Linking WHO control thresholds to morbidity outcomes in urogenital schistosomiasis using an integrated modelling framework.

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The current targets for control of urogenital schistosomiasis specified by the World Health Organization (WHO), including morbidity control and elimination as a public health problem (EPHP), are defined using egg-based prevalence and intensity thresholds. Guidelines focus on reducing prevalence of heavy intensity infections (PHI), defined as more than 50 eggs per 10ml sample of urine, with EPHP defined as less than 1% PHI. Yet morbidity, the outcome that control programmes ultimately seek to reduce, is driven both by the underlying worm burden (rather than directly by observed egg counts), and a host's immune response to worm eggs. Thus, even so-called "light" infections may cause significant morbidity burdens. Worm burdens are latent and highly aggregated within endemic populations, and there is heterogeneity in host immune responses to eggs, meaning the mapping from egg-based surveillance metrics to population-level morbidity is complex and nonlinear. As a result, it remains unclear whether existing WHO thresholds correspond to acceptable reductions in morbidity.

We developed an integrated modelling framework that links Bayesian worm burden inference with agent-based transmission modelling to evaluate WHO control thresholds in terms of their morbidity consequences. We inferred individual-level worm burdens from observed egg counts, accounting for aggregation, sex-structured worm pairing, and density-dependent egg production. Morbidity presence and severity were then modelled as functions of worm burdens, allowing the estimation of the relationships between latent infection intensity and clinically relevant outcomes. These worm burden-morbidity relationships were embedded within a stochastic agent-based transmission model of *Schistosoma haematobium*. By integrating Bayesian inference with transmission modelling, our framework propagates uncertainty from worm burden estimation through to long-term projections of infection and morbidity under a range of control scenarios.

This integrated approach enables direct evaluation of expected morbidity prevalence and severity at the WHO-defined EPHP threshold, as well as post-interruption of transmission (IoT), quantifying how egg-based targets translate into downstream morbidity outcomes over time. By reframing schistosomiasis control thresholds as testable assumptions about morbidity reduction rather than fixed programmatic benchmarks, this framework provides a principled quantitative basis for assessing whether existing WHO targets are epidemiologically aligned with meaningful reductions in population morbidity. More broadly, it establishes a generalisable

approach for connecting surveillance metrics to health impact in neglected tropical disease control.