A conversation with DeWorm3, February 24, 2016

Participants

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- Mr. John Jackson – Head of Science Policy and Communication, The Natural History Museum, London
- Josh Rosenberg – Senior Research Analyst, GiveWell

Note: These notes were compiled by GiveWell and give an overview of the major points made by Dr. Judd Walson and Mr. John Jackson.

Summary

GiveWell spoke with Dr. Walson and Mr. Jackson of DeWorm3 as part of its investigation into deworming. Conversation topics included limitations to the current standard of public health control for intestinal parasite infections, DeWorm3's plans for testing whether the transmission of these infections can be broken, and DeWorm3's funding needs.

Soil-transmitted helminth infections

Current standard for reducing infection rates

Soil-transmitted helminth (STH) infection rates are commonly reduced in two ways: by providing deworming treatments to school-aged children, and/or by drastically improving water quality and sanitation standards.

Providing deworming treatments to school-aged children has a substantial impact on infection rates, but absent major improvements in water quality and sanitation, these treatments must be provided indefinitely.

Conversely, major improvements in water quality and sanitation standards reduce STH infection rates to the point that ongoing deworming campaigns are no longer necessary. In places where STH infections have been greatly reduced, such as Japan, the Southern U.S., and Korea, the reductions were largely attributable to improvements in sanitation. Deworming programs that occurred during the periods of reduction in each of these areas were likely responsible for a minority of the improvement.

Limitations

While improvements in water quality and sanitation standards lead to sustainable reductions in STH infections, these improvements typically happen over multiple decades. DeWorm3 questions whether deworming treatments for school-aged

children is the best way to address these infections in places such as parts of India and Sub-Saharan Africa where it may take 50 years for sanitation standards to be substantially improved.

Many groups, including funders and program implementers working to reduce STH infections, share DeWorm3's concerns that the current strategy of ongoing treatment of school-aged children is not cost-effective or sustainable.

Giving drugs to school-aged children to treat STH infections does not treat the adults in the community. When children go home, they are exposed to soil and water that have been infected by the adults in their households, and they are reinfected. Because reinfection rates are high, school-aged children will need to be repeatedly dewormed until the worm eggs and larvae are removed from the environment.

The children who are at highest risk for STH infections are often not getting treated under the current model because they are not attending school.

DeWorm3 is also concerned that pharmaceutical companies may be fatigued from ongoing requests for donations of deworming medications. This fatigue may lead to a shortage of the medication necessary to operate ongoing treatment programs for school-aged children in the long term.

Charities that invest in the treatment of STH infections have a great deal to gain from understanding how to treat these infections in a way that is more cost-effective and that has a greater impact than the current model. If STH infections could be treated in a more cost-effective way, governments could redirect resources to address other global health needs.

DeWorm3

Objectives

DeWorm3 has three objectives:

1. Define, both epidemiologically and operationally, what it means to break the transmission of STH infections. How would governments measure disease burden and identify when they have broken the transmission of these infections?
2. Conduct field trials to test the feasibility of breaking the transmission of STH infections via an expanded mass drug administration (MDA) program following the transition from a lymphatic filariasis (LF) focus to an STH focus.
3. Work with governments, the WHO, and NGO partners to develop clear implementation strategies to move from controlling STH infections with an indefinite supply of drugs to eliminating these infections. DeWorm3 will also work with these partners to identify the level of evidence necessary to change STH infection policies to focus on elimination rather than control, and will frame its research to generate this level of evidence.

DeWorm3 plans to leverage the momentum of LF community MDA treatment programs in its STH MDA programs. LF MDA programs have successfully reduced LF

infections in some places to the point that the chain of transmission has been broken and the programs have been stopped. By 2021, the transmission of LF infections will likely be either officially interrupted or in the process of being verified as interrupted in all countries around the world.

Planned work

DeWorm3 is currently planning to compare standard MDA targeted at school-aged children to a community-wide MDA approach that aims to break the transmission of the disease.

DeWorm3 will select three or four sites in which to fund randomized controlled trials.

Trials

DeWorm3 plans to conduct a series of high-quality cluster randomized controlled trials (RCTs) in Sub-Saharan Africa and Asia to demonstrate the feasibility of using the LF platform and continuing the MDA model to break the chain of transmission of STH infections.

DeWorm3's trial intervention will include going to households and treating everyone in those households. This methodology is more expensive and resource-intensive than a school-based approach. However, it may be more cost-effective over time. If DeWorm3's method costs four times as much to implement as the traditional school-based approach but is able to eliminate transmission within three years, it becomes more cost-effective after just 12 years.

Measuring progress

DeWorm3 will measure its progress by tracking both the prevalence and the intensity of infection in its trial populations. The prevalence of infection is the number of people who are infected; the intensity of infection is the number of STHs infected people carry.

The biology of STHs is unique. Both male and female STHs are necessary to create eggs. If someone is infected with 20 STHs, that person ingested or absorbed 20 eggs. However, STHs do not reproduce inside the human body—that is, eggs that are produced inside the human body do not remain there long enough to develop into adult worms.

DeWorm3 plans to reduce the number of STHs in people to the point where the likelihood of male and female worms aligning in one person is very low. While a very small number of people may sporadically become infected with both male and female STHs, the infection rate will not be high enough to sustain the worms in the population.

By tracking the prevalence and intensity of STH infections, DeWorm3 will be able to identify the point at which withdrawing treatment should not result in a resurgence of infections. Once DeWorm3 stops treatment, it will follow people to ensure that

the infection rate does not increase. If the infection rate does not increase, transmission will be considered broken.

After this threshold is reached and DeWorm3 stops treatment, a few people may continue to have STH infections, but this number will not be high enough to lead to an increase in the infection rate.

Timeline

DeWorm3's trials will begin towards the end of 2016 and will run for two to four years, depending on location. Trials that are implemented in areas with higher baseline prevalence of STH infections may need to run for a relatively longer period of time.

DeWorm3 is supporting several ongoing trials that are already halfway through smaller pilot studies. The support center at Imperial College London will model the data from these trials, so DeWorm3 will have results immediately. These results will be continually updated over the course of the trials. DeWorm3 hopes to have definitive results four years from the start of its trials.

Transparency

DeWorm3 plans to pre-register its trials at clinicaltrials.gov once its final partners are chosen and all trial sites can be registered. The trial protocol will be finalized over the next months. The entire protocol, including the analysis plan, will be made available publicly. DeWorm3 will also make interim analyses publicly available through peer-reviewed publications and collaborations with partners such as Children Without Worms (CWW).

Leadership

Dr. Judd Walson is an associate professor at the University of Washington in Seattle, as well as the principal investigator of DeWorm3, a research project at the National History Museum in London. The Bill and Melinda Gates Foundation invited Dr. Walson to lead DeWorm3.

Organizational support

The National History Museum will serve as the hub for DeWorm3. The community supporting DeWorm3 chose the Museum because it is a science-based organization with a long history of disease research and a neutral convening body in the United Kingdom, which is important to the project.

Staff

Hundreds, if not thousands, of people are involved in various ways with DeWorm3.

A team of approximately one dozen individuals at the National History Museum in London will oversee the work of DeWorm3 and coordinate the people working on the project.

Scientists in "support centers" around the world will provide support for the scientific work of DeWorm3. These support centers will include an Implementation science and clinical trials support center at the University of Washington in Seattle, an Economic and cost-effectiveness analysis support center that will likely be at the London School of Hygiene and Tropical Medicine, and a Modeling and trials design support center at Imperial College London.

Support in trial countries

In endemic countries, DeWorm3 will work with focused research teams to conduct the trials. These teams will work closely with a large number of groups, including national Ministries of Health and Education, national centers for vector-borne disease control, Evidence Action, CIFF, and other groups to ensure that the research is directly tied to programmatic work and to policy.

DeWorm3 is working with the WHO and other partners, including CWW, Deworm the World, and others, in endemic countries to ensure that there is strong community involvement and buy-in to the objectives of its work.

Funding needs

DeWorm3 does not have a current need for funding. Its planned trials are fully funded by the Bill & Melinda Gates Foundation, which has invested slightly more than $27 million to launch the project. The Gates Foundation is also receptive to further discussions about additional funding if DeWorm3 needs to extend the trials. DeWorm3 is also in discussion with several other large funding bodies that are interested in funding its work.

However, there are other opportunities related to DeWorm3's work that other funders may consider. Additional funders could expand the number of countries in which DeWorm3 is able to coordinate trials. The number of countries that are currently competing for trial funding is limited by the nature of the existing funding. For example, Latin American countries are currently not able to compete for trial funding because Latin America is not a priority area for the Gates Foundation. Additional funders could make it possible for countries like Haiti, which has high STH infection rates but no current funding for treatment programs, to become DeWorm3 trial sites.

Additional funders could allow DeWorm3 to increase its public communications around global health issues and the diseases of the very poor.

There may also be opportunities for additional funders to support DeWorm3 as it helps governments think about how they may transition from STH control to elimination programs.