Acta Tropica 128 (2013) 423–440

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Time to set the agenda for schistosomiasis elimination

David Rollinson[a,*], Stefanie Knopp[b,c], Sarah Levitz[a], J. Russell Stothard[d], Louis-Albert Tchuem Tchuenté[e,f,g], Amadou Garba[b,c,h], Khalfan A. Mohammed[i], Nadine Schur[b,c], Bobbie Person[j], Daniel G. Colley[k], Jürg Utzinger[b,c]

[a] Wolfson Wellcome Biomedical Laboratories, Department of Zoology, Natural History Museum, Cromwell Road, London SW7 5BD, UK
[b] Department of Epidemiology and Public Health, Swiss Tropical and Public Health Institute, P.O. Box, CH–4002 Basel, Switzerland
[c] University of Basel, P.O. Box, CH-4003 Basel, Switzerland
[d] Centre for Tropical and Infectious Diseases, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, UK
[e] National Programme for the Control of Schistosomiasis and Intestinal Helminthiasis, Ministry of Public Health, Yaoundé, Cameroon
[f] Laboratory of Parasitology and Ecology, University of Yaoundé, Yaoundé, Cameroon
[g] Centre for Schistosomiasis and Parasitology, P.O. Box 7244, Yaoundé, Cameroon
[h] Programme National de Lutte Contre la Bilharziose et les Géohelminthes, Ministère de la Santé Publique et de la Lutte Contre les Endémies, Niamey, Niger
[i] Helminth Control Laboratory Unguja, Ministry of Health, P.O. Box 236, Zanzibar, Tanzania
[j] Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA 30333, USA
[k] Center for Tropical and Emerging Global Diseases and Department of Microbiology, University of Georgia, Athens, GA 30602, USA

ARTICLE INFO

Article history:
Available online 10 May 2012

This paper is dedicated to the memory of Dr Likezo Mubila who passed away on 4 August 2011. Likezo was a strong voice for the control of neglected tropical diseases in Africa. She was central to WHO African Region activities and a greatly respected friend and colleague of many involved in helminth control. A few days before her untimely death, Likezo made a great effort to attend and contribute to the launch of "Tokomeza Kichocho" (roughly translated as "Eliminate Schistosomiasis") on Pemba Island, Zanzibar.

Keywords:
Schistosomiasis
Schistosoma haematobium
Schistosoma japonicum
Schistosoma mansoni
Morbidity control
Transmission control
Elimination

ABSTRACT

It is time to raise global awareness to the possibility of schistosomiasis elimination and to support endemic countries in their quest to determine the most appropriate approaches to eliminate this persistent and debilitating disease. The main interventions for schistosomiasis control are reviewed, including preventive chemotherapy using praziquantel, snail control, sanitation, safe water supplies, and behaviour change strategies supported by information, education and communication (IEC) materials. Differences in the biology and transmission of the three main *Schistosoma* species (i.e. *Schistosoma haematobium*, *S. mansoni* and *S. japonicum*), which impact on control interventions, are considered. Sensitive diagnostic procedures to ensure adequate surveillance in areas attaining low endemicity are required. The importance of capacity building is highlighted. To achieve elimination, an intersectoral approach is necessary, with advocacy and action from local communities and the health community to foster cooperative ventures with engineers, the private sector, governments and non-governmental organizations specialized in water supply and sanitation. Examples of successful schistosomiasis control programmes are reviewed to highlight what has been learnt in terms of strategy for control and elimination. These include St. Lucia and other Caribbean islands, Brazil and Venezuela for *S. mansoni*; Saudi Arabia and Egypt for both *S. mansoni* and *S. haematobium*; Morocco, Tunisia, Algeria, Mauritius and the Islamic Republic of Iran for *S. haematobium*; Japan and the People's Republic of China for *S. japonicum*. Additional targets for elimination or even eradication could be the two minor human schistosome species *S. guineensis* and *S. intercalatum*, which have a restricted distribution in West and Central Africa. The examples show that elimination of schistosomiasis is an achievable and desirable goal requiring full integration of preventive chemotherapy with the tools of transmission control. An agenda for the elimination of schistosomiasis would aim to identify the gaps in knowledge, and define the tools, strategies and guidelines that will help national control programmes move towards elimination, including an internationally accepted mechanism that allows verification/confirmation of elimination.

1. Introduction

Cast an eye back to the Lancet in 1919 and you will find two authoritative articles, one by Hamilton Fairley and a second by Christopherson, accompanied by an optimistic editorial on the treatment and prevention of bilharziasis (schistosomiasis). Following the then recent discovery that the schistosome life-cycle involved freshwater molluscs, and with only antimonium tartaratum for treatment, the Lancet editorial put forth that "By a judicious campaign against mollusks especially in a country like Egypt where the water supplies are all under control, it is now quite within the bounds of possibility that the disease may be largely controlled, if not actually stamped out" (Annon., 1919).

* Corresponding author. Tel.: +44 207 942 5181.
E-mail address: d.rollinson@nhm.ac.uk (D. Rollinson).

0001-706X/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.actatropica.2012.04.013

Now move ahead more than 90 years and you will find in the sister journal Lancet Infectious Diseases that the discussion on schistosomiasis elimination continues. Strikingly different opinions are given by leading researchers and control experts in response to a personal view expressed by Gray et al. (2010), which advocates ideas on an integrated schistosomiasis control model and emphasizes the need to combine large-scale administration of praziquantel with molluscicide, environmental modification, health education and promotion, and improved sanitation to disrupt not only parasite transmission from the definitive mammalian host to the intermediate snail host but also *vice versa*. The authors also encourage the development and incorporation of anti-schistosome vaccines for acceleration of schistosomiasis elimination efforts.

In a response, Fenwick and Savioli (2011) drew attention to the use of praziquantel as the cornerstone of an effective public-health strategy and in the control of urogenital and intestinal schistosomiasis in several committed endemic countries. In defence of this approach they stated that "The suggestion of transmission control with molluscicides drags up obsolete approaches, which have been costly, polluting and ineffective in many countries. To suggest a vaccine will be of use is as far in the future as molluscicides are in the past". On the other hand, Zhang and Jiang (2011) responded positively in relation to successful projects in Japan and the People's Republic of China (P.R. China) "... control of snail populations seems the most effective way to interrupt schistosomiasis transmission cycles for a sustainable control strategy".

Faced with this surprising array of modern-day comment and opinion, one could simply ask what has been learnt over the last decades in terms of strategy for control and elimination of schistosomiasis? Moreover, given the available tools for treatment and monitoring of infection, together with the wealth of past experience, why does this debilitating neglected tropical disease (NTD) continue to persist as a parasitic infection of major public health importance (van der Werf et al., 2003; King et al., 2005; Utzinger et al., 2009)? The answers lie in the huge scale of the problem, the scant resources available for control and the complexity of the disease and its transmission that are governed by social–ecological systems (Utzinger et al., 2011). Shortage of praziquantel (the only presently available anti-schistosomal drug), lack of funds for implementation, monitoring and surveillance of interventions, and missing baseline data can place a huge burden on national NTD control programmes, which may not even exist in some endemic countries. Tough choices must be made concerning the allocation of available funds and the setting of disease control priorities.

Moreover, one has to keep in mind that while schistosomiasis is a useful collective term, it is actually a complex of acute and mainly chronic diseases caused by six *Schistosoma* species, namely *Schistosoma haematobium*, *S. guineensis*, *S. intercalatum*, *S. mansoni*, *S. japonicum* and *S. mekongi* (Davis, 2009). Disease and transmission control strategies may need to be adapted to combat the three major causes of infection in man by *S. haematobium*, *S. japonicum* and *S. mansoni* in specific settings. Fortunately, all three species are sensitive to praziquantel (Chen, 2005; Danso-Appiah et al., 2008; Liu et al., 2011), but key differences exist in transmission, disease pathology, occurrence of reservoir hosts, habitats of intermediate host snails and the age-pattern at which individuals are most likely to become infected and resolve their infections.

In this article we will review schistosomiasis control interventions and elimination efforts in endemic countries, taking into account the idiosyncrasies of the three main human *Schistosoma* species. We emphasize that elimination must be seen as the extreme end of the control spectrum, and is not a new goal by any means, but simply one that now needs greater attention and consideration. Indeed, 10 years ago, Engels et al. (2002) reported that the World Health Organization (WHO) advocated a dual strategy for the control of schistosomiasis: (i) a strategy for morbidity control adapted to the public health context in high-burden areas based on preventive chemotherapy using praziquantel (mainly in sub-Saharan Africa), and (ii) an integrated control strategy in areas where a low endemic level has been reached and elimination may be feasible.

Still today, most countries in sub-Saharan Africa endemic for schistosomiasis are not in a position to establish a country-wide elimination programme due to high prevalence rates and transmission potential. While elimination should be considered at the country or national level, there may be low prevalence areas within each country where elimination could be achieved given adequate resources and political commitment. In some countries, elimination of schistosomiasis is already the declared goal. Hence, although morbidity control is likely to remain the main strategy in most places, it is essential to ensure that adequate tools for transmission control and innovative surveillance-response mechanisms are in place wherever elimination is to be achieved. Lessons learnt from the successes and failures of past control and elimination programmes must not be ignored but rather used to help in guiding future interventions.

Most importantly, and taking our lead from the excellent example of the "Malaria Eradication Research Agenda" (malERA) initiative, published in a special issue of PLoS Medicine (Alonso et al., 2011), we feel that the time has come for the international community to set an agenda for schistosomiasis elimination, to develop strategies and tools that will drive forward this important endeavour on a global scale. In so doing, we will be better prepared to encourage global donors to go the 'extra mile' to ensure evidence-based endpoints are achieved. We believe it is time to strengthen the push towards schistosomiasis elimination and that much can be achieved by linking past experiences and available expertise from many different disciplines, such as biology, ecology, economy, epidemiology, environmental and sanitary engineering, geography, medicine, behaviour and the social sciences.

2. Know thine enemy

Schistosomiasis control and elimination are tasks of extraordinary magnitude. Estimates suggest that an alarming 201.5 million cases of schistosomiasis may occur in Africa alone and that over 90% of all schistosomiasis cases are found in sub-Saharan Africa (Steinmann et al., 2006; Utzinger et al., 2009). It is possible that even these numbers are conservative estimates of the true situation, as currently available diagnostic techniques are not sufficiently sensitive to detect light infections (King, 2010) and there is a paucity of georeferenced data for large parts of Africa (Schur et al., 2013).

Schistosomes are remarkable parasites and considerable foes in that they are exquisitely adapted to their two-host life cycle, which involves substantive population booms and crashes. They undergo a development that allows genetic recombination, prodigious egg laying and a long sheltered life of many years in the definitive mammalian host. Short periods of time in the molluscan intermediate host allow massive asexual multiplication to ensure transfer to new definitive hosts and the successful continuation of the life cycle. Adult worms are able to evade the immune response of the definitive host and the larval stages escape the defence reaction of molluscan hosts. The lack of an appropriate immunological response to infection in children may allow continual re-infection even after treatment, the bane of preventive chemotherapy-based morbidity control programmes.

Importantly, interventions must be tailored to the different *Schistosoma* species, and hence take into account idiosyncrasies of the three main species. For example, some 40 domestic and wild

Box 1: Definition of key terms used in this manuscript, adapted from Dowdle (1998) and Molyneux et al. (2004)

Control: Reduction of schistosomiasis incidence, prevalence and intensity of *Schistosoma* infection, morbidity or mortality to an acceptable level as a result of deliberate efforts (e.g. preventive chemotherapy). Continued intervention measures are required to maintain the reduction.

Elimination as a public health problem: Reduction in the prevalence of *Schistosoma* infection below a certain pre-set threshold (e.g. less than 1% heavy infections) based upon direct egg-detection methods in the school-aged population. Continued intervention measures are required to prevent resurgence of transmission.

Elimination: Reduction to zero of the incidence of *Schistosoma* infection in a defined geographical area as a result of deliberate efforts. Active surveillance and response measures are required to prevent re-establishment of transmission through sporadic or introduced cases.

Eradication: Permanent reduction to zero of the global incidence of human infections with *Schistosoma* species as a result of deliberate efforts. Neither surveillance nor intervention measures are any longer required.

animal species (most important are water buffaloes) may act as reservoir hosts of *S. japonicum* and indeed contribute to over 80% of transmission (Wang et al., 2005), which adds an extra layer of complexity regarding control, let alone elimination. On the other hand, it offers an additional entry point for control, such as mechanizing of agriculture, fencing of water buffaloes and vaccination (Wang et al., 2009a,b; McManus et al., 2009, 2010).

Throughout their long evolutionary history, schistosomes have withstood the selection pressures imposed by the vagaries of climate and environmental changes and numerous fluctuations and perturbations in the population size of their snail and definitive mammalian hosts, including man. In modern times, many changes in human social development have unwittingly favoured the parasite and increased the chances of infection and the prevalence of disease. The creation of freshwater sites via dam construction and irrigation, the close contact of human settlements to freshwater, close living with potential reservoir hosts, large increases in the size and density of human populations, coupled with greater dependency on irrigated agriculture, have created environments in which schistosomes have truly flourished and disease prevalence has soared (Southgate, 1997; Jobin, 1999; Steinmann et al., 2006; Rollinson, 2009). Hence, we need to be well aware that control interventions must exert strong and additional selection pressures if these well-adapted and resilient parasites are to be eliminated.

3. Towards schistosomiasis elimination endpoints

For the purposes of this article, key terms, such as control, elimination and eradication, have been defined and they are summarized in Box 1.

The ultimate goal of all schistosomiasis intervention efforts should be the elimination of this infection, whilst maintaining a rich and diverse environment to provide essential ecosystem services (Stothard et al., 2009a). Elimination has in fact been achieved in certain epidemiological settings and control programmes in many endemic areas are now in the position to work towards elimination after they have successfully reduced morbidity caused by schistosome infections. The countries at the fringe of endemic areas, or those experiencing high socio-economic development, are more likely to achieve elimination (Fenwick et al., 2006). The consideration of local socio-cultural, economic and political factors is essential for the success of elimination programmes, as these factors will influence the application and acceptance of intervention strategies (Aagaard-Hansen et al., 2009). In sub-Saharan Africa in particular, socio-economic development is slow, and may be impeded by the political instability that arises at national levels (Fenwick et al., 2009; Stothard et al., 2009a; Bonfoh et al., 2011).

While eradication of the three major schistosome infections is many years away, those that might become the first targets for eradication in the foreseeable future are *S. guineensis* and *S. intercalatum*, two closely related parasite species in West and Central Africa with limited distributions (Pagès et al., 2003). Despite the extremely wide distribution of their intermediate snail hosts, i.e. *B. forskalii* for *S. guineensis* and *Bulinus globosus* for *S. intercalatum*, the latter schistosome species is known to be present only in the Democratic Republic of the Congo, whereas the former species occurs in Cameroon, Gabon, Equatorial Guinea, Nigeria and São Tomé and Principe. In the 1960s and 1970s, there were sporadic reports of *S. guineensis* infections from other countries such as Angola, Burkina Faso, Central African Republic, Chad, Congo, Mali, Senegal and Uganda but without subsequent confirmation of active transmission foci, which suggests either that the parasite has disappeared from these countries or infections were incorrectly diagnosed (Tchuem Tchuenté et al., 2003). Studies in Cameroon showed high dynamic changes in the epidemiology of *S. guineensis*, which is currently a species in decline. Noteworthy, in some areas of Cameroon, *S. guineensis* has now been eliminated, e.g. the town of Loum in the Littoral region (Tchuem Tchuenté et al., 1997) and the village of Kinding Ndjabi in the Centre region of Cameroon (Tchuem Tchuenté et al., 2001). Furthermore, a significant decrease of *S. guineensis* transmission was observed from several other previous foci (Tchuem Tchuenté et al., 2003, 2012). This overall decrease or cessation of *S. guineensis* transmission in Cameroon strongly suggests the feasibility of its local elimination and supports the idea that this species could be a target for eradication in the near future.

Morbidity control through preventive chemotherapy (i.e. the periodic use of anthelminthic drugs as a public health tool against helminth infections) will remain the main task for most countries in sub-Saharan Africa. To put this into some form of perspective, the World Health Assembly (WHA) resolution 54.19, adopted in mid-2001, encouraged their endemic member states to annually deworm at least 75% of school-aged children who are at-risk of morbidity due to schistosome and soil-transmitted helminth infections. Since then, progress has been made in scaling up schistosomiasis treatment, principally enabled by the Schistosomiasis Control Initiative (SCI), the United States Agency for International Development (USAID) and most recently by the Department for International Development (DFID), UK. Other recent inputs in the fight against schistosomiasis include the distribution of praziquantel donated by Merck Serono, which was initiated by WHO in 2008. In 2009, WHO received reports on treatments from 21 out of the 76 (27.6%) endemic countries, where a total of 19.6 million people were treated, representing a 7.8% increase above the number of people treated in 2008 (WHO, 2011). While this is an encouraging trend, the number of people treated in 2009 was only 8.2% of the estimated number of people infected with schistosomes. Moreover, in the framework of preventive chemotherapy through control programmes, people who may have not been infected will have received treatment. Sadly, due to the current shortage of praziquantel (see http://www.who.int/neglected_diseases/) and funding, many endemic countries do not have sufficient drugs available or may lack the capacity to deliver the drug to those in need, and in many high transmission environments treatment of schistosomiasis in preschool-aged children is still overlooked (Hotez et al., 2010).

4. Interventions

The lifecycle of *Schistosoma* is such that there are four main targets for interventions: (i) kill the adult worms in man, which is currently achieved through praziquantel-based chemotherapy; (ii) kill or replace the snail intermediate hosts by means of biological control (e.g. competitor snails and snail-eating fish), chemical control (i.e. molluscicide) and environmental management; (iii) prevent the snails from getting infected, hence preventing contamination of the water by infected individuals, using information, education and communication (IEC), sanitation and behaviour change; and (iv) stop humans from getting infected, by preventing contact with water containing infected snails or cercariae (achieved through IEC and safe water supplies).

Simple control measures can ameliorate the schistosomiasis burden in high prevalence areas, and can be implemented in all circumstances (WHO, 2002). The following control strategies are recommended in a recent WHO report: preventive chemotherapy, intensified case management, vector control, and provision of safe water, sanitation and hygiene (WHO, 2010).

4.1. Preventive chemotherapy

Praziquantel is the sole drug for treatment and morbidity control of schistosomiasis in sub-Saharan Africa (Fenwick et al., 2003; Doenhoff et al., 2009; Utzinger et al., 2011). Praziquantel is safe, cheap and effective against adult worms. Cure rates of up to 85–90% have been achieved, but complete cures (100%) have seldom, if ever, been recorded in endemic areas (Doenhoff et al., 2009; Olliaro et al., 2011).

The large-scale administration of praziquantel to school-aged children is the mainstay of current programmes focusing on morbidity control (Fenwick et al., 2009). Preventive chemotherapy administered via the school route has a big impact on helminth infections as it targets those at highest risk, and takes advantage of the educational infrastructure and resources already in place (Miguel and Kremer, 2004). The disadvantages of this delivery strategy are that there are inherent age and sex inequalities in children attending school, and that as many as 40% of children in sub-Saharan Africa may not be enrolled in school. Table 1 summarizes country-wide *Schistosoma* prevalence estimates for mid-2003 and 2010, the number of people (mainly school-aged children) treated through control programmes and health facilities in 2010 and the national treatment coverage achieved.

Treatment coverage is an important factor determining the effectiveness of control programmes emphasizing preventive chemotherapy. Coverage can be improved by IEC campaigns, mobilization and community participation (Smits, 2009). For example, Tallo et al. (2008) investigated the effects of community-wide treatment in the Philippines and found that participation in treatment campaigns is determined by individual factors, such as age, gender and knowledge. The authors emphasize that active community involvement including contributions from local authorities and villagers, health education in schools, community-based education, preparation and possibly incentives, are necessary to increase participation and coverage.

A problem of treatment adherence may arise as people may alternate between, or combine, treatments obtained through formal healthcare providers and informal sources, such as traditional herbalists. This is a function of the level of knowledge or education of the patients, their knowledge of infection status, logistics of transport, and their anticipation of the quality and benefits of treatment (Aagaard-Hansen et al., 2009). A more fundamental challenge that needs to be addressed at the individual and community level is an understanding, especially in relatively low prevalence areas, that there is a problem, i.e. that schistosomiasis exists in the community and is a health problem. In many settings, especially in regard to *S. mansoni* infection, the level of the health problem is not appreciated by those who are infected or those around them. Very often, people appreciate that they feel better upon treatment, but did not realize prior to treatment that they were ill.

Even if full coverage was possible, chemotherapy will reduce pathology, but may not adequately reduce transmission without additional control measures (Lardans and Dissous, 1998; Urbani et al., 2002). A single round of treatment in a highly endemic area can result in an extended period of low transmission, but prevalence may increase after initial successes (Smits, 2009). In some endemic areas, once preventive chemotherapy is ceased, prevalence can return to baseline levels within 18 months to 2 years (Gray et al., 2010).

King (2009) refers to large-scale treatment campaigns as a "stop-gap measure". Praziquantel does not prevent reinfection; hence control programmes based solely on morbidity control will be neither completely effective nor sustainable. Moreover, some people infected with immature worms will be receiving the drugs, but will not have parasite clearance, as praziquantel is not effective against schistosomula older than two days (Sabah et al., 1986). Therefore it is particularly important that treatment campaigns are timed appropriately, i.e. in the low transmission season in areas where transmission is seasonal (el Malatawy et al., 1992; Augusto et al., 2009), and that the frequency of treatment is in line with WHO recommendations according to infection prevalence and intensity (WHO, 2006). Retreating people with praziquantel 2–8 weeks after the first dose can increase cure and egg reduction rates in infected populations and thus add a benefit to the health and quality of life of people (King et al., 2011). However, another confounding factor impeding the success of preventive chemotherapy are so-called "super spreaders": people who are heavily infected, unreceptive to health education messages, who do not comply with treatment, and who contaminate water bodies continually, therefore perpetuating transmission, even in an area of high treatment compliance.

Environmental, cultural and social determinants of health are all important in schistosomiasis transmission. Although large-scale distribution of praziquantel has achieved significant reductions in the global health burden of the disease and significantly reduced egg excretion in some areas (Barakat et al., 1995; Zhang et al., 2007; Touré et al., 2008), it has failed to break the transmission cycle in other highly endemic communities (Curtale et al., 2010). Without modification of transmission factors, the best that can be achieved with preventive chemotherapy alone is a low equilibrium of transmission and low level infection for an indefinite period of time; without changes in transmission potential, adequate schistosomiasis control will not be achieved, let alone eliminated (King et al., 2006). However, the example of *S. mekongi* in Cambodia demonstrates that 8 years of annual treatments with praziquantel with coverage between 62% and 86% had a dramatic impact on the disease prevalence with reduction to just three cases in 2005 and no cases of severe morbidity (Sinuon et al., 2007). However, sustained control efforts and rigorous surveillance are still required, particularly in view of remaining disease foci in neighbouring Lao PDR (Muth et al., 2010; Sayasone et al., 2011).

At present, WHO guidelines recommend to treat children once every second year when prevalence is moderate (between 10% and 50%); at low prevalence (<10%), the recommendation is to treat children twice during primary schooling, i.e. ideally upon entry and again before children leave school (WHO, 2002). However, the latter are the very settings where the goal of a control programme might be switched to elimination, in which case the need for targeted treatments will undoubtedly be greater. In that respect, we would like to raise the following three questions that a schistosomiasis elimination agenda might consider in relation to preventive chemotherapy.

Table 1
Schistosomiasis prevalence estimates (in mid-2003 and in 2010) and number of people treated in 2010, stratified by endemic country/territory.

Country	Total population (thousands) in 2010[a]	Estimated country prevalence (%) of schistosomiasis in mid-2003[b]	Control programme	Population infected in 2010[c]	Reported number of people treated in 2010[c]	National treatment coverage (%) in 2010[c]	Estimated country prevalence (%) of schistosomiasis in 2010
Africa							
Algeria	35423	7.7	–				<10*
Angola	18493	44.4	–	5317958			28.8
Benin	9872	35.5	MoH[d]; WHO[e]	3265981	364697	5.0	33.1
Botswana	1953	10.0		197757			10.1
Burkina Faso	16097	60.0	SCI[f]; USAID[g]	4886012	4702956	36.1	30.4
Burundi[h]	9553	13.3	SCI	1135848			11.9
Cameroon	19662	12.0	MoH; USAID	4531896	1048206	6.1	23.1
Cape Verde	567	0	–				Non-endemic
Central African Republic	4592	10.0	MoH; WHO	450595	222981	5.8	9.8
Chad	11715	22.5	–	4997975			42.7
Comoros	902	0	–				Non-endemic
Congo	4011	34.2	–	1286624			32.1
Côte d'Ivoire[i]	20375	40.0	MoH; SCI; WHO	8628298			42.4
Democratic Republic of the Congo	69010	28.2	–	19157807			27.8
Djibouti	877	<10.0	–				Non-endemic
Equatorial Guinea	545	2.0	–	13868			2.5
Eritrea	5323	7.2	–	377288			7.1
Ethiopia	89566	7.1	–	6026639			6.7
Gabon	1390	45.5	–	682394			49.1
Gambia	1845	30.0	–	525220			28.5
Ghana	24890	72.5	MoH; USAID; WHO	17644805	1739837	7.2	70.9
Guinea	10028	25.8	–	2659149			26.5
Guinea-Bissau	1853	30.0	–	494214			26.7
Kenya[h]	40645	23.0	MoH; WHO	9396937			23.1
Lesotho	2044	<10.0	–				Non-endemic
Liberia[h]	4311	24.0	SCI	984424			22.8
Madagascar	21299	55.0	MoH; WHO	11087896	834365	5.2	52.1
Malawi	15037	7.7	MoH; SCI; WHO	6725050	1682361	13.4	44.7
Mali	13506	60.0	SCI; USAID	3996931	4483715	42.1	29.6
Mauritania[h]	3363	27.4	MoH; WHO	921902			27.4
Mauritius	1291	0.9	–				<10*
Mozambique	22635	69.8	MoH; SCI; USAID; WHO	16326177	488359	2.6	72.1
Namibia	2157	0.6	–	13272			0.6
Niger	15791	26.7	MoH; SCI; USAID	2145350	2716775	21.4	13.6
Nigeria	158313	23.2	MoH; WHO	36728013	2297282	1.8	23.2
Rwanda[h]	10601	5.9	SCI	610209			5.8
São Tomé and Principe	165	3.8	–	6361			3.9
Senegal	13311	15.3	MoH; WHO	1966933	564684	5.5	14.8
Seychelles	88	0	–				Non-endemic
Sierra Leone	6185	59.5	MoH; USAID; WHO	3473610	1831383	35.6	56.2
Somalia	9486	18.0	–	1684548	8155	0.2	17.8
South Africa	49278	10.8	–	5475080			11.1
Sudan[k]	41230	14.9	Malaria Consortium[l]	7845817	3841	0.01	19.0
Swaziland	1160	25.6	–	307153			26.5
Togo	7122	26.7	MoH; USAID; WHO	1703276	750508	13.8	23.9
Uganda	34040	20.4	MoH; SCI; RTI[m]	5407434	2655421	9.8	15.9
United Republic of Tanzania	43542	51.5	MoH; SCI; IMA[n]	23189294	1298263	3.6	53.3
Western Sahara	530		–				Not indicated*
Zambia	12625	26.6	MoH; SCI; WHO	3520541	129390	1.2	27.9
Zimbabwe	13760	40.0	–	5057616			36.8

Table 1 (*Continued*)

Country	Total population (thousands) in 2010[a]	Estimated country prevalence (%) of schistosomiasis in mid-2003[b]	Control programme	Population infected in 2010[c]	Reported number of people treated in 2010[c]	National treatment coverage (%) in 2010[c]	Estimated country prevalence (%) of schistosomiasis in 2010
Asia							
Indonesia	239600	<0.1	–	241			<0.01
Thailand	65125	0	–				Non-endemic
Japan	127758	0	–				Non-endemic
Cambodia	15224	0.1	MoH	15053	76731	94.8	0.1
P.R. China	1351512	0.1	MoH	325824	2707865	100	0.02
Lao PDR	6173	<0.1	MoH	32180	58432	54.0	0.5
Malaysia	27920	0	–				Non-endemic
Philippines	93001	0.3	–	586811	530852	7.9	0.6
India	1220182		–				<10*
Pakistan	173351		–				<10*
Europe/Middle East							
Egypt	79537	<3.0	–	253423			0.3
Iraq	30688	0.1	–	37572			0.1
Islamic Republic of Iran	74276	Eliminated	–				Non-endemic
Jordan	6453	<0.1	–				Non-endemic
Lebanon	4227	Eliminated	–				Non-endemic
Libyan Arab Jamahiriya	6530	5.0	–	327281			5.0
Morocco	32381	Transmission interrupted	–				<10*
Oman	2767	<0.1	–	132	1355		<0.01
Saudi Arabia	26416	0.1	–	5249			0.02
Syrian Arab Republic	21428	<0.1	–				<10*
Tunisia	10664	Eliminated	–				Non-endemic
Turkey	77703	Eliminated	–				Non-endemic
Yemen	24475	14.6	SCI; World Bank	3535341	2124436	11.0	14.4
South America							
Antigua and Barbuda	88	0.1	–				Non-endemic
Brazil	198982	0.8	–	6839814	39868	0.1	3.4
Dominican Republic	10191	2.9	–	301521			3.0
Guadeloupe	454	1	–				<10*
Martinique	402	Eliminated	–				Non-endemic
Montserrat	6	Eliminated	–				Non-endemic
Puerto Rico	4056	0.1	–				<10*
St. Lucia	171	<0.1	–				<10*
Surinam	465	0.9	–	4732			1.0
Bolivarian Republic of Venezuela	29045	0.1	–	45238	1470	0.02	0.2

* Prevalence estimates derived from WHO (2011).

[a] Population estimates derived from http://esa.un.org/unup/ (accessed 8 December 2011).

[b] Prevalence estimates for situation in mid-2003 mainly derived from Steinmann et al. (2006).

[c] Numbers derived from PCT database: http://www.who.int/neglected_diseases/preventive_chemotherapy/sch/db/index.html?units=minimal&region=all&country=all&countries=all&year=2010 (accessed 8 December 2011).

[d] MoH, Ministry of Health.

[e] WHO, World Health Organization.

[f] SCI, Schistosomiasis Control Initiative.

[g] USAID, United States Agency for International Development.

[h] Schistosomiasis control programme implemented; however, no treatment data available at PCT database.

[i] Côte d'Ivoire: schistosomiasis control initiated but temporarily interrupted due to armed conflict and war.

[k] Sudan: note that South Sudan got independent on 9 July 2011.

[l] Malaria Consortium is supporting South Sudan only.

[m] RTI: Research Triangle International.

[n] IMA: IMA World Health.

- What level of preventive chemotherapy (i.e. number, time and frequency of treatments) should be introduced and to which target group (i.e. school-aged children or whole communities) to reduce the incidence to near zero?
- At what level of prevalence and intensity of infection in which target group does preventive chemotherapy become unacceptable as a treatment strategy either from cost, ethical reasons or compliance considerations?
- Can sufficient praziquantel be made available and accessed in health care centres to implement a case by case treatment regime (treatment on demand)?

4.2. Snail control

Snail control and/or changes in water use have been shown to interrupt transmission in high-risk communities (King et al., 2006). The application of molluscicides may, however, be beyond the scope or financial means of current control initiatives. That said, snail control measures become highly important in settings where low transmission intensity has been achieved, but where infected people from other endemic areas might immigrate into and which is hence prone to disease resurgence (Fenwick et al., 2006). In addition, intermediate host snail control is useful to enhance the impact and performance of preventive chemotherapy and case management (WHO, 2010). It has been shown that the optimum time for preventive chemotherapy is when there is no risk of reinfection with schistosomes, i.e. when the snails have been reduced and transmission is halted. Hence, it is sensible to reduce snail populations before undertaking a treatment campaign (Sturrock, 1995) and to carry out treatment during the low-transmission season (Augusto et al., 2009).

The molluscicide niclosamide has been found to be highly active against all stages of the snail life cycle, as well as schistosome larvae (McCullough et al., 1980). On the other hand, it is toxic to fish and thus has a negative impact on the environment and biodiversity. Moreover, niclosamide is expensive, partly due to its limited use, and does not prevent snails from recolonizing their original habitats. However, if used in a highly focused manner, ecological modelling indicates that niclosamide can be beneficial (Woolhouse et al., 1998). Indeed, repeated molluscicide can be effective in the long-term management of snail populations (Sturrock, 1995; Lardans and Dissous, 1998; Fenwick et al., 2006), and hence has played a key role in the elimination of schistosomiasis in Morocco and Japan, and in control programmes in Egypt and P.R. China, as discussed in greater detail in Section 8.

Alternatives to synthetic chemical molluscicides for snail control include plant-based derivatives (e.g. endod), environmental management to eliminate snail habitats, and biological control with fish, ducks, crayfish, dominant trematodes and snail competitors (displacement, miracidial sponges). Such integrated snail control gives leverage to further accelerate control programmes towards elimination.

An agenda for snail control interventions related to schistosomiasis elimination might consider the following points (also see Utzinger et al., 2005).

- Development of new snail interventions and new cheap molluscicides of plant and synthetic origins.
- Malacological training for helminth control staff to enable identification of snails responsible for transmission and to identify transmission sites.
- Increased targeting of transmission sites using geographical information systems (GIS) and remote sensing at high spatial and temporal resolution. Since transmission of schistosomiasis is highly focal, to be effective and affordable, molluscicide should mirror this situation.
- Development of inexpensive, field-applicable diagnostic assays for the large-scale screening of individual or pooled snails from transmission sites to detect the presence of parasites.
- Greater focus on habitat changes by creating better links between community leaders, health workers and engineers.

4.3. Hygiene, water and sanitation

Hygiene, water and sanitation have recently been phrased "the forgotten foundations of health" (Bartram and Cairncross, 2010). Indeed, access to and use of clean water and improved sanitation are essential in preventing re-emergence of helminthic diseases after successful treatment campaigns (Asaolu and Ofoezie, 2003; Utzinger et al., 2003; Singer and Castro, 2007; Smits, 2009; Ziegelbauer et al., 2012) and would also aid in combating numerous other pathogens that are transmitted by the faecal-oral route. A literature review published in the early 1990s documented a substantial reduction of schistosomiasis (77%) and a particular notable impact on egg counts and thus disease severity due to improved water supply and sanitation facilities (Esrey et al., 1991). Improvements in water and sanitation often go hand-in-hand with a general increase in economic development (Bergquist, 2001; Knopp et al., 2013). Although improvement of access to safe water is imperative, many authorities only pay lip service to that effect, and such improvement is still hard to achieve in many parts of sub-Saharan Africa. Indeed, the WHO targets for safe water, sanitation and hygiene are far from being met, and without access to clean water, elimination of schistosomiasis will remain a distant goal (WHO, 2010).

It must be noted, however, that better access to safe water and sanitation does not necessarily impact favourably on schistosomiasis transmission, since many factors are involved in people's choice of water source for difference purposes. For example, provision of latrines does not mean that they will be used as intended. People may fear them, or not use them if they are not convenient. Latrines may also be poorly maintained and so people will be less likely to visit them (Aagaard-Hansen et al., 2009). Also, while latrines may impact on the transmission of intestinal schistosomiasis, it remains likely that they may not have an equal impact on transmission of urogenital schistosomiasis caused by *S. haematobium*.

While improved sanitation is central to sustainable control, if water contact remains high, transmission is likely to persist even if latrines are available (Rollinson, 2009). In relation to schistosomiasis elimination, it is crucial to monitor and encourage improvements in the provision of water and sanitation, as changes in use of water may have a considerable impact on transmission at the local level. Intersectoral collaboration and community participation are essential for the design, implementation and long-term monitoring of the impact and cost-effectiveness of hygiene, water and sanitation interventions on schistosomiasis and a host of other diseases (Holveck et al., 2007; Wang et al., 2009b).

4.4. Health education and behavioural change

Open water contact in most rural settings is inevitable; therefore a change in behaviour of the population is necessary to stop the contamination of open water bodies with excreta. In theory, the non-contamination of open water bodies is an easy and simple way to stop transmission, but in practice it is very difficult to achieve, even in the face of health education, and access to safe water and sanitation (Jordan, 1985; Fenwick et al., 2006). Children will always play in water and void their bladders, releasing *S. haematobium* eggs into the environment. Similarly, despite sanitation and hygiene

measures, eggs of *S. mansoni* may remain on the perianal folds, so providing a transmission risk.

There is a need for greater and more comprehensive health education for both children and adults to guide behavioural change, especially in relation to reduction of water contact, to minimize the risk of schistosomiasis transmission (Stothard et al., 2006, 2009b). Sanitation hinges on health education, with active teaching methods focusing on personal hygiene (Lansdown et al., 2002; Nock et al., 2006). Education has been found to impact health-seeking behaviour, which may have an effect on prevalence of infection (Lansdown et al., 2002; Aagaard-Hansen et al., 2009). It also provides the impetus behind the success of deworming programmes, preventing the contamination of the environment, and hence transmission (Nock et al., 2006).

However, human behaviour is resistant to change, and behavioural modification will be achieved only with an increase in the knowledge and understanding of schistosomiasis transmission in conjunction with an increase in standards of living (Fenwick et al., 2006; Rollinson, 2009). Thus, although education has been successful in promoting behavioural change, it may have a limited impact on the prevalence or intensity of infection without access to appropriate infrastructure. Health education should be relevant to local knowledge and practices, and should be a "health communication" dialogue, as opposed to "health instruction", which is one-directional (Aagaard-Hansen et al., 2009).

Any agenda for schistosomiasis elimination must encourage greater efforts and explore novel and innovative ways to change human behaviour as it relates to both water contamination and water exposure and thus reduce transmission of schistosomiasis. The social–ecological contexts must be taken into considerations and the tools require careful development and validation for cultural sensitivity.

5. Diagnostics

Development and implementation of optimal methodologies for diagnosis is crucial in all aspects of schistosomiasis control and high sensitivity, as well as absolute specificity, will be needed as programmes shift their emphasis from control to elimination (Utzinger et al., 2011). Evaluation of the efficacy of any intervention measures and the determination of resurgence require appropriate diagnostic tools, which must adapt to changing control situations and objectives (Bergquist et al., 2009). Initial disease surveillance must be enhanced so that drug delivery can be focused (Stothard, 2009).

In the case of morbidity control, rapid identification of high-risk communities with school-based questionnaires, microscopy and, for urogenital schistosomiasis, with reagent strips suffices, as this is generally accurate and cost-effective with regard to this objective (Bergquist et al., 2009; Brooker et al., 2009). However, transmission control requires more accurate and precise tests, especially in low prevalence areas. A low positive predictive value (sensitivity) will impede further progress in disease control, and hence elimination (Bergquist et al., 2009).

Microscopy to detect excreted schistosome eggs in urine and/or faeces is direct and specific, it requires a minimum of tools (e.g. microscope and mainly reusable laboratory equipment) and well-trained staff, but both may be lacking in resource-poor settings in rural Africa. Moreover, although considered the 'gold' standard for the detection of schistosome infections in humans, microscopy may miss infections, especially of those who are lightly infected or where eggs got trapped in tissue, and in areas of low transmission (Doenhoff et al., 2004; Bergquist et al., 2009; Stothard et al., 2009c; Ibironke et al., 2011). Indeed, when levels of excreted eggs fall below less than one egg per gram of stool (EPG) then present methods, e.g. Kato-Katz, will be very unlikely to capture this infection reliably, even when several stool samples are examined consecutively (de Vlas and Gryseels, 1992; Utzinger et al., 2001; Knopp et al., 2011). Similarly, if only one *S. haematobium* egg is present per 10 ml of urine, it will be difficult to reliably detect *S. haematobium* infection with the urine filtration method. It is not yet known if this level of environmental contamination is more than sufficient to ensure infection in local snail intermediate hosts.

Diagnostic tests based on antibody detection are highly sensitive, but they are unable to distinguish past from current infections and are relatively non-specific and prone to cross-reactions with other antigens (Ross et al., 2002; Stothard et al., 2009c). In settings targeted for elimination, positive antibody test results may take an indefinite period of time to convert to negativity after elimination of infection (Abbasi et al., 2010). Also, antibody titres do not reflect the intensity of infection (Doenhoff et al., 2004). However, in settings targeted for elimination, longitudinal monitoring of antibody titres in different age-groups can provide important information about when young children are not exposed to *Schistosoma* anymore.

In contrast, current antigen testing is highly specific, but relatively insensitive (Pontes et al., 2003). That said, Stothard et al. (2009c) found that schistosome egg antigen (SEA)-enzyme-linked immunosorbent assay (ELISA) can be used as a complementary field-based method for monitoring infection, as it performs well over a range of endemic settings and would be best applied to monitor the incidence of 'new' infections in young children in environments where transmission was thought to be interrupted. Another method for the diagnosis of schistosomiasis is the detection of circulating anodic and cathodic antigens (CAA and CCA) in blood or urine (Deelder et al., 1994). Rapid diagnostic tests detecting CCA of *S. mansoni* are now readily available in dipstick or cassette format. Since CCA are only released from living worms, the rapid tests can be used to monitor the dynamics of existing worm burdens, as well as clearance post-treatment. Recent studies carried out in different epidemiological settings of Côte d'Ivoire and Kenya revealed that a single CCA performed on urine samples shows equal or even higher sensitivity for *S. mansoni* diagnosis than multiple Kato-Katz thick smears obtained from stool samples (Coulibaly et al., 2011; Shane et al., 2011).

Polymerase chain reaction (PCR)-based assays that are specific and highly sensitive have been developed for the detection of schistosome DNA in human excreta or sera and plasma (ten Hove et al., 2008; Wichmann et al., 2009; Gomes et al., 2010; Ibironke et al., 2011). However, they need further validation and standardization before being routinely applied for diagnosis of schistosomiasis. Moreover, their application requires expensive high-tech laboratory infrastructure and highly accurate handling of samples, kits and equipment. Hence, PCR is a technique which might be useful for individual patient management, but has limited broad-scale field-applicability at the moment.

When approaching elimination, lower infection levels and the insensitivity of current diagnostic techniques will lead to an inaccurate picture of disease burden, which will threaten the success of the programme (Utzinger et al., 2005; Bergquist et al., 2009). The difficulties in detecting the 'true' prevalence of infection necessitate the development of new techniques and algorithms for monitoring and surveillance (Stothard et al., 2009c). Most importantly these techniques have to be much cheaper than any of the presently available methods. To 'prove' that there are no new infections occurring in areas targeted for transmission control or elimination, large population samples will have to be screened, and the repeated testing of putative infected cases to exclude false positives also needs to be factored in. Mathematical modelling can serve to predict transmission patterns, show if the applied control measures are appropriate, and indicate when elimination may be achieved, and hence guide and support schistosomiasis control and elimination programmes.

6. Monitoring and surveillance

Without monitoring and evaluation, one can expect no reasonable operational efficiency in a control programme, let alone longer-term elimination efforts (Yekutiel, 1981; Brooker et al., 2004). There is a need for appropriate pre-control studies to define the micro-epidemiology and transmission patterns of the disease, and collection of scientifically sound and au courant information that can be translated into feasible and adaptable guidelines (Savioli et al., 2009).

Surveillance is essential, and diagnostic procedures must be sufficiently sensitive to detect those individuals with low level infections (Fenwick et al., 2006; Bergquist et al., 2009). It is imperative to know the true infection status of a community so that appropriate control strategies can be implemented. Also, in the end stages of a control programme with the emphasis shifting towards elimination, rigorous monitoring and surveillance systems are necessary to identify rapidly any disease resurgence that can be immediately addressed by appropriate interventions. For this purpose, highly sensitive diagnostic methods allowing the high throughput of large population or intermediate host snail samples are necessary. In this respect, molecular approaches have been developed for the detection of both *S. haematobium*- and *S. mansoni*-infected snails (Hamburger et al., 1998, 2004; Abbasi et al., 2010). Molecular infection detection is more sensitive than the traditionally applied cercarial shedding, as the latter method cannot pick up prepatent infections and thus might underestimate true prevalence (Hamburger et al., 2001; Abbasi et al., 2010). In knowing the snail species present and the level of infection, an area's disease prevalence can be better assessed and areas at greater risk can be highlighted (Melo et al., 2006; Akinwale et al., 2011). Monitoring the transmission potential (prepatent snails) may aid in selecting the most effective modes of targeting and timing chemotherapy, as well as the application of additional snail control measures for preventing infection and disease (King et al., 2006).

Ideally, malacological surveys should be undertaken, not only to identify sites for focal molluscicide, but also because the snail–schistosome relationship is complex in both specificity and compatibility, with many factors determining the small-scale heterogeneities in disease transmission. These must be considered when focusing and improving control strategies at a local level (Rollinson, 2009).

For assessing the extent of schistosome infections in humans, rapid epidemiological appraisal via school questionnaires has been validated across a variety of ecological, epidemiological and sociocultural settings in sub-Saharan Africa for *S. haematobium* (Lengeler et al., 2002a; Brooker et al., 2009). However, risk appraisal via questionnaires for *S. mansoni* does not perform so well (Lengeler et al., 2002b; WHO, 2002). Questionnaires on water contact patterns can be useful to identify high-risk communities, as human behaviour interfaced with the environment will determine small-scale heterogeneities in schistosomiasis transmission (Utzinger et al., 2000; Rudge et al., 2008).

Since schistosomiasis is highly focal, GIS and remote sensing can be used to develop predictive risk maps for targeted control and so determine the optimum allocation of resources (Clements et al., 2009; Simoonga et al., 2009; Schur et al., 2013). The epidemiology of the disease will shift over time as control interventions progress, and in response, strategies and targets will need to be adapted (Utzinger et al., 2009). Surveillance should prioritize the evaluation of environmental risk, pinpointing transmission patterns at the micro-geographical level. Complementary to this, questionnaires can be used in the identification of behaviour patterns. This will serve to focus control and improve the outcomes of interventions (Rudge et al., 2008). In our view, there is a need for innovative surveillance-response approaches that will be able to readily identify remaining and/or re-emerging hot spots and underlying risk factors (e.g. identification of a child with blood in urine due to *S. haematobium* and detection of contaminated freshwater body where water contact occurred), followed by appropriate interventions that are tailored to the local context (e.g. treatment of child with praziquantel, checking whether any other family members are infected and focal molluscicide of the identified freshwater body where transmission occurred) (Knopp et al., 2013). The feasibility and cost-effectiveness of strengthening diagnostic capacity and provision of praziquantel at primary health care level needs to be determined as a means for surveillance of schistosomiasis in low transmission areas.

7. Capacity building

Infrastructure development and poverty reduction are required to eventually break the local transmission cycles of schistosomiasis (King et al., 2006). A lack of resources, inadequate capacity and political commitment regarding schistosomiasis control can often hinder progress especially in sub-Saharan Africa (Utzinger et al., 2003). Furthermore, a national financing capacity is essential for sustainability of control programmes (WHO, 2002).

It is widely acknowledged that community involvement and capacity building are imperative for successful control and elimination (Ndekha et al., 2003; Parker et al., 2008; Aagaard-Hansen et al., 2009). Control and elimination activities will work best where intersectoral collaborations between health, education and water sectors for development and planning are in place to prioritize needs and to allocate financial resources (Holveck et al., 2007; Aagaard-Hansen et al., 2009). Currently the connection between vertical control programmes centred on morbidity control, and strategies based on clean water and sanitation is absent or insufficiently developed. To remedy this, it is necessary to take an intersectoral approach, with advocacy and action from local communities and the health community to foster cooperative ventures with engineers, the private sector, governments and non-governmental organizations (NGOs) specialized in water supply and sanitation (Singer and Castro, 2007; Utzinger et al., 2009).

Integration is of vital importance to both control and elimination campaigns: there must be improved communication and collaboration between donors and international programme managers, improved communication between decision makers in the Ministry of Health (MoH) and national disease control programme managers, NGOs, and international agencies, strengthened health systems and linked control efforts within health sector frameworks, and lastly a synergy of interventions (Fenwick et al., 2006).

Partnerships must be fostered that seek solutions for implementation and translation into policies adaptable to different social-ecological settings. Also the mobilization of resources and involvement of committed partners around a common objective must be promoted (Savioli et al., 2009). Institutional partnerships should and can be strengthened through the establishment of enduring infrastructure for research (Stothard et al., 2009a).

8. Lessons from successful schistosomiasis elimination

Although schistosomiasis continues to be a public health problem, particularly in sub-Saharan Africa, and there are signs of disease (re-)emergence due to major demographic and ecological transformations, incidence has been reduced in many countries, and local elimination has been achieved in some countries. It is important to review experiences from successful past elimination efforts, as the lessons learnt can shape the contemporary schistosomiasis elimination agenda. Fig. 1 shows a world map, highlighting those countries where schistosomiasis elimination

Table 2
Key features of past successful schistosomiasis control and elimination programmes, stratified by country and/or territory.

Country, territory	Time period	Parasite	Intermediate host snail	Control strategy	Reference(s)
St. Kitts	1945-	*S. mansoni*	*Biomphalaria* spp.	Snail control (biological control (competitor snails), chemical control (molluscicides)) and environmental management	Ferguson et al. (1960)
Martinique and Guadeloupe	n.d.	*S. mansoni*	*Biomphalaria* spp.	Snail control (biological control (competitor snails))	Pointier and Jourdane (2000)
St. Lucia and other Caribbean islands	1966–1981	*S. mansoni*	*Biomphalaria* spp.	Snail control (molluscicide), morbidity control (chemotherapy) and provision of safe water supplies for households and communities. Subsequently, integrated control (combination of aforementioned interventions whenever appropriate, coupled with health education)	Jordan (1985)
Brazil	1975–1993	*S. mansoni*	*Biomphalaria* spp.	Morbidity control (preventive chemotherapy using oxaminquine), health education, water supply and sanitation. Additionally, limited snail control (chemical control using niclosamide)	Katz (1998); WHO (2009); Sarvel et al. (2011)
	1993-			Control programme decentralized and integrated into primary health care system. Case detection and treatment campaigns in endemic areas: early detection and treatment of carriers, search for and control of intermediate host snails, health education and sanitation	WHO (2009); Reis et al. (2010)
Venezuela	First control efforts: 1920s				
	Control programme started in 1943	*S. mansoni*	*Biomphalaria glabrata*	Snail control (chemical control using molluscicides) and environmental management; occasionally chemotherapy and health education. Later, biological control (competitor snails)	Alarcon de Noya et al. (1992); Alarcón de Noya et al. (1999)
Saudi Arabia	n.d.	*S. haematobium* and *S. mansoni*	*Bulinus* spp. and *Biomphalaria* spp.	Vertical programme consisting of case detection and treatment (praziquantel) and snail control (chemical) and environmental management	Al Ghahtani and Amin (2005)
Morocco	1970s-	*S. haematobium*	*Bulinus* spp.	Four-pronged control strategy: (i) annual screening and treatment of humans, including increased intensity of case detection in health centres and by mobile teams; (ii) transmission control (molluscicide and environmental management); (iii) health education and community participation; and (iv) intersectoral collaboration (health, agriculture, education and administration)	Laamrani et al. (2000); Amarir et al. (2011)
Tunisia	1970s-	*S. haematobium*	*Bulinus truncatus*	Control programme focussed on molluscicide, treating all infected people and was linked to efforts to improve water resources and agricultural infrastructure. Last autochthonous cases occurred in 1981–1982 but risk of reintroduction remains	WHO (2009)
Egypt	1976	*S. mansoni* and *S. haematobium*	*Bulinus truncatus* and *Biomphalaria alexandrina*	Case detection and treatment, supplemented by focal molluscicide	EMRO/WHO (2007)
	1997			Preventive chemotherapy using praziquantel, along with focal molluscicide using niclosamide	EMRO/WHO (2007)
	2003			Implementation of annual monitoring surveys	EMRO/WHO (2007)
	2010			Multisectoral approach, integrating sanitation, environmental interventions and health education into preventive chemotherapy campaigns, thus ensuring mobilization of all stakeholders	Curtale et al. (2010)
Mauritius	1988-	*S. haematobium*	*Bulinus cernicus*	Control programme focussing on screening for microhaematuria and/or eggs in urine, health education and molluscicide. Treatment of all positive cases, health education, improvement in water supplies and living standards. Socio-economic development, with a change from a sugar/irrigation-based economy impacted on schistosomiasis transmission	Dhunputh (1994)
Islamic Republic of Iran	1959-	*S. haematobium*	*Bulinus truncatus*	Nationwide health care project comprising public health education, environment decontamination, case finding, screening and chemotherapy	Mombeni and Kheradmand (2005)
Japan	1950–1990s	*S. japonicum*	*Oncomelania* spp.	Nationwide, interdisciplinary, multisector public health campaign to combat parasitic diseases, including *S. japonicum* and soil-transmitted helminthiasis. In 1977, schistosomiasis was declared eliminated. Active surveillance for infected snails was maintained until the early 1990s. Interventions included active case detection and large-scale treatment, lining canals with cement, drainage and filling swamps, molluscicide, and an improvement in standards of living	Kasai et al. (2007); Takeuchi et al. (2007); Kojima et al. (2007)
P.R. China	Late 1940s-	*S. japonicum*	*Oncomelania* spp.	Transmission control targeting intermediate host snail, using chemical molluscicides and environmental management and involving large-scale community participation. Interventions targeting domestic reservoir animals (e.g. mechanization of agriculture, fencing of water buffaloes and vaccination)	Utzinger et al. (2005); Wang et al. (2008, 2009a,b); McManus et al., 2009, 2010)

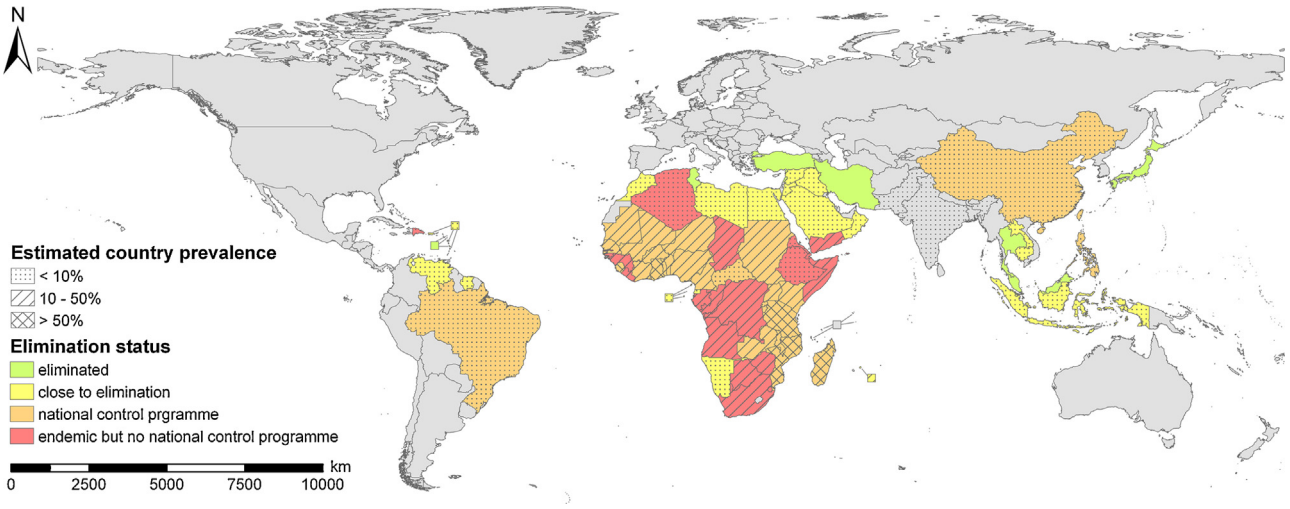

Fig. 1. World map, highlighting countries where schistosomiasis has been eliminated (green colour), is close to elimination (yellow colour) or where national control programmes or at least some sort of preventive chemotherapy are in place (orange colour). Marked in red are countries where schistosomiasis is endemic, but where national control programmes have yet to be implemented. Hatchures indicate countries with a low (prevalence <10%; pointed hatchures), moderate (prevalence 10–50%; dashed hatchures) and high schistosomiasis endemicity (prevalence >50%; crossed hatchures).

has been achieved (green colour), or where the goal of elimination is being targeted (yellow colour). Highlighted using orange colour are those countries where national schistosomiasis control programmes are in place or at least some level of preventive chemotherapy using praziquantel is being implemented. Countries highlighted in red are those where no or only very limited efforts are currently in place for schistosomiasis control. Moreover, countries are stratified into low (<10%), moderate (10–50%) or highly endemic for schistosomiasis (>50%). Table 2 summarizes key features of past successful schistosomiasis control and elimination programmes, stratified by country and/or territory.

8.1. St. Lucia and other Caribbean islands

In 1902 Sir Patrick Manson reported finding lateral-spined schistosome eggs in the stool of a 38-year-old man who had previously lived in St. Kitts and Antigua (Manson, 1902). Further surveys showed that while schistosomiasis had been a significant health problem in St. Kitts by the mid-1940s, the disease had naturally declined and snail habitats had been considerably reduced by construction of aqueducts, chemical treatment and the introduction of competitor snails (Ferguson et al., 1960). In Martinique and Guadeloupe, disease in people has been eliminated from previously endemic areas and biological control using competitive snails has played a role in the reduction (Pointier and Jourdane, 2000). However, there needs to be confirmation of the absence of schistosomiasis in other countries in the Caribbean, such as in the Dominican Republic and Puerto Rico where the disease was formerly present (Schneider et al., 2011).

In St. Lucia many distinct valleys and watersheds result from its central mountain range and in the late 1960s and early 1970s the overall prevalence of intestinal schistosomiasis due to *S. mansoni* in some valleys was greater than 50%. The St. Lucia Research and Control project (a joint project of the MoH of St. Lucia and the Rockefeller Foundation) was therefore instigated between the years 1966 and 1981 to evaluate the effects of different interventions on transmission of intestinal schistosomiasis and their benefits in various situations, so that resource-poor countries would have a rational basis to design an appropriate strategy of attacking their own parasites and intermediate hosts. Based on prior surveys, three intensive strategies were planned on this Caribbean island, designed to have the maximum impact, namely (i) mollusciciding; (ii) chemotherapy; and (iii) provision of safe water supplies for households and communities. Combinations of interventions were implemented where appropriate. A recommendation was that molluscicide should be used in conjunction with chemotherapy, and also with the provision of safe water, especially in areas of high transmission (Jordan, 1985).

With regard to snail control, the first strategy was blanket molluscicide, followed by surveillance to detect snails and finally rapid retreatment of the area if recolonized. This strategy was found to reduce significantly the prevalence of schistosomiasis. Following on from this intervention, a more focal, and hence less expensive, method of molluscicide was adopted, in concert with two intensive preventive chemotherapy campaigns. These actions further reduced the prevalence of *S. mansoni* infections. It was also found that in individual households provided with piped water and in communities with laundry and shower facilities, and if the people had been educated on their proper use and why they are preferable to natural water bodies, exposure to infection could be reduced and the resurgence of transmission prevented (Jordan, 1985). However, between 1995 and 2007 a total of 106 *S. mansoni* cases have been reported, with an incidence rate of six cases per 100,000 in 2007 (PAHO/WHO, 2007). In 2010, a limited school-based study, enrolling 550 children in three villages revealed four active infections, for a prevalence of 0.6% (Kurup and Hunjan, 2010). This example shows that long-term surveillance and monitoring and continued application of control measures are essential to achieve complete elimination.

8.2. Brazil

The Brazilian schistosomiasis control programme was planned in the 1970s, with the main objective to reduce hepatosplenic schistosomiasis due to *S. mansoni* infection. In 1975, the Special Programme for Schistosomiasis Control was introduced in six north-eastern states of Brazil (Katz, 1998). This vertical programme, implemented from 1976 to 1979, integrated mass treatment with oxaminiquine in all communities with prevalences above 50%, health education aimed to prevent the disease, construction of sanitary facilities and provision of potable water in every municipality (WHO, 2009). Control of the intermediate host snail with molluscicides was, at that time, limited due to environmental laws. However, to some extent and irregularly, molluscicide using

niclosamide was applied as intervention strategy (Sarvel et al., 2011). Since 1993, the schistosomiasis control programme (SCP) has undergone decentralization and has been integrated into the primary health care system, with the focus on improving access to diagnostic services, treatment and health education (Reis et al., 2010). Objectives of the SCP are to reduce mortality and morbidity, to reduce prevalence in hyper-endemic areas, to prevent and reduce the spread of schistosomiasis and to eliminate schistosomiasis in isolated areas with low intensity transmission (Katz, 1998; WHO, 2009). Control measures include the early detection and treatment of carriers, the search for and control of intermediate host snails, health education to the at-risk population, and sanitation procedures to change household and environmental factors that favour transmission (WHO, 2009). In non-endemic areas, cases are detected in primary health care units, and in endemic settings through surveys conducted by the SCP. Cases are reported through the national notifiable diseases information system and registered in the information system of the SCP. The applied measures were able to control morbidity but transmission of schistosomiasis persists in vast areas of Brazil. As a result of the decentralization, health seeking behaviour has changed and access to diagnosis and treatment has been weakened in some rural populations (Reis et al., 2010). In the surveys conducted by SCP, the *S. mansoni* prevalence decreased from 23% to 6% between 1977 and 2005. Today, elimination of schistosomiasis seems feasible in five of 14 states of the country (WHO, 2009).

8.3. Venezuela

The first human case of schistosomiasis in Venezuela was discovered in 1905. Control efforts were launched in the early 1920s, whereas a formal schistosomiasis control programme, institutionalized within the MoH, was put in place in 1943. It was then estimated that the schistosomiasis-endemic area covered an area of 15,000 km^2, there were 70,000 human cases and the prevalence of *S. mansoni* in the endemic area was 14%. In 1984, the 'Schistosomiasis Research Group' (SRG) was born, bringing together researchers and interested people related to the schistosomiasis control programme. By 1996, the prevalence of *S. mansoni* infections in the endemic area fell to 1.4%. However, it has been suggested that the true prevalence may be underestimated, and that those people excreting less than 100 EPG may be maintaining foci and impeding the impact of control measures to achieve elimination (Alarcón de Noya et al., 1999).

The control programme initially focused on elimination of the snail intermediate hosts with chemical molluscicides and sanitary engineering, the latter aimed at reducing human contact with contaminated water. In addition, there was occasional health education and drug administration. Diagnosis, initially, was based on stool examinations, but since the early 1980s, was gradually replaced by serology and follow-up stool examination of seropositive individuals. Treatment was either selective or given en masse, based on coprological and serological findings. Despite the marked reduction in the prevalence of *S. mansoni* infection, the size of the endemic area remained unchanged (Alarcón de Noya et al., 1999). Moreover, there was an increase in the transmission risk in some areas, due to the adaptation of the intermediate host snail, *Biomphalaria glabrata*, to sub-urban environments and other areas outside of the original endemic area (Alarcon de Noya et al., 1992). To counter this, competitor snails (i.e. *Melanoides tuberculata* and *Thiara granifera*) were introduced to some areas as a method of biological control and it was indeed found that *Biomphalaria* spp. were reduced or even eliminated in certain environments (Alarcón de Noya et al., 1999).

8.4. Saudi Arabia

Both urogenital and intestinal schistosomiasis have been reported in Saudi Arabia, although the distributions do not appear to overlap. Epidemiological surveys conducted in the 1970s, revealed that both *S. haematobium* and *S. mansoni* were endemic in 12 regions, with prevalences reaching 40% in some areas (EMRO/WHO, 2007). The highest rates of infection were found in the Aseer region (Shati, 2009). The initial programme to control schistosomiasis in Saudi Arabia was vertical, based on case detection, morbidity control (treatment with praziquantel), chemical snail control and environmental management. Eventually, the programme was integrated into the primary health care system, resulting in increased coverage and maintenance of low infection prevalence (Al Ghahtani and Amin, 2005).

Snail control was guided by the local epidemiology of the disease in humans, and was supported by identification and regular treatment of snail-infected water bodies as well as treatment of those infected. With socio-economic development came improved sanitation and water supplies, medical care and health education, the combination of which led to the interruption of transmission of *S. haematobium* in the Jazan region of Saudi Arabia (Al Ghahtani and Amin, 2005).

However, migration from endemic neighbouring areas accounts for new cases of both urogenital and intestinal schistosomiasis in the absence of cross-country control programmes. To remedy this problem, cross-border collaboration is necessary, with regular long-term surveillance to detect and treat any new or residual infections (Al-Madani and Mahfouz, 1997; Al Ghahtani and Amin, 2005). In 2005, a national programme for elimination of schistosomiasis was initiated in the 12 endemic regions and, in 2007, six regions were believed to be schistosomiasis free. The strategy for disease elimination in the remaining regions entails active case detection and treatment by examining 80–100% of the endemic population (annually) and schoolchildren (twice a year), access to safe drinking water and good sanitation to endemic communities, snail control and health education through different channels (EMRO/WHO, 2007).

8.5. Morocco

In Morocco, the first cases of *S. haematobium* were discovered in 1914 and urogenital schistosomiasis has been a problem in the southern parts of the country since then. In the face of large water resource development projects, starting in the late 1960s, urogenital schistosomiasis spread to new foci in central and northern Morocco. Consequently, in the early 1970s, an integrated control programme was launched, which became fully operational in 1982. A four-pronged control strategy was employed, consisting of (i) annual screening and treatment of humans free of charge, including increased intensity of case detection in health centres and by mobile teams; (ii) transmission control by means of mollusciciding and environmental management, depending on the ecological setting; (iii) health education and community participation; and (iv) intersectoral collaboration with involvement of services for administration, health, agriculture and education, at local and provincial levels (Laamrani et al., 2000; Amarir et al., 2011).

Sustainability and compatibility with other health programmes was ensured, as all staff and facilities were part of the regular resources of the local and provincial health services, and having provincial health authorities with a national programme team in a consultative role. However, there was a decrease in motivation and compliance of both the population and the health workers with a decrease in perceived risk, and thus the risk of resurgence. To rectify this, an information campaign was introduced, and the intensity of activities for the remaining foci was stepped up (Laamrani et al.,

2000). Moreover, in the mid-1990s, the MoH announced its plan for schistosomiasis elimination. Large-scale serological surveys conducted between 2005 and 2009 revealed an interruption of disease transmission at the national level, with only very few residual cases. A serological survey carried out in mid-2009 on more than 2000 children, aged 1–16 years, who were selected in the remaining disease-endemic foci, found no *S. haematobium*-specific antibodies in any of the serum samples. Hence, schistosomiasis transmission has been interrupted within the last disease endemic foci (Amarir et al., 2011).

8.6. Tunisia and Algeria

Both countries were previously associated with urogenital schistosomiasis (Doumenge et al., 1987). However, there were relatively few foci in Algeria and it is not clear whether there have ever been active campaigns to address schistosomiasis in this country. In Tunisia, on the other hand, the government decided already in 1969 to eliminate schistosomiasis (WHO, 2009). The transmission of *S. haematobium* was restricted to a few oases, where the intermediate host snail, *Bulinus truncatus*, occurred. The schistosomiasis control programme in Tunisia was implemented from 1970 onwards and aimed to control and interrupt transmission by using molluscicides and treating all infected people (WHO, 2009). Moreover, it was linked to efforts to improve water resources and agricultural infrastructure. Today, Tunisia is considered to have eliminated schistosomiasis, and the last autochthonous cases occurred in 1981–1982 (WHO, 2009). Noteworthy is that a natural shortage of surface water limits snail habitats and water contact but irrigation for agriculture can create new habitats for *B. truncatus* and so the risk of reintroduction remains. Imported *S. haematobium* cases are annually reported in Tunisia (Ben Hariz et al., 2007).

8.7. Egypt

For the MoH in Egypt, schistosomiasis control has high priority. Before the national schistosomiasis control programme (NSCP) started in 1976, the prevalence of the disease was estimated to be around 40% (EMRO/WHO, 2007). The NSPC was based on case detection and treatment. By 1989, the provision of free praziquantel treatment through government health facilities to those infected with *S. mansoni* or *S. haematobium* was initiated (EMRO/WHO, 2007). Chemotherapy was often supplemented with focal molluscicide to control intermediate host snails. Following a ministerial decree, from October 1997, it was authorized that praziquantel could be distributed regardless of infection status to endemic populations. Since the late 1980s, more than 50 million doses of praziquantel have been administered and these treatment campaigns, along with focal molluscicide using niclosamide, greatly reduced prevalence. Between 1988 and 2001, the prevalence of *S. mansoni* dropped from 16.4% to 1.6%, and that of *S. haematobium* was reduced from 11.9% to 1.3% (El Khoby et al., 1998; Fenwick et al., 2003). In 2003, a more targeted approach was adopted, based on annual monitoring surveys. Although more complicated and expensive, it further reduced the prevalence of infection. In 2006, the overall prevalence in Egypt dropped to <3%, but hot-spot transmission sites with prevalences of about 10% still exist (EMRO/WHO, 2007). The control efforts have not halted transmission, and only if the programme is continued, perhaps for another 10–20 years, elimination might be achieved and certified (Curtale et al., 2010).

The new plan of action is a multisectoral approach, integrating sanitation, environmental interventions and health education into preventive chemotherapy campaigns, thus ensuring mobilization of all stakeholders. The ultimate goal is comprehensive primary health care and improvement in living conditions, to raise sanitation as well as social and economic standards in infection hotspots, and so to stop transmission (Curtale et al., 2010). It is hoped that the current socio-political changes will not negatively impact on schistosomiasis and other helminthic diseases.

8.8. Mauritius

For many years, urogenital schistosomiasis was associated with certain areas of Mauritius where the intermediate snail host *Bulinus cernicus* was found (Rollinson and Wright, 1984). Until 1988, the disease was mainly managed in hospitals and associated institutions. Subsequently, a special control programme, focussing on screening for microhaematuria and/or *S. haematobium* eggs in urine, health education and molluscicide was implemented (Dhunputh, 1994). The disease began to decline already in the early 1980s and no cases of *S. haematobium* were observed by egg detection in schoolchildren in 1991. The successful treatment of all positive cases with praziquantel, health education, improvement in water supplies and living standards together with a decline in snail populations are all believed to have played a role in the decline (Dhunputh, 1994). Socio-economic development, with a shift away from a sugar/irrigation-based economy also had an impact on schistosomiasis transmission.

8.9. Islamic Republic of Iran

First attempts to control urinary schistosomiasis in the Islamic Republic of Iran were started in 1959 and control measures, including anti-schistosomal treatment, improvement of the sanitary infrastructure, environmental measurements and focal molluscicide, were implemented from 1968 onwards (Massoud et al., 1969, 1982). The prevalence of *S. haematobium* infection declined from 8.3% in 1970 to 0.7% in 1979 (Massoud et al., 1982). Studies in Khuzestan province have shown that *S. haematobium* can be eliminated by the provision of a nationwide health care project comprising public health education, environment decontamination, case finding, screening and chemotherapy (Mombeni and Kheradmand, 2005). In a follow-up study, Gholamreza et al. (2008) were unable to find any infected urine out of 3400 specimens examined and also suggested that total elimination of urogenital schistosomiasis would be possible if the health authorities in neighbouring areas can be persuaded to adopt a similar strategy of integrated control. The plan for the future is to continue monitoring transmission, by passive surveys in local health centres and active case-finding among schoolchildren, and to continue surveillance, including snail sampling and focal molluscicide, if required.

8.10. Japan

At the end of World War II, the health indicators in Japan were similar to those seen in developing countries today, with a high burden of communicable diseases and many people lacking access to basic health facilities and services (Takeuchi et al., 2007; Ikeda et al., 2011). In 1950, the Japanese government launched a nationwide, interdisciplinary, multisector public health campaign to combat parasitic diseases, which reduced the prevalence of *S. japonicum* and soil-transmitted helminth infections dramatically. Indeed, in 1977, schistosomiasis was declared eliminated (Kasai et al., 2007; Takeuchi et al., 2007). It is important to realize that even though declared eliminated, active surveillance for infected snails was maintained in formerly high transmission areas until the early 1990s. Interventions against schistosomiasis included active case detection and treatment, lining canals with cement, drainage and filling swamps, molluscicide, and an improvement in standards of living (Kojima et al., 2007). Parasite research and control programmes were priorities in Japan, and there was close

collaboration between researchers and disease control managers. Indeed, research continually informed policy (Kasai et al., 2007).

Also crucial to the control programmes was the close collaboration between the education and health sectors. Schools were targeted for deworming, and health education was provided by schoolteachers and supported by researchers. This school health-based approach allowed access to the community, which then led to empowerment (Kojima et al., 2007; Kasai et al., 2007).

What can be learned from Japan's engagement in communicable disease control in general, and schistosomiasis control in particular, is the importance of a comprehensive and coordinated programme, with the cooperation of voluntary organizations, national and local governments, and the private sector in educating, motivating and engaging communities, with scientists involved at every stage and thus informing policy (Kojima et al., 2007). Moreover, continued high level surveillance is mandatory after the accomplishment of elimination.

8.11. P.R. China

As was the case in Japan, schistosomiasis in P.R. China is caused by infections with *S. japonicum*. Intermediate hosts are *Oncomelania* snails, which are amphibious and so can colonize many habitats, including lakes, marshes and microhabitats in hilly and mountainous areas (Wang et al., 2008). *S. japonicum* infections are zoonotic with a wide range of mammalian reservoirs, the most important one being water buffalo, which can contribute to up to 90% of egg contamination in an area (McManus et al., 2009). Schistosomiasis is recognized as a public health problem in P.R. China, and its control has received sustained commitment of the central government since the late 1940s (Utzinger et al., 2005; Wang et al., 2008, 2009a,b).

Between the 1950s and the 1980s, efforts focused on transmission control targeting the intermediate host snail, using molluscicides and environmental management of *Oncomelania* habitats, which involved large-scale community participation. Consequently, as snail habitats were reduced, so were human infection rates (Wang et al., 2008, 2009a). Snail control was and continues to be an integral part in the control of schistosomiasis and interruption of transmission in P.R. China (Utzinger et al., 2005).

In the 1990s with the World Bank Loan Project (WBLP), the methodology shifted to morbidity control with praziquantel and health education in line with WHO guidelines (Utzinger et al., 2005; Wang et al., 2008). However, after WBLP terminated, control efforts were reduced, and because WBLP did not permanently change all snail habitats, schistosomiasis re-emerged (Zhou et al., 2005). Consequently, control efforts were identified, implementing an integrated programme with the declared goal to reduce infection prevalence among humans in all endemic areas to below 1% (Wang et al., 2009a,b).

The positive points of P.R. China's schistosomiasis control programme are (i) the sustained, multifaceted national strategy, adapted to different social–ecological systems (Utzinger et al., 2005); (ii) periodic policy reviews to keep the control strategy on track with changing field realities, and adaptation of approaches to prevailing economic, epidemiological and socio-political conditions (Wang et al., 2009b); and (iii) sufficient flexibility in the approach so that it can be revised and adapted as new evidence is revealed and the needs of the control programme change (Utzinger et al., 2005; Wang et al., 2009a).

A lesson to adopt from P.R. China's schistosomiasis campaign is the continued commitment by the relevant authorities, supported by local resources leading to stewardship and responsibility of the local population, the coordinated efforts of dedicated health workers, communities and the government being central to success (McManus et al., 2009; Wang et al., 2009b).

9. Developing an agenda for schistosomiasis elimination

As reviewed in the previous section, elimination of schistosomiasis is possible and, also if not fully documented or certified, extremely low levels of transmission have been achieved in certain areas or countries for each of the three major species: *S. mansoni* in the Americas, *S. haematobium* in Africa and *S. japonicum* in Asia. The examples of successful control programmes show that elimination of schistosomiasis requires a concerted effort and full integration of preventive chemotherapy with the tools of transmission control. Moreover, control programmes must be flexible and adaptable, and must be tailored to local conditions, taking into account the relative importance of behaviour and environment to local patterns of infection. Most importantly, there is now ample evidence to show that schistosomiasis elimination is an achievable and desirable goal. It is clear that once control of morbidity has been achieved by chemotherapy, the focus must shift to curbing transmission rates with a view to elimination (Savioli et al., 2009) using additional interventions in conjunction with treatment programmes.

The prerequisites for schistosomiasis control and elimination include recognition of the public health importance of the disease by both those infected and those in authority, together with the political will and commitment to use local resources, plus a readily available public health infrastructure for the delivery and maintenance of interventions (Engels et al., 2002; Utzinger et al., 2003; Wang et al., 2008), together with a combination of biomedical, educational and engineering strategies and geospatial tools (Utzinger et al., 2009). Elimination programmes must grow within communities; the long-term health and financial benefits of a successful programme must be promoted to assure local ownership and the necessary long-term commitment. Sustainability of control efforts is key to achieving elimination, progressing from a low prevalence situation to elimination will be challenging, but the long-term benefits and financial savings can be significant (Croce et al., 2010).

There is a need for international approval of a definition of schistosomiasis elimination, guidelines as to whether or not elimination has been achieved, and a confirmation/verification process to recognize this status is also required. This is a pressing need for those countries which are well advanced in the schistosomiasis elimination process, as well as for those about to set the elimination goal.

While there is still much to be done in terms of morbidity control across large areas of Africa and elimination is not yet in sight in most places, it is beneficial and timely to look more closely at the tools and methods that must be implemented to achieve elimination. An agenda for the elimination of schistosomiasis would aim to identify the gaps in knowledge, and define the strategies, tools and guidelines that will help national control programmes to step up a gear and move towards elimination. Ten key general points that the schistosomiasis elimination agenda might consider are listed in Box 2.

Such an agenda for schistosomiasis elimination could follow the example of malERA (Alonso et al., 2011) and would complement the existing schistosomiasis research agenda (Colley and Secor, 2007). Research, including investigations pursued by a multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa (CONTRAST), large-scale intervention studies on schistosomiasis control and elimination initiated by the Schistosomiasis Consortium for Operational Research and Evaluation (SCORE), and efforts to develop and validate new diagnostics, drugs and vaccines against

Box 2: Ten key questions for the schistosomiasis elimination agenda

1 At what point should a country switch from control of morbidity to elimination of schistosomiasis? Initially this would involve elimination of morbidity as a public health problem followed by the complete interruption of transmission.
2 What are the long-term health and socio-economic benefits of achieving elimination? How do programmes ensure compliance with elimination measures as infection and morbidity decline during an elimination programme?
3 What additional public health interventions are required to complement preventive chemotherapy? How can snail control, environmental management and behavioural change interventions be integrated into current control programmes?
4 In areas where animal reservoirs of infection are found, what additional steps must be taken to eliminate the disease? Are different control measures needed to eliminate the main schistosome species?
5 Are currently available tools and techniques adequate to monitor a decline and cessation in transmission? Are new diagnostic tests needed to detect light infections in humans with high accuracy? Can the detection of schistosomes within snails help identify hot-spots of transmission?
6 What is the role of surveillance-response platforms within an elimination agenda and what level of post-elimination surveillance is required, and for how long must this continue to verify that transmission has ceased?
7 What measures are required should the disease be re-introduced to combat resurgence of transmission?
8 What are the financial costs involved in achieving and sustaining an elimination programme and what are the realistic time-lines for achieving elimination in different endemic settings?
9 Is there sufficient technical capacity to implement and monitor elimination within endemic countries?
10 Are new diagnostics, drugs and vaccines required to achieve the long-term elimination goals?

schistosomiasis (for which only scarce funding is available at present; Keiser and Utzinger, 2012) is an essential feature in defining the schistosomiasis elimination agenda that must accompany its implementation in the years to come.

Acknowledgements

Many of the ideas presented here arose thanks to funding from the European Union (EU)-funded Specific Targeted Research Project FP6-2004-DEV-3/PL032203 (CONTRAST: http://www.eu-contrast.eu) programme and the Schistosomiasis Consortium for Operational Research and Evaluation (SCORE: http://score.uga.edu) funded through the University of Georgia Research Foundation. S. Knopp was supported by the "Forschungsfonds der Universität Basel" and by a sub-award (no. RR374-053/4787996) from the University of Georgia, which is awarded by the Bill & Melinda Gates Foundation (prime award no. 50816). We are grateful to Dr. Lester Chitsulo from WHO and three anonymous referees for a series of helpful comments and suggestions.

References

Aagaard-Hansen, J., Mwanga, J.R., Bruun, B., 2009. Social science perspectives on schistosomiasis control in Africa: past trends and future directions. Parasitology 136, 1747–1758.
Abbasi, I., King, C.H., Muchiri, E.M., Hamburger, J., 2010. Detection of *Schistosoma mansoni* and *Schistosoma haematobium* DNA by loop-mediated isothermal amplification: identification of infected snails from early prepatency. Am. J. Trop. Med. Hyg. 83, 427–432.
Akinwale, O.P., Kane, R.A., Rollinson, D., Stothard, J.R., Ajayi, M.B., Akande, D.O., Ogungbemi, M.O., Duker, C., Gyang, P.V., Adeleke, M.A., 2011. Molecular approaches to the identification of *Bulinus* species in south-west Nigeria and observations on natural snail infections with schistosomes. J. Helminthol. 85, 283–293.
Al Ghahtani, A.G., Amin, M.A., 2005. Progress achieved in the elimination of schistosomiasis from the Jazan region of Saudi Arabia. Ann. Trop. Med. Parasitol. 99, 483–490.
Al-Madani, A.A., Mahfouz, A.A.R., 1997. Schistosomiasis and other intestinal parasitic infections among Yemenis in Abha district, Saudi Arabia: an epidemiological study. Saudi Med. J. 18, 158–160.
Alarcón de Noya, B., Balzan, C., Arteaga, C., Cesari, I., Noya, O., 1999. The last fifteen years of schistosomiasis in Venezuela: features and evolution. Mem. Inst. Oswaldo Cruz 94, 139–146.
Alarcon de Noya, B., Noya, O., Balzan, C., Cesari, I.M., 1992. New approaches for the control and eradication of schistosomiasis in Venezuela. Mem. Inst. Oswaldo Cruz 87 (Suppl. 4), 227–231.
Alonso, P.L., Brown, G., Arevalo-Herrera, M., Binka, F., Chitnis, C., Collins, F., Doumbo, O.K., Greenwood, B., Hall, B.F., Levine, M.M., Mendis, K., Newman, R.D., Plowe, C.V., Rodríguez, M.H., Sinden, R., Slutsker, L., Tanner, M., 2011. A research agenda to underpin malaria eradication. PLoS Med. 8, e1000406.
Amarir, F., El Mansouri, B., Fellah, H., Sebti, F., Mohammed, L., Handali, S., Wilkins, P., El Idrissi, A.L., Sadak, A., Rhajaoui, M., 2011. National serologic survey of haematobium schistosomiasis in Morocco: evidence for elimination. Am. J. Trop. Med. Hyg. 84, 15–19.
Annon., 1919. Bilharziasis: its prevention and treatment. Lancet 193, 1032.
Asaolu, S.O., Ofoezie, I.E., 2003. The role of health education and sanitation in the control of helminth infections. Acta Trop. 86, 283–294.
Augusto, G., Magnussen, P., Kristensen, T.K., Appleton, C.C., Vennervald, B.J., 2009. The influence of transmission season on parasitological cure rates and intensity of infection after praziquantel treatment of *Schistosoma haematobium*-infected schoolchildren in Mozambique. Parasitology 136, 1771–1779.
Barakat, R., el Masry, A.G., Farghaly, A., el Morshidy, H.N., elSayed, M.K., Husein, M.H., Miller, F.D., 1995. Impact of population-based selective chemotherapy on prevalence and intensity of *Schistosoma mansoni* infections in the Nile Delta: Kafr El Sheikh. Trop. Geogr. Med. 47, 266–270.
Bartram, J., Cairncross, S., 2010. Hygiene, sanitation, and water: forgotten foundations of health. PLoS Med. 7, e1000367.
Ben Hariz, M., Ben Farhat, L., Hlioui, S., Chourou, O., Essafi-Kallel, K., Mahjoub, A., Chaker, E., Ben Ammar, B., Maherzi, A., 2007. La bilharziose urinaire: à propos de 9 cas importés. Tunis. Med. 85, 150–154.
Bergquist, R., 2001. Strategies for control of infection and disease: current practice and future potential. In: Mahmoud, A.A.F. (Ed.), Schistosomiasis. Imperial College Press, London, pp. 413–469.
Bergquist, R., Johansen, M.V., Utzinger, J., 2009. Diagnostic dilemmas in helminthology: what tools to use and when? Trends Parasitol. 25, 151–156.
Bonfoh, B., Raso, G., Koné, I., Dao, D., Girardin, O., Cissé, G., Zinsstag, J., Utzinger, J., Tanner, M., 2011. Research in a war zone. Nature 474, 569–571.
Brooker, S., Kabatereine, N.B., Gyapong, J.O., Stothard, J.R., Utzinger, J., 2009. Rapid mapping of schistosomiasis and other neglected tropical diseases in the context of integrated control programmes in Africa. Parasitology 136, 1707–1718.
Brooker, S., Whawell, S., Kabatereine, N.B., Fenwick, A., Anderson, R.M., 2004. Evaluating the epidemiological impact of national control programmes for helminths. Trends Parasitol. 20, 537–545.
Chen, M.G., 2005. Use of praziquantel for clinical treatment and morbidity control of schistosomiasis japonica in China: a review of 30 years' experience. Acta Trop. 96, 168–176.
Clements, A.C.A., Firth, S., Dembelé, R., Garba, A., Touré, S., Sacko, M., Landouré, A., Bosqué-Oliva, E., Barnett, A.G., Brooker, S., Fenwick, A., 2009. Use of Bayesian geostatistical prediction to estimate local variations in *Schistosoma haematobium* infection in western Africa. Bull. World Health Org. 87, 921–929.
Colley, D.G., Secor, W.E., 2007. A schistosomiasis research agenda. PLoS Negl. Trop. Dis. 1, e32.
Coulibaly, J.T., Knopp, S., N'Guessan, N.A., Silué, K.D., Fürst, T., Lohourignon, L.K., Brou, J.K., N'Gbesso, Y.K., Vounatsou, P., N'Goran, E.K., Utzinger, J., 2011. Accuracy of urine circulating cathodic antigen (CCA) test for *Schistosoma mansoni* diagnosis in different settings of Côte d'Ivoire. PLoS Negl. Trop. Dis. 5, e1384.
Croce, D., Porazzi, E., Foglia, E., Restelli, U., Sinuon, M., Socheat, D., Montresor, A., 2010. Cost-effectiveness of a successful schistosomiasis control programme in Cambodia (1995-2006). Acta Trop. 113, 279–284.
Curtale, F., Mohamed, M.Y., Youssef, Z.N., 2010. Comprehensive primary health care, a viable strategy for the elimination of schistosomiasis. Trans. R. Soc. Trop. Med. Hyg. 104, 70–72.
Danso-Appiah, A., Utzinger, J., Liu, J., Olliaro, P., 2008. Drugs for treating urinary schistosomiasis. Cochrane Database Syst. Rev. C, CD000053.
Davis, A., 2009. Schistosomiasis. In: Cook, G.C., Zumla, A.I. (Eds.), Manson's Tropical Diseases. Saunders Elsevier, pp. 1425–1460.
Deelder, A.M., Qian, Z.L., Kremsner, P.G., Acosta, L., Rabello, A.L., Enyong, P., Simarro, P.P., van Etten, E.C., Krijger, F.W., Rotmans, J.P., Fillie, Y.E., de Jonge, N., Agnew, A.M., van Lieshout, L., 1994. Quantitative diagnosis of *Schistosoma* infections by measurement of circulating antigens in serum and urine. Trop. Geogr. Med. 46, 233–238.
de Vlas, S.J., Gryseels, B., 1992. Underestimation of *Schistosoma mansoni* prevalences. Parasitol. Today 8, 274–277.

Dhunputh, J., 1994. Progress in the control of schistosomiasis in Mauritius. Trans. R. Soc. Trop. Med. Hyg. 88, 507–509.

Doenhoff, M.J., Chiodini, P.L., Hamilton, J.V., 2004. Specific and sensitive diagnosis of schistosome infection: can it be done with antibodies? Trends Parasitol. 20, 35–39.

Doenhoff, M.J., Hagan, P., Cioli, D., Southgate, V., Pica-Mattoccia, L., Botros, S., Coles, G., Tchuem Tchuenté, L.A., Mbaye, A., Engels, D., 2009. Praziquantel: its use in control of schistosomiasis in sub-Saharan Africa and current research needs. Parasitology 136, 1825–1835.

Doumenge, J.P., Mott, K.E., Cheung, C., Villenave, D., Chapuis, O., Perrin, M.F., Reaud-Thomas, G., 1987. Atlas of the Global Distribution of Schistosomiasis. Talence, CEGET-CNRS; Geneve, OMS/WHO, 400 pp.

Dowdle, W.R., 1998. The principles of disease elimination and eradication. Bull. World Health Org. 76, 22–25.

el Malatawy, A., el Habashy, A., Lechine, N., Dixon, H., Davis, A., Mott, K.E., 1992. Selective population chemotherapy among schoolchildren in Beheira governorate: the UNICEF/Arab Republic of Egypt/WHO Schistosomiasis Control Project. Bull. World Health Org. 70, 47–56.

El Khoby, T., Galal, N., Fenwick, A., 1998. The USAID/Government of Egypt's schistosomiasis research project (SRP). Parasitolol. Today 14, 92–96.

EMRO/WHO, 2007. Inter-Country Meeting on Strategies to Eliminate Schistosomiasis from the Eastern Mediterranean Region , Muscat, Oman, p. 34.

Engels, D., Chitsulo, L., Montresor, A., Savioli, L., 2002. The global epidemiological situation of schistosomiasis and new approaches to control and research. Acta Trop. 82, 139–146.

Esrey, S.A., Potash, J.B., Roberts, L., Shiff, C., 1991. Effects of improved water supply and sanitation on ascariasis, diarrhoea, dracunculiasis, hookworm infection, schistosomiasis, and trachoma. Bull. World Health Org. 69, 609–621.

Fenwick, A., Rollinson, D., Southgate, V., 2006. Implementation of human schistosomiasis control: challenges and prospects. Adv. Parasitol. 61, 567–622.

Fenwick, A., Savioli, L., 2011. Schistosomiasis elimination. Lancet Infect. Dis. 11, 346.

Fenwick, A., Savioli, L., Engels, D., Bergquist, N.R., Todd, M.H., 2003. Drugs for the control of parasitic diseases: current status and development in schistosomiasis. Trends Parasitol. 19, 509–515.

Fenwick, A., Webster, J.P., Bosque-Oliva, E., Blair, L., Fleming, F.M., Zhang, Y., Garba, A., Stothard, J.R., Gabrielli, A.F., Clements, A.C.A., Kabatereine, N.B., Toure, S., Dembele, R., Nyandindi, U., Mwansa, J., Koukounari, A., 2009. The Schistosomiasis Control Initiative (SCI): rationale, development and implementation from 2002–2008. Parasitology 136, 1719–1730.

Ferguson, F.F., Richards, C.S., Sebastian, S.T., Buchanan, I.C., 1960. Natural abatement of schistosomiasis in St Kitts, British West Indies. Public Health 74, 261–265.

Gholamreza, M., Jafar, M., Allahbedasht, M., Nikkhooy, A., Mohammad, K.A., Rokni, M.B., 2008. Survey of urinary schistosomiasis in Iran. Pak. J. Med. Sci. 24, 857–860.

Gomes, L.I., Dos Santos Marques, L.H., Enk, M.J., de Oliveira, M.C., Coelho, P.M., Rabello, A., 2010. Development and evaluation of a sensitive PCR-ELISA system for detection of *Schistosoma* infection in feces. PLoS Negl. Trop. Dis. 4, e664.

Gray, D.J., McManus, D.P., Li, Y., Williams, G.M., Bergquist, R., Ross, A.G., 2010. Schistosomiasis elimination: lessons from the past guide the future. Lancet Infect. Dis. 10, 733–736.

Hamburger, J., He, N., Xin, X.Y., Ramzy, R.M., Jourdane, J., Ruppel, A., 1998. A polymerase chain reaction assay for detecting snails infected with bilharzia parasites (*Schistosoma mansoni*) from very early prepatency. Am. J. Trop. Med. Hyg. 59, 872–876.

Hamburger, J., He-Na Abbasi, I., Ramzy, R.M., Jourdane, J., Ruppel, A., 2001. Polymerase chain reaction assay based on a highly repeated sequence of *Schistosoma haematobium*: a potential tool for monitoring schistosome-infested water. Am. J. Trop. Med. Hyg. 65, 907–911.

Hamburger, J., Hoffman, O., Kariuki, H.C., Muchiri, E.M., Ouma, J.H., Koech, D.K., Sturrock, R.F., King, C.H., 2004. Large-scale, polymerase chain reaction-based surveillance of *Schistosoma haematobium* DNA in snails from transmission sites in coastal Kenya: a new tool for studying the dynamics of snail infection. Am. J. Trop. Med. Hyg. 71, 765–773.

Holveck, J.C., Ehrenberg, J.P., Ault, S.K., Rojas, R., Vasquez, J., Cerqueira, M.T., Ippolito-Shepherd, J., Genovese, M.A., Periago, M.R., 2007. Prevention, control, and elimination of neglected diseases in the Americas: pathways to integrated, inter-programmatic, inter-sectoral action for health and development. BMC Public Health 7, 6.

Hotez, P.J., Engels, D., Fenwick, A., Savioli, L., 2010. Africa is desperate for praziquantel. Lancet 376, 496–498.

Ibironke, O.A., Phillips, A.E., Garba, A., Lamine, S.M., Shiff, C., 2011. Diagnosis of *Schistosoma haematobium* by detection of specific DNA fragments from filtered urine samples. Am. J. Trop. Med. Hyg. 84, 998–1001.

Ikeda, N., Saito, E., Kondo, N., Inoue, M., Ikeda, S., Satoh, T., Wada, K., Stickley, A., Katanoda, K., Mizoue, T., Noda, M., Iso, H., Fujino, Y., Sobue, T., Tsugane, S., Naghavi, M., Ezzati, M., Shibuya, K., 2011. What has made the population of Japan healthy? Lancet 378, 1094–1105.

Jobin, W., 1999. Dams and Disease: Ecological Design and Health Impacts of Large Dams, Canals and Irrigation Systems. E & FN Spon, London and New York.

Jordan, P., 1985. Schistosomiasis: The St. Lucia Project. Cambridge University Press, U.K.

Kasai, T., Nakatani, H., Takeuchi, T., Crump, A., 2007. Research and control of parasitic diseases in Japan: current position and future perspectives. Trends Parasitol. 23, 230–235.

Katz, N., 1998. Schistosomiasis control in Brazil. Mem. Inst. Oswaldo Cruz 93 (Suppl. 1), 33–35.

Keiser, J., Utzinger, J., 2012. Antimalarials in the treatment of schistosomiasis. Curr. Pharmaceut. Design 18, 3531–3538.

King, C.H., 2009. Toward the elimination of schistosomiasis. N. Engl. J. Med. 360, 106–109.

King, C.H., 2010. Parasites and poverty: the case of schistosomiasis. Acta Trop. 113, 95–104.

King, C.H., Dickman, K., Tisch, D.J., 2005. Reassessment of the cost of chronic helmintic infection: a meta-analysis of disability-related outcomes in endemic schistosomiasis. Lancet 365, 1561–1569.

King, C.H., Sturrock, R.F., Kariuki, H.C., Hamburger, J., 2006. Transmission control for schistosomiasis–why it matters now. Trends Parasitol. 22, 575–582.

King, C.H., Olbrych, S.K., Soon, M., Singer, M.E., Carter, J., Colley, D.G., 2011. Utility of repeated praziquantel dosing in the treatment of schistosomiasis in high-risk communities in Africa: a systematic review. PLoS Negl. Trop. Dis. 5, e1321.

Knopp, S., Speich, B., Hattendorf, J., Rinaldi, L., Mohammed, K.A., Khamis, I.S., Mohammed, A.S., Albonico, M., Rollinson, D., Marti, H., Utzinger, J., 2011. Diagnostic accuracy of Kato-Katz and FLOTAC for assessing anthelmintic drug efficacy. PLoS Negl. Trop. Dis. 5, e1036.

Knopp, S., Stothard, J.R., Rollinson, D., Mohammed, K.A., Khamis, I.S., Marti, H., Utzinger, J., 2013. From morbidity control to transmission control: time to change tactics against helminths in Unguja, Tanzania. Acta Trop 128, 412–422.

Kojima, S., Aoki, Y., Ohta, N., Tateno, S., Takeuchi, T., 2007. School-health-based parasite control initiatives: extending successful Japanese policies to Asia and Africa. Trends Parasitol. 23, 54–57.

Kurup, R., Hunjan, G.S., 2010. Epidemiology and control of schistosomiasis and other intestinal parasitic infections among school children in three rural villages of south Saint Lucia. J. Vector Borne Dis. 47, 228–234.

Laamrani, H., Mahjour, J., Madsen, H., Khallaayoune, K., Gryseels, B., 2000. *Schistosoma haematobium* in Morocco: moving from control to elimination. Parasitol. Today 16, 257–260.

Lansdown, R., Ledward, A., Hall, A., Issae, W., Yona, E., Matulu, J., Mweta, M., Kihamia, C., Nyandindi, U., Bundy, D., 2002. Schistosomiasis, helminth infection and health education in Tanzania: achieving behaviour change in primary schools. Health Educ. Res. 17, 425–433.

Lardans, V., Dissous, C., 1998. Snail control strategies for reduction of schistosomiasis transmission. Parasitol. Today 14, 413–417.

Lengeler, C., Utzinger, J., Tanner, M., 2002a. Questionnaires for rapid screening of schistosomiasis in sub-Saharan Africa. Bull. World Health Org. 80, 235–242.

Lengeler, C., Utzinger, J., Tanner, M., 2002b. Screening for schistosomiasis with questionnaires. Trends Parasitol. 18, 375–377.

Liu, R., Dong, H.F., Guo, Y., Zhao, Q.P., Jiang, M.S., 2011. Efficacy of praziquantel and artemisinin derivatives for the treatment and prevention of human schistosomiasis: a systematic review and meta-analysis. Parasit. Vectors 4, 201.

Manson, P., 1902. Report of a case of bilharzia from the West Indies. J. Trop. Med. 5, 384.

Massoud, J., Chu, K.Y., Arfaa, F., 1969. Field trials of Bayluscide, sodium pentachlorophenate and copper sulphate in standing waters in Iran. Ann. Trop. Med. Parasitol. 63, 189–194.

Massoud, J., Arfaa, F., Farahmandian, I., Ardalan, A., Mansoorian, A., 1982. Progress in the national schistosomiasis control programme of Iran. Bull. World Health Org. 60, 577–582.

McCullough, F.S., Gayral, P., Duncan, J., Christie, J.D., 1980. Molluscicides in schistosomiasis control. Bull. World Health Org. 58, 681–689.

McManus, D.P., Gray, D.J., Li, Y., Feng, Z., Williams, G.M., Stewart, D., Rey-Ladino, J., Ross, A.G., 2010. Schistosomiasis in the People's Republic of China: the era of the Three Gorges Dam. Clin. Microbiol. Rev. 23, 442–466.

McManus, D.P., Li, Y., Gray, D.J., Ross, A.G., 2009. Conquering snail fever: schistosomiasis and its control in China. Expert Rev. Anti. Infect. Ther. 7, 473–485.

Melo, F.L., Gomes, A.V., Barbosa, C.S., Werkhauser, R.P., Abath, F.G.C., 2006. Development of molecular approaches for the identification of transmission sites of schistosomiasis. Trans. R. Soc. Trop. Med. Hyg. 100, 1049–1055.

Miguel, E., Kremer, M., 2004. Worms: identifying impacts on education and health in the presence of treatment externalities. Econometrica 72, 159–217.

Molyneux, D.H., Hopkins, D.R., Zagaria, N., 2004. Disease eradication, elimination and control: the need for accurate and consistent usage. Trends Parasitol. 20, 347–351.

Mombeni, H., Kheradmand, A., 2005. *Schistosoma haematobium* control in Khoozestan province in Iran: prosperities and failures. Med. J. Islamic Rep. Iran 19, 19–22.

Muth, S., Sayasone, S., Odermatt-Biays, S., Phompida, S., Duong, S., Odermatt, P., 2010. *Schistosoma mekongi* in Cambodia and Lao People's Democratic Republic. Adv. Parasitol. 72, 179–203.

Ndekha, A., Hansen, E.H., Mølgaard, P., Woelk, G., Furu, P., 2003. Community participation as an interactive learning process: experiences from a schistosomiasis control project in Zimbabwe. Acta Trop. 85, 325–338.

Nock, I.H., Aken'Ova, T., Galadima, M., 2006. Deworming: adding public health education to the equation. Trends Parasitol. 22, 7–8.

Olliaro, P.L., Vaillant, M.T., Belizario, V.J., Lwambo, N.J., Ouldabdallahi, M., Pieri, O.S., Amarillo, M.L., Kaatano, G.M., Diaw, M., Domingues, A.C., Favre, T.C., Lapujade, O., Alves, F., Chitsulo, L., 2011. A multicentre randomized controlled trial of the efficacy and safety of single-dose praziquantel at 40 mg/kg vs. 60 mg/kg for treating intestinal schistosomiasis in the Philippines, Mauritania, Tanzania and Brazil. PLoS Negl. Trop. Dis. 5, e1165.

Pagès, J.R., Jourdane, J., Southgate, V.R., Tchuem Tchuenté, L.A., 2003. Reconnaissance de deux espèces jumelles au sein du taxon *Schistosoma intercalatum* Fisher, 1934, agent de la schistosomose humaine rectale en Afrique, Description de

Schistosoma guineensis n. sp. In: Combes, C., Jourdane, J. (Eds.), Taxonomy, Ecology and Evolution of Metazoan Parasites. Presses Universitaires de Perpignan, Perpignan.
PAHO/WHO, 2007. PAHO/WHO Preparatory Meeting on Epidemiological Data Needed to Plan Elimination of Schistosomiasis in the Caribbean. Pan American Health Organization, Grenada.
Parker, M., Allen, T., Hastings, J., 2008. Resisting control of neglected tropical diseases: dilemmas in the mass treatment of schistosomiasis and soil-transmitted helminths in north-west Uganda. J. Biosoc. Sci. 40, 161–181.
Pointier, J.P., Jourdane, J., 2000. Biological control of the snail hosts of schistosomiasis in areas of low transmission: the example of the Caribbean area. Acta Trop. 77, 53–60.
Pontes, L.A., Oliveira, M.C., Katz, N., Dias-Neto, E., Rabello, A.N.A., 2003. Comparison of a polymerase chain reaction and the Kato-Katz technique for diagnosing infection with *Schistosoma mansoni*. Am. J. Trop. Med. Hyg. 68, 652–656.
Reis, D.C., Kloos, H., King, C., Quites, H.F., Matoso, L.F., Coelho, K.R., Gazzinelli, A., 2010. Accessibility to and utilisation of schistosomiasis-related health services in a rural area of state of Minas Gerais, Brazil. Mem. Inst. Oswaldo Cruz 105, 587–597.
Rollinson, D., 2009. A wake up call for urinary schistosomiasis: reconciling research effort with public health importance. Parasitology 136, 1593–1610.
Rollinson, D., Wright, C.A., 1984. Population studies on *Bulinus cernicus* from Mauritius. Malacologies 25, 447–463.
Ross, A.G.P., Bartley, P.B., Sleigh, A.C., Olds, G.R., Li, Y.S., Williams, G.M., McManus, D.P., 2002. Schistosomiasis. N. Engl. J. Med. 346, 1212–1220.
Rudge, J.W., Stothard, J.R., Basáñez, M.G., Mgeni, A.F., Khamis, I.S., Khamis, A.N., Rollinson, D., 2008. Micro-epidemiology of urinary schistosomiasis in Zanzibar: local risk factors associated with distribution of infections among schoolchildren and relevance for control. Acta Trop. 105, 45–54.
Sabah, A.A., Fletcher, C., Webbe, G., Doenhoff, M.J., 1986. *Schistosoma mansoni*: chemotherapy of infections of different ages. Exp. Parasitol. 61, 294–303.
Sarvel, A.K., Oliveira, A.A., Silva, A.R., Lima, A.C., Katz, N., 2011. Evaluation of a 25-year-program for the control of schistosomiasis mansoni in an endemic area in Brazil. PLoS Negl. Trop. Dis. 5, e990.
Savioli, L., Gabrielli, A.F., Montresor, A., Chitsulo, L., Engels, D., 2009. Schistosomiasis control in Africa: 8 years after World Health Assembly Resolution 54.19. Parasitology 136, 1677–1681.
Sayasone, S., Mak, T.K., Vanmany, M., Rasphone, O., Vounatsou, P., Utzinger, J., Akkhavong, K., Odermatt, P., 2011. Helminth and intestinal protozoa infections, multiparasitism and risk factors in Champasack province, Lao People's Democratic Republic. PLoS Negl. Trop. Dis. 5, e1037.
Schneider, M.C., Aguilera, X.P., da Silva, J.B., Ault, S.K., Najera, P., Requejo, J.M.R., Nicholls, R.S., Yadon, Z., Silva, J.C., Leanes, L.F., Periago, M.P., 2011. Elimination of neglected diseases in Latin America and the Caribbean: a mapping of selected diseases. PLoS Negl. Trop. Dis. 5, e964.
Schur, N., Hürlimann, E., Stensgaard, A.S., Chimfwembe, K., Mushinge, G., Simoonga, C., Kabatereine, N.B., Kristensen, T.K., Utzinger, J., Vounatsou, P., 2013. Spatially explicit *Schistosoma* infection risk in eastern Africa based on Bayesian geostatistical modelling. Acta Trop. 128, 365–377.
Shane, H.L., Verani, J.R., Abudho, B., Montgomery, S.P., Blackstock, A.J., Mwinzi, P.N., Butler, S.E., Karanja, D.M., Secor, W.E., 2011. Evaluation of urine CCA assays for detection of *Schistosoma mansoni* infection in western Kenya. PLoS Negl. Trop. Dis. 5, e951.
Shati, A.A., 2009. Factors affecting the prevalence of human schistosomiaisis in Aseer region, Saudi Arabia. J. Biolog. Sci. 9, 815–819.
Simoonga, C., Utzinger, J., Brooker, S., Vounatsou, P., Appleton, C.C., Stensgaard, A.S., Olsen, A., Kristensen, T.K., 2009. Remote sensing, geographical information system and spatial analysis for schistosomiasis epidemiology and ecology in Africa. Parasitology 136, 1683–1693.
Singer, B.H., Castro, M.C., 2007. Bridges to sustainable tropical health. Proc. Natl. Acad. Sci. U.S.A 104, 16038–16043.
Sinuon, M., Tsuyuoka, R., Socheat, D., Odermatt, P., Ohmae, H., Matsuda, H., Montresor, A., Palmer, K., 2007. Control of *Schistosoma mekongi* in Cambodia: results of eight years of control activities in the two endemic provinces. Trans. R. Soc. Trop. Med. Hyg. 101, 34–39.
Smits, H.L., 2009. Prospects for the control of neglected tropical diseases by mass drug administration. Expert Rev. Anti. Infect. Ther. 7, 37–56.
Southgate, V.R., 1997. Schistosomiasis in the Senegal River Basin: before and after the construction of the dams at Diama, Senegal and Manantali, Mali and future prospects. J Helminthol. 71, 125–132.
Steinmann, P., Keiser, J., Bos, R., Tanner, M., Utzinger, J., 2006. Schistosomiasis and water resources development: systematic review, meta-analysis, and estimates of people at risk. Lancet Infect. Dis. 6, 411–425.
Stothard, J.R., 2009. Improving control of African schistosomiasis: towards effective use of rapid diagnostic tests within an appropriate disease surveillance model. Trans. R. Soc. Trop. Med. Hyg. 103, 325–332.
Stothard, J.R., Chitsulo, L., Kristensen, T.K., Utzinger, J., 2009a. Control of schistosomiasis in sub-Saharan Africa: progress made, new opportunities and remaining challenges. Parasitology 136, 1665–1675.
Stothard, J.R., French, M.D., Khamis, I.S., Basáñez, M.G., Rollinson, D., 2009b. The epidemiology and control of urinary schistosomiasis and soil-transmitted helminthiasis in schoolchildren on Unguja Island, Zanzibar. Trans. R. Soc. Trop. Med. Hyg. 103, 1031–1044.
Stothard, J.R., Mook, P., Mgeni, A.F., Khamis, I.S., Khamis, A.N., Rollinson, D., 2006. Control of urinary schistosomiasis on Zanzibar (Unguja Island): a pilot evaluation of the educational impact of the Juma na Kichocho health booklet within primary schools. Mem. Inst. Oswaldo Cruz 101 (Suppl. 1), 119–124.
Stothard, J.R., Sousa-Figueiredo, J.C., Standley, C., Van Dam, G.J., Knopp, S., Utzinger, J., Ameri, H., Khamis, A.N., Khamis, I.S., Deelder, A.M., Mohammed, K.A., Rollinson, D., 2009c. An evaluation of urine-CCA strip test and fingerprick blood SEA-ELISA for detection of urinary schistosomiasis in schoolchildren in Zanzibar. Acta Trop. 111, 64–70.
Sturrock, R.F., 1995. Current concepts of snail control. Mem. Inst. Oswaldo Cruz 90, 241–248.
Takeuchi, T., Nozaki, S., Crump, A., 2007. Past Japanese successes show the way to accomplish future goals. Trends Parasitol. 23, 260–267.
Tallo, V.L., Carabin, H., Alday, P.P., Balolong, E., Olveda, R.M., McGarvey, S.T., 2008. Is mass treatment the appropriate schistosomiasis elimination strategy? Bull. World Health Org. 86, 765–771.
Tchuem Tchuenté, L.A., Southgate, V.R., Njiokou, F., Njiné, T., Kouemeni, L.E., Jourdane, J., 1997. The evolution of schistosomiasis at Loum, Cameroon: replacement of *Schistosoma intercalatum* by *S. haematobium* through introgressive hybridisation. Trans. R. Soc. Trop. Med. Hyg. 91, 664–665.
Tchuem Tchuenté, L.A., Southgate, V.R., Webster, B.L., De Bont, J., Vercruysse, J., 2001. Impact of installation of a water pump on schistosomiasis transmission in a focus of Cameroon. Trans. R. Soc. Trop. Med. Hyg. 95, 255–256.
Tchuem Tchuenté, L.A., Ngassam, R.I.K., Sumo, L., Ngassam, P., Noumedem, C.D., Nzu, D.D.L., Dankoni, E., Kenfack, C.M., Gipwe, N.F., Akame, J., Tarini, A., Zhang, Y., Angwafo, F.F.III, 2012. Mapping of schistosomiasis and soil-transmitted helminthiasis in the regions of Centre, East and West Cameroon. PLoS Negl. Trop. Dis. 6, e1553.
Tchuem Tchuenté, L.A., Southgate, V.R., Jourdane, J., Webster, B.L., Vercruysse, J., 2003. *Schistosoma intercalatum*: an endangered species in Cameroon? Trends Parasitol. 19, 389–393.
ten Hove, R.J., Verweij, J.J., Vereecken, K., Polman, K., Dieye, L., van Lieshout, L., 2008. Multiplex real-time PCR for the detection and quantification of *Schistosoma mansoni* and *S. haematobium* infection in stool samples collected in northern Senegal. Trans. R. Soc. Trop. Med. Hyg. 102, 179–185.
Touré, S., Zhang, Y., Bosque-Oliva, E., Ky, C., Ouedraogo, A., Koukounari, A., Gabrielli, A.F., Bertrand, S., Webster, J.P., Fenwick, A., 2008. Two-year impact of single praziquantel treatment on infection in the national control programme on schistosomiasis in Burkina Faso. Bull. World Health Org. 86, 780–787.
Urbani, C., Sinoun, M., Socheat, D., Pholsena, K., Strandgaard, H., Odermatt, P., Hatz, C., 2002. Epidemiology and control of mekongi schistosomiasis. Acta Trop. 82, 157–168.
Utzinger, J., N'Goran, E.K., Tanner, M., Lengeler, C., 2000. Simple anamnestic questions and recalled water-contact patterns for self-diagnosis of *Schistosoma mansoni* infection among schoolchildren in western Côte d'Ivoire. Am. J. Trop. Med. Hyg. 62, 649–655.
Utzinger, J., Booth, M., N'Goran, E.K., Müller, I., Tanner, M., Lengeler, C., 2001. Relative contribution of day-to-day and intra-specimen variation in faecal egg counts of *Schistosoma mansoni* before and after treatment with praziquantel. Parasitology 122, 537–544.
Utzinger, J., Bergquist, R., Xiao, S.H., Singer, B.H., Tanner, M., 2003. Sustainable schistosomiasis control: the way forward. Lancet 362, 1932–1934.
Utzinger, J., Zhou, X.N., Chen, M.G., Bergquist, R., 2005. Conquering schistosomiasis in China: the long march. Acta Trop. 96, 69–96.
Utzinger, J., Raso, G., Brooker, S., de Savigny, D., Tanner, M., Ørnbjerg, N., Singer, B.H., N'Goran, E.K., 2009. Schistosomiasis and neglected tropical diseases: towards integrated and sustainable control and a word of caution. Parasitology 136, 1859–1874.
Utzinger, J., N'Goran, E.K., Caffrey, C.R., Keiser, J., 2011. From innovation to application: social-ecological context, diagnostics, drugs and integrated control of schistosomiasis. Acta Trop. 120 (Suppl. 1), S121–S137.
van der Werf, M.J., de Vlas, S.J., Brooker, S., Looman, C.W.N., Nagelkerke, N.J.D., Habbema, J.D.F., Engels, D., 2003. Quantification of clinical morbidity associated with schistosome infection in sub-Saharan Africa. Acta Trop. 86, 125–139.
Wang, L.D., Chen, H.G., Guo, J.G., Zeng, X.J., Hong, X.L., Xiong, J.J., Wu, X.H., Wang, X.H., Wang, L.Y., Xia, G., Hao, Y., Chin, D.P., Zhou, X.N., 2009a. A strategy to control transmission of *Schistosoma japonicum* in China. N. Engl. J. Med. 360, 121–128.
Wang, L.D., Guo, J.G., Wu, X.H., Chen, H.G., Wang, T.P., Zhu, S.P., Zhang, Z.H., Steinmann, P., Yang, G.J., Wang, S.P., Wu, Z.D., Wang, L.Y., Hao, Y., Bergquist, R., Utzinger, J., Zhou, X.N., 2009b. China's new strategy to block *Schistosoma japonicum* transmission: experiences and impact beyond schistosomiasis. Trop. Med. Int. Health 14, 1475–1483.
Wang, L.D., Utzinger, J., Zhou, X.N., 2008. Schistosomiasis control: experiences and lessons from China. Lancet 372, 1793–1795.
Wang, T.P., Johansen, M.V., Zhang, S.Q., Wang, F.F., Wu, W.D., Zhang, G.H., Pan, X.P., Ju, Y., Ørnbjerg, N., 2005. Transmission of *Schistosoma japonicum* by humans and domestic animals in the Yangtze River valley, Anhui province China. Acta Trop. 96, 198–204.
WHO, 2002. Prevention and control of schistosomiasis and soil-transmitted helminthiasis: report of a WHO expert committee. WHO Tech. Rep. Ser. 912, 1–57.
WHO, 2006. Preventive Chemotherapy in Human Helminthiasis: Coordinated Use of Anthelminthic Drugs in Control Interventions: A Manual For Health Professionals and Programme Managers. World Health Organization, Geneva.
WHO, 2009. Elimination of Schistosomiasis from Low Transmission Areas. Report of a WHO Informal Consultation. World Health Organization, Brazil.

WHO, 2010. First WHO Report on Neglected Tropical Diseases 2010: Working to Overcome the Global Impact of Neglected Tropical Diseases. World Health Organization, Geneva.

WHO, 2011. Schistosomiasis number of people treated 2009. Wkly. Epidemiol. Rec. 86, 73–80.

Wichmann, D., Panning, M., Quack, T., Kramme, S., Burchard, G.D., Grevelding, C., Drosten, C., 2009. Diagnosing schistosomiasis by detection of cell-free parasite DNA in human plasma. PLoS Negl. Trop. Dis. 3, e422.

Woolhouse, M.E.J., Etard, J.F., Dietz, K., Ndhlovu, P.D., Chandiwana, S.K., 1998. Heterogeneities in schistosome transmission dynamics and control. Parasitology 117, 475–482.

Yekutiel, P., 1981. Lessons from the big eradication campaigns. World Health Forum 2, 465–490.

Ziegelbauer, K., Speich, B., Mäusezahl, D., Bos, R., Keiser, J., Utzinger, J., 2012. Effect of sanitation on soil-transmitted helminth infection: systematic review and meta-analysis. PLoS Med. 9, e1001162.

Zhang, Y., Koukounari, A., Kabatereine, N., Fleming, F., Kazibwe, F., Tukahebwa, E., Stothard, J.R., Webster, J.P., Fenwick, A., 2007. Parasitological impact of 2-year preventive chemotherapy on schistosomiasis and soil-transmitted helminthiasis in Uganda. BMC Med. 5, 27.

Zhang, Z., Jiang, Q., 2011. Schistosomiasis elimination. Lancet Infect. Dis. 11, 345.

Zhou, X.N., Wang, L.Y., Chen, M.G., Wu, X.H., Jiang, Q.W., Chen, X.Y., Zheng, J., Utzinger, J., 2005. The public health significance and control of schistosomiasis in China–then and now. Acta Trop. 96, 97–105.