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RESEARCH ARTICLE

A health decision analytical model to evaluate the cost-effectiveness of female genital schistosomiasis screening strategies: The female genital schistosomiasis SCREEN framework

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Abstract

Female genital schistosomiasis is a chronic gynaecological disease caused by the waterborne parasite *Schistosoma* (*S.*) *haematobium*. It affects an estimated 30–56 million girls and women globally, mostly in sub-Saharan Africa where it is endemic, and negatively impacts their sexual and reproductive life. Recent studies found evidence of an association between female genital schistosomiasis and increased prevalence of HIV and cervical precancer lesions. Despite the large population at risk, the burden and impact of female genital schistosomiasis are scarcely documented, resulting in neglect and insufficient resource allocation. There is currently no standardised method for individual or population-based female genital schistosomiasis screening and diagnosis which hinders accurate assessment of disease burden in endemic countries. To optimise financial allocations for female genital schistosomiasis screening, it is necessary to explore the cost-effectiveness of different strategies by combining cost and impact estimates. Yet, no economic evaluation has explored the value for money of alternative screening methods. This paper describes a novel application of health decision analytical modelling to evaluate the cost-effectiveness of different female genital schistosomiasis screening strategies across endemic settings. The model combines a decision tree for female genital schistosomiasis screening strategies, and a Markov model for the natural history of cervical cancer to estimate the cost per disability-adjusted life-years averted for different screening strategies, stratified by HIV status. It is a starting point for discussion and for supporting priority setting in a data-sparse environment.

KEYWORDS
cervical cancer, cost-effectiveness analysis, decision tree models, economic evaluation, female genital schistosomiasis, high-risk human papillomavirus, HIV, home-based self-sampling, Markov model, screening

INTRODUCTION

Female genital schistosomiasis is a disabling chronic gynaecological disease affecting an estimated 30–56 million women globally, mostly in sub-Saharan Africa. Female genital schistosomiasis is caused by egg-deposition of the parasite *Schistosoma* (*S.*) *haematobium* in the female genital tract [1]. Exposure to *S. haematobium* occurs through skin contact with larvae (cercariae) in contaminated freshwater [1, 2]. Inside the human host, the parasites mature into adults and live in the blood vessels, where female worms produce eggs [1–3]. Instead of being excreted through urines, eggs get trapped in the urinary and genital tract, causing inflammation, granuloma formation and pathological fibrotic changes

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[1–3]. Signs and symptoms of urogenital schistosomiasis include haematuria, abdominal pain and difficulties in passing urine [2]. Between 30% and 75% of women with *S. haematobium* infection are estimated to develop female genital schistosomiasis [2]. Untreated female genital schistosomiasis is associated with sexual dysfunction and reproductive tract morbidity, including infertility, stillbirth, ectopic pregnancies and spontaneous abortions, conditions with negative social and psychological impacts [1]. Female genital schistosomiasis clinical manifestations include abdominal pain and genital symptoms such as vaginal bleeding and itching, which are often wrongly attributed to sexually transmitted infections by both healthcare professionals and patients [1, 4, 5]. Current female genital schistosomiasis treatment strategies follow schistosomiasis public health guidelines, which recommend mass drug administration of praziquantel as preventive chemotherapy to school-aged children [1]. However, the effectiveness of praziquantel in reversing or preventing female genital schistosomiasis lesions remains largely unknown [1]. Importantly, the pathological changes and chronic genital inflammation in women with female genital schistosomiasis are associated with increased prevalence of both HIV and high-risk (HR-) human papillomavirus (HPV), the primary aetiological agent of cervical precancer [1, 2, 6].

Despite the negative health outcomes of female genital schistosomiasis, control of this disease is challenging due to the lack of standardised screening and diagnosis guidelines in *S. haematobium* endemic settings [1, 5, 7]. Conventional diagnosis involves pelvic examination by a healthcare professional in a clinic or hospital to capture images of the cervix and the vagina using a colposcope [1, 5]. Images are then analysed by trained medical experts and classified as suggestive *'visual female genital schistosomiasis'* if classic female genital schistosomiasis lesions are observed [1, 5]. This method requires expensive equipment operated by highly specialised healthcare workers (gynaecologists) and advanced clinical infrastructure, often unavailable in rural *S. haematobium* endemic settings [1, 5]. In addition, the typical female genital schistosomiasis lesions are non-specific and can be wrongly attributed to other sexually transmitted infections and even cervical cancer, limiting the correct identification and treatment of female genital schistosomiasis [8]. Molecular testing using polymerase chain reaction (PCR) for *S. haematobium* DNA detection from genital samples is an alternative highly specific method for female genital schistosomiasis diagnosis [5]. Genital samples can be obtained by a healthcare worker in a clinic or self-collected at home by the participant [5]. Notably, home-based self-sampling may be more affordable and scalable compared to clinic-based sampling, given that it removes the need for a pelvic exam, potentially decreasing the costs incurred by both health providers and patients [5]. A study in Zambia validated home-based self-sampling as an effective female genital schistosomiasis screening strategy [5]. Yet, to date, no study has evaluated the *affordability* and *cost-effectiveness* of female genital schistosomiasis screening strategies, hindering the implementation of new interventions [9]. This gap is attributable to female genital schistosomiasis being a neglected and under-researched disease, limiting the available information on its natural history, symptomatology, and association with other conditions, as well as on the effectiveness of screening strategies. This paper presents a novel health decision analytical framework to evaluate the cost-effectiveness of female genital schistosomiasis screening strategies. The aim is to illustrate an approach for generating model-based evidence to support priority setting and the establishment of effective female genital schistosomiasis screening guidelines in a data-scarce environment. Importantly, this aligns with the objective of the Sustainable Development Goals on health promotion and women empowerment, as well as the 2030 World Health Organisation's (WHO) targets for schistosomiasis control and elimination [10, 11].

ECONOMIC EVALUATIONS OF NEW HEALTHCARE INTERVENTIONS

Given the scarcity of healthcare resources relative to the growing demand within the overburdened healthcare systems in sub-Saharan Africa, it is essential to evaluate the value for money of alternative investment options [12]. Health economic evaluations systematically compare the costs and health outcomes associated with different interventions [12]. The incremental cost-effectiveness ratio is key to economic evaluation, representing the economic value of a healthcare strategy compared to an alternative (e.g., standard of care) [12, 13].

Cost-utility analysis, which values the health outcomes from an intervention in terms of both the additional life expectancy and the quality of life gained, is the most common approach for economic evaluations seeking to inform sectoral allocations [12, 14]. Health utility metrics are advantageous as they standardise disability burden valuations across health conditions, allowing the comparison of interventions in different disease areas [15]. Disability-adjusted life-years are the most common health utility used in economic evaluations in low- and middle-income countries, where local health state valuations are often unavailable [1, 4, 9]. One disability-adjusted life-years corresponds to one year of healthy life lost, calculated by summing the person-years of life lost to premature death and the person-years lived with a disability from the disease (Data S1) [14]. Years of life lost are estimated based on life expectancy at the age of death. Years lived with a disability consider the age- and sex-specific incidence for the disease, its typical duration and its disability weights, values available 'off the shelf' for disease states described in the Global Burden of Disease study (Data S1) [15, 16].

BUILDING A HEALTH DECISION ANALYTICAL MODEL

Health decision analytical models use setting-specific epidemiological and health utility, and cost data to extend economic evaluation beyond empirical studies [17]. The initial

TABLE 1 Steps and components for developing a health decision model for the cost-effectiveness of female genital schistosomiasis screening strategies. The model was adapted from Campos et al. [18] and Briggs et al. [19].

Steps	Components [20, 21]	Application to female genital schistosomiasis health-decision model for the cost-effectiveness of screening interventions
1. Model conceptualization	a. Frame the health decision problem/policy question. b. Specify key elements of the decision problem. c. Define the population of interest. d. Define the interventions to be evaluated and the comparator.	a. To evaluate the cost-effectiveness of different screening strategies for female genital schistosomiasis b. There are currently no standardised guidelines available for female genital schistosomiasis screening in *S. haematobium* endemic settings. Data from large epidemiological studies is limited. There is no health state description for female genital schistosomiasis in the Global Burden of Disease study, which is used to assign disability weights, making DALY calculations difficult c. Women living in a *S. haematobium* endemic country. d. Home-based self-sampling, clinic-based sampling vs. no screening (current standard of care).
2. Model building and testing	a. Structure the model based on what is known about the natural history of the disease of interest disease b. Define the potential variables that can modify the transition between states c. Estimate the transition probabilities between the states	a. No longitudinal data is available to fully understand the natural history of female genital schistosomiasis. Therefore, the history of disease is based on the association with other sexual and reproductive health conditions. b. Female genital schistosomiasis prevalence; HPV-specific genotypes and their prevalence in the population; association between female genital schistosomiasis and HR-HPV; HIV status and age. c. Transition probabilities between health states in Markov model derived from local published estimates and large epidemiological studies from similar settings
3. Impact evaluation of the different interventions	a. Estimate the performance of the defined interventions based on where and how early they interrupt the history of disease. b. Measure coverage, costs and health outcomes of the intervention considered across different regions	a. Evaluate the sensitivity and specificity of different female genital schistosomiasis screening strategies, the associations between female genital schistosomiasis and HR-HPV, and the impact that female genital schistosomiasis screening has on cervical cancer progression. b. Perform a cost-utility analysis. Measure coverage based on ongoing epidemiological studies and published estimates.
4. Health decision modelling analysis and comparison of different strategies	a. Run the decision analytic model to project costs and health outcomes under different intervention scenarios. b. Compare strategies incrementally in terms of their costs and health outcomes. c. Identify cost-effective strategies based on the willingness-to-pay threshold in the context of the specific setting of interest. In absence of threshold in certain settings, the incremental cost-effectiveness ratio can be compared to a range of monetary thresholds identified using the WHO CHOICE method, the consumption value of health or health opportunity costs. d. Perform sensitivity and scenario analyses.	a. Run the decision model. Project costs and health outcomes for home-based self-sampling, clinic-based sampling and a no-screening approach, separately. b. Compare the two screening strategies to a do-nothing approach using the incremental cost-effectiveness ratio. c. Compare incremental cost-effectiveness ratios to locally relevant cost-effectiveness thresholds. d. Explore different parameter ranges and scenarios in univariate and probabilistic sensitivity analysis.

step involves defining the health decision problem, target population and interventions to compare (Table 1) [19, 20]. Then, decision trees and/or Markov models are developed and tested to reflect the decision problem and disease progression [18, 20]. Decision trees structure the decision problem with branches representing events and outcomes over time [19]. Branch points are described as nodes and represent either a decision about an alternative intervention to use or a chance event (i.e. an event happening or not governed by chance) [19]. The options at each chance node are assumed to be mutually exclusive and their probabilities must add up to one [19]. Each branch ends with a terminal node where patient pathway cost and morbidity are noted [19]. To calculate the cost-effectiveness of an intervention using a decision tree, the costs and outcomes for the different branches are multiplied by the branch probability, summed for each intervention, and compared [19]. Decision trees model interventions that have measurable outcomes at specific time points [19]. Conversely, Markov models simulate a population or an individual's transition between pre-defined and mutually exclusive health states during a specific time interval [19]. Time is considered as discrete

periods called 'cycles', and movement between states is governed by transition probabilities [19, 21]. Time spent in each disease state for a single model cycle is associated with a cost and health outcome which are then aggregated for the modelled cohort of patients over successive cycles and compared for different interventions [18, 20]. Data to populate decision trees and Markov models are collected alongside or extrapolated from epidemiological studies [18, 20].

This paper proposes a health decision analytical framework to evaluate the cost-utility of female genital schistosomiasis screening strategies by considering the costs and health outcomes associated with *home-based genital self-sampling* and *clinic-based sampling* compared to a '*do-nothing*' approach. The '*do-nothing*' comparator is chosen given the lack of a recognised standard of care for female genital schistosomiasis screening and diagnosis. Health outcomes are expressed as incremental disability-adjusted life-years averted by different female genital schistosomiasis screening strategies. Incremental cost-effectiveness ratio from the cost-utility analysis are then compared to cost-effectiveness thresholds, based on willingness-to-pay or opportunity cost, to assess whether an intervention is cost-effective and thus should be adopted in a specific context [14, 22, 23].

ISSUES WITH BUILDING FEMALE GENITAL SCHISTOSOMIASIS HEALTH ANALYTICAL MODELS

The lack of standardised guidelines for female genital schistosomiasis screening and diagnosis in endemic countries hinders accurate estimation of the population-based prevalence (Table 2) [1, 5, 7]. Moreover, the natural history of disease and the longitudinal associations between female genital schistosomiasis and other Sexual and Reproductive Health and Research conditions (including HIV and HR-HPV) remain largely unknown due to the limited epidemiological data available and the absence of cohort studies (Table 2). Measuring female genital schistosomiasis—related disability-adjusted life-years is challenging since disability weights for female genital schistosomiasis are not available, and its morbidity is not included in the 1.44 million disability-adjusted life-years global burden of disease estimate for schistosomiasis [1]. Past efforts to quantify disability caused by schistosomiasis focused solely on acute infection morbidity and mortality, without considering the lifetime persistence of chronic sequelae [24]. This approach underestimates the overall burden, as it fails to account for some severe and chronic clinical outcomes of schistosomiasis, such as female genital schistosomiasis [24]. Our framework suggests calculating the population-based prevalence of female genital schistosomiasis as the combined prevalence measured by all possible screening strategies, and using cross-sectional evidence to estimate the potential natural history of the disease. To estimate the female genital schistosomiasis disability-adjusted life-years and improve the accuracy of disease burden estimation, we propose mapping female genital schistosomiasis symptoms onto the existing Global Burden of Disease health states.

MODELLING HEALTH OUTCOMES FOR FEMALE GENITAL SCHISTOSOMIASIS AND CERVICAL CANCER

We developed a novel health decision analytical model to evaluate the cost per disability-adjusted life-years averted (cost-utility) for female genital schistosomiasis screening strategies (Figure 1). Model validity was tested with preliminary data, and it will be implemented to evaluate the cost-effectiveness of female genital schistosomiasis screening strategies using data from an ongoing study in Zambia [25]. This model combines a decision tree, considering the different female genital schistosomiasis screening strategies, with a Markov model for the natural history of cervical cancer stratified by female genital schistosomiasis status. The combined female genital schistosomiasis and cervical cancer model should also be stratified by HIV status, especially in HIV-endemic settings. This would account for the association between female genital schistosomiasis, HIV, HR-HPV and cervical cancer progression. Initially, an asymptomatic girl or woman enters the decision tree, which simulates the sensitivity and specificity of the screening methods under evaluation. Branches represent the probability of being HR-HPV positive or negative, given female genital schistosomiasis status. Individuals exit the decision tree and enter the corresponding state in the Markov model, representing the natural history of HPV and cervical cancer. The disease states in this model include: (1) infection with a specific type of carcinogenic or HR-HPV, (2) precancer, defined as persistent HR-HPV infection associated with lesions at a high likelihood of invasion if left untreated and (3) invasive cervical cancer [18, 26]. Across the different states, individuals have a probability of moving to the death state, the absorbing state, for which the probability of moving to any other state is 0 and the probability of remaining in the state is 1 [27].

Movements between cervical cancer health states are governed by transition probabilities, describing the risk of moving between states over a cycle [18]. Regression between states is also possible, including HR-HPV viral clearance and the regression of precancer and cervical cancer to a normal cervix [18]. In the absence of co-infection with female genital schistosomiasis, women transition from a normal cervix to an HR-HPV-infected state based on the underlying population's incidence of HR-HPV [28]. Infection with female genital schistosomiasis is assumed to modify the natural history of cervical cancer by increasing the incidence and prevalence of HR-HPV infection [18].

Health utility metrics are then calculated for the different health states in the model and compared across strategies. Since female genital schistosomiasis outcomes are not yet included in the Global Burden of Disease study, specific disability weights for female genital schistosomiasis are derived by combining weights from conditions described in the 2019 Global Burden of Disease study that share similar sexual and reproductive tract morbidity with female genital schistosomiasis [29]. For example, the disability weights for '*mild chlamydial infection*' and '*primary infertility due to sexually transmitted infections*' can be used and combined

TABLE 2 Decision analytical model inputs and output reporting standards.

Model inputs	Description	Research gaps	Assumptions adopted
Population considered for evaluating the intervention	Define eligibility criteria, age-groups and geographical location for the female genital schistosomiasis intervention evaluated		
Population-based prevalence of female genital schistosomiasis in the setting of interest	Report population-based prevalence of female genital schistosomiasis. This will be based on prevalence estimates different screening methods evaluated, which should be reported separately	Population-based female genital schistosomiasis prevalence across *S. haematobium* endemic settings (i.e. the underlying prevalence without the intervention across geographical areas) is unknown	Given that there are no standardised methods for population-based female genital schistosomiasis screening and diagnosis, consider the population-based prevalence of female genital schistosomiasis as the combined prevalence measured by all possible screening strategies evaluated.
Accuracy of screening methods	Report the sensitivity and specificity of different screening strategies	No gold standard for female genital schistosomiasis screening and diagnosis to calculate accurate sensitivity and specificity estimates	1. Consider the composite diagnosis of home-based and clinic-based swabs as the reference standard for calculating the sensitivity and specificity 2. Consider the sensitivity and specificity of screening strategies when implementing an female genital schistosomiasis screening algorithm. This involves pre-screening with CCA or urine microscopy to detect active schistosome infection follow by female genital schistosomiasis screening at home or clinic.
Association between female genital schistosomiasis and HR-HPV infection and natural history of cervical cancer by female genital schistosomiasis status	1. HR-HPV incidence, persistence, and progression/regression to/from precancer and cervical cancer by female genital schistosomiasis status 2. Stratify the associations and natural history of disease by different HPV genotypes, when possible.	1. No longitudinal data available on the temporal association between female genital schistosomiasis and HR-HPV incidence, persistence and cervical cancer progression. 2. Limited country-specific data on natural history of cervical cancer by HPV genotype	1. Use cross sectional associations of female genital schistosomiasis with HR-HPV infection using different female genital schistosomiasis screening methods. 2. Use available data from similar settings
Disability weight (DW)	Weight factor calculated as part of the global burden of disease (GBD) studies to reflect the severity of health states from a disease or injury.	Specific female genital schistosomiasis disability weights are not available as female genital schistosomiasis is not included in the GBD study.	Female genital schistosomiasis disability weights were derived by combining weights from conditions with similar sexual and reproductive tract health state description from the GBD study.
Costs of female genital schistosomiasis screening	Unit costs per woman screened for different female genital schistosomiasis screening strategies. Currency and year, methods for inflation adjustment. Indicate willingness to pay thresholds (WTP) to help inform decision making.	Lack of standardised WTP in many countries where *S. haematobium* is endemic.	Use cost-effectiveness thresholds which reflect the health opportunity cost in the country of interest. Other threshold can then be considered for illustrative purposes as appropriate in different contexts depending on available data and policy interest.
Uncertainty intervals around input measures	Uncertainty intervals and confidence intervals around the input values to run the sensitivity analyses		

Outputs	Description
Total annual cost of each strategy	Total annual cost for the different female genital schistosomiasis screening interventions
Years of life lived with disability (YLDs)	YLDs consider the age-specific incidence for duration, its typical duration and its disability weights. From the decision tree individuals exit with a specific female genital schistosomiasis YLD which is then summed to the cervical cancer YLDs found at the end of the Markov model.
Years of life lost due to premature death (YLLs)	This measure is estimated based on life expectancy at age of death because of female genital schistosomiasis. Female genital schistosomiasis is associated with high morbidity but low mortality, therefore the YLLs for cervical cancer are used as an approximation of the female genital schistosomiasis YLLs.

(Continues)

TABLE 2 (Continued)

Outputs	Description
Disability adjusted life years (DALYs)	DALYs are calculated as the sum of YLDs and YLLs.
Sensitivity analysis on key inputs	Report results from probabilistic sensitivity analysis to identify drivers of uncertainty in cost-effectiveness estimates. Conduct a scenario analysis considering different input ranges
Incremental cost-effectiveness ratios and costs saved	Calculate the incremental cost-effectiveness ratio for economic evaluations and compare it to willingness to pay thresholds to help inform decision making.

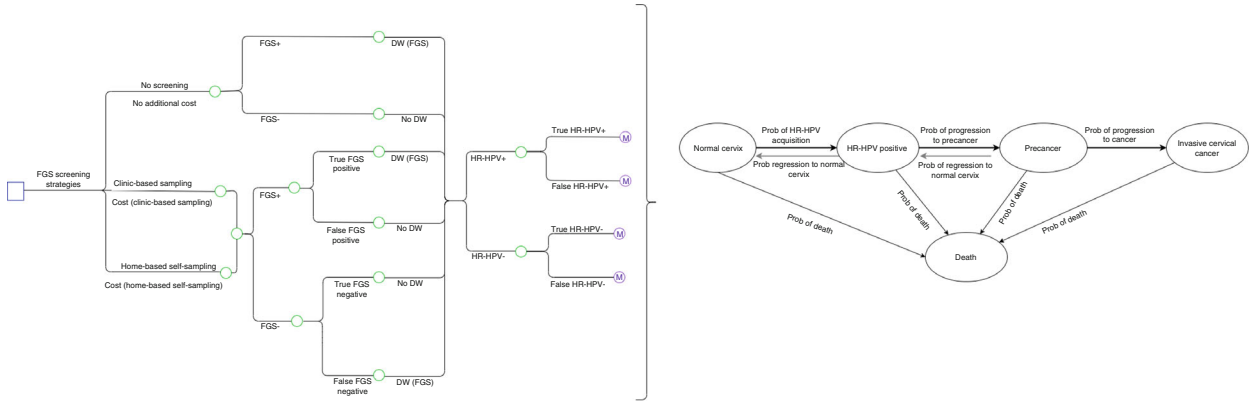

FIGURE 1 Combined decision tree and Markov models use to evaluate the cost-effectiveness of female genital schistosomiasis screening strategies. In settings with high HIV prevalence, the model can be stratified by HIV status by using the same model for HIV positive and HIV negative women. DW, Disability weight; FGS, Female genital schistosomiasis; HR-HPV, High-risk human papillomavirus.

using a multiplicative approach (S1 text and S1 table) [30]. Years lived with a disability are then calculated by multiplying the disability weights with the number of individuals in the different health states ($n_{s,i}$) [30]. A sensitivity analysis using a range of possible disability weights, taken from different conditions (for example, trichomoniasis infection, chlamydia, and genital herpes), should then be performed to understand the range of years lived with a disability associated with female genital schistosomiasis. Based on the decision tree outcomes, the cohort exits with female genital schistosomiasis-specific years lived with a disability which are then added to the cervical cancer years lived with a disability found at the end of the Markov model. Finally, disability-adjusted life-years are calculated by summing the state-specific years lived with a disability (from the decision tree and Markov model) and the cervical cancer years of life lost, which are used given that female genital schistosomiasis is associated with high morbidity but low mortality.

COST ANALYSIS FOR FEMALE GENITAL SCHISTOSOMIASIS SCREENING STRATEGIES

Cost analyses of novel female genital schistosomiasis control strategies should align with the Global Health Costing Consortium reference case standard for global health costing studies [31]. This costing analysis aims to estimate the incremental economic costs of female genital schistosomiasis screening and to calculate the unit (or average) cost per woman screened for female genital schistosomiasis and per positive case identified *using home-based self-sampling* and *clinic-based sampling* compared to a *do-nothing* alternative. We developed a costing tool in Microsoft Excel to facilitate cost data collection and analysis of female genital schistosomiasis screening strategies (available to download here). The tool allows us to identify, measure and value the variable (e.g., personnel and supplies costs) and fixed costs (e.g., overheads, building and equipment costs) across different settings. Users can input setting-specific data to calculate the total and unit costs. Worksheets for conducting an univariable sensitivity analysis are also provided. A societal costing perspective including both health care provider and patient costs should be adopted when possible [4, 31]. A time horizon of one year should be sufficiently long to capture all relevant costs [31].

KEY STRUCTURAL AND PARAMETER ASSUMPTIONS

Age

The association between female genital schistosomiasis and HR-HPV infection may change across age groups. In a healthy population, the incidence of HR-HPV peaks in the

youngest age groups, typically between ages 25–35 years old, after sexual initiation, and declines with age [32]. Most of these infections (up to 90%) are clear within 2 years, with only a small fraction progressing to persistent infection leading to cervical precancer and cervical cancer. [28, 32]. The presence of female genital schistosomiasis is presumed to modify the natural history of cervical cancer, potentially reducing HPV control [18]. Among women with female genital schistosomiasis, we would expect a higher HPV incidence across all age groups, and a higher probability of progressing to cervical precancer, particularly in younger women (aged 25–35 years old) whose lesions would typically regress to a normal cervix [18]. Yet, the exact effects of female genital schistosomiasis on the natural history of cervical cancer remain largely unknown, emphasising the need for longitudinal cohort studies to assess the temporal effects of female genital schistosomiasis on the natural history of cervical cancer [1, 9].

Female genital schistosomiasis prevalence

Female genital schistosomiasis screening strategies are likely to be more cost-effective in communities with higher female genital schistosomiasis prevalence, as the fixed screening costs will be spread across a larger pool of identified cases. Female genital schistosomiasis prevalence is higher in rural areas near contaminated freshwater bodies [24, 33]. Sensitivity analysis can be conducted to understand the cost-effectiveness across different prevalence scenarios, informing the development and implementation of targeted and cost-effective female genital schistosomiasis screening programmes aligned with population-level prevalence.

Diagnostic accuracy of screening techniques

The cost-effectiveness of screening programmes depends on the diagnostic accuracy of selected strategies (i.e. sensitivity and specificity) and programmatic attributes (screening coverage, uptake, and costs) [34]. The absence of a reference standard for female genital schistosomiasis screening and diagnosis limits the assessment of the diagnostic accuracy of screening strategies [5]. A study in Zambia showed *home-based self-sampling* for female genital schistosomiasis to be highly acceptable, with 90.0% of women preferring it over *clinic-based screening* [35]. The authors found a sensitivity of 57.1% (28.9%–82.3%) and specificity of 97.3% (95.5%–98.5%) compared to clinic-based cervicovaginal lavage (CVL) [5]. Importantly, the sensitivity increased to 88.9% among participants with active schistosome infection determined by detectable urine Circulating Anodic Antigen, positive PCR, or positive microscopy [5]. This indicates that an algorithm with pre-screening for active infection could increase the accuracy of home-based self-swabs, potentially reducing costs and improving the efficiency of resource allocations [5]. A limitation of this screening algorithm is reduced female genital schistosomiasis detection among women without active schistosome infection [5]. Previous studies have shown that older women (aged over 45 years old) often present less active but more chronic *S. haematobium* infections, with egg deposition in the genital tract which is detectable by colposcopy [5, 9, 36]. In contrast, younger women have a higher intensity of active *S. haematobium* infection and a higher rate of Schistosoma DNA retrieval from the genital tract [5, 36, 37]. Consequently, the female genital schistosomiasis screening algorithm could target younger women, while female genital schistosomiasis screening for older women could be integrated into existing cervical cancer screening programmes [1].

To date, no study has evaluated the diagnostic accuracy of clinic-based cervicovaginal swabs for female genital schistosomiasis screening. Research on HPV DNA testing suggested that self-collected genital samples are likely less resource-intensive, and more acceptable than clinic-based screening [34, 38]. However, home-based self-sampling may have slightly lower diagnostic accuracy compared to clinic-based screening [34, 39, 40]. As female genital schistosomiasis screening programmes are developed and implemented across settings, decision-makers must quantify the trade-offs between test performance and practical aspects to inform cost-effectiveness [34].

HIV status

Chronic cervicovaginal inflammation and vascularisation in women with female genital schistosomiasis have been shown to contribute to increased HIV transmission [1, 41, 42]. Cross-sectional studies found a positive and significant association between female genital schistosomiasis and prevalent HIV [1, 41, 42]. Women living with HIV have a higher risk of acquiring HR-HPV and developing cervical cancer compared to HIV-negative women [18, 26]. Considering the associations and synergies between these three conditions, the epidemiological association between female genital schistosomiasis and HR-HPV, on which the proposed health decision analytical model is based, should be stratified by HIV status, particularly in HIV-endemic populations. For the HIV-positive population, HIV disability-adjusted life-years associated with different interventions should be included in the overall health utility metrics. These stratified models can assess the cost-effectiveness of female genital schistosomiasis screening across communities with varying HIV prevalence levels.

HPV genotype

Twelve HPV genotypes are considered high-risk for progression to cervical precancer and cancer (i.e., HPV genotypes 16, 18, 31, 33,35, 39, 45, 51, 52, 56, 58 and 59) [43]. Notably, HPV types 16 and 18 are associated with approximately 75% of cases [43]. The remaining HR-HPV groups fall into

intermediate risk categories, representing less hazardous types [18]. Therefore, if data for the different genotypes is available, the proposed health decision model should be stratified by different HPV genotypes, incorporating transition probabilities that accurately reflect the different risks.

Female genital schistosomiasis and cervical cancer treatment

Treatment for female genital schistosomiasis and for cervical cancer is not considered in the current model, which focuses on evaluating the cost-effectiveness of screening interventions. Due to limited evidence on the effectiveness of praziquantel in reversing female genital schistosomiasis lesions, it is challenging to quantify the effect of treatment on the natural history of female genital schistosomiasis and its associations with other Sexual and Reproductive Health and Research conditions [1]. Additional studies are needed to better understand the effect of treatment strategies on female genital schistosomiasis [1].

Cervical cancer treatment guidelines are better established and follow national treatment algorithms [18]. If data on the costs and effectiveness of treatment is available, it can be incorporated into the proposed Markov model. Specifically, the impact of treatment would influence the transition probabilities for regression to a normal cervix. Incorporating this data into the model requires additional assumptions about treatment coverage based on the accuracy and location of different screening methods [34].

DISCUSSION AND LIMITATIONS

We presented a health decision analytical model to evaluate the cost-utility of different female genital schistosomiasis screening strategies. The model combines a decision tree for female genital schistosomiasis screening strategies, and a Markov model for the natural history of cervical cancer to estimate the cost per disability-adjusted life-years averted (cost-utility) for different screening strategies and stratified by HIV status. Since no female genital schistosomiasis disability weights are available, we proposed to calculate female genital schistosomiasis disability-adjusted life-years using weights from Sexual and Reproductive Health and Research conditions with similar symptoms. While this is probably the most accurate method available, it is likely to underestimate the true disutility of female genital schistosomiasis by failing to measure the full range of chronic morbidities and potential co-infections. Ultimately, this results in an underestimation of the overall cost-effectiveness of female genital schistosomiasis screening strategies. To improve precision, future studies should prioritise estimating the disability weights associated with female genital schistosomiasis and understanding its global burden, considering life-long morbidities, symptoms and co-infections across endemic settings [1, 9].

Further analysis is needed to estimate the financial consequences of different female genital schistosomiasis screening strategies across socioeconomic groups [44]. Policymakers do not base financial allocation solely on findings from cost-effectiveness and cost-utility analyses, but instead, consider a range of criteria including equity and fairness before distributing resources within the health sector [45]. These health dimensions are particularly relevant for female genital schistosomiasis, which affects girls and women living in rural communities with limited access to care. Adopting a societal costing perspective provides an initial understanding of direct and indirect costs incurred by patients to access different screening interventions, which can inform decision-makers on the societal preferences for different screening strategies [31]. Extended analyses should be conducted to further understand the equity and fairness associated with different female genital schistosomiasis screening strategies.

CONCLUSIONS

Cost-effectiveness analyses of female genital schistosomiasis control strategies are essential to inform health policy for the optimal allocation of healthcare resources by comparing the costs and benefits of alternative interventions. To date, there are no estimates of the affordability and cost-effectiveness of different female genital schistosomiasis screening strategies, limiting evidence-based programming of effective control interventions. We presented a framework and health decision analytical model to evaluate the cost-effectiveness of female genital schistosomiasis screening strategies, considering the poor data availability and the resulting uncertainty around key model parameters. Future research should prioritise long-term, longitudinal studies on female genital schistosomiasis-specific outcomes which to inform more accurate cost-effectiveness analyses of control strategies.

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CONFLICT OF INTEREST STATEMENT

There are no competing interests for any author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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