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Commentary: The tide continues to move on mass deworming—where are we now?

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Treating individuals who are known to have parasitic worm infections including hookworm, roundworm, pinworm (all soil-transmitted helminths) and schistosomiasis (a freshwater-associated helminth) is clearly sensible. These organisms can cause a variety of unpleasant, though rarely life-threatening, illnesses. Children in endemic settings who present to health services with symptoms suggestive of worm infection can be routinely dewormed without the need for more expensive laboratory tests. Mass deworming of children in low-income countries in the hope of achieving productivity gains is a different matter.

Many supporters of mass deworming point to evidence of positive short-term effects, like improved health and school attendance, and positive long-term effects, like improved cognitive and labour market outcomes. Enthusiasm for mass deworming interventions was further encouraged in 2008, when the Copenhagen Consensus judged that mass deworming represented the fourth most effective means of advancing international development.

Although almost everyone agrees on the efficacy of drug treatment for deworming helminth-infected children,

many hold differing views on the impacts of mass deworming interventions.¹ Recent systematic reviews from both the Cochrane² and Campbell³ Collaborations find limited evidence of impacts of mass deworming efforts, from both nutritional and mortality perspectives.

So, where are we now? Mass deworming supporters often point to evidence suggestive of later life benefits of the practice, which comes from three influential working papers looking at long-term outcomes arising from deworming in childhood. For those not familiar with the concept, ‘working papers’ are draft versions of research, which social scientists use to garner feedback from others. Working papers often undergo a series of revisions while the authors refine their research and submit it for publication.

This new paper by Jullien *et al.*, a group of independent and experienced assessors from the Cochrane Collaboration, critically appraises the evidence supporting the possible long-term benefits of mass deworming interventions. They find these working papers to be at high risk of bias, and they caution against solely relying on the

existing evidence for policy making. This work corroborates and expands on a similar, though less detailed, appraisal made by Campbell Collaboration researchers. This research is a valuable addition to the evidence base underpinning mass deworming interventions, though it paradoxically leads to greater uncertainty about whether such long-term effects exist.

Research continues to be produced around impacts of mass deworming. We anticipate that an additional impact evaluation, drawn from a large 3ie-funded Chinese mass deworming trial, will provide further evidence on the effectiveness of these types of interventions in the near future.⁴ Proponents of mass deworming will highlight Croke *et al.*,⁵ a systematic review posted as a working paper this year by many of the same authors as the papers critically appraised here. This work suggests some evidence of a nutritional benefit of deworming interventions. We note that this new systematic review appears to lack a pre-analysis plan; these are being increasingly advocated for work in the social sciences.⁶

Throughout history, many - if not all - scientific beliefs have eventually been replaced by new understandings: this is the nature of scientific progress. Revisions and mis-steps along the way have been numerous: this is why modern medical practice is so tightly wedded to the principle of evidenced-based medicine. History is valuable to inform our future progress—so, what have we learned from the numerous evidential enquiries into the effectiveness of mass deworming? We propose some learning points.

One - critical appraisal and independent replication of scientific findings are vital, though these will take different forms in different circumstances. No single scientific authority, no matter how highly regarded, is infallible. Scientists, although creditably innovative and passionate about their fields of expertise, are often not the best appraisers of the overall state of the evidence and can be slow to accept findings contradictory to their own beliefs. It remains the duty of all researchers (and funders of research) to independently appraise and reproduce influential scientific findings until these are beyond any reasonable doubt—and for journals to publish such studies. Much credit is due to the authors of the three papers undergoing this critical appraisal for being so forthcoming with the Cochrane group. Replication of the findings of the Cochrane group in this field, both by the Campbell Collaboration and by other independent scientists, lends greater certainty to their conclusions.

Two - exploratory and confirmatory research, both important in generating new knowledge, should not be confused. The three papers critically appraised by Jullien *et al.* each opportunistically attempt to investigate whether childhood deworming programmes lead to improved long-

term economic productivity outcomes—this generated original and exciting new hypotheses. This kind of work is invaluable in science, regardless of whether or not subsequent research finds supporting evidence. The next step for investigating such new hypotheses should be to establish rigorous experimental studies to test pre-defined hypotheses, such as the trials recently published from a group working in Peru.^{7,8} Promising pilot studies need to be evaluated at scale and in new environments, while bearing in mind that many interventions will turn out to not work as well as anticipated.

Three - to enable the updating of our beliefs as quickly as possible, we support revising the standard epidemiology and economic publishing models. Economic journal editors should encourage shorter papers, which would allow evidence to take less than the current average of 6.2 years to be added to the academic literature.⁹ Epidemiology, and health journal editors more generally, should allow for the public posting of working papers, to enable better understandings of the state of evidence bases as soon as possible.

For those organizations and philanthropists who continue to devote effort and resources to international mass deworming programmes in the hope of achieving long-term productivity gains, we suggest that the evidence of effectiveness in this area remains undetermined. John Maynard Keynes is often quoted as saying ‘When the facts change, I change my mind. What do you do, sir?’ We say it’s time to gather more facts.

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Commentary: Biases in the assessment of long-run effects of deworming

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Introduction

Jullien and colleagues provide a critique of three working papers on the long-run effects of deworming interventions.¹ Despite being unpublished, these three papers have been prominent in the public debate in support of calls for such interventions over the past few years.² What can we really infer from them?

On first read, the critique by Jullien *et al.* is devastating. The three papers appear to have no redeeming qualities: a collection of fished results from poorly implemented and poorly analysed studies whose influence can only be explained by confirmation bias among deworming advocates.

On second read, and going back to the original papers, things are not so simple. A number of concerns described by Jullien *et al.* are on target. But a number seem to be off in ways that cannot be explained by differences in disciplinary norms.

I discuss the evaluation of this evidence according to possible sources of bias (mostly using Jullien *et al.*'s categories but adding some additional considerations).

Sources of Bias

Publicization bias

Consider first a type of publication bias. One might reasonably worry that these three publicized (but unpublished) studies, all displaying positive effects of

deworming, were plucked by deworming advocates from a larger population of unpublished studies with many null or negative effects. However, although clearly it is hard to know where to look for unpublished (and unpublicized) null results, especially in the absence of preregistration norms, the fact that the search by Jullien *et al.* did not uncover any studies other than these three moderately increases confidence that the pattern of positive results is not simply a product of publicization bias.

Confounding bias

Jullien *et al.* worry about unknown bias due to absent baseline data in Baird *et al.*³ For many social science experimentalists, this concern is hard to make sense of (at least if the assignment is considered to be as good as random), since unbiasedness is seen to stem from the assignment procedure, not the realization of assignments.⁴ The concern with confounding in Ozier⁵—that observational variation is mixed up with experimental variation—also seems off. The key analysis provided in Ozier [Figure 1(B1)] clearly focuses on the experimental variation. Moreover, as the regression analysis includes fixed effects for cohorts, cohorts with no variation in treatment should effectively drop out. In both cases the economists could have made things easier by using a better randomization procedure and employing cleaner design-based inference procedures, but in neither case is there clear cause for concern.