Schistosomes, snails and climate change: Current trends and future expectations

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\textbf{ABSTRACT}

The exact impact of climate change on schistosomiasis, a disease caused by a blood fluke that affects more than 250 million people mainly in tropical and subtropical countries, is currently unknown, but likely to vary with the snail-parasite species' specific ecologies and the spatio-temporal scale of investigation. Here, by means of a systematic review to identify studies reporting on impacts of climate change on the agents of schistosomiasis, we provide an updated synthesis of the current knowledge about the climate change-schistosomiasis relation. We found that, despite a recent increase in scientific studies that discuss the potential impact of climate change on schistosomiasis, only a handful of reports have applied modelling and predictive forecasting that provide a quantitative estimate of potential outcomes. The volume and type of evidence associated with climate change responses were found to be variable across geographical regions and snail-parasite taxonomic groups. Indeed, the strongest evidence stems from the People’s Republic of China pertaining to \textit{Schistosoma japonicum}. Some evidence is also available from eastern Africa, mainly for \textit{Schistosoma mansoni}. While studies focused on the northern and southern range margins for schistosomiasis indicate an increase in transmission range as the most likely outcome, there was less agreement about the direction of outcomes from the central and eastern parts of Africa. The current lack of consensus suggests that climate change is more likely to \textit{shift} than to \textit{expand} the geographic ranges of schistosomiasis. A comparison between the current geographical distributions and the thermo-physiological limitations of the two main African schistosome species (\textit{Schistosoma haematobium} and \textit{S. mansoni}) offered additional insights, and showed that both species already exist near their thermo-physiological niche boundaries. The African species both stand to move considerably out of their “thermal comfort zone” in a future, warmer Africa, but \textit{S. haematobium} in particular is likely to experience less favourable climatic temperatures. The consequences for schistosomiasis transmission will, to a large extent, depend on the parasites and snails ability to adapt or move. Based on the identified geographical trends and knowledge gaps about the climate change-schistosomiasis relation, we propose to align efforts to close the current knowledge gaps and focus on areas considered to be the most vulnerable to climate change.

1. Introduction

Shifts in patterns of precipitation, a rise in temperature and an increase in the frequency and severity of extreme climate events (e.g. droughts and flooding) are three major components of ongoing climate change (IPCC, 2013). Numerous studies have documented how climate change is already changing plant and animal species' distribution and phenology as they attempt to adapt or track their climatic optima (Walther et al., 2002). Climate change is also affecting many infectious disease agents, particularly those transmitted via an ectotherm or poikilotherm invertebrate vector or intermediate host, whose distribution and development are inextricably linked with climate (Campbell-Lendrum et al., 2015). Yet, determining the exact effects of climate change on specific human infectious diseases, despite a growing interest from the scientific community, has proven difficult and the debate about the potential health impacts remains polarized (Lafferty and Mordecai, 2016).

This is also the case for snail-borne schistosomiasis that affects more than 250 million people worldwide, particularly in countries of the tropics and subtropics (Hotez et al., 2014). Climate-induced shifts in

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phenology and geographical range of both schistosomes and intermediate host snails are likely to affect disease dynamics. Of prospective scenarios, snails and parasites could be introduced into currently non-endemic areas as environmental conditions become more suitable (Gautret et al., 2015). Hence, accurate predictions of these outcomes and their geographical location play an essential role in alerting health authorities to potential future risks, and have important implications for the feasibility of schistosomiasis control and elimination efforts. A sound knowledge of the functional relationship between the biology and ecology of the parasites, their intermediate hosts and the major climatic drivers is pivotal to build accurate models of climate change impact on schistosomiasis. However, the social-ecological context and multifactorial nature of schistosomiasis (Utzinger et al., 2011; McManus et al., 2018) make it difficult to detect climate-mediated changes, and it is currently unclear what the dominant outcome and net effect of climate change on schistosomiasis distribution and transmission will be.

Hence, there is a pressing need to review our current understanding of the potential effects of climate change, particularly global warming, on schistosomiasis and our capacity to predict future impacts. To this end, we systematically reviewed and summarised the principal findings of climate change-schistosomiasis research published in the peer-reviewed literature to date. Specifically, our review was motivated by asking the following questions. First, what is the current scientific consensus/evidence (if any) about the effect and direction of climate on schistosomiasis? Second, do outcomes vary across geographical location, modelling methods and parasite-snail species? Third, can we use our current understanding of the intra-specific variation in schistosome-snail species’ thermostolerances, ecology and climatic niches to inform our expectations about future scenarios for the main Schistosoma species affecting humans?

Our piece consists of two main parts: we begin by reviewing and summarising the principal findings and specificities of studies investigating the effect of climate change on the three main human Schistosoma species (i.e. Schistosoma haematobium, S. japonicum and S. mansoni) and their specific intermediate host snail species, to determine how many studies, and if any trends (taxonomically, geographically or methodologically) are prevalent. Then, focusing on the impacts of global warming, we synthesise experimental evidence about the effect of temperature on the performance of these schistosome species to look for differences in thermal tolerances, by identifying key points on each species thermal performance curves (Box 1). We compare these findings with empirical data on their geographical distribution and climatic niches to identify any differences that could provide new insights into schistosome species’ specific responses to the rising, global temperatures.

**Box 1: Generalized thermal performance curve of a hypothetical ectotherm.**

The relationship between environmental temperature and an organism’s performance (measured, for example, as fecundity, growth and metabolic rate) can be expressed as a thermal performance curve (TPC) (grey line). The optimum temperature ($T_{opt}$) specifies the temperature at maximum performance. The ecophysiological key characteristics, critical thermal minimum ($CT_{min}$) and maximum ($CT_{max}$), delimit an organism’s thermal tolerance. The shape and range of TPCs most likely vary between species of parasites and intermediate host snail species, and determine where climatic suitability for transmission and snail proliferation will increase or decrease with climate warming. The colored squares represent different climatic scenarios in a given location: red: prevailing/current climatic conditions that is suboptimal for the given species; yellow: warming scenario that give optimal conditions for the species in that geographical location, and green: warming scenario where temperatures become too hot.

2. **Methods**

2.1. **Search strategy and selection criteria**

We systematically reviewed the peer-reviewed literature to identify relevant publications pertaining to climate change and schistosomiasis. A systematic search of the extant literature on PubMed and Web of Science databases was conducted on all available published literature up to 31 December 2017 using the following search terms in various combinations and Boolean operators (OR, AND): Schistosom*, Bulinus, Biomphalaria, Oncomelania, Climat* change, warming. Identified articles were screened by reading through the titles and abstracts. In addition, reference lists of the identified articles were screened for any additional relevant studies for inclusion. Full text articles were retrieved and managed in EndNote reference manager version X7 (Clarivate Analytics; Philadelphia, PA, USA). Two reviewers (ASS and MES) independently examined the full text of publications included for qualitative review ($n = 103$) to extract information about the reported direction of climate change on schistosomiasis and intermediate host snails (i.e. overall positive, negative or uncertain/both directions possible).

2.2. **Comparison of geographical distributions, climatic variability and thermostolerances of the schistosome species**

In addition to reviewing climate change-schistosomiasis research with an emphasis on a potential impact of climate change, we also synthesised current knowledge about the thermo-physiological performance/tolerance of the three most important human schistosome species. We compared this information with empirical observations of schistosomiasis to look for any intraspecific differences between species that might impact future patterns (i.e. assess for any difference with regards to their sensitivity to warming), or explain discrepancies between the direction of impacts found in our literature review.

To do so, we downloaded geographically referenced point-based prevalence data for S. haematobium and S. mansoni from the Global Neglected Tropical Disease (GNTD) database (Hürlimann et al., 2011); restricting our search spatially to Africa. At present, more than 10,000 unique survey locations (mainly on S. mansoni and S. haematobium in Africa) are included in the GNTD database (www.gntd.org). For each survey point with at least 5% prevalence (chosen as the cut-off value to represent locations with endemic transmission), we extracted both current and future bioclimatic temperatures. All bioclimatic data were acquired from the Worldclim dataset (www.worldclim.org) (Hijmans et al., 2005). Future temperatures were based on downscaled climatic conditions for the time period 2070 (average 2061–2080) for RCP 8.5, readily obtained from the Coupled Model Intercomparison Project phase 5 (CMIP5), as presented by the Intergovernmental Panel on Climate Change (IPCC, 2013).
3. Trends in climate change-schistosomiasis research over two decades

Our systematic review identified 386 peer-reviewed publications. These were narrowed down to 183 relevant studies referring to climate change and schistosomiasis. Eighty of these studies were excluded, since they lacked any direction of the change. The remaining 103 studies were included in the qualitative review synthesis, while 20 of these studies were retained for the final review (Fig. 1).

The oldest published articles referring to the topic of climate change impacts on schistosomiasis were published in the early and mid-1990s. Subsequently, an exponential increase in articles pertaining to climate change and schistosomiasis occurred. In 2015 and 2016, there were 19 papers in each year focusing on climate change and schistosomiasis, while this number slightly decreased in 2017. About half of the published papers constitute original research articles, the rest being reviews, commentaries, editorials and the likes (Fig. 2).

Martens and colleagues were the first to apply a global modelling approach to the study of impact of climate change on schistosomiasis (Martens et al., 1995, 1997). In their first study, they linked global circulation model-based scenarios of climate change with a model of the relationship between climate variables (temperature and precipitation) and the parasite’s basic reproduction rate (R₀). They found that the world’s population at risk of schistosomiasis might increase by 0.7–3.3%, due to expanding ranges of schistosomiasis into higher latitudes (North and South) and higher altitudes. However, in a follow-up study published two years later, using a slightly different modelling approach, they concluded that schistosomiasis transmission potential is likely to decrease by 11–17% by 2050. Yet, they emphasised that transmission of schistosomiasis in countries in which, until recently, pockets of transmission occurred (e.g. Japan and southern European countries) are likely to increase, a scenario that came true with the outbreak of urogenital schistosomiasis in Corsica in 2015 (Boissier et al., 2015).

About a decade later, researchers from the People’s Republic of China put forth a series of publication pertaining to climate change and *S. japonicum* (Yang et al., 2005, 2006; Zhou et al., 2008). In a first study (Yang et al., 2005), it was shown that the historical isotherm (freezing line), considered to be the approximate northern limit of *S. japonicum* transmission in the People’s Republic of China, had shifted from 33°15’ N latitude to 33°41’ N, expanding the potential transmission area by 41,335 km², which corresponds to approximately the size of Switzerland. This translated to an additional 20.7 million people at risk of schistosomiasis in the People’s Republic of China. Subsequently, using a growing degree day (GDD) modelling approach, the authors hypothesised that the number of *S. japonicum* parasite generations, as measured by GDDs summed over a year (i.e. annual growing degree day, AGDD in short) would increase in the future by speeding up their development in longer growing seasons and extending the current area where both parasites and intermediate host snail can proliferate (Yang et al., 2006). GDD is a unit used to express the amount of heat energy an organism can accumulate, and AGDD is an important aggregate measure that has been found to correlate with the distributional patterns of many living organisms (Malone and Zukowski, 1992). The approach is based on the
assumption that a snail only develops when the environmental temperature is higher than a certain minimal threshold and that the thermal total energy required for development is constant (Malone et al., 2006). This was then confirmed by Zhou et al. in 2008, who forecasted an expansion of schistosomiasis transmission into currently non-endemic areas in the northern part of the People’s Republic of China, with an additional risk area of 783,883 km² by 2050 (Zhou et al., 2008).

The first decade in the new millennium saw an increased publication output, particularly with regard to reviews and commentaries, highlighting the sensitivity of infectious and vector-borne diseases in general. Referring to schistosomiasis (i.e. Sutherst, 2004; Kelly-Hope, 2008; Mas-Coma et al., 2008, 2009), many of them concluded that the most likely scenario of a future warmer world would be that of expanded schistosomiasis transmission.

Next, a suite of statistical modelling papers focusing on Africa emerged, initiated by Stensgaard and colleagues (2013). The authors combined GDD models for S. mansoni with snail habitat suitability models for several intermediate host snail species and showed that, overall, conditions for most of the S. mansoni intermediate host snails could decrease (by as much as 43% for Biomphalaria pfeifferi, the most important intermediate host snail for S. mansoni in Africa) under future climate change scenarios for the African continent. The study also highlighted the importance of accounting for other environmental factors relating to the snail habitats, such as environmental modifications, land use and water availability. Most studies published by then, in particular those applying dynamic, mathematical modelling, primarily employed temperature as the only driving factor (see, for example, Mangal et al., 2008) without accounting for other potential modifiers. Additionally, the studies lacked species specificity (Fig. 3 left), particularly with regard to intermediate host snails.

An overview of the identified 20 papers that apply quantitative analysis and/or modelling to predict a potential impact of climate change on schistosomiasis is given in Table 1.

3.1. Species trends: are some species more in focus than others?

Most human schistosomiasis cases are caused by infection with any one of the three species S. mansoni (Africa, Brazil and the Caribbean), S. haematobium (Africa and the Middle East) or S. japonicum (People’s Republic of China and The Philippines). Snails of the genera Biomphalaria, Bulinus and Oncomelania act as intermediate hosts for S. mansoni, S. haematobium and S. japonicum, respectively. Within each genus, there are several species of snails capable of acting as an intermediate host for schistosomes. For instance, there are as many as 12 suitable Biomphalaria host species for S. mansoni in Africa alone, and these different snail species all have different ecological requirements (Brown, 1994). Given their different habitat preferences, it is therefore not unlikely that these snails will be affected differently by changing climatic conditions. This was, for instance, evident from a study on climate change impacts on S. mansoni and intermediate host snails in Africa (Stensgaard et al., 2013), showing that the expected effects of climate change will lead to a reduction in suitable habitats for four out of five species of intermediate host snails for the parasite, as current living areas become too hot for the snails. This study underlined the importance of including biological knowledge of different intermediate host snail species in the models to gain a deeper insight of how rising temperatures might govern schistosomiasis transmission.

However, our review revealed that a considerable number of studies on the climate change-schistosomiasis nexus do not even differentiate between the parasite species, but merely refer to impacts on schistosomiasis (Fig. 3). Of the relatively few studies that do focus on specific species, there was an overweight of studies concerned with S. japonicum and its intermediate host snail species, Oncomelania hupensis. This observation is explained by the fact that most climate change-schistosomiasis studies thus far were conducted in the People’s Republic of China.
Table 1
Summary of published studies that assessed the effect of climate change on schistosomiasis between 1992 and 2017, using quantitative/analytical approaches to determine/back-up the concluded outcome.

<table>
<thead>
<tr>
<th>Study</th>
<th>Place</th>
<th>Parasite species</th>
<th>Snail species</th>
<th>Response type investigated</th>
<th>Main factors drivers/predictors</th>
<th>Method</th>
<th>Time period (model)</th>
<th>Results</th>
<th>Overall outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martens et al. (1995)</td>
<td>Global</td>
<td>Non-specific schistosome species</td>
<td>-</td>
<td>Geographical risk areas and number of people at risk</td>
<td>Temp + precip</td>
<td>Mathematical model</td>
<td>2050/2100 relative to 1990 (UKMOGCM &amp; ECHAM1-A-GCM)</td>
<td>Predicted extension of areas conducive to schistosomiasis transmission. Overall increase in populations at risk of schistosomiasis</td>
<td>-</td>
</tr>
<tr>
<td>Yang et al. (2005)</td>
<td>People's Republic of China</td>
<td>S. japonicum</td>
<td>O. hupensis</td>
<td>Geographical area suitable for snail and number of people at risk</td>
<td>Temp only</td>
<td>Trend analysis and kriging of temperature surfaces</td>
<td>1971-2000 relative to 1961–1990 (meteorological station data)</td>
<td>Predicted expansion of potential transmission area. Increase in number of people at risk</td>
<td>-</td>
</tr>
<tr>
<td>Yang et al. (2006)</td>
<td>People's Republic of China (Jiangsu province)</td>
<td>S. japonicum</td>
<td>O. hupensis</td>
<td>Change in AGDD</td>
<td>Temp only</td>
<td>Growing degree day model (GDD)</td>
<td>2006 relative to 2003</td>
<td>Predicted increase in AGDD</td>
<td>-</td>
</tr>
<tr>
<td>Zhou et al. (2008)</td>
<td>People's Republic of China</td>
<td>S. mansoni</td>
<td>O. hupensis</td>
<td>Potential transmission index (PTI)</td>
<td>Temp only</td>
<td>Growing degree day model (GDD)</td>
<td>2050 relative to 2000</td>
<td>Predicted expansion of schistosomiasis transmission area (north)</td>
<td>-</td>
</tr>
<tr>
<td>Mangal et al. (2008)</td>
<td>-</td>
<td>S. mansoni</td>
<td>Biomphalaria spp.</td>
<td>Non specific</td>
<td>Parasite prevalence and abundance</td>
<td>Temp only</td>
<td>Mathematical model</td>
<td>No specified time period</td>
<td>Observed altitudinal change in transmission risk areas (above 1400 m)</td>
</tr>
<tr>
<td>John et al. (2008)</td>
<td>Uganda</td>
<td>S. mansoni</td>
<td>-</td>
<td>Altitudinal transmission risk area</td>
<td>Hum (parasitological data) only</td>
<td>Epidemiological survey</td>
<td>2008 (compared to 1998-2002)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Stensgaard et al. (2013)</td>
<td>Sub-Saharan Africa</td>
<td>S. mansoni</td>
<td>(in B. pfeifferi)</td>
<td>Potential transmission index (PTI)</td>
<td>Temp + precip + env + hum</td>
<td>Hybrid (GDD + SDM model)</td>
<td>2070-2099 relative to 1950/1990 (HADCM3)</td>
<td>Predicted decrease in PTI with up to 19% overall</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B. pfeifferi</td>
<td>-</td>
<td>Range size/suitable snail habitat</td>
<td>Temp + precip + env + hum</td>
<td>SDM</td>
<td>2070-2099 relative to 1950/1990 (HADCM3)</td>
<td>Predicted decrease in suitable snail habitat with up to 43%</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B. sudanica</td>
<td>-</td>
<td>Range size/suitable snail habitat</td>
<td>Temp + precip + env + hum</td>
<td>SDM</td>
<td>2070-2099 relative to 1950/1990 (HADCM3)</td>
<td>Predicted increase in suitable snail habitat with up to 14%</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B. alexandrina</td>
<td>-</td>
<td>Range size/suitable snail habitat</td>
<td>Temp + precip + env + hum</td>
<td>SDM</td>
<td>2070-2099 relative to 1950/1990 (HADCM3)</td>
<td>Predicted decrease in suitable snail habitat with up to 15%</td>
<td>-</td>
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<tr>
<td></td>
<td></td>
<td>B. choanomphala</td>
<td>-</td>
<td>Range size/suitable snail habitat</td>
<td>Temp + precip + env + hum</td>
<td>SDM</td>
<td>2070-2099 relative to 1950/1990 (HADCM3)</td>
<td>Predicted decrease in suitable snail habitat with up to 45%</td>
<td>-</td>
</tr>
<tr>
<td>McCrcheon et al. (2014a)</td>
<td>Africa</td>
<td>S. mansoni</td>
<td>B. pfeifferi</td>
<td>Infection risk</td>
<td>Temp only</td>
<td>Mathematical model (agent-based)</td>
<td>No specified time period</td>
<td>Predicted potential increase in schistosomiasis risk in flowing water in cooler areas, but decrease in temperature in areas at/near the currents limits of schistosomiasis transmission</td>
<td>-</td>
</tr>
<tr>
<td>McCrcheon and Booth (2014b)</td>
<td>Africa</td>
<td>S. mansoni</td>
<td>B. glabrata</td>
<td>Infection risk</td>
<td>Temp only</td>
<td>Mathematical model (agent-based)</td>
<td>No specified time period</td>
<td>Infection risk may increase dramatically with small increases in temperature in areas at/near the currents limits of schistosomiasis transmission</td>
<td>-</td>
</tr>
<tr>
<td>Pedersen et al. (2014a)</td>
<td>Zimbabwe</td>
<td>-</td>
<td>Bu. globosus</td>
<td>Area of suitable snail habitat</td>
<td>Clim + env</td>
<td>SDM</td>
<td>2050 + 2100 vs present (HIRHAM RCM &amp; GCM)</td>
<td>Predicted reduction in area suitable for snail habitat</td>
<td>-</td>
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<tr>
<td>Pedersen et al. (2014b)</td>
<td>Zimbabwe</td>
<td>-</td>
<td>B. pfeifferi</td>
<td>Area of suitable snail habitat</td>
<td>Clim + env</td>
<td>SDM</td>
<td>2050 and 2100 vs present (HIRHAM RCM &amp; GCM?)</td>
<td>Predicted increase in areas of suitable habitat in 2055, but decline towards 2100</td>
<td>-</td>
</tr>
<tr>
<td>Pedersen et al. (2014b)</td>
<td>Zimbabwe</td>
<td>-</td>
<td>Bu. globosus</td>
<td>Area of suitable snail habitat</td>
<td>Clim + env</td>
<td>SDM</td>
<td>2012 relative to 1988</td>
<td>Predicted decrease in favourable</td>
<td>-</td>
</tr>
<tr>
<td>Pedersen et al. (2014b)</td>
<td>Zimbabwe</td>
<td>-</td>
<td>B. pfeifferi</td>
<td>Area of suitable snail habitat</td>
<td>Clim + env</td>
<td>SDM</td>
<td>2012 relative to 1988</td>
<td>Predicted decrease in favourable</td>
<td>-</td>
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<th>Time period (model)</th>
<th>Results</th>
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<tr>
<td>Stengsgaard et al. (2016)</td>
<td>Eastern Africa</td>
<td>S. mansoni</td>
<td>Bi. pfeifferi</td>
<td>Infection risk and snail habitat suitability</td>
<td>Temp + precip + env + hum</td>
<td>Hybrid (SDM + agent-based model)</td>
<td>2026-2035 &amp; 2056-2065 relative to baseline 2006-2015 (RCM: RCA4 &amp; AOGCM – EC-EARTH)</td>
<td>Predicted increase in overall risk areas in 63% of total area vs predicted decrease risk in 37% of the total area in eastern Africa</td>
</tr>
<tr>
<td>Pedersen et al. (2017)</td>
<td>Zimbabwe</td>
<td>S. mansoni</td>
<td></td>
<td>Overall prevalence</td>
<td>Temp + precip + env + hum</td>
<td>Geostatistical model</td>
<td>2010 relative to 1981</td>
<td>Observed decline in overall prevalence (9.4% in 1981 to 5.1% in 2010)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. haematobium</td>
<td></td>
<td>Overall prevalence</td>
<td>Temp + precip + env + hum</td>
<td>Geostatistical model</td>
<td>2010 relative to 1981</td>
<td>Observed decline in overall prevalence (41.5% in 1981 to 17.3% in 2010)</td>
</tr>
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<td>Casimiro et al. (2006)</td>
<td>Portugal</td>
<td>S. haematobium</td>
<td></td>
<td>Percentage of days/year within favourable temperature range for parasite survival</td>
<td>Temp only</td>
<td>Ecologic scenarios based on temperature thresholds</td>
<td>2040-2049 &amp; 2080-2100 (HadRM2 and PROMES)</td>
<td>Increased percentage of days/year within favourable temperature range for parasite survival</td>
</tr>
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<td></td>
<td></td>
<td>S. japonicum</td>
<td></td>
<td>Future potential transmission potential</td>
<td>Temp + precip</td>
<td>Estimated based on modelled future snail species distribution (above)</td>
<td>2050/2060 and 2080/2090</td>
<td>Predicted northwards expansion of transmission areas</td>
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<td>Stanton et al. (2017)</td>
<td>Uganda</td>
<td>S. mansoni</td>
<td>Biomphalaria spp.</td>
<td>Altitudinal transmission risk area</td>
<td>None</td>
<td>Empirical observations (parasitological and malacological surveys)</td>
<td>Present</td>
<td>Observed natural transmission of intestinal schistosomiasis</td>
</tr>
<tr>
<td>Poulin (2006)</td>
<td></td>
<td>Schistosoma spp.</td>
<td></td>
<td>Cercarial output</td>
<td>Temp only</td>
<td>Computed Q10 for cercarial production rates</td>
<td>No specific time-period</td>
<td>Predicted increase in cercarial output with increases in environmental temperatures</td>
</tr>
</tbody>
</table>

Abbreviations: Env, other environmental factors; GDD, growing degree day (model); Hum, human; Precip, precipitation; SDM, species distribution model; Temp, temperature.
The second most important set of studies pertained to climate change and its potential impact on S. mansoni, including the most important intermediate host snail species Bi. pfeifferi and Bi. glabrata with 35 out of 103 studies that conclude on the direction of impacts of climate change on schistosomiasis. The outcomes of these studies were distributed approximately equally among the categories “positive”, “negative” and “uncertain/both outcomes likely” scenarios. Far fewer studies dealt with S. haematobium, and in particular studies looking at potential impacts on Bulinus, are currently heavily underrepresented (Fig. 3). Indeed, only two out of 20 modelling studies (Table 1) have dealt with S. haematobium: the first from Portugal indicated an increased potential for S. haematobium under future climatic conditions in Europe (Casimiro et al., 2006). The second study was conducted in Zimbabwe, and observed a decline in urogenital schistosomiasis over the last three decades (41.5% in 1981; 17.3% in 2010), in a period with an increasingly drier and warmer climate (Pedersen et al., 2017).

Thus, if schistosomiasis is currently constrained in range at the northern range margin (i.e. People’s Republic of China and Europe) and southern range margin (i.e. southern Africa), also referred to as the leading edges of distribution, due to unfavourable climatic conditions (i.e. too cold), we would expect schistosomiasis to expand pole-ward in face of rising temperature. This is in accordance with the observed pattern of studies in Fig. 4, but also with a recent outbreak of urogenital schistosomiasis in Corsica (Boissier et al., 2015).

### 3.2. Geographical trends in climate change-schistosomiasis research and outcomes

As pointed out, most studies identified in the current review focussed on the People’s Republic of China, and hence, S. japonicum. These studies (n = 30, Fig. 4), consistently point to an increased risk of schistosomiasis with climate change. This, however, is not reflected in the current situation in the country, as the estimated number of people infected with S. japonicum decreased from more than 10 million in the mid-1950s to 1.52 million in the 1980s (Chen and Feng, 1999), a period that has experienced general global warming (IPCC, 2013). The decrease in schistosomiasis is attributed to a sustained, large-scale, multifaceted control programme carried out in endemic provinces (Zhou et al., 2007). This highlights the importance of accounting for human/societal factors in combination with environmental drivers when attempting to predict realistic outcomes of climate change impacts.

On the African continent, a total of 23 studies were identified, approximately equally divided with regards to the direction of the predicted outcome (positive, negative and uncertain). Breaking these studies down by region in Africa, revealed that particular studies from low-latitude countries/areas showed little consensus with regards to the direction of the predicted outcome of climate change on schistosomiasis, whereas the studies from i.e. South Africa point towards a negative outcome (increased risk with climate change) (Fig. 4).

3.3. Modelling trends in climate change-schistosomiasis research

Currently, two broad types of approach for predicting the impact of climate change on vector-borne diseases in general, and schistosomiasis in particular, can be distinguished. First, empirical-statistical (correlative) approaches that use statistical models of relationships between snail and/or parasite distribution and environmental factors. Second, process-based (mechanistic) approaches that seek to simulate detailed biophysical/epidemiological processes by explicitly incorporating associations between environmental conditions and organismal performance estimated independently of current distributions (Kearney and Porter, 2009; Dormann et al., 2012; Stensgaard et al., 2016). However, both approaches have strengths and limitations, and value in assessing the response of both parasite snail species to climate change (Purse and Golding, 2015; Stensgaard et al., 2016).
apply quantitatively modelling and/or prediction, a total of 20 studies on the impact of climate change of either schistosomiasis or intermediate host snail species remained. The main features, including the choice of modelling of these studies, are summarised in Table 1.

Of the modelling papers, 10 used a correlative modelling approach based on empirically observed data on snail and/or parasite current/historical distributions (hereof six studies that used a species distribution modelling (SDM) approach) and eight used a process-based modelling approach (i.e. temperature-driven mathematical or GDD model), while only three studies also used a combination/hybrid modelling approach (Table 1, Fig. 5).

The trend that emerges from Fig. 5 and Table 1 is a tendency for correlative modelling studies (typically applying species distribution models to intermediate host snail distributions) to predict negative outcomes (i.e. shrinking suitable snail habitats as in Stensgaard et al. (2013) and Pedersen et al. (2014a,b) more often than positive outcomes. The opposite seem to apply to the process-based models (i.e. temperature driven mathematical models such as in McCreesh et al. (2015).

SDMs are among the most widely applied modelling approach used in conservation biology. The approach benefits from straightforward pairing of distribution data with readily available climate data, but can have weak predictive power when projected to novel climates and give little insight into the causal mechanisms that underlie changes in species ranges (Dormann et al., 2012). Hence, there have been recent calls to improve this methodology (Fordham et al., 2013; Pacifici et al., 2015) and appeals to incorporate more physiology-based knowledge (i.e. species thermotolerances) as a means to increase the accuracy of SDMs (Buckley et al., 2011; Huey et al., 2012; Sunday et al., 2014).

On the other hand, mathematical models that have temperature as the only environmental driver, while able to capture the complex and non-linear relationship between the full spectrums of life cycle stages and temperature in great detail (i.e. McCreesh et al., 2015), run the risk of over-simplification. This can also explain the observed differences in outcomes between the models reviewed in the current study; by far the majority of the process-based studies reviewed focus primarily on ambient temperature as the main environmental explanatory factor, and thus fail to incorporate other important (climatic and non-climatic) environmental drivers that may impact and even limit the distribution of the intermediate host snails (e.g. land cover, soil properties and water availability). Ignoring rainfall and the absolute necessity of appropriate aquatic habitats for the intermediate host snails will arguably lead to unrealistic (overly “optimistic”) predictions about the ability of the parasite to establish itself in areas unsuitable for the survival and proliferation of the intermediate host snail species.

In the climate change-schistosomiasis field, only a few studies have attempted to take advantage of the full spectrum of models, i.e. in “hybrid modelling” (Stensgaard et al., 2013, 2016), that combine SDMs with physiology-driven mechanistic models. Studies using this modelling approach indicate that climate change seems more likely to shift than to expand the geographic ranges of schistosomiasis, compared with models at the extremes on the correlative-process model continuum (Fig. 5), which may be a more realistic scenario (Lafferty, 2009; Purse and Golding, 2015). In fact, Stensgaard et al. (2016) showed that combining a mathematical agent-based model of the temperature-sensitive stages of the S. mansoni and intermediate host snail lifecycles, with a snail species distribution model for eastern Africa, significantly improved model predictions for current conditions. The functional relationship between the biology of schistosomes, snails and temperature form a fundamental part of such process-based niche models.

4. Thermotolerances, geographical distributions and climatic niche space of the schistosome species

The physiological processes of the free-living and intra-molluscan stages of the schistosome parasites are highly sensitive to temperature, and upper/lower thermal thresholds (Box 1) determine their ability to remain active, infective and survive under extreme climatic conditions. Hence, detailed, species-specific information about the relationship between the biology of the various life cycle stages of the parasites and the different intermediate host snails and temperature is adamant to develop more accurate prediction models (i.e. McCreesh and Booth, 2013; Stensgaard et al., 2013; McCreesh et al., 2015). Furthermore, any differences in thermo-tolerances may hint at which Schistosoma-snail species that may stand to “lose or gain” in a warming world and may offer clarifying insights into the seemingly contradictory results from climate change-schistosomiasis studies from Africa especially. To this end, we here summarise experimental evidence about the effect of temperature on the performance of the main human schistosome species to highlight key points on each species’ thermal performance curves (Box 1).

4.1. Experimentally established effects of temperature on schistosome life history stages

In the schistosome life cycle there are several stages that are sensitive to temperatures in the environment, such as the miracidia and cercariae as these are free living stages, and will be exposed directly to ambient temperature changes. Furthermore, all intra-molluscan stages are sensitive to environmental temperatures, as the snail intermediate hosts are poikilotherms and their internal temperature therefore follows the environmental temperatures. Numerous experimental studies have been performed to investigate the effect of temperature on the different stages of the Schistosoma life cycle. Temperature can influence the performance of all the different stages of the Schistosoma life cycle: from the survival of the free-swimming miracidia larvae, the speed of development into mature cercariae inside the molluscan intermediate host, the number of released cercariae and the survival and infectivity of the free-swimming cercariae once shed from the snail. Finally, temperature influences the intermediate host snails’ growth, fecundity and survival, as recently reviewed and synthesised by Kalinda et al. (2017). However, one of the most important effects of temperature...
pertaining to intra-molluscan larval stages is the length of the so-called prepatent period, which is the time it takes from miracidia infection of the snail until cercarial shedding. The effect of temperature on the prepatent period has been investigated by experimental manipulation of the snail-parasite system by many researchers. In Table 2, we summarised some of the main findings of these studies for the three main human schistosome species, focusing on establishing the lower temperature threshold (MinDDT), optimum temperature (OptDDT) and maximum temperature/onset of slowdown of parasite development (MaxDDT) for intra-molluscan Schistosoma parasite development.

Gordon et al. (1934) for instance, infected Bi. pfefferi with S. mansoni at a range of temperatures from 14 °C to 37 °C, and found that increased temperatures up to 32–33 °C shortened the prepatent period to 15 days, from 31 to 35 days at 20–22 °C. However, a further increase of temperature to 34–35 °C was associated with a slowed development speed. Some of these results were further confirmed by Foster in 1964, and Pflüger in 1980 and 1981 (Foster, 1964; Pflüger, 1980, 1981). Moreover, Pflüger (1980) showed that the development speed peaks at 32–33 °C and starts to slow down at 34–35 °C for S. mansoni in Bi. glabrata. The effect of temperature on S. haematobium development shows the same pattern with shorter prepatent periods at higher temperatures. For S. haematobium in Bu. globosus, Gordon and colleagues reported that temperatures of 20–22 °C resulted in a prepatent period of 66–68 days, while considerably shorter durations (22–27 days) were observed at higher temperatures (34–35 °C) (Gordon et al., 1934). Pflüger et al. reported that the relationship between S. haematobium development speed and temperature was linear between 18 °C and 32 °C in Bu. truncatus (Pflüger et al., 1984). With a prepatent period of 106–113 days at 18 °C and 17–20 days at 32 °C, the results show that the overall prepatent period is longer for S. haematobium compared to S. mansoni. Furthermore, combining the results from Gordon et al. (1934) and Pflüger (1984), their data indicate that the development speed peaks around 32–33 °C for S. haematobium.

### 4.2. Link between thermophysiological limitations and geographical distribution of schistosome species in Africa

To compare the climatic niche space of the two main African schistosome species under current and future climatic conditions, we plotted the summarised, experimentally established thermo-physiological lower and upper thresholds of the individual species of schistosomes against bioclimatic temperature data extracted from georeferenced prevalence points with known endemic transmission of schistosomiasis (Fig. 6). We used the mean temperature of the warmest and coldest quarter (bioclim 10 and bioclim 11, respectively) to represent the maximum and minimum temperatures currently experienced by the schistosome species. Interestingly, we observe that under current temperature regimes, both species are very close to their upper thermal threshold for parasite development. S. haematobium, however, seem to occur in slightly warmer areas, and even somewhat above (according to the 95% ellipse). Since the parasites have quite similar physiological thermal performance values, the difference in their climatic epidemiology must be strongly related to differences in their intermediate host snails environmental tolerances and preferences.

Indeed, the emerging picture from Fig. 6 is well in accordance with observations that high temperatures may explain the absence of the main S. mansoni intermediate host snail species, Biomphalaria spp., from coastal East Africa and the consequent absence of S. mansoni transmission in the same areas (Sturrock, 1966). Similarly, high mortality of Bi. pfefferi in South Africa have been linked to periods of continuous high temperatures (Appleton, 1977). Other studies have shown that there can be great variability in how well the Bulinus intermediate host snails of S. haematobium can tolerate temperatures. The optimum temperature for growth and reproduction of Bu. truncatus and Bi. alexandrina has been found to be similar (at 26–28 °C), whereas both were considerably less heat tolerant than the competing snail species Helisoma daryi in laboratory investigations (El-Emam and Madsen, 1982).

The higher tolerance of Bulinus snails to high temperatures, and hence, the occurrence of S. haematobium in warmer areas than S. mansoni, could also be due to the general higher ability of Bulinus snails to aestivate (i.e. survive buried in the soil/mud) (Rubaba et al., 2016), highlighting another key parameter that needs to be taken into account: the behavioural ability of the snails to adapt, thus tolerating heat waves and other climate extremes.

As shown in Fig. 6, it is also evident that schistosomiasis transmission is currently taking place somewhere outside the lower thermo-threshold for parasite development. This is, however, not surprising as both snail survival and parasite development are possible at lower, fluctuating temperatures. For instance, with temperature fluctuations of ± 10 °C, S. mansoni can complete its life cycle even at very low (11.5 °C) or very high temperatures (40 °C) (Pflüger, 1981). The mapped temperatures (bioclim 10 and bioclim 11) depict averages over a 3-month period, and hence, do not capture these fluctuations.

The fact that S. haematobium under the current climate is already found so close to its thermal maximum (even slightly over), could also explain the result of Schur et al. (2013) that indicates a significant decrease in S. haematobium infection risk in Africa from the beginning of the 1990s onwards. The authors also note that in the 1950s and 1970s, higher prevalence of S. haematobium compared to S. mansoni was found in the Lango region of central-northern Uganda, while recent investigations in the same area only detected few S. haematobium cases, and that the underlying reasons for this decline is unresolved.

Also, as suggested by the right pane in Fig. 6, the two main schistosome species in Africa will experience temperatures over their MaxDDT under future global warming scenarios. This indicates that future climatic conditions for schistosomiasis might become less suitable with regard to maximum temperatures over large parts of Africa,

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**Table 2** Experimentally observed critical thermal thresholds for parasite intra-molluscan development for the three main species of human schistosomes.

<table>
<thead>
<tr>
<th>Parasite species</th>
<th>Development in molluscan host</th>
<th>MinDDT (°C)</th>
<th>OptDDT (°C)</th>
<th>MaxDDT (°C)</th>
<th>Thermal tolerance breadth (°C)</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bu. pfefferi</td>
<td>&lt; 16</td>
<td>32-33</td>
<td>&gt; 34–35</td>
<td>&gt; 19</td>
<td>Gordon et al. (1934), Foster (1964)</td>
</tr>
<tr>
<td>S. haematobium</td>
<td>Bu. truncatus</td>
<td>15.3</td>
<td>30-32</td>
<td>33</td>
<td>17.7</td>
<td>Pflüger et al. (1984)</td>
</tr>
<tr>
<td></td>
<td>Bu. globosus</td>
<td>15.5</td>
<td>31</td>
<td>&gt; 34–35</td>
<td>19.5</td>
<td>Gordon et al. (1934), Kalinda et al. (2017)</td>
</tr>
<tr>
<td>S. japonicum</td>
<td>O. hupensis</td>
<td>15.3</td>
<td>30</td>
<td>-</td>
<td>-</td>
<td>Yang et al. (2006)</td>
</tr>
</tbody>
</table>

* MinDDT, the minimum development temperature threshold for intra-molluscan parasite development (“developmental null point”).

* OptDDT, temperature where development speed peaks (shortest prepatent period).

* MaxDDT, temperature above which development is inhibited or starts to slow down significantly.
Fig. 6. Climatic (temperature) windows for *Schistosoma mansoni* and *Schistosoma haematobium* on the African continent. The mean temperature (°C) of the warmest quarter and the mean temperature (°C) of the coldest quarter are depicted for each coordinate with parasite presence for *S. mansoni* (orange) and *S. haematobium* (grey). The upper and lower physiological thermal thresholds for parasite development in the intermediate snails host (MDTTmax, horizontal dashed lines; MDTTmin, vertical dashed lines for each species) define the potential maximum thermotolerance range (as described in Table 2). Left: under current climatic conditions; right: under future climatic conditions (prediction for year 2070). Ellipses enclose 95% of the presence data for each parasite species.

particularly for *S. haematobium*. This could indicate that a mean higher impact of climate change on *S. haematobium* compared to *S. mansoni* in Africa. On the other hand, a smaller proportion of schistosomiasis transmission sites will be located in areas with temperatures below the MinDTT, but given the shape of the thermal performance curve (Box 1: note the sharp drop in performance after Topt), the exceedence of the MaxDDT could have a higher impact overall on schistosomiasis transmission.

5. Conclusions and outlook

Scrutinizing more than two decades of research at the climate change-schistosomiasis interface, we note the following: despite a gradual increase in scientific articles that show concern for a potential impact of climate change on schistosomiasis, there are only few original research papers, and even fewer that employ an advanced modelling approach to give a quantitative estimate of the observed or expected impacts. We found that most research efforts focused on the People’s Republic of China, despite the fact that schistosomiasis remains a much larger public health problem in Africa. Additionally, Africa is considered one of the most vulnerable continents to climate change and climate variability, which, coupled with a low adaptive capacity to deal with the negative impacts of climate change, further aggravates the situation (Preston et al., 2011; IPCC, 2013).

As such, we found that there is a mismatch between knowledge supply and need, and more emphasis should be directed towards understanding the implications of climate change on schistosomiasis in the most vulnerable regions. We also identified a bias with regards to the schistosome species studied: only few publications pertained to climate change and *S. haematobium* and its intermediate host snails (Fig. 3), and none using predictive modelling, despite the fact that it is precisely this species that currently is emerging in Europe (Boissier et al., 2015). One explanation could be a limited availability of studies on the effect of temperature on the development of various life cycle stages of *S. haematobium*, not least within the broad range of Bulinus intermediate host snails. Furthermore, there is little updated and synthesised data on the geographical distribution of Bulinus intermediate host snails in Africa, and close to none in Europe (Kincaid-Smith et al., 2017). This observation represents a considerable gap in our knowledge required to improve predictions of the effect of global warming on future distribution and transmission of urogenital schistosomiasis in particular.

Finally we note that a higher proportion of studies predict a decrease in schistosomiasis risk with climate change in the central and eastern parts of Africa, compared to studies located at higher latitudes, which in part can be explained by *S. mansoni* and *S. haematobium* being near/over their upper thermal threshold for parasite development (Fig. 6). We emphasise that the physiological differences in thermal relationships across snail and schistosome species need to be taken into account in future predictions of their geographical distribution and spread under the effects of global climate change.

An alternative, more holistic approach to the prevailing “single-species” climate change impact modelling approach, would be to fully embrace that all organisms are part of complex social-ecological systems and that the interconnectedness between species need to be accounted for, as recently advocated by the emerging field of ecohealth (Bergquist et al., 2017). The next generation of climate change impact assessment methods should thus ideally take into account the full complexity of schistosomiasis transmission dynamics, including the effects of the broader social-ecological contexts in which transmission occurs.

As a way forward, we suggest a combination and synthesis of statistical-empirical distribution modelling with process-based models of snail lifecycles and parasite development, underpinned by a solid knowledge of snail ecology, be further explored. Yet, a significant challenge to overcome before we can take full advantage of more complex modelling approaches is the scarcity of historical, long-term data-series on schistosomiasis and not least on the geographical distribution of the many species of schistosome intermediate host snails. While the first challenge is currently being dealt with through the construction of open-access databases such as the GNTD database initiative (Hürlimann et al., 2011), the latter is challenged by the cumbersome methods currently available to collect and identify snail species (Kincaid-Smith et al., 2017). Newly developed molecular tools,
such as environmental DNA (eDNA) holds promise to detect both intermediate host snails, parasites and even reservoir hosts at large spatial and temporal scales, which could prove very useful as inputs to climate change-schistosomiasis impact models (Bass et al., 2015).

5.1. Schistosomiasis in a warmer world: risk or opportunity?

The outstanding question then is what the net effect of climate change on schistosomiasis will be. There is little doubt that a changing climate will alter the availability of schistosomae parasite-snail niche space, and that this will vary according to the different ecologies of the many different intermediate host snail species of schistosomiasis. While research thus far indicate a mixed picture, with a potentially decreasing availability of climatic niche space, especially for *S. haematobium*, at lower latitudes in Africa, we see that this species has been able to resurface in colder climates, as witnessed by a recent outbreak of urogenital schistosomiasis in southern Europe. The establishment of transmission on Corsica was possible because suitable snail species already existed there, and due to the dispersion of the parasite with the increased movement of people from endemic areas in West Africa (Boissier et al., 2016). In conjunction with an increased window of transmission in which the parasite cercariae may be emitted by the snails as the potential transmission seasons get warmer and longer, this is expected to provide more optimal conditions for the parasite to establish and spread in Europe (Kincad-Smith et al., 2017).

Opposite to these effects, there could be a “beneficial” role for climate change since suitable areas for snail survival and parasite development, could be lost from large areas in West and Central Africa (Stensgaard et al., 2013). However, this could easily be offset by an increased creation of freshwater sites via dam construction and irrigation schemes, as dependency on irrigated agriculture grow and hydropower production with the predicted increases in dry spells in many parts of Africa with climate change, which have been known to create environments in which schistosomes and snails flourish and disease prevalence soared (Steinmann et al., 2000; Diakité et al., 2017). Whether or not climate change will work for or against the efforts to control and eventually eliminate schistosomiasis in 2025 thus remains an outstanding, but pressing question (WHO, 2012).

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