

Title

Reproducibility matters: intra- and inter-sample variation of the point-of-care circulating cathodic antigen test in two *Schistosoma mansoni* endemic areas in Uganda

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Abstract

Over 240 million people are infected with schistosomiasis. Detecting *Schistosoma mansoni* eggs in stool using Kato-Katz thick smears (Kato-Katzs) is highly specific but lacks sensitivity. The urine-based point-of-care circulating cathodic antigen test (POC-CCA) has higher sensitivity, but issues include specificity, discrepancy between batches and interpretation of trace results. A semi-quantitative G-score and latent class analyses making no assumptions about trace readings have helped address some of these issues. However, intra-sample and inter-sample variation remains unknown for POC-CCAs. We collected 3 days of stool and urine from 349 and 621 participants, from high- and moderate-endemicity areas, respectively. We performed duplicate Kato-Katzs and one POC-CCA per sample. In the high-endemicity community, we also performed three POC-CCA technical replicates on one urine sample per participant. Latent class analysis was performed to estimate the relative contribution of intra- (test technical reproducibility) and inter-sample (day-to-day) variation on sensitivity and specificity. Within-sample variation for Kato-Katzs was higher than between-sample, with the opposite true for POC-CCAs. A single POC-CCA per person with a G3 threshold most accurately assesses individual infections and provides a good prevalence estimate. However, to reach the WHO target product profile requirement of 95% specificity for monitoring and evaluation, at least 2 days of urine sampling, 2 POC-CCAs per person, and the less sensitive threshold of G4 are needed.

Keywords

Schistosomiasis - *Schistosoma mansoni* - Diagnostics - Point-of-care - POC-CCA - Circulating Cathodic Antigen - Latent Class Analysis - Sensitivity - Specificity - WHO Target Product Profile - Monitoring and Evaluation

Results

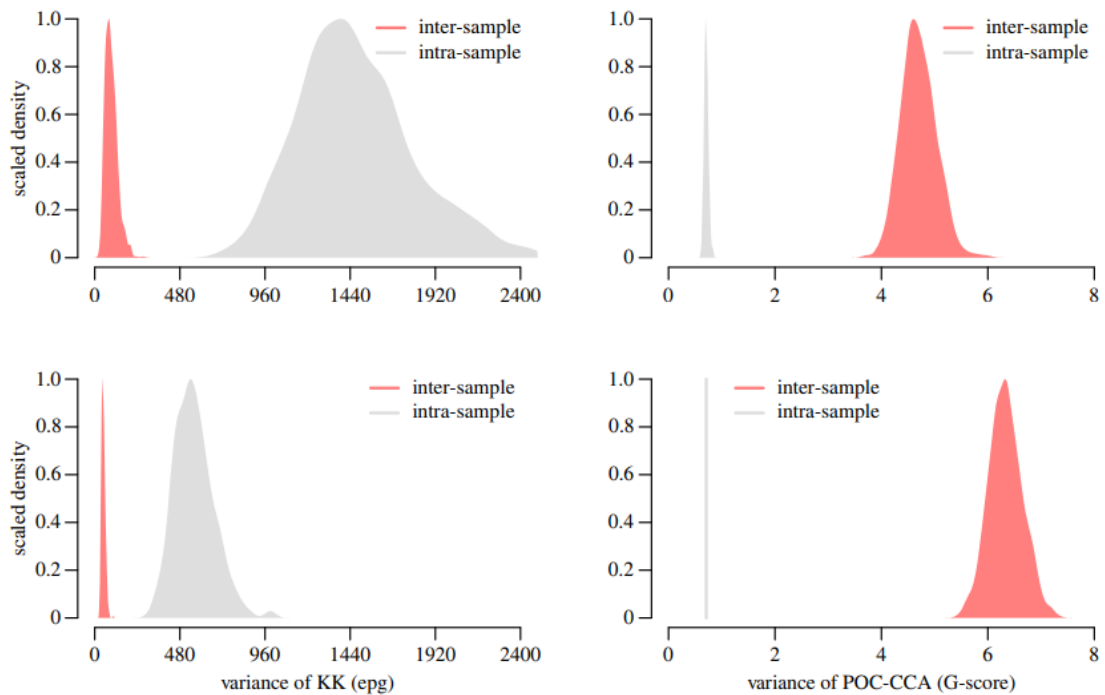


Figure 1. Inter-sample (red) and intra-sample (grey) variance for the Kato–Katz thick smears (KK, left) and point-of-care circulating cathodic antigen test (POC-CCA, right), for Mayuge (top) and Tororo (bottom). epg: eggs per gram in stool. G-score: a semi-quantitative scale of antigen concentration from G1 to G10. Note: the intra-sample variation of POC-CCA in Tororo was fixed to the mean value from Mayuge, as no repeated tests were performed on the same day and sample in Tororo.

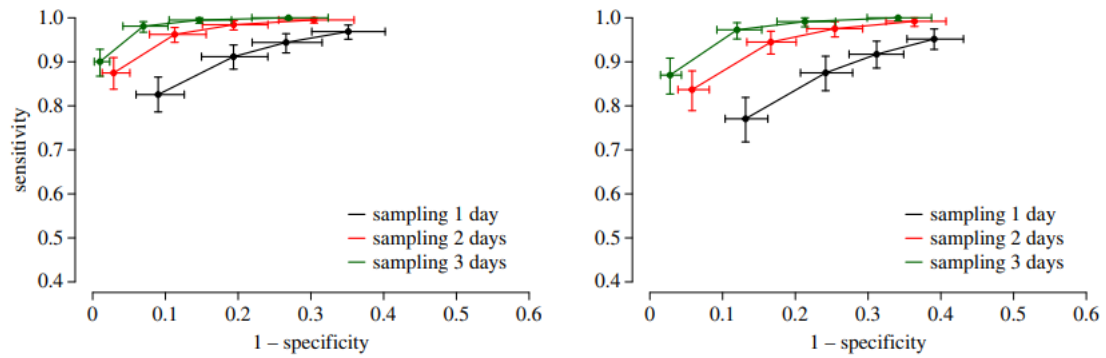


Figure 2. Receiver operating characteristic curves for the point-of-care circulating cathodic antigen test (POC-CCA) diagnostic depending on the number of sampling days (top—green—3 days, middle—red—2 days and black—bottom—1 day). The G-score threshold used, moving from left (G4) to right (G2), for each colour was G4, G3, G2.5 and G2, respectively). Mayuge presented on the left, Tororo on the right.

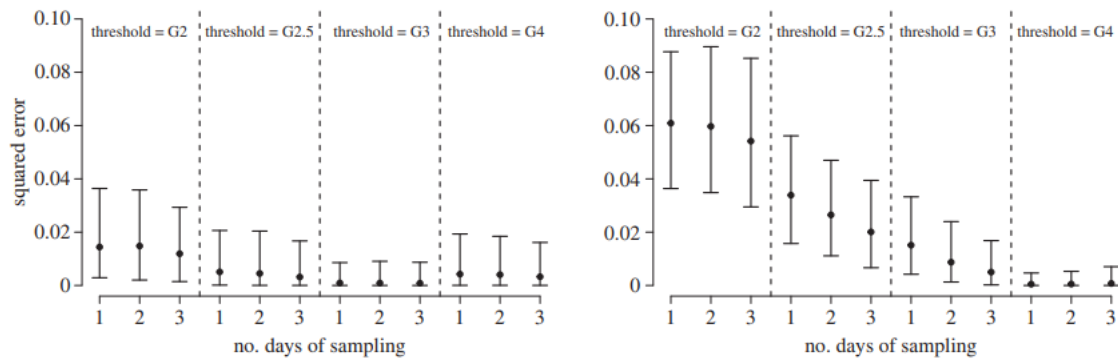


Figure 3. Squared error in the estimation of *Schistosoma mansoni* prevalence using point-of-care circulating cathodic antigen tests (POC-CCAs) depending on the number of days of sampling and the threshold used for the G-score, for Mayuge (left) and Tororo (right). The error is calculated by squaring the difference between the simulated prevalence and the estimated prevalence obtained from the diagnostic.

Notes

- Additional information available at the published article:
<https://doi.org/10.1098/rstb.2022.0275>
- The oral presentation could be based fully or partially on this published article, and other aspects related to POC-CCA could be commented during the presentation.