.
- 45 Hotez PJ. NTDs V.2.0: “Blue Marble Health”—neglected tropical disease control and elimination in a shifting health policy landscape. *PLoS Negl Trop Dis* 2013; **7**: e2570.
- 46 Savioli L, Albonico M, Daumerie D, et al. Review of the 2017 WHO guideline: preventive chemotherapy to control soil-transmitted helminth infections in at-risk population groups. An opportunity lost in translation. *PLoS Negl Trop Dis* 2018; **12**: e0006296.
- 47 WHO. Integrating neglected tropical diseases into global health and development. Geneva: World Health Organization. 2017. https://www.who.int/neglected_diseases/resources/9789241565448/en/ (accessed April 25, 2019).
- 48 Tchuem Tchuente L-A, Stothard JR, Rollinson D, Reinhard-Rupp J. Precision mapping: an innovative tool and way forward to shrink the map, better target interventions, and accelerate toward the elimination of schistosomiasis. *PLoS Negl Trop Dis* 2018; **12**: e0006563.
- 49 Sansom C. Neglected tropical diseases: securing sustainability. *Lancet Infect Dis* 2018; **18**: 502–03.
- 50 Anderson R, Farrell S, Turner H, Walson J, Donnelly CA, Truscott J. Assessing the interruption of the transmission of human helminths with mass drug administration alone: optimizing the design of cluster randomized trials. *Parasit Vectors* 2017; **10**: 93.

- 51 WHO, International Bank for Reconstruction and Development/The World Bank. Healthy systems for universal health coverage—a joint vision for healthy lives. Geneva. 2017. https://www.uhc2030.org/fileadmin/uploads/uhc2030/Documents/About_UHC2030/mgt_arrangemts_docs/UHC2030_Official_documents/UHC2030_vision_paper_WEB2.pdf (accessed April 25, 2019).
- 52 Fitzpatrick C, Bangert M, Mbabazi PS, et al. Monitoring equity in universal health coverage with essential services for neglected tropical diseases: an analysis of data reported for five diseases in 123 countries over 9 years. *Lancet Glob Health* 2018; **6**: e980–88.
- 53 WHO. WHO model list of essential medicines: 20th list. Geneva: World Health Organization. 2017. <https://apps.who.int/iris/bitstream/handle/10665/273826/EML-20-eng.pdf?ua=1> (accessed April 25, 2019).
- 54 World Health Assembly. Prophylactic and therapeutic substances: World Health Organization. 1975. <https://apps.who.int/iris/handle/10665/147731> (accessed April 25, 2019).
- 55 King CL, Suamani J, Sanuku N, et al. A trial of a triple-drug treatment for lymphatic filariasis. *N Engl J Med* 2018; **379**: 1801–10.
- 56 Thomsen EK, Sanuku N, Baea M, et al. Efficacy, safety, and pharmacokinetics of coadministered diethylcarbamazine, albendazole, and ivermectin for treatment of bancroftian filariasis. *Clin Infect Dis* 2015; **62**: 334–41.
- 57 Irvine MA, Stolk WA, Smith ME, et al. Effectiveness of a triple-drug regimen for global elimination of lymphatic filariasis: a modelling study. *Lancet Infect Dis* 2017; **17**: 451–58.
- 58 Ridley DB. Priorities for the priority review voucher. *Am J Trop Med Hyg* 2017; **96**: 14–15.
- 59 Kesselheim AS, Maggs LR, Sarpatwari A. Experience with the priority review voucher program for drug development. *JAMA* 2015; **314**: 1687–88.
- 60 Johnston KL, Ford L, Taylor MJ. Overcoming the challenges of drug discovery for neglected tropical diseases: the A·WOL Experience. *J Biomol Screen* 2013; **19**: 335–43.
- 61 Chatelain E, Ioset J-R. Drug discovery and development for neglected diseases: the DNDi model. *Drug Des Devel Ther* 2011; **5**: 175–81.
- 62 Merck KGaA. New public-private partnership to develop a treatment for schistosomiasis-infected preschool children. Pediatric Praziquantel Consortium. 2012. <https://www.pediatricpraziquantelconsortium.org/news-events/new-public-private-partnership-develop-treatment-schistosomiasis-infected-preschool> (accessed April 25, 2019).
- 63 Reinhard-Rupp J, Klohe K. Developing a comprehensive response for treatment of children under 6 years of age with schistosomiasis: research and development of a pediatric formulation of praziquantel. *Infect Dis Poverty* 2017; **6**: 122.
- 64 Chami G. Access to Medicines for Neglected Tropical Diseases. Cambridge, UK. 2018. <https://soundcloud.com/user-506806647-613533892/access-to-medicines-for-neglected-tropical-diseases> (accessed April 25, 2019).
- 65 Dowell SF, Blazes D, Desmond-Hellmann S. Four steps to precision public health. *Nature* 2016; **540**: 189–91.
- 66 Dean L, Page S, Hawkins K, et al. Tailoring mass drug administration to context: implementation research is critical in achieving equitable progress in the control and elimination of helminth neglected tropical diseases in sub-Saharan Africa. *Int Health* 2016; **8**: 233–34.
- 67 Bundy DAP, Appleby LJ, Bradley M, et al. 100 Years of mass deworming programmes: a policy perspective from the world bank's disease control priorities analyses. *Adv Parasitol* 2018; **100**: 127–54.
- 68 Bundy D, Jacobson J. Translating the London Declaration into action. Washington, DC: World Bank. 2012. https://unitingtocombatntds.org/wp-content/uploads/2017/11/translating_the_london_declaration_into_action_summary.pdf (accessed April 25, 2019).
- 69 Zouré HG, Wanji S, Noma M, et al. The geographic distribution of *Loa loa* in Africa: results of large-scale implementation of the rapid assessment procedure for loiasis (RAPLOA). *PLoS Negl Trop Dis* 2011; **5**: e1210.
- 70 Stanton M, Molineux A, Mackenzie C, Kelly-Hope L. Mobile technology for empowering health workers in underserved communities: new approaches to facilitate the elimination of neglected tropical diseases. *JMIR Public Health Surveill* 2016; **2**: e2.
- 71 Biometrics in a data driven world: trends, technologies, and challenges. Boca Raton, FL: Taylor & Francis Group; 2017.
- 72 Bockarie MJ, Pedersen EM, White GB, Michael E. Role of vector control in the global program to eliminate lymphatic filariasis. *Annu Rev Entomol* 2009; **54**: 469–87.
- 73 WHO. WASH and health working together: a 'how-to' guide for neglected tropical disease programmes. Geneva: World Health Organization. 2018. <https://apps.who.int/iris/handle/10665/279913> (accessed April 25, 2019).
- 74 WHO. Accelerating work to overcome the global impact of neglected tropical diseases: a roadmap for implementation. Geneva: World Health Organization. 2012. https://www.who.int/neglected_diseases/NTD_RoadMap_2012_Fullversion.pdf?ua=1 (accessed April 25, 2019).

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