<u>Predicting the Potential Distribution of Soil Transmitted Helminths</u> in the United States

Kelsey McDaid Envs 196 May 4, 2019

Background

The impact of intestinal worms is seen as a thing of the past in the United States, but recent studies convey that, while the disease burden may not be as high as a century ago, there is persistence of intestinal worms in pockets of impoverished communities in the United States. Soil Transmitted Helminths (STHs) are a family of intestinal worms that include *Ascaris lumbricoides* (roundworm), *Trichuris trichiura* (whipworm), *Ancylostoma duodenale* and *Necator americanus* (hookworms), in addition to Strongyloidiasis. While all are transmitted through contact with feces, hookworms and Strongyloidiasis both infect hosts through the penetration of their skin as young larvae (Brooker et al, 2004).

Globally, interventions are hindered by a poor understanding of the precise distributions of these infections, limiting the ability to combat them(Brooker 2006). This is not to say the infections are not widespread. Strongyloidiasis infects more than 100 million people worldwide, but is difficult to diagnose and has a high potential for fatal complications including "chronic persistent infection and with special characteristic features of autoinfection, hyperinfection involving pulmonary and gastrointestinal systems, and disseminated infection involving other organs" (Puthiyakunnon et. al, 2014, Vadlamudi & Krishnaswamy, 2006). For hookworm, the correlation of treatment with positive outcomes, such as improvements in schooling outcomes and long term income has been noted after hookworm eradication programs (McKenna et. al,

2017), hookworm is estimated to infect 740 million people (Brooker, 2004). In the early 1900's, the discovery that health problems affecting southerners could be attributed to hookworm resulted in the donation of a substantial sum of money and the formation of the Rockefeller Sanitation Commission. This eradication program provided free dewormings, and provided education to recognize the symptoms of the disease, so that fewer cases went untreated (Bleakly 2007),

The current prevalence of infection in the United States has limited insight, but recent research into the intestinal parasite burden in Lowndes County, Alabama provides some evidence for a renewed need for awareness about the infection in parts of the U.S.. Due to the dearth of data from the last several decades, little is known about the prevalence of STHs in the, but the "socioeconomic and environmental conditions may remain conducive to ongoing infection" (Starr & Montgomery 2011). This is supported by a study performed by researchers from Baylor College of Medicine, which looked at the intestinal parasite burden of an at-risk group of residents of Lowndes County Alabama, where the results showed 34.5% tested positive for N. Americanus and 7.3% for Strongyloides stercoralis (McKenna et. al 2017). This is backed up by a study that found the Strongyloidiasis infection in the Appalachian region "mainly Eastern Kentucky and rural Tennessee with a prevalence of 4% and 2.5–3% respectively" (Vadlamudi & Krishnaswamy 2006). As such it is estimated there are 68,000 to 110,000 Appalachians infected with S. stercoralis (Hotez 2008). The potential presence of hookworm infection, remains largely undocumented. As noted by Starr & Montgomery in 2011, the most recent high quality study for inclusion in their review was published in 1982. Infection means that the eradication efforts were insufficient and that there is some likelihood that STHs

could have a low-level prevalence in the endemic regions in the US, data for which is scarce, as there has been limited monitoring for decades. This is compounded with how, in the study done, with *N.Americanus* as the primary infection, the endemic species is still present. As such, the evaluation of where there may be other renewals of STH infections in impoverished communities, even at low parasite burdens.

Studies of STHs have relied upon the use of microscopy in the analysis of fecal samples, a method that has a diagnostic sensitivity of 30-50% and thus possible underreporting (Starr & Montgomery, 2011). However, advancements in the field of diagnostics has resulted in the development of qPCR, the use of which as a diagnostic tool detects polyparasitism better and has "increased detection rates and significantly increased specificity," in addition to a decreased cost of analysis in comparison to microscopy (Vicuña et. al, 2013). These methods provide an opportunity to perform analysis on whether there is a even a low level parasite burden in regions of the United States.

Data

The project will be concerned with the potential prevalence and distribution of soil transmitted helminths (STHs) in the United States. It will take into account both environmental factors and socioeconomic factors to create a site suitability model to convey the potential areas where conditions are amenable to the persistence of the STH life cycle and transmission to human hosts. This project will inquire into into whether there are regions in which there is potentially suitable habitat for STHs or a likelihood that the conditions would be met that would facilitate STHs persistence/reemergence in a region.

With poverty being a crucial factor in the transmission cycles of these parasites, finding areas of poverty and determining clustered areas of poverty will be performed through spatial autocorrelation. The methods will be similar to those done by James Holt in 2007 for the CDC, who computed a Local Moran's I for each county in the US and then used inverse weighting to compare the similarities between neighbors. The values were subsequently converted to z scores, which were then converted to bivariate categorical values (Holt, 2007). This permitted the identification of very high and extremely high poverty counties, with subsequent identification of clusters. For later steps in the study, the study area will be narrowed down to the relevant areas through the use of a binary to classify whether a specific county is in poverty/ not in poverty.

Provided the data can be found, the access to adequate sewage systems municipal sewage systems and affordability of septic systems in the area (whether the soil requires a specialized septic system, and whether they have no or failing sewage system) will be used to model where the cycle of transmission from soil-host can persist.

The environmental factors to account for are rainfall, soil type and temperature.

For the flooding and risks posed by heavy rainfall, a floodplain model will be created using elevation and past or predicted hydrological data to see where there is rainfall above a threshold that would overwhelm their sewage disposal methods and/or cause outright flooding in the dwellings.

The temperature in the regions and its variability will be incorporated into the model with allowances made for variation outside the range. The preferential habitat of hookworm larvae was found to be 20-30 °C, but "required a much smaller (8 week) window of thermal suitability

for transmission and so were able to persist even when the period available for development was of the order of ten weeks" (Brooker et. al 2006).

Data on soil types will be used to map the range of adequate and preferred soil types, as hookworm prevalence is associated with sandy soil, as it permits rapid migration in response to temperature and moisture, action which is inhibited by clay soil (Brooker et al, 2004). However, other soil types seem to be amenable to the worms as well, as the soil in Lowndes county "is composed of a firm sedimentary limestone bed overlain with a layer of dark, rich soils" (McKenna et. al, 2017)

Limitations in this study include different years of data collection, and the different specific habitats of STHs. The scope of the study does not include zoonotic STHs, for while they may have an impact on some of the populations and regions in question, their methods of and limits on transmission are not the same as the human-specific parasites. While there is the exposure to farm waste in impoverished rural areas, there is exposure to other waste in poor urban areas. This could confound the analyses of parasite distribution due to habitat, as the hookworm species which are entirely non-zoonotic and depend on poor access to adequate sanitation, something that is a greater problem in poor rural areas. Another limitation is that there may not be sufficient tracking of septic system usage or connection into municipal waste treatment.

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