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DETECTION AND ATTRIBUTION OF CLIMATE CHANGE EFFECTS ON INFECTIOUS DISEASES

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Abstract

Infectious agents are likely to be sensitive to climate change if their life cycle includes periods of exposure to ambient conditions. Several studies have attempted to attribute changes in patterns of infectious diseases to recent climate change, such as resurgent malaria in the East African Highlands and the northward expansion of tick-borne encephalitis and Lyme disease in Europe and Canada. However, debate continues over the relative importance of climate change compared to social, demographic and other factors. Methods for the detection and attribution of climate change impacts on human infectious diseases have not been clearly defined. There are several areas of contention in the literature on appropriate methods for the detection of climate change effects on infectious diseases, including the availability and appropriate use of climate data, identifying regions where changes are most likely to be observed and the biological importance of small temperature increases and threshold effects. Definitions and strategies for the detection and attribution of climate change impacts on human infectious diseases are discussed and compared to approaches to the detection and attribution of climate change impacts in other fields. 'Consistency analysis' is proposed as a feasible methodological approach to address research questions about the impact of recent climate change on infectious diseases.

Introduction

Infectious agents whose life cycle includes a life stage or extended periods exposed to ambient weather conditions (including time within vectors or hosts) are sensitive to climate variability. Anthropogenic (or human-induced) climate change will alter the patterns of many human infectious diseases, because the development rates, lifespan and reproductive capacity of climate-sensitive infectious agents, their vectors and hosts are influenced by higher temperatures and increased climate variability (Hoberg et al., 2008; Costello et al., 2009).

Most research on climate change and infectious disease has focused on vector-borne diseases (Kovats et al., 2001; Gage et al., 2008). For example, evidence has emerged of an influence of recent regional climate change on malaria occurrence in the East African Highlands (Pascual et al., 2006; Alonso et al., 2010; Chaves and Koenraadt, 2010). Earlier studies that did not find an association (Hay et al., 2002; Shanks et al., 2002) have been criticised (Patz et al., 2002; Pascual et al., 2006; Omumbo et al., 2011). Even so, the global impact of climate change on malaria, compared to interventions and economic development that have led to malaria control, remains unclear (Gething et al., 2010; Béguin et al., 2011).

There is similar debate regarding climate in relation to tick-borne diseases. Northward expansion of the tick vectors of tick-borne encephalitis (TBE) has been documented in Europe (Lindgren et al., 2000; Lindgren and Gustafson, 2001; Daniel et al., 2003; Danielová et al., 2006), while other authors argue that the spatial and temporal heterogeneity evident in the European-wide TBE resurgence is not consistent with the relatively uniform climate change that has occurred in this region (Sumilo et al., 2007; Randolph, 2010).

In relation to the detection and attribution of climate change impacts, other climate-sensitive diseases considered include cholera (Lipp et al., 2002; Rodo et al., 2002), dengue, other waterborne infections (Hunter, 2003), food-borne infections (Tirado et al., 2010) and soil-transmitted helminthiases (Weaver et al., 2010).

Methods for the detection and attribution of climate change impacts on human health are not as well developed as in fields such as ecology (Parmesan and Yohe, 2003), perhaps due to the greater complexity in disease systems where human behaviours and ethical and logistical issues of accessing health data and working within health systems, must also be considered. Contested methodological issues for detecting climate change influences on infectious diseases include the appropriate use of climate data, the geographical range over which changes in incidence are likely to be observed, the requisite length of time-series data and the biological importance of small temperature increases and threshold effects. We discuss here the difficulties in the detection and attribution of the impact of recent climate change on infectious diseases. This is part of a larger ongoing challenge for climate change-related research in various topic areas seeking to establish methods and criteria for assessing the climate attributability of observed changes in physical, biological and ecological systems.

Climate change is important for, and, ultimately, critical to, long-term human well-being and survival. While uncertainties exist about the detailed nature of climate impacts, impacts on infectious diseases are anticipated to pose significant, increasing, perceived and real threats. Our purpose in this chapter is to highlight the challenges in studying climate change impacts on infectious diseases. We suggest that new approaches will produce a less polarised and more productive discussion of climate change impacts on infectious diseases. Improved understanding of these impacts and further projected risks should increase the impetus for mitigation and facilitate the development of strategies for adaptation.

Detection

Climate change detection is the process of demonstrating that the climate has changed significantly, relative to natural climate variability, and that the change has persisted for several decades (Hegerl et al., 2006; Stott et al., 2010). In climate and health studies, detection is the process of demonstrating that significant changes in disease incidence or transmission risk (such as change in the distribution of vectors) are congruous with demonstrated climate change in space and time. Correlation must be supported with evidence for climate sensitivity of the agents, vectors and hosts of the disease (Kovats et al., 2001).

Climate change has heterogeneous impacts on infectious disease transmission, due to regional differences in the extent of warming, exposure to ambient conditions during the life cycle of infectious agents and the interaction between climate and other factors that affect incidence. The detection of climate change effects on infectious diseases is governed by the interaction between extrinsic and intrinsic biological factors[1] and the role of social conditions (Weiss and McMichael, 2004). Change in incidence will occur when environmental conditions reach or exceed the thermal and moisture tolerances of diseases. For example, rising temperatures have led to the altitudinal expansion of malaria in the East African Highlands (Pascual et al., 2006; Alonso et al., 2010), yet prolonged drought is

1 Extrinsic factors, including temperature, water availability, soil structure, pH and sunlight, determine the favourability of the environmental conditions that influence the development and reproductive rates of the agents, vectors and hosts of infectious diseases. Intrinsic factors include ecological regulation of the agent, vector and host populations; for example, the availability of food, water and breeding sites limit maximum population size.

associated with the contraction of the malaria transmission range in the Sahel (Mouchet et al., 1996). As incidence increases, intrinsic biological factors, including herd immunity, limit transmission. Conversely, range contractions may lead to reduced population immunity over time if endemic transmission ceases, which leaves populations vulnerable to infrequent epidemics (Bangs and Subianto, 1999). Table 25.1 presents a schematic to highlight how extrinsic climate influences and intrinsic saturation effects may interact to alter infectious disease transmission under a changing climate, using the example of herd immunity.

Table 25.1 Interaction between extrinsic climate influences and intrinsic herd immunity (saturation) effects.

	Potential effects of warming on infectious disease incidence	
Climate context[a]	Low herd immunity (epidemic transmission)	High herd immunity (endemic transmission)
Cool climate + warming	Transmission thresholds reached, virgin soil epidemics may occur	Minimal increased incidence, endemic transmission maintained
Warm climate + warming	Larger epidemics, increased duration of epidemic season endemic transmission	Minimal increased incidence, endemic transmission maintained
Hot climate + warming	Transmission thresholds exceeded. Partial or full range contraction may occur, with risk of infrequent epidemics	Partial or full range contraction of host or disease, with subsequent decrease in immunity, leaving population at risk of epidemics

[a] Cool, warm and hot climate defined with respect to the thermal tolerances of the disease agent, vector or host; for example, much of Europe may become a 'hot' climate for TBE (Randolph, 2004). Regions where high herd immunity prevents increased incidence may nonetheless experience an increased abundance of vector/host populations. This may make long-term control or eradication efforts substantially more difficult.

Source: Authors' work.

Climate-sensitive diseases with high incidence, due to short duration of immunity (such as malaria and cholera), are particularly likely to alter in incidence consequent upon climate change (Dobson, 2009). Similarly, incidence changes in infectious diseases that have short incubation periods and epidemic transmission will be more readily detectable than diseases with long incubation periods and/or endemic transmission, such as lymphatic filariasis (Gage et al., 2008).

In contrast, the provision of health services, sanitation and other public health strategies may reduce disease transmission, and these non-climate societal factors may mask the effect of climate change. In this case, climate change potentiates transmission, but no change in incidence is currently detectable. However, if a decline in the quality of health service provision occurs, then climate change impacts may become apparent over a relatively short period. Therefore, when discussing climate change influences on infectious diseases, we need to be aware of the difference between climate change influences and our ability to detect this influence, which may be masked by improvements in health service delivery. Analysis of malaria in 27 African countries demonstrates that climate change has heterogeneous observable impacts on malaria incidence against diverse economic backgrounds (Egbendewe-Mondzozo et al., 2011). The finding that TBE in endemic regions of Europe has not responded consistently to climate change (Sumilo et al., 2007) may nonetheless be an expected *observable* impact of climate change due to interactions between biological factors and social conditions.

Assuming climate change impacts on infectious diseases are most likely to be observed where extrinsic factors are a dominant influence on disease, the most likely types of changes to infectious diseases to be observed under climate change include:

- Range shifts: spatial changes in the incidence of infectious diseases are most likely to occur at the edge of currently known geographical ranges, where unstable epidemic transmission occurs and conditions may be marginal for transmission (Chaves and Koenraadt, 2010).
- Seasonal shifts: climate change may induce changes in the duration of the transmission season.
- Changes in transmission intensity: regions that currently experience epidemic transmission may shift to endemic transmission.

Scale Effects

To correlate regional anthropogenic warming with changes in infectious diseases, a minimum of 20 years of data is required, preferably 50 years (Hegerl et al., 2006). As the climate is currently unstable, attempts to detect a statistically significant warming trend in conjunction with changes in disease incidence need to be updated regularly (Stott et al., 2010).

The spatial scale of climate and disease data has also been shown to be critical for detecting climate change impacts on infectious diseases. Continental-scale maps and indices of malaria transmission risk are too coarse to capture transmission dynamics at the margins of current distributions, where local malaria transmission can be maintained by small numbers of vectors and climate change, weather anomalies and diurnal temperature variations have a marked effect on transmission intensity (Pascual and Bouma, 2009; Paaijmans et al., 2010). The application of malaria suitability indices (developed for use at large spatial scales; Hay et al., 2002) has been criticised (Patz et al., 2002;

Pascual et al., 2006). Similarly, the use of global climate gridded data sets at coarse resolution for studies on regional climate change and malaria trends has been criticised (Patz et al., 2002; Omumbo et al., 2011). Global gridded climate data sets provide spatially interpolated climate data that are reliable at continental and global scales but not at regional scales, particularly in regions with steep climate gradients and sparse local meteorological stations that provide input data to the global climate models (Patz et al., 2002; Omumbo et al., 2011).

Threshold Effects

Non-stationarity such as threshold effects in time-series data adds further complexity. Non-stationarity describes shifts in the dominant influence on the periodicity of epidemic infectious diseases over time (Cazelles et al., 2005). The absence of a significant correlation between climate change and disease transmission over the full length of a time series may mask significant effects in discrete intervals within the time series, particularly when the largest outbreaks coincide with conditions that deviate substantially from the climate average. Rodo et al. (2002) demonstrated a strong correlation between cholera incidence and climate conditions during El Niño Southern Oscillation (ENSO) events at three- to four-year cycles, but weak correlation at other times. There may be thresholds at which major influences on transmission change from factors such as vector control, which may co-occur with environmental conditions that are suitable for transmission, to environmental conditions being dominant influences that overwhelm attempts to adapt to increased transmission. Existing studies may need to be re-evaluated using statistical methods that can detect the climate thresholds at which discernible impacts on infectious diseases occur, such as transient climate-disease couplings (Rodo et al., 2002).

Climate Change: Weak but Persistent Signal

A further difficulty in detection studies is assessing the importance of small, 'non-significant' climate trends. Tests of statistical significance do not reveal the biological importance of small trends in average climate conditions. Zhou et al. (2004) showed that although statistically significant temperature increases occurred for only three sites of seven across the East African Highlands, climate variability increased significantly in five of seven sites, and that increased climate variability correlated with the increased frequency of malaria epidemics. Furthermore, Pascual et al. (2006) showed that a 0.5°C increase in monthly average temperatures increased *Anopheles* mosquito abundance by 30–40 per cent in a mosquito simulation model. Given that Bouma (2003) reports a non-significant

0.5°C rise in minimum December and January temperatures in Madagascar (months predictive of malaria incidence in his statistical model), climate warming may need to be reconsidered as a contributing factor to malaria resurgence in highland provinces of Madagascar. Further complexity is introduced by the effect of diurnal temperature ranges; if small temperature increases occur in regions with cool mean temperatures (<18°C), then the effect of diurnal temperature variation has been demonstrated to increase substantially the potential for malaria transmission (Paaijmans et al., 2009, 2010).

Sampling Effects

Compounding the difficulty of identifying significant climate trends, several factors can increase the risk of false positive (chance) findings in the search for climate change impacts on infectious diseases. As the number of observers increases, it becomes increasingly likely that agents, vectors or hosts may be found outside the presumed range; however, this may reflect either an observation at the extreme end of a stable distribution or an observation within the true range assumed novel due to inaccurate existing data. Population growth can produce similar risks of false positive findings through the increased density of agents, vectors or hosts at the edge of the known distribution. Many published studies are the result of opportunistic surveillance of diseases with good baseline data and for which changes have already been noted, rather than systematic analysis of any positive, negative or neutral impacts of climate change on the incidence and range of climate-sensitive diseases, as has been done in ecology (Parmesan and Yohe, 2003). Surveillance for range shifts may minimise the confounding effects of non-climate factors within the known range.

Attribution

Attribution is 'the process of establishing the most likely causes for a detected change with some level of confidence' (Stott et al., 2010). Significant correlation between changes in disease incidence and regional climate change (i.e. detection) is not sufficient to attribute a causal relationship. Kovats et al. (2001) suggest that attribution would require a 'trend in disease over many years which is significantly correlated with a change in climate, but not with any other potential driving mechanism'. A rigorous definition of attribution would require establishing an unbiased, causal relationship between observed changes in infectious diseases and climate change *and* establishing that the observed climate change is anthropogenic in origin. However, there are considerable difficulties in achieving this standard in epidemiology. Changes in infectious diseases are reported at regional scales at which anthropogenic climate change may be difficult to detect above the level of natural variability, and also factors other than anthropogenic greenhouse gas emissions may influence regional climate trends (Stott et al., 2010).

The scientific consensus on anthropogenic global change emerged through the collation of thousands of observations from individual sites; the attribution of warming trends to anthropogenic influences at any one site would not be possible. Similarly, attribution cannot be demonstrated formally for any single study, or possibly even any single disease. The causal effects of climate change on infectious disease may become unambiguously apparent by conducting a systematic analysis of trends across diverse diseases and geographic regions. Uncertainty in attribution for individual studies does not prohibit achieving an acceptable level of confidence in attribution based on cumulative synthesis (Parmesan and Yohe, 2003). No meta-analysis has been published of the magnitude of range shifts or other changes in multiple infectious diseases due to climate change. As with analyses of the impacts of climate change on species ecology (Parmesan and Yohe, 2003), the most systematic method for assessing whether climate change is impacting infectious diseases is to assess whether the changes observed for diverse climate-sensitive infectious diseases are consistent with the predicted effects of climate change. This represents a departure from previous debates in the literature, particularly for TBE (Randolph, 2010), that have focused on the unique, especially entomological, characteristics of particular diseases rather than assessing whether climate change has similar distributional effects on a number of infectious diseases.

Full attribution of changes in infectious diseases to climate change requires:

- meteorological evidence of climate change at regional scales
- spatiotemporally correlated change in infectious disease frequencies
- evidence that other factors cannot account for all of the observed change.

A simpler alternative for the detection and attribution of climate change impacts, called consistency analysis, has been proposed in ecology (Parmesan and Yohe, 2003), and we suggest could also be applied to infectious diseases. Consistency analyses involve demonstrating a significant relationship between regional climate change and changes to infectious diseases that are not fully explained by other factors. Consistency analyses are strengthened considerably when similar effects are observed for several diseases in multiple regions. Few individual studies can demonstrate all aspects of a consistency analysis, though the work of Alonso et al. (2010) is a notable exception. The finding that warming in the East African Highlands accounts for approximately 40 per cent of the observed increase in malaria cases is a substantial contribution to the field (Alonso et al., 2010). It should be noted that authors disputing a correlation between climate change and malaria in the East African Highlands have not quantified other possible contributing factors to malaria resurgence at a regional scale. On a global scale, the impact of economic development on reducing the global malaria burden has been estimated (Gething et al., 2010), but this finding cannot explain local increases in malaria incidence.

A qualitative assessment of consistencies in the types of changes in infectious diseases observed under recent climate change may be a good starting point for analysis. An example of a qualitative assessment measure is 'sign switching' (Parmesan and Yohe, 2003). Range expansion along the warming margins of the current distribution and range contraction along the cooling margins has been defined as a diagnostic 'fingerprint' of climate change impacts on species distribution (Parmesan and Yohe, 2003) and is applicable to infectious diseases. Several studies documenting altitudinal and latitudinal range shifts for several diseases and their vectors have been discussed previously in this chapter. Temporal sign switching may be evident for malaria in the East African Highlands; malaria incidence increased in the East African Highlands in the 1940s–50s and from the 1970s onwards, but decreased in the 1960s (Malakooti et al., 1998), which is broadly consistent with 20th-century temperature trends. Rigorous analysis is required to test whether temperature trends explain apparent sign-switching variation in malaria incidence after controlling for other factors such as malaria control and demographic change. A consistency analysis would require demonstrating regional climate change in each of these instances, and also assessing the overall coherence of the changes. Coherence would emerge if the overall pattern of change were consistent with predictions under climate change, such as both altitudinal and latitudinal shifts (i.e. coherent direction of change) are observed for several diseases.

The feasibility of quantitative consistency analysis of the recent impacts of climate change on infectious diseases is limited by the relatively small number of studies that have been published, and the risk of publication bias. Numerical estimates of mean range shifts, changes in duration of transmission season or net changes in incidence are not yet possible, though a method for this type of assessment has been presented for natural systems (Parmesan and Yohe, 2003).

Future Work

We suggest that it is now possible to document systematically consistent changes in infectious diseases in response to climate change across diverse agents, vectors and hosts using consistency analysis, and that this is a more appropriate and informative approach than the usual disease-specific research. Detecting a climate change signal in global changes in infectious diseases' incidence will require interdisciplinary collaboration with common understanding of priority regions for human health. Targeted surveillance efforts, including geographical information system mapping and molecular surveillance, should be integrated with archival distribution records to establish baseline geographic distributions and to monitor change (Hoberg et al., 2008; Weaver et al., 2010). Multi-disease, multi-site studies that document infectious disease shifts that are consistent, neutral or inconsistent with the predicted effects of climate change should be prioritised, and the effect of climate change needs to be quantified relative to the effect of other factors.

Although full attribution of changes in infectious diseases to recent climate change may not yet be possible for most diseases, it is timely to move beyond polarised debates about whether climate or other influences dominate (Brisbois and Ali, 2010). The approaches discussed here may offer a way forward to improved methods for the detection and attribution of recent climate change effects on infectious diseases, which will narrow uncertainty boundaries for projections of future transmission under climate change.

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