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CHARTING A PATH TOWARDS STH ELIMINATION



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WELCOME

Welcome to DeWorm3

An estimated 1.5 billion people, representing a quarter of the world's population, are infected with intestinal worms, known as soil-transmitted helminths (STH)¹. These parasites disproportionately affect disadvantaged populations, particularly people in impoverished communities living without access to adequate water and sanitation. People with heavy or chronic STH infections are at risk of experiencing significant disease and disability, particularly children and women of reproductive age. Economic development, improvements in water and sanitation, and intermittent targeted mass treatment (deworming) can help prevent the morbidity associated with these infections. However, in many places the reach of these programs is insufficient or may need to be continued for the foreseeable future as infections persist. A fundamental rethink of the approach to STH infections is needed if we are to develop effective, sustainable and scalable solutions to address this enormous public health problem.

The Natural History Museum, supported by funding from the Bill & Melinda Gates Foundation, launched the DeWorm3 project to test a strategy designed to move beyond the control of these infections,



establishing whether the spread of these diseases in specific locations can be stopped and the problem eliminated. In collaboration with governments, charities and an international network of universities, a multi-country, community-based trial is underway. DeWorm3 differs from previous initiatives in scale and scope. In sites across Benin, India and Malawi not only the children most affected by these infections are being targeted but all members of the communities (including adolescents and adults) where these infections occur. DeWorm3 aims to determine if it is possible to not just control but to eliminate these debilitating infections, removing them from daily life and relegating them to history.

Data collected as part of the DeWorm3 trial are already shaping how STH and other diseases are approached globally. We look forward to continued collaboration with policymakers, organisations and individuals to achieve the goal of eliminating STH, changing lives across the world for the better.

Judd Walson
Principal investigator



Judd Walson - Principal investigator

DeWorm3

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¹ World Health Organization (WHO) (2019) Soil-transmitted helminth infections [Online]. Available at: <https://www.who.int/news-room/fact-sheets/detail/soil-transmitted-helminth-infections> (Accessed: 10 January 2020).



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THE CHALLENGE

STH are transmitted through eggs present in the faeces of infected individuals. Adult worms live in the intestine, where thousands of eggs are produced each day. In areas where there is open defecation and a lack of access to hygienic sanitation, eggs are widely present in the environment. People unknowingly ingest eggs from contaminated hands and food that has not been adequately washed. Some worms, such as hookworm, can also penetrate the skin of people walking barefoot. Children are especially susceptible as they may be walking or playing in contaminated soil.

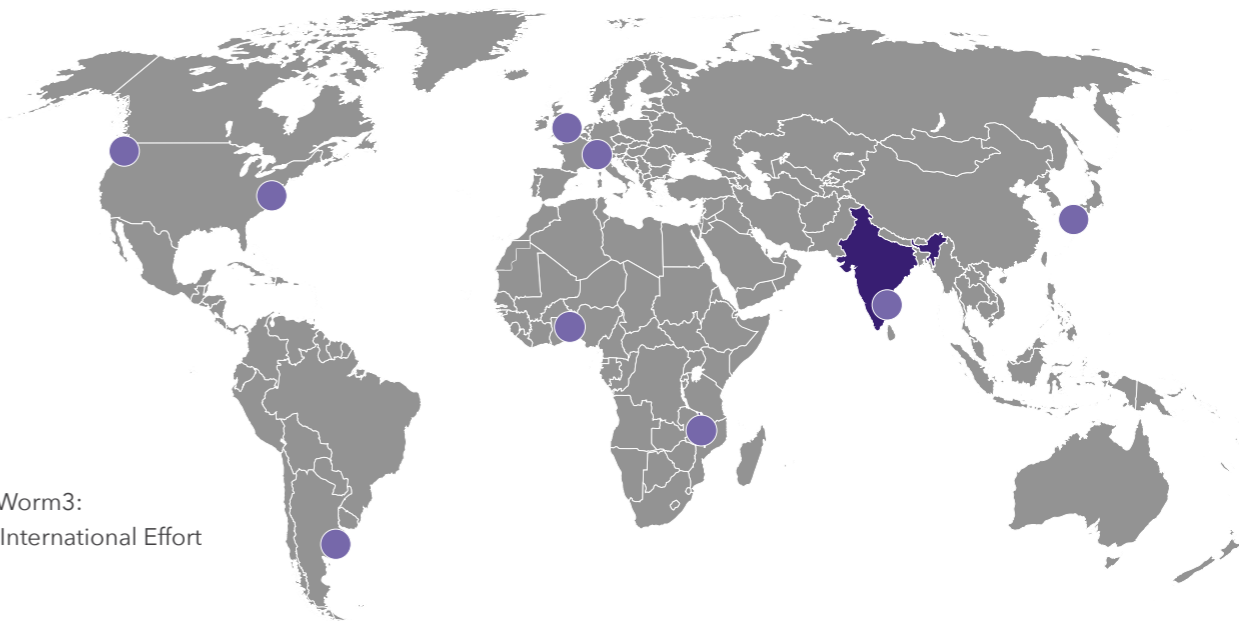
The four main species of STH—roundworm, whipworm and two species of hookworm—thrive in sub-Saharan Africa, east and southeast Asia and Latin America, where people lack access to clean water and sanitation is poor.¹ While all individuals in some communities are at risk of infection, children and women of reproductive age suffer disproportionately from the negative consequences of these parasite

infections. Women of reproductive age and young children with worms are at increased risk of malnutrition and anaemia. In addition, these STH infections also result in lower school attendance and achievement as well as reduced income earning potential when infected children become adults. The debilitating effects of worms contribute to a cycle of poverty in already deprived communities.

The current WHO strategy is one of morbidity control, targeting pre-school and school-age children, women of reproductive age, pregnant women and adults in high-risk occupations with repeat treatment of deworming medications². The strategy has been effective in controlling morbidity and spread of the disease; however, it is unlikely to break transmission of STH. Adults also harbour STH infections, particularly hookworm. As a result, children are easily re-infected when they return to their households and communities.

“STH infections also result in lower school attendance and achievement as well as reduced income earning potential when infected children become adults.”

DeWorm3:
An International Effort



Without substantial economic development and improvements to sanitation the current school-based, targeted strategy supported by drug donation programs will need to continue for the foreseeable future to control the negative health effects of these infections.

Using existing tools and novel delivery strategies the focus of DeWorm3 is to determine whether we can interrupt the transmission of STH infections sufficiently to eliminate these diseases.

WHERE TO BEGIN?

The DeWorm3 Project uses a community-wide drug administration approach to determine whether deworming both children and adults can begin to disrupt the STH transmission cycle. We selected sites across three countries – India, Malawi and Benin – to conduct community cluster randomized trials comparing the school-based strategy to community-wide deworming.

Researchers from Imperial College have informed important aspects of the project’s design. Using data from previous studies, they have provided evidence-based estimates of the frequency, duration and scale of treatment likely to result in transmission interruption. They have addressed questions including how to interrupt the infection cycle and how extensive the drug programme will need to be to suppress STH prevalence, without risk of bounce back once deworming stops. These analyses are instrumental to the success of the DeWorm3 project and any future STH programme guidelines.



²WHO (2017) Guideline: Preventive Chemotherapy to Control Soil-Transmitted Helminth Infections in At-Risk Population Groups. Geneva: World Health Organization.

A NEW APPROACH

Trials for the DeWorm3 Project have now begun in Benin, Malawi and India. Collaborators include the Ministry of Health, Institut de Recherche Clinique du Bénin and Institut de Recherche pour le Développement in Benin; Blantyre Institute for Community Outreach, London School of Hygiene and Tropical Medicine, Ministry of Health and Ministry of Education in Malawi; and Christian Medical College, Vellore in India. These strategic partners have established in-country research sites. Each site has unique epidemiological, cultural, socio-economic and geographical differences that will enable the study team to determine which factors are critical to the interruption of STH transmission.

We began by conducting a census at each of the three study sites to register all residents—more than 370,000 people—and to assess relevant STH transmission factors such as access to clean water and sanitation, recent deworming and other key demographic characteristics. Using an electronic data collection system developed with the LSHTM Data Support Unit, study communities have been mapped in detail, including the coordinates of every household. This allows the study team to monitor the progress of treatment in real-time as we conduct

“ Study sites have total populations ranging from 90,000-140,000 people ”

drug administration. A random sample of individuals in each site was asked to provide stool samples to determine the baseline STH infection status in each area. These individuals have been asked to continue providing stool samples annually and again two years after the trial concludes to assess the rate of change of STH prevalence in each site.

Each study involves a population of over 80,000 people divided into 40 total clusters. Clusters are randomized to receive either the current WHO approach providing deworming medication to school-aged children, while other clusters receive community-wide deworming across all ages. This two-level approach will continue for three years. Once this treatment is complete, no deworming will occur for two years, after which the prevalence of STH infection at each site will be examined to assess success.

MAKING A BIG IMPACT QUICKLY

It can take more than a decade for the results of trials such as this to be implemented at scale and supported by policy. The DeWorm3 trials aim to bridge this “know-do” gap by incorporating implementation science research to contextualize the clinical research findings. Collaborators at each of the sites, in collaboration with the Global Health Implementation Program at the University of Washington in Seattle (USA) will describe the implementation environment and conduct research such as stakeholder mapping, qualitative interviews and economic evaluations to identify effective strategies to scale-up and sustain community-wide deworming programs efficiently. We believe that these data will help policymakers and implementers deliver high-quality, effective programmes across all affected countries.



FUTURE OUTLOOK

The DeWorm3 Project is bringing rigorous research at scale to address an issue of global public health concern. To date, the project has been successful in achieving remarkably consistent and high coverage of drug delivery across the study sites. The data collected as part of the trial and the associated implementation science research are already shaping how MDA for STH and for other diseases is approached globally.

We look forward to continued collaboration with communities, governments, multilaterals, non-profits and individuals as we seek to address one of the most common and debilitating human infections across the globe.



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DEAN JAMISON explains the move from control to elimination

In 2013, The Lancet published the report of its Commission on investing in health, named Global Health 2035, in which it argued that a 'grand convergence' on infectious disease was technically and financially feasible. By aligning health investments, it suggested country governments and donors could reduce avoidable infectious, maternal and child deaths to universally low levels in both low-income and lower middle-income countries.

In the case of STH infections Global Health 2035 identified deworming as a highly cost-effective intervention, and suggested five years as an impactful timeframe in which to operate such an intervention. A subsequent report of the Commission, in 2018 reported an impressive 8.3% per year increase in mass

drug administrations (MDAs) for control of helminthic infection in recent years. However, the current focus on deworming children rather than both children and adults means in many settings, the cycle of infection may never be broken.

DeWorm3 is an opportunity for us to test the idea that we might one day actually eliminate these infections—in particular *Ascaris lumbricoides* (roundworm), hookworm, and *Trichuris trichiura* (whipworm). By providing a cost-effective solution for the most vulnerable populations, community-wide MDAs offer the potential to break the deadlock, over a short period of time, and thereby eliminate future drug expenditure.

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NILANTHI DE SILVA explains how WHO might use the findings of DeWorm3

Professor of Parasitology at the University of Kelaniya, Sri Lanka, serves on the World Health Organisation's Expert Advisory Panel on Parasitic Diseases and is a member of the DeWorm3 Strategic Advisory Group.

The World Health Organization (WHO) recommendations to combat STH infections currently focus on control and reduction of morbidity, in the knowledge that deworming is known to dramatically reduce the number of adult worms, and therefore to reduce the risk of illness such as anaemia, intestinal obstruction, dysentery and more.

However, because environmental contamination and re-infection are so common, deworming needs to be repeated every four to 12 months, to keep the worm count low. With the current strategy of targeting only at-risk groups, it is inevitable that environmental contamination and re-infection will continue. Therefore, the need for periodic, large-scale deworming will also continue, as will the risk of donor fatigue or anthelmintic resistance.

If DeWorm3 can demonstrate that transmission can be interrupted through deworming programmes that target the entire community rather than selected populations, and that this is also programmatically feasible, that would lead to a major shift in WHO recommendations to member states. A time-bound target that requires periodic deworming for a limited number of years, followed by cessation of the deworming programme, will always be the preferred option. But whatever the results from DeWorm3, even if they indicate interruption of STH transmission through mass deworming alone is not really feasible, the data generated will certainly help to fill current gaps in knowledge, helping WHO to make better, more evidence-based recommendations.



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KHUMBO KALUA describes the census process in Malawi
Principal Investigator for the Malawi DeWorm3 site researches neglected tropical diseases, focusing on trachoma, schistosomiasis and STH

Conducting a census is no easy task at the best of times. In Malawi we faced many obstacles, including unseasonably heavy rainfall. We also began our DeWorm3 efforts during farming season, when many families were already out in their fields. We knew we had many households to visit and because many people were not at home, we often needed to visit households several times to ensure every person was reached.

Once all households in the location had been visited and information on household members' age, sex, education and toilet access had been collected, the teams reported back to the office to meticulously upload data from the consent forms—and to make note of all the households we would need to revisit! It was a monumental task that could not have been achieved without the tireless work of our staff and volunteers.

We began by identifying 40 locations in the study site and employed 10 teams of four to visit each site. These teams were equipped with a Samsung Galaxy J2 phone, log forms, consent forms, a pen, a bag for carrying supplies and a vehicle. Leaving the office at 7am each day, they began by meeting a village volunteer to guide them around the various households at their location. As was custom, our teams always started at the chief's house as a way to ensure community-leader buy-in. These volunteers also acted as a witness if there was no-one literate over the age of 16 living at the address to sign the consent form.



MOUDACHIROU IBIKOUNLÉ

talks about mass drug administration (MDA) in Benin.
Principal Investigator for the Benin DeWorm3 site; neglected tropical disease research focuses on lymphatic filariasis, schistosomiasis and STH control and elimination.

Several successful mass drug administration (MDA) treatments for lymphatic filariasis, caused by a thread like worm, have been carried out in Benin. Prior to DeWorm3, there have been as many as six rounds of MDA in the Comé district providing a good foundation for the project trials.

work smoothly, through what's known as sensitisation. We've identified people who can help influence the community to accept this approach and therefore help ensure consistent data collection between the community clusters.

Although the Comé community is familiar with deworming, the challenge of the DeWorm3 project will be to manage the two-level approach within the same community: the one that works across many ages, and the one focused on children. We've sought help from all levels of village administration to make it

Sensitisation activities are jointly led by an advisory board and the project core team. The board is made up of local authorities, traditional leaders and local health centre managers. Together the teams help prepare communities for the census, trial monitoring and drug administration. This might involve broadcasts on local radio, in the churches or in the mosques.





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HOW CAN SENSITISATION ENCOURAGE PEOPLE TO TAKE PART IN THE TRIAL?

Moudachirou Ibikounlé and Adrian Luty, the Benin site principal investigators, have experience in preparing, or sensitising, their local communities to large-scale treatment campaigns. Their efforts ensure the required number of individuals across a large age range agree to take medication, and in some cases provide urine and stool samples, during the trial period.

To help launch the Benin DeWorm3 project, they worked with a local youth group, creating an awareness song that was launched at a community event in front of a live crowd. The chorus says, 'we need to eliminate' and 'we need to get treatment' while the main lyrics talk about the DeWorm3 project, the effects intestinal worms may have on people's health and urges people to listen to experts for a better future. The piece was so well received that it was professionally recorded by the youth group members and is now regularly played across Comé district. Feedback from community members revealed that it has led to increased education, especially among teenagers, about intestinal worms and the aims of the deworming campaign.

CHORUS

Cette mauvaise maladie
On doit éliminer.
On doit se faire soigner (x3)
Dans tout Comé
Dans tout le Benin

English translation:

This nasty sickness
We must eliminate.
We need to get treated (x3)
In the whole of Comé
In the whole of Benin

Above: Members of Carrefour Jeunesse Comé performing the DeWorm3 song at a community event.

SITARA SR AJJAMPUR talks about parasite survey techniques in India

Principal Investigator for the India DeWorm3 site, researches diarrheal diseases and oversees a busy parasitology diagnostics laboratory.

Collecting and examining stools is how we assess the number of worms in a population. For the DeWorm3 trial in India these are assessed at Christian Medical College (CMC), Vellore and at a "field lab" in Jawadhu Hills.

Once a participant has been recorded on the census and selected for a survey, they are asked if they are willing to provide stool samples. They are then given a questionnaire and a home stool collection kit with a unique barcode. These are later scanned and carefully transported in a cooler box to one of our laboratories.

Rapid and appropriate sample transport is vital to the success of a project, as is effective and precise examination. Once the samples reach the lab they are scanned, then screened. We test the samples for soil-transmitted helminths and other helminth ova, and meticulously record anything we find. With a study of

“ More than 100 samples screened each day ”

this scale (more than 100 samples screened each day) we rely on a large number of well-trained technical staff. Stool sampling is critical to the Deworm3 project objectives, particularly in understanding prevalence of each STH species and determining if STH transmission has been successfully interrupted.

WHO 2017. Guideline: Preventive Chemotherapy to Control Soil-Transmitted Helminth Infections in At-Risk Population Groups. Geneva: World Health Organization.



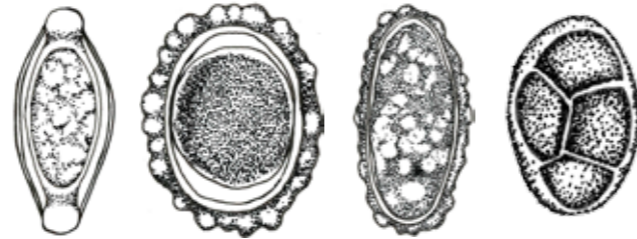
CONCLUSION

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The Natural History Museum (NHM) is proud to have been invited to develop and lead DeWorm3 on behalf of the Bill & Melinda Gates Foundation. United towards eliminating infections of intestinal worms across the world, DeWorm3 has become more than the sum of its parts yet firmly focused on its goals. DeWorm3 focuses on sites in Benin, India and Malawi, but its partnerships and tireless collaborators span the globe; representing expertise in clinical trials, public health, epidemiology, modelling, social sciences, molecular biology, diagnostics and many other disciplines.

Over 300 people are involved in delivering this investment. I applaud the PIs and their teams across all the institutions delivering and supporting DeWorm3. To date the project has been an unprecedented success with sustained, and even improved performance across the board. Without the generous drug donations from GlaxoSmithKline DeWorm3 would not be able to implement such an enormous clinical trial and we thank them for help in treating over 300,000 people for STH.

In January 2020 the NHM launched its new strategy in response to a growing planetary emergency. From climate change, pollution, habitat and biodiversity



loss to an ever-growing human population we must respond collaboratively and effectively if we are to secure a future where both people and planet thrive. DeWorm3 is a prime example of our commitment to attaining the United Nations Sustainable Development Goals - especially SDG 3 'good health and well-being'.

The NHM's science has long focused on agents of disease and how they interact in the natural environment; whether identifying parasites or vectors, uncovering parasite and pathogen life cycles, revealing patterns of evolutionary radiation or ecological dispersal, or engaging with elimination and control programmes. The NHM's 80 million natural history specimens represent a global resource tracking global change. We host over 15,000 science visitor research days, loan over 40,000 items and engage with well over 5 million visitors to our galleries each year. Our digital reach is global and growing via the internet, social and other media. Our new collections enable genetic, genomic and environmental analyses, drive discovery and help track change in a rapidly changing world.

What we collect and share today - samples, specimens, data, information, knowledge - will help shape our tomorrow. DeWorm3 is providing a platform for positive change.

Tim Littlewood
Executive Director of Science, NHM



Tim Littlewood
Executive Director of Science, NHM



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A SPECIAL THANK YOU TO ALL OF OUR COLLABORATORS

