Comment

A single dose of ivermectin is sufficient for strongyloidiasis

Human strongyloidiasis, caused by infection with *Strongyloides stercoralis*, belongs to the soil-transmitted helminthiases and affects up to 100 million people in the tropics and subtropics.[1] Control of *S stercoralis* lags behind efforts to tackle the common soil-transmitted helminths, including the hookworms, *Ascaris lumbricoides*, and *Trichuris trichiura*. This difference is related to the difficult detection of an active infection with *S stercoralis*, which involves a battery of faecal and serological tests.[1] For therapy, the current gold standard in terms of efficacy and safety is ivermectin given as a single dose of 200 µg/kg; however, there is a need for further investigation of optimal doses and treatment regimens.[2]

In *The Lancet Infectious Diseases*, Dora Buonfrate and colleagues[3] explored whether multiple doses of ivermectin would be superior to a single dose in terms of infection clearance at 12 months post-treatment against *S stercoralis*. A rigorous diagnostic approach was followed, with use of coprological techniques (ie, stool culture and PCR), together with serology, at baseline, 6 months, and 12 months after treatment. Another study strength was that participants were recruited from European sites (ie, referral centres for tropical parasitic diseases in Italy, Spain, and the UK) where *S stercoralis* is not endemic and re-infection could thus be excluded as a reason for continued positive infection status. The authors found similar efficacy (risk difference 1·48%, 95% CI –7·55 to 10·52; p=0·75) for the single dose (86%; 102 of 118 responded to treatment) and multiple dose (85%; 96 of 113 responded to treatment) groups in 231 participants who completed follow-up at 12 months, leading the trial steering committee to halt recruitment at a planned interim analysis before the target sample size of 400 participants was reached. After a subgroup analysis by diagnostic result and an exploratory analysis of efficacy at 6 months, no additional benefit from providing multiple doses on clearance rates could be found. Although ivermectin proved to be safe, with only few adverse events of mostly mild intensity reported in both groups, the authors showed that a single dose was better tolerated than multiple doses, adding further support to the use of a single dose rather than multiple doses.

A limitation of the study is that about half of the patients (n=163) had suspected strongyloidiasis (ie, positive serology but no detection of larvae in faeces, which is the gold-standard for diagnosis of strongyloidiasis). The analysis of multiple stool samples or PCR analysis across all sites might have helped to overcome this diagnostic limitation. Serology tends to overestimate the burden of disease because of its potential for cross-reactivity with other helminth infections, and therefore treatment efficacy might have been underestimated.[4] The use of high serological cutoff values by the authors undoubtedly limited the inclusion of false-positive cases and probably also the number of patients with light *S stercoralis* infections, as infection intensity can strongly affect the treatment efficacy of anthelmintics.[5] Moreover, the authors selected a lengthy four-dose regimen of 200 µg/kg given on days 1, 2, 15, and 16, which is specifically recommended for patients with *S stercoralis* hyperinfection who are immunocompromised. For patients who are immunocompetent, such a regimen is deemed unnecessary.[6] Notably, this multiple dose treatment schedule would not be compatible with treatment programmes in endemic countries and might also face adherence issues in the management of patients. In Buonfrate and colleagues' study, direct observation of tablet intake was only possible for the first dose, which might have affected the outcome of the multiple dose group.

The effectiveness of ivermectin given as a single dose makes it an excellent drug to be used in preventive chemotherapy. Ivermectin has been used for decades in programmes of preventive chemotherapy against lymphatic filariasis and onchocerciasis. In 2017, ivermectin was added to the WHO essential medicines list to treat strongyloidiasis and, in combination with albendazole, to treat soil-transmitted helminth infections,[7] paving the way for integrated use of ivermectin in existing control strategies for soil-transmitted helminths. The use of ivermectin with albendazole would not only allow simultaneous tackling of *S stercoralis* and other soil-transmitted helminth species but also enhance efficacy of single albendazole against *T trichiura*.[8]

Yet, treatment of strongyloidiasis remains a challenge in endemic countries. Merck does not donate ivermectin for this indication, and hence ongoing efforts to obtain WHO prequalification of generic ivermectin are

applauded.[9] Similarly, efforts to add moxidectin, a new treatment for onchocerciasis, to the currently inadequate therapeutic armamentarium for strongyloidiasis should be supported.[10] The epidemiology of strongyloidiasis should be defined, including its endemicity and areas at high risk, which will also aid to forecast the amount of drug needed, before a well designed control strategy can be implemented.

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Tuberculosis testing and migrant health

Global migration is increasing. Current estimates suggest that some 244 million people, representing 3·3% of the world's population, are living as international migrants.[1] Migration has important implications for tuberculosis control because a high proportion of tuberculosis cases in low-incidence countries are in people who have migrated from countries where the disease is more frequent.[2] Countries with a low incidence of tuberculosis have adopted policies for targeted testing of prospective migrants for active or latent tuberculosis infection, but these policies are inconsistent in their specification of migrant countries of origin, the categories of migrants to be tested, and the tuberculosis tests to be used.[3] In the UK, a system of pre-entry screening for active pulmonary tuberculosis is used,[4] together with testing for latent infection in individuals aged 16–35 years arriving from high-incidence countries.[5] Policies for tuberculosis testing in migrants need to be informed by better evidence, but randomised controlled trials are seldom feasible and non-randomised studies require large sample sizes and long follow-up. Tuberculosis testing also needs to be understood in the broader context of communicable disease control. In its 2018 guidance on infectious diseases in newly arrived migrants, the

European Centre for Disease Prevention and Control made recommendations for testing for HIV, hepatitis, and parasitic and vaccine-preventable diseases, in addition to tuberculosis.[6]

In *The Lancet Infectious Diseases,* Luis Berrocal-Almanza and colleagues[7] use for epidemiological analysis a substantial dataset derived from migrant tuberculosis testing and primary care registration in the UK. The study cohort included 224 234 migrants who tested negative on pre-entry screening for active tuberculosis between Jan 1, 2011, and Dec 31, 2014, with follow-up until Aug 31, 2017. This cohort was compared with a group of 118 738 new migrants identified from the population-based system of health-care registration in England who were not screened for active tuberculosis. The study included 2451 participants who were tested for latent tuberculosis infection through a programme of migrant testing being rolled out in England,[5] of whom 1404 had also been tested for active tuberculosis infection. Analysis of 1771 incident active tuberculosis cases that were identified during follow-up revealed several important findings. First, socioeconomic conditions after arrival were associated with tuber-culosis risk: migrants who were able to live in the least deprived areas in the UK had a lower risk of active