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Journal

Frontiers of Biogeography, 9(4)

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Publication Date

2018

DOI

10.21425/F59436623

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Disease biogeography: spatial and temporal analyses of infectious disease burden at the country-level scale provides new insights and challenges

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Abstract. In a recent study, Wood et al. (2017 *Phil. Trans. Roy. Soc. B* 372, 20160122) utilized a novel set of spatial and temporal analyses to identify which factors were most strongly correlated with changes in human infectious disease burdens from 1990 to 2010 in 60 countries. Using the statistical analyses and findings of this article as a framework, I have identified three important insights and challenges that this research presents for disease biogeography moving forward. First, the main factor still limiting disease biogeography research progress is underreported or absent data – particularly in the case of neglected tropical diseases. Second, the use of disability-adjusted life years instead of indirect measures of disease burden should be a focal point of disease biogeography research since it allows for comparisons of lethal and non-lethal diseases. Finally, disease biogeography studies that utilize country-level statistical analyses may be better at identifying demographic and economic drivers than environmental or biological drivers.

Keywords. Disease, biogeography, pathogen

Understanding what factors drive global variation in human infectious disease burden has historically been challenging. In most cases, the central limitation is a lack of epidemiological data, including location and prevalence rates of different diseases (Murray et al. 2012, Kirk et al. 2015, Aarestrup and Koopmans 2016). This is particularly true for regions/countries that do not have strong public health programs and often for Neglected Tropical Diseases (NTDs), which by their nature are understudied and poorly represented in health surveys (Hotez et al. 2014, Stensgaard et al. 2017). Understanding what drives disease burden is also challenging because diseases can be impacted by ecological, economic, and demographic factors (Sachs and Malaney 2002, Jones et al. 2008, Murray et al.

2015, Stephens et al. 2016). Therefore, studies that try to identify global drivers of infectious diseases must find ways to deal with data limitations and factors that are operating at different spatial and temporal scales.

In the last decade, there have been numerous studies that have attempted to tease apart the effects of ecological, economic, and demographic drivers on human infectious disease burdens (Jones et al. 2008, Dunn et al. 2010, Smith et al. 2014, Stephens et al. 2016, Garchitorena et al. 2017). However, a recent paper by Wood et al. (2017) utilizes a novel approach to estimate what the contribution is of each of these putative factors to the variation in human infectious disease burden between countries over time. Here, I dis-

cuss the benefits and limitations of this approach and how this research can provide insight into future studies on human and wildlife disease biogeography.

In their manuscript, Wood et al. (2017) examine how a number of factors including population density, temperature and precipitation per unit area, percent of people living in urban areas, bird/mammal species richness per unit area, forest cover per unit area, and per capita wealth drive spatial and temporal variation in human infectious disease burden. To do this, the authors analyzed recently published information on disability-adjusted life years (DALYs, i.e., the total number of years lost to death/disability) from 1990 and 2010 for 24 infectious diseases tracked by the World Health Organization's Global Burden of Disease Database in 60 countries of similar geographic size.

Using this novel spatial and temporal approach, the authors identify three main findings. First, the majority of the putative factors had different associations with each of the 24 different diseases. This finding is important because it is consistent with recent work on human pathogen geography, which suggests that though there are biogeographic trends with diseases (e.g., pathogen diversity decreases with latitude), many diseases have different factors that can affect their impact on human health (Dunn et al. 2010, Stephens et al. 2016). Furthermore, this finding suggests that there will continue to be challenges for public health agencies looking for singular efforts that will reduce the impacts of multiple diseases simultaneously.

Second, conservation efforts including reforestation and increases in biodiversity over time may not improve human health. At first glance, this finding may be unsurprising as human infectious disease burden can be correlated with increases in the number of potential hosts (Jones et al. 2008, Dunn et al. 2010, Murray et al. 2015). However, this finding also conflicts directly with the dilution effect hypothesis (Keesing et al. 2010) and the decoy hypothesis (Stensgaard et al. 2016), which suggests that increases in the number of hosts is likely to reduce subsequent disease risk in

alternative hosts. Collectively, this finding indicates that public health and conservation goals could be in conflict and may pose challenges in the future.

Finally, and perhaps most interestingly, the authors determined that urbanization showed the strongest effect of all the investigated drivers and was associated with decreases in disease burden across space and time. This result is important because it contradicts the idea that urbanization may cause increases in disease transmission and outbreaks (Hassell et al. 2017). However, it also may imply that decreasing contact with zoonotic disease hosts or increasing access to health care are likely to outweigh any potential disease risks from increased human population.

One of the factors that makes this study novel is that the authors utilized DALYs instead of other indirect measures of human disease burden (e.g., prevalence or outbreak frequency). This approach is ideal for disease biogeography research because infectious diseases are idiosyncratic in nature and can have significant variation in both impact on hosts and in transmission route. As a result, this study allows for comparison between different diseases – especially those that are lethal and non-lethal, which is something that should be increasingly done in future disease biogeography research.

However, while the use of DALYs helps to draw generalized conclusions about drivers of human infectious disease burden at the country-scale, this metric also has an important caveat for future disease research studies. Despite their widespread usage since the mid-1990s, recent research has shown that DALYs data can vary in quality and quantity depending on the type of disease and geographic location. For example, many NTDs (e.g. Chagas disease and schistosomiasis, both of which were utilized in this study) may be underreported or impact marginalized people who are not represented in national health surveys (Schratz et al. 2010, Hotez et al. 2014). This finding reveals that while we are moving forward in our understanding of how to analyze and compare different types of disease, the main thing holding research back is still the lack of adequate

epidemiological data. And this conclusion extends well beyond this study as there are no similar metrics to DALYs for non-human disease research.

The final challenge this study addresses is the utility and accuracy of the country as a unit of replicate for disease biogeography studies. In particular, Wood et al. (2017) suggest that while countries may not be ideal units of replication at this scale there are strong correlations between infectious disease burden and demographic and economic factors. This finding is incredibly important as countries are often the scale at which conservation and public health decisions are made. However, as is suggested above with the DALYs data, it may not always be possible to conduct complete and thorough analyses because of differences in levels of data collection, their potential lack of independence, and variation in size/disease burden. In addition, the authors findings also suggest that due to the idiosyncratic nature of infectious diseases, countries may not be an ideal unit of replication for exploring environmental drivers of disease burden. Collectively, these two conclusions suggest that as people continue to engage in disease biogeography research moving forward, they must acknowledge that different drivers may be operating at fundamentally different spatial scales and that it may be difficult to come to general conclusions with a single analysis.

Ultimately, Wood et al. (2017) provide important and thought provoking conclusions for the field of disease biogeography. These include the idea that new statistical approaches are still needed to understand what factors drive human (and non-human) infectious disease dynamics across the world. In addition, they suggest that while we are increasing our understanding of how disease burdens are changing over time, we still lack data on neglected diseases and in underreported regions that may help us to further identify trends in both human and non-human disease impacts over time. Finally, they suggest that while countries may be difficult to compare for social, geographic, and economic reasons, they can provide useful information about global disease trends and should continue to be an important part of disease biogeography research in the future.

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Submitted: 02 October 2017

First decision: 29 October 2017

Accepted: 27 December 2017

Edited by Michael N Dawson