Is that really a neglected disease?

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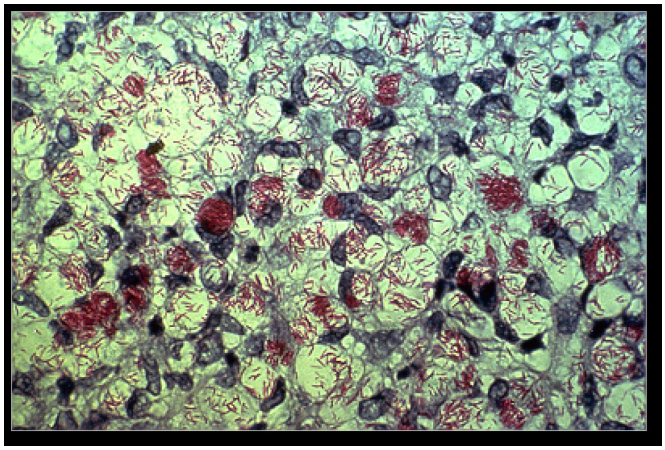

M. leprae, one of the causative agents of leprosy. Credit: Public Domain

Dangerous infectious diseases such as AIDS/HIV, Zika, Ebola and influenza frequently make headlines, and it seems as if there is no end of media attention and research interest focused on them. Conversely, diseases like leishmaniasis, Chagas and rabies seem to receive relatively little attention and research activity in relation to their perceived disease burden, and have hence been considered by many to be "neglected tropical diseases (NTDs)." But is this perception accurate?

In a fascinating analysis of 52 infectious diseases published recently in *PNAS*, Japanese researcher Yuki Furuse sought to answer this question and to rank these diseases with regard to their actual disease burden in relation to published research findings.

Infectious diseases were responsible for 20% of deaths worldwide in 2016, as well as significant disability in the case of non-fatal diseases—blindness resulting from trachoma, for example. For this reason Furuse chose disease-adjusted life years (DALYs) as a measure of disease burden to represents both mortality and significant disability incurred by infectious disease.

For an indicator of research intensity in a given region, the five countries with the highest number of medical research publications were considered representative of that region, and the first author of each study was used as a surrogate for determining nationality. Publications released between 2010 and 2017 from 45 countries in 10 regions were reviewed.

By applying linear and logistic regression techniques to these data, Furuse was able to thus establish a burden-adjusted research intensity (BARI) index to more accurately assess disease burden in relation to research intensity at national, regional, and global levels. His analysis tracked BARIs from the 1990s through the present decade and highlighted diseases with extreme burden at either the high or low end of the research intensity scale.

About these findings the author noted that "No clear universal feature determined the BARI for a disease. The reason for high or low BARI may be specific to each disease." Nevertheless, six general patterns emerged from an evaluation of the data: 1) BARI is high in most countries, e.g. AIDS/HIV; 2) BARI is moderate in most countries, e.g. chlamydia; 3) BARI is low in most countries, e.g. tetanus; 4) BARI varies depending on regional economic level, e.g. Campylobacter enteritis research intensity is high in high-income countries but not in low-income countries; 5) BARI is high in affected countries with considerable research also from non-affected countries, e.g. malaria; 6) BARI is low or middle with regard to affected countries with considerable research from non-affected countries, e.g. the NTD ascariasis.

Interestingly, the study revealed that several so-called NTDs—Chagas, leishmaniasis, and leprosy—actually had a high BARI. On the other hand, Furuse's research revealed that paratyphoid fever, a non-NTD with a low BARI, received scant attention from researchers.

While HIV/AIDS research has actually decreased in

intensity in recent years, it still scored exceptionally high even in relation to its already high disease burden. Tuberculosis also rated a high BARI.

Influenza was identified as an infectious disease with a justifiably high global BARI for several reasons. Because the virus is rapidly evolving and new vaccines must be formulated every year, flu research is a perennial worldwide infectious disease priority. Recent pandemic outbreaks such as avian flu and swine flu, which are particularly concerning with regard to their pathogenicity, are also drivers for the continuous high level of research intensity for this disease state.

Other headline-grabbing diseases such as Ebola and Zika have not yet caused significant DALYs, and thus were not included in the study—however, their virulence and pandemic potential already merit significant research interest.

In discussing some of the weaknesses of his study, Furuse notes that, for diseases with an already high burden, his data don't specify how much compensatory research activity they should receive if they are lacking. Using DALYs as a statistical measure also has a downside in that it may misrepresent or underestimate the disease burden from some types of disease. For example, renal disease deaths brought on by schistosomiasis may be mistakenly misclassified as simply renal disease deaths. Furuse also acknowledged the potential for confusion inherent in using the first author's institutional affiliation as a surrogate for country of nationality.

All things considered however, this study provides valuable insight into the relationship between a quantified burden for a number of infectious diseases and its corresponding research intensity—or lack thereof. In closing, the author concludes "Despite its limitations, our study identified infectious diseases that have received research attention or have been neglected by researchers from one viewpoint. We hope these findings provide a basis for further discussions about the more appropriate allocation of research resources to infectious diseases."

More information: Yuki Furuse. Analysis of research intensity on infectious disease by disease burden reveals which infectious diseases are neglected by researchers. *PNAS*. January 8, 2019 116 (2) 478-483; published ahead of print December 31, 2018
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