REVIEWS

Impact of regional climate change on human health

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The World Health Organisation estimates that the warming and precipitation trends due to anthropogenic climate change of the past 30 years already claim over 150,000 lives annually. Many prevalent human diseases are linked to climate fluctuations, from cardiovascular mortality and respiratory illnesses due to heatwaves, to altered transmission of infectious diseases and malnutrition from crop failures. Uncertainty remains in attributing the expansion or resurgence of diseases to climate change, owing to lack of long-term, high-quality data sets as well as the large influence of socio-economic factors and changes in immunity and drug resistance. Here we review the growing evidence that climate–health relationships pose increasing health risks under future projections of climate change and that the warming trend over recent decades has already contributed to increased morbidity and mortality in many regions of the world. Potentially vulnerable regions include the temperate latitudes, which are projected to warm disproportionately, the regions around the Pacific and Indian oceans that are currently subjected to large rainfall variability due to the El Niño/Southern Oscillation sub-Saharan Africa and sprawling cities where the urban heat island effect could intensify extreme climatic events.

Global average temperatures are projected to increase between 1.4 and 5.8 °C by the end of this century[1]; an associated rise in sea level is also expected. The number of people at risk from flooding by coastal storm surges is projected to increase from the current 75 million to 200 million in a scenario of mid-range climate changes, in which a rise in the sea level of 40 cm is envisaged by the 2080s (ref. 2). Extremes of the hydrologic cycle (such as floods and droughts) are projected to increase with warmer ambient temperatures. Evidence is mounting that such changes in the broad-scale climate system may already be affecting human health, including mortality and morbidity from extreme heat, cold, drought or storms; changes in air and water quality; and changes in the ecology of infectious diseases[3–5].

We reviewed both empirical studies of past observations of climate-health relationships, and model simulation studies of projected health risks and regional vulnerability associated with future climate change. Here we focus on the health implications of climate variability, past and present climate change impacts on human health, future projections and uncertainties. This review primarily examines relatively direct-acting temperature effects, while recognizing that other major risk pathways exist, for instance, altered storm patterns, hydrologic extremes, and sea-level rise.

Health implications of climate variability

Non-infectious health effects. The summer of 2003 was probably Europe's hottest summer in over 500 years, with average temperatures 3.5 °C above normal[6–8]. With approximately 22,000 to 45,000 heat-related deaths occurring across Europe over two weeks in August 2003 (refs 9 and 10), this is the most striking recent example of health risks directly resulting from temperature change. Judging from this extreme event, changes in climate variability associated with long-term climate change could be at least as important for future risk assessment as upward trends in mean temperature.

The European heatwave in 2003 was well outside the range of expected climate variability[8]. In addition, comparisons of climate model outputs with and without anthropogenic drivers show that the risk of a heatwave of that magnitude had more than doubled by 2003 as a result of human-induced climate change[3]. The demonstration of a causal link between global warming and the occurrence of regional heatwaves indicates a potential for more frequent and/or more severe heatwaves in a future warmer world.

On local and regional scales, changes in land cover can sometimes exacerbate the effect of greenhouse-gas-induced warming, or even exert the largest impact on climatic conditions. For example, urban 'heat islands' result from lowered evaporative cooling, increased heat storage and sensible heat flux caused by the lowered vegetation cover, increased impervious cover and complex surfaces of the cityscape. Dark surfaces such as asphalt roads or rooftops can reach temperatures 30–40 °C higher than surrounding air[11]. Most cities show a large heat island effect, registering 5–11 °C warmer than surrounding rural areas[12]. But the effects of land cover change on climate are not limited to small areas: at the scale of the entire continental USA, Kalnay and Cai[13] estimated that land-cover changes (from both agriculture and urban areas) caused a surface warming of ~0.27 °C per century. Also, in southeast China, a warming of ~0.05 °C per decade since 1978 has been attributed to land-use change from urban sprawl[14].

Exposure to both extreme hot and cold weather is associated with increased morbidity and mortality, compared to an intermediate 'comfortable' temperature range[15]. Heat mortality follows a J-shaped function with a steeper slope at higher temperatures[16]. The comfortable or safest temperature range is closely related to mean temperature, with an upper bound from as low as 16.5 °C for the Netherlands and 19 °C for London[17], to as high as 29 °C in Taiwan[18]. Hot days occurring earlier in the summer season have a larger effect than those occurring later[17]. It should be noted that although the majority of temperature–mortality studies have taken place in developed

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countries and in regions with temperate climates, the same pattern of temperature–mortality relationship found in European and North American cities occurs in São Paulo, Brazil, a developing city with subtropical conditions[19].

In summary, although most studies to date show clear vulnerability to heat in cooler temperate regions, tropical regions may well show a similar sensitivity as location-specific temperatures rise.

Climatic influences on regional famines are another well-recognized climate–health association. Malnutrition remains one of the largest health crises worldwide and according to the WHO, approximately 800 million people are currently undernourished, with close to half of these living in Africa[20]. Droughts and other climate extremes have direct impacts on food crops, and can also influence food supply indirectly by altering the ecology of plant pathogens. Projections of the effect of climate change on food crop yield production globally appear to be broadly neutral, but climate change will probably exacerbate regional food supply inequalities[21].

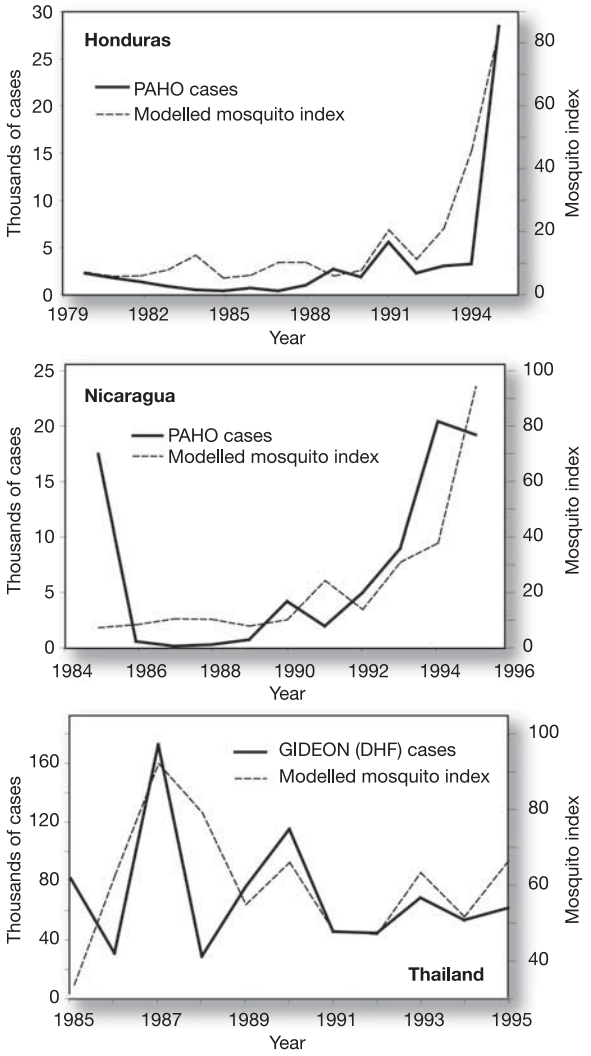

Figure 1 | Correlation between simulated, climate-driven variations in *Aedes aegypti* mosquito density and observed variations in dengue and DHF cases. Using a computer model of mosquito physiology and development, estimated changes in the relative abundance of *Aedes aegypti* that were driven only by month-to-month and year-to-year variations in temperature, humidity, solar radiation and rainfall were analysed. The simulated, climate-induced variations in mosquito density were then compared to reported cases of dengue and DHF across many nations of the world that covered at least one degree of latitude and longitude and had at least five years of dengue caseload data. In many countries of Central America and Southeast Asia, the relationship is statistically significant ($P < 0.05$). For example, climate-driven fluctuations in *Ae. aegypti* densities appear to be related to annual variations in dengue/DHF cases in Honduras, Nicaragua and Thailand as shown. These represent relatively small-area countries; for larger countries endemic for dengue such as Brazil, China, India and Mexico, the association is not significant, as might be expected because the disease data was at the country level. Graphs adapted from ref. 32.

Infectious diseases. Climatic variations and extreme weather events have profound impacts on infectious disease. Infectious agents (such as protozoa, bacteria and viruses) and their associated vector organisms (such as mosquitoes, ticks and sandflies) are devoid of thermostatic mechanisms, and reproduction and survival rates are thus strongly affected by fluctuations in temperature[4,22]. Temperature dependencies are seen in correlations between disease rates and weather variations over weeks, months or years[23] and in close geographic associations between key climate variables and the distributions of important vector-borne diseases[24,25].

Malaria transmission has been associated with anomalies of maximum temperature in the highlands of Kenya[26]. Several studies of long-term trends in malaria incidence and climate in Africa, however, have not found a link to temperature trends, emphasizing instead the importance of including other key determinants of malaria risk such as drug resistance, human migration and immune status, inconsistent vector- or disease-control programmes, and local land-use changes[27–30]. However, in the highland Debre Zeit sector of central Ethiopia an association has been documented between increasing malaria prevalence and incidence with concomitant warming trends from 1968 to 1993 (ref. 31). Controlling for confounding factors, the association could not be explained by drug resistance, population migration, or level of vector-control efforts. In short, studies of the association of malaria and past climate in the African Highlands remains controversial in part due to varying quality of long-term disease data across sites in Africa, and in part due to the difficulty in adequately controlling for demographic and biological (drug resistance) data. A definitive role of long-term climate trends has not been ascertained.

Dengue fever and the more serious form of this disease, dengue haemorrhagic fever (DHF), are caused by the world's most prevalent mosquito-borne virus. All strains of the dengue virus are carried principally by the *Aedes aegypti* mosquito. This mosquito is strongly affected by ecological and human drivers, particularly the density of water-bearing containers, but is also influenced by climate, including variability in temperature, moisture and solar radiation. For relatively small countries with presumably some climate uniformity, a climate-based dengue model has been developed that strongly correlates with the inter-annual variability in dengue cases reported at the national level (Fig. 1)[32].

A few examples of other vector-borne diseases demonstrating variance with climate include the Ross River virus in Australia[33,34], and plague[35] in the American southwest. Bluetongue, a disease of livestock, has increased its northern range in Europe since 1998, paralleling trends in warming and controlling for many biological and socioeconomic factors[36].

Temperature has also been found to affect food-borne infectious diseases. For example, higher than average temperatures contribute to an estimated 30% of reported cases of salmonellosis across much of continental Europe[37]. In the UK, the monthly incidence of food poisoning is most strongly associated with the temperatures occurring in the previous two to five weeks[38].

El Niño/Southern Oscillation and infectious diseases. With the exception of seasonal variability, the El Niño/Southern Oscillation (ENSO) is the strongest naturally occurring source of climate variability around the globe[39]. Studies of malaria have revealed the health impacts of interannual climate variability associated with El Niño, including large epidemics on the Indian subcontinent[40], in Colombia[41], Venezuela[42] and Uganda[43]. Rift Valley fever epidemics

between 1950 and 1998 have coincided with unusually high rainfall in East Africa associated with ENSO-related Pacific and Indian Ocean sea surface temperature (SST) anomalies[44]. While more than three quarters of the Rift Valley Fever outbreaks between 1950 and 1988 occurred during warm ENSO event periods[45], some epidemics have also occurred in years with no El Niño, and the model has not been validated against new epidemics.

A 'wavelet analysis' method was recently used to incorporate host immunity and pathogen population dynamics of DHF in Thailand. A spatial-temporal travelling wave explained a three-year period cycle in disease incidence, starting in Bangkok, moving radially at a speed of 148 km per month[46]. In a subsequent study that controlled for this intrinsic synchronization, El Niño remained as a significant determinant of dengue epidemics that cycled every two to three years from 1986 to 1992 in Thailand[47].

Hantavirus pulmonary syndrome in the American southwest can be predicted on the basis of ENSO events; following the 1991–92 El Niño, associated heavy rainfall led to an increase in the

Table 1 | Global burden of climate-change-attributable disease

Region	CVD		Diarrhoea			Malaria			Floods			
	Mortality*	Risk‡	Mortality*	Disease†	Risk‡	Mortality*	Disease†	Risk‡	Mortality*	Disease†	Risk‡	
											Inland	Coastal
AFR-D	1	1.007	5	154	1.08	5	178	1.02	0	1	1.36	1.64
AFR-E	1	1.005	8	260	1.08	18	682	1.14	0	3	1.48	1.18
AMR-A	0	1	0	0	1	0	0	1.51	0	4	4.93	1.19
AMR-B	1	1.004	0	0	1	0	3	1.15	1	67	2.13	2.27
AMR-D	0	1.005	1	17	1.02	0	0	1.08	0	5	1.78	4.64
EMR-B	0	1.003	0	14	1	0	0	1	0	6	2.67	1.75
EMR-D	1	1.003	8	277	1.09	3	112	1.29	1	46	3.05	3.91
EUR-A	0	0.999	0	0	1	0	0	1	0	3	3.55	1.14
EUR-B	0	0.999	0	6	1.01	0	0	1	0	4	1.82	6.31
EUR-C	0	0.998	0	3	1	0	0	1.48	0	1	2.35	1.04
SEAR-B	1	1.007	1	28	1	0	0	1	0	6	1.79	1.39
SEAR-D	7	1.007	22	612	1.09	0	0	1.01	0	8	1.12	1.04
WPR-A	0	0.999	0	0	1	0	0	1.48	0	1	1.76	1.04
WPR-B	0	1	2	89	1.01	1	43	1.42	0	37	1.62	1.05
World	12§	–	47	1,459	–	27	1,018	–	2	193	–	–

Region	Malnutrition			All causes		Total deaths per million	Total DALYs per million
	Mortality*	Disease†	Risk‡	Mortality*	Disease†	Mortality*	Disease†
AFR-D	8	293	1.02	19	626	66.83	2,185.78
AFR-E	9	323	1.02	36	1,267	109.4	3,839.58
AMR-A	0	0	1	0	4	0.15	11.85
AMR-B	0	0	1	2	71	3.74	166.62
AMR-D	0	0	1	1	23	10.28	324.15
EMR-B	0	0	1	1	20	5.65	147.57
EMR-D	9	313	1.08	21	748	61.3	2,145.91
EUR-A	0	0	1	0	3	0.07	6.66
EUR-B	0	0	1	0	10	1.04	48.13
EUR-C	0	0	1	0	4	0.29	14.93
SEAR-B	0	0	1	2	34	7.91	117.19
SEAR-D	52	1,918	1.17	80	2,538	65.79	2,080.84
WPR-A	0	0	1	0	1	0.09	8.69
WPR-B	0	0	0.99	3	169	2.16	111.36
World	77	2,846	–	166	5,517	27.82	925.35

*Estimated mortality in thousands attributable to climate change in 2000 (compared to baseline climate of 1961–1990).
†Estimated disease burden in thousands of DALYs attributable to climate change in 2000.
‡Projected changes in relative risk for 2030.
§Heat-related deaths without subtracting potential reductions in cold-related deaths; this value was therefore not included in the aggregate estimates of mortality due to climate change.
The data in Table 1 are taken from ref. 57. The region key is taken from ref. 57. AFR-D: Algeria, Angola, Benin, Burkina Faso, Cameroon, Cape Verde, Chad, Comoros, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Guines-Bissau, Liberia, Madagascar, Mali, Mauritania, Mauritius, Niger, Nigeria, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, Togo.
AFR-E: Botswana, Burundi, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Eritrea, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia, Zimbabwe.
AMR-A: Cuba, Canada, United States of America.
AMR-B: Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Brazil, Chile, Colombia, Costa Rica, Dominica, Dominican Republic, El Salvador, Grenada, Guyana, Honduras, Jamaica, Mexico, Panama, Paraguay, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, Uruguay, Venezuela.
AMR-D: Bolivia, Ecuador, Guatemala, Haiti, Nicaragua, Peru.
EMR-B: Bahrain, Cyprus, Iran, Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Oman, Qatar, Saudi Arabia, Syrian Arab Republic, Tunisia, United Arab Emirates.
EMR-D: Afghanistan, Djibouti, Egypt, Iraq, Morocco, Pakistan, Somalia, Sudan, Yemen.
EUR-A: Andorra, Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, the Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom.
EUR-B: Albania, Armenia, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Georgia, Kyrgystan, Poland, Romania, Slovakia, Tajikistan, Macedonia, Turkey, Turkmenistan, Uzbekistan, Yugoslavia.
EUR-C: Belarus, Estonia, Hungary, Kazakhstan, Latvia, Lithuania, Moldova, Russian Federation, Ukraine.
SEAR-B: Indonesia, Sri Lanka, Thailand.
SEAR-D: Bangladesh, Bhutan (Democratic People's Republic of), Korea, India, Maldives, Myanmar, Nepal.
WPR-A: Australia, Brunei, Darussalam, Japan, New Zealand, Singapore.
WPR-B: Cambodia, China, Cook Islands, Fiji, Kiribati, Lao, Malaysia, Marshall Islands, Micronesia, Mongolia, Nauru, Niue, Palau, Papua New Guinea, Philippines, Republic of Korea, Samoa, Solomon Islands, Tonga, Tuvalu, Vanuatu, Vietnam.

rodent populations that preceded human cases of disease[48]. Based on these climate/ecology/disease relationships, a climate- and GIS (Geographic Information System)-based model was developed that predicted disease risk reasonably well for the following strong El Niño event of 1997–98 (ref. 49).

Waterborne diseases, such as childhood diarrhoeal disease, are also influenced by El Niño, as was observed with the 1997–98 El Niño event in Peru. During that unseasonable winter, the ambient temperature in Lima increased more than 5 °C above normal, and the number of daily admissions for diarrhoea increased by more than twofold, compared to expected trends[50].

Cholera has varied with climatic fluctuations and SSTs affected by the ENSO phenomenon over multi-decadal time periods in Bangladesh[51]. In the Bay of Bengal, upward trends in cholera also have been linked to longer-term climate changes (that is, changes over approximately a century), with weak cholera/ENSO links found during 1893–1940, and strong and consistent associations occurring during the more pronounced ENSO fluctuations between 1980–2001 (ref. 52). One ecologically based hypothesis for this link involves copepods (zooplankton), which feed on algae, and can serve as reservoirs for *Vibrio cholerae* and other enteric pathogens[53]; copepods bloom in response to the warming SSTs generally associated with El Niño.

Understanding interannual cycles of cholera and other infectious diseases (as seen above for dengue fever), however, requires the combined analyses of both environmental exposures and intrinsic host immunity to a disease. When these factors are considered together, interannual variability of cholera is strongly correlated to SSTs in the Bay of Bengal, ENSO, the extent of flooding in Bangladesh across short time periods (<7 years), and to monsoon rains and Brahmaputra river discharge for longer period climate patterns (>7 years)[54].

Although it is not clear whether and how ENSO dynamics will change in a warmer world, regions that are currently strongly affected by ENSO (for example, southeast Asia, southern and east Africa, the southwest USA, and various regions of South America) could experience heightened risks if ENSO variability, or the strength of El Niño events intensifies.

Land use, local climate and infectious disease. Just as the 'urban heat island' (mentioned above) exacerbates heatwaves, so too can land use change influence transmission of infectious diseases. Land cover may affect mosquito habitat by changing local temperature and humidity. For example, temperatures were significantly higher in communities in highland Uganda bordering cultivated swamps compared with natural ones[55], and average minimum temperatures were associated with the number of *Anopheles gambiae sensu lato* (*s.l.*) mosquitoes per house after adjustment for potential confounding variables. Of course, in some locations, rainfall is more important than temperatures or land use, and in some locations malaria epidemics in the highlands of Africa are more influenced by changing disease-control efforts than any other factors[29].

Past and present climate-change impacts

In the most comprehensive, peer-reviewed and quantitative climate–health assessment to date, the World Health Organization (WHO) examined the global burden of disease already attributable to anthropogenic climate change up to the year 2000 (ref. 20); WHO also made model-based forecasts of the health risks from global climate change until 2030 (refs 56, 57).

The study made generally conservative assumptions about climate–health relationships (for example, that socioeconomic conditions would prevent a climate-driven spread of vector-borne disease from endemic tropical regions to temperate regions), and health impacts were included only if quantitative models were available. An assessment over such a broad range of health impacts is by nature approximate, as there are significant uncertainties in all climate change–disease models. The study indicates that the climatic changes that have occurred since the mid-1970s could already be causing over 150,000 deaths and approximately five million 'disability-adjusted life years' (DALYs) per year through increasing incidences of diseases such as diarrhoea (temperature effects only), malaria and malnutrition that occur mainly in developing countries[57] (Table 1, Fig. 2).

The WHO assessment emphasized that actions to adapt to a changing climate will require regional assessments of vulnerability to specific health risks, and interventions that are geographically and temporally targeted on highly susceptible populations.

Future projections and uncertainties

The WHO extended its estimates of morbidity and mortality caused by human-induced climate change to the year 2030, following

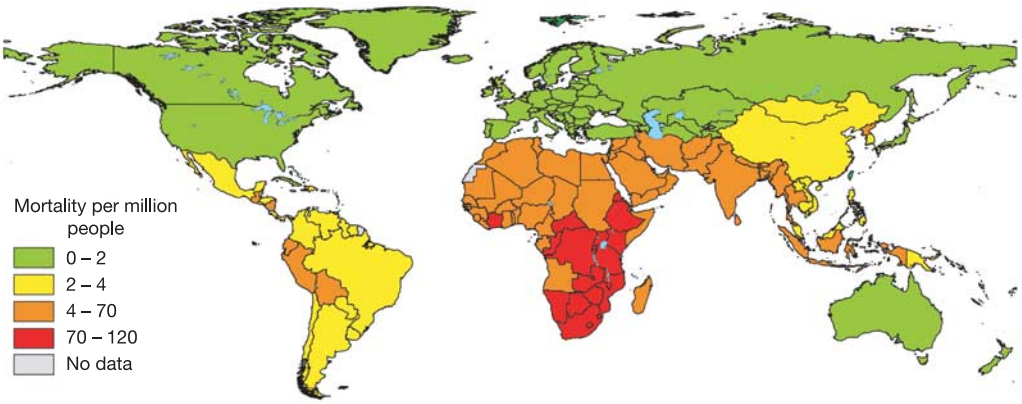

Figure 2 | WHO estimated mortality (per million people) attributable to climate change by the year 2000. The IPCC 'business as usual' greenhouse gas emissions scenario, 'IS92a' and the HadCM2 GCM of the UK Hadley Centre were used to estimate climate changes relative to 'baseline' 1961–1990 levels of greenhouse gases and associated climate conditions. Existing quantitative studies of climate–health relationships were used to estimate relative changes in a range of climate-sensitive health outcomes including: cardiovascular diseases, diarrhoea, malaria, inland and coastal flooding, and malnutrition, for the years 2000 to 2030. This is only a partial list of potential health outcomes, and there are significant uncertainties in all of the underlying models. These estimates should therefore be considered as a conservative, approximate, estimate of the health burden of climate change. Even so, the total mortality due to anthropogenic climate change by 2000 is estimated to be at least 150,000 people per year. Details on the methodology are contained in ref. 57.

Hadley Centre global climate model (GCM) projections for a range of greenhouse-gas emissions scenarios[58]. It estimates that the climate-change-induced excess risk of the various health outcomes will more than double by the year 2030 (ref. 57). Large increases are predicted for the relative risk of flooding and more modest changes in diseases such as malaria, malnutrition and diarrhoea (Table 1). However, it is important to note that these small relative changes may actually cause far greater aggregate disease burdens. In sub-Saharan Africa, for example, flooding currently kills less than one person per million annually, while malaria kills over 1,600 per million and diarrhoea kills over 1,000 per million (ref. 57).

To consider changes in future heatwave probabilities, GCM projections of future climate for conditions contributing to heatwaves are now capable of estimating the occurrence of stagnant, warm air masses that can determine the severity of a heatwave, including variables such as consecutive nights (three or more) with high minimum night-time temperatures[59]. A recent analysis of the 1995 Chicago and 2003 Europe heatwaves predicted intensified magnitude and duration of heatwaves over portions of Europe and the United States, suggesting that heatwaves in Chicago and Paris will be 25% and 31% more frequent, respectively, by 2090 and that the average length of a heatwave in Paris will have increased from 8–13 days to 11–17 days. Large increases in heatwaves were also projected for the western and southern USA and the Mediterranean region[59].

Data from the MARA (Mapping Malaria Risk in Africa) project have been applied to global climate projections to examine potential changes in malaria risk over regions of Africa[60]. Excluding any increase in population, an increase of 16–28% in person-month exposure (number of people exposed per month) to malaria risk by year 2100 was determined[60]. However, like all previous continental or global models of malaria–climate relationships, the study fails to account for non-climatic determinants or the variation of specific climate–disease relationships among locations[61,62].

Extrapolation from statistically based models into the future is of limited value. There may be evidence that malaria is increasing in the highlands of Africa owing to climate change, but methods used to detect it are still controversial and do not convincingly prove or disprove the association. To assess the health risks of mid- to long-term future climate projections, a concerted effort combining the use of process-based models (capturing the biology of the malaria system) alongside statistical modelling will be needed.

Regional assessments of health impacts. Climate-change projections from GCMs, such as a recent set of simulations performed in preparation for the Intergovernmental Panel on Climate Change (IPCC) Fourth Assessment Report[63], are increasing in resolution, but are still not appropriate for analysing disease patterns at scales smaller than a few grid boxes of area 250 km^2. For example, local patterns of climate that are strongly influenced by subtle changes in topography (slope and aspect, rainshadow effects, orographic precipitation), large water bodies, coastlines and other geographic features may be important determinants of disease ecology.

Moving from large-scale climate projections to smaller spatial scales requires the application of 'downscaling' techniques that bring additional information to bear on the region in question. Downscaling methods fall into two broad categories: dynamical downscaling, using high-resolution, regional climate models[64,65], and statistical downscaling, based on statistical relationships between large-scale predictor variables and regional predictants (Table 2).

A dynamical downscaling study with the aim of determining the impact of potential climate changes over the next 50 years on air pollution in the eastern USA[66] reported that under the high-emission 'A2' IPCC scenarios, daily average ozone levels increase by 3.7 p.p.b. across the eastern USA, with the most polluted cities today experiencing the greatest increase in temperature-related ozone pollution (Fig. 3). Across 15 selected cities in this region, the average number of days exceeding the 8-hour ozone standard increased by 60%—from 12 to almost 20 days per summer by the 2050s (ref. 67). Assuming constant population and dose–response characteristics, an independent dynamical downscaling study[64] (refs 64 and 67 both stem from the modeling work of ref. 66) projected that ozone-related deaths from climate change will increase by ~4.5% for the mid-2050s (using the 'A2' emissions scenario), compared with the levels of the 1990s. Considering the potential population exposed to outdoor air pollution (in the millions), this seemingly small relative risk actually translates to quite a substantial attributable health risk. There is significant uncertainty associated with these findings, as they are based on a single emissions scenario, one GCM simulation, and many assumptions about regional ozone precursor emissions.

Table 2 | Differences between dynamical and statistical downscaling

	Benefits	Drawbacks	Applications
Dynamical downscaling	• Simulates climate mechanisms • No *a priori* assumptions about how current and future climate are related • 'State of the science' tools • Continually advancing computers are making RCMs faster and cheaper to run • Encourages collaborations between health and climate scientists	• Expensive, in terms of computer resources and professional expertise • Results may be sensitive to uncertain parameterisations • Biases in the GCM (providing boundary conditions) may propagate to regional scale • Output from models may not be in a format well-suited to health analysis—additional data processing often required	• Health responses associated with climate extremes and nonlinear variability • Data-poor areas • Connecting outcomes with climate processes • Include land-use impacts on climate or health outcomes
Statistical downscaling (especially regression methods)	• Much cheaper (runs quickly on desktop computers with free software) • Builds on the statistical expertise common among public health researchers • May correct for biases in GCM • Allows for the assessment of climate results over a range of GCMs and emission scenarios	• Assumes relationships between local and large-scale climate remain constant • Does not capture climate mechanisms • Not well suited to capturing variance or extreme events	• Climate means, and variability with some limitations • Data-rich regions, especially Northern Hemisphere mid-latitudes • Compare present with projected climate in a consistent framework • Test a range of inputs • Variable scales, down to individual measurement sites

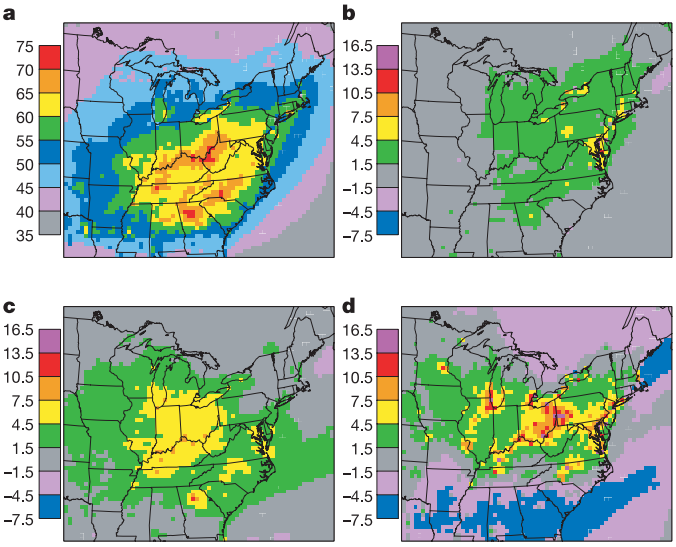

Figure 3 | Simulated ozone air pollution over the eastern United States by using a downscaled climate model linked to a regional air pollution model. **a**, Baseline summertime average daily maximum 8-hour O_3 concentrations for the 1990s. **b**–**d**, The following panels show changes in summertime-average daily maximum 8-hour O_3 concentrations for the 2020s (**b**), the 2050s (**c**), and the 2080s (**d**) over the region based on IPCC A2 scenario simulations relative to the 1990s, in parts per billion. Five consecutive summer seasons were simulated in each decade starting with the NASA Goddard Institute for Space Studies (GISS) Atmosphere-Ocean Global Climate Model, with results subsequently downscaled using the mesoscale regional climate model (MM5), and finally coupled to the Community Multiscale Air Quality (CMAQ) model. Simulation results for the 2020s, 2050s and 2080s indicate that summertime average daily maximum 8-hour O_3 concentrations increase by 2.7, 4.2 and 5.0 p.p.b., respectively, as a result of regional climate change. The data were taken from ref. 66.

Statistical downscaling is most useful for health assessment in data-rich regions. On the basis of statistical downscaling techniques, heat-related deaths in California are estimated to more than double by the year 2100 (ref. 68).

Pursuing early warning systems. Current early warning systems for infectious diseases are beginning to show some utility. For example, over two-thirds of the inter-annual variability of malaria in Botswana can be predicted from the SSTs and associated monthly rainfall[69]. For more direct health impacts from heatwaves, although uncertainty still remains as to which weather parameters are most hazardous, a number of studies have consistently identified high minimum (night-time) temperatures, duration, and early seasonal occurrence of heatwaves as particularly dangerous conditions[70]. Therefore, early warning systems may offer some health protection from the effects of heatwaves. For example, after the 1995 heatwave in the United States, the city of Milwaukee initiated an 'extreme heat conditions plan' involving local agencies, communications tests, stepped responses to early forecasts, a 24-hour 'hotline' and other interventions. Reductions in heat-related morbidity (measured by emergency ambulance runs) and mortality were reduced by 49% from expected levels during a heatwave in 1999, and were not attributable to differences in heat levels alone[71].

Currently, over two dozen cities worldwide have a 'synoptic-based' weather-watch warning system, which focuses monitoring on dangerous air masses[72]. These systems successfully forecast most days with excess deaths in Rome during the 2003 heatwave[73], and have been implemented successfully in Shanghai, for example[74]. However, variability in predictability between cities suggests that systems must be location-specific, requiring the input of considerable amounts of health-related and meteorological data for each locale[75].

Health and regional climate change

Two main climatic impacts on health at a regional scale emerge from this review: direct heat-related mortality and morbidity, and a climate-mediated change in the incidence of infectious diseases.

Heat-related mortality is dominated by the difference between temperature extremes and the mean climate—especially early in summer when people have not yet become accustomed to higher temperatures—rather than by gradual increases in mean temperatures. Projections of future climate suggest such increases in extremes in relation to mean temperatures may occur particularly in the mid-latitudes. In addition, the effect of heatwaves is exacerbated in large cities owing to the urban heat island effect. As urban areas and urban population grow, vulnerability to heat-related mortality seems likely to increase in the future.

Studies of climatic influences on infectious diseases have mainly focused on the influence of ENSO. ENSO has been found to be related to incidences of malaria in South America, rift valley fever in east Africa, dengue fever in Thailand, hantavirus pulmonary syndrome in the southwestern USA, childhood diarrhoeal disease in Peru and cholera in Bangladesh. It is unclear at this stage whether global warming will significantly increase the amplitude of ENSO variability, but if so, the regions surrounding the Pacific and Indian oceans are expected to be most vulnerable to the associated changes in health risks.

Potential impacts of long-term trends in mean temperatures on health, for example, on malaria incidence in the African highlands, have not been reliably detected. The data available at present do not allow robust control for non-climatic confounding factors such as socio-economic influences, immunity patterns and drug resistance effects. However, regions bordering areas with high endemicity of climate-sensitive diseases, where temperatures at present limit the geographic distribution of disease (such as malaria in the African highlands) could be at risk in a warmer climate.

Early warning systems both for heatwaves and for expected outbreaks of infectious diseases can help to adapt to some of the effects of a changing climate, through measures such as opening air-conditioned shopping malls at night-time to those who are most vulnerable to heat, or providing prophylactic treatment to those in danger from infectious diseases. However, population vulnerability still greatly depends on economic and other determinants of a society's capacity to provide such measures.

Land use and land cover change, as mentioned above, can magnify the effects of extreme climatic events, both on direct health outcomes (for example, heat mortality), and on ecologically mediated infectious diseases in any region of the world. Therefore, to assess accurately future climate-change impacts on health, future projections of land-use change must be considered as well.

As illustrated in Fig. 2, the regions with the greatest burden of climate-sensitive diseases are also the regions with the lowest capacity to adapt to the new risks. Africa—the continent where an estimated 90% of malaria occurs—has some of the lowest per capita emissions of the greenhouse gases that cause global warming. In this sense, global climate change not only presents new region-specific health risks, but also a global ethical challenge. To meet this challenge, precautionary approaches to mitigating anthropogenic greenhouse gases will be necessary, while research continues on the full range of climate–health mechanisms and potential future health impacts.

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