

- 2 Parola P, de Lamballerie X, Jourdan J, et al. Novel chikungunya virus variant in travelers returning from Indian Ocean islands. *Emerg Infect Dis* 2006; **12**: 1493–99.
- 3 Musso D, Gubler DJ. Zika virus. *Clin Microbiol Rev* 2016; **29**: 487–524.
- 4 Angelakis E, Mediannikov O, Parola P, Raoult D. *Rickettsia felis*: the complex journey of an emergent human pathogen. *Trends Parasitol* 2016; **32**: 554–64.
- 5 Dieme C, Bechah Y, Socolovski C, et al. Transmission potential of *Rickettsia felis* infection by *Anopheles gambiae* mosquitoes. *Proc Natl Acad Sci USA* 2015; **112**: 8088–93.

Finding undiagnosed leprosy cases

We share the concerns raised by Claudio Salgado and colleagues¹ about the real-world leprosy situation. Indeed, the absence of reported cases is not the same as the absence of leprosy. The annual reported number of cases and new case detection rates largely reflect the current case finding efforts. A study estimated that more than 4 million cases will be missed worldwide between 2000 and 2020.²

However, we disagree about the interpretation of our recent publications, cited by the authors, in which we predict the leprosy trends in Pará State, Brazil, using mathematical

modelling.^{3,4} Salgado and colleagues¹ state that these predictions are not based on what is truly occurring in practice (ie, under-reporting of leprosy cases). However, our model does account for the large number of missed cases through an internal process including case detection delays and imperfect contact tracing based on available data. Moreover, such mathematical modelling can even help to provide estimates of the number of undiagnosed cases. To illustrate this, we present the annual number of new undiagnosed leprosy cases (per 100 000 population) based on the same model (figure).^{3,4} The predicted rate of new undiagnosed leprosy cases is at least twice that of diagnosed cases. About half of the undiagnosed cases are symptomatic, which clearly indicates the failure of practice to identify all cases.

Furthermore, the overall declining trend in new case detection rates should not be considered as a call to discourage further active surveillance or contact tracing. Zero transmission in Pará State will not likely occur in the coming decades (figure). Moreover, in our model we assumed, based on actual data, a continuation

of a detection delay of 3 years and household contact tracing with 58% coverage. If case finding rates are worse, then we can expect even higher numbers of both diagnosed and undiagnosed cases. Therefore, earlier diagnosis of leprosy cases remains crucial for the attainment of zero transmission.⁵ Clearly, additional strategies remain necessary, such as providing chemoprophylaxis to household contacts and preferably a wider range of contacts, as well as active case finding in identified high-risk populations.^{4,5}

We declare no competing interests.

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- 1 Salgado CG, Barreto JG, da Silva MB, Frade MA, Spencer JS. What do we actually know about leprosy worldwide? *Lancet Infect Dis* 2016; **16**: 778.
- 2 Smith WC, van Brakel W, Gillis T, Saunderson P, Richardus JH. The missing millions: a threat to the elimination of leprosy. *PLoS Negl Trop Dis* 2015; **9**: e0003658.
- 3 Blok DJ, De Vlas SJ, Richardus JH. Global elimination of leprosy by 2020: are we on track? *Parasit Vectors* 2015; **8**: 548.
- 4 de Matos HJ, Blok DJ, de Vlas SJ, Richardus JH. Leprosy new case detection trends and the future effect of preventive interventions in Para State, Brazil: a modelling study. *PLoS Negl Trop Dis* 2016; **10**: e0004507.
- 5 Smith CS, Aerts A, Kita E, Virmond M. Time to define leprosy elimination as zero leprosy transmission? *Lancet Infect Dis* 2016; **16**: 398–99.

Global burden on neglected tropical diseases

Neglected tropical diseases (NTDs) are a diverse group of infectious diseases prevailing in tropical and subtropical areas that affect more than 1 billion people, disproportionately those living in poverty.¹ NTDs are included in the Sustainable Development Goals (SDG),² with goal 3.3 to end the epidemics of AIDS, tuberculosis, malaria, and neglected tropical

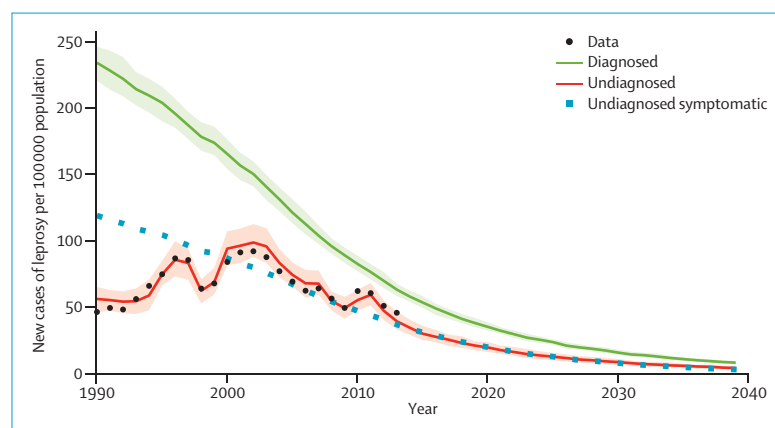


Figure: Predicted trend of diagnosed and undiagnosed new cases of leprosy (per 100 000) in Pará State, Brazil

The new case detection rate (NCDR) of diagnosed leprosy cases (red line) was fitted to the reported NCDR obtained from the SINAN database (black dots). The green line represents the corresponding estimated trend of total undiagnosed cases (ie, asymptomatic and symptomatic). The blue dotted line provides the NCDR of undiagnosed symptomatic cases. The estimated numbers of diagnosed and undiagnosed cases are determined by a process of case finding incorporated by the model, which concerns a passive case detection delay for symptomatic cases of on average 3 years and household contact tracing with 58% coverage, based on empirical evidence. Shaded areas indicate 90% confidence intervals.

diseases and combat hepatitis, water-borne diseases, and other communicable diseases by 2030.

The Global Burden of Disease 2013 study contained estimation of the burden of 17 NTDs.³ In *The Lancet Infectious Diseases*, the disability-adjusted life years (DALYs) for dengue and cutaneous leishmaniasis were evaluated in more detail in two Articles.^{4,5} These individual analyses were of value for many reasons. First, only in these Articles could methodology be described in deep detail. Typically, corresponding to the feature of being neglected, collection of accurate data for morbidity and mortality is challenging for NTDs. Thus, data missing in countries without surveillance and under-reporting in those with surveillance are unavoidable. In these Articles, the application of extrapolation could be explained and the use of under-reporting factors could be shown. Similarly, the estimation of cases by different severity, the corresponding disease duration, and disability weight could also be provided here. Obviously, full demonstration of these contents increases transparency, which provides the chance for argument and the space for future improvement.

Second, the full demonstration of disease burden by sex and age benefits

the application of targeted control measurements. Particularly, the disease burden map will provide the insight for international and regional organisations to formulate control strategy. Third, these Articles offer comparison of the literature available for diseases. The data for NTDs are relatively few, which hinders the accurate evaluation of disease burden. These comparisons will increase our understanding of complexity in data collection and analysis on NTDs, which would encourage the improvement in the future.

Of the 17 NTDs included in the Global Burden of Disease 2013, dengue and cutaneous leishmaniasis were ranked ninth and 16th, and the corresponding shares in all NTDs (including 17 definite ones above and one group of others) were 4.54% and 0.17%, respectively (appendix).³ Obviously, individual analyses for other NTDs are also expected and this methodology could be used.

A comprehensive database for all NTDs should be established and updated periodically based on data from the Global Burden of Disease 2013. This database should include a special section for each neglected tropical disease. More research is needed to improve the construction of modelling, collection of

epidemiological data, and refine other parameters for these diseases. These steps will promote accurate evaluation of global burden for NTDs and any subsequent application of appropriate control or elimination strategy, which will finally promote the achievement of the SDGs.

We declare no competing interests.

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- 1 WHO. Neglected tropical diseases. http://www.who.int/neglected_diseases/diseases/en (accessed Feb 21, 2016).
- 2 UN. Sustainable development goals. <http://www.un.org/sustainabledevelopment> (accessed Feb 21, 2016).
- 3 GBD 2013 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. *Lancet* 2015; **386**: 2145–91.
- 4 Stanaway JD, Shepard DS, Undurraga EA, et al. The global burden of dengue: an analysis from the Global Burden of Disease Study 2013. *Lancet Infect Dis* 2016; **16**: 712–23.
- 5 Karimkhani C, Wanga V, Coffeng LE, Naghavi P, Dellavalle RP, Naghavi M. Global burden of cutaneous leishmaniasis: a cross-sectional analysis from the Global Burden of Disease Study 2013. *Lancet Infect Dis* 2016; **16**: 584–91.

See Online for appendix