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A strengthening evidence-base for mass deworming, but questions remain

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Soil-transmitted helminths (STH), a group of three intestinal worms are estimated to affect up to a billion people globally, predominantly in low-income settings. The world's largest deworming program has been the lymphatic filariasis elimination programme, which provides community-wide treatment with treatments that also affect STH. As these programmes scale back due to successful control of lymphatic filariasis there is a question of whether, and how, to continue or expand deworming for STH, usually delivered through school-based deworming.

Shifting from school-based to community deworming is an area of on-going debate. In this issue, Clarke et al. provide a review of empirical evidence on community-wide and child-targeted treatment strategies and show that treating adults in addition to children will have indirect benefits for children, particularly for roundworm [1]. This meta-analysis validates existing mathematical modelling [2] and cost-effectiveness analyses [3, 4] highlighting the potential benefits of expanding of STH control programmes to all age groups. However, questions remain about how to scale-up to mass treatment, and whether this would really allow programmes to become finite in their scope, meaning breaking transmission. There is also limited synthesis of available data on the potential role of water, sanitation and hygiene.

Clarke et al's meta-analysis [1] is an example of providing an explicit and transparent link between the policies being advocated and a reliable evidence base in a field where there has previously been some criticism [5]. We urgently need specific policy options guided by further reliable evidence base to support the long-term credibility and optimal implementation of STH control programmes. For instance, the current study [1] and others have pleaded for properly conducted randomized controlled trials to address evidence gaps [6, 7, 5, 8]. Are we absolutely clear though about which anthelmintic drugs or which combinations of those to use in future trials and thus by extension in control programs? Some conclusions about the superiority of some anthelmintic drugs over others have been drawn on mainly comparisons with placebo [7]. On the other hand, treatment networks to illustrate the types and numbers of treatments compared so far (so-called "geometry" of evidence) has also been provided for major neglected tropical diseases, highlighting the study of soil transmitted helminth infections through 160 trials, including 46,887 participants [6]. Recently a comparative appraisal of three broad-spectrum anthelmintic drug combinations on 440 children with a randomized controlled design has been applied for trichuriasis [8]. Can we not now evaluate all this evidence for each of these worms in the most adequate statistical way before we give exact recommendations for future clinical trials? The latter should not be designed as stand-alone experiments ignoring previous evidence. We should aim for minimum monetary and human cost involved and efficient future research planning. The use of network metanalysis [9] - a methodological tool which can include many competing treatments and make use of a wider evidence space by including direct and indirect comparisons could be a promising vehicle to answer some of these key questions.

Furthermore, at the heart of current debates are questions around the health impact of STH and whether the target of the global programme should be minimising morbidity in children through

long-term deworming or breaking transmission [2]. Precise estimates for pathways from infection with STH to poor child development, as well as the mediating effects of nutrition and anaemia, are still lacking. Researchers in The Cochrane Collaboration reviewed the effects of school-based deworming programmes on children's health, ability to learn, and school attendance, through 45 randomized trials, concluding non consistent benefits and highlighting very low, low or moderate quality of evidence [10]. Clarke et al [1], and others [11] stress the risks of using imperfect diagnostic tools for the detection of STH within research and control. Measurement error problems are highly pertinent in child development too; this construct is complex, encompassing cognitive, sensorimotor and social-emotional domains [12] and culturally appropriate child assessment instruments should be also considered in the design of future clinical trials as well as the collaborative involvement of endemic country mental health researchers and developmental psychologists in order to successfully overcome these challenges.

There are signs that the evidence base for deworming is being strengthened, through evidence synthesis and fruitful debates. Continuing research will allow programs to move forward with well-designed interventions to prevent STH infection and loss of human potential around the globe.

References

1. Clarke NE, Clements CA, Doi SA, Wang D, Campbell SJ, Gray D et al. Differential impact of mass and targeted deworming campaigns for soil transmitted helminth control in children: A systematic review and meta-analysis. *The Lancet*. 2016.
2. Anderson RM, Turner HC, Truscott JE, Hollingsworth TD, Brooker SJ. Should the Goal for the Treatment of Soil Transmitted Helminth (STH) Infections Be Changed from Morbidity Control in Children to Community-Wide Transmission Elimination? *PLoS Negl Trop Dis*. 2015 9(8):e0003897. doi:10.1371/journal.pntd.0003897. eCollection 2015.
3. Lo NC, Bogoch II, Blackburn BG, Raso G, N'Goran EK, Coulibaly JT et al. Comparison of community-wide, integrated mass drug administration strategies for schistosomiasis and soil-transmitted helminthiasis: a cost-effectiveness modelling study. *Lancet Glob Health*. 2015; 3(10):e629-38. doi:10.1016/S2214-109X(15)00047-9.
4. Turner HC, Truscott JE, Bettis AA, Shuford KV, Dunn JC, Hollingsworth TD et al. An economic evaluation of expanding hookworm control strategies to target the whole community. *Parasit Vectors*. 2015 8:570. doi:10.1186/s13071-015-1187-5.
5. Nagpal S, Sinclair D, Garne P. Has the NTD Community Neglected Evidence-Based Policy? *PLoS Negl Trop Dis*. 2013;7(7):e2238. doi:10.1371/journal.pntd.0002238.
6. Kappagoda S, Ioannidis JP. Neglected tropical diseases: survey and geometry of randomised evidence. *BMJ*. 2012;345:e6512. doi:10.1136/bmj.e6512.
7. Keiser J, Utzinger J. Efficacy of current drugs against soil-transmitted helminth infections: systematic review and meta-analysis. *JAMA*. 2008;299(16):1937-48. doi:10.1001/jama.299.16.1937.
8. Speich B, Ali SM, Ame SM, Bogoch, II, Alles R, Huwyler J et al. Efficacy and safety of albendazole plus ivermectin, albendazole plus mebendazole, albendazole plus oxantel pamoate, and mebendazole alone against *Trichuris trichiura* and concomitant soil-transmitted helminth infections: a four-arm, randomised controlled trial. *Lancet Infect Dis*. 2015;15(3):277-84. doi:10.1016/S1473-3099(14)71050-3.
9. Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. *Res Synth Methods*. 2012;3(2):80-97. doi:10.1002/jrsm.1037.
10. Taylor-Robinson DC, Maayan N, Soares-Weiser K, Donegan S, Garner P. Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin, and school performance. *Cochrane Database Syst Rev*. 2015(7):CD000371. doi:10.1002/14651858.CD000371.pub6.

11. Levecke B, Brooker SJ, Knopp S, Steinmann P, Sousa-Figueiredo JC, Stothard JR et al. Effect of sampling and diagnostic effort on the assessment of schistosomiasis and soil-transmitted helminthiasis and drug efficacy: a meta-analysis of six drug efficacy trials and one epidemiological survey. *Parasitology*. 2014 141(14):1826-40. doi:10.1017/S0031182013002266.
12. Walker SP, Wachs TD, Gardner JM, Lozoff B, Wasserman GA, Pollitt E et al. Child development: risk factors for adverse outcomes in developing countries. *The Lancet*. 2007;369(9556):145-57. doi:10.1016/S0140-6736(07)60076-2.

Conflict of interest

The authors declare no conflict of interest.