IOPS Statistical Consulting Report: Project 5 Schistosomiasis

Angelika M. Stefan[a], Mihai A. Constantin[b]

[a] Department of Psychology, University of Amsterdam, The Netherlands

[b] Tilburg School of Social and Behavioral Sciences, Tilburg University, The Netherlands

Correspondence may be addressed to a.m.stefan@uva.nl (AMS) or mihai.a.constantin@gmail.com (MAC).
Associated materials can be found at https://github.com/mihaiconstantin/iops-statistical-consulting.

Abstract

ABSTRACT PLACEHOLDER

Keywords

Schistosomiasis; Parasitology; Latent Class Analysis; Diagnostic Accuracy

Study description

Schistosomiasis is a parasitic disease mainly prevalent in Sub-Saharan Africa. It is caused by the parasitic worm *Schistosoma* nesting in the human body. The current project focuses on the species *Schistosoma mansoni*.

The WHO-recommended gold standard for the diagnosis of *Schistosoma mansoni* in humans is the detection of parasite eggs in stool samples through microscopy using the Kato-Katz technique. The advantage of the Kato-Katz method is that the rate of false positive results is extremely low because a trained expert can unequivocally identify eggs in the sample. However, especially when the load of parasites is low, there is a chance that no eggs are detected with the microscope method, thus leading to false negative results. In other words, the microscopy method tends to result in high levels of specificity with somewhat lower levels of sensitivity. Thus, previous studies investigating the effectiveness of treatments for *Schistosoma mansoni* infections using microscopy diagnosis might have overestimated the cure rates due to false negative results.

The department of parasitology at the Leiden University Medical Center developed a sensitive new diagnostic test for schistosomiasis based on the CAA (circulating anodic antigen) method. To test the application of the method in the field, it was incorporated in a clinical trial on the efficiency of repeated treatment of praziquantel for schistosomiasis (RePST study). The participants of the study were school children (age 5-15) who were selected because they showed positive results on two tests for schistosomiasis: a rapid field test on urine and the stool microscopy method. Upon study entry, participants were randomly assigned one out of two treatment groups. The first group received one praziquantel treatment, the second group received four treatments at two week intervals. The study included repeated tests for schistosomiasis with four diagnostic methods:

- Stool Microscopy (Kato-Katz method)
- Rapid antigen detection test in urine samples (point-of-care circulating cathodic antigen test)

- CAA in urine samples
- Polymerase chain reaction (PCR) on stool samples

Measurements based on stool samples were repeated during treatment weeks (weeks 0, 2, 4, 6). Measurements based on urine samples were repeated every week. It can be expected that the rate of true positive testing results decreases and the rate of true negative testing results increases due to the medication participants received.

Research question

The goal of the current project is to assess the accuracy of each of the four tests used in the clinical trial. The challenge is that none of the methods yields a perfect diagnosis. Therefore, the accuracy needs to be estimated from the data. In previous research, Latent Class Analysis has been used to answer this question.

Consultancy Project Scope

We will inspect and clean the data, and suggest statistical analysis options to determine the accuracy of the four diagnostic methods. In close collaboration with LUMC researchers (responsible: Pytsje Hoekstra), we will decide on a suitable analysis method and conduct the analysis. We will further present the analysis results and provide access to the analysis code. We will not be involved in the primary objective of the clinical trial, that is, the determination of effectiveness of a multi-dose treatment regimen of preziquantel for schistosomiasis.

Conducting a Latent Class Analysis for Schistosoma Diagnosis

Get the code and install relevant programs

- Download the code from GitHub *explain here how to download the code*
- Install R *link: How to install R and RStudio*
- Install JAGS *link: where to install JAGS*

- Install relevant R-packages: R2jags, dplyr, ...

Get the data

- If data are already available: Use function to clean bring data in appropriate format (pattern table with counts)
- If data are not yet available: Simulate data using *sim_LCAsimple_RCode.R*

Analyze the data

There are different ways to analyze the data with Latent Class Analyses. It is probably best to run all analyses to investigate the robustness of results to the analysis type. The first decision to make is whether trace results should be considered as positive results or as negative results. This decision affects the data structure: If trace results are considered positive, patterns with more positive results (e.g., 1-1-1-0) will occur more often. The second decision we can make is whether or not dependency between the tests should be estimated. Dependency means that two tests yield similar results independent of their sensitivity or specificity. The problem with test dependency is that there are more parameters than we can estimate, so we need to add constraints to the model. We can either set constraints to the specificity / sensitivity of the tests, or we can define constraints on the dependency of tests. Another decision we need to make is whether or not to use informed prior distributions. Informed prior distributions can make models more diagnostic, but they also introduce external information

References