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Authors' response

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In agreement with McKenzie's interesting letter,[1] and as set forth in our paper,[2] it is useful to reiterate upfront that polyparasitism is very common across different ecological, epidemiological, and socio-cultural settings, particularly in the developing world. We have encountered this phenomenon—without exception—in every cross-sectional survey carried out in the western part of Côte d'Ivoire regardless of whether emphasis was placed on school-age children or entire communities.[3,4] Our observations therefore support the seven reports from the 1990s cited by McKenzie,[1] and more recent results obtained from cross-sectional surveys done elsewhere in sub-Saharan Africa,[5] Southeast Asia,[6] and South America.[7]

It is important to highlight two shortcomings of our work that also apply to all of the above mentioned reports. First, our population sample was selectively screened for 'only' 15 different parasite species, namely *Schistosoma mansoni*, soil-transmitted helminths ($n = 3$), intestinal protozoa ($n = 8$) and *Plasmodium* ($n = 3$). The diagnostic approach adopted was microscopic examination of stool and blood samples that were collected and processed according to standardized, quality-controlled, techniques. Almost 90% of the study participants harboured a polyparasitic infection, whereas three-quarters were infected with three or more parasites concurrently.[2] Had other parasites also been investigated, e.g. food-borne trematodes, the frequency of polyparasitism would have been even higher. Second, the frequency of multiple parasite infections not only depends on the epidemiological setting, but is also a function of the sensitivity and specificity of the diagnostic tool, as well as the sampling effort. This issue is well documented in the case of the Kato-Katz technique for diagnosis of *S. mansoni* and soil-transmitted helminths, particularly in areas where light infection intensities predominate. We have recently documented very low sensitivities of a single Kato-Katz thick smear for detection of *S. mansoni* or hookworm, namely 22.4% and 8.0%, respectively.[8] Consequently, the observed infection prevalence of a concurrent infection with *S. mansoni* and hookworm increased several-fold when the sampling effort was intensified from a single Kato-Katz thick smear to 25 smears prepared from five stool samples collected over consecutive days.[8] Employing a latent-class model, the 'true' concurrent infection prevalence increased further.[8]

To remedy these shortcomings, the following points are offered for discussion. First, we would like to encourage other investigators engaged in parasitic disease research and control to place more pointed emphasis on the issue of multiparasitism, with an attempt to screen at least for those parasites that are most common in a given epidemiological setting. We believe that many researchers will find that their previously collected datasets already contain the necessary information to carry forward analyses similar to ours[2] or those of others cited above, i.e. determination of significant pair-wise parasite associations. Results from such analyses will enhance our understanding of host-to-parasite crosstalks in a polyparasitic landscape. Such findings, in turn, can provide insights to design and implement sound research and control programmes for malaria, schistosomiasis, soil-transmitted helminthiasis and other parasitic diseases that are of public health and economic significance. Second, there is a pressing need for novel diagnostic tools with high sensitivity and high specificity. We currently pursue a multi-pronged approach to investigate whether nuclear magnetic resonance (NMR) spectroscopy-based and mass spectrometry (MS)-based metabonomic approaches can play a seminal role for biomarker identification;[9] hence we are in the process of evaluating the overall metabolic consequences of evolving human internal ecosystems that encompass microfloral-parasite-host interactions. Recently, we have reported the metabolic signature of an *S. mansoni* infection in the mouse by analysing urine samples with high field ^{1}H NMR spectroscopy and multivariate pattern recognition techniques.[10]

In view of polyparasitism being so common in the developing world, several important implications need to be discussed. First, there is growing recognition in public health circles for integrated and combined control approaches, so that pro-poor

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health benefits can be maximized with scarce resources. Molineux and Nantulya (2004) recently suggested combining the filariasis elimination programme with control efforts aimed at malaria, which was, among other reasons, justified on technical similarities of current interventions.[11] Further support for combined control approaches can be obtained from recent data in Senegal; severe malaria attacks were significantly lower among individuals free of helminth infections, thus treatment against soil-transmitted helminths might protect from malaria episodes.[12] However, our own work in Côte d'Ivoire and that of others in Uganda do not support this observation, as no significant associations were found between either *Plasmodium* infection or clinical malaria and any of the soil-transmitted helminths investigated.[2,13]

Second, at a more fundamental level, new research is required to understand the physiology of homeostatic balance among multiple parasites and a host organism. This should reveal the nature of mutualistic adaptation between parasites and hosts, where, as a consequence of their vastly different evolutionary paces, the burden of adaptation falls largely on the shoulders of the parasites. This point of view[14] has yet to be fully taken up by the scientific community, but it would inevitably provide for a much deeper understanding of multiparasitism than heretofore.

Finally, it is important to note that historically, polyparasitism was the norm rather than the exception also in temperate zones, as several species of intestinal parasites were widely distributed across Europe and the US.[15] However, the industrial revolution paved the way for social and economic advances, environmental sanitation, use of preventive measures, improved hygiene behaviour and, finally, development and access to efficacious drugs. The frequency of parasitic infections and hence polyparasitism decreased in response to these economic and social changes. This illustrates that without addressing the root ecological and behavioural causes, i.e. improved access to clean water and sanitation, coupled with sound hygiene behaviour, multiparasitism will remain common in the developing world.

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