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OPEN LETTER

REVISED How modelling can help steer the course set by the World Health Organization 2021-2030 roadmap on neglected tropical diseases [version 2; peer review: 2 approved]

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Abstract

The World Health Organization recently launched its 2021-2030 roadmap, *Ending the Neglect to Attain the Sustainable Development Goals,* an updated call to arms to end the suffering caused by neglected tropical diseases. Modelling and quantitative analyses played a significant role in forming these latest goals. In this collection, we discuss the insights, the resulting recommendations and identified challenges of public health modelling for 13 of the target diseases: Chagas disease, dengue, *gambiense* human African trypanosomiasis (gHAT), lymphatic filariasis (LF), onchocerciasis, rabies, scabies, schistosomiasis, soil-transmitted helminthiases (STH),

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Taenia solium taeniasis/ cysticercosis, trachoma, visceral leishmaniasis (VL) and yaws. This piece reflects the three cross-cutting themes identified across the collection, regarding the contribution that modelling can make to timelines, programme design, drug development and clinical trials.

Keywords
Mathematical, Statistical, Targets, Public Health, Elimination, Transmission, Cross-cutting, NTD

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Any reports and responses or comments on the article can be found at the end of the article.

This article is included in the 2030 goals for neglected tropical diseases collection.

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REVISED **Amendments from Version 1**

Following reviewer advice, the largest change is the addition of a new paragraph in challenges, that broaches two non-mutually exclusive issues; 1) model-use hierarchy, from broad large-scale guidance to ground-level implementation and 2) model access at localised levels to aid decision making.

Other changes include the clarification of misleading text.

Any further responses from the reviewers can be found at the end of the article

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A renewed roadmap for a new decade

The World Health Organization's (WHO) 2021-2030 Neglected Tropical Disease (NTD) Roadmap was launched on January 28th, 2021, renewing the commitment of the global NTD community to end the suffering caused by these diseases[1]. The development of the roadmap was guided by extensive global stakeholder consultation, including consultation with mathematical and statistical modellers. Modellers were asked to assess the technical feasibility of proposed goals, to identify major challenges for achieving the new goals from a transmission dynamics perspective, possible acceleration strategies, and key outstanding research questions[2]. Technical commentaries have been published as a collection in Gates Open Research[3–15], which detail these insights for 13 NTDs: Chagas disease, dengue, *gambiense* human African trypanosomiasis (gHAT), lymphatic filariasis (LF), onchocerciasis, rabies, scabies, schistosomiasis, soil transmitted helminthiases (STH), *Taenia solium* taeniasis/cysticercosis, trachoma, visceral leishmaniasis (VL) and yaws.

Neglected tropical diseases continue to affect over one billion people[16] as the result of the considerable inequalities in global healthcare systems that fail to support those most in need[17]. The burden of NTDs falls largely on the poorest communities, resulting in an unrelenting cycle of poverty that is driven by negative social, health and economic impacts of infection on individuals and families, augmenting existing social divides. For infections with a substantial zoonotic component, morbidity and mortality among livestock also affect people's livelihood with economic impacts that transcend medical implications. Notable progress to reduce the burden of NTDs has been made as a result of the commitments made in 2012 through the WHO 2020 NTD Roadmap[18] and the London Declaration on NTDs[19]. As a result, 500 million people no longer require interventions against several NTDs and 40 countries, territories and areas have eliminated at least one disease[1]. These wins are the outcome of concerted and consolidated efforts from endemic communities and invaluable volunteers, governments, donor agencies and the pharmaceutical industry. Despite such early gains, reaching the endgame presents some of the greatest challenges – namely sustaining those early gains whilst identifying and averting small numbers of sparsely distributed cases. The 2030 roadmap is shaped around three pillars that aim to support global efforts to maintain the gains, address the challenges and ultimately combat NTDs[1]: 1. Accelerating programmatic action. 2. Intensifying cross-cutting approaches and 3. Shifting operating models and culture to facilitate in country ownership.

The use of mathematical and statistical modelling in NTD research and policy has until recently, and with a few exceptions (e.g., onchocerciasis[20]), lagged behind other groups of infectious diseases that receive more focus and funding (often, diseases that impact wealthier individuals and nations, or those perceived to potentially impact these). However, this is changing with the advent of groups like the NTD Modelling Consortium[21], who have developed the Policy-Relevant Items for Reporting Models in Epidemiology of Neglected Tropical Diseases (PRIME-NTD) principles, as a guide to communicate the quality and relevance of modelling to stakeholders[20]. This has added clout to the call for modelling in the policy arena as well as setting a high bar of best practice for the wider modelling community. Having now gained significant traction, the use of modelling in NTD policy has contributed to new intervention tools[22], vector control strategies[23–26], shaped policy responding to COVID-19-related programme disruptions[27–35] and has aided in the development of WHO guidelines[36,37]. For this positive relationship to continue, it is imperative to invest in a mutual understanding through ongoing conversation between policy-makers and modellers, to determine what kind of questions are the "right" questions, how to interpret uncertainty and what the models can and cannot be used for.

This piece introduces a collection of papers borne of a meeting in Geneva, in April 2019 attended, among others, by the NTD Modelling Consortium and convened by the WHO: *Achieving NTD control, Elimination and Eradication Targets Post-2020; Modelling Perspectives & Priorities*[2]. As new management targets and strategies took shape, the meeting provided policy makers and modellers the space to ask and answer specific questions regarding the proposed 2030 goals and the intended strategies to achieve them. Although the roadmap covers a range of diseases with diverse epidemiologies and differing management recommendations, the priority questions identified by modelers and stakeholders during the 2019 meeting and echoed by the authors of the technical commentaries shared three similar themes that should be considered in NTD modelling moving forward: timelines, programme design, and clinical study design.

Timelines

Goals are only worth setting in the context of time. It is therefore not surprising that many of the technical commentaries in this collection identified timelines as a priority issue. The public health and economic benefits of reaching goals are innumerable but can only be achieved by the target year through appropriate mobilisation of diverse resources. Modelling in the forms of past inference and forward projections can align

many moving parts (for example epidemiological, demographic, and social considerations) to inform our understanding of the reasons why programmes succeed or fail[38,39]. Forecasts have played a crucial role in understanding whether the 2020[40] and associated collection[41,42], 2025[43] and 2030[3–15,34] goals can be reached under current strategies with the caveat that long-term predictions naturally become more uncertain.

In some instances, whether a goal can or will be met on time is relatively easy to ascertain – for example it is a resounding no for leprosy and rabies, which are hindered by passive case control, long quiescent incubation periods, and inadequate investment in interventions[15,44]. Alternatively, the goals for schistosomiasis[11], STH[8], and onchocerciasis[13] seem achievable in some or most settings, depending on localised parameters like baseline prevalence, and already experienced duration of and adherence to mass drug administration (MDA) programmes. In the case of *T. solium*, a lack of internationally agreed goals for elimination or control curtails the ability to effectively model timelines; for example, the 2021-2030 NTD roadmap proposes the overall milestone of achieving "intensified control in hyperendemic areas", without agreeing on technical definitions for *T. solium* endemicity levels, or defining measurable criteria for attaining "intensified" control[14].

Programme design

The diseases considered by the London Declaration and WHO roadmaps are at differing stages in their trajectories. Whilst some are on the cusp of achieving their goals, others face political and epidemiological barriers to progress. Both scenarios raise several priority questions regarding programme design, where 'programme' can mean intervention or surveillance. In addition to determining success or failure within the defined intervention time frames, modelling has provided insights into key factors of operational design like the treatment coverage necessary to reach goals in a given setting. Where it may not be possible, models can be used to test the efficacy of separate and combined chemotherapeutic[37] and non-pharmaceutical interventions[23,45,46], including combined interventions that target multi-host systems for zoonotic NTDs[14]. Additionally, deciding the optimal timing[47] or frequency[48,49] of treatment, and knowing who to treat[50,51] are essential to the success of all interventions. Of course, the intervention strategies most likely to lead to achievement of the goals may not be sustainable in terms of cost to individuals, governments, or donors. By partnering highly detailed transmission models with cost-effectiveness analysis, modelling can also contribute to tailored insights regarding the affordability and benefits versus costs of interventions[52–62]. Models can also be used to explore integration between NTD programmes, or to understand the potential cross-utility of existing NTD programmes on other helminth species, such as exploring the additional benefit of national schistosomiasis control programmes using praziquantel on *T. solium* prevalence in co-endemic areas[14]. Understanding this cross-utility is vital to intensifying cross-cutting approaches – one of the three core pillars of the roadmap, that differentiates the framework from its predecessor.

These are all very practical features of intervention programmes that can in principle be planned for, but underlying features of target populations and human nature can undermine this. Survey data in recent years have made it evident that whilst the aim may be to deliver treatment at a certain geographical and therapeutic coverage, it is not analogous with consumption, as treatment is systematically not ingested by some[63,64], or is not disseminated to the full intended group, reducing the true coverage. There are a variety of reasons for this[65,66], but it is likely that similar mechanisms impact participation in surveillance, therefore biasing the estimates of prevalence, particularly when treatment and surveillance are co-occurring (e.g., gHAT[9,67], rabies[15,68]). Modelling shows that the impact of this variable effective coverage depends on the pathogen in question and transmission intensity[64,69–71] but it undoubtedly has an impact on reaching public health goals[72,73], and on the reliability of the projected intervention intensity needed to reach them. It has also been suggested (in the context of VL though applicable beyond), that modelling results – and therefore policy based on them – may be erroneous without better capturing socio-economic and human behaviour risk factors, including feedback loops of behaviour change as a result of perceived risk[74]. This also highlights the need for ongoing surveillance and the use of modelling throughout to provide real-time insight into post-intervention population-level infection dynamics.

Once a strategy has been deemed effective and prevalence targets are attained, it is likely that these interventions either transition, such as going from MDA to identified case management, or they stop all together. Establishing robust surveillance strategies at this point is vital, but obviously not everyone can be regularly sampled and not every incident infection case will be detected. Stochastic events like reinfection and reintroduction are risks that can drive resurgence. Modelling can support the identification of the optimal surveillance strategy and determine which prevalence or intensity indicators need to be monitored to ensure the desired public health goal[75–77], although challenges remain in developing long-term strategies[78]. Modelling can make useful contributions in developing sustainable, effective interventions and surveillance strategies and should therefore be included in any programmatic design from the start. As embodied by the 2021-2030 NTD roadmap, impactful interventions cannot be achieved by working in silos, but instead require continuous communication between all parties of an interdisciplinary team.

Drug development and clinical study design

Though modelling is increasingly used in public health decision making, the use of modelling to direct clinical trial design and drug development is not so common, and even less so for NTDs. Chemotherapeutic interventions are the cornerstone of large-scale intervention strategies to reach goals like elimination as a public health programme or elimination of transmission. Though treatment options are limited for the likes of STH, LF and trachoma, they are themselves considered sufficiently effective at reducing prevalence and

transmission. There is therefore a cautiously sanguine view that consistent application and uptake is enough to reach target public health goals[1,4,5]. However, confidence in the existing treatment for onchocerciasis (targeted for elimination of transmission) is less apparent because the standard ivermectin dose only kills skin dwelling transmission stages with sub-optimal efficacy against adult stages. Modelling suggests this will not be sufficient to reach public health goals[13,79], pressing the need for novel chemotherapeutics. However, financial returns on investments into NTDs are limited and therefore largely unappealing, particularly because of the heavy reliance by endemic nations on donations from pharmaceutical producers. Increased use of mathematical modelling could reduce the financial waste associated with the drug-development-to-distribution-pipeline[79]. If we consider this pipeline in three parts; pre-clinical, clinical trial and distribution, it is clear that modelling can provide valuable insight at each stage. Onchocerciasis and LF have recently benefited from pharmacokinetic-pharmacodynamics modelling, translating pre-clinical non-human experimental results into quantitative insights relevant to human treatment[80]. Clinical trial simulations are designed to include all aspects of a clinical trial protocol including (but not limited to) recruitment criteria, drug properties/effectiveness and follow-up times[81], providing valuable guidance that translates into more effective, efficient, cost-efficient and robust clinical trials. In addition to providing insight into the optimal distribution of new drugs[82], rethinking the distribution of existing drugs to achieve public health targets can also be guided by modelling[37,48].

Challenges

Modelling has certainly addressed many of the key questions asked of modellers at the 2019 meeting[2]. However, cross-disease challenges remain[83]. The most common of these, highlighted by all groups involved in the meeting report[2] and this collection, is undoubtedly a lack of data or poor data quality. This could be because certain parameters simply cannot be measured; because of vast heterogeneity or because they have yet to be collected[84]. A previous collection details the data needs to improve modelling[51,84–94], across the NTDs, so great detail will not be provided here. However, for example, VL has a highly variable incubation period, unknown duration of asymptomatic infection and estimates for the duration of lasting immunity are ill-defined[6,85,95], introducing uncertainty into the temporal dynamics underlying any projections. Chagas disease, gHAT and leprosy also suffer from r elatively long, but indeterminate incubation periods[9,12,21] impacting case detection and adding greater uncertainty in epidemiological estimates fitted to by models[85,96]. Asymptomatic or pre-symptomatic infection is common of many NTDs and presents a significant challenge to their management. For example, asymptomatic VL infections cannot be treated, whereas it is possible to treat asymptomatic gHAT but only if it is able to be detected. Identifying their respective proportions in an infected population, particularly in the absence of high surveillance coverage, means accounting for this group using roundabout methods and proxy diagnostics[6,9].

Many diagnostics are indirect, proxy measures of case detection, often with less than perfect sensitivity or specificity[97,98], and have a direct effect on perceived prevalence and individual burdens of infection[99,100]. Given that models are only as good as the data to which they are fitted, this has a significant impact on the utility of model results. For example, in the instances of STH and intestinal schistosomiasis (*Schistosoma mansoni*), WHO targets are given in terms of eggs per gram of faecal matter as detected with the Kato-Katz method, which notoriously suffers from poor sensitivity, particularly for low intensity infections[101], invariably underestimating prevalence. Where a multi-host system is present for zoonotic NTDs, though it is possible to measure infection through direct observation of parasite stages in the animal host(s)[14], via necropsy or other methods[102], it is likely that this approach is inappropriate for monitoring and evaluating the likes of *T. solium* control programmes, due to the large animal sample sizes required to detect a statistically meaningful impact on transmission, especially in low prevalence settings[14]. Molecular xenomonitoring (testing vectors for the parasite instead of human hosts) for LF and onchocerciasis has shown promise[103] but operational research gaps remain, impacting large-scale utilisation[104]. Reconciling these different streams of imperfect diagnostic data will be key to their utility in modelling and indeed to reaching and sustaining public health goals.

The operational units over which epidemiological data are collected, and projections made are also often over somewhat arbitrary administrative borders that infectious diseases do not adhere to. For rabies, non-spatial models are inadequate for capturing the low-endemicity incidence rates[15] such that more data-intensive modelling approaches are required. In addition to questionable detection success, VL surveillance has operated over geographical units that are too large to evaluate the success of control methods[6], despite modelling showing that transmission is highly localised over smaller spatial scales (i.e. 85% of inferred transmission distances ≤300m)[105]. Similarly for onchocerciasis, modelling shows that the rate at which interventions can be scaled down depend strongly on the spatial units of assessment[13,106]. Clustering of *T. solium* porcine cysticercosis around human taeniasis carriers, particularly evident in South American communities, demonstrates the need for spatially explicit models in certain settings[14,107], such as the recently developed CystiAgent model for Peru[108], capable of testing spatially structured interventions. From this it is evident that whilst spatial heterogeneity requires nuanced model structure, the leading challenge here is the paucity of data at the spatial level necessary to parameterise the models for spatially relevant insights. This will become ever more important as all NTDs move towards low-prevalence and spatially-heterogenous incidence patterns.

The assumptions made to overcome these uncertainties often differ across models – which then produce differing results. This is somewhat overcome by the practice of model comparison[109,110], which highlights important biological and population processes that impact epidemiological trajectories, Understanding

where these differences in modelling results come from and what these differences can tell us is critical to the interpretation of modelling results. This waves a clear flag for collaborative opportunities between modellers, field epidemiologists and clinicians, to generate the necessary data to inform model parameters, or provide setting-specific insight, improving projections and the cross-discipline understanding of model results. Indeed, the optimal working relationship is a synergistic pathway, where the model's needs drive data collection, the data shapes further model iterations, and these then inform policy and the outcomes at the programmatic and clinical level[51,83–94]. Improving communication between these groups is critical to achieving the desired public health gains[20].

The integration of modelling across public health hierarchy is also crucial but is an ongoing challenge. Whilst leading global health bodies like the WHO use modelling results to generate broad guidance at the international level, the truth is that this one-size-fits-all approach is unlikely to sufficiently describe intervention needs in every setting, such that local decision makers may be unsure why interventions – as advised by modelling – have not reached public health targets, when to stop MDA[79], or why resurgence occurs. This is not necessarily a failure of the modelling process, but of the framework in which modelling results are used and the way in which model results are accessed. One way to overcome this, and indeed many of the above challenges, is to provide in-country/ local decisions makers with modelling tools, making clear what data are needed to provide location-specific insights. Such tools do exist and efforts to extend the availability of these are ongoing where research and public health funding allow; for gHAT across the Democratic Republic of Congo, modelling has been used to identify target health zones, accompanied by an interactive visual tool[111]. A tool for LF is also available[112], however the authors highlight the advantages and disadvantages associated with such tools. For example, the level of expertise needed to harness the tool and interpret the results will depend on the level of automation[113] – which itself creates further trade-offs between usability and correct model specification, with fewer parameters available for change within an interface, limiting calibration to local settings. There is also an increased risk of incorrect interpretation including poor understanding of uncertainty and where it comes from, which could lead to reduced trust in the results and modelling methods. It is therefore imperative to balance the availability of tools at local scales with the expertise to use the models correctly.

Conclusion

The increased use of mathematical and statistical modelling over the last decade has helped move the field of NTDs into a more quantitative space, providing the link between epidemiological concepts and observed reality. For modelling to continue to fill this role and influence decision-making, ongoing conversations and engagement between all parties will be paramount. These will, in turn, overcome the continuous challenges of data quality and access, and the consequent model assumptions required. As programme and disease management move towards a country-ownership framework under the new roadmap, it will be key that modelling follows suit, overcoming systematic notions of knowledge ownership and challenging associated power dynamics[114–116]. In this way, future modelling will work to support this new NTD landscape.

Data availability

No data are associated with this article.

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References

1. World Health Organization: **Ending the neglect to attain the sustainable development goals: a road map for neglected tropical diseases 2021-2030**. Geneva: World Health Organization, 2020; License: CC BY-NC-SA 3.0 IGO.
Reference Source

2. NTD Modelling Consortium, WHO Department of Control of Neglected Tropical Diseases: **Achieving NTD Control, Elimination and Eradication Targets Post-2020 Modelling Perspectives and Priorities**. Geneva, 2019 15th - 16th April 2019.
Publisher Full Text

3. Collaborating Group on Dengue Disease Modelling: **Considerations for the 2030 Sustainable Development Goals for dengue [version 1; peer review: 2 approved with reservations].** *Gates Open Res.* 2019; **3**.
Publisher Full Text

4. NTD Modelling Consortium Lymphatic Filariasis Group: **The roadmap towards elimination of lymphatic filariasis by 2030: insights from quantitative and mathematical modelling [version 1; peer review: 2 approved].** *Gates Open Res.* 2019; **3**: 1538.
PubMed Abstract | Publisher Full Text | Free Full Text

5. NTD Modelling Consortium discussion group on Trachoma: **Insights from mathematical modelling and quantitative analysis on the proposed 2030 goals for trachoma [version 2; peer review: 2 approved].** *Gates Open Res.* 2021; **3**: 1721.
PubMed Abstract | Publisher Full Text | Free Full Text

6. NTD Modelling Consortium Visceral Leishmaniasis Group: **Insights from mathematical modelling and quantitative analysis on the proposed WHO 2030 targets for visceral leishmaniasis on the Indian subcontinent [version 1; peer review: 3 approved, 1 approved with reservations].** *Gates Open Res.* 2019; **3**: 1651.
PubMed Abstract | Publisher Full Text | Free Full Text

7. Marks M, McVernon J, Engelman D, *et al.*: **Insights from mathematical modelling on the proposed WHO 2030 goals for scabies [version 1; peer review: 3 approved].** *Gates Open Res.* 2019; **3**: 1542.
PubMed Abstract | Publisher Full Text | Free Full Text

8. NTD Modelling Consortium discussion group on soil-transmitted helminthes: **Insights from quantitative analysis and mathematical modelling on the proposed WHO 2030 goals for soil-transmitted helminths [version 2; peer review: 2 approved].** *Gates Open Res.* 2019; **3**: 1632.
PubMed Abstract | Publisher Full Text | Free Full Text

9. NTD Modelling Consortium Discussion Group on *Gambiense* Human African Trypanosomiasis: **Insights from quantitative and mathematical modelling on the proposed 2030 goal for *gambiense* human African trypanosomiasis (gHAT) [version 2; peer review: 2 approved]**. *Gates Open Res.* 2020; **3**: 1553.
PubMed Abstract | Publisher Full Text | Free Full Text

10. Dyson L, Mooring EQ, Holmes A, *et al.*: **Insights from quantitative and mathematical modelling on the proposed 2030 goals for Yaws [version 1; peer review: 2 approved].** *Gates Open Res.* 2019; **3**: 1576.
PubMed Abstract | Publisher Full Text | Free Full Text

11. NTD Modelling Consortium Schistosomiasis Group: **Insights from quantitative and mathematical modelling on the proposed WHO 2030 goal for schistosomiasis [version 2; peer review: 3 approved].** *Gates Open Res.* 2019; **3**: 1517.
PubMed Abstract | Publisher Full Text | Free Full Text

12. Collaborating Group on Chagas Disease Modelling: **Insights from quantitative and mathematical modelling on the proposed WHO 2030 goals for Chagas disease [version 1; peer review: 2 approved].** *Gates Open Res.* 2019; **3**: 1539.
PubMed Abstract | Publisher Full Text | Free Full Text

13. NTD Modelling Consortium Onchocerciasis Group: **The World Health Organization 2030 goals for onchocerciasis: Insights and perspectives from mathematical modelling [version 1; peer review: 3 approved].** *Gates Open Res.* 2019; **3**: 1545.
PubMed Abstract | Publisher Full Text | Free Full Text

14. CystiTeam Group for Epidemiology and Modelling of *Taenia solium*/Taeniasis Cysticercosis: **The World Health Organization 2030 goals for *Taenia solium*: Insights and perspectives from transmission dynamics modelling [version 2; peer review: 3 approved].** *Gates Open Res.* 2019; **3**: 1546.
PubMed Abstract | Publisher Full Text | Free Full Text

15. World Health Organization Rabies Modelling Consortium: **Zero human deaths from dog-mediated rabies by 2030: perspectives from quantitative and mathematical modelling [version 2; peer review: 3 approved, 1 approved with reservations].** *Gates Open Res.* 2020; **3**: 1564.
PubMed Abstract | Publisher Full Text | Free Full Text

16. World Health Organization: **Global update on implementation of preventive chemotherapy against neglected tropical diseases in 2018.** *Weekly Epidemiological Record.* 2019; **38**(94): 425–40.
Reference Source

17. Hotez PJ, Ottesen E, Fenwick A, *et al.*: **The neglected tropical diseases: the ancient afflictions of stigma and poverty and the prospects for their control and elimination.** In: Pollard AJ, Finn A. (eds.) *Adv Exp Med Biol.* 2006; **582**: 23–33. Boston, MA: Springer.
PubMed Abstract | Publisher Full Text

18. World Health Organization: **Accelerating Work to Overcome the Global Impact of Neglected Tropical Diseases – A Roadmap for Implementation.** Geneva. Geneva. 2012.
Reference Source

19. Uniting to Combat NTDs: **London Declaration on Neglected Tropical Diseases.** 2012.
Reference Source

20. Behrend MR, Basáñez MG, Hamley JID, *et al.*: **Modelling for policy: The five principles of the Neglected Tropical Diseases Modelling Consortium.** *PLoS Negl Trop Dis.* 2020; **14**(4): e0008033.
PubMed Abstract | Publisher Full Text | Free Full Text

21. Hollingsworth TD, Adams ER, Anderson RM, *et al.*: **Quantitative analyses and modelling to support achievement of the 2020 goals for nine neglected**

tropical diseases. *Parasit Vectors.* 2015; **8**: 630.
PubMed Abstract | Publisher Full Text | Free Full Text

22. Stylianou A, Hadjichrysanthou C, Truscott JE, *et al.*: **Developing a mathematical model for the evaluation of the potential impact of a partially efficacious vaccine on the transmission dynamics of *Schistosoma mansoni* in human communities.** *Parasit Vectors.* 2017; **10**(1): 294.
PubMed Abstract | Publisher Full Text | Free Full Text

23. Rock KS, Ndeffo-Mbah ML, Castaño S, *et al.*: **Assessing strategies against *gambiense* sleeping sickness through mathematical modeling.** *Clin Infect Dis.* 2018; **66**(suppl_4): S286–S92.
PubMed Abstract | Publisher Full Text | Free Full Text

24. Mahamat MH, Peka M, Rayaisse JB, *et al.*: **Adding tsetse control to medical activities contributes to decreasing transmission of sleeping sickness in the Mandoul focus (Chad).** *PLoS Negl Trop Dis.* 2017; **11**(7): e0005792.
PubMed Abstract | Publisher Full Text | Free Full Text

25. Rock KS, Torr SJ, Lumbala C, *et al.*: **Predicting the impact of intervention strategies for sleeping sickness in two high-endemicity health zones of the Democratic Republic of Congo.** *PLoS Negl Trop Dis.* 2017; **11**(1): e0005162.
PubMed Abstract | Publisher Full Text | Free Full Text

26. Rock KS, Torr SJ, Lumbala C, *et al.*: **Quantitative evaluation of the strategy to eliminate human African trypanosomiasis in the Democratic Republic of Congo.** *Parasit Vectors.* 2015; **8**: 532.
PubMed Abstract | Publisher Full Text | Free Full Text

27. Toor J, Adams ER, Aliee M, *et al.*: **Predicted impact of COVID-19 on neglected tropical disease programs and the opportunity for innovation.** *Clin Infect Dis.* 2020; **72**(8): 1463–6.
PubMed Abstract | Publisher Full Text | Free Full Text

28. Kura K, Ayabina D, Toor J, *et al.*: **Disruptions to schistosomiasis programmes due to COVID-19: an analysis of potential impact and mitigation strategies.** *Trans R Soc Trop Med Hyg.* 2021; **115**(3): 236–44.
PubMed Abstract | Publisher Full Text | Free Full Text

29. Aliee M, Castaño S, Davis CN, *et al.*: **Predicting the impact of COVID-19 interruptions on transmission of *gambiense* human African trypanosomiasis in two health zones of the Democratic Republic of Congo.** *Trans R Soc Trop Med Hyg.* 2021; **115**(3): 245–52.
PubMed Abstract | Publisher Full Text | Free Full Text

30. Blumberg S, Borlase A, Prada JM, *et al.*: **Implications of the COVID-19 pandemic in eliminating trachoma as a public health problem.** *Trans R Soc Trop Med Hyg.* 2021; **115**(3): 222–8.
PubMed Abstract | Publisher Full Text | Free Full Text

31. Borlase A, Blumberg S, Callahan EK, *et al.*: **Modelling trachoma post-2020: opportunities for mitigating the impact of COVID-19 and accelerating progress towards elimination.** *Trans R Soc Trop Med Hyg.* 2021; **115**(3): 213–21.
PubMed Abstract | Publisher Full Text | Free Full Text

32. Hamley JID, Blok DJ, Walker M, *et al.*: **What does the COVID-19 pandemic mean for the next decade of onchocerciasis control and elimination?** *Trans R Soc Trop Med Hyg.* 2021; **115**(3): 269–80.
PubMed Abstract | Publisher Full Text | Free Full Text

33. Le Rutte EA, Coffeng LE, Munoz J, *et al.*: **Modelling the impact of COVID-19-related programme interruptions on visceral leishmaniasis in India.** *Trans R Soc Trop Med Hyg.* 2021; **115**(3): 229–35.
PubMed Abstract | Publisher Full Text | Free Full Text

34. Malizia V, Giardina F, Vegvari C, *et al.*: **Modelling the impact of COVID-19-related control programme interruptions on progress towards the WHO 2030 target for soil-transmitted helminths.** *Trans R Soc Trop Med Hyg.* 2021; **115**(3): 253–60.
PubMed Abstract | Publisher Full Text | Free Full Text

35. Prada JM, Stolk WA, Davis EL, *et al.*: **Delays in lymphatic filariasis elimination programmes due to COVID-19, and possible mitigation strategies.** *Trans R Soc Trop Med Hyg.* 2021; **115**(3): 261–8.
PubMed Abstract | Publisher Full Text | Free Full Text

36. World Health Organization: **Guideline: Alternative mass drug administration regimens to eliminate Lymphatic Filariasis.** 2017.
Reference Source

37. 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**(4): 451–8.
PubMed Abstract | Publisher Full Text

38. Bartsch SM, Peterson JK, Hertenstein DL, *et al.*: **Comparison and validation of two computational models of Chagas disease: A thirty year perspective from Venezuela.** *Epidemics.* 2017; **18**: 81–91.
PubMed Abstract | Publisher Full Text | Free Full Text

39. Cucunubá ZM, Nouvellet P, Peterson JK, *et al.*: **Complementary Paths to Chagas Disease Elimination: The Impact of Combining Vector Control With Etiological Treatment.** *Clin Infect Dis.* 2018; **66**(suppl_4): S293–S300.
PubMed Abstract | Publisher Full Text | Free Full Text

40. 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**(suppl_4): S237–S244.
PubMed Abstract | Publisher Full Text | Free Full Text

41. Gambhir M, Pinsent A: **Possible changes in the transmissibility of trachoma following MDA and transmission reduction: implications for the GET2020 goals.** *Parasit Vectors.* 2015; **8**: 530.
PubMed Abstract | Publisher Full Text | Free Full Text

42. Toor J, Alsallaq R, Truscott JE, *et al.*: **Are We on Our Way to Achieving the 2020 Goals for Schistosomiasis Morbidity Control Using Current World Health Organization Guidelines?** *Clin Infect Dis.* 2018; **66**(suppl_4): S245–S52.
PubMed Abstract | Publisher Full Text | Free Full Text

43. Deol AK, Fleming FM, Calvo-Urbano B, *et al.*: **Schistosomiasis - Assessing Progress toward the 2020 and 2025 Global Goals.** *N Engl J Med.* 2019; **381**(26): 2519–28.
PubMed Abstract | Publisher Full Text | Free Full Text

44. Medley GF, Blok DJ, Crump RE, *et al.*: **Policy Lessons From Quantitative Modeling of Leprosy.** *Clin Infect Dis.* 2018; **66**(suppl_4): S281–S285.
PubMed Abstract | Publisher Full Text | Free Full Text

45. Verver S, Walker M, Kim YE, *et al.*: **How can onchocerciasis elimination in Africa be accelerated? Modeling the impact of increased Ivermectin treatment frequency and complementary vector control.** *Clin Infect Dis.* 2018; **66**(suppl_4): S267–S274.
PubMed Abstract | Publisher Full Text | Free Full Text

46. Kumar V, Siddiqui NA, Pollington TM, *et al.*: **Impact of intensified control strategies on incidence of visceral leishmaniasis in a highly endemic district of Bihar, India**. An interrupted time series analysis to assess interventions as new WHO 2021 – 2030 elimination goals are agreed. ResearchGate Preprint. 2020.
Reference Source

47. Davis EL, Danon L, Prada JM, *et al.*: **Seasonally timed treatment programs for Ascaris lumbricoides to increase impact-An investigation using mathematical models.** *PLoS Negl Trop Dis.* 2018; **12**(1): e0006195.
PubMed Abstract | Publisher Full Text | Free Full Text

48. Walker M, Pion SDS, Fang H, *et al.*: **Macrofilaricidal efficacy of repeated doses of Ivermectin for the treatment of river blindness.** *Clin Infect Dis.* 2017; **65**(12): 2026–34.
PubMed Abstract | Publisher Full Text | Free Full Text

49. Anderson R, Truscott J, Hollingsworth TD: **The coverage and frequency of mass drug administration required to eliminate persistent transmission of soil-transmitted helminths.** *Philos Trans R Soc Lond B Biol Sci.* 2014; **369**(1645): 20130435.
PubMed Abstract | Publisher Full Text | Free Full Text

50. Farrell SH, Coffeng L, Truscott J, *et al.*: **Investigating the effectiveness of current and modified world health organization guidelines for the control of soil-transmitted helminth infections.** *Clin Infect Dis.* 2018; **66**(suppl_4): S253–S259.
PubMed Abstract | Publisher Full Text | Free Full Text

51. Toor J, Turner HC, Truscott JE, *et al.*: **The design of schistosomiasis monitoring and evaluation programmes: The importance of collecting adult data to inform treatment strategies for *Schistosoma mansoni*.** *PLoS Negl Trop Dis.* 2018; **12**(10): e0006717.
PubMed Abstract | Publisher Full Text | Free Full Text

52. Turner HC, Truscott JE, Fleming FM, *et al.*: **Cost-effectiveness of scaling up mass drug administration for the control of soil-transmitted helminths: a comparison of cost function and constant costs analyses.** *Lancet Infect Dis.* 2016; **16**(7): 838–46.
PubMed Abstract | Publisher Full Text

53. 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.
PubMed Abstract | Publisher Full Text | Free Full Text

54. Davis CN, Rock KS, Antillón M, *et al.*: **Cost-effectiveness modelling to optimise active screening strategy for *gambiense* human African trypanosomiasis in endemic areas of the Democratic Republic of Congo.** *BMC Med.* 2021; **19**(1): 86.
PubMed Abstract | Publisher Full Text | Free Full Text

55. Lenk EJ, Redekop WK, Luyendijk M, *et al.*: **Socioeconomic benefit to individuals of achieving 2020 targets for four neglected tropical diseases controlled/eliminated by innovative and intensified disease management: Human African trypanosomiasis, leprosy, visceral leishmaniasis, Chagas disease.** *PLoS Negl Trop Dis.* 2018; **12**(3): e0006250.
PubMed Abstract | Publisher Full Text | Free Full Text

56. Kim YE, Stolk WA, Tanner M, *et al.*: **Modelling the health and economic impacts of the elimination of river blindness (onchocerciasis) in Africa.** *BMJ Glob Health.* 2017; **2**(2): e000158.
PubMed Abstract | Publisher Full Text | Free Full Text

57. Lo NC, Gurarie D, Yoon N, *et al.*: **Impact and cost-effectiveness of snail control to achieve disease control targets for schistosomiasis.** *Proc Natl Acad Sci U S A.* 2018; **115**(4): E584–E591.
PubMed Abstract | Publisher Full Text | Free Full Text

58. Lo NC, Lai YS, Karagiannis-Voules DA, *et al.*: **Assessment of global guidelines for preventive chemotherapy against schistosomiasis and soil-transmitted helminthiasis: a cost-effectiveness modelling study.** *Lancet Infect Dis.* 2016; **16**(9): 1065–75.
PubMed Abstract | Publisher Full Text

59. Turner HC, Truscott JE, Hollingsworth TD, *et al.*: **Cost and cost-effectiveness of soil-transmitted helminth treatment programmes: systematic review and research needs.** *Parasit Vectors.* 2015; **8**: 355.
PubMed Abstract | Publisher Full Text | Free Full Text

60. Turner HC, Walker M, French MD, *et al.*: **Neglected tools for neglected diseases: mathematical models in economic evaluations.** *Trends Parasitol.* 2014; **30**(12): 562–70.
PubMed Abstract | Publisher Full Text

61. Smith JL, Sturrock HJW, Assefa L, *et al.*: **Factors associated with the performance and cost-effectiveness of using lymphatic filariasis transmission assessment surveys for monitoring soil-transmitted helminths: a case study in Kenya.** *Am J Trop Med Hyg.* 2015; **92**(2): 342–53.
PubMed Abstract | Publisher Full Text | Free Full Text

62. Stone CM, Kastner R, Steinmann P, *et al.*: **Modelling the health impact and cost-effectiveness of lymphatic filariasis eradication under varying levels of mass drug administration scale-up and geographic coverage.** *BMJ Glob Health.* 2016; **1**(1): e000021.
PubMed Abstract | Publisher Full Text | Free Full Text

63. Babu BV, Babu GR: **Coverage of, and compliance with, mass drug administration under the programme to eliminate lymphatic filariasis in India: a systematic review.** *Trans R Soc Trop Med Hyg.* 2014; **108**(9): 538–49.
PubMed Abstract | Publisher Full Text

64. Plaisier AP, Stolk WA, van Oortmarssen GJ, *et al.*: **Effectiveness of annual Ivermectin treatment for *Wuchereria bancrofti* infection.** *Parasitol Today.* 2000; **16**(7): 298–302.
PubMed Abstract | Publisher Full Text

65. Nandha B, Meenakshy V, Abdul Khader N, *et al.*: **Bridging the gap in outreach and compliance with mass drug administration for lymphatic filariasis elimination in an endemic district in Kerala, India: an intervention research approach.** *Health Educ Res.* 2019; **34**(3): 300–9.
PubMed Abstract | Publisher Full Text

66. Chami GF, Kabatereine NB, Tukahebwa EM: **The division of labour between community medicine distributors influences the reach of mass drug administration: A cross-sectional study in rural Uganda.** *PLoS Negl Trop Dis.* 2019; **13**(9): e0007685.
PubMed Abstract | Publisher Full Text | Free Full Text

67. Crump RE, Huang CI, Knock ES, *et al.*: **Quantifying epidemiological drivers of *gambiense* human African Trypanosomiasis across the Democratic Republic of Congo.** *PLoS Comput Biol.* 2021; **17**(1): e1008532.
PubMed Abstract | Publisher Full Text | Free Full Text

68. Rajeev M, Guis H, Edosoa GT, *et al.*: **How geographic access to care shapes disease burden: The current impact of post-exposure prophylaxis and potential for expanded access to prevent human rabies deaths in Madagascar.** *PLoS Negl Trop Dis.* 2021; **15**(4): e0008821.
PubMed Abstract | Publisher Full Text | Free Full Text

69. Farrell SH, Truscott JE, Anderson RM: **The importance of patient compliance in repeated rounds of mass drug administration (MDA) for the elimination of intestinal helminth transmission.** *Parasit Vectors.* 2017; **10**(1): 291.
PubMed Abstract | Publisher Full Text | Free Full Text

70. Hardwick RJ, Truscott JE, Oswald WE, *et al.*: **Individual adherence to mass drug administration in neglected tropical disease control: A probability model conditional on past behaviour.** *PLoS Negl Trop Dis.* 2021; **15**(1): e0009112.
PubMed Abstract | Publisher Full Text | Free Full Text

71. Stolk WA, Prada JM, Smith ME, *et al.*: **Are alternative strategies required to accelerate the global elimination of lymphatic filariasis? Insights from mathematical models.** *Clin Infect Dis.* 2018; **66**(suppl_4): S260–S6.
PubMed Abstract | Publisher Full Text | Free Full Text

72. Irvine MA, Reimer LJ, Njenga SM, *et al.*: **Modelling strategies to break transmission of lymphatic filariasis--aggregation, adherence and vector competence greatly alter elimination.** *Parasit Vectors.* 2015; **8**: 547.
PubMed Abstract | Publisher Full Text | Free Full Text

73. Dyson L, Stolk WA, Farrell SH, *et al.*: **Measuring and modelling the effects of systematic non-adherence to mass drug administration.** *Epidemics.* 2017; **18**: 56–66.
PubMed Abstract | Publisher Full Text | Free Full Text

74. DebRoy S, Prosper O, Mishoe A, *et al.*: **Challenges in modeling complexity of neglected tropical diseases: a review of dynamics of visceral leishmaniasis in resource limited settings.** *Emerg Themes Epidemiol.* 2017; **14**: 10.
PubMed Abstract | Publisher Full Text | Free Full Text

75. Toor J, Coffeng LE, Hamley JID, *et al.*: **When, Who, and How to Sample: Designing Practical Surveillance for 7 Neglected Tropical Diseases as We Approach Elimination.** *J Infect Dis.* 2020; **221**(Suppl 5): S499–S502.
PubMed Abstract | Publisher Full Text | Free Full Text

76. Werkman M, Toor J, Vegvari C, *et al.*: **Defining stopping criteria for ending randomized clinical trials that investigate the interruption of transmission of soil-transmitted helminths employing mass drug administration.** *PLoS Negl Trop Dis.* 2018; **12**(10): e0006864.
PubMed Abstract | Publisher Full Text | Free Full Text

77. Toor J, Truscott JE, Werkman M, *et al.*: **Determining post-treatment surveillance criteria for predicting the elimination of *Schistosoma mansoni* transmission.** *Parasit Vectors.* 2019; **12**(1): 437.
PubMed Abstract | Publisher Full Text | Free Full Text

78. Minter A, Pellis L, Medley GF, *et al.*: **What Can Modeling Tell Us About Sustainable End Points for Neglected Tropical Diseases?** *Clin Infect Dis.* 2021; **72**(Suppl 3): S129–S33.
PubMed Abstract | Publisher Full Text | Free Full Text

79. Walker M, Hamley JID, Milton P, *et al.*: **Supporting drug development for neglected tropical diseases using mathematical modeling.** *Clin Infect Dis.* 2021; **73**(6): e1391–e1396.
PubMed Abstract | Publisher Full Text | Free Full Text

80. Aljayyoussi G, Tyrer HE, Ford L, *et al.*: **Short-course, high-dose Rifampicin achieves *Wolbachia* depletion predictive of curative outcomes in preclinical models of lymphatic filariasis and onchocerciasis.** *Sci Rep.* 2017; **7**(1): 210.
PubMed Abstract | Publisher Full Text | Free Full Text

81. Walker M, Hamley JID, Milton P, *et al.*: **Designing antifilarial drug trials using clinical trial simulators.** *Nat Commun.* 2020; **11**(1): 2685.
PubMed Abstract | Publisher Full Text | Free Full Text

82. Turner HC, Walker M, Attah SK, *et al.*: **The potential impact of moxidectin on onchocerciasis elimination in Africa: an economic evaluation based on the Phase II clinical trial data.** *Parasit Vectors.* 2015; **8**: 167.
PubMed Abstract | Publisher Full Text | Free Full Text

83. Hollingsworth TD, Pulliam JR, Funk S, *et al.*: **Seven challenges for modelling indirect transmission: vector-borne diseases, macroparasites and neglected tropical diseases.** *Epidemics.* 2015; **10**: 16–20.
PubMed Abstract | Publisher Full Text | Free Full Text

84. Toor J, Hamley JID, Fronterre C, *et al.*: **Strengthening data collection for neglected tropical diseases: What data are needed for models to better inform tailored intervention programmes?** *PLoS Negl Trop Dis.* 2021; **15**(5): e0009351.
PubMed Abstract | Publisher Full Text | Free Full Text

85. Chapman LAC, Jewell CP, Spencer SEF, *et al.*: **The role of case proximity in transmission of visceral leishmaniasis in a highly endemic village in Bangladesh.** *PLoS Negl Trop Dis.* 2018; **12**(10): e0006453.
PubMed Abstract | Publisher Full Text | Free Full Text

86. Giardina F, Coffeng LE, Farrell SH, *et al.*: **Sampling strategies for monitoring and evaluation of morbidity targets for soil-transmitted helminths.** *PLoS Negl Trop Dis.* 2019; **13**(6): e0007514.
PubMed Abstract | Publisher Full Text | Free Full Text

87. Pinsent A, Hollingsworth TD: **Optimising sampling regimes and data collection to inform surveillance for trachoma control.** *PLoS Negl Trop Dis.* 2018; **12**(10): e0006531.
PubMed Abstract | Publisher Full Text | Free Full Text

88. Michael E, Sharma S, Smith ME, *et al.*: **Quantifying the value of surveillance data for improving model predictions of lymphatic filariasis elimination.** *PLoS Negl Trop Dis.* 2018; **12**(10): e0006674.
PubMed Abstract | Publisher Full Text | Free Full Text

89. Chapman LAC, Morgan ALK, Adams ER, *et al.*: **Age trends in asymptomatic and symptomatic *Leishmania donovani* infection in the Indian subcontinent: A review and analysis of data from diagnostic and epidemiological studies.** *PLoS Negl Trop Dis.* 2018; **12**(12): e0006803.
PubMed Abstract | Publisher Full Text | Free Full Text

90. Hamley JID, Milton P, Walker M, *et al.*: **Modelling exposure heterogeneity and density dependence in onchocerciasis using a novel individual-based transmission model, EPIONCHO-IBM: Implications for elimination and data needs.** *PLoS Negl Trop Dis.* 2019; **13**(12): e0007557.
PubMed Abstract | Publisher Full Text | Free Full Text

91. Lietman TM, Deiner MS, Oldenburg CE, *et al.*: **Identifying a sufficient core group for trachoma transmission.** *PLoS Negl Trop Dis.* 2018; **12**(10): e0006478.
PubMed Abstract | Publisher Full Text | Free Full Text

92. Bulstra CA, Le Rutte EA, Malaviya P, *et al.*: **Visceral leishmaniasis: Spatiotemporal heterogeneity and drivers underlying the hotspots in Muzaffarpur, Bihar, India.** *PLoS Negl Trop Dis.* 2018; **12**(12): e0006888.
PubMed Abstract | Publisher Full Text | Free Full Text

93. Coffeng LE, Vaz Nery S, Gray DJ, *et al.*: **Predicted short and long-term impact of deworming and water, hygiene, and sanitation on transmission of soil-transmitted helminths.** *PLoS Negl Trop Dis.* 2018; **12**(12): e0006758.
PubMed Abstract | Publisher Full Text | Free Full Text

94. de Vos AS, Stolk WA, de Vlas SJ, *et al.*: **The effect of assortative mixing on stability of low helminth transmission levels and on the impact of mass drug administration: Model explorations for onchocerciasis.** *PLoS Negl Trop Dis.* 2018; **12**(10): e0006624.
PubMed Abstract | Publisher Full Text | Free Full Text

95. Le Rutte EA, Chapman LAC, Coffeng LE, *et al.*: **Policy Recommendations From Transmission Modeling for the Elimination of Visceral Leishmaniasis in the Indian Subcontinent.** *Clin Infect Dis.* 2018; **66**(suppl_4): S301–S8.
PubMed Abstract | Publisher Full Text | Free Full Text

96. Nery JS, Ramond A, Pescarini JM, *et al.*: **Socioeconomic determinants of leprosy new case detection in the 100 Million Brazilian Cohort: a population-based linkage study.** *Lancet Glob Health.* 2019; **7**(9): e1226–e36.
PubMed Abstract | Publisher Full Text | Free Full Text

97. Clark J, Arinaitwe M, Nankasi A, *et al.*: **Reconciling egg- and antigen-based estimates of *Schistosoma mansoni* clearance and reinfection: a modelling study.** *Clin Infect Dis.* 2021; ciab679.
PubMed Abstract | Publisher Full Text

98. Lamberton PHL, Kabatereine NB, Oguttu DW, *et al.*: **Sensitivity and Specificity of multiple kato-katz thick smears and a circulating cathodic antigen test for *Schistosoma mansoni* diagnosis pre- and post-repeated-Praziquantel treatment.** *PLoS Negl Trop Dis.* 2014; **8**(9): e3139.
PubMed Abstract | Publisher Full Text | Free Full Text

99. Medley GF, Turner HC, Baggaley RF, *et al.*: **The Role of More Sensitive Helminth Diagnostics in Mass Drug Administration Campaigns: Elimination and Health Impacts.** *Adv Parasitol.* 2016; **94**: 343–92.
PubMed Abstract | Publisher Full Text

100. Stuyver LJ, Levecke B: **The role of diagnostic technologies to measure progress toward WHO 2030 targets for soil-transmitted helminth control**

programs. *PLoS Negl Trop Dis.* 2021; **15**(6): e0009422.
PubMed Abstract | Publisher Full Text | Free Full Text

101. Lindholz CG, Favero V, de Marco Verissimo C, *et al.*: **Study of diagnostic accuracy of Helmintex, Kato-Katz, and POC-CCA methods for diagnosing intestinal schistosomiasis in Candeal, a low intensity transmission area in northeastern Brazil.** *PLoS Negl Trop Dis.* 2018; **12**(3): e0006274.
PubMed Abstract | Publisher Full Text | Free Full Text

102. Rudge JW, Webster JP, Lu DB, *et al.*: **Identifying host species driving transmission of schistosomiasis japonica, a multihost parasite system, in China.** *Proc Natl Acad Sci U S A.* 2013; **110**(28): 11457–62.
PubMed Abstract | Publisher Full Text | Free Full Text

103. Pryce J, Reimer LJ: **Evaluating the diagnostic test accuracy of molecular xenomonitoring methods for characterizing community burden of lymphatic filariasis.** *Clin Infect Dis.* 2021; **72**(Suppl 3): S203–S209.
PubMed Abstract | Publisher Full Text | Free Full Text

104. Pilotte N, Unnasch TR, Williams SA: **The Current Status of Molecular Xenomonitoring for Lymphatic Filariasis and Onchocerciasis.** *Trends Parasitol.* 2017; **33**(10): 788–98.
PubMed Abstract | Publisher Full Text

105. Chapman LAC, Spencer SEF, Pollington TM, *et al.*: **Inferring transmission trees to guide targeting of interventions against visceral leishmaniasis and post-kala-azar dermal leishmaniasis.** *Proc Natl Acad Sci U S A.* 2020; **117**(41): 25742–50.
PubMed Abstract | Publisher Full Text | Free Full Text

106. Stolk WA, Blok DJ, Hamley JID, *et al.*: **Scaling-down mass ivermectin treatment for onchocerciasis elimination: modeling the impact of the geographical unit for decision making.** *Clin Infect Dis.* 2021; **72**(Suppl 3): S165–S171.
PubMed Abstract | Publisher Full Text | Free Full Text

107. Dixon MA, Braae UC, Winskill P, *et al.*: **Strategies for tackling *Taenia solium* taeniosis/cysticercosis: A systematic review and comparison of transmission models, including an assessment of the wider Taeniidae family transmission models.** *PLoS Negl Trop Dis.* 2019; **13**(4): e0007301.
PubMed Abstract | Publisher Full Text | Free Full Text

108. Pray IW, Wakeland W, Pan W, *et al.*: **Understanding transmission and control of the pork tapeworm with CystiAgent: a spatially explicit agent-based model.** *Parasit Vectors.* 2020; **13**(1): 372.
PubMed Abstract | Publisher Full Text | Free Full Text

109. Hollingsworth TD, Medley GF: **Learning from multi-model comparisons: Collaboration leads to insights, but limitations remain.** *Epidemics.* 2017; **18**: 1–3.
PubMed Abstract | Publisher Full Text

110. Hamley JID, Walker M, Coffeng LE, *et al.*: **Structural Uncertainty in Onchocerciasis Transmission Models Influences the Estimation of Elimination Thresholds and Selection of Age Groups for Seromonitoring.** *J Infect Dis.* 2020; **221**(Suppl 5): S510–S8.
PubMed Abstract | Publisher Full Text | Free Full Text

111. Huang CI, Crump RE, Brown PE, *et al.*: **Identifying regions for enhanced control of gambiense sleeping sickness in the Democratic Republic of Congo.** *medRxiv.* 2021; 2020.07.03.20145847.
Publisher Full Text

112. Irvine MA, Hollingsworth TD: **Making Transmission Models Accessible to End-Users: The Example of TRANSFIL.** *PLoS Negl Trop Dis.* 2017; **11**(2): e0005206.
PubMed Abstract | Publisher Full Text | Free Full Text

113. Hollingsworth TD, Langley I, Nokes DJ, *et al.*: **Infectious disease and health systems modelling for local decision making to control neglected tropical diseases.** *BMC Proc.* 2015; **9**(Suppl 10): S6.
PubMed Abstract | Publisher Full Text | Free Full Text

114. Abimbola S, Asthana S, Montenegro C, *et al.*: **Addressing power asymmetries in global health: Imperatives in the wake of the COVID-19 pandemic.** *PLoS Med.* 2021; **18**(4): e1003604.
PubMed Abstract | Publisher Full Text | Free Full Text

115. Adetokunboh OO, Mthombothi ZE, Dominic EM, *et al.*: **African based researchers' output on models for the transmission dynamics of infectious diseases and public health interventions: A scoping review.** *PLoS One.* 2021; **16**(5): e0250086.
PubMed Abstract | Publisher Full Text | Free Full Text

116. Iyer AR: **Authorship trends in *The Lancet Global Health.*** *Lancet Glob Health.* 2018; **6**(2): e142.
PubMed Abstract | Publisher Full Text

Open Peer Review

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Version 2

Reviewer Report 04 February 2022

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✔ **Angus McLure**
National Centre for Epidemiology and Population Health, Australian National University, Acton, ACT, Australia

The changes implemented by the authors have addressed my (minor) reservations.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Infectious disease modelling broadly, with some experience with LF but not the other NTDs covered by this letter.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 04 January 2022

https://doi.org/10.21956/gatesopenres.14570.r31306

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✔ **Margaret C. Baker**
Georgetown University, Washington, DC, USA

This article is an introduction to the series of articles that have been published describing the role of mathematical modelling in the development of the goals and objectives set by the World Health

Organization in the 2021-2030 roadmap for NTDs. The article provides a good overview of the series which in turn provides welcome visibility into how mathematical models informed the development of the 2030 roadmap.The article makes the case for use of modeling in regards to informing: 1) Programmatic timelines, 2) Program design and 3) Drug development.

With regard to the first 2 items (timelines and program design), the case is clearly made for the potential of modeling to inform these, at least at a global level. What is less clear is how modeling can inform decision making at a national level to answer similar questions. This would require the use of an interactive tool that can be used by NTD program managers and their partners to input their parameters (e.g. disease agent, vector species, baseline prevalence, different intervention details, etc). They would in turn be provided with predictions on timelines and answers to questions such as: what would be the impact of: increasing coverage? Reducing those never treated by x %? Adding complimentary control methods? Increasing frequency of treatment? Such tools are available for other health areas like maternal and neonatal health (e.g http://www.healthpolicyplus.com/ns/pubs/18466-18842_MHTools.pdf; http://www.mandate4mnh.org/; Jones-Hepler *et al.*, 2017[1])

With regards to drug development I am not aware of the need for new drugs for LF or trachoma (the references provided did not collaborate and these are not listed as challenges in the Roadmap).

As a reviewer I was asked to comment on whether the article adequately referenced different views and opinions, to which I respond, only partially. The article is authored by modellers who have a much clearer insight into the pro modelling perspective. There are still many in the NTD community who remain skeptical - due to one of the challenges that is clearly presented in this article, that is the reliability of the data on which the models are built. It would be helpful to have all the assumptions, parameters, and data sources used in the models published online in one easy-to-access place. This would enable more informed discussions to take place, across a wider group of participants, as existing evidence is weighed in making policy decisions. It would also be helpful to have a summary from this of the biggest evidence gaps - to drive research and documentation of programmatic results.

References

1. Jones-Hepler B, Moran K, Griffin J, McClure E, et al.: Maternal and Neonatal Directed Assessment of Technologies (MANDATE): Methods and Assumptions for a Predictive Model for Maternal, Fetal, and Neonatal Mortality Interventions. *Global Health: Science and Practice*. 2017; **5** (4): 571-580 Publisher Full Text

Is the rationale for the Open Letter provided in sufficient detail?

Yes

Does the article adequately reference differing views and opinions?

Partly

Are all factual statements correct, and are statements and arguments made adequately supported by citations?

Partly

Is the Open Letter written in accessible language?
Yes

Where applicable, are recommendations and next steps explained clearly for others to follow?
Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: PC NTDs, implementation science, design and evaluation of infectious disease control programs

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 28 Jan 2022

Jessica Clark, University of Oxford, Old Road Campus, Headington, UK

What is less clear is how modeling can inform decision making at a national level to answer similar questions. This would require the use of an interactive tool that can be used by NTD program managers and their partners to input their parameters (e.g. disease agent, vector species, baseline prevalence, different intervention details, etc). They would in turn be provided with predictions on timelines and answers to questions such as: what would be the impact of: increasing coverage? Reducing those never treated by x %? Adding complimentary control methods? Increasing frequency of treatment? Such tools are available for other health areas like maternal and neonatal health (e.g http://www.healthpolicyplus.com/ns/pubs/18466-18842_MHTools.pdf; http://www.mandate4mnh.org/; Jones-Hepler et al., 2017[1])

A similar point has been raised by reviewer 1. A new final paragraph of the C*hallenges* section has been added. In short, the translation of international-level policy to local-level implementation does mean that local-level specific details are often overlooked, and general policy recommendations fail to meet all conditions of that setting. Whilst providing tools locally is an obvious path to improve national (or smaller) level control, it comes with a trade-off. In making the models more user-friendly, some of the complexities that allow for fine scale tuning of certain parameters may have to become fixed, such that the insight is less specific. There is also the matter of interpretation and understandings the limitations of the models. As such, local expertise is still necessary even in the hands of decision-makers.

With regards to drug development I am not aware of the need for new drugs for LF or trachoma (the references provided did not collaborate and these are not listed as challenges in the Roadmap).

This misunderstanding was a result of poor sentence structure. We have rectified this by rewriting the opening to the *Drug development and clinical study design* section.

As a reviewer I was asked to comment on whether the article adequately referenced different views and opinions, to which I respond, only partially. The article is authored by modellers who have a much clearer insight into the pro modelling perspective. There are still many in the NTD community who remain skeptical - due to one of the challenges that is clearly presented in this article, that is the reliability of the data on which the models are built. It would be helpful to have all the assumptions, parameters, and data sources used in the models published online in one easy-to-access place. This would enable more informed discussions to take place, across a wider group of participants, as existing evidence is weighed in making policy decisions. It would also be helpful to have a summary from this of the biggest evidence gaps - to drive research and documentation of programmatic results.

It is out with the scope of this article to provide a thorough overview of the data needs to improve modelling insights. There is however a PLoS NTD collection that was cited in the main text. To make this clearer, text has been added text to the *Challenges* section, directing the reader to this in-depth collection. With regards to the assumptions, parameters and data sources; these are provided in every publication that presents modelling results, and the code for each model is public. These are not included here because there are no models specifically presented here.

Competing Interests: No competing interests were disclosed.

Reviewer Report 14 December 2021

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Angus McLure
National Centre for Epidemiology and Population Health, Australian National University, Acton, ACT, Australia

This open letter summarises the contributions of (infectious) disease modelling to inform elimination efforts for Neglected Tropical Diseases (NTDs), highlighting key areas of contributions (timelines/forecasts/predictions, Programme/intervention/surveillance design, and drug development) and naming some of the key challenges. To be frank, it appears to me the kind of letter that doesn't fit very well into the peer-review paradigm as the goal is primarily to introduce a collection of papers. However, I have tried to answer the peer-review questions as posed and provide constructive feedback where I can. I should note that my relevant area of knowledge is mostly around LF and infectious disease modelling more broadly, so my review is skewed towards topics most relevant to LF.

Regarding the correctness of all statements, to my knowledge, nearly all the statements are correct. However, I would like to highlight one statement which seemed at odds with the literature. The line comes in paragraph 10: 'To reach goals like elimination as a public health

programme (trachoma, STH, schistosomiasis and LF) and elimination of transmission (onchocerciasis) novel drug development will be critical'. With regards to LF, I don't agree with this statement, i.e. I don't think new drug development is critical for the elimination of LF as a public health problem. Moreover the statement appears to contradict the Consortium's recent paper specifically on LF elimination targets (NTD Modelling Consortium Lymphatic Filariasis Group, 2019 [1]). From my knowledge of LF, the existing drugs (ivermectin, albendazole, and diethylcarbamazine) work well and as long as drugs are matched to the setting, side effects are not major concerns. The Consortium's existing work suggests that the 2030 goals can be achieved with these existing drugs if programmes can effectively deliver enough rounds of MDA before 2030. The main barrier to this elimination campaign is achieving high coverage (with the existing drugs) and reaching areas or people who have consistently low treatment coverage. Even a 100% effective and safe medicine won't help if some people or foci aren't being treated. Whether this criticism can be extended to the other diseases mentioned here is beyond my knowledge. This is the only point in the paper I have real reservations about.

I have indicated in my review that the letter only *partly* references differing views and opinions. Though I don't think this represents a major defect of the letter, I should explain why I chose this response. As the main thrust of the letter is that modelling has been and can continue to be useful for directing elimination efforts, presenting differing views and opinions would involve finding examples of where models have *mis*directed elimination efforts or sharing the opinions those who hold that 'models are a waste of time'. While I have certainly come across those who hold the latter view, they tend not to express their view in the form of citable literature, so the absence of their opinions is perhaps to be expected! However, as regards instances where models have misdirected elimination efforts, given the large volume of literature covered, there are probably examples of this — i.e. where a model recommended an intervention that turned out to be far from adequate. Whether these examples are publicly available and known to the authors is another question. If they know of good examples, the authors might consider including these, perhaps with a note about how these failures have informed future modelling work.

Having said all this, I think the 'challenges' section of the paper covers the major challenges reasonably enough. This section can perhaps be improved by giving more examples of how these challenges translate into things that models *cannot* or have not yet been able to do; currently the section feels a little too modelling-centric rather than programme-centric. An example of something models have not been able to do (that I am aware of) is around critical prevalence thresholds for LF/oncho elimination. Various models investigating these have found that the critical threshold varies substantially based on setting-specific assumptions. However, knowing that the threshold will be different in different settings doesn't really help you pick a target threshold that's appropriate for *your* setting. And since there haven't been resources in place to fit models to every setting, we have ended up with the very crude 1/2% prevalence thresholds which will be unnecessarily low in some settings and too high in others (e.g. places with high and highly heterogenous biting rates). This to me is an example not of the failure of *modellers*, but a limitation of modelling as an approach to help inform *specific* interventions/programmes. You might argue that the 1%/2% thresholds are targets not *necessarily* meant to be identified with critical transmission tipping points. However my reading of the non-modelling literature and conversations with non-modellers suggests that many people believe that the 1%/2% target thresholds entail the interruption of transmission and that many believe that the universal application of these thresholds have a rigorous evidence base. Moreover, discussion of resurgence often blame failure to achieve the threshold rather than suggesting that the threshold

might be wrong for the setting. Again this perhaps points to a failure of communication rather than a failure of the modelling itself, but as this letter is about how modelling informs practice, this example (or better example along a similar line) may be relevant for inclusion (if they can manage to express it more succinctly than I have!).

A final minor point:
P10. Misplaced comma in "by endemic nations, on donations".

References

1. NTD Modelling Consortium Lymphatic Filariasis Group: The roadmap towards elimination of lymphatic filariasis by 2030: insights from quantitative and mathematical modelling.*Gates Open Res* . 2019; **3**: 1538 PubMed Abstract | Publisher Full Text

Is the rationale for the Open Letter provided in sufficient detail?
Yes

Does the article adequately reference differing views and opinions?
Partly

Are all factual statements correct, and are statements and arguments made adequately supported by citations?
Partly

Is the Open Letter written in accessible language?
Yes

Where applicable, are recommendations and next steps explained clearly for others to follow?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Infectious disease modelling broadly, with some experience with LF but not the other NTDs covered by this letter.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 28 Jan 2022

Jessica Clark, University of Oxford, Old Road Campus, Headington, UK

Regarding the correctness of all statements, to my knowledge, nearly all the statements are correct. However, I would like to highlight one statement which seemed at odds with the literature. The line comes in paragraph 10: 'To reach goals like elimination as a public health programme (trachoma, STH, schistosomiasis and LF) and elimination of

transmission (onchocerciasis) novel drug development will be critical'. With regards to LF, I don't agree with this statement, i.e. I don't think new drug development is critical for the elimination of LF as a public health problem. Moreover the statement appears to contradict the Consortium's recent paper specifically on LF elimination targets (NTD Modelling Consortium Lymphatic Filariasis Group, 2019[1]). From my knowledge of LF, the existing drugs (ivermectin, albendazole, and diethylcarbamazine) work well and as long as drugs are matched to the setting, side effects are not major concerns. The Consortium's existing work suggests that the 2030 goals can be achieved with these existing drugs if programmes can effectively deliver enough rounds of MDA before 2030. The main barrier to this elimination campaign is achieving high coverage (with the existing drugs) and reaching areas or people who have consistently low treatment coverage. Even a 100% effective and safe medicine won't help if some people or foci aren't being treated. Whether this criticism can be extended to the other diseases mentioned here is beyond my knowledge. This is the only point in the paper I have real reservations about.

The reference to LF was with regards to the fact that it has been targeted for elimination as a public health problem, rather than the need for new therapeutics specifically for LF. However, we acknowledge that the sentence was misleading and have rewritten the opening to the *Drug development and clinical study design* section.

I have indicated in my review that the letter only partly references differing views and opinions. Though I don't think this represents a major defect of the letter, I should explain why I chose this response. As the main thrust of the letter is that modelling has been and can continue to be useful for directing elimination efforts, presenting differing views and opinions would involve finding examples of where models have misdirected elimination efforts or sharing the opinions those who hold that 'models are a waste of time'. While I have certainly come across those who hold the latter view, they tend not to express their view in the form of citable literature, so the absence of their opinions is perhaps to be expected! However, as regards instances where models have misdirected elimination efforts, given the large volume of literature covered, there are probably examples of this — i.e. where a model recommended an intervention that turned out to be far from adequate. Whether these examples are publicly available and known to the authors is another question. If they know of good examples, the authors might consider including these, perhaps with a note about how these failures have informed future modelling work.

The second paragraph of *Programme design*highlighted some of the ways in which inherent features of the target populations (largely related to behaviour – adherence, treatment access etc) can impact the model projections. This has been made more explicit with the addition of a specific example regarding VL.

Having said all this, I think the 'challenges' section of the paper covers the major challenges reasonably enough. This section can perhaps be improved by giving more examples of how these challenges translate into things that models cannot or have not yet been able to do; currently the section feels a little too modelling-centric rather than programme-centric. An example of something models have not been able to do (that I am aware of) is around critical prevalence thresholds for LF/oncho elimination. Various models investigating these have found that the critical threshold varies substantially based on setting-specific assumptions. However, knowing that the threshold will be different in different settings doesn't really help you pick a target threshold that's appropriate for your setting. And since there haven't been resources in place to fit models to every setting, we have ended up with the very crude 1/2% prevalence thresholds which will be unnecessarily low in some settings and too high in others (e.g. places with high and highly heterogenous biting rates). This to me is an example not of the failure of modellers, but a limitation of modelling as an approach to help inform specific interventions/programmes. You might argue that the 1%/2% thresholds are targets not necessarily meant to be identified with critical transmission tipping points. However my reading of the non-modelling literature and conversations with non-modellers suggests that many people believe

that the 1%/2% target thresholds entail the interruption of transmission and that many believe that the universal application of these thresholds have a rigorous evidence base. Moreover, discussion of resurgence often blame failure to achieve the threshold rather than suggesting that the threshold might be wrong for the setting. Again this perhaps points to a failure of communication rather than a failure of the modelling itself, but as this letter is about how modelling informs practice, this example (or better example along a similar line) may be relevant for inclusion (if they can manage to express it more succinctly than I have!).

This is an interesting point and, if we have distilled it correctly, we completely agree. What you describe is perhaps not so much a failure of modelling, or something models cannot do, but is a symptom of the framework in which we apply mathematical modelling to NTDs. Large-scale international-level policy and guidance is the outcome of mathematical models that are indeed fit to data from specific locations, likely using more than one model, however it is unlikely that this insight will adequately describe all settings. So, there is a disparity across the public health hierarchy from international-level modelling use to a local level. The point you raise about non-modellers then using certain values as wrote is, as you rightfully state, an outcome of communication and understanding. This is a nuanced point connected to local access to, and use of, models. Reviewer two has raised the point that a discussion should be had in this letter around the topic of making models available as tools. These two comments are not mutually exclusive. We have therefore addressed them simultaneously in an new final paragraph of the *Challenges* section.

A final minor point:
P10. Misplaced comma in "by endemic nations, on donations".

This has been rectified, thank you.

Competing Interests: No competing interests were disclosed.