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Seasonal forecasting and health impact models: challenges and opportunities

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After several decades of intensive research, steady improvements in understanding and modeling the climate system have led to the development of the first generation of operational health early warning systems in the era of climate services. These schemes are based on collaborations across scientific disciplines, bringing together real-time climate and health data collection, state-of-the-art seasonal climate predictions, epidemiological impact models based on historical data, and an understanding of end user and stakeholder needs. In this review, we discuss the challenges and opportunities of this complex, multidisciplinary collaboration, with a focus on the factors limiting seasonal forecasting as a source of predictability for climate impact models.

Keywords: climate variability; seasonal forecasting; climate services; health impacts; statistical models

Introduction

The environmental consequences of climate change—sea-level rise, flooding and drought, more intense hurricanes and storms, heat waves, and degraded air quality—substantially impact human well-being,¹ with some of the health effects including population displacement; injury and death related to extreme weather events; changes in the prevalence and geographical distribution of food-, water-, and vector-borne diseases; increased respiratory and cardiovascular disease; and threats to mental health.^{2,3} Climate change has a potentially large impact on the incidence of vector-borne diseases, such as dengue and malaria,⁴ either directly, by affecting the developmental rates and survival of both the mosquito and pathogen, or indirectly, through changes in land-cover and land-surface characteristics, which affect the availability of mosquito breeding sites.^{5,6} In addition, climate interacts with local conditions and population herd immunity, affecting not only mosquito infestation

but also human susceptibility and the contact rate between mosquitoes and humans.⁷

In addition to climate variability and change, infectious disease emergence and spread can be exacerbated by anthropogenic activities, such as deforestation, mining, urbanization, and human mobility.⁸ For example, the global expansion of the mosquito-transmitted viral disease, dengue fever, and the recent spread of chikungunya and Zika viruses to the Americas have been attributed, in part, to international travel and ineffective vector control.⁹ In Europe, the climate is becoming increasingly suitable for the mosquito species *Aedes albopictus*, which is already established in several Southern European countries. In 2010, locally acquired dengue infections were reported in France and Croatia, and in 2012, an outbreak of more than 2000 dengue cases occurred in Madeira, Portugal, in areas where *Aedes aegypti* exists.¹⁰ Deforestation and mining activities in the Amazon rainforest have coincided with an upsurge of malaria, owing to the creation of natural and human-made mosquito breeding sites and clustering of nonimmune migrants close to these sites.^{11,12} For some diseases, the most important factors may be contact among people

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and wildlife that harbor zoonotic pathogens.¹³ For example, in tropical urban slum environments, epidemics of the bacterial disease leptospirosis can occur during periods of heavy rainfall,¹⁴ and flooding can lead to human infection after direct contact with flood waters contaminated with the urine of infected rats. On the other hand, the transmission of water- and food-borne bacterial diseases, such as cholera or *Escherichia coli* infections, is exacerbated by poor sanitation and hygiene.¹⁵

Mitigation of climate change and adaptation to its negative effects are public health priorities in the coming decades. The impacts of climate on health are felt across all sectors of society, from the local to the global level, and climate change is becoming a central issue in public health and global political agendas.¹⁶ Infectious disease epidemics and extreme temperature-related mortality have a direct impact on the health of local populations, strain healthcare systems, and cause substantial economic loss.^{17,18} Many policy makers are aware of the effects of climate on the dynamics of many diseases and health outcomes; however, climate information is rarely exploited as a means to help prevent and control such health risks.¹⁹ In order to improve the ability to adapt to a changing climate and to mitigate its effects, it is necessary to improve the link between the production and supply of climate science information and its accommodation to the needs of end users. Climate services, which aim to provide timely, tailored information and decision-support tools to decision makers, are an important part of improving our capacity to manage climate-related risk.²⁰ For example, the Global Framework for Climate Services (GFCS), a climate service coordinating body created in 2012 and led by the World Meteorological Organization,²¹ aims to create a structure to support better, more informed decisions, with the ultimate goal of saving lives, protecting the environment, and improving economic development. The GFCS has so far focused efforts on developing countries, with health being one of its priority sectors.

In this article, we discuss the challenges associated with incorporating climate information in health impact models to understand variations in health risks. We first discuss spatiotemporal modeling tools of climate impacts and diseases, and then outline some of the factors limiting seasonal forecasting as a source of predictability for these climate impact models, such as the transfer of predictable

information, the transient nature of climate teleconnections, or the time-varying relationship between climate and associated impacts.

Spatiotemporal modeling of climate impacts and diseases

Infectious diseases can be modeled by spatiotemporal statistical methods,²² which tend to be empirical rather than rooted in scientific mechanisms and are widely used in both environmental and health sciences applications. In considering the many possible statistical models for disease processes, the distinction between empirical and mechanistic models is important. An empirical model seeks only to describe the spatiotemporal structure of the process, whereas a mechanistic model seeks to explain it. For example, an empirical model might represent the behavior of the disease process by specifying the mean value at every time and location as a regression on one or more spatially and/or temporally varying covariates, and the covariance between any two values as a function of their spatiotemporal distance; whereas, a mechanistic model would more likely incorporate an explicit and asymmetric dependence between the present and past, for example, by specifying disease risk at any particular time and location, conditional on the historical incidence pattern.

The distinction between empirical and mechanistic modeling is sometimes equated to the distinction between mathematical and statistical modeling, respectively. But this is, at best, an oversimplification. Data relating to the scientific process of interest are invariably noisy; therefore, whichever approach is taken to model the scientific process, it is necessary to supplement the process model by a data model, which specifies the joint distribution of the data, conditional on the underlying temporal sequence of spatial states of the process, and this model is inherently statistical. In practice, this hierarchical structure, combining a process model with a data model conditional on the unobserved state of the process, is particularly important when analyzing data with a relatively low signal-to-noise ratio. The data model is typically of limited scientific interest in itself, but is essential to the delivery of valid inferences about the underlying process.

Empirical spatiotemporal models typically take the form of generalized linear models, in which either the regression parameters or the residuals

are replaced by stochastic processes. In particular, Bayesian geostatistical approaches, which replace the residual by a spatially and/or temporally correlated stochastic process, are increasingly used for mapping the incidence of both infectious and non-infectious diseases.²³ These methods can be used for the identification of important covariates along with estimation of their regression parameters, and for the prediction and mapping of future unobserved values of the response variable of interest. Also, they can provide valuable information for improving the design of future studies by identifying and quantifying sources of variation that could be better controlled, or even eliminated altogether.

In contrast, mechanistic models typically use deterministic or stochastic differential equations to express the dynamics of an underlying infectious disease process. Early accounts of this approach^{24,25} and a more recent book-length account²⁶ have previously been published. When locations and times of individual cases are available, mechanistic models can be formulated as spatiotemporal point processes, in which the current incidence depends explicitly on the locations and times of past cases. This approach has been used to model the spread of the 2001 foot-and-mouth epidemic in the United Kingdom.²⁷ The ability to combine mechanistic models with principled (i.e., likelihood-based) methods of statistical inference is relatively recent. The potential use of a partial likelihood method²⁸ to fit the model used to study the 2001 foot-and-mouth epidemic²⁷ has been shown.²⁸ The widely used empirical models of spatial correlation can be derived as the solutions to particular kinds of stochastic differential equations,²⁹ thereby rendering these models amenable to likelihood-based inference.

A versatile modeling procedure was recently developed to determine the most important drivers of spatiotemporal variability in disease risk.³⁰ The model framework combines climatic and nonclimatic factors in the model parameterization to correctly quantify variability captured by climate information, and the methodology exploits recent advances in spatiotemporal hierarchical mixed modeling. An advantage of implementing the model in a Bayesian framework is the ability to address specific public health issues in terms of probabilities. Explanatory variables at various spatial and temporal resolutions (e.g., data on climate, land

use, socioeconomic conditions, health infrastructure) can be incorporated and tested in the model framework in order to select a suitable combination of statistically significant variables. However, when health outcome and climate data are both available, they are not necessarily measured at the same set of spatiotemporal points; therefore, a scale mismatch often exists. More generally, either the health outcome or climate data, or both, may take the form of spatial averages rather than point-referenced measurements. For example, a common scenario is that health outcomes are recorded as case counts and population denominators on a set of small-area units that partition the region of interest, while ground truth meteorological data are collected as time series at each location in an irregular network of weather-recording stations. These data typically suffer from either measurement error or microscale fluctuations, or both, that distort the underlying correct value. Data that are both spatially incomplete and error prone are not necessarily more useful than proxies such as remotely sensed images or the outputs from physically based climate models, which are usually calculated on a raster grid.³¹

In principle, an extension of the above-mentioned hierarchical approach can accommodate multiple spatially misaligned data sources by combining a spatially and temporally continuous process model with a collection of spatially and temporally discrete data models, one for each data source.³² More pragmatically, gridded data (e.g., climate or topographical) can be reconciled with spatial area data (e.g., disease counts and demographic characteristics) using interpolation methods,³³ or by assigning a grid point to each spatial polygon on the basis of the shortest Euclidean distance between the area centroid and neighboring grid points.³⁴ Once all available explanatory data have been transformed to the same spatial and temporal resolution as the response variable, it can be incorporated into the model framework to account for confounding factors and help more correctly attribute variations in disease risk to variation in climatic factors.

In many cases, data on important drivers of disease systems are not routinely collected or readily available, a limitation that typically detracts from adequate progress in developing useful prediction systems at the local scale of cities or small regions. To overcome this problem, spatiotemporal random effects can be included in the model

framework. Unstructured random effects help account for unknown or unobserved disease risk factors (e.g., mosquito abundance, population immunity, healthcare inequalities and interventions) and introduce an extra source of variability (a latent effect) into the model, which can assist in modeling overdispersion. To allow for correlated heterogeneity between locations or spatial clustering, which is a typical feature of infectious disease dynamics, structured random effects can be included in the model. One way to impose a spatial dependency structure is to assume a Gaussian intrinsic conditional autoregressive model prior to distribution for the spatial effects,³⁵ which accounts for spatial dependence by specifying a neighborhood structure of the area under consideration. Once unknown structures are accounted for, one can identify which of the available indicators could significantly contribute to an effective early warning system.

Factors limiting seasonal forecasting as a source of predictability for climate impact models

Seasonal forecasts of the climate with lead times up to several months,^{36–38} along with strong public health surveillance systems, provide the opportunity to issue timely early warnings of imminent threats.^{39,40} Several studies have investigated the use of climate information in early warning systems for diseases such as malaria and Rift Valley fever.^{41,42} The efficacy of any climate-driven early warning system, however, strongly depends on the underlying skill of the climate forecasting system. Seasonal climate forecasts have been reported to have skill in tropical regions of Brazil and, to a lesser extent, in extratropical regions.^{43,44} For example, in a recent study, real-time seasonal climate forecasts and disease surveillance data were integrated into a spatiotemporal model framework,⁴⁵ to provide a dengue forecast for Brazil, 3 months in advance of a major global event (e.g., the 2014 FIFA World Cup⁴⁶). The probability of dengue incidence falling into predefined categories of low, medium, and high risk was mapped using a visualization technique, in which color saturation expresses forecast certainty.⁴⁷ As an indication of the level of trust a decision maker can place in the dengue predictions for a specific location, the forecast map was accompanied by a verification map, expressing the past performance of the model (Fig. 1). This climate-

driven dengue early warning was used to support the decisions of the National Dengue Control Programme several months ahead of the event, to help direct mitigation and control actions to those areas with a higher probability of dengue outbreaks. The early warnings were also disseminated to the general public via the media and visitors traveling to Brazil.⁴⁸ This example of a successful early warning system illustrates the potential of climate services to benefit public health. Nonetheless, there are several theoretical and practical issues to be considered that largely limit the operational value of some of these schemes. These factors mainly refer to the scale mismatch and the transfer of predictable information from climate forecasts to the abovementioned models of climate-driven impacts and diseases, as further discussed in the following sections.

Sources of climate predictability and transfer of predictable information

Although weather phenomena are not predictable at lead times beyond 2 weeks (i.e., the atmosphere is chaotic⁴⁹), average values of climate variables are potentially predictable months, years, and even decades in advance.⁵⁰ Nevertheless, the longer the lead time of the prediction, the longer the time period for which the variable needs to be averaged. The tropical belt plays a key role in the predictability of climate variables⁵¹ and exerts an influence worldwide through the activation of atmospheric responses when thermally driven processes exceed certain thresholds. This region is largely influenced by the incident solar radiation that heats the ocean surface, which, in turn, drives the atmospheric circulation, both locally and at distant regions through large-scale teleconnections.^{52,53} Ocean anomalies and, thus, these thermally driven atmospheric patterns persist over longer periods than weather phenomena. Therefore, atmospheric variables are, to some extent, predictable at lead times of months, years, and decades.⁵⁴ Climate forecasts at seasonal time scales provide an opportunity to anticipate potential health threats several months in advance. These forecasts occupy an intermediate zone between weather forecasting and long-term climate projections, and are typically used to issue probabilistic statements of the expected climate conditions for the next 1–6 months.⁵⁴ These forecasts are particularly useful for certain seasons and locations around the world.

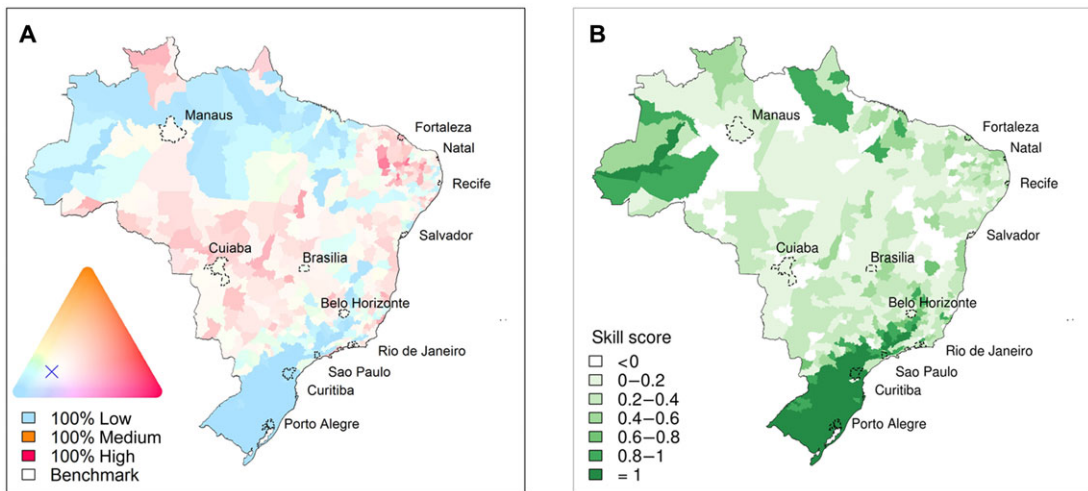


Figure 1. (A) Probabilistic dengue forecast in June 2014 for Brazil. The continuous color palette (ternary phase diagram) conveys the probabilities assigned to low-risk, medium-risk, and high-risk dengue categories. Category boundaries are defined as 100 cases per 100,000 inhabitants and 300 cases per 100,000 inhabitants. The greater the color saturation, the more certain the forecast of a particular outcome. Dark red shows a high probability of high dengue risk. Dark blue indicates a high probability of low dengue risk. Colors close to white indicate a forecast similar to the benchmark (i.e., long-term average distribution of dengue incidence in Brazil, marked by a cross). (B) Evaluation of past performance for each area based on out-of-sample retrospective dengue forecasts, June 2000–2013. The skill score takes the value 1 for a perfect forecast and 0 for the benchmark (long-term average) forecast. The darker the shade of green, the greater the skill of the forecasting system. Negative values (white) show areas where the model did worse than using the benchmark. Adapted, with permission, from Ref. 46.

For example, El Niño–Southern Oscillation (ENSO) is a predictable phenomenon^{55,56} that is key to seasonal climate forecasting worldwide.^{57,58} ENSO is a coupled oceanic–atmospheric phenomenon, characterized by sustained fluctuations between unusually warm (El Niño) and cold (La Niña) sea surface temperature conditions in the central and eastern tropical Pacific Ocean.^{59,60} ENSO influences the interannual variability in weather patterns and the likelihood of activation, enhancement, weakening, and/or displacement of regional extreme events, such as droughts and floods, across the globe.^{61–63} The associations that can be found between ENSO events and climate variables at distant regions several months later are exemplified in Figure 2A and B. A negative relationship between Pacific sea surface temperatures in December–February and precipitation the following March–May is observed for North Brazil, Southeast Africa, and Southeast Asia, implying dry conditions during El Niño events and wet conditions during La Niña events (Fig. 2A). At the same time of year, El Niño conditions are associated with anomalous warming over much of

the Amazon, Southeast Africa and Asia, and North Australia (Fig. 2B). An association between ENSO and a heightened risk of certain vector-borne,^{64,65} water-borne,^{66,67} and wind-borne^{51,68,69} diseases has been identified in specific geographical areas, where climate anomalies and ENSO are linked.

The potential predictability of climate variables in the tropics, particularly that derived from ENSO, is therefore key for the development of modeling tools to predict climate impacts and design early warning systems.^{41,46,70} Nonetheless, there are other sources of predictability that can be explored to support climate services,⁷¹ particularly in the midlatitudes, where weaker atmospheric flow instabilities in the summer favor the influence of long memory drivers, such as soil moisture.⁷² Thus, the amount of available soil moisture controls the fraction of heat that is released as latent and sensible heat fluxes, so that the frequency and intensity of summer heat waves are largely controlled by the rainfall in the preceding winter and spring.^{73,74} Some researchers have, however, highlighted the complexity of this delayed association, and despite recent advances in the prediction of heat waves, such as the record-breaking

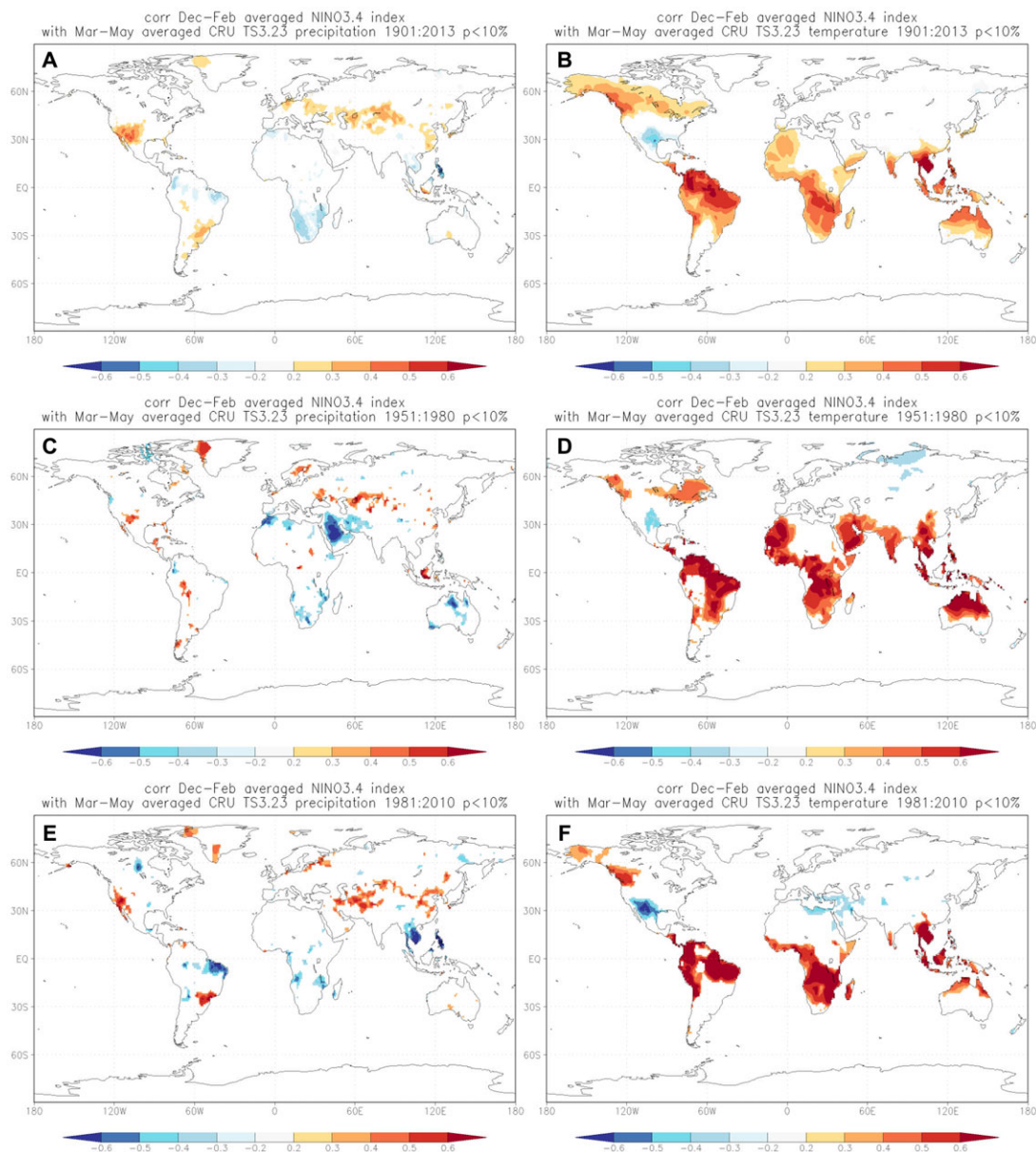


Figure 2. Maps of statistically significant correlations (at the 10% level) between December–February sea surface temperature anomalies in the Nino3.4 region (170–120W, 5S–5N) and March–May (A, C, E) global precipitation and (B, D, F) temperature. Data are taken from the Climatic Research Unit dataset for (A, B) 1901–2013, (C, D) 1951–1980, and (E, F) 1981–2010, and maps were produced using KNMI Climate Explorer (<http://climexp.knmi.nl>).

2003 summer event in Europe,⁷⁵ the skill of these predictions remains rather poor. For example, rainy winter/spring seasons over Southern Europe inhibit hot summer days, whereas dry seasons are followed by either a high or a low frequency of hot days.⁷⁶ It was later shown that summer heat is more sen-

sitive to the occurrence of specific weather regimes in initially dry cases than wet cases,⁷⁷ inducing an asymmetry in summer heat predictability.

The poor predictability of these forecasts represents a serious constraint for the applicability of seasonal forecasts in the domain of climate services.

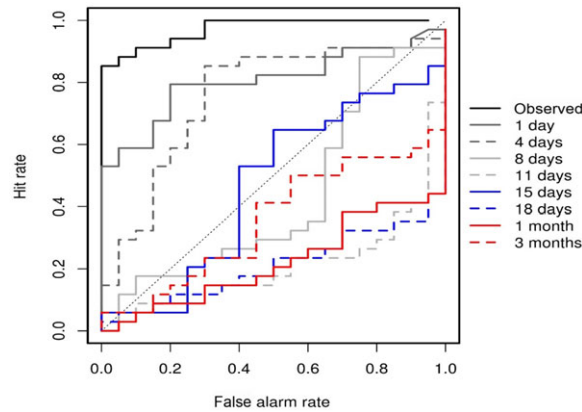


Figure 3. Receiver operating characteristic (ROC) curves for the binary event of exceeding an emergency mortality threshold in Europe for a heat wave scenario (August 1–15, 2003), using a probabilistic mortality model driven by climate forecast data at lead times ranging from 1 day to 3 months. The ROC curve for the mortality model driven by observed climate data is shown for reference (black curve). Adapted, with permission, from Ref. 79.

For example, as part of the EUPORIAS (European Provision of Regional Impact Assessment on a Seasonal-to-Decadal Timescale) project,⁷⁸ a climate service tool was developed to provide probabilistic predictions of exceeding emergency mortality thresholds for heat wave scenarios.⁷⁹ The predictions were based on subseasonal to seasonal temperature forecasts, to support decision making for the preparedness of health services and protection of vulnerable communities ahead of future extreme temperature events.^{79–81} The tool was designed to provide multilead probabilistic forecasts of mortality risk ahead of the peak summer season. In general, a decreasing transition in skill was found between excellent predictions when using observed temperature or subseasonal climate forecasts at very short lead times as driving climate conditions for the temperature-related mortality model, and predictions with no skill when using forecast temperature with lead times greater than 1 week (Fig. 3). These results showed that the performance of climate services is, in some cases, more limited by the predictability of the climate variables than by the impact model itself.

The transient nature of climate variability and teleconnections

Although a clear window of opportunity for climate services emerges during El Niño and La Niña years in those areas with both climate predictability and large climate-driven disease incidence, there

are several factors limiting the potential use of this information in climate services. For example, predictability is generally greater for surface air temperature than for precipitation, and therefore, the areas with large potential predictability coincident in both variables are rather small. More importantly, ENSO should be seen as a nonstationary mode of variability whose potential predictability and teleconnections change at the decadal and longer timescales. Figure 2C–F illustrates the time-varying relationship between ENSO and climate variables for two consecutive 30-year time periods, showing the transient nature of ENSO dynamics and teleconnections. While there are large areas in the tropics with significant correlations with temperature in both periods (cf. Fig. 2D–F), we see no overlapping regions in the precipitation maps (cf. Fig. 2C–E). We found, for example, that a multidecade regime shift in the late 1970s decreased the relationship between ENSO and the Asian monsoons⁸² (cf. Fig. 2D–F) and that global warming is expected to favor the relative occurrence of central Pacific El Niño events (also referred to as El Niño Modoki⁸³) to the detriment of the canonical type in the Eastern Pacific.^{84,85} These changes modify the areas and time lags that characterize the associated teleconnections, whose nonstationary nature imposes a strong constraint to the calibration and application of climate-driven impact models, which are sensitive to regime shifts in the ENSO phenomenon and, in general, in the climate system.

ENSO also exemplifies the intermittent relationship between climate and associated impacts at the interannual timescale, for which El Niño and La Niña define transient windows of opportunity for enhanced predictability. Despite the active search for climatic drivers of infectious diseases, the irregularity of this link and the temporal scales of these windows impose a limit in the ability to anticipate disease risk, which typically leads to low reported correlations between disease descriptors and climatic variables. Different factors could explain these low values, including climatic variables being inherently weak drivers of the dynamics of the disease, or being strong modulators operating in a nonlinear way. The former can take place when the forcing occurs only during limited intervals of time (e.g., during El Niño or La Niña episodes) or when local variation in environmental factors and the immunological status of the at-risk population mask the underlying climate-related dynamics.⁸⁶ The latter implies an association between variables that is not fully addressed by standard statistical techniques and can therefore be incorrectly interpreted as a weak dynamical association. It is critical to distinguish between these different outcomes, given that the information provided on the underlying processes is radically different. A strong coupling between climate and disease variables, albeit transient in time or imperfectly measured, can provide potential for long-lead disease forecasting.

A clear example was provided by the study of population dynamics of cholera epidemics in Bangladesh,⁶⁶ which demonstrated an influence of the ENSO phenomenon on the disease. However, this study could not address the strength of this influence, given that the effect of the different independent variables was not additive in the model, and changed over time. The clear relationship between temperature and the amplification of cholera incidence worldwide has since been well documented.^{67,87,88} Nevertheless, there seems to be an apparent discrepancy between known aspects of cholera epidemiology and the low values obtained in correlations reported by many studies. This discrepancy can be also seen, for example, in the relationship between cholera and rainfall in Zanzibar, where attained significance levels were low despite the known strong relationships between extreme rainfall and the disease.⁸⁹

The time-varying association between climate variability and impacts

In addition to the transient nature of climate variability and associated teleconnections, temporal changes in the association between climate metrics and impacts on health can also affect the applicability of climate forecast information in impact models. Apart from secular changes in infrastructure and public health, anthropogenic global warming due to human activities can also redefine these associations, whose future evolution is not easy to anticipate because either the relationships are not fully understood or the changes in the key driving climate variables are still unclear.^{51,68} In addition, the future evolution of the incidence of certain diseases is closely determined by the degree of exposure of human individuals and societies, which can change through a natural response of body metabolism,⁹⁰ the adoption of new habits by individuals and populations,⁹¹ or the design of societal strategies and measures aimed at reducing the vulnerability of their citizens.^{92,93}

We illustrate these points here with regard to temperature-related mortality, whose expected increase in summer probably represents the most direct consequence of temperature rise to human health.^{18,94} Recent heat waves suggest that changes in the degree of exposure of human populations are not only the result of a slow and progressive process due to background temperatures, but also a relatively rapid response to large impact events. For example, a model that successfully predicted the death toll associated with the record-breaking 2003 summer heat wave in France showed that the impact of heat waves changed after the event: excess mortality predictions for the following heat wave in 2006 (6452 deaths) were found to largely exceed the observed mortality (2065 cases).⁹² The study concluded that the overestimation in the prediction was attributed to a decline in the vulnerability to heat, the increase in the awareness of the risk, the adoption of preventive measures, and the implementation of a coordinated early warning system.

These results suggest that the relation between climate variables and human mortality is constantly being redefined, and therefore, climate impact models need to be recalibrated accordingly.⁹⁵ For example, in a study using spatiotemporal climate and mortality data in France to describe the dependency between long-term changes in heat stress factors

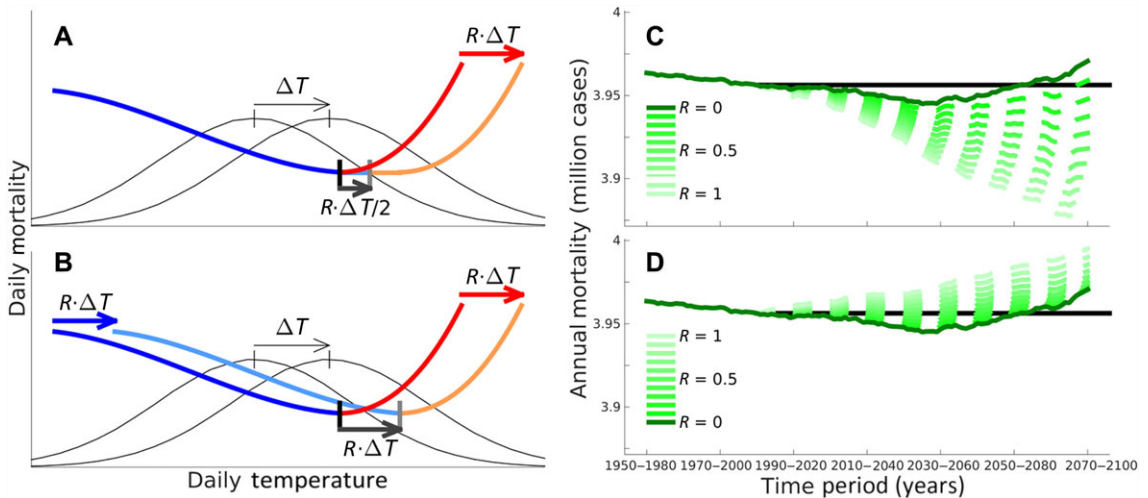


Figure 4. Scenarios of acclimatization to warm and/or cold temperatures. Panel A corresponds to a scenario with only decreased exposure to warm temperatures, while in panel B, the sensitivity to cold temperatures is also increased. Acclimatization is expressed as the shift along the temperature axis of the temperature–mortality relationship by a fraction ($0 \leq R \leq 1$) of the increase in annual mean temperatures (ΔT). This fraction is equal to 0(1) for a scenario with no (immediate) gain or loss of acclimatization to warmer summer or winter temperatures, respectively. Panels C and D correspond to the projections of annual mortality for Western Europe according to these scenarios of acclimatization. Adapted, with permission, from Ref. 80.

and their relationship with mortality,⁹⁶ the $+1.2^\circ\text{C}$ warming in mean temperatures observed in recent decades was associated with a $+0.7^\circ\text{C}$ warming in the comfort temperature (i.e., temperature of minimum mortality), suggesting that human populations have experienced a set of long-term acclimatization mechanisms to slow-varying background temperatures. The response ratio $0.7/1.2 \approx 0.58$ is found to be lower than 1, suggesting that this set of slow-varying acclimatization processes might be partially limited by other factors, for example, mechanisms linked to the physiology of the human body and/or the natural dynamics of the pathogens associated with the seasonal rise of mortality in winter.⁹⁷

In this context, a qualitative conceptual model has been proposed,⁵ in which the degree of exposure of a society to summer temperatures is reduced under warming conditions (Fig. 4A), and a scenario in which the rise in winter temperatures increases the sensitivity of individuals to cold events was later hypothesized (Fig. 4B).⁸⁰ These scenarios of exposure to warm and/or cold temperatures were used to infer long-term projections of future annual mortality in Europe,⁸⁰ showing that the rise in heat-related mortality will start to completely compensate for the reduction of deaths from cold during the sec-

ond half of the century ($R = 0$ in Fig. 4C and D). Nevertheless, changes in annual mortality are seen to be small compared to those that are inferred from scenarios of immediate gain or loss of acclimatization to warmer summer or winter temperatures, respectively ($R = 1$ in Fig. 4C and D). These results highlight the key importance of uncertainties associated with the relationship between climate variability and impacts for the study of some health effects.

Conclusions and future work

The health sector is starting to benefit from tailored climate services based on climate forecasts, which support decision making at local, regional, national, and global levels. Health stakeholders, such as government ministries and departments, hospitals, and other health services,⁹⁸ are starting to make use of climate impact indicators to optimize resources in the health system and to enforce preventive measures to improve quality of life, particularly for the most vulnerable sectors of society. However, information from climate forecasts used in operational early warning systems requires a rigorous assessment of its real predictability and applicability. Moreover, factors determining the vulnerability to adverse health effects, including

biological susceptibility, socioeconomic status, and the built environment, also need to be considered in the decision-making process. By integrating useful climate and nonclimate information in decision-support systems, policy makers will be better positioned to efficiently mitigate and facilitate adaptation to the environmental effects of climate change. Despite some progress in demonstrating the potential for incorporating climate information into public health decision-making processes, there remain substantial challenges to the implementation of sustainable operational early warning systems, which require significant financial resources and long-lasting interagency collaboration to stand a chance of being successful. Further, effective communication of tailored climate information,⁹⁹ an iterative evaluation of the efficacy of the system,²⁰ and local capacity building are necessary components to achieve effective and sustainable services.

The many potential drivers of complex health systems, both extrinsic (e.g., climate and socioeconomic factors) and intrinsic (e.g., population immunity, vulnerability, and demography), are often difficult to disentangle. Spatiotemporal modeling tools are therefore required to simultaneously consider the complex interaction of climate hazards, disease transmission, socioeconomic disparities, and human vulnerability in predictive health risk models. However, there is an urgent need for more interdisciplinary collaboration to make available global datasets of important health risk factors and to understand the caveats associated with each dataset before embarking on modeling exercises. New endeavors are required to synthesize data collection and modeling efforts and to design health early warning systems in close collaboration with public health decision makers.

These initiatives also depend on the availability of accurate climate information and skillful climate forecasts for the implementation of operational early warning systems. There are windows of opportunity for the prediction of climate variables with lead times ranging from months to a few seasons, especially during El Niño and La Niña episodes and in ENSO-affected regions. Climate forecasts are found to be more accurate during these events, particularly in the tropics where climate-sensitive diseases pose the largest burden to public health. When these events occur, there is a clear opportunity to incorporate climate information into decision-

making processes for climate-sensitive sectors, also out of the tropics due to the nature of atmospheric teleconnections. Nonetheless, this information is subject to large uncertainties associated with the complex and nonstationary nature of the climate system. Moreover, the skill of the climate forecasts rapidly decreases when these windows of opportunity close, which, in many cases, can make the information provided in the climate service system no better than the information derived from a coin toss. In that regard, the skill of climate model simulations and predictions still represents a major research area for improving the usefulness of health early warning systems to public health decision makers, particularly in the numerous regions and time scales for which climate forecast skill is low or nonexistent.

Future endeavors aimed at developing new scientific tools and platforms for the mitigation of climate-related health risks and the adaptation of society to environmental emergencies will require the close coordination of climate modelers and scientists, epidemiologists, hospitals, public health agencies, and governments. This coordination will help ensure the successful implementation and delivery of useful tools for the well-being and adaptation of society to the threats posed by climate change.

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Conflicts of interest

The authors declare no conflicts of interest.

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