



## Current Opinion

## Schistosomiasis elimination by 2020 or 2030?



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## ABSTRACT

Schistosomiasis has been a public health burden in a number of countries across the globe for centuries and probably beyond. The World Health Organization and partners are currently preparing to move towards elimination of this disease. However, given the historical challenges and barriers to ridding areas of this water-borne parasite infection, we question whether the current targets for eliminating schistosomiasis as a global health problem can be achieved.

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Three species of schistosomiasis have been a health scourge globally; in China, the Philippines and Japan (*Schistosoma japonicum*), in Egypt, Sudan and in sub-Saharan Africa (*Schistosoma haematobium* and *Schistosoma mansoni*), and in parts of the Caribbean and South America, particularly Brazil (*S. mansoni*) (Gryseels et al., 2006). By 2001, however, the World Health Organization (WHO) was calling for countries to be implementing programmes to control morbidity caused by schistosomiasis, and by 2012, the World Health Assembly (WHA) endorsed the elimination of schistosomiasis as a public health problem ([http://www.who.int/neglected\\_diseases/mediacentre/WHA\\_65.21\\_Eng.pdf](http://www.who.int/neglected_diseases/mediacentre/WHA_65.21_Eng.pdf)). This was in part motivated by the fact that Japan had already eliminated schistosomiasis, and that China, Egypt and parts of South America had greatly reduced prevalence by a combination of treatment and improved socio-economic conditions (Rollinson et al., 2013). Additionally however, this was based on findings that show that treatment reduces common serious complications of schistosomiasis such as periportal fibrosis and hepatomegaly in intestinal schistosomiasis (Homeida et al., 1988; Wu et al., 2015) and vesico-urethero-nephropathy in urogenital infection (Rasendramino et al., 1998; Subramanian et al., 1999) in both children and adults (Hatz et al., 1998; Magak et al., 2015). The effect of anti-schistosomal treatment on genital morbidity in men and women

is still not yet well understood (Leutscher et al., 2000; Kjetland et al., 2006).

For other neglected tropical diseases (NTDs), lymphatic filariasis (LF), onchocerciasis and trachoma in particular, the year 2020 was seen as a feasible target to reach elimination of transmission (WHO, 2012) ([http://www.who.int/neglected\\_diseases/NTD\\_Road-Map\\_2012\\_Fullversion.pdf](http://www.who.int/neglected_diseases/NTD_Road-Map_2012_Fullversion.pdf)). Whereas this might be achievable for those diseases, most scientists involved with promoting control programmes believe that 2020 is an unachievable target for the elimination of schistosomiasis as a public health problem, and indeed for the three soil-transmitted helminth infections (STHs) or intestinal worms, *Ascaris* spp., *Trichuris* spp. and hookworm (*Necator* and *Ancylostoma* spp.), even 2030 might be too ambitious a target (Ross et al., 2015a).

In fact, because schistosomiasis (and STHs) are highly focal in distribution and the power of transmission depends on so many factors, different target dates could and should be set for different countries, districts and ecological zones (French et al., 2015).

Some of the factors that determine the prevalence and intensity of infection in a given ecological setting include, but are not necessarily limited to, the following (in no particular order of importance) (Gryseels et al., 2006): (i) human population density; (ii) human fresh water contact (fishing, agriculture, livestock, domestic activities, leisure); (iii) the presence or absence of piped water (school, health centre, village and household levels); (iv) the presence or absence of sanitation facilities, including quality and cleanliness; (v) the type of habitat for intermediate hosts (snails) and

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distance from human habitation (lakeshore, river, stream, pond, irrigation canal, drain, etc); (vi) snail density and seasonal variation in snail population linked to vegetation and temperature; and (vii) snail control methods which might be effective (vegetation clearance, competitive snails, predators such as ducks, fish, crustaceans, canal lining, mollusciciding).

WHO currently recommends preventive chemotherapy (PC) or mass drug administration (MDA) for the control of schistosomiasis, combined with access to safe water, improved sanitation, hygiene education and snail control (WHO, 2015). [http://www.who.int/neglected\\_diseases/NTD\\_RoadMap\\_2012\\_Fullversion.pdf](http://www.who.int/neglected_diseases/NTD_RoadMap_2012_Fullversion.pdf) Praziquantel (PZQ) is the drug of choice; not only is it safe and effective, but since 2003, increasing quantities of drugs have been made available free of charge through generous donations by pharmaceutical companies. In 2002, the Schistosomiasis Control Initiative (SCI) was established at Imperial College London, UK (<http://www3.imperial.ac.uk/schisto>) with the aim of providing treatment with PZQ to infected and at-risk children in sub-Saharan African countries to improve their immediate health and to protect them from the chronic consequences of disease (Fenwick et al., 2009). However, the increase in PZQ demand led to a scarcity of PZQ supply becoming a constraint in controlling schistosomiasis at the global level.

In 1988, PZQ was marketed by Bayer (pharmaceutical) at a price of USD 1.00 per tablet, but by 2003, PZQ was available at a price of approximately USD 0.08 per tablet, which equates to USD 0.20 cents a dose per school-age child treated. However, the market was not stable or predictable because it depended on the regular availability of funding to purchase the drug, and this funding was itself scarce and variable. Other NTDs have benefitted from pharmaceutical company donations, onchocerciasis treated with Mectizan (ivermectin) donated by Merck in the USA since 1986; LF from treatment with Mectizan (Merck) and albendazole from GlaxoSmithKline (GSK) donations since the late 1990s, and trachoma donated by Zithromax (azithromycin) from Pfizer since 1998. The Bill & Melinda Gates Foundation (BMGF) first awarded a grant for NTD control in 2001, and by 2003 BMGF had invested their funds in NTDs and really led the way towards implementation of control programmes. For schistosomiasis, BMGF funds were awarded to SCI, Imperial College London, and used to purchase generic PZQ for six countries in sub-Saharan Africa. Initially, PZQ was not donated by any pharmaceutical company until Merck KGaA stepped up with a relatively small donation of 20 million tablets annually of PZQ through WHO from 2007 to 2010 (Table 1). At about the same time, Johnson and Johnson, followed by GSK, targeted STHs for the first time with donated mebendazole and albendazole, respectively. In 2010, the major breakthrough came

for schistosomiasis with several milestone announcements. The first was the expanded commitment by Merck KGaA to incrementally increase their donation from 20 million tablets of PZQ per year to reach 250 million tablets by 2016 and beyond; the second was an increase by the governments of the UK and USA in funds targeting the control of NTDs, in particular for the purchase and delivery of PZQ to infected and at-risk individuals in sub-Saharan Africa. The third event was the World Bank agreement to fund the treatment of schistosomiasis in Yemen. A fourth event was the arrival of a philanthropic organisation willing to support NTD control (Legatum, which led to the launch of the EndFund), and the final event was the launch of the Global Network for NTDs which has become a major global advocacy organisation (Molyneux, 2014). Looking forward, the development of an appropriate formulation of PZQ for treatment of preschool children may further improve treatment coverage of younger populations at risk of schistosomiasis (Trastullo et al., 2015).

In 2012, Bill Gates convened a meeting in London which led to the London declaration against NTDs and WHO taking a massive initiative to encourage every endemic country to develop a national plan for NTD control (UK Coalition against Neglected Tropical Diseases, 2012. London Declaration on Neglected Tropical Diseases) (<http://ntd-coalition.org>). So from a situation in 2000, where only Egypt, Brazil, China and the Philippines were implementing schistosomiasis control, by 2015, every endemic African country had developed a national plan for control of NTDs including schistosomiasis and many had at least started implementation of their schistosomiasis control programmes. The WHA resolutions, together with funding from the BMGF, USAID and UK all played their part, as has additional funding from the newly created ENDFUND, and the support for deworming by independent charity evaluators (Liese et al., 2014).

Despite this massive support for NTD and schistosomiasis control, the question remains whether all this is enough to allow us to even move toward elimination of schistosomiasis as a public health problem. And if not, what is missing? In our opinion, there are a number of barriers still preventing us from eliminating schistosomiasis as a public health problem in the near future.

Governmental commitment is still insufficient to permit the elimination of schistosomiasis, and while many governments welcome the implementation of NTD control programmes in their countries, domestic financial support is still too limited to implement sustainable control programmes, and schistosomiasis remains a neglected tropical disease. This applies both to single-disease programmes, and to integrated programmes targeting multiple diseases through the same programme structure. Several countries in Africa are suffering from political instability and civil

**Table 1**  
Past, current and future praziquantel (PZQ) commitments for mass treatment of schistosomiasis.

PZQ producer	Past 30 years	Current donations	Next 10 years <sup>a</sup>
Bayer Merck	Sell PZQ at USD 1.00 per tablet Donated 20 million PZQ tablets per year 2007/2010	None 20 million PZQ tablets in 2007, rising to 103 million tablets in 2015	Unlikely to donate Pledged to donate 250 million PZQ tablets per year through 2020
MedPharm Shin Poong Pharm	Donated 13 million PZQ tablets in 2004 Reduced the price of PZQ to USD 0.08 a tablet by 2000	None None	Unlikely to donate Sells PZQ to WHO for Yemen, unlikely to donate
Micro Labs Limited	Started selling PZQ in 2010 at USD 0.08 a tablet	None	Will be a competitive bidder for selling PZQ, unlikely to donate
Cipla Limited	Started selling PZQ in 2002 at USD 0.08 a tablet	None	The first registered PZQ with WHO - the price is likely to rise to about 12 US cents, unlikely to donate

WHO, World Health Organization.

<sup>a</sup> Authors' predictions based on current situation and trends.

unrest, as well as epidemics of infectious diseases such as ebola, which lead to a breakdown of health delivery services. Public health services need to be further strengthened to endure such shocks, and to ensure the delivery of donated drugs to maintain the trust of donors and the sustainability of control programmes. Many programmes are only school-based interventions – they bring improved health and quality of life to children in school but do not reach children out of school, preschool children or adults who are commonly infected and in need of treatment in order to reduce transmission in endemic areas.

Further evidence is needed on the ideal frequency, dosage and efficacy of PZQ on the respective schistosomiasis species and their related morbidity, including that of different schistosome hybrids (Webster et al., 2013; Zwang and Olliaro, 2014; Ross et al., 2015b); but the frequency and indeed any change from the recommended 40 mg/kg will be dependent on the aim of the intervention, be it for morbidity control or to achieve elimination of transmission.

As endemic countries scale up control programmes and potentially move towards elimination, validated and highly sensitive and specific diagnostic field-friendly tools are required to enable monitoring and evaluation of disease elimination (Colley et al., 2013; Knopp et al., 2015). Climatic changes and global movement of people have recently shown that sustained commitment will be needed if global elimination of schistosomiasis shall be achieved (Boissier et al., 2015). Finally, elimination of this ancient parasite infection will require a substantial scale-up of the skill-base both in endemic countries and among international stakeholders, and will need to be further strengthened through consortiums such as Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) (<http://score.uga.edu>), SCI and others. In every country the expertise to treat schistosomiasis has increased since 2000, but to achieve elimination, a broader base of expertise will be needed among all NTD elimination stakeholders.

So, can we hope to achieve elimination of schistosomiasis as a public health problem in Africa by 2020 and globally by 2025 as targeted by WHO, or even by 2030 as targeted by the sustainable development goals (SDGs) (United Nations, <http://www.un.org/sustainabledevelopment/sustainable-development-goals/>). Retrieved 28 December, 2015) (<http://apps.who.int/iris/handle/10665/78074>) In Zanzibar, on the two islands of Unguja and Pemba where *S. haematobium* infection was previously recognised as rife, treatment had been intermittent through until 2005 when SCI (schisto.org) with funding from the BMGF started a regular treatment programme. Since 2011, with further funding from BMGF, a SCORE consortium (score.uga.edu) project led by Professor Daniel Colley at the University of Georgia (UGA), Athens, Georgia, USA has attempted to eliminate schistosomiasis by MDA with PZQ, snail control using molluscicides and behaviour change to prevent snail infections and human transmission (Knopp et al., 2013). Prevalence and intensity of infection is now very low compared with levels before treatments were offered; however, reaching zero prevalence is proving difficult and transmission has yet to be interrupted (Dr David Rollinson, personal communication).

There is no doubt that in order to achieve elimination of schistosomiasis, either as a public health problem or by breaking transmission, a marked improvement in socio-economic conditions, improved water supplies and sanitation facilities are going to be needed in addition to MDA (Bockarie et al., 2013). It has happened in Japan and in Puerto Rico. It has happened in many parts of China, although even in China some stubborn hotspots remain (Zou and Ruan, 2015). Our prediction is therefore that, if elimination of schistosomiasis is to be possible, we as stakeholders must ensure that treatment reaches all population groups at risk, and that a game-changer in the provision of water, sanitation and hygiene

facilities will be needed. If not, it is highly probable we might not even move beyond hotspots of schistosomiasis by 2030.

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