Gender-related differences in prevalence, intensity and associated risk factors of *Schistosoma* infections in Africa: A systematic review and meta-analysis

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Abstract

Background

Schistosomiasis remains a global-health problem with over 90% of its burden concentrated in Africa. Field studies reflect the complex ways in which socio-cultural and socio-economic variables, affect the distribution of *Schistosoma* infections across different populations. This review set out to systematically investigate and quantify the differences in *Schistosoma* infection burdens between males and females in Africa for two of the most prevalent *Schistosoma* species—*Schistosoma mansoni* and *Schistosoma haematobium*.

Methodology

We searched (from inception to 11th March 2020) Embase, MEDLINE, PubMed, and Web of Science for relevant studies on schistosomiasis. We included studies that report *S. mansoni* and/or *S. haematobium* prevalence and/or intensity data distributed between males and females. We conducted meta-analyses on the male to female (M:F) prevalence of infection ratios. Subgroup analyses were performed according to study baseline prevalence, sample size and the lower and upper age limit of study participants. We also present a descriptive analysis of differential risk and intensity of infection across males and females. Evidence for differences in the prevalence of schistosomiasis infection between males and females is presented, stratified by *Schistosoma* species.

Result

We identified 128 relevant studies, with over 200,000 participants across 23 countries. Of all the reported differences in the prevalence of infection between males and females, only

41% and 34% were statistically significant for *S. mansoni* and *S. haematobium*, respectively. Similar proportions of studies (27% and 34% for for *S. haematobium* and *S. mansoni*, respectively) of the reported differences in intensity of infection between males and females were statistically significant. The meta-analyses summarized a higher prevalence of infection in males; pooled random-effects weighted M:F prevalence of infection ratios were 1.20 (95% CI 1.11–1.29) for *S. haematobium* and 1.15 (95% CI 1.08–1.22) for *S. mansoni*. However, females are underrepresented in some of the studies. Additionally, there was significant heterogeneity across studies (Higgins I^2 statistic (p-values < 0.001, I^2 values >95%)). Results of the subgroup analysis showed that the baseline prevalence influenced the *M:F* prevalence ratios for *S. haematobium* and *S. mansoni*, with higher M:F prevalence of infection ratios in settings with a lower baseline prevalence of infection. Across the studies, we identified four major risk factors associated with infection rates: occupational and recreational water contact, knowledge, socio-economic factors and demographic factors. The effect of these risk factors on the burden of infection in males and females varied across studies.

Conclusions

We find evidence of differences in prevalence of infection between males and females which may reflect differences in gender norms and water contact activities, suggesting that policy changes at the regional level may help ameliorate gender-related disparities in schistosomiasis infection burden. Collecting, robustly analysing, and reporting, sex-disaggregated epidemiological data, is currently lacking, but would be highly informative for planning effective treatment programmes and establishing those most at risk of schistosomiasis infections.

Author summary

Schistosomiasis is a parasitic waterborne disease affecting more than 240 million people worldwide every year, especially in sub-Saharan Africa. The difference in *schistosoma* infection prevalence, infection intensity and risk between males and females has rarely been quantified. In this study, we aim to qualitatively and quantitatively synthesise published studies that present sex-disaggregated epidemiological data and investigate gender differences (e.g. those driven by social and cultural norms) that predispose males or females to higher risk of infection. Based on the 123 studies included in our meta-analysis, we found a higher prevalence of Schistosoma (*S. mansoni* and *S. haematobium*) in males.

Introduction

Schistosomiasis is a neglected tropical disease (NTD) with over 240 million people infected. Over the last decade, progress has been made towards achieving schistosomiasis morbidity control in several countries in the sub-Saharan African region, although more remains to be done [1]. The World Health Organisation (WHO) strategy for schistosomiasis control focuses on reducing disease through periodic, targeted treatment with praziquantel through the large-scale treatment (preventive chemotherapy) of affected populations. About 92% of those

requiring preventive treatment live in sub-Saharan Africa [2]. Generally, the highest prevalence and intensity of infections have been found in school-aged children (SAC; 5–14 years old) [3], though pre-SAC and adults can also be highly infected [4,5]. The disease is caused by parasitic flukes of the genus *Schistosoma* and manifests in two forms; urogenital schistosomiasis (*Schistosoma haematobium*) and intestinal schistosomiasis (*Schistosoma mansoni*, *Schistosoma japonicum*, *Schistosoma mekongi*, *Schistosoma guineensis* and *Schistosoma intercalatum*). Although the epidemiology of each species differs to a certain extent, transmission requires contamination of fresh water by faeces (intestinal) or urine (urogenital) containing eggs, an intermediate snail host, and human contact with that contaminated water inhabited by the intermediate host snail. Humans are infected by the cercarial aquatic larval stage of the parasite, with exposure depending on a range of factors which could be based on individual, socio-economic or socio-cultural behaviours. The two major *Schistosoma* species prevalent in sub-Saharan Africa are *S. mansoni* and *S. haematobium* which are transmitted via intermediate snail hosts *Biomphalaria sp*. and *Bulinus sp*., respectively [6].

Host gender shapes peoples risk of *schistosoma* infections [7]. Local differences in prevalence and intensity observed between men and women may, in part, be explained by differences in the social and occupational roles taken up by men and women affecting water-related contact, including frequency, duration and level of submergence, which can all be influenced by age and cultural beliefs [8]. For example, in many African countries, activities including washing clothes, bathing children and rice cultivation are mostly carried out by women and girls, thus increasing their risk of schistosomiasis [9]. On the other hand, previous work has suggested that males typically suffer from a higher parasitic infection risk than females [10] and based on studies in Puerto Rico and Brazil, fishing and swimming are more often associated with males [9]. Additionally, as children mature, the frequency and duration of water contact can change, dependent on age and gender, resulting in divergent infection dynamics [11]. Despite these general observations, the difference in *schistosoma* infection prevalence, infection intensity and risk between males and females has rarely been quantified [8]. A review by Sevilimedu et al [12], on the gender distribution of diarrheal disease-causing pathogens showed higher prevalence of *S. mansoni* in males. This study was geographically broad however it did not include *S. haematobium*. Given the prevalence of infection in Africa and that the *Schistosoma* species most prevalent in Africa are *S. mansoni* and *S. haematobium*, there is a need to provide updated findings specifically for Africa, whilst also expanding these results to include *S. haematobium* as well as *S. mansoni*.

The aim of this study is to investigate the differences in prevalence and intensity of *S. mansoni* and *S. haematobium* infections between males and females in Africa. The question which we aim to answer is: in individuals that have *Schistosoma* infections (*S. haematobium* or *S. mansoni*), do males or females have significantly higher prevalence and/or intensity of infection? We aim to qualitatively and quantitatively synthesise published studies that present sex-disaggregated epidemiological data and investigate gender differences (e.g. those driven by social and cultural norms) that predispose males or females to higher risk of infection. We note that, whilst the burden of schistosomiasis can be considered in many forms (e.g. infection prevalence, intensity, morbidity, or socio-economic), and whilst none of these are mutually exclusive, investigating gender-related differences in all of these simultaneously, is outwith the scope of this paper. Understanding the distribution of *Schistosoma* infection prevalence and intensity between males and females can support programmes to understand and identify who is most infected with *S. mansoni* and *S. haematobium*, contributing to transmission and subsequent morbidity.

Methods

This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, the completed checklist for which is in S1 Table. A protocol was prospectively registered in PROSPERO, registration number: CRD42020175165.

Search strategy

The lead author, DA, searched the following databases (from inception to 31st March 2020): Embase, MEDLINE, PubMed, and Web of Science. The search terms used were derived from two general sections: the disease and the epidemiological measures of interest. Variations on the following keywords were used for the search "schistosomiasis", "prevalence" and "intensity". We used Boolean operators "AND" to combine the categories and "OR" to join the terms within each category. Exact search terms are provided in S1 Text. To not limit the span of the search we did not include search terms relating to Africa, or specific countries within Africa. Based on expert recommendation, we also manually searched the Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) for any additional papers not picked by our search strategy. Identified studies were imported into EndNote X9 (Thomson Reuters, New York, USA) and duplicates were removed.

Selection criteria

The remaining unique studies were reviewed by titles, abstracts, figures and tables by DA, JC and JT independently and in duplicate. In case of any disagreement, a final decision was reached by team consensus. Following the participants, intervention, comparison, outcomes, study (PICOS) design criteria, we included studies assessing the following:

- Population: Human population (no age or geographical restriction) diagnosed with *Schistosoma* infections (*S. haematobium* or *S. mansoni*).

- Intervention or exposure: Exposure to *S. haematobium* or *S. mansoni*.

- Comparison: The comparison will be *Schistosoma* infection prevalence and/or intensity between male and female participants.

- Outcomes: The outcome measures are the male to female ratios of prevalence and/or intensity of infection.

- Study design: Observational studies.

   We included observational studies written in English (for details on any publication bias, see S2 Text and S1 and S2 Figs), that reported the prevalence and/or intensity of *Schistosoma* infections (*S. mansoni* and/or *S. haematobium*) in males and females in Africa. We excluded studies that (i) did not report prevalence and/or intensity separately for males and females (or men and women, boys and girls), (ii) full publication could not be obtained, (iii) extended analysis of previously published studies, (iv) previously published reviews on the epidemiology of schistosomiasis as these papers did not contain any new data, (v) non-human studies, and (vi) studies on human schistosomiasis caused by other *Schistosoma* species. Unpublished manuscripts, conference proceedings, conference abstracts, editorials, commentaries, letters to editors and author replies were also excluded.

Data extraction

Relevant data were extracted from eligible publications into a predefined Microsoft Excel extraction sheet developed for this review. For each full text included, the following information was extracted:

1. Publication details: title, journal, author(s), year of publication, country and year in which study was carried out

2. Study design: type of study, sampling method, *Schistosoma* species, diagnostic method(s)

3. Study population demographics (participants): number of individuals in study, population characteristics including age and demographic information.

4. Outcome measures: the main outcome variables extracted were male and female prevalence, and mean intensity of infection (defined as the mean number of schistosome eggs per gram of stool (for *S. mansoni*) and eggs per 10 millilitres of urine (for *S. haematobium*) in a population). We use the prevalence of infection and intensity of infection in males and females to calculate the male to female (*M:F*) prevalence and intensity of infection ratios. We did not differentiate between studies which presented results based on host sex (male/female) or gender (man/woman, boy/girl) and as we are not looking at specific biological risk factors, we do not differentiate between sex and gender in our results and discussion.

For cross-sectional studies, we extracted study population demographics and outcome measures of each study area separately where available. For longitudinal studies, we extracted this information only at baseline. Data extraction was performed independently, and a small random proportion was performed in duplicate by four reviewers (DA, JC, HB and JT). The methodological quality of the included studies was also assessed using the Joanna Briggs Institute critical appraisal (assessment of risk of bias) checklist for studies that report prevalence data [13]. The critical appraisal checklist has nine criteria with options of Yes, No, Unclear or Not Applicable for each individual study. The global rating for each article was given based on the number of 'Yes' (0–3: poor quality, 4–7: moderate quality and 8–9: High quality). In studies where *M:F* prevalence of infection and/or infection intensity ratios were not provided directly, we calculated these using the data provided.

Data synthesis

We did not carry out a meta-analysis on the intensity of infection *M:F* ratios for either *Schistosoma* species due to paucity of data. Amongst studies that report the mean intensity of infection, only 16 studies report the standard deviation of the mean intensity of infection in males and **females**. In addition to this, the studies differ in the way they calculate intensity of infection with some studies excluding zero counts and others including them. Instead, we present a descriptive summary of the results. In line with the aim of the paper, we provide an overview of the included studies and stratify results according to type of *Schistosoma* species and significance of the difference in *M:F* intensity of infection ratios. Statistical significance was defined as significance at 5% level as documented by all the individual studies. We also present a descriptive analysis of how risk factors varied between males and females.

We carried out a meta-analysis of the *M:F* prevalence of infection ratio to generate a pooled estimate for both *Schistosoma* species using the approach and adapted code provided by [14]. Heterogeneity was assessed using Higgin's I^2 statistic with $I^2 > 50\%$ indicating significant heterogeneity [15]. The R^2 (amount of heterogeneity accounted for by each factor or the combination of all significant factors) values were also calculated. For publication bias, we used Egger's method [16] with significance p-value < 0.05. We employed the random-effects model for meta-analyses, weighting for the inverse of the variance using the R function 'rma' with the inverse of the variance of each study as the study weight. Some studies (cross-sectional) were entered into the model multiple times to account for multiple communities being reported. Using this function, we also conducted a meta-regression analysis with *M:F* prevalence ratios

as the primary outcome of interest and age, quality rating, and baseline prevalence of the study area as the explanatory variables (S3 Text). Forest plots were created using the 'forest' function and all analyses were coded using R 4.0.1 [17].

Results

Overview of studies

The search strategy yielded 2246 papers across the three databases, with four papers added from previous reviews. In addition to this we also had 3 papers from additional sources based on expert recommendation. After removing 1440 duplicates, 809 titles and abstracts were screened. After abstract screening, 625 further papers were excluded for reasons previously stated under Selection Criteria. The remaining 184 papers were assessed for full eligibility. Of these 184 papers, 56 papers were excluded because they did not match the inclusion criteria (Fig 1). A total of 128 papers were included in this systematic review. These 128 studies were identified from a total of 23 countries, with the majority undertaken in Nigeria (30 papers, 23.4%) and Ethiopia (16 papers, 12.5%) (Fig 2). Included papers were published between the years 1980 and 2020, with the majority published in the 21st century as most of the earlier published studies did not report sex-disaggregated prevalence and/or intensity data (Fig 3). 63 papers focused on *S. haematobium* only, while the remaining studies were focused on solely *S. mansoni* (51 papers) or both species (14 papers). The included studies covered a wide range of age groups including Pre-SAC, SAC and/or adults. One study indicated an age range of 0–91 years but no mean age [18]. Study sample size ranged from 83 [19] to 49,822 [20]. In total,
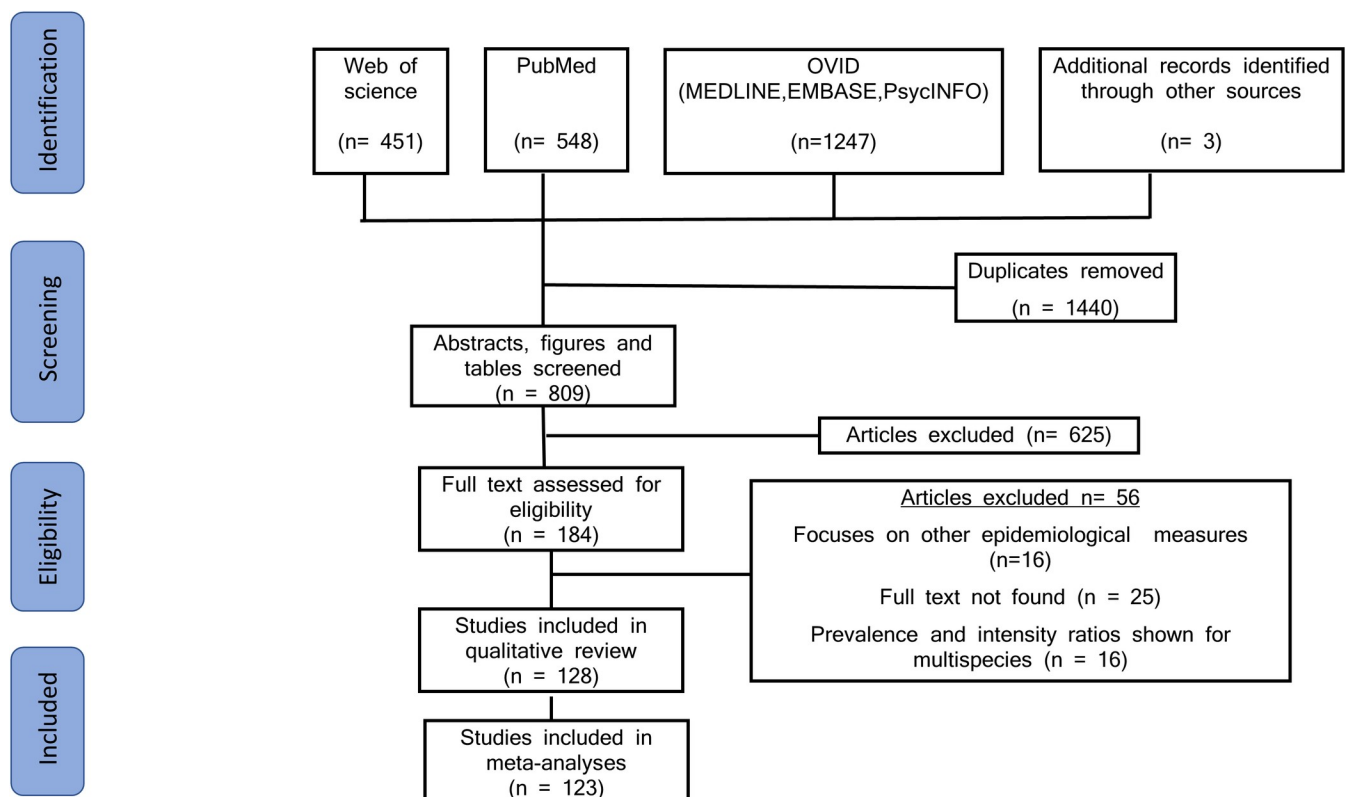
Fig 1. PRISMA diagram summarising inclusion and exclusion of all identified papers.
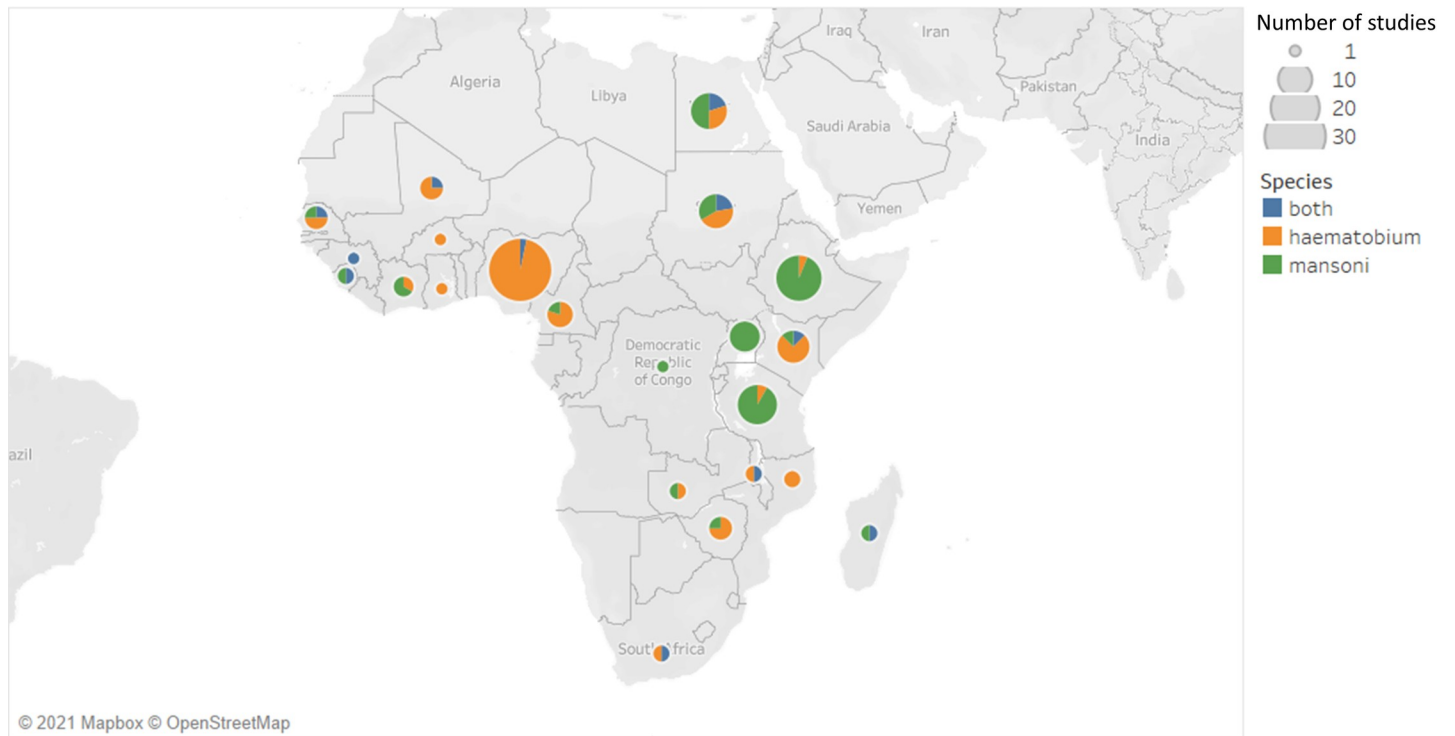
Fig 2. Map showing the geographical distribution across Africa of all papers included in this final review (n = 128). The size of each marker is proportional to the total number of studies conducted in each country and the colour corresponds to the species. This map was created using our data and the Tableau software [21]. Mapbox and OpenStreetMap are available by default in the Tableau Software Map Layers pane. Each Tableau software map built-in includes acknowledgements of Mapbox (https://www.mapbox.com/tableau/) and OpenStreetMap (https://www.openstreetmap.org/). OpenStreetMap is free to use under an open license.

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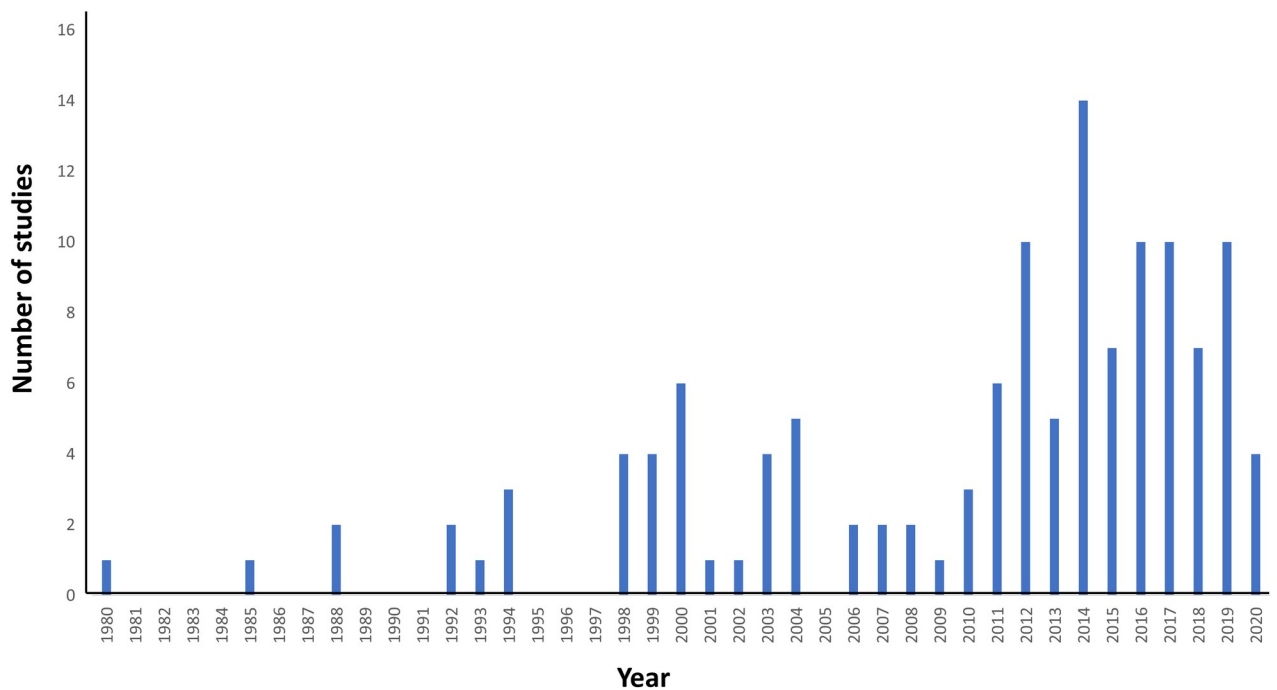
Fig 3. Distribution of publication year for the included papers (n = 128).

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there were 210,851 male participants and 195,988 female participants across the included studies. Most of the studies carried out statistical analysis on their data with respect to differences in male and females, mostly using a χ^2 test for categorical variables.

Quality of included studies

S2 Table provides the overall quality score for each study included in the review. Only 33 (around 25%) of the included studies met the threshold for high quality with eight studies obtaining the highest scores of 9/9 [22–29]. 85 studies were found to be of moderate quality. The remaining ten studies had poor quality particularly because there was a poor description of the study population (how and why participants were sampled, adequacy of sample size and coverage) and statistical methods.

Summary of identified risk factors

Thirty-five of the included studies conducted a risk factor analysis to determine factors associated with *Schistosoma* infection. We summarise the risk factors found to be associated with *Schistosoma* infection, across the included studies (Table 1). These can be grouped into five major categories: (1) occupational and recreational water contact patterns such as fishing, swimming, laundry, farming [29–36]; (2) knowledge and beliefs such as education level [37,38]; (3) socio-economic factors such as income, occupation of parents [39–41]; (4) demographic factors such as age [30,35,42–49]; and (5) climatic and environmental factors such as availability of a nearby tap water source [50]. Two studies, one on *S. haematobium* in Zambia [51] and the other on *S. mansoni* in Uganda [52], found high altitudes to be significantly associated with higher infection rates, contrary to previous findings that climatic and environmental conditions at such high altitiudes are not favourable for schistosomiasis transmission [53,54]. This was attributed to snail abundance in temporary water bodies in both studies. Amongst the studies that report a significantly higher prevalence of infection in males, 16 studies [22,38,40,41,43,50,55–64], attribute this difference to gender-specific water-contact activities in which males tend to have more frequent water contact either because of cultural or religious beliefs, occupational reasons, or social roles.

Table 1. Risk factors and how they vary between males and females in included studies for *S. haematobium* and *S. mansoni*.

Risk factor	Males	Females
(1) Occupational and recreational	More males were reported to have water contact during activities such as swimming and agricultural activities and fishing [30–32,35,43,57,59] Farming as father's occupation was significantly associated with higher infection rate [41]	Females were more involved in household duties [31] When women take up typical male roles such as fishing and farming, it increases their risk [58]
(2) Knowledge and socio-cultural beliefs	Male children considered haematuria (blood with urine) as a sign of maturity instead of a symptom of infection [38]; cultural practices predispose males to higher exposure [41,55]	Females were prohibited from bathing in open water sources due to religious beliefs [43]
	Increasing literacy level of family head (males or females) was associated with lower risk to infection [39]	
(3) Demographic factors	The male sex was found to be a significant risk factor associated with a higher risk of infection [38,40]	-
	Pre-SAC ($\leq$ 5 *years*) males and females display almost similar water contact activities and many are infected when being washed or when accompanying their caregivers to contaminated water bodies [29,34] Young adults and the elderly were less likely to be infected than SAC [39]	
(4) Socio-economic factors	Low household income predisposed individuals to higher risk of infection [39]	
(5) Climatic and environmental factors	-	The absence of tap water predisposed females to higher risk as they are burdened with responsibility of fetching water from contaminated water sources [50]
	High altitudes were found to be significantly associated with higher infection rates in males and females [51]	

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S. haematobium results

Sex-disaggregated prevalence and/or intensity data for *S. haematobium* was reported by 77 papers. Five [36,65–68] of these papers do not report carrying out any statistical analysis on their data with respect to gender. Of the remaining 72 that do report this information, 70 report sex-disaggregated prevalence data, while only 41 report sex-disaggregated intensity of infection data. All the studies that reported differences which were found to statistically significant indicate that there is a higher prevalence and intensity of infection in males than females.

Of the 41 studies which reported their *M:F* intensity of infection ratios, these ratios ranged from 0.5 in a study in Sierra Leone [69] to 10.14 a study in Nigeria [41]. Only one of these extremes was statistically significant, with males showing a statistically higher intensity of infection [41]. In all the studies that reported a significant difference in intensity of infection between males and females, males were reported to have a higher mean intensity of infection.

Of the 70 studies which reported the *M:F* prevalence of infection ratios these ranged from 0.7 observed in a study in Zimbabwe [70] to 7.75 in a study in Nigeria [56]. While the difference was reported to be statistically significant in the Nigerian study with males being seven times more likely to be infected than females due to their water contact patterns, the study in Zimbabwe reported that the observed difference was not statistically significant. Most of the studies (76%) reported a sex ratio greater than 1, indicating a greater prevalence of infection in males than females although only 41% of these were reported to be statistically significant. Three studies [33,71,72] reported a significantly higher prevalence of infection in females. The age of the study participants in these three studies ranged from 4–21 years and so it is conceivable that differences in water contact patterns between males and females could explain this due to higher infection risk behaviours in young children. However, only one of the studies [33] reported this interaction and their results suggest that although within the study population, males had less prevalence of infection than females, females may have had less exposure (as measured by frequency of water contact) to the parasite than males.

The random effects weighted model of *M:F* prevalence of infection ratios (including all studies regardless of whether the differences in prevalence of infection between males and females is reported to be significant or not) showed a significantly higher prevalence in males compared to females (1.20, 95% CI: 1.11–1.29) (Fig 4). The heterogeneity test statistic showed significant heterogeneity between publications $I^2 = 95.95\%$. As a result of such substantial heterogeneity, we conduct subgroup analysis to investigate what factors contribute to this heterogeneity. The univariate subgroup analysis (S3 Table) showed that the baseline prevalence, the lower age bound of the study participants and the sample size were significantly associated with *M:F* prevalence of infection ratios. The amount of heterogeneity contributed by the baseline prevalence, lower age bound of participants and sample size of study were 17.51%, 18.96% and 11.79% respectively (S3 Table). A larger sample size and a higher lower bound of the study participants each led to higher M:F prevalence of infection ratios (S3 and S4 Figs). On the other hand, a lower baseline prevalence leads to a higher *M:F* prevalence of infection ratios (S5 Fig).

S. mansoni results

A total of 65 papers report sex-disaggregated prevalence and/or intensity of infection data for *S. mansoni*. Of these papers, 57 carried out statistical analyses relating to the differences in males and females. Of these 57 studies, 56 reported sex-disaggregated prevalence data, while only 35 reported sex-disaggregated intensity of infection data. 39% of the 56 studies reported a significant difference in prevalence of infection between males and females, while 31% of the 35 studies reported a significant difference in intensity of infection between males and females.
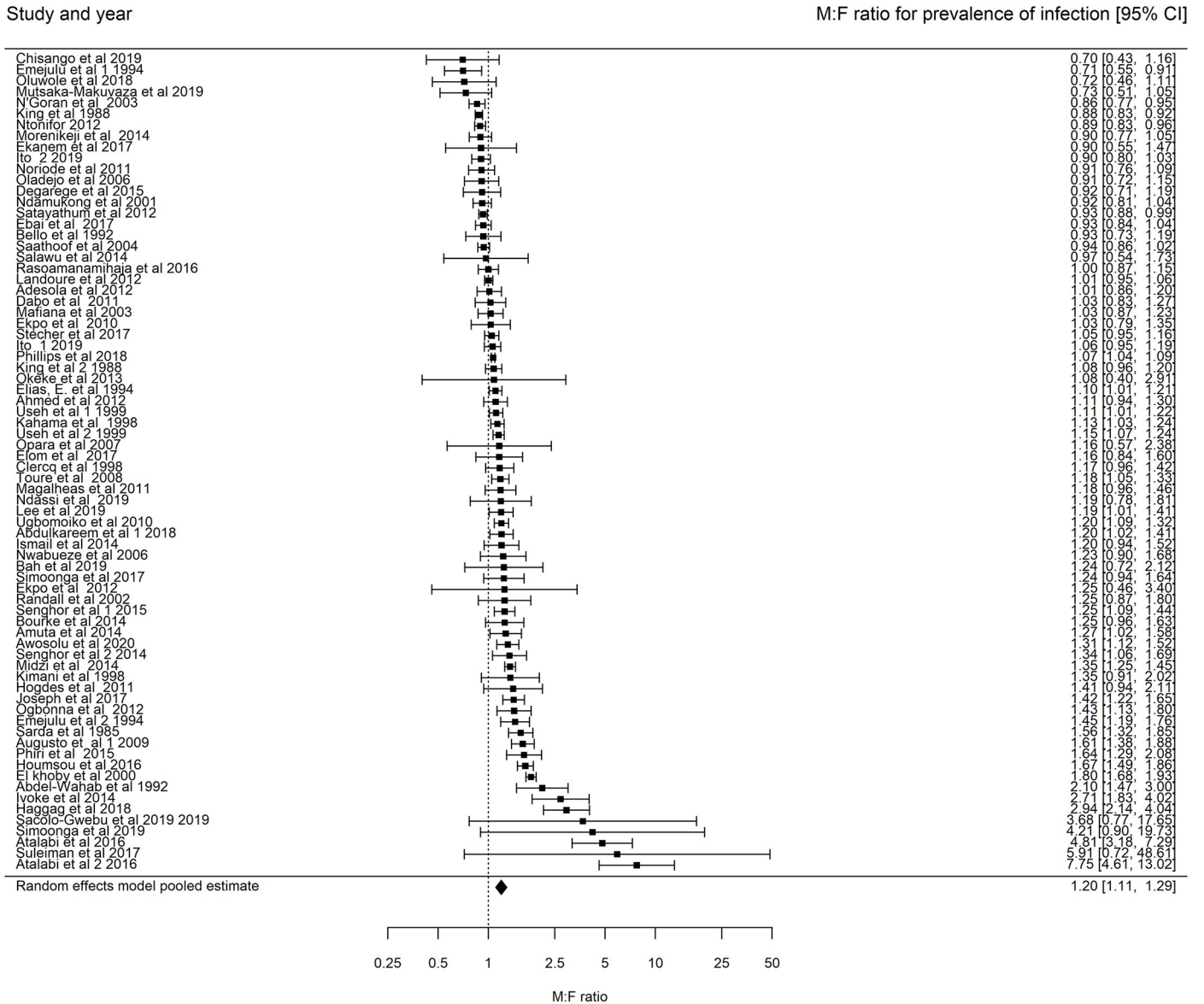
Study and year

M:F ratio for prevalence of infection [95% CI]

| Study	M:F ratio [95% CI]
Chisango et al 2019	0.70 [0.43, 1.16]
Emejulu et l 1994	0.71 [0.55, 0.91]
Oluwole et al 2018	0.72 [0.46, 1.11]
Mutsaka-Makuvaza et al 2019	0.73 [0.51, 1.05]
N'Goran et al 2003	0.86 [0.77, 0.95]
King et al 1988	0.88 [0.83, 0.92]
Ntonifor 2012	0.89 [0.83, 0.96]
Morenikeji et al 2014	0.90 [0.77, 1.05]
Ekanem et al 2017	0.90 [0.55, 1.47]
Ito 2 2019	0.90 [0.80, 1.03]
Noriode et al 2011	0.91 [0.76, 1.09]
Oladejo et al 2006	0.91 [0.72, 1.15]
Degarege et al 2015	0.92 [0.71, 1.19]
Ndamukong et al 2001	0.92 [0.81, 1.04]
Satayathum et al 2012	0.93 [0.88, 0.99]
Ebai et al 2017	0.93 [0.84, 1.04]
Bello et al 1992	0.93 [0.73, 1.19]
Saathoof et al 2004	0.94 [0.86, 1.02]
Salawu et al 2014	0.97 [0.54, 1.73]
Rasoamanamihaja et al 2016	1.00 [0.87, 1.15]
Landoure et al 2012	1.01 [0.95, 1.06]
Adesola et al 2012	1.01 [0.86, 1.20]
Dabo et al 2011	1.03 [0.83, 1.27]
Mafiana et al 2003	1.03 [0.87, 1.23]
Ekpo et al 2010	1.03 [0.79, 1.35]
Stecher et al 2017	1.05 [0.95, 1.16]
Ito 1 2019	1.06 [0.95, 1.19]
Phillips et al 2018	1.07 [1.04, 1.09]
King et al 2 1988	1.08 [0.96, 1.20]
Okeke et al 2013	1.08 [0.40, 2.91]
Elias, E. et al 1994	1.10 [1.01, 1.21]
Ahmed et al 2012	1.11 [0.94, 1.30]
Useh et al 1 1999	1.11 [1.01, 1.22]
Kahama et al 1998	1.13 [1.03, 1.24]
Useh et al 2 1999	1.15 [1.07, 1.24]
Opara et al 2007	1.16 [0.57, 2.38]
Efom et al 2017	1.16 [0.84, 1.60]
Clercq et al 1998	1.17 [0.96, 1.42]
Toure et al 2008	1.18 [1.05, 1.33]
Magalheas et al 2011	1.18 [0.96, 1.46]
Ndassi et al 2019	1.19 [0.78, 1.81]
Lee et al 2019	1.19 [1.01, 1.41]
Ugbomoiko et al 2010	1.20 [1.09, 1.32]
Abdulkareem et al 1 2018	1.20 [1.02, 1.41]
Ismail et al 2014	1.20 [0.94, 1.52]
Nwabueze et al 2006	1.23 [0.90, 1.68]
Bah et al 2019	1.24 [0.72, 2.12]
Simoonga et al 2017	1.24 [0.94, 1.64]
Ekpo et al 2012	1.25 [0.46, 3.40]
Randall et al 2002	1.25 [0.87, 1.80]
Senghor et al 1 2015	1.25 [1.09, 1.44]
Bourke et al 2014	1.25 [0.96, 1.63]
Amuta et al 2014	1.27 [1.02, 1.58]
Awosolu et al 2020	1.31 [1.12, 1.52]
Senghor et al 2 2014	1.34 [1.06, 1.69]
Midzi et al 2014	1.35 [1.25, 1.45]
Kimani et al 1998	1.35 [0.91, 2.02]
Hogdes et al 2011	1.41 [0.94, 2.11]
Joseph et al 2017	1.42 [1.22, 1.65]
Ogbonna et al 2012	1.43 [1.13, 1.80]
Emejulu et al 2 1994	1.45 [1.19, 1.76]
Sarda et al 1985	1.56 [1.32, 1.85]
Augusto et al 1 2009	1.61 [1.38, 1.88]
Phiri et al 2015	1.64 [1.29, 2.08]
Houmsou et al 2016	1.67 [1.49, 1.86]
El khoby et al 2000	1.80 [1.68, 1.93]
Abdel-Wahab et al 1992	2.10 [1.47, 3.00]
Ivoke et al 2014	2.71 [1.83, 4.00]
Haggag et al 2018	2.94 [2.14, 4.04]
Sacolo-Gwebu et al 2019 2019	3.68 [0.77, 17.65]
Simoonga et al 2019	4.21 [0.90, 19.73]
Atalabi et al 2016	4.81 [3.18, 7.29]
Suleiman et al 2017	5.91 [0.72, 48.61]
Atalabi et al 2 2016	7.75 [4.61, 13.02]
Random effects model pooled estimate	1.20 [1.11, 1.29]

M:F ratio

Fig 4. Forest plots showing the M:F prevalence of infection ratios and 95% CI for Schistosoma haematobium (74 communities and n = 71 studies, pooled M:F prevalence ratio is (1.19, 95% CI 1.11–1.29), heterogeneity: I^2 = 95.95%). Points further to the right indicate higher prevalence in males. Analysis includes studies that report the number of males and females who were screened for S. haematobium infection and the fraction who tested positive regardless of the reported significance of the difference in M:F prevalence of infection ratios.

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The *M:F* intensity of infection ratios in the 35 studies that reported it ranged from 0.55 to 2.79 observed in a study in Sudan [73] and a study in Uganda [23] respectively. Only one of these were statistically significant: the study in Uganda where males had on average three times higher egg counts than females. Males had a higher mean intensity of infection in all but one study that reported a significant difference in intensity of infection between males and females. This study was in a community in Sudan [64] where females had higher egg counts than males even though the observed prevalence was significantly higher in males. This was attributed to the duration spent on household chores such as laundry at the local canal by females in the study population.

The *M:F* prevalence of infection ratios in the 57 studies which reported these ratios ranged from 0.31 to 3.93 observed in a study in Sudan [73] and South Africa [49] respectively. Both studies report that the difference in prevalence between males and females was statistically significant. Females had a higher prevalence of infection than males in only three [73–75] of the studies. The ages of the participants in these studies ranged from 6 to above 40 (SAC and adults).

The random effects weighted model on *M:F* prevalence of infection ratios (including all studies regardless of whether the differences in prevalence of infection between males and females was reported to be significant or not) showed a significantly higher prevalence in males compared to females (1.15, 95% CI: 1.08–1.22; Fig 5). The heterogeneity test statistic test
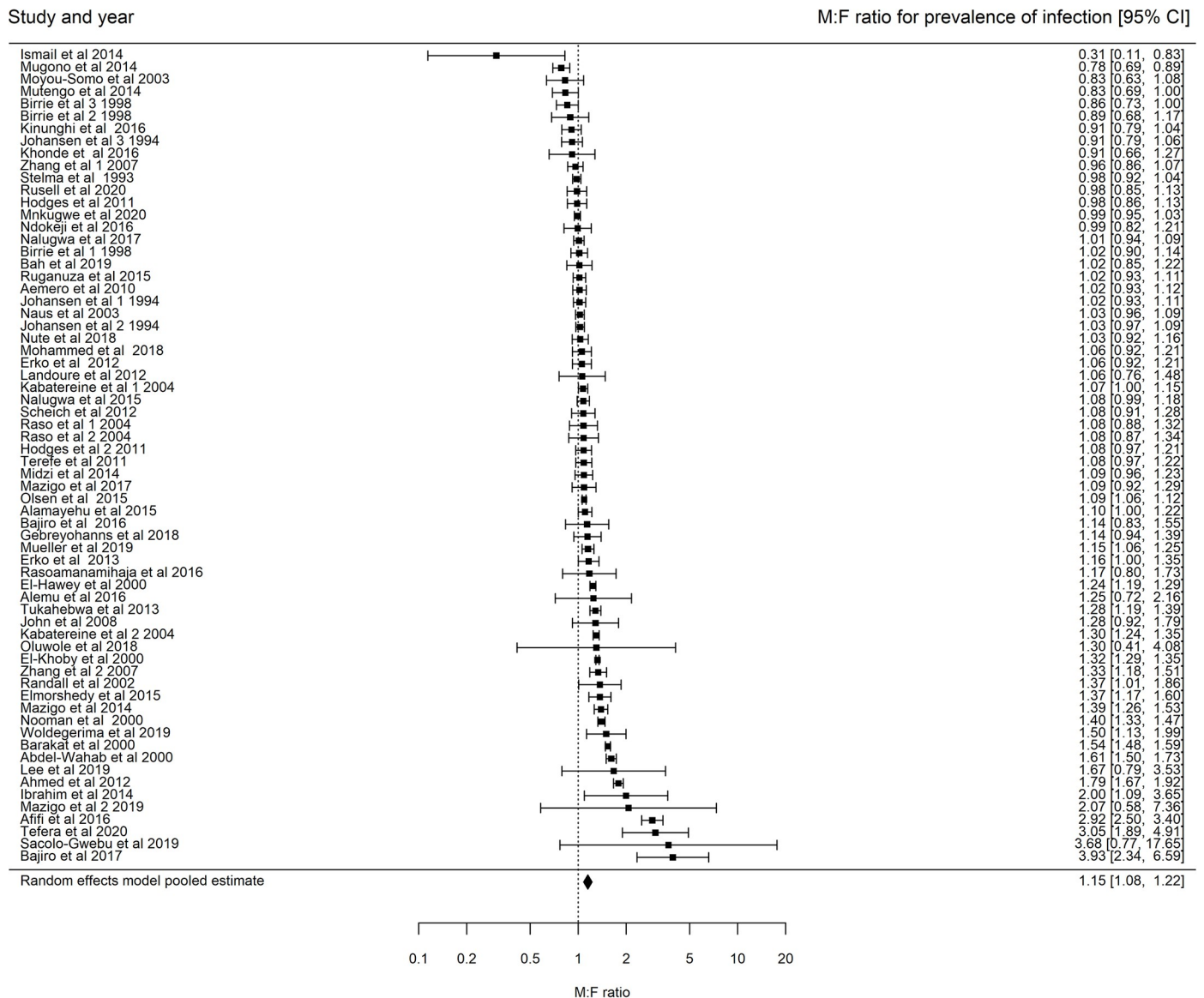
Fig 5. Forest plots showing the M:F prevalence of infection ratios and 95% CI for Schistosoma mansoni (66 communities and n = 61 studies, pooled M:F prevalence ratio is (1.15, 95% CI 1.08–1.22), heterogeneity: I² = 96.43%). Points further to the right indicate higher prevalence in males. Analysis includes studies that report the number of males and females who were screened for S. mansoni infection and the fraction who tested positive regardless of the reported significance of the difference in M:F prevalence of infection ratio.

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showed consistent heterogeneity of publications I^2 = 96.43%. Due to the presence of high heterogeneity, subgroup analysis was performed to check for important contributing factors. The univariate subgroup analysis (S4 Table) showed that baseline prevalence of studies was significantly associated with *M:F* prevalence of infection ratios, while the other tested factors (sample size, lower and upper age limit of study participants) were not. The amount of heterogeneity contributed by the baseline prevalence was 10.5% (S4 Table). A higher baseline prevalence corresponds to a lower *M:F* prevalence of infection ratio (S6 Fig).

Discussion

In this systematic review, we analysed studies reporting prevalence and intensity of *S. haematobium* and *S. mansoni* infection in Africa, quantifying the differences between males and females. We conducted a meta-analysis on the *M:F* prevalence of infection ratios obtained from the eligible studies, separately for both *Schistosoma* species using a random-effects model. We also conducted a univariate meta-regression analysis to determine what variables are associated with differences in male and female prevalence of infection. Our findings suggest that males are significantly more likely to be infected than females and that the higher the baseline prevalence, the lower the *M:F* prevalence of infection ratios for both *Schistosoma* species.

Our results suggest males are at an increased risk of exposure to contaminated water bodies. One plausible explanation is gender-related occupational roles, for example, in some of the studies, men spent more time fishing and practicing irrigation farming [30,42,73,76]. Also, in some study areas due to religious and sociocultural reasons, females are prohibited or at least discouraged from participating in activities such as swimming and fishing and are therefore exposed less often to infection [43,77]. Although females have some exposure activities which are particular to them, such as household chores, like washing dishes and doing laundry in contaminated water bodies, this seems to not be enough to increase their probability of infection beyond that of their male counterparts within the same communities. This has been attributed to the fact that their water contact activities involve the use of soap which may have a cercaricidal effect and thus reduce their risk whilst exposed to contaminated water [78]. There are, however, instances where this does not hold true—in a Kenyan study, a higher prevalence of infection in females was not directly linked to exposure patterns [33]—females had a significantly higher prevalence of *S. haematobium* infection even though males were reported to have more water contact.

It has been shown that males are less likely to participate in MDA programmes [79,80] and are thus may be be important maintainers of infections and transmission in some settings. Indeed the lower rate of male treatment, may in turn be contributing to their higher prevalence. We were unable to investigate this further here, but it is worth noting that the higher risk for males was documented before widespread MDA began from ~2002/3 indicating that even if this is involved it is unlikely to be a key driver. We also aimed to analyse the data pre and post MDA initiation, however as the timing of the study in relation to MDA was almost never reported, this was not possible. Our findings show that higher or lower prevalence of infection in one sex did not always translate to higher or lower mean egg counts in that sex when compared to the opposite sex. However, a paucity of adequately reported intensity sex dis-aggregated data meant we could not conduct a meta-analysis or regression on the intensity of infection ratios. Improvements to sex-disaggregated data reporting and susequent analysis is needed to elucidate this relationship. It is therefore evident that whilst water contact goes some way to explaining these sex-specific infection patterns, there are other risk factors to be considered.

An important factor this review cannot disentangle, is the difference in infection prevalence and/ or intensity in males and females by age. Results of the meta-regression analyses show that while the lower age limit of the study cohort was not significantly associated with higher *M:F* prevalence of infection for *S. mansoni*, it was for *S. haematobium*. Water-associated behaviors are possibly similar for very young males and females thereby leading to *M:F* prevalence of infection ratios closer to one. Whilst our initial aim had been to report data dis-aggregated by sex and age, we however found only 13 studies [20,23,29,44,45,55,81–87], that reported prevalence of infection data in males and females, stratified by age. This was not a sufficient number of studies, or a sufficient level of detail, to conduct a robust analysis. Additionally, the age stratifications vary greatly across studies, negatively impacting comparisons and analyses into the specific shape of the sex-age-infection profile. The risk of infection is generally believed to be higher for children, with infection intensity thought to peak between 10 and 20 years of age [88,89]. In conjunction with our results supporting higher infection risk for males, this highlights the necessity for studies to be designed with these age-varying patterns explicitly considered, and for these data to be reported in a consistent manner.

We note several limitations of this study. First of all, females were underrepresented, particularly in some studies [41,56,69,71,74,84,90,91] which may imply a sampling bias in the study designs themselves, which we could not overcome. Additionally, here we focus on infection intensity and infection prevalence, and do not investigate this relationship with the prevalence of morbidity, where there is some evidence to suggest in cases such as gential schistosomiasis, that females shoulder the burden of morbidity more so than males [92,93]. Along the same lines, the paucity of infection intensity data meant that we could not quantitatively investigate the relationship between host sex and infection intensity. These are important and undoubtedly interconnected points. In mixed sex studies, infection intensity and morbidity are not linearly related [94], but understanding sex differences across infection intensity and the manfestation of that as clinical morbidity will be vital to the understanding the distribution of the true, multidimensional burden of infection. Additionally, although we have focused our discussion on gender and the associated behavioural differences, we acknowledge that biological differences between the sexes may also contribute to the observed differences. For example different immune responses between the sexes have been argued to be an important factor in the observed differences in intensity of infection between males and females [95].

Some limitations related to data and study quality were also observed in the included studies. Using the Joanna Briggs Institute critical appraisal for studies that report prevalence data, showed that 72.9% of the studies had low to moderate quality. This was most often because numerous studies had either poorly conducted, poorly reported or completely un conducted/ reported statistical analysis of prevalence and/or infection data in males and females. This was particularly evident in intensity of infection data as most studies did not report the standard deviation of the mean intensity of infection. Inappropriate analytical methods were more common in older studies, prior to the computational power for analysis we have now. Though it is worth mentioning that this was not always the case, and that unsuitable methods of analysis were used even in more recent works, presumably because the analyses are based on older papers/ methods. Alternative meta-analysis methods, like those making use of entire datasets could overcome these issues [96], though could also significantly limit the scope of the papers included if original datasets were not sharable (digitalised for example) or accessible. Papers also scored poorly for quality because a formal sample size calculation was rarely carried out.

We also observed some level of publication bias for studies on *S. haematobium*. Publication bias may exist when there is a preference to publish studies with significant findings. There is generally no preference to publish studies with specific *M:F* prevalence of infection ratios and

in addition to this, not all subgroup analyses showed publication bias. Therefore, we believe that publication bias is unlikely to have distorted our results.

Given the high heterogeneity between the studies, the pooled *M:F* prevalence estimate should be interpreted with caution. Such variation may partially be attributed to factors including the baseline prevalence of the study areas, the age (lower age bound or upper age bound) of study participants or bias introduced by the sample size of each study. Based on the baseline prevalence, the pooled *M:F* prevalence of infection ratios decreased significantly from 1.34 and 1.25 in study areas with baseline prevalence less than 50% to 1.09 and 1.06 in study areas with baseline prevalence greater than 50% for *S. haematobium* and *S. mansoni* respectively. This may be because in areas of high endemicity, the infection is widespread such that the difference in prevalence between males and females is not so obvious. In relation to sample size and the lower age bound, it was observed that the larger the sample size or the higher the lower age bound of the studies, the higher the *M:F* prevalence of infection ratios and vice versa for *S. haematobium* only.

To conclude, our study highlights the importance of collecting, reporting and analysing unbiased sex-disaggregated data. Our results also expose a distinct lack of age by sex data collection and reporting [97]. Finally, through our quality assessment, we also highlight the need for improved statistical methods and reporting. Addressing these challenges will help to characterise the distribution of *Schistosoma* infection across demographic groups, which in turn will be vital for understanding how current intervention programmes can be improved to access and treat those most in need.

Supporting information

S1 Table. PRISMA guidelines completed checklist.
(DOCX)

S2 Table. All references included in the qualitative assessment of differences in infection prevalence and intensity between males and females as reported by the individual studies. Baseline prevalence is scored in keeping with the World Health Organization prevalence categories, where Mod is an abbreviation of moderate. Study size is broken down by males (M) and females (F). The quality scoring system follows that in the main text methods, with Poor = 0–3, medium = 4–7 (abbreviated as med here), and high = 8–9. *S. m* is the abbreviation for *Schistosoma mansoni*, nd *S. h* is the abbreviation for *Schistosoma haematobium*. Papers are listed in alphabetical order by title. Nr = Not reported.
(DOCX)

S3 Table. Results of univariate meta-regression analysis showing the effect of age (lower and upper age limit of included studies), baseline prevalence and sample size on the *M:F* prevalence of infection ratio of *S. haematobium*. DF = degrees of freedom, * *depicts p-value < 0.05*.
(DOCX)

S4 Table. Results of univariate meta-regression analysis showing the effect of age (lower and upper age limit of included studies), baseline prevalence and sample size on the *M:F* prevalence of infection ratio of *S. mansoni*. DF = degrees of freedom, * *depicts p-value < 0.05*.
(DOCX)

S1 Text. Search strategy.
(DOCX)

S2 Text. Publication bias.
(DOCX)

S3 Text. Univariate meta-regression analysis.
(DOCX)

S1 Fig. Funnel plot for assessing publication bias in meta-analysis of 71 epidemiological studies in Africa of *S. haematobium*. The funnel graph shows the effect measure (*M:F* prevalence ratio) and standard error (S.E.) for each study.
(DOCX)

S2 Fig. Funnel plot for assessing publication bias in meta-analysis of 61 epidemiological studies in Africa of *S. mansoni*. The funnel graph shows the effect measure (*M:F* prevalence ratio) and standard error (S.E.) for each study.
(DOCX)

S3 Fig. Forest plots showing the *M:F* prevalence ratios and 95% CI for *S. haematobium* according to sample size; a) Studies with sample size less than 2251(mean sample size of included studies), pooled *M:F* prevalence ratio is 1.17 (95% *CI* 1.08–1.27), I^2 = 93.15%, and b) studies with sample size greater than 2251; *M:F* prevalence of infection ratio is 1.31 (95% *CI* 1.08–1.59), I^2 = 98%.
(DOCX)

S4 Fig. Forest plots showing the *M:F* prevalence ratios and 95% CI for *S. haematobium* for studies where the lower age limit is greater than 5 years (21 communities and n = 19 studies, pooled *M:F* prevalence ratio is 1.54 (95% *CI* 1.24–1.91), heterogeneity: I^2 = 97.85%). Analysis includes studies that report the number of individuals who were screened for *S. haematobium* infection and the fraction who tested positive distributed by sex regardless of the reported significance of the difference in *M:F* prevalence ratios.
(DOCX)

S5 Fig. Forest plots showing the *M:F* prevalence ratios and 95% CI for *S. haematobium* according to baseline prevalence; a) Studies with baseline prevalence greater than 50% pooled *M:F* prevalence ratio is 1.09 (95% *CI* 1.03–1.15), I^2 = 91.40%, and b) studies with baseline prevalence less than 50%; *M:F* prevalence of infection ratio is 1.34 (95% *CI* 1.16–1.55), I^2 = 94.42%. Analyses includes studies that report the number of individuals who were screened for *S. haematobium* infection and the fraction who tested positive distributed by sex regardless of the reported significance of the difference in *M:F* prevalence ratios.
(DOCX)

S6 Fig. Forest plots showing the *M:F* prevalence ratios and 95% CI for *S. mansoni* according to baseline prevalence; a) Studies with baseline prevalence greater than 50% pooled *M:F* prevalence ratio is 1.06 (95% *CI* 0.99–1.12), I^2 = 90.38%, and b) studies with baseline prevalence less than 50%; *M:F* prevalence of infection ratio is 1.25 (95% *CI* 1.14–1.39), I^2 = 97.84%.
(DOCX)

Author Contributions

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Formal analysis: Diepreye Victoria Ayabina.

References

1. Deol AK, Fleming FM, Calvo-Urbano B, Walker M, Bucumi V, Gnandou I, et al. Schistosomiasis—assessing progress toward the 2020 and 2025 global goals. New England Journal of Medicine. 2019; 381(26):2519–28. https://doi.org/10.1056/NEJMoa1812165 PMID: 31881138

2. GBD Disease and Injury IaPC. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017; 390(10100):1211–59. https://doi.org/10.1016/S0140-6736(17)32154-2 PMID: 28919117

3. Adenowo AF, Oyinloye BE, Ogunyinka BI, Kappo AP. Impact of human schistosomiasis in sub-Saharan Africa. Brazilian Journal of Infectious Diseases. 2015; 19(2):196–205. https://doi.org/10.1016/j.bjid.2014.11.004 PMID: 25636189

4. Poole H, Terlouw DJ, Naunje A, Mzembe K, Stanton M, Betson M, et al. Schistosomiasis in pre-school-age children and their mothers in Chikhwawa district, Malawi with notes on characterization of schistosomes and snails. Parasites & vectors. 2014; 7(1):153. https://doi.org/10.1186/1756-3305-7-153 PMID: 24690282

5. Toor J, Turner HC, Truscott JE, Werkman M, Phillips AE, Alsallaq R, et al. The design of schistosomiasis monitoring and evaluation programmes: The importance of collecting adult data to inform treatment strategies for Schistosoma mansoni. PLoS neglected tropical diseases. 2018; 12(10):e0006717. https://doi.org/10.1371/journal.pntd.0006717 PMID: 30296257

6. Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. The Lancet. 2014; 383 (9936):2253–64.

7. Trienekens SC, Faust CL, Meginnis K, Pickering L, Ericsson O, Nankasi A, et al. Impacts of host gender on Schistosoma mansoni risk in rural Uganda—A mixed-methods approach. PLoS neglected tropical diseases. 2020; 14(5):e0008266. https://doi.org/10.1371/journal.pntd.0008266 PMID: 32401770

8. Organization WH. The social context of schistosomiasis and its control: an introduction and annotated bibliography: World Health Organization; 2008.

9. Michelson EH. Adam's rib awry? Women and schistosomiasis. Social Science and Medicine. 1993; 37 (4):493–501. https://doi.org/10.1016/0277-9536(93)90284-b PMID: 8211261

10. Bernin H, Lotter H. Sex bias in the outcome of human tropical infectious diseases: influence of steroid hormones. J Infect Dis. 2014; 209 Suppl 3:S107–13. https://doi.org/10.1093/infdis/jit610 PMID: 24966190

11. Musuva RM, Awiti A, Omedo M, Ogutu M, Secor WE, Montgomery SP, et al. Community knowledge, attitudes and practices on schistosomiasis in western Kenya—the SCORE Project. The American journal of tropical medicine and hygiene. 2014; 90(4):646–52. https://doi.org/10.4269/ajtmh.13-0488 PMID: 24534810

12. Sevilimedu V, Pressley KD, Snook KR, Hogges JV, Politis MD, Sexton JK, et al. Gender-based differences in water, sanitation and hygiene-related diarrheal disease and helminthic infections: a systematic review and meta-analysis. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2016; 110(11):637–48. https://doi.org/10.1093/trstmh/trw080 PMID: 28115686

13. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. International journal of evidence-based healthcare. 2015; 13(3):147–53. https://doi.org/10.1097/XEB.0000000000000054 PMID: 26317388

14. Horton KC, MacPherson P, Houben RM, White RG, Corbett EL. Sex differences in tuberculosis burden and notifications in low-and middle-income countries: a systematic review and meta-analysis. PLoS medicine. 2016; 13(9):e1002119. https://doi.org/10.1371/journal.pmed.1002119 PMID: 27598345

15. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. Bmj. 2003; 327(7414):557–60. https://doi.org/10.1136/bmj.327.7414.557 PMID: 12958120

16. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. Bmj. 1997; 315(7109):629–34. https://doi.org/10.1136/bmj.315.7109.629 PMID: 9310563

17. Team RC. R: A language and environment for statistical computing. Vienna, Austria; 2013.

18. Raso G, N'Goran E, Toty A, Luginbuhl A, Adjoua CA, Tian-Bi NT, et al. Efficacy and side effects of praziquantel against Schistosoma mansoni in a community of western Cote d'Ivoire. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2004; 98(1):18–27. https://doi.org/10.1016/s0035-9203(03)00003-8 PMID: 14702835

19. Ekpo UF, Alabi OM, Oluwole AS, Sam-Wobo SO. Schistosoma haematobium infections in preschool children from two rural communities in Ijebu East, south-western Nigeria. Journal of Helminthology. 2012; 86(3):323–8. https://doi.org/10.1017/S0022149X11000459 PMID: 22824258

20. Abdel-Wahab MF, Esmat G, Ramzy I, Narooz S, Medhat E, Ibrahim M, et al. The epidemiology of schistosomiasis in Egypt: Fayoum Governorate. American Journal of Tropical Medicine and Hygiene. 2000; 62(2 SUPPL.):55–64. https://doi.org/10.4269/ajtmh.2000.62.55 PMID: 10813501

21. Chabot C, Stolte C, Hanrahan P. Tableau software. Tableau Software. 2003;6.

22. Awosolu OB, Shariman YZ, Farah Haziqah MT, Olusi TA. Will nigerians win the war against urinary schistosomiasis? Prevalence, intensity, risk factors and knowledge assessment among some rural communities in Southwestern Nigeria. Pathogens. 2020; 9(2):128. https://doi.org/10.3390/pathogens9020128 PMID: 32079189

23. Tukahebwa EM, Magnussen P, Madsen H, Kabatereine NB, Nuwaha F, Wilson S, et al. A very high infection intensity of Schistosoma mansoni in a Ugandan Lake Victoria Fishing Community is required for association with highly prevalent organ related morbidity. PLoS Neglected Tropical Diseases. 2013; 7(7):e2268. https://doi.org/10.1371/journal.pntd.0002268 PMID: 23936559

24. Mutsaka-Makuvaza MJ, Matsena-Zingoni Z, Katsidzira A, Tshuma C, Chin'Ombe N, Zhou XN, et al. Urogenital schistosomiasis and risk factors of infection in mothers and preschool children in an endemic district in Zimbabwe. Parasites and Vectors. 2019; 12(1):427. https://doi.org/10.1186/s13071-019-3667-5 PMID: 31477172

25. Adesola H, Uduak N, Olajumoke M, Roseangela N, Chiaka A, Sunday A, et al. Urine turbidity and Microhaematuria as rapid assessment indicators for Schistosoma haematobium infection among school children in endemic areas. American Journal of Infectious Diseases. 2012; 8(1):60–4.

26. Alemayehu B, Tomass Z. Schistosoma mansoni infection prevalence and associated risk factors among schoolchildren in Demba Girara, Damot Woide District of Wolaita Zone, Southern Ethiopia. Asian Pacific Journal of Tropical Medicine. 2015; 8(6):457–63. https://doi.org/10.1016/j.apjtm.2015.05.009 PMID: 26194830

27. Mwandawiro CS, Nikolay B, Kihara JH, Ozier O, Mukoko DA, Mwanje MT, et al. Monitoring and evaluating the impact of national school-based deworming in Kenya: Study design and baseline results. Parasites and Vectors. 2013; 6(1):198. https://doi.org/10.1186/1756-3305-6-198 PMID: 23829767

28. Magalhaes RJS, Biritwum NK, Gyapong JO, Brooker S, Zhang Y, Blair L, et al. Mapping Helminth co-infection and co-intensity: Geostatistical prediction in Ghana. PLoS Neglected Tropical Diseases. 2011; 5(6):e1200. https://doi.org/10.1371/journal.pntd.0001200 PMID: 21666800

29. Nalugwa A, Olsen A, Tukahebwa ME, Nuwaha F. Intestinal schistosomiasis among preschool children along the shores of Lake Victoria in Uganda. Acta Tropica. 2015; 142:115–21. https://doi.org/10.1016/j.actatropica.2014.11.014 PMID: 25454166

30. Tefera A, Belay T, Bajiro M. Epidemiology of Schistosoma mansoni infection and associated risk factors among school children attending primary schools nearby rivers in Jimma town, an urban setting, Southwest Ethiopia. PLoS One. 2020; 15(2):e0228007. https://doi.org/10.1371/journal.pone.0228007 PMID: 32107485

31. Nooman ZM, Hasan AH, Waheeb Y, Mishriky AM, Ragheb M, Abu-Saif AN, et al. The epidemiology of schistosomiasis in Egypt: Ismailia Governorate. American Journal of Tropical Medicine and Hygiene. 2000; 62(2 SUPPL.):35–41. https://doi.org/10.4269/ajtmh.2000.62.35 PMID: 10813498

32. Sulieman Y, Eltayeb RE, Pengsakul T, Afifi A, Zakaria MA. Epidemiology of urinary schistosomiasis among school children in the alsaial Alsagair village, River nile state, Sudan. Iranian Journal of Parasitology. 2017; 12(2):284–91. PMID: 28761490

33. Satayathum SA, Muchiri EM, Ouma JH, Whalen CC, King CH. Factors affecting infection or reinfection with Schistosoma haematobium in coastal Kenya: survival analysis during a nine-year, school-based

treatment program. The American journal of tropical medicine and hygiene. 2006; 75(1):83–92. PMID: 16837713

34. Ndokeji S, Mazigo HD, Temu M, Kishamawe C, Malenganisho W, Todd J, et al. Prevalence and intensity of schistosoma mansoni and hookworm infections among pre-school and school-aged children in Ilemela district, north-western Tanzania. Tanzania Journal of Health Research. 2016; 18(2).

35. Gebreyohanns A, Legese MH, Wolde M, Leta G, Tasew G. Prevalence of intestinal parasites versus knowledge, attitude and practices (KAPs) with special emphasis to Schistosoma mansoni among individuals who have river water contact in Addiremets town, Western Tigray, Ethiopia. PLoS One. 2018; 13(9):e0204259. https://doi.org/10.1371/journal.pone.0204259 PMID: 30252865

36. Phiri BBW, Ngwira B, Kazembe LN. Analysing risk factors of co-occurrence of schistosomiasis haematobium and hookworm using bivariate regression models: Case study of Chikwawa, Malawi. Parasite Epidemiology and Control. 2016; 1(2):149–58. https://doi.org/10.1016/j.parepi.2016.02.001 PMID: 29988186

37. Mohammed J, Weldegebreal F, Teklemariam Z, Mitiku H. Clinico-epidemiology, malacology and community awareness of Schistosoma mansoni in Haradenaba and Dertoramis kebeles in Bedeno district, eastern Ethiopia. SAGE Open Medicine. 2018;6. https://doi.org/10.1177/2050312118786748 PMID: 30034806

38. Abdulkareem BO, Habeeb KO, Kazeem A, Adam AO, Samuel UU. Urogenital Schistosomiasis among Schoolchildren and the Associated Risk Factors in Selected Rural Communities of Kwara State, Nigeria. Journal of Tropical Medicine. 2018; 2018:6913918. https://doi.org/10.1155/2018/6913918 PMID: 29853921

39. Ugbomoiko US, Ofoezie IE, Okoye IC, Heukelbach J. Factors associated with urinary schistosomiasis in two peri-urban communities in south-western Nigeria. Annals of Tropical Medicine and Parasitology. 2010; 104(5):409–19. https://doi.org/10.1179/136485910X12743554760469 PMID: 20819309

40. Mugono M, Konje E, Kuhn S, Mpogoro FJ, Morona D, Mazigo HD. Intestinal schistosomiasis and geohelminths of Ukara Island, North-Western Tanzania: Prevalence, intensity of infection and associated risk factors among school children. Parasites and Vectors. 2014; 7(1):612.

41. Atalabi TE, Lawal U, Ipinlaye SJ. Prevalence and intensity of genito-urinary schistosomiasis and associated risk factors among junior high school students in two local government areas around Zobe Dam in Katsina State, Nigeria. Parasites and Vectors. 2016; 9(1):388. https://doi.org/10.1186/s13071-016-1672-5 PMID: 27388007

42. Mazigo HD, Dunne DW, Wilson S, Kinung'hi SM, Pinot de Moira A, Jones FM, et al. Co-infection with Schistosoma mansoni and Human Immunodeficiency Virus-1 (HIV-1) among residents of fishing villages of north-western Tanzania. Parasites & vectors. 2014; 7:587. https://doi.org/10.1186/s13071-014-0587-2 PMID: 25511298

43. Lee YH, Lee JS, Jeoung HG, Kwon IS, Mohamed AAWS, Hong ST. Epidemiological survey on schistosomiasis and intestinal helminthiasis among village residents of the rural river basin area in White Nile state, Sudan. Korean Journal of Parasitology. 2019; 57(2):135–44. https://doi.org/10.3347/kjp.2019.57.2.135 PMID: 31104405

44. Abdel-Wahab MF, Esmat G, Medhat E, Narooz S, Ramzy I, El-Boraey Y, et al. The epidemiology of schistosomiasis in Egypt: Menofia Governorate. American Journal of Tropical Medicine and Hygiene. 2000; 62(2 SUPPL.):28–34. https://doi.org/10.4269/ajtmh.2000.62.28 PMID: 10813497

45. Barakat R, Farghaly A, El Masry AG, El-Sayed MK, Hussein MH. The epidemiology of schistosomiasis in Egypt: Patterns of Schistosoma mansoni infection and morbidity in Kafr El-Sheikh. American Journal of Tropical Medicine and Hygiene. 2000; 62(2 SUPPL.):21–7.

46. El-Khoby T, Galal N, Fenwick A, Barakat R, El-Hawey A, Nooman Z, et al. The epidemiology of schistosomiasis in Egypt: Summary findings in nine governorates. American Journal of Tropical Medicine and Hygiene. 2000; 62(2 SUPPL.):88–99. https://doi.org/10.4269/ajtmh.2000.62.88 PMID: 10813505

47. Mueller A, Fuss A, Ziegler U, Kaatano GM, Mazigo HD. Intestinal schistosomiasis of Ijinga Island, north-western Tanzania: prevalence, intensity of infection, hepatosplenic morbidities and their associated factors. BMC Infectious Diseases. 2019; 19(1):832. https://doi.org/10.1186/s12879-019-4451-z PMID: 31590657

48. Mnkugwe RH, Minzi OS, Kinung'hi SM, Kamuhabwa AA, Aklillu E. Prevalence and correlates of intestinal schistosomiasis infection among school-aged children in North-Western Tanzania. PLoS One. 2020; 15(2):e0228770. https://doi.org/10.1371/journal.pone.0228770 PMID: 32023307

49. Sacolo-Gwebu H, Chimbari M, Kalinda C. Prevalence and risk factors of schistosomiasis and soil-transmitted helminthiases among preschool aged children (1–5 years) in rural KwaZulu-Natal, South Africa: a cross-sectional study. Infectious Diseases of Poverty. 2019; 8(1):47. https://doi.org/10.1186/s40249-019-0561-5 PMID: 31202273

50. Senghor B, Diallo A, Sylla SN, Doucoure S, Ndiath MO, Gaayeb L, et al. Prevalence and intensity of urinary schistosomiasis among school children in the district of Niakhar, region of Fatick, Senegal. Parasites and Vectors. 2014; 7(1):5. https://doi.org/10.1186/1756-3305-7-5 PMID: 24387599

51. Simoonga C, Kazembe LN. Using the hierarchical ordinal regression model to analyse the intensity of urinary schistosomiasis infection in school children in Lusaka Province, Zambia. Infectious diseases of poverty. 2017; 6(1):43. https://doi.org/10.1186/s40249-017-0262-x PMID: 28219411

52. John R, Ezekiel M, Philbert C, Andrew A. Schistosomiasis transmission at high altitude crater lakes in western Uganda. BMC Infectious Diseases. 2008; 8:110. https://doi.org/10.1186/1471-2334-8-110 PMID: 18694485

53. Kabatereine NB, Brooker S, Tukahebwa EM, Kazibwe F, Onapa AW. Epidemiology and geography of Schistosoma mansoni in Uganda: implications for planning control. Tropical Medicine & International Health. 2004; 9(3):372–80.

54. Stensgaard A, Jorgensen A, Kabatareine N, Malone J, Kristensen T. Modeling the distribution of Schistosoma mansoni and host snails in Uganda using satellite sensor data and Geographical Information Systems. Parassitologia. 2005; 47(1):115. PMID: 16044680

55. Phillips AE, Gazzinelli-Guimaraes PH, Aurelio HO, Dhanani N, Ferro J, Nala R, et al. Urogenital schistosomiasis in Cabo Delgado, northern Mozambique: Baseline findings from the SCORE study. Parasites and Vectors. 2018; 11(1):30. https://doi.org/10.1186/s13071-017-2592-8 PMID: 29316983

56. Atalabi TE, Lawal U, Akinluyi FO. Urogenital schistosomiasis and associated determinant factors among senior high school students in the Dutsin-Ma and Safana Local Government Areas of Katsina State, Nigeria. Infectious Diseases of Poverty. 2016; 5(1):69. https://doi.org/10.1186/s40249-016-0158-1 PMID: 27480058

57. Okoli EI, Odaibo AB. Urinary schistosomiasis among schoolchildren in Ibadan, an urban community in south-western Nigeria. Tropical Medicine and International Health. 1999; 4(4):308–15. https://doi.org/10.1046/j.1365-3156.1999.00388.x PMID: 10320657

58. Amuta EU, Houmsou RS. Prevalence, intensity of infection and risk factors of urinary schistosomiasis in pre-school and school aged children in Guma Local Government Area, Nigeria. Asian Pacific Journal of Tropical Medicine. 2014; 7(1):34–9. https://doi.org/10.1016/S1995-7645(13)60188-1 PMID: 24418080

59. Ivoke N, Ivoke ON, Nwani CD, Ekeh FN, Asogwa CN, Atama CI, et al. Prevalence and transmission dynamics of Schistosoma haematobium infection in a rural community of southwestern Ebonyi State, Nigeria. Tropical biomedicine. 2014; 31(1):77–88. PMID: 24862047

60. Nwabueze AA, Opara KN. Outbreak of urinary schistosomiasis among school children in riverine communities of Delta State, Nigeria: Impact of road and bridge construction. Journal of Medical Sciences. 2007; 7(4):572–8.

61. Senghor B, Diaw OT, Doucoure S, Sylla SN, Seye M, Talla I, et al. Efficacy of praziquantel against urinary schistosomiasis and reinfection in Senegalese school children where there is a single well-defined transmission period. Parasites and Vectors. 2015; 8(1):362. https://doi.org/10.1186/s13071-015-0980-5 PMID: 26156522

62. Joseph SO, Abdulkareem BO, Samuel UU. Distribution pattern of human urinary schistosomiasis in Kwara State, Nigeria. American Journal of Infectious Diseases. 2017; 13(4):38–44.

63. Barbosa LM, Silva LK, Reis EA, Azevedo TM, Costa JM, Blank WA, et al. Characteristics of the human host have little influence on which local Schistosoma mansoni populations are acquired. PLoS Neglected Tropical Diseases. 2013; 7(12):e2572. https://doi.org/10.1371/journal.pntd.0002572 PMID: 24340115

64. Afifi A, Ahmed AA, Sulieman Y, Pengsakul T. Epidemiology of Schistosomiasis among Villagers of the New Halfa Agricultural Scheme, Sudan. Iran J Parasitol. 2016; 11(1):110–5. PMID: 27095977

65. De Clercq D, Vercruysse J, Picquet M, Shaw DJ, Diop M, Ly A, et al. The epidemiology of a recent focus of mixed Schistosoma haematobium and Schistosoma mansoni infections around the 'Lac de Guiers' in the Senegal River Basin, Senegal. Tropical Medicine and International Health. 1999; 4(8):544–50. https://doi.org/10.1046/j.1365-3156.1999.00444.x PMID: 10499077

66. Saathoff E, Olsen A, Magnussen P, Becker W, Appleton CC. Patterns of Schistosoma haematobium infection, impact of praziquantel treatment and re-infection after treatment in a cohort of schoolchildren from rural KwaZulu-Natal/South Africa. BMC Infectious Diseases. 2004; 4:40. https://doi.org/10.1186/1471-2334-4-40 PMID: 15471549

67. Toure S, Zhang Y, Bosque-Oliva E, Ky C, Ouedraogo A, Koukounari A, et al. Two-year impact of single praziquantel treatment on infection in the national control programme on schistosomiasis in Burkina Faso. Bulletin of the World Health Organization. 2008; 86(10):780–7. https://doi.org/10.2471/blt.07.048694 PMID: 18949215

68. Kinung'hi S, Magnussen P, Kaatano G, Olsen A. Infection with Schistosoma mansoni has an effect on quality of life, but not on physical fitness in schoolchildren in Mwanza region, north-western Tanzania: a

cross-sectional study. PLoS neglected tropical diseases. 2016; 10(12):e0005257. https://doi.org/10.1371/journal.pntd.0005257 PMID: 28027317

69. Bah YM, Paye J, Bah MS, Conteh A, Saffa S, Tia A, et al. Schistosomiasis in School Age Children in Sierra Leone After 6 Years of Mass Drug Administration With Praziquantel. Frontiers in public health. 2019; 7:1. https://doi.org/10.3389/fpubh.2019.00001 PMID: 30809516

70. Chisango TJ, Ndlovu B, Vengesai A, Nhidza AF, Sibanda EP, Zhou D, et al. Benefits of annual chemotherapeutic control of schistosomiasis on the development of protective immunity. BMC Infectious Diseases. 2019; 19(1). https://doi.org/10.1186/s12879-019-3811-z PMID: 30832614

71. King CH, Lombardi G, Lombardi C, Greenblatt R, Hodder S, Kinyanjui H, et al. Chemotherapy-based control of schistosomiasis haematobia. I. Metrifonate versus praziquantel in control of intensity and prevalence of infection. American Journal of Tropical Medicine and Hygiene. 1988; 39(3):295–305.

72. N'Goran EK, Gnaka HN, Tanner M, Utzinger J. Efficacy and side-effects of two praziquantel treatments against Schistosoma haematobium infection, among schoolchildren from Cote d'Ivoire. Annals of Tropical Medicine and Parasitology. 2003; 97(1):37–51. https://doi.org/10.1179/000349803125002553 PMID: 12662421

73. Ismail HA, Hong ST, Babiker AT, Hassan RM, Sulaiman MA, Jeong HG, et al. Prevalence, risk factors, and clinical manifestations of schistosomiasis among school children in the White Nile River basin, Sudan. Parasites & vectors. 2014; 7:478.

74. Erko B, Degarege A, Tadesse K, Mathiwos A, Legesse M. Efficacy and side effects of praziquantel in the treatment of Schistosomiasis mansoni in schoolchildren in Shesha Kekele Elementary School, Wondo Genet, Southern Ethiopia. Asian Pacific Journal of Tropical Biomedicine. 2012; 2(3):235–9. https://doi.org/10.1016/S2221-1691(12)60049-5 PMID: 23569905

75. Birre H, Abebe F, Gundersen SG, Medhin G, Berhe N, Gemetchu T. Epidemiology of Schistosomiasis mansoni in three endemic communities in north-east Ethiopia: Baseline characteristics before endod based intervention. Ethiopian Medical Journal. 1998; 36(2):101–11. PMID: 10214452

76. Russell HJ, Penney JMS, Linder C, Joekes EC, Bustinduy AL, Stothard JR, et al. A cross-sectional study of periportal fibrosis and Schistosoma mansoni infection among school-aged children in a hard-to-reach area of Madagascar. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2020.

77. Sulieman Y, Eltayeb RE, Pengsakul T, Afifi A, Zakaria MA. Epidemiology of urinary schistosomiasis among school children in the Alsaial Alsagair village, River Nile State, Sudan. Iranian journal of parasitology. 2017; 12(2):284. PMID: 28761490

78. Sow S, de Vlas SJ, Stelma F, Vereecken K, Gryseels B, Polman K. The contribution of water contact behavior to the high Schistosoma mansoni Infection rates observed in the Senegal River Basin. BMC infectious diseases. 2011; 11(1):1–11. https://doi.org/10.1186/1471-2334-11-198 PMID: 21767372

79. Randjelovic A, Frønæs S, Munsami M, Kvalsvig J, Zulu S, Gagai S, et al. A study of hurdles in mass treatment of schistosomiasis in KwaZulu-Natal, South Africa. South African Family Practice. 2015; 57(2):57–61.

80. Rilkoff H, Tukahebwa EM, Fleming FM, Leslie J, Cole DC. Exploring gender dimensions of treatment programmes for neglected tropical diseases in Uganda. PLoS Negl Trop Dis. 2013; 7(7):e2312. https://doi.org/10.1371/journal.pntd.0002312 PMID: 23875047

81. King CH, Keating CE, Muruka JF, Ouma JH, Houser H, Arap Siongok TK, et al. Urinary tract morbidity in schistosomiasis haematobia: Associations with age and intensity of infection in an endemic area of Coast Province, Kenya. American Journal of Tropical Medicine and Hygiene. 1988; 39(4):361–8.

82. Ekanem EE, Akapan FM, Eyong ME. Urinary schistosomiasis in school children of a southern nigerian community 8 years after the provision of potable water. The Nigerian postgraduate medical journal. 2017; 24(4):201–4. https://doi.org/10.4103/npmj.npmj_136_17 PMID: 29355157

83. Opara KN, Udoidung NI, Ukpong IG. Genitourinary schistosomiasis among pre-primary schoolchildren in a rural community within the Cross River Basin, Nigeria. Journal of Helminthology. 2007; 81(4):393–7. https://doi.org/10.1017/S0022149X07853521 PMID: 18005467

84. Elias E, Daffalla A, Lassen JM, Madsen H, Christensen NO. Schistosoma haematobium infection patterns in the Rahad Irrigation Scheme, Sudan. Acta Tropica. 1994; 58(2):115–25. https://doi.org/10.1016/0001-706x(94)90051-5 PMID: 7887337

85. El-Hawey AM, Amr MM, Abdel-Rahman AH, El-Ibiary SA, Agina AM, Abdel-Hafez MA, et al. The epidemiology of schistosomiasis in Egypt: Gharbia Governorate. American Journal of Tropical Medicine and Hygiene. 2000; 62(2 SUPPL.):42–8. https://doi.org/10.4269/ajtmh.2000.62.42 PMID: 10813499

86. Mutengo MM, Mwansa JCL, Mduluza T, Sianongo S, Chipeta J. High Schistosoma mansoni Disease Burden in a Rural District of Western Zambia. American Journal of Tropical Medicine and Hygiene. 2014; 91(5):965–72.

87. Mohamed-Ali Q, Elwali NEMA, Abdelhameed AA, Mergani A, Rahoud S, Elagib KE, et al. Susceptibility to periportal (Symmers) fibrosis in human Schistosoma mansoni infections: Evidence that intensity and duration of infection, gender, and inherited factors are critical in disease progression. Journal of Infectious Diseases. 1999; 180(4):1298–306.

88. Woolhouse M, Taylor P, Matanhire D, Chandiwana S. Acquired immunity and epidemiology of Schistosoma haematobium. Nature. 1991; 351(6329):757–9. https://doi.org/10.1038/351757a0 PMID: 1905786

89. Guerrant RL, Walker DH, Weller PF. Tropical Infectious Diseases: Principles, Pathogens and Practice E-Book: Elsevier Health Sciences; 2011.

90. Oluwole AS, Adeniran AA, Mogaji HO, Olabinke DB, Abe EM, Bankole SO, et al. Prevalence, intensity and spatial co-distribution of schistosomiasis and soil transmitted helminths infections in Ogun state, Nigeria. Parasitology Open. 2018; 4:e8.

91. Sarda RK, Simonsen PE, Mahikwano LF. Urban transmission of urinary schistosomiasis in Dar es Salaam, Tanzania. Acta tropica. 1985; 42(1):71–8. PMID: 2859753

92. Nour NM. Schistosomiasis: health effects on women. Reviews in Obstetrics and Gynecology. 2010; 3 (1):28. PMID: 20508780

93. Clements AC, Barnett AG, Nyandindi U, Lwambo NJ, Kihamia CM, Blair L. Age and gender effects in self-reported urinary schistosomiasis in Tanzania. Tropical Medicine & International Health. 2008; 13 (5):713–21.

94. Wiegand RE, Secor WE, Fleming FM, French MD, King CH, Deol AK, et al. Associations between infection intensity categories and morbidity prevalence in school-age children are much stronger for Schistosoma haematobium than for S. mansoni. PLoS neglected tropical diseases. 2021; 15(5):e0009444. https://doi.org/10.1371/journal.pntd.0009444 PMID: 34033646

95. Marguerite M, Gallissot MC, Diagne M, Moreau C, Diakkhate MM, Roberts M, et al. Cellular immune responses of a Senegalese community recently exposed to Schistosoma mansoni: correlations of infection level with age and inflammatory cytokine production by soluble egg antigen-specific cells. Tropical Medicine & International Health. 1999; 4(8):530–43. https://doi.org/10.1046/j.1365-3156.1999.00443.x PMID: 10499076

96. Nakagawa S, Poulin R, Mengersen K, Reinhold K, Engqvist L, Lagisz M, et al. Meta-analysis of variation: ecological and evolutionary applications and beyond. Methods in Ecology and Evolution. 2015; 6 (2):143–52.

97. Diaz T, Strong KL, Cao B, Guthold R, Moran AC, Moller A-B, et al. A call for standardised age-disaggregated health data. The Lancet Healthy Longevity. 2021; 2(7):e436–e43. https://doi.org/10.1016/S2666-7568(21)00115-X PMID: 34240065