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REVIEW

Climate change epidemiology: methodological challenges

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Abstract Climate change is now thought to be unequivocal, while its potential effects on global and public health cannot be ignored. However, the complexities of the causal webs, the dynamics of the interactions and unpredictability mean that climate change presents new challenges to epidemiology and magnifies existing methodological problems. This article reviews a number of such challenges, including topics such as exposure assessment, bias, confounding, causal complexities and uncertainties, with examples and recommendations provided where appropriate. Hence, epidemiology must continue to adapt by developing new approaches and the integration of other disciplines such as geography and climatology, with an emphasis on informing policy-making and disseminating knowledge beyond the field.

Keywords Climate change · Epidemiology · Methodology · Bias · Confounding

Introduction

Today, population health scientists are faced with challenges on an unprecedented scale, in the form of global climate change. The increases in average air and sea temperatures observed in the last several decades have been confirmed as "unequivocal", and attributable to human activity by the Intergovernmental Panel for Climate Change (IPCC). Temperatures are predicted to further increase significantly over the next century (IPCC 2001, 2007; WHO 2008). Direct impacts on human health include increased frequency and severity of extreme weather events such as heat waves, droughts, storms, and floods, while indirect impacts can be mediated through the various biological systems that sustain life on Earth. Significant threats to human health highlighted by the IPCC and WHO include: temperature extremes and other extreme weather events, air pollution (ground ozone), water- and food-borne diseases, rodent- and vector-borne diseases, and disruptions of food and water supplies, along with effects of social, cultural, and political changes such as migration and conflicts (IPCC 2001, 2007; Martens and McMichael 2002; McMichael et al. 2003).

These expected outcomes imply that to assess the predicted impacts of climate change on human health, we must consider both the temporal and spatial scales over which risks and effects are likely to occur, the multifactorial sources and pathways that contribute to health change, and the dynamic and complex interactions between them. This clearly presents new challenges not only to current epidemiological methods regarding disease causation, but also to the type of approaches required to reliably investigate climate–health relationships (Baker and Nieuwenhuijsen 2008; March and Susser 2006; McMichael 1999; Pekkanen and Pearce 2001). Here, our aim is to review some key challenges that climate change presents to epidemiology.

This paper belongs to the special issue "Climate changes health".

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Key challenges and their methodological implications

Scale of study

The scales involved in investigating climate–health relationships, in terms of time-span and geographical spread,

are largely unfamiliar to population health scientists. Climate impacts on populations rather than individuals, therefore within a given area, identifying "unexposed" control group is often difficult as risks will be characterized by small yet significant differences in exposure among individuals. Assessment of likely risk is also complicated by the long-time scales involved in both risk evolution and disease causation as a result of climate change, necessitating long-term study designs (Baker and Nieuwenhuijsen 2008; March and Susser 2006). Hence, not only is there a need to carefully define the appropriate spatial–temporal scales for investigating climate–health relationships, but also the development of methods and frameworks to conduct research and combine evidence from various scales, from both the macro-population level to the micro-individual and even molecular levels (Pekkanen and Pearce 2001). Other related issues include to enable assessments of health over the life span perhaps using life-course approaches and historical trend analysis, and the use of multilevel modelling approaches to better relate macro causes (e.g. environmental and societal changes) and micro causes (e.g. individual vulnerability) of health change.

Exposure assessment

Although the recent unusual climatic trends have been confirmed by various international panels and organisations, translating climate and its alterations into meaningful exposure assessments presents challenges to epidemiologists. Climate is naturally variable, sometimes considerably so. It is defined using a set of weather "norms": the expected averages values for a specific time-period and location. As weather and climate can vary over spatial (local, national, global) and temporal (day, season, year) scales, it is crucial that climate variability and climate change are clearly distinguished, as the effects of the latter are gradual and occur on decadal time-scales. Extensive and standardised data collection for extended periods of observation is required in order to establish baseline values, against which future climate changes can be measured (IPCC 2001, 2007; Martens and McMichael 2002).

Even in the case of extreme weather events, standardised definitions can be difficult as each phenomenon has features unique to its locality and time-span. Consider the example of a heat waves (Appendix 1): the absolute temperatures, duration, and even impact could be used to describe such an event, and all of the aforementioned defining factors can vary between geographical locations and time. Hence, a truly useful definition needs to be locality specific and take into account other relevant indicators like physiological, behavioural and other characteristics including adaptations of its population. Appendix 1 reviews of some current national heat-wave response plans with a focus on how they are defined.

The definition of exposure must also vary according to the type of health outcome to be studied. For example, many communities, especially in developing countries, are particularly vulnerable to rapid-onset flash floods, as by nature they provide little warning (Few et al. 2004) and therefore making preventative measures very difficult. The majority of flash-flood-related deaths are from drowning and injuries. This differs from slow-onset floods that are less likely to cause immediate mortality and morbidity in the onset phase (Few et al. 2004). In this case, a likely health outcome is the subsequent outbreak of an infectious disease. It is important to distinguish between the types of flood exposures for directing response measures and response planning following flood events.

Ecological and atomistic fallacies

Pure ecological approaches that lack the incorporation of any individual-level information tend to be prone to a methodological shortfall: the ecological bias (sometimes referred to as "ecological fallacy" or "cross-level bias"). This occurs when aggregate or group level assessments are used to infer associations at the individual level. Its implications for epidemiological research have been discussed in depth elsewhere (Greenland 2001; Portnov et al. 2007; Wakefield 2008). An approach to minimising such bias is to increase inter-group and reduce intra-group variance in exposure (i.e. more "centres" of internally equally exposed individuals). However, ecological bias could still arise from the loss of information and the reduction in exposure variance resulting from aggregation of data, a common practice due to practicality, confidentiality, or contextual reasons which directly define variables at the group level (i.e. the presence of a health-related resource at neighbourhood-level). This can distort the magnitude and even the direction of the ecological-level association observed in contrast to individual-level association, depending on the rate and distribution of these factors in the control population. Modern ecological studies routinely incorporate individual-level data to minimise ecological bias, and these are often referred to as "semi-individual" studies. However, this does not eliminate the problem of bias altogether. Abrahamowicz et al. (2004) simulated a semi-individual study with cluster level exposure and individual outcome measure and performed Cox regression analysis, a routine approach when investigating causal relationships in environmental epidemiology. They found that aggregation of individual data resulted in systematic underestimation of the causal relationship between exposure and outcome, which differed from confounding.

However, the preceding does not imply that aggregate-level data should never be used in epidemiological studies; sometimes it is the only form of information available. On the other hand, it is also important to consider populations not only as a collection of individuals, but also as entities with their own unique culture, history, and attributes (Pearce 1996). Population characteristics can have effects independent of the individual. This is demonstrated by McMichael (1999) using the example of herd immunity in the case of infectious diseases suggesting that inferring causation at the population level from individual level comparisons can lead to what has been termed as "atomistic fallacy" by Susser (1973). Any practical and cost-effective health intervention will no doubt also need to address the population as well as individuals. This has resulted in proposals for epidemiology to lean towards ecological or population-based study designs, while also incorporating multi-level information and interdisciplinary approaches, in order to rise to the challenges climate change presents (McMichael et al. 2003; McMichael 1999; Rothman 1993). In a two-pronged approach, one would thus use individual data as much as possible for initial aetiological research to identify any important associations (including vulnerability), while group-level data would be used for studies that ultimately aim to inform policy makers and adaptation, set at the level of populations.

Confounding and effect modification

Climate change research can be especially prone to certain causes of artefactual association: confounding and effect modification. A confounder is an independent risk factor for the outcome that is also associated with exposure, while an effect modifier is a third factor acting within the casual pathway that affects the outcome.

Relationships between climate and health are often mediated via complex webs of diffused and indirect pathways and cascades (i.e. through ecosystems), frequently with prolonged time-span for the associated impacts to become evident. Attribution to a particular exposure would thus be difficult as there would be many competing explanations for observed associations, which cannot be clearly and easily specified. Other complexities such as simultaneous exposures make attribution to each individual hazard using existing quantitative methods difficult.

Figure 1 illustrates the complexity of performing studies in real-life climate change scenario of saltwater intrusion in Bangladesh. For decades, salinity levels in surface and groundwater in coastal Bangladesh have been rising at unprecedented rates (Mirza 2004; Tanner et al. 2007). Higher sea levels are likely to increase salinization (Mondal et al. 2001; Salim et al. 2007). Saltwater from the Bay of Bengal is reported to have penetrated over 100 km

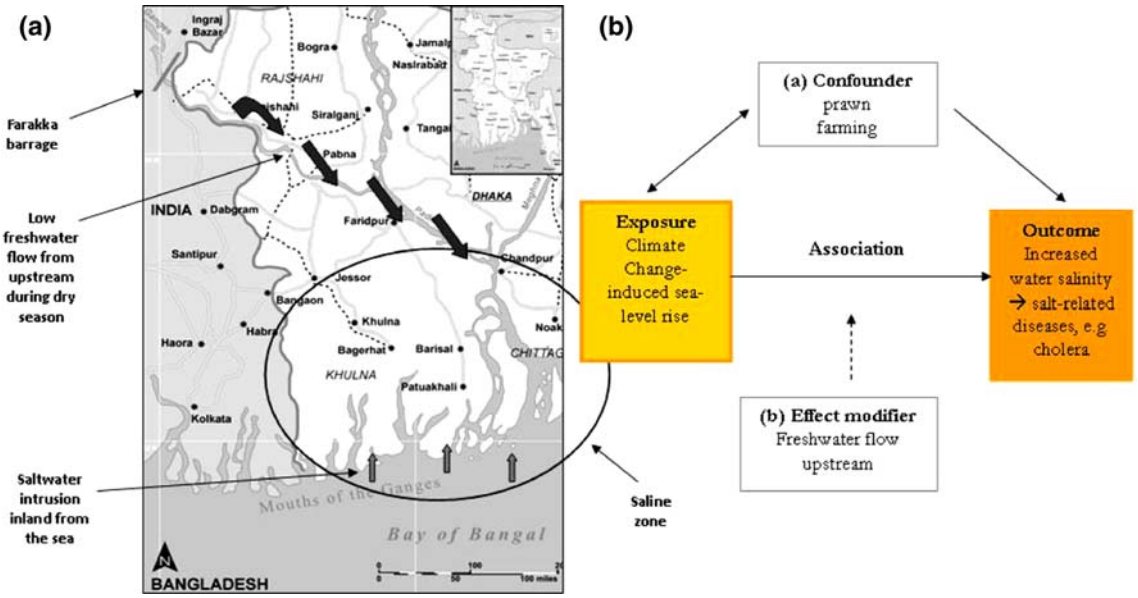

Fig. 1 Confounder and effect modifier in epidemiology. **a** Salinity in surface water and its related health impacts are determined by several factors including (1) rising sea levels (2) shrimp and prawn cultivation in the coast, and (3) reduced freshwater flow from upstream, partly controlled by the *Farakka* barrage. The causal pathway between sea-level rise (SLR) and salinity-related health effects is complex; health effects differ for varying levels of other factors. **b** To investigate the association between climate change/SLR and water salinity related diseases, banned antibiotics used in prawn farming (climate change and SLR can lead to lower productivity of rice growing farms (i.e. through droughts and salinization of soil) so that rice fields are converted for shrimp and prawn farms, which in turn, lead to salinization) would be considered as (*a*) a 'confounder', while the 'freshwater flow upstream' would be considered as (*b*) an effect modifier. *Asterisks* climate change and SLR can lead to lower productivity of rice growing farms (i.e. through droughts and salinization of soil) so that rice fields are converted for shrimp and prawn farms, which in turn, lead to salinization

along tributary channels currently affecting 20 million people and 830,000 hectare of arable land by varying degree of salinity in Bangladesh (Muir and Allison 2006). This has raised serious public health concerns as various salt-related diseases have been reported in those areas, specifically hypertension and eclampsia in pregnancy (Khan et al. 2008), and cholera outbreaks as a consequence of changes in water quality and temperature that facilitate the proliferation of *Vibrio cholerae* (Khan et al. 2008).

Other factors also contribute to the effects of climate change. In particular, the shrimp farming business, which requires high levels of salt in pond water for cultivation, has risen in the same region and has become a major export industry (Mondal et al. 2001), thus further worsening the ecological situation. In addition, farming of the freshwater prawn (*Macrobrachium rosenbergii*) has spread in the region, and the latter group of farmers have started using banned antibiotics like nitrofurans, due to temperature-related bacterial proliferation (Ahmed et al. 2008). The diseased prawns that are rejected from international markets (sometimes found to be contaminated with bacteria like *V. cholerae*) are distributed and consumed by the local communities, resulting in outbreaks of cholera, diarrhoea, dysentery, and skin diseases (Ahmed et al. 2008; USAID 2006). The causal pathway between SLR and salinity-related health effects is therefore confounded by this complex scenario, since cholera outbreaks can either be due to climate change (via modifications in water salinity, pH, and temperature) or to the consumption of infected shrimps, and can even be exacerbated by exposure to antibiotics. The association becomes even more complex when we address additional factors that modify the salinity and health relationship, as illustrated in Fig. 1.

The case-crossover study design maybe used to overcome some of the challenges related to confounding by combining elements from the case–control and cross-over designs. Pioneered by Maclure (1991); here cases serve as their own controls as they pass between windows of exposure and non-exposure. Exposure is then related to the subsequent occurrence of the event of interest. The strengths of this study design include overcoming the difficulty of finding appropriate controls and eliminating within-individual confounding by personal characteristics that remain constant in the short term; also its bi-directional selection of control periods allows adjustment for seasonal and secular trends (Jaakkola 2003). However, it is best applied to relatively rapid-onset, transient, and/or reversible health impacts such as cholera outbreaks; it is unsuitable for many diseases that are chronic in nature (with long lag-times) and have complex aetiology involving many causal factors, such as hypertension.

Bias in climate change

In addition to the issue of confounding as suggested previously, climate change research is affected by potential bias in still unexplored ways. A common classification of bias includes selection bias (in study conception, design and realization), and information bias. Selection bias occurs when the groups that are compared (e.g. exposed and unexposed) are recruited in a way that leads to an artificially unbalanced representation of the outcome variable. According to Rothman (1993), selection bias is "a distortion of the effect measured, resulting from procedures used to select subjects that lead to an effect estimate among subjects included in the study different from the estimate obtainable from the entire population theoretically targeted for the study". For example, in a cohort study for mortality, if a national death registry is not available, then it is necessary to attempt to contact each subject or his next-of-kin to verify vital status (i.e. whether the subject is still alive). Bias could occur if the response rate is higher in the exposed persons with the disease (i.e. participation depends on exposure and disease status).

In the case of climate, in an extreme example subjects exposed to high climate variability can be selected from an area with endemic malaria while subjects "unexposed" to weather variability are selected from a non-malarial area. This will of course lead to a gross overestimation of the association between malaria and climate changes.

Formally speaking, the probability of being "represented" in the sample should be the same for all the subjects who are eligible (e.g. as controls in a case–control study), i.e. the probability should be equal to the sampling fraction. Sampling should not be influenced by disease status in a cohort or by exposure status in a case–control study. Information bias arises when information, e.g. on the outcome variable, is influenced by knowledge of exposure status. For example, clinical data on hypertension can be collected with great accuracy from an area affected by water salinization, while incomplete hospital records will be used to identify those with hypertension in an unexposed area. Such extreme cases of bias rarely occur, while more commonly selection bias is related to low response rates in interview-based epidemiological studies. Table 1 shows how response rates in epidemiological research are associated with social class (deprivation index), thus creating opportunities for both selection and information bias (Goodman and Gatward 2008).

The increasing use of objective information such as GIS-based maps and routinely collected data makes both selection and information bias less likely, but there are exceptions. Appendix 2 shows two examples of potentially biased research on the field of climate change.

Table 1 Non-participation rate in children by deprivation index IMD decile. (Goodman and Gatward 2008)

IMD	Non-participation rate (%)
1 least deprived	7.3
2	6.7
3	7.1
4	7.9
5	8.8
6	9.1
7	11.7
8	10.7
9	14.2
10 most deprived	15.7

IMD index of multiple deprivation

Complexities: nonlinearity and vulnerability

Many exposure–response relationships in epidemiology often do not follow linear trends, but rather have more complicated dynamics; well known examples include correlations between body mass index and all cause mortality (Engeland et al. 2003), alcohol intake and coronary heart disease (Bagnardi et al. 2008), and air pollution (particulate matter) and daily mortality (Daniels et al. 2000), to name a few. To put this in the context of climate change, this means that it is not sufficient for epidemiological studies to identify associations but to characterise observed relationships in enough detail in order to be informative for public health policy-making. Appendix 3 illustrates this in more detail using the example of heat-waves Heat-Health Watch Warning Systems example continued from Appendix 1.

Also, the relevance of purely aetiological research on health effects of climate change is dwindling, given that intertwining social, cultural, and other determinants of health within populations are also central to their susceptibility. Population vulnerability is an important characteristic which is difficult to assess using traditional quantitative methods and whose definition varies across different disciplines (Martens and McMichael 2002). It is a product of the extent a group of individuals will be exposed to the change in climate, as well as the sensitivity to the potential impacts of such changes, with adaptive capacity, the ability to cope and minimise impacts (IPCC 2001; WHO 2000). In terms of health research, vulnerability is shaped by the risk related to exposures (e.g. geographical location), current status of health, economic growth, healthcare infrastructure, availability and security of resources, along with various political, social, and cultural characteristics that determine the distribution of the above factors within a population (Fig. 2).

For instance, poverty is widely considered to effectuate inequalities for a large number of health determinants

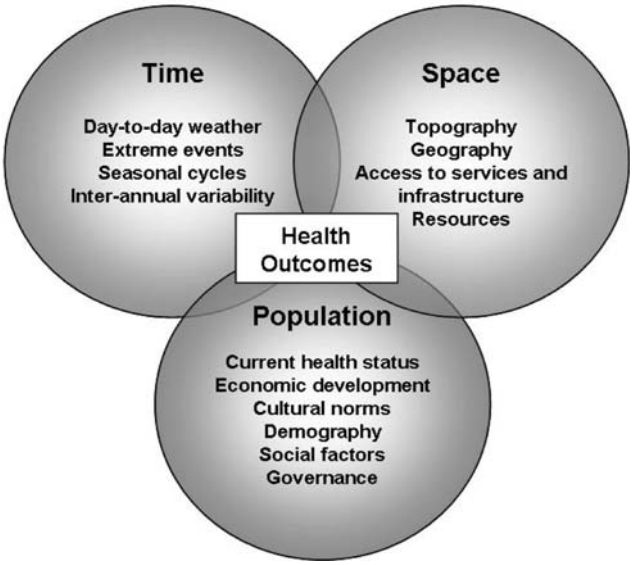

Fig. 2 Population vulnerability interaction diagram. Also see Fig. 3 for a specific example in the case of cholera

including: access to healthcare, poor occupational health, low social capital, low education attainment and health literacy, slow uptake of beneficial interventions and lifestyle, all of which can hinder effective adaptation (O'Neill et al. 2007). Many impoverished populations already shoulder a large share of harmful exposures, such as: environmental and occupational pollution, experiences of food- and water-stresses, and settlements on hazardous sites (e.g. low-lying lands and hillsides) which are more prone to natural disasters. They also tend to rely heavily on climate-dependent industries such as agriculture for livelihood, which is predicted to be most severely affected by the alterations in precipitation and temperature in long-term climate change (Stern 2006). Gender is another known factor that can introduce inequalities in population health and shares many of its mechanistic pathways with poverty. Women have been found to be over-represented in agricultural and other informal labour forces compared to men (Costello et al. 2009; Stern 2006). In disaster events, women have shown increased likelihood of experiencing domestic abuse, post-traumatic stress disorders, and displacement (Dankelman et al. 2008). However, they are also central to local post-event-management and adaptation, while social networks maintained by women can be greatly beneficial, as seen in recent cyclones and floods in India and Pakistan, respectively (Briceño 2002; IPCC 2007).

Use of epidemiology in health impact assessment

Risk assessment aims to comparably identify, characterise, and control environmental risks to health, and it is consequently heavily reliant on epidemiology (Nurminen et al. 1999). By the addition of a comparative element, the

comparative risk assessment (CRA) enables quantification of the contributions to overall disease burden from a number of risk factors (Murray et al. 2003). Alternatively, the health impact assessment (HIA) framework, which is defined by a consensus as "a combination of procedures, methods and tools by which a policy, programme or project may be judged as to its potential effects on the health of a population, and the distribution of those effects within the population" (WHO 1999). It is traditionally a way to systematically assess impacts of a policy or intervention on health in a given community, and its multidisciplinary approach makes it appropriate to investigate the real-life complexity associated with climate change and other environmental issues since it evaluates the contribution of a wide range of health determinants, including economical, social, psychological, environmental, and organisational factors (Scott-Samuel et al. 2006). In the case of climate change, these may be adaptive and mitigative strategies. Yet, there are inherent drawbacks to these approaches, for example, the convention for HIA is to assess impacts of individual factors rather than complex causal webs, and it has also been criticised to lack quantitative rigour (Veerman et al. 2005).

A methodology for an integrated conceptual and analytic framework to assess health impacts of certain environmental exposures has been proposed recently. Briggs (2008) describes an integrated environmental HIA as "a measure of assessing health-related problems deriving from the environment, in ways that take account of the complexities, interdependencies and uncertainties of the real world". It combines a number of existing methodologies to provide a more comprehensive assessment framework that encompasses comparative risk- and health impact-assessments, adaptive responses and policy-making, which is specifically focused for environmental health risks.

An alternative conceptual approach to deal with complexities in causal relationships of interest is to take a less reductionism view of causality. One can imagine instances in climate change research, where interactions between risk factors for the same and even different endpoints, can be just as interesting in regards of their potential as targets for prevention or adaptation measures. For example, a flood can directly cause immediate death, physical injury, and disruption to infrastructure, which can then lead to communicable diseases, poisoning in the short term, and also post-traumatic stress disorders in the long term. In addition, the attributable fraction of each factor may add up to more than 100%, and results will also vary with time and place of study, making interpretation difficult.

Uncertainties and unpredictable outcomes

Accounting for the inherent uncertainty in models of ecological and physical processes related to global climate change is necessary but difficult in practice. Uncertainties exist regarding climate–health relationships, as well as around the extent that socioeconomic adaptation, technological advances, and human behaviour will influence such relationships in the future (Haines et al. 2006). Recent work in the area of climate change and health has raised the importance of dealing with 'biocomplexity', defined as "properties of a system emerging from the interplay of behavioural, biological, chemical, physical, and social interactions that affect, sustain, or are modified by living organisms" (Martens and Huynen 2008; McMichael 2001; Michener et al. 2001). This increasing focus on understanding the biocomplexities of the climate–health relationship first came about from the growing awareness that traditional study methods principally based on empirical observations, which by definition, cannot be readily used to predict future events and their impacts, as a result of system uncertainties, interactions spanning multiple hierarchical levels as well as temporal and spatial scales, and complex dynamics leading to multiple emergent states (Michener et al. 2001). Some uncertainties generally occur from deficient understanding of the actual processes, such as ascertaining key parameter values in models, reasonably foreseeing the future (as population vulnerability may change over time), and sampling variation. Highly non-linear interactions and feedback loops between various components and pathways linked to the health impact of climate change would lead to the occurrence of chaotic and even unpredictable behaviours and thresholds for health change between populations. This system dynamics perspective suggests that ultimately the study of climate–health relationship will need to move beyond simply using empirical studies to the use of a systems approach based on well-validated mathematical modelling (Costello et al. 2009). Indeed, the challenge here is how best to use empirical studies to inform, validate, and test a mathematical modelling approach to enhance our understanding of climate epidemiology.

The recent studies of cholera outbreaks provide a good example of how our understanding of an infectious disease has evolved from a linear empirical model based on oral-faecal transmission of a water-borne bacterium to a human host, to a more complex ecological model based on the climatic, chemical, biological and social factors that underpin transmission. Figure 3 adapted from Wilcox and Colwell (2005), illustrates specificities of the multi-factorial cross-scale environmental transmission of cholera and the hierarchical multi-level analysis framework required to investigate such diseases).

Knowledge dissemination

The prompt dissemination of knowledge and experience gained through climate change research to governments and

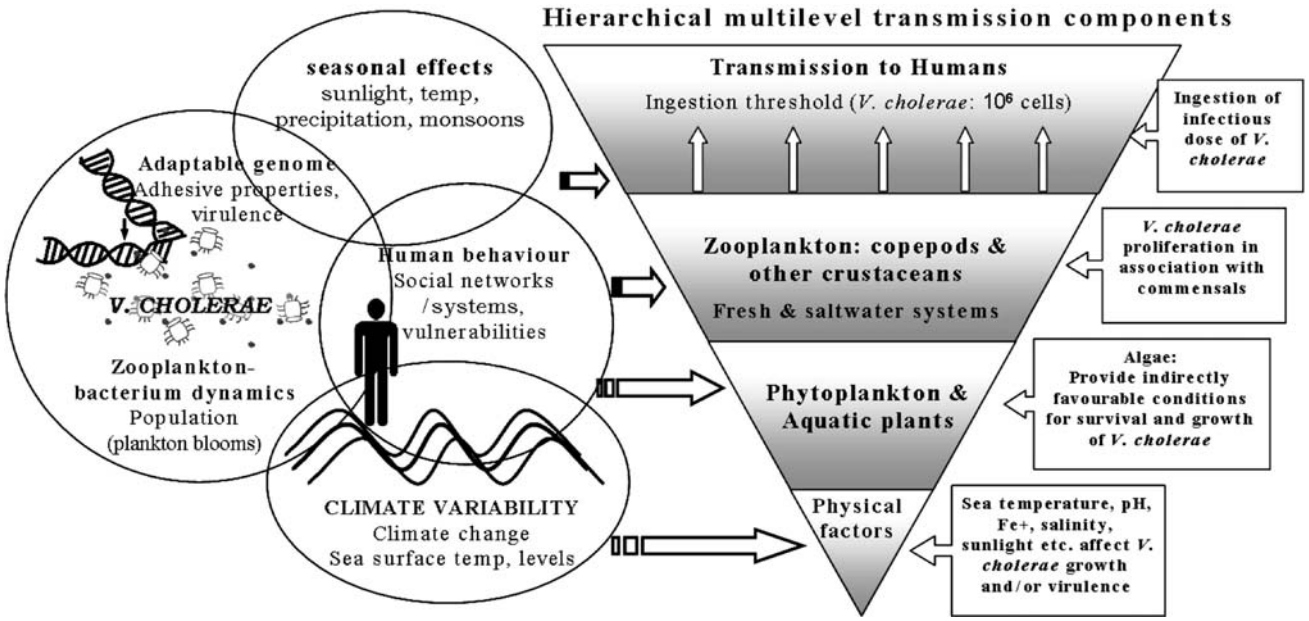

Fig. 3 Biocomplexity and cholera. This figure illustrates the interwoven climatic, biological and social influences of cholera transmission, and the hierarchical multilevel framework approach needed for investigating climate–cholera relationships successfully. Adapted from Wilcox and Colwell (2005) [34]

health organisations around the world is imperative. In addition to the climate change-health working groups already established such as the IPCC and at WHO, a number of international databases have been set up to promote the sharing of knowledge such as the UK Climate Impacts Programme and the Copenhagen UN Framework Convention on Climate Change (UNFCCC) (Costello et al. 2009).

In order for the significance of epidemiological findings to translate to a wider audience (i.e. other than fellow scientists), the traditional effect-indicators used for reporting findings, such as the odds ratio and risk ratio may need to be extended to measures of health impacts such as attributable risk fraction in terms of disease burden, or even quality-adjusted-life-years (QALY's) and disability-adjusted-life-years (DALY's), where possible and appropriate. Causal diagrams can also be valuable tools for describing complex causal systems and for controlling confounding (Joffe 2006), by incorporate changing scenarios: (1) spontaneous natural changes, which could include weather fluctuations, climate change, and population growth, (2) policy-induced changes, and (3) scenarios for use in modelling (Joffe 2006). The use of causal diagrams is considered to be advantageous because they are tractable and can readily connect with policies and other initiatives that could affect health.

Conclusions

Gaining a comprehensive a priori knowledge of well-validated relationships between climate-related factors and health, even in the absence of climate change, should be a high priority for health researchers. To ensure the best chances of success in detecting early climate-related changes, the choice of health outcomes needs to be based, at least in part, on a priori knowledge of the mechanisms of pathogenesis: i.e. diseases that have shown climate- or weather-sensitivity either directly (e.g. temperature extremes-related mortality) or have such a component within their aetiological pathways (e.g. cholera outbreaks). The International Institute for Environment and Development (IIED), IPCC and WHO have recommended a number of priority disease categories: heat- and cold-stresses; allergic disorders from natural and anthropogenic sources; natural disasters (sea-level rises, wind, storms, droughts, floods); food security and safety; water- and vector-borne diseases and ultraviolet radiation.

Perhaps the most unfamiliar challenge for epidemiologists is the need for integration into the wider context of public health and aim to inform policy, through effective dissemination of epidemiological knowledge beyond the specialist field.

In summary, climate change requires epidemiology to endeavour to identify research needs and gaps in empirical knowledge and prioritise according to need, to develop methodologies that address the "real-world" complexities such as multi-factorial causal webs and non-linear dose–response relationships, and to make communication and dissemination of results more accessible to a wider audience.

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Conflict of interest statement The authors declare no conflicts of interest.

Appendix 1

What is a heat-wave?

The World Meteorological Organisation (WMO) has no formal definition for the term "Heat-wave", since the characteristics tend to be event-specific (WHO 2009). Table 2 describes, with an emphasis on the methods used to derive criteria for triggering such systems, some national Heat-Health Watch Warning Systems (HHWS) in operation from five countries. All information presented is from a non-systematic search using publicly available sources such as national institutional and ministerial websites.

HHWS for Europe has been reviewed previously by Kovats and Kristie (2006) as well as WHO's EuroHEAT project. It is clear that according to the examples of HHWS's presented in the table below, the definitions of heat-waves differ markedly, in the type and number of meteorological variables taken into account, absolute thresholds, duration, as well as the weight given to implications of health effects. It would seem that regional- or city- specific warning plans tend to involve more sophisticated approaches to determine criteria for triggering alerts: examples include Shanghai (Tan et al. 2004) and Philadelphia (Kalkstein et al. 1996), which use synoptic approaches to identify air masses that have been associated with increased mortality.

But does increased complexity in the methods of heat-wave prediction add value to HHWS's? The EuroHEAT project investigated the predictive value of a number of meteorological characteristics used by current HHWS and their associations with increased mortality (WHO 2009); these include heat-wave duration, intensity, maximum and minimum temperatures (90th percentile of daily distribution), and interval between heat-wave episodes. It was found that maximum and minimum temperatures and duration were significantly associated. This result suggests that perhaps the simplest definitions are adequate for the purpose of public-health planning which is the primary aim of any HHWS's. Also predictions of simple meteorological variables such as temperatures are usually of higher confidence, with the added advantage of a longer lead-time (WHO 2009), to enable timely implementation of planned actions. However, real-time health-surveillance for the duration of alerts as seen in the French systems may be the most fitting way to maintain reactivity to events such as heat-waves that could quickly escalate into crisis.

Appendix 2—Examples of bias

Example 1

Balanyà et al. (2006) tested the hypothesis that chromosomal inversion polymorphisms of *Drosophila subobscura* are evolving in response to global warming. However, according to a critique (Rodríguez-Trelles 2007), their conclusions may not be adequately supported by their data owing to a potential systematic bias in their sampling approach. Balanyà et al. compared inversion frequency records collected up to 50 years ago latitudinally across three continents with the corresponding current records gathered on the same dates. Using calendar dates instead of climatological or biological dates could be systematically misleading for two reasons. First, because global climate warming has lengthened the growing season, increasingly at higher latitudes, current biological dates are not expected to represent their corresponding calendar dates from decades ago, the disparity being greater toward the poles. Second, because chromosomal inversion polymorphisms of *D. subobscura*, a temperate zone species, undergo pronounced seasonal cycles, with seasonal transitions in inversion frequencies occurring in a matter of weeks. Thus, according to the critique, it is possible that the long-term global genetic shift reported by Balanyà et al. is, at least in part, a sampling artefact ensuing from a biological lag between the old and new samples—especially those from higher latitudes(Rodríguez-Trelles 2007). The new samples were collected systematically later than the old ones with respect to the historical onset of the biological spring.

Example 2

Global climate model (GCM) -based output grids can bias the area identified as suitable when these are used as predictor variables for species distribution, because GCM outputs, typically at least 50×50 km, are biologically coarse. Seo et al. (2009) tested the assumption that species ranges can be equally well portrayed in species distribution operating on base data of different grid sizes by comparing species distribution statistics and areas selected by four species distribution models run at seven grid sizes, for nine species of contrasting range size. Area selected was disproportionately larger for distribution models run on larger grid sizes, indicating a cut-off point above which model results were less reliable. Up to 2.89 times more species range area was selected by distribution models operating on grids above 50×50 km, compared to distribution

Table 2 An example of operational HHWS systems in five countries

National programmes	Time of operation	Trigger	Alert levels	Action links	Regional adaptation	Last update	Taken from
China		Predicted T_{max} breach 37°C and 40°C in the forthcoming 24 h	2, colour-coded	Interventions to reduce risk in vulnerable groups, warning to electric suppliers and fire prevention services	Specific drought-prone areas can raise alert level depending on situation, with approval from China Meteorological Administration	2008	突发气象灾害预警信号发布试行办法
France	01 June–31 Aug	When thresholds for observed or predicted 3-day average of T_{max} and T_{min} are exceeded on the day (thresholds corresponds to expected excess daily mortality to be 50–100% of historical records form the last 30 years)	3, colour-coded	Graduated response at every level: from national and local public health, media and social services leading to possible crisis management	Temperature thresholds set by region, which can activate alerts at the local level using local indicators	2008	Le Plan National Canicule Version 2008
Portugal	15 May–30 Sept	Trigger consists of a combination of absolute T_{max} (observed and predicted), speed of elevation, duration, occurring in early or late summer, expected effect on mortality and other factors such as air pollution, UV and local events	3, colour-coded	Links with the ministries of labour and social affairs, environment, health and public administrations to reach the most vulnerable, such as the elderly, children and those with morbidity	Temperature thresholds derived by province	2008	Plano de Contingência para as Ondas de Calor de 2008
UK	01 June–15 Sept	In the event of T_{max} and T_{min} threshold breaches or 60% likelihood in 3 days	4, colour-coded; one emergency level	Actions orientated around high risk groups and settings, via links to Department of Health, Health Protection Agency, Health Authorities, Primary Care Trusts and local Social Services	Temperature thresholds set for specific geographical regions by the Met office	2008	Heatwave plan for England 2008
USA		Using the Heat Index (HI), represents of air temperature and relative humidity as in "apparent temperature". Maximum daytime HI >40.5°C for northern areas to 43.3°C for southern areas for at least two consecutive days; T_{min} night-time exceeds 23.9°C		Media forecast of HI, issue warning	Coverage to include approximately 70 vulnerable urban cities across the continental U.S. with mostly populations of 500,000 or more. Use location-specific temperature threshold	2003	A National Health/Health Warning System: Improvement Over Current System

T_{max} and T_{min} stand for maximum temperature and minimum temperature, respectively

Information sources respectively by country: China Meteorological Administration, French Ministry of Health, Portuguese Ministry of health, Department of Health UK, National Weather Service, Office of Climate, Water and Weather Services USA

models operating at 1 km^2. Spatial congruence between areas selected as range also diverged as grid size increased, particularly for species with ranges between 20,000 and 90,000 km^2.

Appendix 3

Heat-waves—non-linearity

The PHEWE (Assessment and Prevention of acute Heath Effects of Weather conditions in Europe) project assessed the effect of the "apparent" maximum temperatures (represents the combined discomfort due to heat and humidity) and mortality in 15 countries. It was found that despite differences between the minimum mortality thresholds between the cities, the shapes of the heat-health dose–response curves were remarkably consistent: they were V- or J-shaped curves (Baccini et al. 2008), mirroring results from another large international study, the ISOTHURM project (McMichael et al. 2008). In addition, when the PHEWE cities were stratified into "Mediterranean" and "Northern-Continental" by meteorology and geography, the meta-analytic curves suggest that the heat effect, defined as change in mortality associated with 1°C increase in maximum apparent temperature above city specific threshold, is larger in Mediterranean (3.12%, 95% CI 0.60–5.72) than Northern-Continental (1.84%, 95% CI 0.06–3.64), despite potential acclimatization, which contradicts a previous study in the US (Curriero et al. 2002).

Results such as this have important implications for public health policies, as some national heat-health response plans reply on simple temperature thresholds for activation (Appendix1) and their tiered alert structure also needs to take into account the non-linearity described above to set appropriate thresholds for each level of response. For instance, by identifying the minimum mortality threshold and slope of the response curves by city or region, extrapolation from an analogue location can be misleading due to differences between the distribution of characteristics such as socio-economic-status, demographics, underlying morbidity, race, and adaptation such as use of air conditioning (Kinney et al. 2008).

Moreover, how far should an alert threshold for HHWS stray from minimum mortality threshold on a heat-mortality curve? Although the most reliable evidence of correlation between heat-waves and health is restricted to mortality only, there are a small number of recent studies that suggest that this may extend to morbidity. The association between heat and respiratory mortality was also seen with hospitalization in the PHEWE study (Baccini et al. 2008) and in the elderly (Kovats et al. 2004; Linares and Díaz 2008). While for cardiovascular and circulatory admissions, the evidence is more contradictory (Kovats et al. 2004; Linares and Díaz 2008; Michelozzi et al. 2009; Panagiotakos et al. 2004; Schwartz et al. 2004), although potential biological plausibility has been proposed previously (Pan et al. 1995). This is thought to be attributed to the speed of progression of such events being exacerbated by the high temperature and therefore manifest as mortality instead (Kovats et al. 2004; Linares and Díaz 2008; WHO 2009).

References

Abrahamowicz M, Du Berger R, Krewski D, Burnett R, Bartlett G, Tamblyn RM, Leffondre K (2004) Bias due to aggregation of individual covariates in the Cox regression model. Am J Epidemiol 160:696–706

Ahmed N, Demaine H, Muir J (2008) Freshwater prawn farming in Bangladesh: history, present status and future prospects. Aquac Res 39:806–819

Baccini M, Biggeri A, Accetta G, Kosatsky T, Katsouyanni K, Analitis A, Anderson H, Bisanti L, D'Ippoliti D, Danova J, Forsberg B, Medina S, Paldy A, Rabczenko D, Schindler C, Michelozzi P (2008) Heat effects on mortality in 15 European cities. Epidemiology 19:711–719

Bagnardi V, Zatonski W, Scotti L, La Vecchia C, Corrao G (2008) Does drinking pattern modify the effect of alcohol on the risk of coronary heart disease? Evidence from a meta-analysis. J Epidemiol Community Health 62:615–619

Baker D, Nieuwenhuijsen MJ (2008) Environmental epidemiology: study methods and application. Oxford University Press, Oxford

Balanyá J, Oller J, Huey R, Gilchrist G, Serra L (2006) Global genetic change tracks global climate warming in *Drosophila subobscura*. Science 313:1773–1775

Briceño S (2002) Gender mainstreaming in disaster reduction. United Nations-International Strategy for Disaster Reduction, Geneva

Briggs D (2008) A framework for integrated environmental health impact assessment of systemic risks. Environmental Health 7

Costello A, Abbas M, Allen A, Ball S, Bell S, Bellamy R, Friel S, Groce N, Johnson A, Kett M, Lee M, Levy C, Maslin M, McCoy D, McGuire B, Montgomery H, Napier D, Pagel C, Patel J, de Oliveira JA, Redclift N, Rees H, Rogger D, Scott J, Stephenson J, Twigg J, Wolff J, Patterson C (2009) Managing the health effects of climate change. Lancet 373:1693–1733

Curriero F, Heiner K, Samet J, Zeger S, Strug L, Patz J (2002) Temperature and mortality in 11 cities of the eastern United States. Am J Epidemiol 155:80–87

Daniels M, Dominici F, Samet J, Zeger S (2000) Estimating particulate matter-mortality dose-response curves and threshold levels: an analysis of daily time-series for the 20 largest US cities. Am J Epidemiol 152:397–406

Dankelman I, Alam K, Ahmed WB, Gueye YD, Fatema N, Mensah-Kutin R (2008) Gender, climate change and human security-lessons from Bangladesh, Ghana and Senegal. In: Grossman A, C. O (eds). The Women's Environment and Development Organization (WEDO)

Engeland A, Bjørge T, Selmer R, Tverda lA (2003) Height and body mass index in relation to total mortality. Epidemiology 14:293–299

Few R, Ahern M, Matthies F, Kovats S (2004) Floods, health and climate change: a strategic review. Working Paper 63, November 2004 edn. Tyndall Centre for Climate Change Research

Goodman A, Gatward R (2008) Who are we missing? Area deprivation and survey participation. Eur J Epidemiol 23:379–387
Greenland S (2001) Ecologic versus individual-level sources of bias in ecologic estimates of contextual health effects. Int J Epidemiol 30:1343–1350
Haines A, Kovats RS, Campbell-Lendrum D, Corvalan C (2006) Climate change and human health: impacts, vulnerability, and mitigation. Lancet 367:2101–2109
IPCC (2001) IPCC third assessment report: climate change 2001. International Panel on Climate Change
IPCC (2007) IPCC fourth assessment report: climate change 2007. International Panel on Climate Change
Jaakkola JJ (2003) Case-crossover design in air pollution epidemiology. Eur Respir J Suppl 40:81s–85s
Joffe M (2006) Complex causal process diagrams for analyzing the health impacts of policy interventions. Am J Public Health 96:473–479
Kalkstein LS, Jamason PF, Greene JS, Libby J, Robinson L (1996) The Philadelphia hot weather-health watch/warning system: development and application, summer 1995. Bull Am Meteorol Soc 77:1519–1528
Khan A, Mojumder S, Kovats S, Vineis P (2008) Saline contamination of drinking water in Bangladesh. Lancet 371
Kinney PL, O'Neill MS, Bell ML, Schwartz J (2008) Approaches for estimating effects of climate change on heat-related deaths: challenges and opportunities. Environ Sci Policy 11:87–96
Kovats RS, Kristie LE (2006) Heatwaves and public health in Europe. Eur J Pub Health 16:592–599
Kovats R, Hajat S, Wilkinson P (2004) Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK. Occup Environ Med 61:893–898
Linares C, Díaz J (2008) Impact of high temperatures on hospital admissions: comparative analysis with previous studies about mortality (Madrid). Eur J Pub Health 18:317–322
Maclure M (1991) The case-crossover design: a method for studying transient effects on the risk of acute events. Am J Epidemiol 133:144–153
March D, Susser E (2006) The eco- in eco-epidemiology. Int J Epidemiol 35:1379–1383
Martens P, Huynen M (2008) Using integrated assessment to analyze and forecast the future effects of global environmental change. In: Baker D, Nieuwenhuijsen MJ (eds) Environmental epidemiology: study methods and application. Oxford University Press, Oxford, pp 349–364
Martens P, McMichael A (2002) Environmental change, climate and health—issues and research methods. Cambridge University Press, Cambridge
McMichael AJ (1999) Prisoners of the proximate: loosening the constraints on epidemiology in an age of change. Am J Epidemiol 149:887–897
McMichael AJ (2001) Global environmental change as "risk factor": can epidemiology cope? Am J Public Health 91:1172–1174
McMichael A, Campbell-Lendrum D, Corvalán C, Ebi K, Githeko A, Scheraga J, Woodward A (2003) Climate change and human health—risks and responses. In: WHO (ed) World Health Organization (WHO), Geneva
McMichael A, Wilkinson P, Kovats R, Pattenden S, Hajat S, Armstrong B, Vajanapoom N, Niciu E, Mahomed H, Kingkeow C, Kosnik M, O'Neill M, Romieu I, Ramirez-Aguilar M, Barreto M, Gouveia N, Nikiforov B (2008) International study of temperature, heat and urban mortality: the 'ISOTHURM' project. Int J Epidemiol 37:1121–1131
Michelozzi P, Accetta G, De Sario M, D'Ippoliti D, Marino C, Baccini M, Biggeri A, Anderson HR, Katsouyanni K, Ballester F, Bisanti L, Cadum E, Forsberg B, Forastiere F, Goodman PG, Hojs A, Kirchmayer U, Medina S, Paldy A, Schindler C, Sunyer J, Perucci CA, PHEWE Collaborative Group (2009) High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. Am J Respir Crit Care Med 179:383–389
Michener WK, Baerwald TJ, Firth P, Palmer MA, Rosenberger JL, Sandlin EA, Zimmerman H (2001) Defining and unraveling biocomplexity. Bioscience 51:1018–1023
Mirza M (2004) The Ganges water diversion: environmental effects and implications—an introduction. Springer, Dordrecht
Mondal M, Bhuiyan S, Franco D (2001) Soil salinity reduction and prediction of salt dynamics in the coastal ricelands of Bangladesh. Agric Water Manage 47:9–23
Muir J, Allison E (2006) The threat to fisheries and aquaculture from climate change—World Fish Centre Policy Brief. Word Fish Centre, Penang, p 8
Murray C, Ezzati M, Lopez A, Rodgers A, Vander HS (2003) Comparative quantification of health risks: conceptual framework and methodological issues. Popul Health Metrics 1:1
Nurminen M, Nurminen T, Corvalan C (1999) Methodologic issues in epidemiologic risk assessment. Epidemiology 10:585–593
O'Neill MS, McMichael AJ, Schwartz J, Wartenberg D (2007) Poverty, environment, and health: the role of environmental epidemiology and environmental epidemiologists. Epidemiology 18:664–668
Pan W, Li L, Tsai M (1995) Temperature extremes and mortality from coronary heart disease and cerebral infarction in elderly Chinese. Lancet 345:353–355
Panagiotakos DB, Chrysohoou C, Pitsavos C, Nastos P, Anadiotis A, Tentolouris C, Stefanadis C, Toutouzas P, Paliatsos A (2004) Climatological variations in daily hospital admissions for acute coronary syndromes. Int J Cardiol 94:229–233
Pearce N (1996) Traditional epidemiology, modern epidemiology, and public health. Am J Public Health 86:678–683
Pekkanen J, Pearce N (2001) Environmental epidemiology: challenges and opportunities. Environ Health Perspect 109:1–5
Portnov BA, Dubnov J, Barchana M (2007) On ecological fallacy, assessment errors stemming from misguided variable selection, and the effect of aggregation on the outcome of epidemiological study. J Expo Sci Environ Epidemiol 17:106–121
Rodríguez-Trelles R (2007) Comment on "Global genetic change tracks global climate warming in *Drosophila subobscura*". Science 315
Rothman KJ (1993) Methodologic frontiers in environmental epidemiology. Environ Health Perspect 101(Suppl 4):19–21
Salim M, Maruf B, Chowdhury A, Babul S (2007) Increasing salinity threatens productivity of Bangladesh: COAST trust. COAST position papers 3. COAST Trust, Bangladesh
Schwartz J, Samet JM, Patz JA (2004) Hospital admissions for heart disease: the effects of temperature and humidity. Epidemiology 15:755–761
Scott-Samuel A, Ardern K, Birley M (2006) Assessing health impacts on a population. In: Pencheon D (ed) Oxford handbook of public health practice, 2nd edn. Oxford University Press, Oxford, pp 43–55
Seo C, Thorne JH, Hannah L, Thuiller W (2009) Scale effects in species distribution models: implications for conservation planning under climate change. Biol Lett 5:39–43
Stern N (2006) Stern review on the economics of climate change. Office of Climate Change, UK
Susser M (1973) Thinking in the health sciences: concepts and strategies of epidemiology. Oxford University Press, New York
Tan J, Kalkstein LS, Huang J, Lin S, Yin H, Shao D (2004) An operational heat/health warning system in Shanghai. Int J Biometeorol 48:157–162
Tanner T, Hassan A, Islam K, Conway D, Mechler R, Ahmed A, Alam M (2007) ORCHID: piloting climate risk screening in

DFID Bangladesh. Detailed Research Report April 2007. Institute of Development Studies (IDS), Dhaka

USAID (2006) A pro-poor analysis of the shrimp sector in Bangladesh. The United States Agency for International Development (USAID). Development and training services. USAID Bangladesh, Arlington, Virginia, USA

Veerman J, Barendregt J, Mackenbach J (2005) Quantitative health impact assessment: current practice and future directions. J Epidemiol Community Health 59:361–370

Wakefield J (2008) Ecologic studies revisited. Annu Rev Public Health 29:75–90

WHO (1999) Health impact assessment Gothenburg consensus paper. WHO European Centre for Health Policy, Brussels

WHO (2000) Climate change and human health: impact and adaptation. World Health Organisation (WHO), Regional Office for Europe, Geneva

WHO (2008) Climate change and health report. World health Organisation (WHO)

WHO (2009) Improving public health responses to extreme weather/heat-waves—EuroHEAT. Technical Summary. World Health Organization (WHO) Regional Office for Europe

Wilcox BA, Colwell RR (2005) Emerging and reemerging infectious diseases: biocomplexity as an interdisciplinary paradigm. Ecohealth 2:244–257