LONDON CENTRE FOR NEGLECTED TROPICAL DISEASE RESEARCH

An innovative research collaboration:

Selected research highlights 2021






@NTDResearch

Imperial College London

NATURAL HISTORY MUSEUM

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

RVC Royal Veterinary College University of London

Contents




Director's note

The year 2020 has been a very challenging one with the SARS-CoV-2 pandemic causing so much suffering in every region of the world. We now understand that 2021 will also be a difficult year, as appreciation that the virus will become endemic worldwide grows and the threat of continual evolution threatens the hope that vaccines will provide a quick solution to control viral spread. The greatest impact has been in the resource-poor settings of the world where lack of healthcare facilities and shortages of personal protective equipment (PPE) for healthcare workers have exacerbated the impact of the virus. This is not just in terms of mortality and morbidity, but also with respect to trade, tourism and manufacturing which often sustain economic performance in many developing countries as growth worldwide slows.

In terms of NTD control, as detailed in a recent report from the Bill and Melinda Gates Foundation-funded NTD Modelling Consortium, on the impact of the pandemic on interventions in countries with endemic NTD infections, the spread of the coronavirus has caused delays in many mass drug administration and treatment programmes but not all[1]. These setbacks can be remedied in the coming years by increasing the frequency of treatment and expanding treatment coverage, but such adjustments will require extra resources to be made available not just to provide PPE equipment but also to cover the associated additional logistical costs.

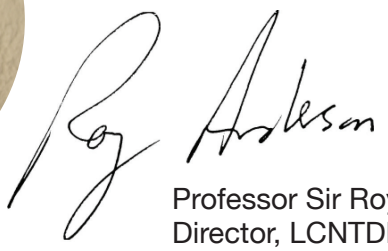
The effectiveness of such remedies will of course also depend on vaccines to protect against SARS-CoV-2 infection being made available to developing countries on the same scale as to the rich nations of the world. The unit of vaccination to create sufficient herd immunity to greatly restrict viral transmission is the world, not any individual country. Our strong connectedness between countries ensures rapid spread via corridors of air transport.

As recently noted by the Director General of the World Health Organization, Dr Tedros Adhanom Ghebreyesus, in his opening remarks at the 148th session of the Executive Board, 'vaccine equity' is not just a moral imperative, it is a strategic and economic imperative. A recent study estimated that the economic benefits of equitable vaccine allocation for 10 high-income countries would be at least 153 billion U.S. dollars in 2021, rising to 466 billion dollars by 2025.

Some positives may eventually emerge from the COVID-19 pandemic including an increased focus globally on health care infrastructure. In the NTD world, we should all look to see how our experiences and research can benefit the immediate task of vaccinating populations in resource-poor settings to ensure populations can be adequately protected. It is only then that a refocus on NTD control and morbidity elimination can occur.

One obvious example for us all to consider is how the delivery platforms for NTD control, so effectively built up over the past decade, can also be employed to help deliver vaccines. Current mass vaccination programmes to protect against the common viral infections, such as measles and diphtheria, are targeted at young children. For the novel coronavirus it is the older age groups who are most in need of protection. Given that in many areas of NTD control, such as the MDA programmes for lymphatic filariasis and onchocerciasis, community-wide treatment is required, these platforms could play an important role in helping to roll out SARS-CoV-2 vaccination.

Multi-use delivery infrastructures are of obvious importance more generally in NTD control, as we move into a period where, seeking ways to reduce costs in health care delivery, we try to see how NTD platforms can be adapted, not just to treat one infection, but many at the same time as outlined in the new WHO 2021-2030 road map for NTDs. By building capacity and health care infrastructure for NTD control we will also help to deliver mass vaccination to protect against COVID-19. We must constantly seek synergies for control across diseases rather than staying in a disease-specific silo.



Professor Sir Roy Anderson FRS FMedSci
Director, LCNTDR

1 Predicted Impact of COVID-19 on Neglected Tropical Disease Programs and the Opportunity for Innovation. DOI: 10.1093/cid/ciaa933

Reaching elimination of transmission of onchocerciasis by 2030: What is the impact of the COVID-19 pandemic?

Jonathan I.D. Hamley, Imperial College London
Martin Walker, Royal Veterinary College
Philip Milton, Imperial College London
Maria-Gloria Basáñez, Imperial College London
With David J. Blok, Adrian D. Hopkins, Louise C. Hamill, Philip Downs, Wilma A. Stolk

What is the research?

The SARS-CoV-2 (COVID-19) pandemic has led to severe disruptions to routine public health services on a global scale. These disruptions are expected to be particularly pronounced in low- and middle-income countries due to already under-resourced healthcare systems. Mathematical models of onchocerciasis transmission provide a useful predictive tool for understanding the impacts of interruptions to ivermectin mass drug administration (MDA) in the short-term (increases in transmission intensity) and long-term (elimination prospects).

We used two transmission models (EPIONCHO-IBM, developed at Imperial College London and ONCHOSIM, developed at Erasmus Medical Centre) to quantify where (in terms of transmission setting and treatment history) the impact of interruptions to ivermectin MDA for onchocerciasis will be most pronounced, allowing better planning and prioritisation of ivermectin distribution and treatment programmes upon safe resumption of MDA. Additionally, we investigated how mitigation strategies based on increased frequency (from annual to biannual MDA) or increased coverage (from 65% to 75% of total population) can help programmes to get back on track.

Why is this research necessary?

Although so-called 'lockdowns' and delayed MDA might be necessary for reducing the transmission of SARS-CoV-2, there will be implications for onchocerciasis programmes. Delayed ivermectin MDA, or reduced treatment coverage, could result not only from population-wide lockdowns to reduce COVID-19 transmission and the resulting redirection or disruption of health services, but also from shortages in drug availability (due to slower production and supply chains, or exceeded drug shelf-life by the time MDA recommences). There are concerns that delaying MDA might increase onchocerciasis morbidity and undermine the progress made towards the 2030 elimination of transmission (EOT) goals proposed in the recently launched WHO NTD road map 2021-2030. Therefore, investigating the impact of the COVID-19 pandemic on the progress of onchocerciasis control and elimination programmes, as well as identifying the best remedial strategies is crucial for endemic countries.

Community volunteer for COVID-19 awareness campaign speaks to community members in Nimba County, Liberia.
Photo credit: Ascend West and Central Africa Programme, Sightsavers

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

Both EPIONCHO-IBM and ONCHOSIM models predict that programmes with shorter (annual) MDA histories (i.e. those with fewer years of ivermectin MDA prior to the interruption) and settings with high pre-intervention (baseline) endemicity will be the most affected if one or two rounds of annual MDA are missed entirely. The impacts of missed routine MDA rounds can be seen not only in short-term increases in microfilarial prevalence, but also in reduced elimination prospects by 2030. Programmes with longer history of ivermectin MDA and those which had already switched to biannual MDA with high therapeutic coverage prior to COVID-19 would be less affected.

Biannual MDA at 65% coverage for one or two years following the MDA interruption is predicted to be more effective than increasing therapeutic coverage (from 65% to 75%) for mitigating COVID-19's impact on short-term infection dynamics and long-term elimination.

These results will be tested in endemic communities and will help country programmes to plan and implement remedial strategies to progress towards the achievement of the 2030 NTD road map goals for onchocerciasis.

DeWorm3: Charting a path towards the elimination of soil transmitted helminths

Leanne Doran, Natural History Museum

What is the research

The DeWorm3 Programme is a large-scale, five-year, community cluster randomised trial in India, Malawi and Benin which seeks to determine the feasibility of interrupting the transmission of soil-transmitted helminth infections (STH). Managed from a central hub at the Natural History Museum since 2015, DeWorm3 is supported by a vast array of international partnerships with governments, research institutes and global disease experts, and was designed to achieve three core objectives:

1. **Define STH transmission interruption**
   To quantify epidemiological and operational targets for STH transmission interruption, DeWorm3 had to define a STH transmission breakpoint, develop tools and methods to measure STH transmission interruption, and identify the prevalence and intensity of baseline STH infections.

2. **Demonstrate the feasibility of interrupting STH transmission through MDA-based approaches**
   The DeWorm3 intervention approach used a baseline census to divide the study sites into 40 clusters which were randomised to either receive twice yearly community-wide MDA with albendazole (GSK) targeting eligible individuals of all ages (20 clusters), or the standard-of-case deworming programme targeting children provided in each county (20 clusters). To date, all three DeWorm3 sites have successfully conducted their six rounds of MDA with consistently high coverage and compliance and a stalwart reputation with local communities.

3. **Recommend a feasible and effective approach for scaling STH transmission interruption programmes**
   DeWorm3 is a hybrid trial with implementation sciences studies being conducted alongside the core trial to generate evidence of sustainable and scalable models for STH transmission interruption.

Why is this research necessary?

STH are among the most common infectious organisms of humans, and in many low-resource settings these infections can result in considerable morbidity with global control efforts largely focusing on targeted treatment of high-risk groups such as children and pregnant women. However, this approach may not reduce the overall prevalence of infection below levels needed to interrupt transmission, with poor sanitation and hygiene coupled with large reservoirs of infection in untreated individuals perpetuating transmission. Furthermore, it is currently not clear when morbidity-control programmes can be discontinued, leading to concerns over the sustainability of these strategies. An estimated 1.45 billion people are infected globally with STH, and with mathematical models suggesting that transmission interruption may be possible with MDA alone, DeWorm3 could contribute to the shift from STH control to elimination.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

STH is targeted for elimination as a public health problem in the WHO NTD road map 2021-2030. If DeWorm3 is successful, it could contribute towards the overarching global targets by reducing the amount of people requiring STH interventions, reducing the disability-adjusted life years related to STH and contributing to the overall elimination of STH transmission. The NTD road map advocates integrated approaches, multisectoral coordination and country ownership, factors which are integral to the success of DeWorm3, which thrives because of its international partnerships, collaborations and focus on capacity-building.

Mass drug administration in Benin. A special thank you to our core partners: London School of Hygiene and Tropical Medicine, Blantyre Institute for Community Ophthalmology, Institut de Recherche pour le Développement, Institut De Recherche Clinique Du Benin, Christian Medical College Vellore, University of Washington and Imperial College London. Photo credit: DeWorm3 Benin Trials Team

Guiding targeting of interventions against visceral leishmaniasis using modelling

Dr Lloyd Chapman, London School of Hygiene & Tropical Medicine
Professor Mary Cameron, London School of Hygiene & Tropical Medicine
Professor Graham Medley, London School of Hygiene & Tropical Medicine
With Professor Déirdre Hollingsworth, Simon Spencer, Timothy Pollington, Chris Jewell, Caryn Bern

What is the research?

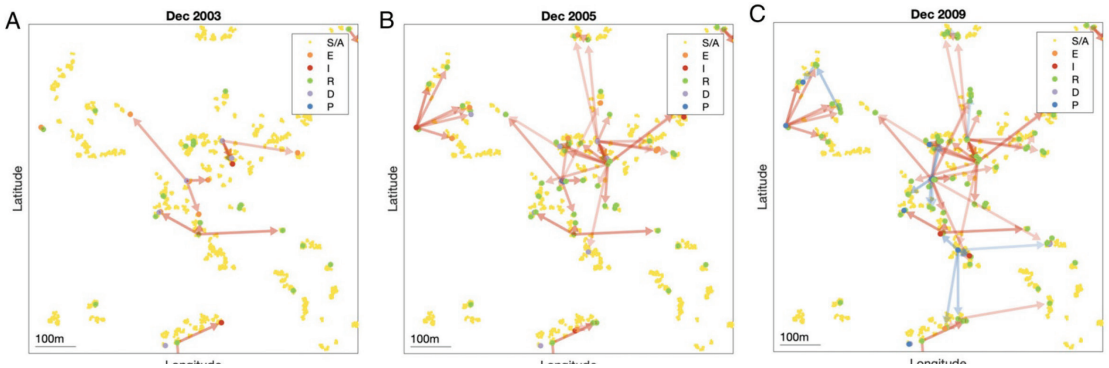
Visceral leishmaniasis (VL) is a deadly sandfly-borne parasitic disease characterised by strongly spatiotemporally clustered incidence and a high proportion of asymptomatic infection (75-95%). In 5-20% of treated cases in the Indian subcontinent, it leads to a secondary skin condition, post-kala-azar dermal leishmaniasis (PKDL), that is infectious to sandflies but often goes undiagnosed. We developed a mathematical modelling and statistical inference framework to estimate the rate of spread of infection around VL and PKDL cases and asymptomatic individuals in space and time using detailed data on VL and PKDL incidence from a highly endemic community in Bangladesh and infectiousness data from recent xenodiagnosis studies. We found that the contribution of PKDL cases to transmission increases significantly as VL incidence decreases in the downward phase of an epidemic cycle (reaching 55% in this setting) and that the contribution of asymptomatic individuals is low. Most transmission occurs <300m from cases within a few months of symptom onset for VL but after longer times for PKDL. VL and PKDL cases with long diagnosis delays generate large numbers of secondary cases. We estimated that VL incidence would have been reduced by 9% by halving the average duration of infectiousness of PKDL and by 25% by preventing PKDL altogether.

Why is this research necessary?

Establishing how far and fast infection spreads around individuals infected with the parasite that causes VL and how much different infection states contribute to transmission of VL is key to targeting interventions in space and time to eliminate the disease. This is not straightforward as most infections are asymptomatic and therefore unobserved, and the incubation period for symptomatic VL is long and variable. Novel inference methods to account for this missing data are therefore required. Furthermore, it is believed that PKDL cases and asymptomatic individuals can sustain transmission in periods of low VL incidence, but their contribution to transmission has till now not been accurately quantified since existing models have not accounted for spatiotemporal heterogeneity and data on infectiousness has been limited.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

Despite significant progress towards the WHO 2020 target for elimination of VL as a public health problem (<1 case/10,000 people/year at subdistrict level), no country has yet been validated for elimination and the target has been renewed for 2030. Ongoing transmission and sporadic outbreaks in less endemic areas suggest that improvements in control interventions are required to achieve the target and maintain low incidence. Targeting interventions will become increasingly important as the number of cases continues to decrease. This research provides estimates of the radius and time horizon within which interventions need to be performed around VL and PKDL cases to prevent transmission. It also highlights the need to improve active case detection for VL and PKDL to reduce diagnosis delays and suggests that control efforts should focus on active case detection rather than indoor residual spraying of insecticide, given the low estimated relative contribution of asymptomatic individuals to transmission.



Inferred transmission tree for visceral leishmaniasis cases in part of the study area in Bangladesh at different stages of the epidemic wave between 2002 and 2010. Dots show individuals colored by their infection state: S/A, susceptible or asymptomatic; E, pre-symptomatic; I, symptomatic visceral leishmaniasis; R, recovered; D, dormantly infected; P, post-kala-azar dermal leishmaniasis. Arrows show the most likely source of infection for each case infected up to that point in time, shaded according to the certainty of the infection source (darker shading indicating greater certainty).

The schistosome and snail resource

Dr Bonnie Webster, Natural History Museum
Dr Aidan Emery, Natural History Museum
Dr Amaya Bustinduy, London School of Hygiene & Tropical Medicine

What is the research?

Funded through the Wellcome Trust Biomedical Resource Scheme, this project contributes to schistosomiasis research by:

1. Maintaining lifecycles of the two "standard" *Schistosoma* species and their snail hosts, currently used as the model systems, but whose availability are limited;
2. Initiating and maintaining lifecycles of key African *Schistosoma* species, of medical/veterinary importance, not currently maintained/available;
3. Creating cultures of key freshwater snail vectors, the majority of which are not currently available; and
4. Providing a platform for fundamental schistosomiasis research that relies on live *Schistosoma* species and snails, creating a resource of material to support internal and collaborative research programmes.

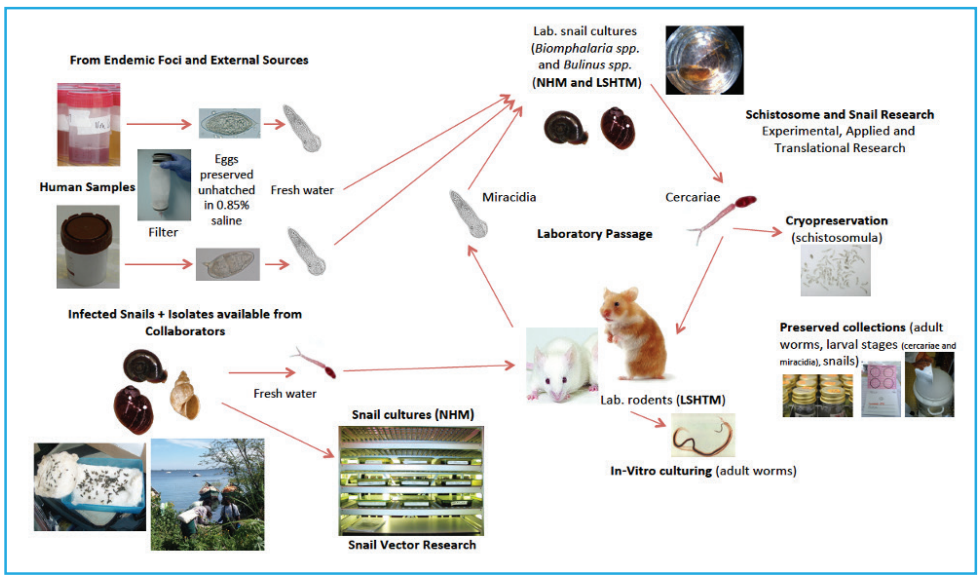
Why is the research necessary?

Schistosomiasis is a term used to encapsulate a disease that is highly diverse in its pathology, cause and epidemiology, depending on the various *Schistosoma* and snail vector species involved. The main distinction made for human schistosomiasis is as either urogenital or intestinal manifestations, which are species specific. This simplifies a more complex picture involving at least six Schistosoma species (four in Africa, *Schistosoma mansoni, S. guineensis, S. intercalatum* (intestinal) and *S. haematobium* (urogenital)) each with their own variants and interactions. Additionally, another 18 species infect animals, with substantial veterinary and zoonotic impact.

The value of laboratory lifecycles for human parasitic diseases should not be underestimated, particularly for a complex disease such as schistosomiasis. However, even "standard" schistosomes and snails are not simple to maintain, requiring attention to detail and expert knowledge of the nuances of different aspects of the lifecycle and breeding of the snail hosts. The "standard", *Schistosoma mansoni-Biomphalaria glabrata* system, isolated from Puerto Rico in the 1950's, has been the subject of most schistosomiasis research, from providing insights into schistosome biology and intra-molluscan development to developing therapeutics (drugs and vaccines). The other important human Schistosoma species, also available as a lifecycle system, *S. haematobium-Bulinus truncatus*, isolated from Egypt in the 1980's, is used far less, mainly due to its more complicated maintenance. Other African *Schistosoma* species are not available as live resources/cultures for laboratory research. Through the creation of this resource of "standard' and "non-standard' schistosomes and snails we will facilitate many avenues of schistosomiasis research that rely of live material.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

This study will be valuable for research activities and capacity of many laboratories particularly in the UK and Europe where these lifecycles are limited or unavailable, whilst its unique focus on diversity will be of global benefit. This kind of central resource relieves the financial, infrastructure and technical burden faced by many research groups that wish to conduct research reliant on lifecycles, live material and the diverse range of schistosomes and snails involved in disease. The diverse range of schistosomes and snails within the SSR will be valuable both to teaching activities but also for capacity building in endemic low and middle income countries.



Schematic showing the planned SSR laboratory lifecycle system.

Spatial analysis to support trachoma elimination and surveillance

Clara R. Burgert-Brucker, London School of Hygiene & Tropical Medicine, RTI International
Emma M. Harding-Esch, London School of Hygiene & Tropical Medicine
With Donal Bisanzio, Jeremiah Ngondi, Anthony W. Solomon

What is the research?

Trachoma, caused by ocular infection with the bacterium *Chlamydia trachomatis*, is the leading infectious cause of blindness worldwide. Using high-quality standardised trachoma data collected in population-based prevalence surveys supported by the Global Trachoma Mapping Project (GTMP) and Tropical Data, and geospatial covariates reflecting climatic, environmental, and socio-demographic information; this study aims to measure trachoma prevalence clustering and associations with geospatial factors at village-level. Spatial data analysis techniques will be used to identify the spatial structure among survey locations (villages) with varying trachomatous inflammation – follicular prevalence in children aged 1–9 years (TF1–9) in 24 trachoma endemic countries. Furthermore, the spatial relationships of survey location prevalence and geospatial covariates will be examined to identify potential factors associated with TF1–9. This research will leverage spatial analysis approaches and methods along with non-spatial correlation and regression methods.

Why is this research necessary?

Although the World Health Organization (WHO) SAFE strategy for trachoma elimination works in the majority of settings, some districts do not reach elimination thresholds (TF1–9 <5%) despite years of mass drug administration (MDA), while others experience “recrudescence”, where prevalence returns from <5% to ≥5%. Understanding the village prevalence spatial heterogeneity and relationships to environmental and socio-economic factors can help inform decision-making for reaching and maintaining trachoma elimination endgame targets. For example, the results of this analysis can help better understand areas of ongoing risk of trachoma, or areas at risk of recrudescence. This research is also crucial for conducting advanced spatial modelling approaches to refine trachoma decision-making to achieve elimination, or for surveillance in a post-validation context.

A woman in Ethiopia has her eyes checked for signs of trachoma.
Photo credit: RTI International/Yonas Getachew

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

The WHO NTD road map 2021-2030 targets trachoma for elimination as a public health problem in all trachoma-endemic countries by 2030. Trachoma prevalence surveys are essential to target and prioritise interventions, measure progress toward trachoma elimination goals, and help validate a country as having eliminated trachoma as a public health problem. These surveys are representative at the evaluation unit (EU) level, which is the level at which programmatic decision-making for trachoma is made. In an increasingly resource-constrained global health programme environment, there is a need for enhanced tools to identify areas of high trachoma prevalence or areas at risk of recrudescence within EUs, before and after the elimination validation period. Spatial analysis approaches using village-level data do not replace the need for survey fieldwork but do allow for the increased utility of existing survey data at sub-EU level, in turn allowing for cost efficiencies. This work builds on approaches and methods used for other NTDs such as lymphatic filariasis, as well as other health areas such as malaria. Furthermore, the results of this research could allow for further integration and cross-cutting approaches with other NTDs.

Reservoir dynamics of rabies in southeast Tanzania: Understanding the role of wildlife and implications for elimination

Sarah Hayes, Imperial College London
Prof. Christl A. Donnelly, Imperial College London and University of Oxford
With Kennedy Lushasi, Dr. Katie Hampson, Dr. Pierre Nouvellet

What is the research?

This study is a collaboration between Imperial College London, the University of Glasgow and the Ifakara Health Institute, Tanzania. It was undertaken from January 2011 to July 2019 across 13 districts of a previously unstudied area of southeast Tanzania and was funded by the Wellcome Trust. Contact tracing of animal-bite victims presenting to health facilities for rabies post-exposure prophylaxis was used to identify probable rabies exposures in humans and probable animal rabies cases. This coincided with a World Health Organization (WHO) coordinated domestic dog vaccination programme implemented by the Government of Tanzania and funded by the Bill and Melinda Gates Foundation.

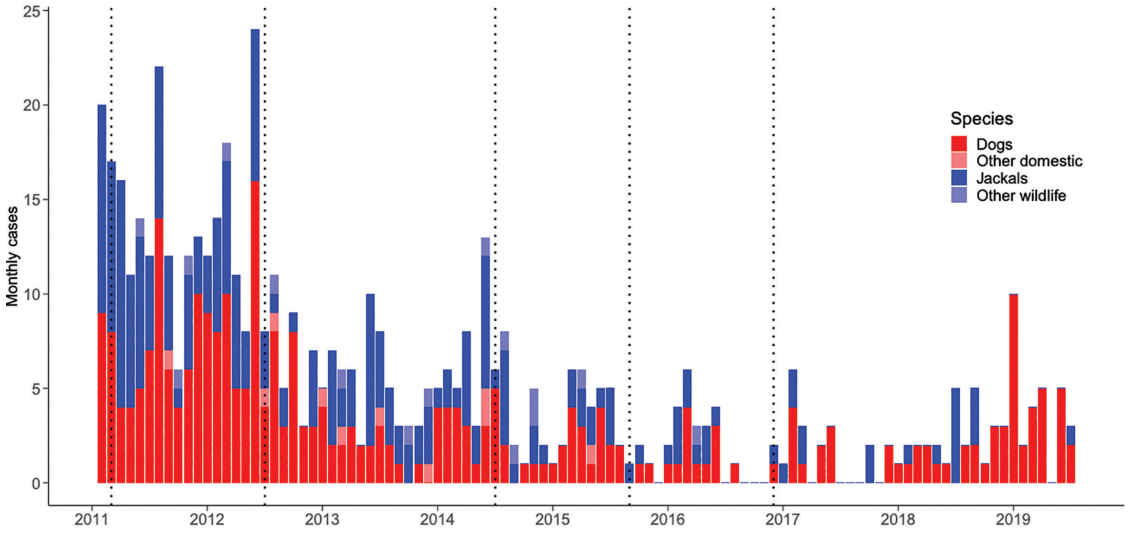
Trends in probable human rabies exposures and probable animal rabies cases and their association with domestic dog vaccination were assessed. Data on the timing, location and species of rabid animals were used to reconstruct probabilistic transmission trees to infer who infected whom and to estimate the relative frequencies of within- and between-species transmission. This information was used to further our understanding of the reservoir dynamics of rabies virus within this area of southeast Tanzania.

Why is this research necessary?

Despite the existence of effective rabies vaccines for more than a century, rabies still kills an estimated 59,000 people per year. Poor, rural populations throughout Africa and Asia bear the highest burden of disease. WHO estimates that 99% of human rabies cases are caused by transmission from domestic dogs and across most of Africa domestic dogs are considered the key species in maintaining rabies circulation. Consequently, domestic dog vaccination is a vital component of many rabies control programmes. In southeast Tanzania, a large proportion of the probable animal rabies cases reported occurred in jackals, prompting questions regarding the role of wildlife in rabies transmission in this region. If additional species can maintain infection independently of domestic dogs, it could complicate control strategies centred around domestic dog vaccination.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

Rabies is targeted for elimination as a public health problem in the WHO NTD road map 2021- 2030, with the aim of achieving zero human deaths from rabies in at least 155 (92%) countries globally by 2030. This research will support this target in two ways. Firstly, surveillance is a vital component of control programmes, essential both in assessing their impact and signalling when targets have been achieved. This research is the first to report on rabies incidence in this area of southeast Tanzania and to report changes in incidence following implementation of domestic dog vaccination programmes. Secondly, we show that despite a high proportion of probable animal rabies cases occurring in wildlife, domestic dog vaccination appeared to reduce the public health threat posed by rabies and led to a decrease in rabies incidence in all species. This supports the use of domestic dog vaccination as an integral part of rabies control strategies, even in areas where wildlife may be contributing to the disease reservoir.



Probable animal rabies cases by species recorded from January 2011 to July 2019 in Lindi and Mtwara regions of southeast Tanzania. Dashed lines indicate the timing of mass domestic dog vaccination campaigns.

Atomic force microscopy identifies a novel glycan to glycan mode of attachment between Leishmania and the sand fly midgut

Dr Matthew Rogers, London School of Hygiene & Tropical Medicine
Laith Yakob, London School of Hygiene & Tropical Medicine
With Mark Geoghegan, Newcastle University

What is the research?

There are approximately 70 species of phlebotomine sand flies worldwide that have been identified as vectors of leishmaniasis. To allow transmission, the flagellated promastigote forms of *Leishmania* must first attach to the midgut epithelium of the sand fly vector or be expelled during defecation. This represents a major barrier for the parasite and an opportunity for control. *Leishmania* utilises its surface glycocalyx of lipophophoglycan (LPG) to bind to the sand fly gut. In restrictive sand fly species, attachment is provided by LPG binding to a gut-expressed lectin receptor, resulting in the selective transmission of only one parasite species. In contrast, most sand flies are more permissive and can host a wide range of *Leishmania* species through an unknown mechanism.

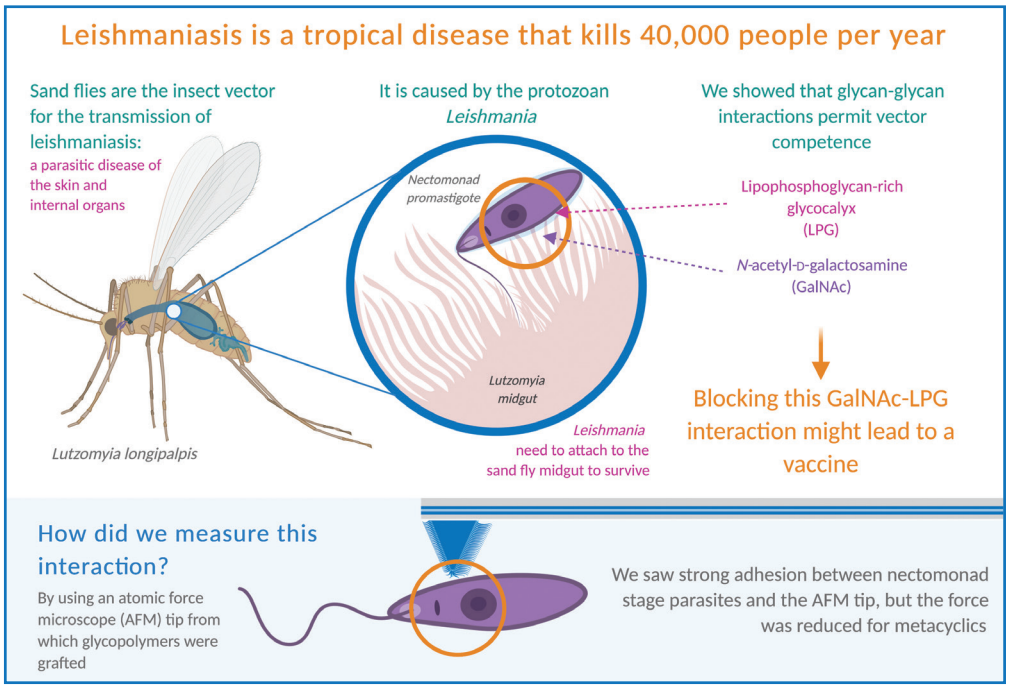
We build on previous research that showed that permissive vectors line their gut with a mucus containing an abundance of *N*-acetyl-*D*-galactosamine (GalNAc). Using atomic force microscopy (AFM), we probed the surface of promastigotes with GalNAc mimics and showed that there was direct interaction between this sugar and LPG. We found that this mode of binding was restricted to the gut adherent promastigote stages and modelling revealed that it could be a good target as a transmission blocking vaccine (TBV) against leishmaniasis.

Why is this research necessary?

Identifying the specific interactions between the parasite and its vector has considerable implications for a TBV. By identifying the key interaction, it may be possible to impede *Leishmania* attachment to the sand fly. Were a TBV to be developed, it would have to be effective. As part of this work, modelling demonstrated that a partially effective TBV would actually reduce sand fly mortality by reducing parasite load: the more parasites the fly carries, the greater its burden. A partially effective TBV would simply reduce that burden and may exacerbate the problem. Nevertheless, an effective vaccine would reduce *Leishmania* transmission.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

NTD research is critical to alleviate the human and economic burden NTDs impose on the world's poorest communities. The WHO NTD road map 2021-2030 includes basic research into the transmission of NTDs, encompassing vector incrimination and surveillance. This study unlocks the mechanism by which the majority of sand fly species can vector leishmaniasis. This represents a paradigm shift in our understanding of the vectorial competency of sand flies as it challenges the text-book thinking of a protein-based receptor-ligand model of attachment by showing that direct glycan-glycan interactions are involved. Such basic science underpins our knowledge of the epidemiology of pathogens and will contribute to the 'momentum' required to drive innovation for future control.



Graphical abstract from: Hall et al. "Glycan-glycan interactions determine *Leishmania* attachment to the midgut of permissive sand fly vectors" Chem. Sci. 11 10973-83 (2020). https://doi.org/10.1039/D0SC03298K

Force-of-Infection of *Taenia solium* porcine cysticercosis: a modelling analysis to assess global incidence and prevalence trends

Matthew Dixon-Zegeye, Imperial College London
Peter Winskill, Imperial College London
Charles Whittaker, Imperial College London
Martin Walker, Imperial College London
María-Gloria Basáñez, Imperial College London
With Wendy E. Harrison, Veronika Schmidt, Elsa Sarti, Saw Bawm, Michel M. Dione, Lian F. Thomas

What is the research?

Human neurocysticercosis, caused by the cestode *Taenia solium*, is responsible for approximately a third of preventable epilepsy cases in endemic settings, and is a zoonotic neglected tropical disease (zNTD). *T. solium* also causes taeniasis in humans and cysticercosis in pigs. Pigs are exposed to infective stages (eggs and proglottids) in the environment because of their free-roaming behaviour in endemic communities (Figure 1).

This study used a modelling approach to estimate the average, per susceptible rate at which pigs become exposed (antibody positive) and infected (antigen and necropsy positive), and how this rate varies between different epidemiological and geographical locations globally. This rate, known as the force-of-infection (FoI), was estimated by fitting, using a Bayesian framework, catalytic models to age-stratified prevalence data obtained from a systematic literature review and through collaborators, incorporating uncertainty in diagnostic sensitivity and specificity. To better understand immunity and infection dynamics in the porcine intermediate host, the models tested whether, in addition to antibody seroconversion and infection acquisition, pigs also experience seroreversion (from antibody data) and infection loss (from antigen and necropsy data).

Why is this research necessary?

Infection with *T. solium* is responsible for a substantial global human health and economic burden resulting from direct human health costs and impacts on the livelihoods of smallholder pig farmers in endemic settings. In 2012, the World Health Organization (WHO) called for a validated strategy towards *T. solium* taeniasis/cysticercosis control and elimination, and in 2020, for intensified control in hyperendemic areas. To support control efforts, more information is required to determine whether and how *T. solium* interventions need to be tailored to different epidemiological, socio-economic and cultural settings. Understanding patterns of incidence (from FoI estimates) across different settings is an important step in this process.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

The WHO NTD road map 2021-2030 proposes milestones for *T. solium* based on achieving intensified control in hyperendemic areas. However, it is not clear what constitutes hyper-endemicity or which combination of interventions are optimal for achieving intensified control. The results of this study indicate marked geographical heterogeneity in FoI, supporting the tailoring of interventions for specific locations. In addition, FoI estimates can help to define levels of endemicity and parameterise transmission dynamics models towards projecting the impact of *T. solium* control and elimination strategies over the 2021-2030 period.

The study highlights that substantial uncertainty surrounds the parameter estimates obtained from fitting the catalytic models to existing datasets, signalling that concerted efforts should be made to collect more robust data using improved diagnostics. There is a pressing need for modellers to work more closely with field epidemiologists, with the aim of developing prevalence survey sampling strategies that generate high-quality age-stratified prevalence data to improve FoI estimations. Initiatives such as the **CystiTeam**, conceived by the authors of this report, seek to synergise collaborative research in the *T. solium* taeniasis/cysticercosis field to support the achievement of road map targets.

Figure 1. Pigs roaming freely in endemic communities of Tumbes region, Northern Peru. Photo credit: Matt Dixon, following a visit to the Cysticercosis Working Group in Peru (CWG), 2017.

Understanding the role of disease knowledge and risk perception in shaping preventive behaviour for selected vector-borne diseases in Guyana

Elisa Sicuri, Imperial College London & Barcelona Institute for Global Health (ISGlobal)
With Céline Aerts, Horace Cox, Javin Chandrabose, Laetitia Duval, Krijn Paaijmans, Mélanie Revilla

What is the research?

This study explored whether the adoption of preventive measures such as bed nets, mosquito coils or skin repellent is responsive to risk perception, taking into account the links with disease knowledge and controlling for individuals' socioeconomic and demographic characteristics. To do so, primary data were collected from 800 participants over three waves on knowledge, risk perception and use of preventive measures for four diseases: malaria, dengue fever, Zika virus and cutaneous leishmaniasis. Those data were collected from communities in four regions (two coastal and two interior) of Guyana, South America, each of which has different characteristics (e.g., main economic activity and disease incidence).

Early data analysis consisted in a structural equation model applied to the first data wave. We found evidence of the expected bidirectional association between risk perception and preventive behaviour. A one-unit increase in risk perception translated into a 0.53 unit increase in self-reported preventive behaviour, while a one-unit increase in behaviour led to a 0.46 unit decrease in risk perception for all diseases. A higher knowledge of the disease's symptoms and causes encouraged a positive behaviour but only if the perceived risk was high enough. We also found that bed nets donated by the government were widely used among the population.

Why is this research necessary?

Understanding the drivers of choices about prevention is crucial to enhancing control and moving towards the elimination of NTDs. Until now, research is lacking on the complex links between behaviour, knowledge and risk perception in the context of NTDs, and of infectious diseases more broadly. A low-risk perception is likely to diminish the use of preventive measures, which has important implications in a context of elimination. In such a context, risk perception is likely to be lower (as the actual risk is lower) and government action aimed at promoting a preventive behaviour may be even more important than during high transmission periods.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

The control, elimination and eradication of NTDs will require collaboration with local communities, a collaboration that ought to be driven by positive behaviour. This study found that people acted according to their perceived risk. They also acted according to their knowledge, but only if the perceived risk was sufficiently high. Consequently, one key recommendation for achieving NTD road map targets is effective communication with at-risk populations, particularly during the so-called 'last mile'. In this context, it is essential for governments to promote knowledge and risk awareness among the population in order to avoid a decrease in preventive behaviour arising from a lower risk perception. Promoting access to and/or donation of preventive tools will also be of considerable help in that endeavour.

Conjunctival scarring, corneal pannus and Herbert's pits in adolescent children in trachoma-endemic populations of the Solomon Islands and Vanuatu

Dr Robert Butcher, London School of Hygiene & Tropical Medicine
Professor David Mabey, London School of Hygiene & Tropical Medicine
Dr Chrissy Roberts, London School of Hygiene & Tropical Medicine

What is the research?

The prevalence of trachomatous trichiasis (TT), the sight-threatening stage of trachoma, are below the target for elimination of trachoma as a public health problem in all surveyed areas of Papua New Guinea, Solomon Islands and Vanuatu. Despite this, the clinical sign trachomatous inflammation—follicular (TF) is common in young children, and widely above the recommended threshold for multiple rounds of mass drug administration with azithromycin.

One possible implication of these data is that people experiencing TF in childhood in the Pacific are not progressing to conjunctival scarring and TT as we might expect them to in sub-Saharan Africa. However, empirical longitudinal data to test this hypothesis are not available. To enable trachoma programmes in the Pacific to progress in the immediate term, an alternative approach was recommended by the World Health Organization (WHO) Western Pacific Regional Office, the results of which are presented in this study.

The purpose of this research was to look for early signs of pathology (conjunctival scarring) from trachoma in older children living in communities in Solomon Island and Vanuatu with high levels of TF. Clinical signs at the sclerocorneal junction were incorporated into the grading scheme for these children to ensure maximum specificity for trachoma. The prevalence of concurrent conjunctival scarring and sclerocorneal junction signs in older children was low. Pathogenesis due to trachoma is therefore concluded to be less common than would be expected given the prevalence of TF and, as a result, further MDA is not necessary.

Why is this research necessary?

The SAFE strategy (surgery, antibiotics, facial cleanliness, environmental improvement) is the WHO-recommended approach to reducing the prevalence of blindness from trachoma. Despite ocular *C. trachomatis* being the target of the A, F and E components of SAFE strategy, it is not practically possible to test for infection at the scale trachoma programmes work at, so programmes instead rely on the clinical sign trachomatous inflammation – follicular (TF) to guide interventions. However, a number of settings have now been identified where high TF prevalence does not appear to predict high *C. trachomatis* prevalence, for example low-prevalence and post-treatment settings. Some Pacific Island countries exhibit a similar conundrum: the TF prevalence suggests treatment is needed but the prevalence of *C. trachomatis* is very low and age-specific serological profiles suggest transmission is low. There is a critical need for innovative and practical solutions to give these countries paths to elimination of trachoma as a public health problem. This study demonstrates one such approach from the Pacific.

How will the research support the achievement of 2030 NTD road map targets?

A direct benefit from this research is to provide an immediate guidance to health ministries in the Pacific to help them progress towards elimination of trachoma as a public health problem. A broader, longer-term benefit is to highlight to the global trachoma community that TF may not be a universally appropriate diagnostic tool to guide interventions. Identification of other settings where TF may not be appropriate and development of new tools which may be useful in its place are needed to continue global progress towards elimination.

Point-of-care diagnostics and environmental monitoring of schistosomiasis transmission

Dr Bonnie Webster, Natural History Museum
Dr Aidan Emery, Natural History Museum
Dr Fiona Allan, Natural History Museum
Dr Tom Pennance, Natural History Museum
Zikmund Bartonicek, Natural History Museum
John Archer, Natural History Museum

What is the research?

One focus of our research is the development and deployment of portable isothermal diagnostic technologies for the molecular diagnosis of human schistosomiasis. Current analyses using a Recombinase Polymerase Amplification (RPA) assay, have shown a sensitivity and specificity of 93.7% and 100% respectively when compared to urine filtration, and work continues to optimise the assay to facilitate test and treat in elimination settings. Additionally, this technology is being used to diagnose female genital schistosomiasis (FGS) to enable targeted interventions in Zambia in collaboration with Amaya Bustinduy at the London School of Hygiene & Tropical Medicine.

In parallel to this, we are developing transmission monitoring protocols using molecular methods. For example using DNA-based methods for screening freshwater snail vectors, xenomonitoring. One assay we have recently developed has been used to determine which freshwater bodies are involved with ongoing transmission in the elimination setting of Pemba Island, Zanzibar. Furthermore, we are expanding the transmission surveillance toolbox by developing several molecular detection methods, with colleagues at Imperial College London to identify parasites and intermediate host snails within the environment through environmental DNA (eDNA). These methods can be used to validate water, sanitation and hygiene (WaSH) technologies alongside potentially being of use for ongoing monitoring and surveillance of transmission.

Why is the research necessary?

The assessment of critical actions required to meet the WHO 2030 targets for schistosomiasis elimination as a public health problem outline the need for sensitive point-of-care diagnostics and the development of molecular tests for xenomonitoring and transmission surveillance.

In endemic areas, appropriate diagnostic/transmission detection tools are required that can be readily adapted at different stages of a control programme. Sensitive and specific diagnostic tests are needed to prevent false negative diagnosis. Additionally, diagnosis needs to be performed at the point-of-care so that infected individuals can be treated on the spot. This will not only support the move towards elimination, but will also restrain transmission resurgence, a real risk for schistosomiasis.

Prolific water contact at a water body on Pemba Island, Zanzibar. Point-of-care diagnostics and monitoring of transmission will support elimination is these settings. Photo credit: Dr Bonnie Webster

Snail xenomonitoring and eDNA methods are needed to not only detect transmission and to enable targeted interventions, but to help better understand the local transmission dynamics of different schistosome species. Moreover, these tools for assessing *Schistosoma* transmission could eventually be used during elimination programmes to identify focal areas of persisting transmission or certify elimination and/or transmission interruption.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

Currently the diagnosis of schistosomiasis, based on microscopic egg detection, leads to a gross underestimation of true prevalence. Particularly in elimination settings, there is a critical need to implement test and treat scenarios so that the few individuals that are maintaining transmission are treated. This research aims to fill some diagnostic gaps needed for sustained schistosomiasis elimination. Additionally, this research is being adapted for the difficult diagnosis of related pathologies, including FGS, with an aim to empower women to seek appropriate support.

The provision of advanced methodologies for the detection of schistosomiasis transmission, via snail xenomonitoring and environmental detection will further provide the much needed surveillance tools necessary for succeeding in and certifying the 2030 control and elimination goals set by the World Health Organization.

BILHIV in YourSelf: Integrating schistosomiasis self-testing into reproductive health in Zambia

Dr Amaya Bustinduy, London School of Hygiene & Tropical Medicine

What is the research?

As part of a seven-year UKRI Future Leaders Fellowship, the 'BILHIV in YourSelf study' (Bilharzia and HIV) aims to test and develop a *one-stop*, cost-effective package for self-sampling and self-testing at home for the detection of multiple reproductive tract infections in Zambian women. Importantly, the strategy will include combined self-sampling of an NTD, female genital schistosomiasis (FGS) and human papillomavirus (HPV), etiological agent for cervical cancer. Self-testing for HIV and Trichomonas, a common sexually transmitted infection (STI) will also be offered. This is a partnership between the London School of Hygiene & Tropical Medicine and the ZAMBART research institute in Lusaka, which has implemented world leading trials on community-based prevention of HIV, TB and STIs. Co-habiting males will be later surveyed for the presence of male genital schistosomiasis and we will analyse its relative contribution to HIV transmission.

The project will focus on health economics to achieve sustainability. It will also include the development of a point of care molecular field-applicable testing for Schistosoma haematobium(Sh) and HPV in collaboration with Dr Bonnie Webster at the Natural History Museum.

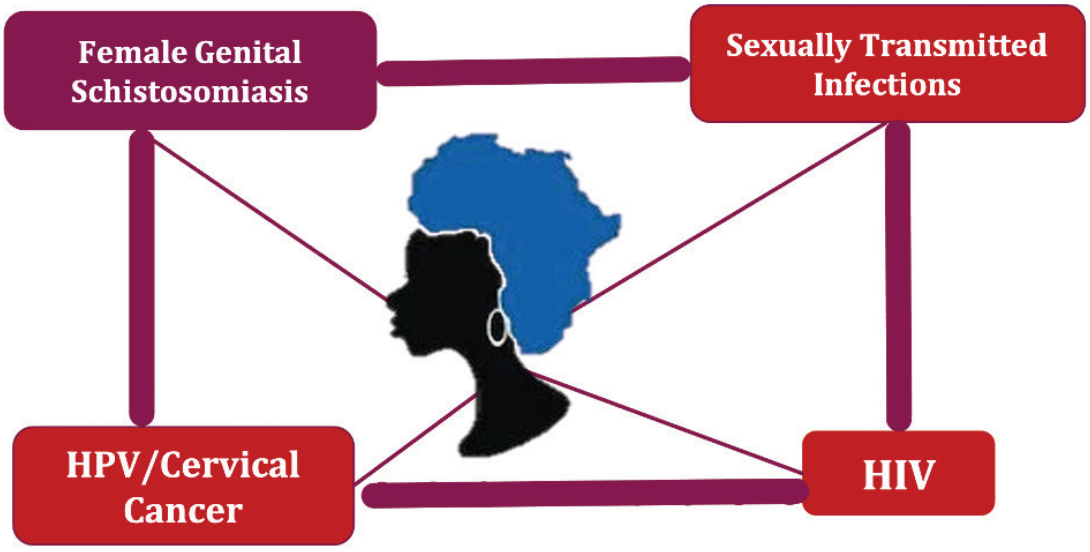
Why is this research necessary?

It is estimated that around 40 million women living in sub-Saharan Africa are affected by FGS, a chronic and neglected gynaecological disease caused by a waterborne parasite, *Schistosoma haematobium (Sh)*. FGS is associated with infertility, dyspareunia and symptoms mimicking STIs. Conventional FGS diagnosis is challenging, as it relies on costly equipment and high-level specialised training seldom available in resource-limited countries. Cervical cancer is the fourth leading cause of death in women worldwide, with an estimated 311,000 deaths/year. The highest regional incidence and mortality rates are seen in Africa. Despite the regional overlap of FGS and HPV, there have been no efforts to integrate cervical cancer within other sexual and reproductive health screening strategies making this project an unmissable opportunity to support and expand FGS/cervical cancer screening at scale.

Genital self-sampling has been recently validated for the detection of *Sh* DNA from genital samples in **our previous study**, and is highly acceptable. Self-sampling strategies have been validated for the detection of oncogenic HPV genotypes, allowing for possible community-based screening. HIV and Trichomonas self-testing are already commercially available.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

This project aims to demonstrate that integration of home self-sampling for the screening of FGS with HPV and self-testing for HIV and STIs is a feasible, cost-effective and self-empowering strategy that will increase the detection of cases and improve access to care for girls and women of reproductive age in sub-Saharan Africa. Our aims fall into the remit of the three pillars set out in the new WHO NTD road map, by setting the foundation for a national roll-out of an integrative multidisciplinary programme. Our ultimate goal is to empower African women in their holistic paths to health.



Schematic representation of the multi-disease screening of the 'BILHIV in Yourself' study.
Photo credit: Amaya Bustinduy

Anticipating the impact of global change on snakebite envenoming

Dr Gerardo Martín, Imperial College London
Dr Kris Murray, Imperial College London, MRC Unit The Gambia at London School of Hygiene and Tropical Medicine

What is the research?

Snakebite envenoming is the only non-infectious neglected tropical disease (NTD). The geographic patterns of envenoming and their severity vary as a result of the distribution, abundance, ecology and behaviour of different venomous snake species. Given that snakes are ectothermic and have specific habitat preferences, their abundance and distributions are being affected by global change (global warming, land use and demographic changes). Naturally, these processes are also expected to gradually change the geographic patterns of snakebite burden. However, due to the current lack of process-based epidemiological frameworks for the study of snakebite, changes in snakebite risk are difficult to track or forecast. This study aims to develop a framework based on models for the transmission of infectious diseases, which represents snakebites as the product and outcome of human-snake encounters. The model is fully parameterised using data on observed snakebite envenoming incidence, estimates of snake abundance, prevailing land cover and human population density in Sri Lanka. The developed framework allows us to infer some of the potential implications of global change for snakebite envenoming.

Young adult of Hypnale zara, one of the three hump-nosed viper species, which are among the leading cause of snakebite envenoming across the wet, western region of Sri Lanka. Photo credit: Gerardo Martín.

Why is this research necessary?

Global sustainability goals encompass curbing global climate change, protecting biodiversity and human health. As global change is the greatest force driving biodiversity loss, it is natural that diseases related to biodiversity, such as snakebite, will also be affected. Other NTDs are expected to shift to higher or lower elevations or latitudes in response to changes in climate, while habitat discontinuities are known determinants of vector and host species distributions. In contrast, snakebite is still poorly understood ecologically and epidemiologically, hampering efforts to infer how its burden will change in future as a result of global change. Being able to predict these changes is necessary in order to optimise the allocation of post-bite treatments in regions affected by some of the many venomous snake species, and to design novel and locally appropriate strategies for prevention informed by patterns of risk.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

This research provides a baseline estimate of the expected trends of envenoming incidence under a series of scenarios of climate, land use change and human population growth. The predictions shed light on current burden distribution and potential future changes in risk, which can help fine tune the allocation and distribution of prevention and treatment options. These could include anticipating changes in species-specific antivenom requirements or for communicating risk patterns, contributing to the WHO NTD road map 2021-2030 targets for reducing the unacceptable burden of snakebite.

A spatio-temporal approach to short-term forecasting of visceral leishmaniasis diagnoses in India

Emily Nightingale, London School of Hygiene & Tropical Medicine

What is the research?

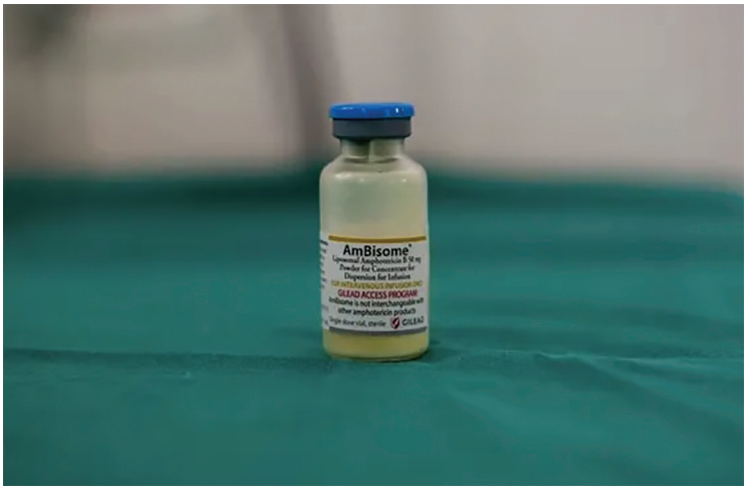
In India, elimination of visceral leishmaniasis as a public health problem (VL-EPHP) is defined as being below a threshold incidence of one case per 10,000 in every sub-district (block). We demonstrate a framework for prediction of new diagnoses up to four months ahead of time, based on seasonal trends and previous incidence both within a block and across its neighbours. Comparable predictive power between one, three and four-month time horizons demonstrated the value of such predictions despite lags in the diagnosis data of up to several weeks. We identified that incorporating information from recent incidence in neighbouring blocks improved predictive power relative to a temporal only model, suggesting that spatial correlation in incidence across the region should be an important consideration for future analyses.

Why is this research necessary?

Many elements of VL transmission and control are not well understood, therefore interpretation of mathematical models of incidence can be limited by the need for strong underlying assumptions, perhaps unsupported by quantitative evidence. This study took a purely data-driven approach which exploits patterns of spatial and temporal correlation in the observed counts for the purposes of prediction, without attempting to explain underlying biological mechanisms. These predictions can provide insight into the relative progress of each endemic block towards target incidence levels, and could have value for guiding operations as resource limitations require interventions to become more focal.

How will the research support the achievement of targets set in the WHO NTD road map 2021-2030?

As the Indian sub-continent approaches its targets for VL-EPHP it is vital to monitor routinely-collected data in near real-time to evaluate progress and identify regions diverging from the overall trends. In the absence of more detailed understanding of transmission processes, the approach described here offers a way to anticipate likely numbers of new diagnoses up to four months ahead of time, and gives an insight into possible timelines for reaching the elimination targets. Both other Member States in the regional Kala-Azar Elimination Programme – Nepal and Bangladesh – have been successful in achieving target incidence in all sub-districts while areas of two of the four endemic states in India 'Bihar and Jharkhand', remain persistently above the threshold, reasons for which are not entirely clear. Projecting forward from our final model to the end of 2020, we found that smaller blocks were less likely to achieve target incidence than larger blocks. This is likely due to the fact that the 1/10,000 target is particularly stringent when population size is only in the tens of thousands; VL often occurs in village-level clusters, just one of which could easily tip such a block over the threshold. This research provides motivation for future work towards understanding the spatial distribution of incidence at a more granular level, which may help us to understand inconsistencies in block-level progress towards the new WHO NTD road map 2021-2030 targets and contribute to addressing the gaps in our knowledge of VL transmission.



Recommended first-line treatment for visceral leishmaniasis in India is single dose Ambisome. As well as being useful for monitoring progress towards elimination targets, local-level incidence forecasts could help to more efficiently direct the distribution of resources across an increasingly heterogeneously-affected region.

New research highlights the importance of a One Health approach to reach the NTD road map targets for elimination of schistosomiasis

Professor Joanne P Webster, Dr Elsa Leger, Dr Stefano Catalano, Dr Anna Borlase, Lucy Yasenev,
Alice Morrell – Royal Veterinary College
Prof David Rollinson, Dr Aidan Emery, Muriel Rabone – Natural History Museum
Dr James W. Rudge – London School of Hygiene & Tropical Medicine
Duncan Berger – Wellcome Sanger Institute
With Mariama Sene-Wade Khalilou Ba, Nicolas Diouf, Samba Diop, Cheikh Thiam, Alassane Ndiaye

What is the research?

Schistosomiasis, caused by *Schistosoma* spp. trematode parasites, is a major neglected tropical disease (NTD) of global medical and veterinary importance. Despite almost twenty years of mass administration of the anthelmintic praziquantel to, predominantly, school-aged children, the burden of schistosomiasis remains extremely high in certain regions of sub-Saharan Africa (SSA). In endemic regions of Asia, animal hosts are acknowledged as important zoonotic reservoirs for schistosomiasis, with recent indications of a potentially increasing risk for ongoing transmission posed through rodent reservoirs. Withing SSA, in contrast, the zoonotic component of schistosomiasis transmission and the implications of the multi-host aspects of schistosomiasis for disease control and reaching the elimination targets has been largely ignored. However, zoonotic transmission from both wildlife and/or domestic animal reservoirs, particularly when considering the emerging risk raised by viable hybridization between human with livestock schistosomes, are all be predicted to represent a continued risk to public health.

A recent comprehensive programme of research, led by LCNTDR researchers at the Royal Veterinary College, combined parasitological, epidemiological, and molecular data to evaluate the occurrence and distribution of *Schistosoma* species and hybrids across potential key definitive host species (humans, domestic livestock and rodent wildlife) and snail intermediate hosts in Senegal. The prevalence of schistosomiasis was observed to extremely high in human (both children and adults), livestock and sympatric rodent populations. Viable hybrids between *S. haematobium* and *S. bovis* (and/or *S. curassoni*) occurred frequently in humans, but were not found in livestock, suggesting they originated via zoonotic spillover from livestock. The same hybrids were also found to be shed by snail intermediate hosts. Hybrids between livestock schistosomes (*S. bovis* with *S. curassoni)*, which this team had previously demonstrated to infect humans, were also identified in all livestock species. Additionally, matching genotypes of *Schistosoma mansoni*, indicative of shared transmission, were found in rodents, humans and snail intermediate hosts in the same areas.

Why is the research necessary?

Despite almost twenty years of intensive human-centric schistosomiasis control activities in Senegal, this research highlighted the ongoing burden of human schistosomiasis amongst both children (urogenital schistosomiasis prevalence was up to 88%, with large proportions of hybridized schistosomes) and, though often excluded from control and research programmes, adults. Moreover, a very high burden of livestock schistosomiasis was observed (with S. *bovis* prevalence up to 94% in cattle), as well as within sympatric wildlife (up to 52% in rodents), which revealed the multi-host, multi-parasite aspects of schistosomiasis and the potential implications for control. Furthermore, the high burden of schistosomiasis observed in livestock populations reflected the considerable socioeconomic and welfare consequences for underserved livestock-keeping communities.

Photo credit: Dr Elsa Leger

How will the research support the achievement of 2030 NTD road map targets?

By elucidating the role and dynamics of inter-specific hybridization and zoonotic transmission amongst these areas of persistently high schistosomiasis prevalence and intensities, this research highlights the need for all age groups and all potential host species to be included in future efforts within SSA and beyond. Taken together, this research emphasizes that a truly multi-disciplinary One Health perspective must be implemented in order to achieve both the 2030 WHO Roadmap targets of elimination as a public health problem and ultimately towards interruption of schistosomiasis transmission and its subsequent verification.

New research highlights considerable burden of neuropsychiatric disease caused by neglected parasitic infection

Gregory Milne, Royal Veterinary College
Professor Joanne P Webster, Royal Veterinary College
Martin Walker, Royal Veterinary College

What is the research?

Toxoplasmosis, caused by the Apicomplexan protozoan parasite *Toxoplasma gondii*, is considered one of the five neglected parasitic diseases of the USA, with research in other areas of the globe indicating that the disease disproportionately affects poorer communities, characteristic of all the major neglected tropical diseases (NTDs).

In humans, postnatally/adult-acquired *T. gondii* infections - which occur predominantly through consumption of either infected undercooked/raw meat or by food and water contaminated with faeces of infected felines – is well known to cause a large burden of disease in immunocompromised hosts, in pregnant women and their foetuses (with over 190,000 congenital infections occurring every year) and even in immunocompetent hosts, particularly during outbreaks.

A gathering body of research over many decades has also gradually revealed the parasite's association with a variety of host behavioural changes, particularly in relation to an increased risk of schizophrenia in some *T. gondii*–infected individuals.

Furthermore, a recent study by researchers at the Royal Veterinary College, University of London, highlighted the substantial diversity of human conditions associated with *T. gondii* infection, including bipolar disorder, depression and traffic accidents (Figure 1).

Why is this research necessary?

The research demonstrated the lack of data available on the associations between *T. gondii* infection and various neuropsychiatric disorders in certain regions of the globe, including sub-Saharan Africa. This is particularly pertinent as *T. gondii* seroprevalence levels across sub-Saharan Africa are among the highest in the world, a region where there is also likely to be considerable under-diagnosis and misclassification of mental health disorders in general as well as directly in relation to NTDs.

Such research is necessary as it reveals that *T. gondii*, one of the most widespread parasitic zoonoses globally, may be responsible for a dramatic burden of disease, not only in terms of congenital disease and disease in immunocompromised hosts, but also in terms of an underappreciated burden of neuropsychiatric conditions (including cases caused by postnatally acquired infections). Ameliorating this burden will require an improved understanding of the parasite, through epidemiological and basic science studies performed in global regions that are underrepresented in research efforts to-date. These studies will help to better understand the causes and effects of *T. gondii* infection.

How will the research support the achievement of 2030 NTD road map targets?

Through better understanding of the biological and epidemiological underpinnings of the associations between *T. gondii* infection and various disability-causing conditions, including neuropsychiatric disorders, this research will help to reduce the disability-adjusted life years (DALYs) related to NTDs. In this respect, this research contributes to the 2030 WH0 NTD road map target of reducing NTD-related DALYs by 75% as well as to that of the current WHO call for attention and research into the association between NTDs and mental health.

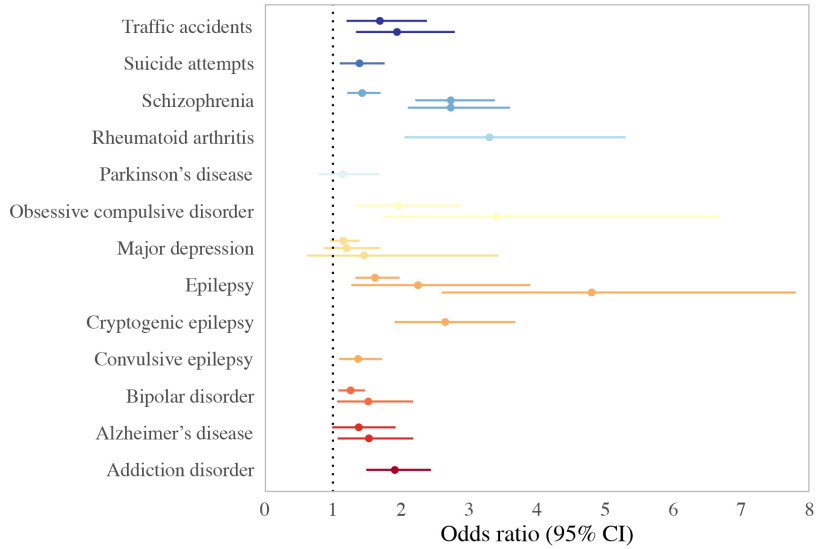


Figure 1. Odds ratios (ORs) for the association between Toxoplasma gondii infection and a variety of human conditions. Each point represents an OR from a published meta-analysis (*n*=15), with error bars representing 95% confidence intervals (CIs). Intervals overlapping the dotted line at OR=1 represent no association between infection and the named condition.[4]

LONDON CENTRE FOR NEGLECTED TROPICAL DISEASE RESEARCH

An innovative research collaboration bringing together leading experts to tackle NTDs

The London Centre for Neglected Tropical Disease Research (LCNTDR) is an innovative research collaboration that brings together leading experts to conduct cutting-edge research to build the evidence base around the design, implementation and evaluation of neglected tropical disease (NTD) control and elimination programmes.

LCNTDR facilitates coordination of NTD research activities between its members, with its priority being to enhance efforts to control some of the most neglected diseases worldwide.

The centre's core objectives include:

- **Providing evidence-based technical and training support to countries investing in national NTD programmes;**
- **Supporting harmonisation of multi-sectoral partnerships and collaborations;**
- **Acting as an NTD knowledge base for disseminating innovative and evidence-based information for policy and programme formulation;**
- **Providing a neutral coordinating platform for partner collaboration on NTD control and prevention efforts;**
- **Carrying out research on new approaches to the study of the geography, transmission dynamics and control of NTDs, with a particular focus on integrated diagnosis and mapping and integrated control of more than one NTD.**

Learn more about LCNTDR at **www.londonNTD.org**

@NTDResearch

Imperial College London

NATURAL HISTORY MUSEUM

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

RVC Royal Veterinary College University of London