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Infectious Diseases

A systematic review and meta-analysis of ambient temperature and diarrhoeal diseases

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Abstract

Background: Global climate change is expected to increase the risk of diarrhoeal diseases, a leading cause of childhood mortality. However, there is considerable uncertainty about the magnitude of these effects and which populations bear the greatest risks.

Methods: We conducted a systematic review using defined search terms across four major databases and, additionally, examined the references of 54 review articles captured by the search. We evaluated sources of heterogeneity by pathogen taxon, exposure measure, study quality, country income level and regional climate, and estimated pooled effect estimates for the subgroups identified in the heterogeneity analysis, using meta-analysis methods.

Results: We identified 26 studies with 49 estimates. Pathogen taxa were a source of heterogeneity. There was a positive association between ambient temperature and all-cause diarrhoea (incidence rate ratio (IRR) 1.07; 95% confidence interval (CI) 1.03, 1.10) and bacterial diarrhoea (IRR 1.07; 95% CI 1.04, 1.10), but not viral diarrhoea (IRR 0.96; 95% CI 0.82, 1.11). These associations were observed in low-, middle- and high-income countries. Only one study of protozoan diarrhoea was identified.

Conclusions: Changes in temperature due to global climate change can and may already be affecting diarrhoeal disease incidence. The vulnerability of populations may depend, in part, on local pathogen distribution. However, evidence of publication bias and the uneven geographical distribution of studies limit the precision and generalizability of the pooled estimates.

Key words: Ambient temperature, weather, diarrhoea, climate change, vulnerability

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Key Messages

- The relationship between ambient temperature and diarrhoeal diseases is variable and this variability is due in part to pathogen taxon, based on a review of 26 manuscripts.
- Increases in ambient temperature were generally associated with increases in all-cause and bacterial diarrhoea.
- Increases in ambient temperature were not associated with increases in viral diarrhoea.
- There was insufficient evidence to evaluate relationships between ambient temperature and protozoan diarrhoea.
- The impact of climate change on diarrhoeal diseases may vary regionally due, in part, to spatial variability in the distribution of pathogens. More research is needed to understand how infectious disease risks due to climate change vary across other factors such as access to safe water and sanitation, demographics and local climate norms.

Introduction

Global climate change is expected to increase the risk of diarrhoeal diseases,[1] the second leading cause of death in children under 5 years of age.[2] Diarrhoea accounted for 3.6% of the global disease burden in 2010, with much of this burden concentrated in low-resource settings.[3] Even modest changes in diarrhoea risk can yield large changes in morbidity and mortality.

Attempts to quantify the potential impacts of climate change on diarrhoea have been hampered by uncertainties regarding climate-disease relationships. Recent estimates of global health risk factors excluded climate change, because of the scarcity of empirical evidence regarding climate-disease relationships.[4] Another study concluded that the greatest sources of uncertainty in projecting the impact of climate change on diarrhoeal diseases were due not to climate models but to gaps in scientific evidence linking temperature and diarrhoeal diseases.[5] Reviews have evaluated the relationship between temperature and diarrhoea, focusing on specific pathogens[6] and exposure pathways,[7,8] but systematic review and quantitative synthesis are needed.

The complexity of diarrhoea aetiology and transmission makes evaluating the empirical relationships between diarrhoeal diseases and climatic factors challenging. Infectious diarrhoea can be caused by a range of pathogens whose relative importance varies regionally.[9,10] Infection can be acquired through multiple exposure pathways including food, water, person-to-person contact and direct exposure to fecal waste—pathways linked to safe water and sanitation infrastructure.[11] Host susceptibility also plays a key role in diarrhoeal diseases.[10,12] Changes in ambient temperature, precipitation and the frequency of extreme weather events may alter the distribution, survival and virulence of diarrhoeal pathogens, change host exposure patterns and compromise infrastructure. Given this complexity, the effect of temperature on diarrhoeal diseases may not be uniform across all pathogens, host populations and environments.

Here, we present a comprehensive systematic review and meta-analysis of the literature describing the relationship between ambient temperature and diarrhoea. We synthesized the available literature, identified key gaps and evaluated sources of heterogeneity in an effort to advance our ability to predict the potential impacts of climate change on diarrhoeal disease and to highlight research needs.

Methods

Search strategy

As part of a larger systematic review of the relationship between temperature, precipitation and diarrhoeal diseases, we searched for the health outcome terms 'diarrhoea' and 'diarrhea', paired with climate terms: 'climate change', 'temperature', 'rain*', 'precipitation', 'flood*', 'drought*' or 'sea surface temperature', using PubMed, Embase, Web of Science and the Cochrane Collection on 26 November 2013. In addition, we searched the references of 54 review articles identified during the search for additional relevant articles. Test searches using pathogen-specific search terms indicated the inclusion of these additional terms was unlikely to alter the final selection of manuscripts. Figure 1 shows the search strategy.

Eligibility

Studies were included in this meta-analysis if: (i) the outcome measure was incidence or counts of diarrhoea, or a pathogen-specific diarrhoeal disease at a monthly or finer resolution; (ii) the exposure of interest was mean, maximum or minimum ambient temperature; (iii) the study included at least 1 continuous year of data to allow adjustment for seasonality and avoid analyses focused on a single temperature event; (iv) the parameter estimated was an incidence rate ratio (IRR) or it was possible to convert the estimate to an IRR expressing change in diarrhoea incidence per a 1°C increase in temperature; and (v) standard errors and/or confidence intervals were provided. Articles were

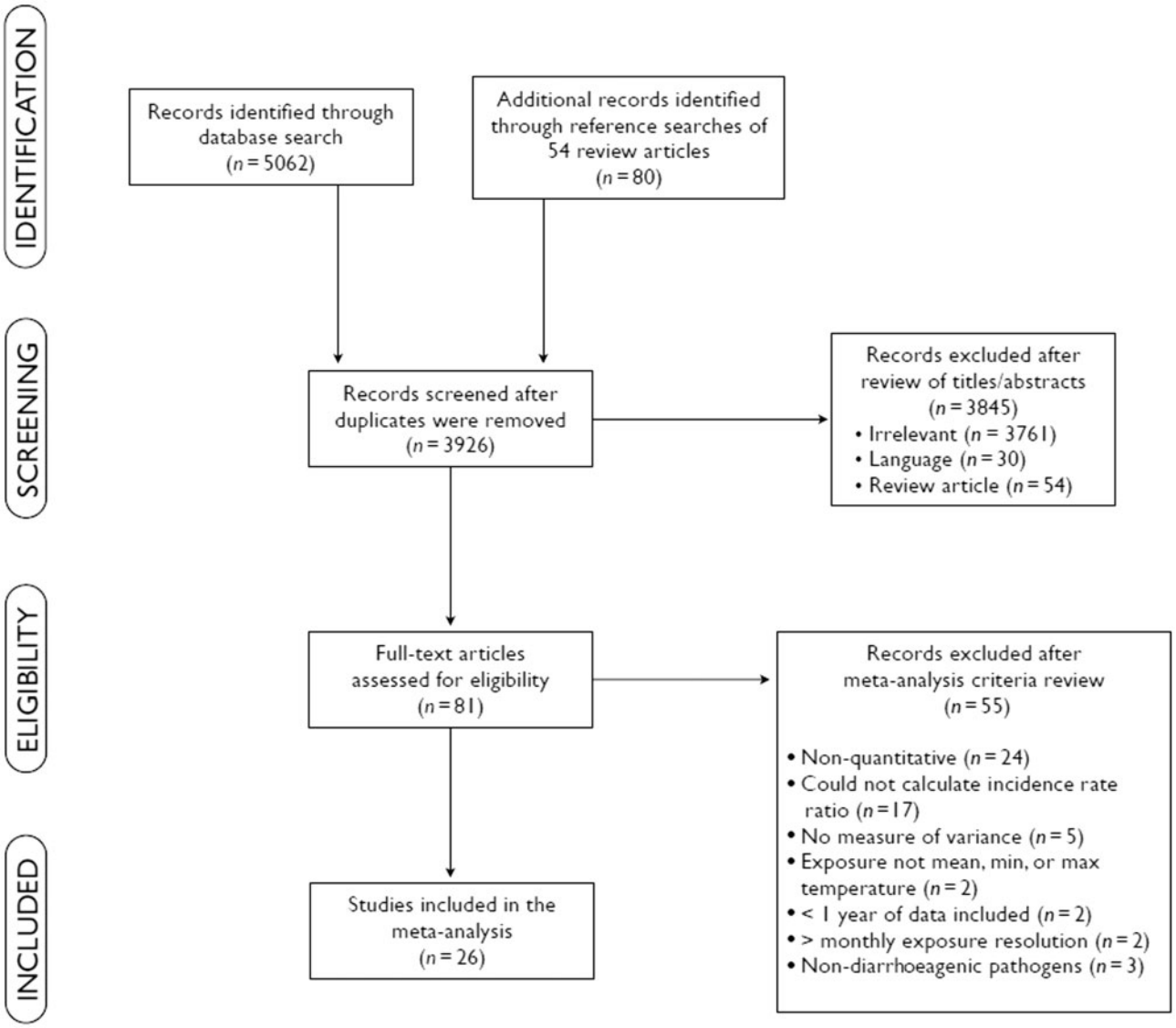

Figure 1. Systematic search and study selection.

limited to English-language publications. Articles initially were screened by APW and RSG, and full-text articles were screened by two reviewers (EJC and APW or RSG).

Data extraction and quality scoring

Data extracted from each study include study location, exposures, outcomes and analytical methods. When regression coefficients were provided instead of IRRs, parameters were converted to IRRs using standard methods.[13] Where multiple estimates were reported, Cochrane Collaboration guidelines[14] determined the criteria for inclusion: we selected the final model as specified by the authors or, if a final model was not specified, the model with the greatest number of relevant covariates. Estimates for distinct geographical regions were extracted separately. In one manuscript,[15] effect estimates were presented for three bacterial pathogens in one province and only one pathogen (*Campylobacter*) in the other. We extracted only the *Campylobacter* estimates to reduce publication bias and population overlap.

In order to evaluate the impact of study quality on pooled estimates, we adapted published instruments following standard guidelines.[14,16,17] Our instrument included nine items assessing reporting quality, bias and external validity, with possible scores ranging from 0 (poor quality) to 10 (high quality) (see Supplementary data, available at *IJE* online). Each manuscript was scored by two independent reviewers (APW and RSG) and discrepancies were resolved jointly.

Meta-analysis

We evaluated heterogeneity in the relationships between temperature and diarrhoea, using forest plots and the Mantel–Haenszel test for heterogeneity.[14] We then analysed sources of heterogeneity using a set of five

variables selected a priori, related to diarrhoea aetiology (pathogen taxon), study design (exposure measure and study quality) and population vulnerability. Measures of vulnerability included country income level based on World Bank classifications of low- or middle-income countries (LMIC) vs high-income countries (HIC)[18] and the predominant climate at each study location (Koppen climate classifications).[19] Because only two studies were conducted in arid regions,[20,21] both in Lima, Peru, we collapsed climate classification into three categories: tropical/arid, temperate and cold/polar. We classified two studies[22,23] that pooled data from multiple countries as tropical, because the majority of sites included in these studies were tropical. We used a Monte Carlo permutation test to evaluate whether the above variables explain variability in the effect estimates, running 10 000 permutations using both univariate and multivariate models, and presenting *p*-values that account for multiple hypothesis testing.[24] Because only one study of protozoan diarrhoea was identified, we excluded this from this heterogeneity analysis.

Meta-analysis was used to estimate pooled effects by variables identified in the heterogeneity analysis. Mantel–Haenszel tests indicated significant heterogeneity within each subgroup ($P < 0.001$), so pooled effects were estimated using DerSimonian and Laird random effects models.[25] We conducted a sensitivity analysis, estimating pooled effect estimates by diarrhoeal pathogen taxon, using robust variance estimate meta-analysis methods,[26,27] to account for potential correlation of estimates within the same publication. We assumed a within-study correlation of 0.1, but evaluated estimates at rho = 0.1, 0.3, 0.5, 0.7 and 0.9 and found that point estimates and confidence intervals varied by < 0.001 across these values. We used the robust variance estimate with small sample size correction; however, estimates using this method are unstable when the number of clusters is limited,[28] so we conducted this sensitivity analysis only on the highest level of stratification. Due to the large number of studies of bacterial diarrhoea captured, we repeated the heterogeneity analysis on these studies using the remaining four covariates.

We used the metan,[29] metareg[30] and robumeta[27] packages in Stata version 13.1. Following previous work,[5] we defined α as the change in the rate ratio of diarrhoea for a 1°C increase in ambient temperature, using the pooled IRR estimates from the meta-analysis. Publication bias was assessed by inspecting funnel plots for asymmetry, which suggests 'small study bias'.[31,32]

Results

We identified 26 manuscripts that met our inclusion criteria (Table 1) and 49 estimates of the relationship between ambient temperature and diarrhoea within these manuscripts (Figure 2). Study locations included low-, middle-and high-income countries and all six inhabited continents; however, research was concentrated in three countries: Bangladesh (five manuscripts), Australia (five) and the UK (four) (Figure 3).

Sources of heterogeneity

There was considerable heterogeneity across the 49 estimates ($P < 0.001$). Pathogen taxa were the only variables that explained heterogeneity ($P = 0.020$ for viral diarrhoea in multivariate analyses, $P < 0.001$ in univariate analyses).

All-cause diarrhoea

We identified ten estimates from seven manuscripts of the relationship between all-cause diarrhoea and temperature. Pooled estimates indicated a positive association between ambient temperature and diarrhea (Table 2). Pooled estimates based on maximum and minimum temperature were more variable than estimates based on mean ambient temperature, though four out of five estimates were derived from a single study that had one of the lowest quality scores.[33] Excluding that study yielded minimal change in the pooled estimate (IRR = 1.06, 95% CI 1.03, 1.09).

Bacterial diarrhoea

We identified 30 estimates from 12 manuscripts of the relationship between temperature and bacterial diarrhoea, including non-typhoidal *Salmonella sp.* (20), *Campylobacter* (5), *Vibrio cholerae* (3), *Salmonella typhi* (1) and *Shigella* (1). Pooled estimates indicated a significant positive association between ambient temperature and bacterial diarrhoea.

Pooled estimates were stable across mean, maximum and minimum temperature, but were modestly higher in lower quality studies, studies conducted in LMIC and in tropical climates (Figure 4). Heterogeneity analysis indicated that study quality and climate were sources of variability in multivariate models ($P = 0.055$ and $P = 0.085$, respectively) although these findings may be due to chance.

Protozoan diarrhoea

Only one estimate of the relationship between temperature and a protozoan pathogen, *Cryptosporidium*, was identified. This study showed a significant positive association between ambient temperature and cryptosporidiosis.

Viral diarrhoea

We identified eight estimates from six manuscripts of the relationship between temperature and viral diarrhoea, including rotavirus (seven) and norovirus (one), all with mean ambient temperature as the exposure. All but one

Table 1. Summary of the 26 publications included in the meta-analysis

Ref.	Location	Study period	Population	Ages	Outcome	Taxonomic class	Exposure definition	Statistical model	Temporal lags[a]	Threshold	Resolution	Climate group[b]	Income group[c]	Quality score
Ali (2013)[47]	Matlab, Bangladesh	1988–2001	4157 cases	All	Cholera cases presenting to treatment centres	Bacterial	Minimum temperature	Seasonal autoregressive integrated moving average (SARIMA) model adjusted for sea surface temperature, season, autocorrelation	None	None	Monthly	A	Low	8
Atchison (2010)[48]	England, Wales, Scotland, The Netherlands	1993–2007	NA	< 5	Reported, lab-confirmed rotavirus	Viral	Population-weighted, mean temperature	Poisson regression model adjusted for relative humidity, rainfall, holidays, long-term trends, season, autocorrelation	1–4 weeks	5°C	Weekly	C	High	9
Bi (2008)[49]	Adelaide and Brisbane, Australia	1990–2005	34 908 cases	All	Reported, lab-confirmed *Campylobacter*	Bacterial	Maximum temperature	Poisson regression model adjusted for rainfall (Adelaide only), humidity (Brisbane only), long-term trends (Brisbane only), season, autocorrelation	9 weeks, Adelaide; 6 weeks, Brisbane	None	Weekly	C	High	8
Britton (2010)[50]	New Zealand	1965–2006	NA	All	Reported *Salmonella*	Bacterial	Mean temperature	Negative binomial regression model adjusted for outbreak periods, long-term trends, season, autocorrelation	None	None	Monthly	C	High	6
Checkley (2000)[20]	Lima, Peru	1993–98	57 331 cases	< 10	Diarrhoea admissions at a children's hospital	All-cause	Mean temperature	Poisson regression	37 days	None	Daily	B	Upper middle	7
Chou (2010)[51]	Taiwan	1996–2007	1.2 million cases	0–64	Hospital admissions for diarrhoea from National Health Insurance Research database	All-cause	Maximum temperature	Poisson regression model adjusted for extreme rainfall, humidity, long-term trends, season, autocorrelation	1 month	None	Monthly	C	High	8
Dewan (2013)[52]	Dhaka, Bangladesh	2005–09	4355 cases	All	Lab-confirmed typhoid cases admitted to 11 hospitals	Bacterial	Mean temperature	Poisson regression model adjusted for rainfall, river level, holidays, long-term trends, season, autocorrelation	0 –4 weeks	None	Weekly	A	Low	9
D'Souza (2004)[53]	Five cities in Australia	1991–2001	27 652 cases	All	Reported *Salmonella*	Bacterial	Mean temperature	Negative binomial regression model adjusted for outbreaks and long-term trends	1 month	None	Monthly	C	High	8
D'Souza (2008)[54]	Brisbane, Canberra and Melbourne, Australia	1993–2003	12 816 cases	< 5	Hospital admissions for rotavirus from state health department records	Viral	Mean temperature	Negative binomial regression model adjusted for humidity, long-term trends, season, autocorrelation	1 week	None	Weekly	C	High	9
Fleury (2006)[15]	Newfoundland-Labrador (NL) and Alberta, Canada	1992–2000	2931 cases[d]	All	Reported, lab-confirmed *Campylobacter*[e]	Bacterial	Mean temperature	Poisson regression model adjusted for holidays, health region, long-term trends, season, autocorrelation	1 week	−10°C Alberta, > 0°C NL	Weekly	D	High	9

(continued)

Table 1. Continued

Ref.	Location	Study period	Population	Ages	Outcome	Taxonomic class	Exposure definition	Statistical model	Temporal lags[a]	Threshold	Resolution	Climate group[b]	Income group[c]	Quality score
Hashizume (2007)[55]	Dhaka, Bangladesh	1996–2002	12 182 cases	All	Non-cholera diarrhoea cases presenting to ICDDR,B Dhaka Hospital	All-cause	Mean temperature	Poisson regression model adjusted for rainfall, holidays, long-term trends, season, autocorrelation	0 –4 weeks	None	Weekly	A	Low	10
Hashizume (2008)[34]	Dhaka, Bangladesh	1996–2001	3115 cases	All	Lab-confirmed rotavirus diarrhoea presenting to ICDDR,B Dhaka Hospital	Viral	Mean temperature	Poisson regression model adjusted for relative humidity, river level, holidays, long-term trends, season, autocorrelation	0–4 weeks	>29°C	Weekly	A	Low	9
Hu (2007)[45]	Brisbane, Australia	1996–2004	NA	All	Reported cryptosporidiosis	Protozoan	Maximum temperature	SARIMA model adjusted for humidity, annual trends, season, autocorrelation	1–3 months	None	Monthly	C	High	7
Jagai (2012)[22]	Six countries in South Asia	1976–2009	47 time series from 39 studies	All	Rotavirus z-score	Viral	Temperature z-score	Linear mixed effects model adjusted for precipitation, vegetation index, distance from the equator	1 month	None	Monthly	A/B/C	Low and lower middle	7
Kovats (2004)[39]	Ten countries in Europe	1983–2002 (varies by country)	NA	All	Reported, lab-confirmed *Salmonella*	Bacterial	Mean temperature	Poisson regression model adjusted for holidays, interannual variation, season, autocorrelation	0–9 weeks	6°C	Weekly[e]	C/D/E	High	7
Lama (2004)[21]	Lima, Peru	1991 –98	40 020cases	13	Emergency department admissions for acute diarrhoea	All-cause	Mean temperature	Log-linear regression model with an interaction term between temperature and cholera in the community[f]	None	None	Monthly	B	Upper middle	6
Levy (2009)[23]	Global tropics	1974–2005	26 studies	All	Rotavirus cases	Viral	Mean temperature	Poisson regression model adjusted for study, within study correlation and autocorrelation	None	None	Monthly	Multiple	Multiple	7
Lopman (2009)[56]	England and Wales	1993 –2006	35 210 cases	All	Reported, lab- confirmed norovirus	Viral	Mean temperature	Poisson regression adjusted for relative humidity, holidays and weekends, epidemic season, use of improved diagnostics, population immunity, long-term trends, season, autocorrelation	49 days	None	Daily	C	High	9
Luque Fernandez (2009)[57]	Lusaka, Zambia	2003–06	13 069 cases	All	Cholera cases at cholera isolation centres	Bacterial	Maximum temperature	Poisson regression adjusted for rainfall, season, autocorrelation	6 weeks	None	Weekly	C	Lower middle	8

(continued)

Table 1. Continued

Ref.	Location	Study period	Population	Ages	Outcome	Taxonomic class	Exposure definition	Statistical model	Temporal lags[a]	Threshold	Resolution	Climate group[b]	Income group[c]	Quality score
Onozuka (2010)[58]	Fukuoka, Japan	1999–2007	422 176 cases	All	Infectious gastroenteritis at 120 sentinel medical institutions	All-cause	Mean temperature	Poisson regression adjusted for relative humidity, long-term trends, season, autocorrelation	0–8 weeks	None	Weekly	D	High	9
Seidu (2013)[33]	Northern Ghana	2008–09	2664 participants	All	Self-reported diarrhoea from bi-weekly interviews	All-cause	Maximum, minimum temperature	Poisson regression model adjusted for maximum and minimum rainfall, maximum and minimum temperature 1–2 bi-weeks earlier, season, autocorrelation[g]	None	None	Bi-weekly	A	Lower middle	5
Singh (2001)[59]	Fiji	1978–98	NA	Infants	Reported diarrhoea	All-cause	Mean temperature	Poisson regression model adjusted for rainfall, season	1 month	None	Monthly	A	Upper middle	5
Tam (2006)[42]	England	1989–99	623 817 cases	All	Reported lab-confirmed *Campylobacter*	Bacterial	Mean temperature	Negative binomial regression model adjusted for relative humidity, holidays, long-term trends, season, autocorrelation	0–6 weeks	< 14°C	Weekly	C	High	9
Traerup (2011)[60]	Tanzania	1998–2004	NA	All	Reported cholera	Bacterial	Maximum temperature	Negative binomial regression adjusted for long-term trends, drought	None	None	Monthly	A	Low	7
Zhang (2008)[61]	Jinan, China	1987–2000	60 905 cases	All	Reported hospital cases of bacillary dysentery	Bacterial	Maximum temperature	SARIMA model adjusted for season and autocorrelation	1 month	None	Monthly	D	Upper middle	6
Zhang (2010)[62]	Brisbane and Townsville, Australia	1990–2005	6464 cases	All	Reported lab-confirmed *Salmonella*	Bacterial	Maximum, minimum temperature	Poisson regression adjusted for rainfall, long-term trends, season, autocorrelation	2 weeks (Brisbane); none (Townsville)	None	Weekly (Brisbane), monthly (Townsville)	A/C	High	8

NA, not available.

[a]Lag between exposure and outcome included in the final model.

[b]Climate categories are based on Koppen-Geiger climate classification where A is tropical, B is arid, C is temperate, D is cold and E is polar.[19]

[c]Categories are based on 2012 gross national income per capita.[18]

[d]The authors reported 6282 cases of *Salmonella*, 1743 cases of *Campylobacter* and 9664 cases of entero-pathogenic *E. coli* in Alberta, and 986 cases of *Salmonella*, 1188 cases of *Campylobacter* and 0 cases of entero-pathogenic *E. coli* in Newfoundland-Labrador. However, the only reported effect estimates available for both provinces described the relationship between *Campylobacter* and temperature (the authors reported a non-significant association between temperature and *Salmonella* in Newfoundland-Labrador, without providing an effect estimate). We therefore restricted the meta-analysis to *Campylobacter* in the two provinces to reduce publication bias and population overlap.

[e]Except Poland (biweekly), Estonia and Slovak Republic (monthly).

[f]Estimates included in this analysis were estimates of the association between temperature and diarrhoea when cholera was not present in the community.

[g]Models fit separately for communities that apply fecal sludge and communities that do not. Autoregressive terms were only included in the former model.

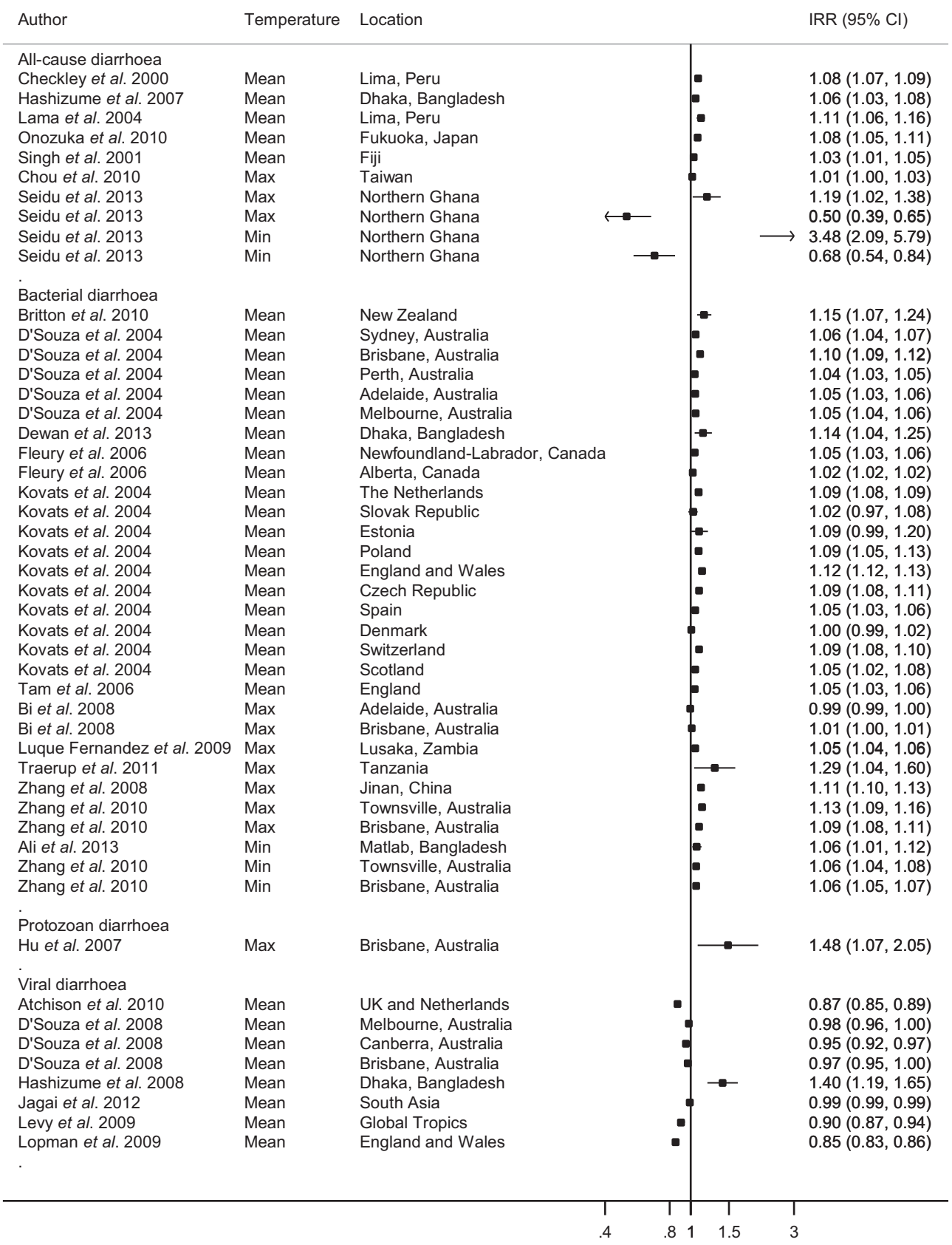

Figure 2. Forest plot showing 49 estimates of the incidence rate ratio (IRR) and 95% confidence Interval (CI) from the 26 studies included in the meta-analysis, by pathogen taxon.

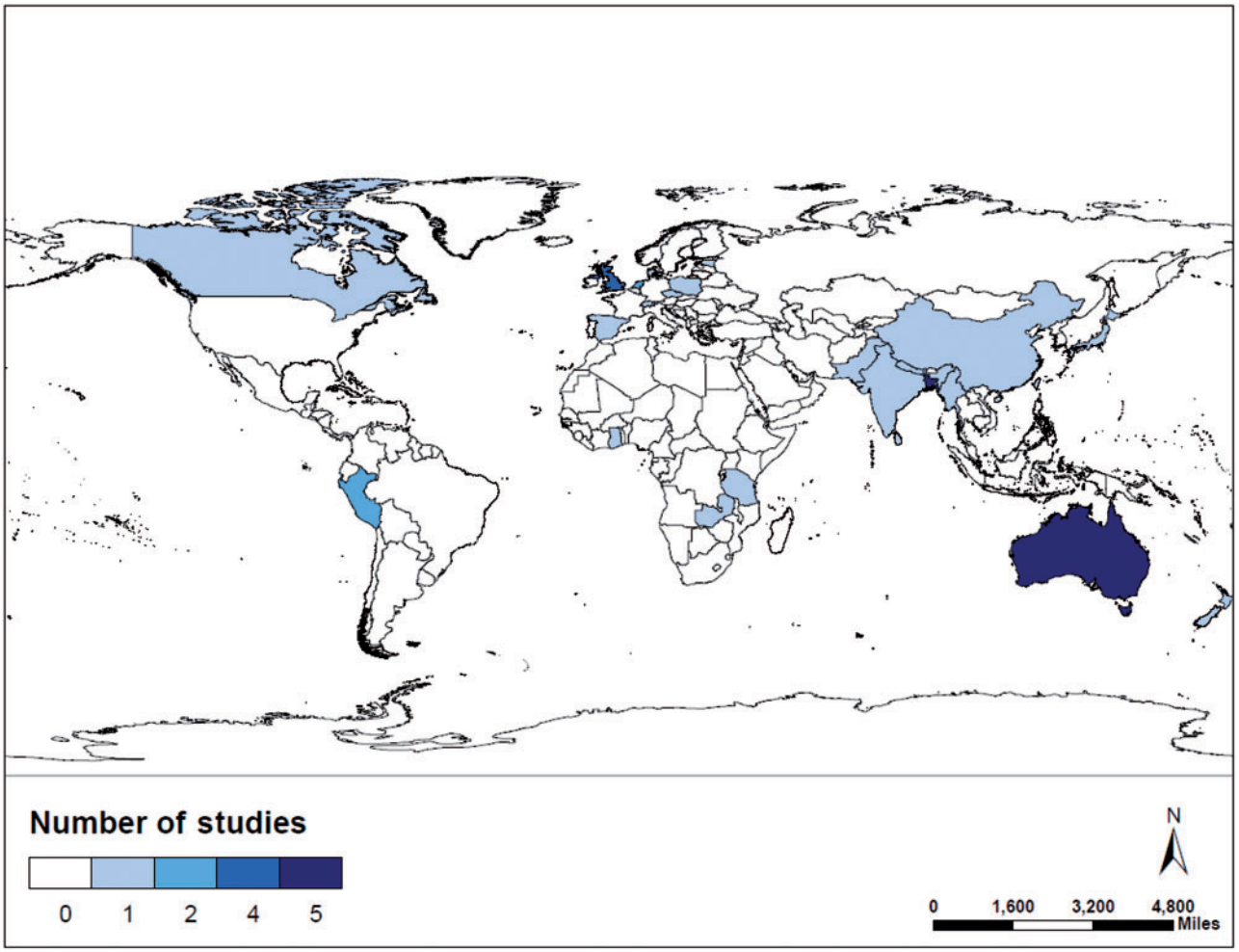

Figure 3. Map displaying the location of studies included in the meta-analysis, by country. The locations from one study that included data from more than 10 countries[23] are excluded from the map. World shape file is from the GADM database of Global Administrative Areas.

Table 2. Pooled effect estimates of the relationship between ambient temperature and diarrhoeal diseases by pathogen taxon

	No. estimates	No. papers	Unadjusted[a]				Adjusted[b]			
			IRR (95% CI)		Alpha[c] (95% CI)		IRR (95% CI)		Alpha[c] (95% CI)	
All-cause diarrhoea										
All exposures	10	7	1.05	(1.01, 1.09)	0.05	(0.01, 0.08)	1.07	(1.03, 1.10)	0.07	(0.03, 0.10)
Mean temperature	5	5	1.07	(1.04, 1.09)	0.07	(0.04, 0.09)				
Bacterial diarrhoea										
All exposures	30	12	1.07	(1.05, 1.08)	0.06	(0.05, 0.08)	1.07	(1.04, 1.10)	0.07	(0.04, 0.10)
Mean temperature	20	6	1.07	(1.05, 1.08)	0.06	(0.05, 0.08)	1.06	(1.03, 1.10)	0.06	(0.03, 0.10)
Protozoan diarrhoea										
All exposures	1	1	1.48	(1.07, 2.05)	0.48	(0.00, 0.96)				
Mean temperature	0	0								
Viral diarrhoea										
Mean temperature	8	6	0.95	(0.90, 1.00)	−0.05	(-0.10, 0.00)	0.96	(0.82, 1.11)	−0.04	(-0.19, 0.10)

[a]Estimated using random effects model of DerSimonian and Laird.[25]

[b]Estimated using robust variance estimation to account for correlation of estimates from the same manuscript. Not calculated for all-cause diarrhoea and mean temperature because each estimate is from a different manuscript. Not calculated for protozoan diarrhoea because only one estimate was available.

[c]Defined as the proportional change in the rate ratio of diarrhoea for a 1°C change in ambient temperature.

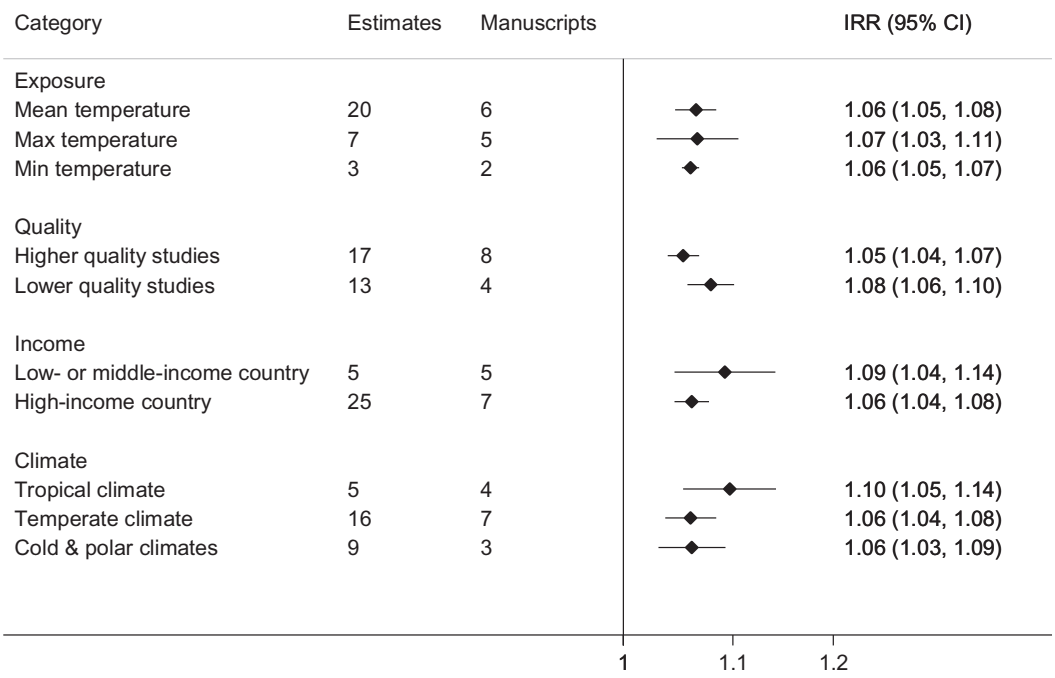

Figure 4. Pooled estimates describing the relationships between ambient temperature and bacterial diarrhea by exposure, study quality, national income and regional climate. Pooled estimates were estimated using DerSimonian and Laird random effects models.[25] High-quality studies were defined as those scored 8 or higher using a 10-point index. Country-level income was defined using World Bank World definitions[18] and climate categories were defined using Koppen climate classifications[19].

estimate indicated a significant negative association, but the confidence intervals of the pooled estimates included the null. The one study with a positive effect employed a threshold analysis where a positive relationship was observed above 29°C.[34] When this study was excluded, pooled estimates were further from the null (unadjusted IRR 0.93, 95% CI 0.88, 0.98; adjusted IRR = 0.91, 95% CI 0.84, 0.99).

Publication bias

Funnel plot asymmetry was observed for studies of bacterial and viral diarrhoeal pathogens, with a greater than expected number of smaller studies showing positive (bacterial) and negative (viral) outcomes than expected (Figure S1, see Supplementary data available at *IJE* online).

Discussion

We found considerable heterogeneity in estimated associations between ambient temperature and diarrhoeal diseases, and this variability was explained, in part, by pathogen taxon. Pooled estimates from 26 studies indicated a significant positive association between temperature and both all-cause and bacterial diarrhoea, but not between temperature and viral diarrhoea. These associations were observed in low-, middle- and high-income countries, suggesting that temperature can affect diarrhoea incidence across a range of conditions. However, the concentration of studies in a few countries and evidence of publication bias raises questions about the generalizability and precision of the pooled estimates. We identified only one study of protozoan diarrhoea that met our inclusion criteria, limiting our ability to evaluate relationships between temperature and this taxon. This is a key gap in the literature, as *Cryptosporidium* is a major cause of diarrhoea in children and immune-compromised populations.[9]

Our findings offer an important advance in estimating the potential change in diarrhoeal disease burden attributable to climate change under different emissions scenarios. Using a cumulative risk assessment framework, climate-attributable disease burden depends on underlying disease rates, projected climatic changes and climate-disease risk parameters, represented here by α. Our findings suggest that assuming a single, fixed value for α is not appropriate. In this study, we found α varies by pathogen taxon. Climate-diarrhoea risk parameters may vary across other parameters beyond the scope of this study, such as individual pathogens, exposure routes and access to water and sanitation infrastructure. Variability in α for diarrhoeal pathogens may also be explained, in part, by regional climate: Our analysis of bacterial diarrhoea suggests that the association between temperature and bacterial diarrhoea was higher in tropical climates, a phenomenon that warrants further evaluation.

Differential risk by climate type may be attributable to differences in pathogen distribution and/or underlying local vulnerabilities.[35] If climate-risk parameters do vary, future climate-attributable diarrhoea disease burden may depend not just on future emission scenarios, but also on changes in socioeconomic and demographic patterns and on public health interventions, as has been demonstrated for malaria and waterborne diseases.[36,37]

Based on the above cumulative risk assessment model, climate-attributable disease burden will be greatest in populations with an already high diarrhoea burden, particularly due to bacterial infections, and in areas with large increases in ambient temperature. Tropical, low-resource settings may bear a triple vulnerability profile due to the higher underlying diarrhea rates, unprecedented future ambient temperatures[38] and possibly greater temperature-diarrhoea risk parameters in these areas.

Limitations

We found evidence of publication bias, including small study publication bias, and of modestly stronger effect estimates in lower quality studies of bacterial diarrhoea. Both may indicate that estimates are inflated away from the null. Most of the studies we captured were secondary data analyses, which may be prone to a focus on significant findings. In our broader systematic review, we found that manuscripts with multiple effect estimates were more likely to include non-significant findings (unpublished data). In this meta-analysis, the only non-significant estimates were from a study that included multiple effects estimates.[39] The inclusion of multiple estimates from the same studies may help mitigate publication bias. Whereas this has the potential to introduce correlation between estimates that, if not accounted for, may introduce bias,[40] inference did not change when we used robust variance estimation models to account for within-study correlation. The publication of estimates that contradict the findings of similar studies, the fact that many studies drew from large, long-term datasets and the consistency of results across research groups, study designs and geographies bolsters confidence in this meta-analysis.[41]

As has been done previously,[5] we assumed a constant change in diarrhoea risk for every 1°C increase in temperature. The true relationship between temperature and diarrhoeal pathogens may be more complex. Fifteen estimates in our meta-analysis were based on threshold models, which account for non-linear exposure-response relationships by assuming linearity only above or below a given threshold. With two exceptions,[34,42] threshold models included in our meta-analysis were based on data from temperate climates with lower thresholds, ranging from -10 to 14°C, suggesting that linear exposure-response relationships may be most appropriate for warmer temperature ranges. Additionally, our estimates of temperature-diarrhoea relationships are limited to the range of observable temperature data under current climate conditions. Although this may be sufficient for near-term predictions of climate-attributable health impacts, some scenarios suggest that temperatures in the tropics will exceed currently observed ranges[38] with consequent health impacts that are difficult to predict. Global climate change will impact on not only temperature but also precipitation patterns, with implications for diarrhoeal diseases that we explore elsewhere.

The studies we captured in our meta-analysis are studies of association. A causal relationship between temperature and diarrhoeal diseases may be due in part to environmental factors, such as the impact of temperature on pathogen survival and reproduction in environmental media, or temperature-mediated virulence of pathogens. It is also possible that temperature-related behavioural or demographic patterns may drive these relationships, as has been suggested for viral diarrhoea.[43] Behavioural and demographic seasonal factors might confound the relationship between ambient temperature and disease detection; however, many of the analyses captured in our study adjusted for season.

Future research

Our analysis offers a step towards understanding variability in temperature-diarrhoea risk parameters. Further research to characterize how the impact of changing temperature varies by pathogen and by known risk factors should be a priority, as it could improve our ability to identify high-risk populations and to prioritize adaptation targets. Large, multinational datasets that capture pathogen-specific diarrhoea could allow for further evaluation of variability in parameter estimates across such factors. Mechanistic transmission models, that integrate parameters from epidemiological and experimental studies, baseline conditions and future climate predictions, can also be used to evaluate the sensitivity of climate-attributable disease estimates to uncertainties in parameter estimates, highlighting future priority research areas.[44] Quantitative analysis is also needed to understand the relationship between protozoan diarrhoea and ambient temperature, particularly in LMICs. The one study we identified[45] and most of the studies identified in a recent review[6] and meta-analysis,[46] showed a positive association, but most of the work to date has been conducted in HICs, making it difficult to generalize these findings.

Conclusions

Studies conducted in Peru during an El Niño event in the 1990s provided early epidemiological evidence of the

potential for temperature anomalies to alter diarrhoea patterns.[20,21] Twenty years later, our synthesis of 26 studies shows rising temperatures due to global climate change can and may already be affecting population health through increased risk of diarrhoeal diseases, particularly bacterial diarrhoea. Populations in tropical settings may be particularly vulnerable. Studies that evaluate heterogeneities in risk are needed to evaluate adaptation and mitigation measures in order to prevent delays or, worse, reversals of progress in reducing diarrhea disease burden.

Supplementary Data

Supplementary data are available at *IJE* online.

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