

What is the impact of climate change on infectious disease?

DISCUSSION

AUTHORS

Jessica P J Larwood
St John's College, University of Oxford

Address for Correspondence:

Jessica P J Larwood
St John's College
University of Oxford
OX13JP

Email: jessica.larwood@sjc.ox.ac.uk

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ABSTRACT

The world is warming at an alarming rate; in October 2018 the Intergovernmental Panel on Climate Change reported a 1°C human-induced warming since the pre-industrial period and a current rise of 0.2°C per decade. The UN secretary-general stated that 'climate change affects every aspect of society, from the health of the global economy, to the health of our children'.

Many in the field hypothesise that the changing climate will lead to an increase in the size of vector-borne disease transmission zones, an appearance of tropical disease in temperate regions and the emergence of native species that have the capacity to transmit tropical pathogens. Although a large proportion of the discussion surrounding climate change and infectious disease focusses on malaria, concern exists surrounding other vector-borne diseases such as tick-borne encephalitis and Lyme disease, and water-borne and respiratory infections. The true effect of climate change on infectious disease is elusive and heavily debated; a comprehensive model including not only temperature, but precipitation, humidity, and extreme weather events is needed to properly evaluate the impact of the warming climate on communicable disease. Whilst the intricacies of the climate and infectious disease is not fully understood, it is important to remember that those most vulnerable to communicable diseases are those living in poverty, so any climate induced increase in transmission will only seek to worsen the already apparent health inequality worldwide.

Introduction

The relationship between climate change and infectious disease is a topic of polarising debate, especially when it comes to human pathogens – socioeconomic drivers, vector-control methods, antimicrobial treatment, and infrastructure can all mask the true climate effect. The relationship between climate and infectious disease is non-linear, with certain factors increasing disease transmission and others limiting it, making the true trajectory difficult to elucidate.

The life-cycle and transmission of many pathogens is tied to climate, whether that be an increase in water-borne disease after extreme weather events or the seasonal cycle of flu outbreaks. Climate has a greater association with disease caused by pathogens that spend part of their lifecycle outside of the host, exposed to the environment, whilst disease transmitted directly between humans has fewer climate associations.

(1) A recent assessment of over 150 high-impact European pathogens concluded that 66% have at least one climate affected variable that impacts disease occurrence and up to 37% of disability-adjusted-life-years arise from human infectious disease sensitive to climate. (2) Nonetheless, the method used to prioritise pathogens for inclusion in this assessment has a number of limitations, including under-representation of newly emerging diseases and bias in results due to trends in interest in diseases. Evidently, there is a relationship between many infectious diseases and the climate, but how a warming climate will impact these pathogens is up for debate. A seminal review published in *Science* in 2002, by Havell et al, concluded that warming can increase pathogen development, survival rates, disease transmission, and host susceptibility; (3) however, these conclusions were drawn from data on both marine and terrestrial biota with cholera the only human disease included. Since the publication of the Havell et al review, numerous studies have explored the impact of a changing climate on individual infectious diseases or mechanisms of transmission, but there is still no consensus on the overall impact of climate change on infectious disease within the human population.

Vector-borne disease

Vector-borne infections are the focus of research when it comes to climate change and infectious disease, and dominate the conversation surrounding the topic. Broadly, there are three expected threats from vector-borne disease under a warming climate: increased risk from endemic disease due to changes in temperature and rainfall, change in geographic range of vectors, and the appearance of exotic diseases in temperate regions due to increased climatic suitability. (4) Although much attention is focused on the threat of invasive species, there is also a risk from native species which may have the potential to become vectors for tropical disease. The endemic UK mosquito, *O. Detritus*, has been shown to be a capable vector for exotic flaviviruses (a genus that includes West Nile Virus and Zika) when under specific temperature conditions. (5) Limitations of this study include unrealistically high temperature conditions that do not mimic current UK climate and a small sample size. Nevertheless, it is an early contribution to knowledge on the competence of native vectors. Understanding the risk posed by native species in the transmission of exotic pathogens is essential in predicting climate-mediated change, especially in temperate regions, such as the U.K, where the impact of vector-borne diseases is currently relatively small.

Malaria is already a great concern to public health. The WHO predicts it is likely to be the vector-borne disease most sensitive to long-term climate change. (6) Malaria is caused by the Plasmodium parasite, a group of single-celled organisms that use mosquitos as mobile vectors, infecting the human host via the mosquito feeding. Plasmodium Falciparum accounts for approximately 75% of human malaria cases and has a high rate of mortality, whilst Plasmodium Vivax accounts for a further 20% of cases and is traditionally thought to cause a milder form of disease. Due to its prevalence in lesser-developed regions, P. Falciparum is often diagnosed clinically; the potential for over-diagnosis can therefore make the true pattern of transmission hard to elucidate.

Malaria is intertwined with many aspects of climate. Research from endemic areas demonstrates clear seasonal variation in disease transmission and analysis has shown that the malaria epidemic risk increases five-fold in the year after an El Nino event, although this may be confounded by human behavioral changes or infrastructure inadequacy. (7) The prevailing forecast for the trajectory of malaria transmission is global expansion, particularly into regions of higher altitudes. (7) However, an alternative approach, using statistical modelling rather than historic biological data, suggests that overall change to malaria transmission due to climate change is likely to be relatively small and any expansion in disease range would be offset by contraction in other geographic locations. (9) A major disadvantage of these models is that they only account for malaria caused by P. Falciparum and neglect malaria caused by other species, including P. Vivax which was once endemic to Northern Europe and requires much lower temperatures for transmission. Therefore, the risk of malaria in a warming climate may be vastly underestimated in areas where P. Vivax poses the greatest risk. Additionally, evidence suggests recent invasion of other mosquito-borne diseases in temperate regions, such as Chikungunya, Dengue fever and West Nile Virus in Europe. It is likely that even if there is no net change to the size of the area suitable for mosquito-borne disease transmission, the impact on previously unaffected communities will be significant. (1)

Mosquitos are not the only vector thought to be vulnerable to climate effects; the possible increase in cases of tick-borne encephalitis (TBE) in Europe is also cause for concern. Viral transmission of TBE occurs between cofeeding larval and nymphal ticks, and synchrony of this feeding is associated with milder winter climates. (10) It is therefore thought that by increasing tick synchrony, climate warming may increase rates of transmission and promote the selection of more virulent strains. (10) This theory is claimed to explain the increased incidence of TBE in Sweden since the 1980s, with a prominent study published in the Lancet reporting a significant relationship between two consecutive mild winters and an increase in disease. (11) However, authors do not account for an increase in TBE vaccination since the mid-1980s or the increase in education and awareness surrounding ticks, meaning the links between climate change and disease incidence may be underestimated. Unsurprisingly, there is division amongst researchers as to whether climate change is the true cause of the increased incidence of TBE in Europe; alternative explanations include changes in land-use, increase in human population in tick-endemic areas, wild-animal population

changes, and increased tourism. Another tick-borne illness with an increasing incidence in Europe is Lyme disease, the most common vector-borne disease in temperate climates. (1) The field is similarly divided as to whether climate change is solely responsible for the increase and poleward spread of disease. Increased surveillance programmes and predictive modelling is needed to better assess the threat from tick-borne infection.

It is difficult to elucidate the impact of climate change on vector-borne disease due to challenges in modelling the multiple possible effects of a changing climate on pathogens, vectors, and host susceptibility, with climate warming often increasing some elements of transmission and decreasing others. During an outbreak of P. Vivax malaria in Greece in 2012, spatial modelling was used to highlight areas of susceptibility based on land temperature and elevation, and ultimately helped to guide the public health response. (12) The major limitation of this technique was the fact it only accounted for environmental suitability, rather than incorporating actual data from vector surveillance or disease incidence. The success of this approach does however demonstrate that even rudimentary models can be useful in directing healthcare responses, initiating vector control, and increasing awareness amongst at-risk populations. Although the outbreak reported in Greece was amongst economic migrants from malaria endemic areas, the spatial modelling demonstrated may be a useful tool in mapping changes in climate suitability over time. Socioeconomic and public health factors such as vector control strategies, vaccination initiatives, inconsistent diagnostic methods, and human migration may mask true patterns of vector-borne disease transmission.

Water-borne disease

Research surrounding vector-borne disease and climate change focusses on a temperature change as a possible driving force behind an increase in disease transmission, however, a warming climate will also affect precipitation, humidity, and the frequency of extreme weather events. Climate change is expected to alter the water cycle and - water-borne enteric diseases are among the expected health implications of this climatic shift. (13) Diarrheal disease already accounts for 10-12% of all deaths in children under the age of five, so even a small increase in diarrhea risk will have a substantial impact on the global disease burden. (13) The WHO estimate that climate change could be responsible for between 20,000 and 86,000 deaths in children globally between the years 2030 and 2050, under a range of socioeconomic growth models. (1) This assessment does not account for the likely co-morbidity of water-borne infection and malnutrition, or the different temperature profiles of individual pathogens. Despite these limitations, it does begin to expose the possible devastation climate change could cause via diarrheal disease.

The first systemic review of water-borne disease and climate change in 2016 showed that heavy rainfall and flooding significantly increase the rate of water-borne disease outbreaks, often due to contamination of the drinking water supply. (13) Additionally, it demonstrated that an increase in temperature may precipitate increased outbreaks of bacterial diarrheal disease whilst having a negative correlation with viral diarrheal disease. This tendency to promote bacterial and inhibit viral disease is possibly

explained by the vulnerability of viruses to higher temperatures compared to more complex survival mechanisms employed by bacteria, including increased bacterial load in hosts and expression of virulence genes. (13) Despite these convincing results, reporting bias – with over-representation of certain geographic regions and surveillance programmes – limits conclusions that can be drawn. Unlike the impact of temperature and precipitation, the impact of drought on water-borne disease is unclear, with sparse and variable epidemiological data. The research is mixed, with some studies demonstrating a clear association between drought and diarrheal disease, possibly explained by increased concentration of pathogens in water sources, though other groups reject this claim. (14) (15) Variability between drought events may explain these inconclusive results; as such, it may be useful to stratify data based on water source used during the drought, length of drought, amount of rainfall at the end of the drought period, etc. Though temperature, flooding, and heavy rainfall are all risk factors for water-borne disease, more research is needed to fully understand the relationship between drought and water-borne infection.

Cholera, a disease caused by the water-borne bacteria *Vibrio Cholerae*, is of heightened interest in the conversation surrounding climate and water-borne disease as it is highly contagious and can be fatal within hours in the most severe cases. *V. Cholerae* is naturally present in estuaries, rivers, and coastal bodies of water, forming a commensal relationship with plankton for its survival and replication. Coastal cholera infection has been associated with plankton blooms, increased sea surface temperature, and extreme storms. (10) Moreover, analysis of monthly data points for cholera cases in Dhaka, Bangladesh between 1980 – 1998, showed a variability in incidence correlating with the frequency of the El Nino weather pattern. (16) However, this is not sufficient evidence to conclude that increased temperature directly increases cholera transmission and alternative explanations consider changes to Himalayan snowpack melting, sanitary conditions, and human interactions with water sources. (16)

The increased risks of cholera in endemic areas is one concern, but there is also evidence of poleward spread of *Vibrio* outbreaks in cold and temperate regions, such as Chile, Northwest US, and Spain. (17) *Vibrio* bacteria preferentially grow in warm, low salinity sea water; increased precipitation reducing salinity in estuaries and wetlands and an increase in temperature due to climate warming may explain how new areas of suitability are emerging in high latitudes. (17) The Baltic sea is of particular interest in the study of *Vibrio* diseases, it is one of the fastest warming marine ecosystems worldwide and long-term warming and extreme heatwaves have been related to an increase in *Vibrio* infections. (17) Predictive models suggest that for every 1°C increase in sea surface temperature, cases of *Vibrio* illness in the Baltic regions could increase two-fold. (17) Despite clear changes to the patterns of *Vibrio* infections, conclusive evidence of a climate related cause remains contentious. This is in part due to lack of full epidemiological data and the possible attribution of cases of *Vibrio* infection in high latitudes to sporadic cause. Cholera and other forms of *Vibrio* infection appear to be susceptible to climate change and further research is needed to exclude alternative drivers such as changes to human interaction with water sources and changes in coastal population density. (17) Looking to the future, it would be helpful to

establish a centralised reporting system for *Vibrio* infections that is consistent between geographic areas and allows analyses alongside climate data, with the ultimate aim of devising an early warning system to advise public health measures.

Respiratory infection

Respiratory infections often follow seasonal cycles of transmission, but whether climate change will impact transmission patterns is purely speculative, with insufficient evidence to draw meaningful conclusions. Pneumonia and influenza are significant contributors to the global burden of disease, with severity and transmission increasing in winter months. Therefore, as suggested by the European Respiratory Journal, climate change could actually have a beneficial effect, with warmer winters reducing disease frequency. (18) Interestingly, an Australian study showed that the most important variable in determining frequency of childhood pneumonia is the temperature drop between neighboring days, suggesting that oscillations in temperature may have the potential to drive increased transmission of respiratory infections. (19) Any conclusions drawn on how respiratory infections are affected by climate change are currently limited and lacking in robust evidence; extensive epidemiological analysis is needed to elucidate true patterns of disease transmission, as well as consideration of other direct and indirect confounding factors such as air pollution, risk of flooding, and changes in human behavior. A better understanding of the relationship between a changing climate and respiratory infections is essential, as such diseases can spread rapidly and cause a huge burden on public health.

A pathogen may emerge as a new public health concern due to changes in its transmission or life cycle, or mutualistic microorganisms may become pathogenic due to changes in host susceptibility to infection. Although there are many causes of new pathogen emergence, it is important to consider the implications of a changing climate on the development of new diseases. Parachlamydia Acanthamoebae is an emerging human respiratory pathogen that relies on warming for the transformation from endosymbiotic to lytic within host amoeba in the human nasal passage, and ultimately conversion from a commensal to pathogenic species. (20) Despite having a temperature component for pathogenesis there is currently no research to determine whether climate change has an impact on disease transmission. Predicting emergence of new diseases is virtually impossible, but it may be useful to develop a database of emerging pathogens with climate dependency in order to increase preparedness for unexpected disease patterns and outbreaks.

Global health

It is important to remember that one of the biggest risk factors for infectious disease is poverty and that any changes to infectious disease burden due to climate change will disproportionately affect the poor. Developing nations are already most at risk from climate change due to their geographical locations, their high dependency on natural resources, and their limited ability to adapt to climate changes. An increase in infectious disease transmission would therefore compound existing adversity. Over 1 billion people live in poverty; in order to protect these communities and alleviate health inequality we need urgent development of intervention strategies and public health initiatives, and continued research and investment to establish the true potential

impact of climate change on infectious disease. (21)

Conclusion

Given the evidence for the sensitivity of many pathogens to climate, it is highly likely that at least some diseases will be affected by climate change. As it stands, the most conclusive evidence is on the link between increased frequency of diarrheal disease and climate warming. The most divided debate surrounds the changes in transmission pattern of vector-borne disease, although many argue there is strong evidence supporting a climate-related cause. Epidemiological data relating climate change and respiratory infection is currently lacking, as is evaluation of the potential of native species to transmit infections, and predictions surrounding the emergence of new pathogens. Additionally, there is a pressing need to develop a model that encompasses all possible climate related diseases and considers not only changes in temperature, but also precipitation, humidity, extreme weather events, and indirect factors like loss of land, migration, and air pollution. The true effect of climate change on infectious disease is notoriously elusive and demands careful consideration of all of the socioeconomic, geographical, and meteorological variables.

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