consumption, not least for acne, are very difficult to ascertain. Third, the use of antibiotics in farming, as cited by the Nast and colleagues, is under increasing scrutiny, and has become acute since the discovery of the MCR-1 mechanism in China as a result of the use of colistin in animal feeds.[3]

With regard to concerns regarding the quality of the Review and its compliance with PRISMA criteria, we submitted a detailed PRISMA checklist on submission and Nast and colleagues' concerns were not shared by any of the reviewers or indeed the journal.[4]

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Treatment of visceral leishmaniasis: pitfalls and stewardship

We recognise and share the concerns expressed by Sujit Bhattacharya and Aditya Dash[1] relating to the optimal choice of treatment for the elimination programme for visceral leishmaniasis in India, Nepal, and Bangladesh.

Widespread use in programmatic settings of a single dose of liposomal amphotericin B (AmBisome) monotherapy, although efficacious in clinical trials, might put the future of this vital drug in the management of visceral leishmaniasis at risk. Difficulties in maintenance of the required cold-chain, combined with the long elimination half-life of the liposomal formulation, could result in subtherapeutic exposure in patients. Clinical drug resistance to amphotericin B in leishmaniasis, albeit not easily achieved, seems nevertheless possible. The availability of alternative generic liposomal amphotericin B formulations, with different compositions, unassessed bioequivalence, and unknown quality assurance, further complicates matters.[2] These points are especially important when considering that 15–20% of patients seek treatment in the—largely unregulated—private sector.

Bhattacharya and Dash discuss the decline in visceral leishmaniasis incidence in south Asia that is attributed to early diagnosis and improved vector control and housing;[1] but which might also be explained by transmission factors unrelated to the elimination programme, such as climate conditions and natural cyclic trends of the epidemics. They further argue that miltefosine was abandoned too early in the elimination initiative, even if the current 28 day oral miltefosine monotherapy regimen is far from optimal. The authors acknowledge miltefosine's teratogenicity, meaning women of child-bearing age need to use contraception until 4 months after therapy. Stigmas surrounding contraceptive use necessitate the availability of alternative treatment options for female patients. More worryingly, we documented a high failure rate (20% at 12 months follow-up) in the region for the standard miltefosine regimen.[3] Treatment failure was more pronounced in children,[4] who typically had reduced exposure to the drug and were probably underdosed.[5] A previously proposed alternative miltefosine dose regimen could be adopted to overcome this difference in miltefosine exposure between children and adults.[6] Although no formal clinical drug resistance of the parasite has been detected,[3] strains more tolerant to miltefosine after treatment have been observed, particularly after treatment of post-kala-azar dermal leishmaniasis.[7] Additionally, miltefosine monotherapy might potentiate the selection of more aggressive and infective leishmania strains: strains from relapsing miltefosine-treated patients exhibited higher virulence.[8]

To safeguard therapies for future use, a combination therapy would be preferable in the elimination programme. Close surveillance of emerging resistance to such a regimen is still highly recommended, because resistant adaptation of *Leishmania donovani* to various combination regimens has already been confirmed experimentally.

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What do we actually know about leprosy worldwide?

A recent Comment[1] in *The Lancet Infectious Diseases* spoke about the possibility of attaining zero leprosy transmission globally. We believe the real-world leprosy situation needs to be considered carefully before conclusions can be made. Since 2009, our group has been doing leprosy field research in several cities in Pará, Brazil, in the Amazon region. Our team consists of three leprologists who are supported by well-trained physiotherapists, nurses, and laboratory personnel. Importantly, they also receive assistance from local community health agents and health authorities from the basic health units who know about the local leprosy situation. Our focus has been to diagnose cases in schoolchildren and then visit their household contacts. During our 1–2 week field trips, the proportion of schoolchildren and their contacts newly diagnosed in all of the cities surveyed ranged from 3·4% in Acará to 13·4% in Senador José Porfírio, and averages 4% in schoolchildren and 8% in household contacts, indicating an extremely high number of hidden leprosy cases. All newly diagnosed cases are reported to the regional leprosy control coordinators with recommendations for multidrug therapy based solely on their clinical signs.

Unfortunately, regional leprosy control coordinators have repeatedly refused to enrol all the cases we diagnose into the national leprosy database (SINAN), and frequently send other physicians to re-examine and validate our diagnoses. For example, Mosqueiro island—an idyllic tourist destination only 1 hour's drive from the state capital, Belém—reportedly had a new case detection rate of 14·1 per 100 000 people in 2013, while the rate in Pará was 50·7 per 100 000. The family health strategy provides basic health coverage for only 50% of the Pará population, and 22% of those residing in Mosqueiro. In May, 2014, our group visited the island and diagnosed 110 new cases out of 1000 individuals examined (11·0%). Only 13 (11·8%) were validated as having leprosy (although only 69 patients were revisited): the remainder were not treated. Using mathematical modelling of the same dataset to project scenarios of leprosy elimination in Pará, two back-to-back reports predicted leprosy elimination by either 2026[2] or 2030.[3] These predictions about case detection rates are not based on what is truly occurring, but these citations might be exploited by health authorities. These reports imply that further active surveillance activity and chemoprophylaxis will not influence the trend substantially, and the disease will subside by continuing and maintaining the present health structure. Conversely, WHO suggests we need early case detection and contact tracing[4] and we completely agree. Our work shows that it is feasible to find more leprosy cases using geographical information systems and serological analysis to target specific schools for surveillance in hyperendemic areas.[5]

Nonetheless, the real question is why the percentage of children with leprosy varies from 1·2% to 39·8% (or why grade 2 disability ranges from 0·0% to 28·0%)[4] in different, but all equally poor, countries? The answers will only be possible when we understand that absence of diagnosis of leprosy is not the same as the absence of leprosy. The elimination target has become the mantra everywhere, but it is now meaningless. Although the zero-transmission strategy[1] is highly desirable, comprehension and acknowledgment of the real worldwide leprosy situation is imperative first.

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