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CLIMATE AND ATOPIC DISEASE IN CHILDREN IN TEMPERATE COUNTRIES

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Abstract

Background: Although atopic diseases exhibit strong seasonal patterns, there is only weak evidence that climate per se is a determinant of the variation in prevalence of wheeze between populations. Previous studies that reported an association between climate factors and wheeze did not take into account other environmental hazards or potential confounding factors. We investigated the impact of climate factors (temperature and humidity) on the prevelance of atopy-related diseases such as asthma and eczema in children.

Methods: We used the PATY combined cross-sectional dataset of respiratory health in children in 10 countries in Europe and North America to investigate the effect of long term climate factors (temperature, relative humidity) on three outcomes: wheeze, woken by wheeze and itchy rash. Study-specific odds ratios for associations with climate factors were estimated using logistic regressions with area-level random effects, controlling for ambient air pollutant exposures and individual risk factors.

Results: Climate exposure had no effect on the prevalence of wheeze or itchy rash. Controlling for NO_2 or PM_{10} did not strongly confound the overall associations between symptoms and climate variables. Climate factors did not modify observed associations between air pollution and children's health.

Conclusions: The prevalence of wheeze or itchy rash is unlikely to be determined by the outdoor climate within mid to high latitude countries in North America and Europe.

Key words: atopic disease, asthma, climate, cold

Introduction

The effect of climate (average long term conditions) as opposed to weather (day to day experiences of temperature and rainfall) on health although studied in the past is currently receiving more attention due to the threat of global climate change.

The indoor environment is known to affect the risk of atopic diseases such as asthma and rhinitis in children. High humidity (dampness) is bad for asthma and good for mould growth (1). Indoor mould is also associated with an increased risk of asthma in children (2). A study using the PATY (Pollution and the Young) dataset, found that the prevalence of asthma symptoms increased by 2.7% with an increase in the estimated annual mean of indoor relative humidity of 10% (3).

The effect of the outdoor climate on the prevalence of atopic disease is less well established. An international comparison using ISAAC (International Study of Asthma and Allergies in Childhood) data from 42 countries found inconsistent results (4). Other studies have found that the prevalence of eczema symptoms correlated with latitude (positively) and mean annual outdoor temperature (negatively) (3). Another international study found asthma symptoms in adults to be positively associated with temperature in the coldest month of the year (5). A positive association between mean annual temperature and the 12 month period-prevalence of wheeze in adults has also been reported in New Zealand (6). A study in Spain, using only 2 locations, reported that mean asthma prevalence was higher at the coast than inland (7). Possible mechanisms for the impact of climate include exposures to allergens (6) or moulds. Sunlight exposure, via production of Vitamin D, has also been suggested to play a role in the aetiology of atopic diseases (8). The direct relationship between indoor and outdoor temperatures and humidity is likely to become less apparent as housing quality improves, with most households having home heating. However, very cold winters were shown to decrease the level of house dust mite allergen in German homes in the following year (9).

Climate therapy, particularly for respiratory diseases, was popular in Europe in the 19th and 20th centuries (10). There is good evidence that high altitude areas (over 1000 m above sea level) have less asthma than other areas, possibly due to reductions in house dust mites (11;12).

Climate is a difficult exposure to assess in epidemiological studies. All persons in single population are exposed to the same climate. Climatologists define climate as the long term average of the weather conditions and the accepted standard is to use a 30-year period. However, this is not useful for health studies where health status can change rapidly within a decade. Year-to-year variability in temperatures also has been shown to affect respiratory health in the US (13) but we are not aware of any studies in Europe. The majority of epidemiological evidence is for acute effects (day to day variations) of low (or high) temperatures on respiratory outcomes (14-18).

It is important to distinguish the mechanisms by which climate (long term exposures over many years) may cause disease from the mechanisms by which acute weather exposures (short-term or daily events) are known to affect health. In the case of respiratory outcomes and air pollution exposures, the acute exposures are thought to act by principally by the exacerbations of a chronic condition (19). Intermediate between these time scales, one can consider inter-annual variability (the seasonal pattern) and inter-annual variability (year to year variation).

The climate-health studies so far have not been able to control for between population variations in air pollution, although some do control for socio-economic factors to a limited extent. The evidence for population socio-economic status or economic development (in terms of GDP per capita) as an explanatory factor for the between population difference in asthma is weak (20). Environmental factors may have a role in explaining the considerable variation in the prevalence of wheeze between populations, but this issue is still unresolved.

The PATY project investigated the environmental determinants of respiratory ill-health in over 58,000 children, by assessing data from cross-sectional studies in Russia, North America, and countries across Eastern and Western Europe (21). We investigated the role of climate in the health of children, and the role of climate factors as modifiers in observed associations between air pollution and children's health.

Methods

Study subjects

This study uses data assembled within the PATY project, in which cross-sectional studies assessed respiratory symptoms (including cough and wheeze), individual risk factors by questionnaire, and allowed calculation of annual mean particulate matter measures by study area. Table 1 describes the studies from 10 countries, which are further detailed in individual country publications (22-27). Three comparable outcomes were analysed: wheeze in the last year, itchy rash ever, and "woken by wheeze in the last year". Further details on the questionnaires are described elsewhere (28). Other information was collected at the individual level including household and family characteristics, parental smoking and pet ownership.

An arithmetic annual mean of daily series for each pollutant were available for each study area within a country (29;30). Comparable measures were used, were possible, to re-construct exposure measures from the original daily air pollution data collected by the individual studies (for further information see individual studies listed above).

Climate exposure assessment

To describe the "climate exposure" for each study area, each was linked to the nearest World Meteorological Organization climate station, using the following criteria:

- nearest (geographic straight-line) and within 300m altitude
- >80% data completeness per calendar year across data period.

Daily meteorological data were obtained from the National Climate Data Center Global Summary of the Day dataset (31). Data series for 10 years (1994-2003) were downloaded for all stations except for 5 stations in which data up to 1999 were only available (6 years). Where two populations were close together, they were linked to same station. The daily series were then collapsed to the average monthly values to describe the relevant climate exposure. The following variables were then created for each survey area:

- mean temperature in coldest month
- mean relative humidity in coldest month
- mean temperature in hottest month
- mean relative humidity in hottest month

As an alternative measure of humidity, we calculated mean dewpoint in the coldest and warmest month for each study area. Information on altitude for each study area was obtained from an online gazetteer (32). However, only one study area [Montana in Switzerland] was more than 1000 metres above sea level. Due to the lack of high altitude populations, it was not possible to analyse the impact of altitude on the health outcomes.

Studies from three PATY countries (Austria, the Czech Republic and the Netherlands) were excluded as it was not possible to link them the study areas to climate stations or the areas were not sufficiently far apart to be allocated different climate exposures.

Statistical Analysis

A two-stage approach was used. First, country-specific effects of temperature were estimated, using logistic regression with area-level random intercept. Second, these estimates and their standard errors were entered into a meta-analysis, obtaining a mean estimate, and a measure and Cochran χ^2 test of heterogeneity. Country-specific effects were assumed to follow a random distribution about a mean. Estimation of this mean (and confidence interval) takes into account both between-study variation in effects and uncertainty (due to sampling variability) of study-specific estimates (33). Analyses were done in STATA v9. Odds ratios are reported per 1 degree increase in temperature or % increase in relative humidity.

We controlled for age, sex, maternal education, paternal education, household-crowding, current parental smoking, mother smoking during pregnancy, gas-cooking, unvented gas/oil/kerosene heater, mould, nationality, birth-order, and ‘ever had a pet’.

Parental illnesses may be a confounder, but over adjustment can occur, since the exposure could affect both children and parents. This variable was therefore excluded from our main model. We tested robustness of results to controlling for parental asthma, month of questionnaire, and area-level response rates. We also tested for effect modification by sex, age, parental smoking, and (since these illnesses may have a strong genetic component) by parental asthma (34).

Meta-regressions assessed associations between country estimates and study/country-characteristics. We examined the following potential causes of heterogeneity between country-specific results: year of study; proportion of younger children (aged 6-8); proportion of questionnaires filled out in the spring, questionnaire-date variability across study areas; high response rate (80+%); response rate variability across study areas; Western/former Eastern bloc country; GDP per capita (35).

We also undertook sensitivity analyses to see if pollutants confounded the climate-health association by adjusting (one at a time) for area-level PM_{10} and NO_2. Individual PATY studies measured different combinations of pollutants, so that some studies are excluded in these pollutant-adjusted models. We therefore present results with and without controlling for the second environmental variable, within the subset of studies for which that second variable is available. We also assessed the degree to which the climate variables confound associations between PM_{10} and symptoms.

As a sensitivity analysis, we tested the effects on symptoms of dewpoint in the hottest and coldest months. Only the main model was run for these exposures.

Results

Variation in climate exposures

The North American data, covering a large geographical area, had the widest range of temperature and humidity exposures (Figure 1), while Germany and Poland had the least variation in climate. The Russian study areas experienced, on average, the lowest temperatures in winter, and also the greatest difference between summer and winter (intra-annual variability), while Italian study areas were the warmest both in summer and winter due to their low latitude. Germany and Poland had the highest winter humidity, and Poland also the highest in summer. The North American study areas were, on average, among the least humid in winter, and among the most humid in summer.

Controlling only for individual risk factors

Figure 2 shows study-specific and mean odds ratios for the four climate exposures, and the three outcomes. Confidence intervals for the effects of summer temperature were wide in some countries, reflecting the lack of variability in temperature between towns. Estimates for other measures were generally more precise.

No consistent associations were seen between any of the climate variables and the three outcomes. Of the 96 country-specific odds ratios, 14 were statistically significant - a greater number than that expected by chance. These significant results were most frequently observed for the effects of winter humidity on itchy rash, and for summer temperature (and to a lesser extent summer humidity) on wheeze. However, these effects were not consistent in direction, and all mean estimates (Table 2) were close to 1 and non-significant.

Heterogeneity between country-specific results

While most country-specific results were homogenous, there was significant between-country heterogeneity in the observed effects of both summer and winter temperatures on wheeze, and also effects of winter humidity on itchy rash (Figure 2, Table 2). However, none of the tested study/country level variables explained or significantly reduced the heterogeneity. Statistically significant estimates of summer temperature effects on wheeze ranged from 0.92 (95% CI 0.86-0.99) per 1°C in Bulgaria to 1.15 (1.02-1.31) in Italy (see Figure 2). (Odds ratios in Poland and Germany were larger, but imprecisely estimated due to the small range in temperatures.) Estimates of winter humidity effects on itchy rash ranged from 0.89 (0.80-0.99) per % increase in Bulgaria to 1.44 (1.14-1.82) in Hungary (Figure 2).

Controlling for outdoor air pollution

Controlling for NO_2 or PM_{10}, although causing some fluctuations in country-specific estimates (not shown), did not strongly confound the overall associations between symptoms and climate variables. Nor did controlling for these pollutants reduce between-country heterogeneity. Table 3 shows mean estimates with and without controlling for pollutants, in those countries with pollution data available.

Confounding of PM_{10} effect by climate variables

Little association was seen between PM_{10} and either wheeze or woken by wheeze, with and without controlling for climate variables. A raised, but non-significant, pooled odds ratio of 1.05 (0.92-1.20) per 10 $\mu g/m^3$ was obtained for the association between PM_{10} and itchy rash. This remained unaltered by controlling for summer or winter temperature, and raised only slightly by controlling for winter humidity. Controlling for summer humidity tended to increase observed PM_{10} effects, but overall the effect did not reach statistical significance, with an adjusted pooled odds ratio of 1.16 (0.90-1.50) per 10 $\mu g/m^3$.

Confounding and effect modification by individual risk factors

There were no consistent patterns of effect modification by parental asthma or sex. Some evidence was seen of stronger effects of increased temperature on older children (results not shown). For all three outcomes, mean interaction terms between age and both summer and winter temperature were weakly significant ($p<0.10$). That is, symptoms were more strongly associated with higher temperatures in older children. This interaction was most notable for itchy rash, and mean odds ratios for the effects of summer and winter temperatures among older children were 1.08 (95% CI 0.99-1.19, $p=0.097$) and 1.07 (1.00-1.14, $p=0.07$) respectively, while no associations were seen among children under 9.

Although self-reported parental asthma was strongly related to reported symptoms in the children, it was not a confounder for the effects of the climate variables, nor was month of questionnaire, or area-level response rate.

Dewpoint

No overall associations were seen between symptoms and either summer or winter dewpoint. Country-specific odds ratios for the effect of winter dewpoint on wheeze were heterogeneous, ranging from 0.83 (0.72-0.97) per degree in Bulgaria to 1.12 (1.02-1.23) in Germany. Odds ratios for the remaining associations showed no evidence of between-country heterogeneity.

Discussion

Overall, our study indicated that climate is not an important determinant of the prevalence of wheeze or itchy rash in children in mid-latitude populations in North America and Europe. This is the first study to control for outdoor air pollutants (NO_2 and PM_{10}), which could be important confounders for associations between climate and respiratory health. Our findings are broadly consistent with other international (multi-centre) studies.

Pooling of studies has both advantages and disadvantages and these may have contributed to the lack of observed associations and to the heterogeneity of some results across countries. Advantages include the large number of children in the study and the range in exposures. Confidence intervals were reasonably small in most though not all countries. A major concern with meta-analyses in general is comparability of studies and this applies to our study as well. Because the same statistical model and the same confounder model were used for all countries, the current analyses will be more comparable than a traditional meta-analysis where only published effect estimate are compared across studies. Since our studies were initiated independently, they sometimes differed in design and in wording of questionnaires. We assessed symptom and confounder questions to extract the symptoms thought to be most comparable across studies. Much of the systematic differences in study methodologies were taken care of by the design of the analysis, specifically the analysis of associations per country, followed by a formal meta-analysis, with the impact on results of differences between studies. As the same exposure variables are used for all symptoms, errors in exposure assessment are an unlikely source of the pattern of association seen in our study.

Confounding by unmeasured area-related factors cannot be discounted. Such a confounder should be strongly related both to climate and to the symptom, and so the credibility of observed associations is enhanced by being measured across more areas, and by consistency across more countries. Exposure data on tropospheric ozone were not available, although the concentration of this pollutant is known to be affected by weather.

Differing response rates between study areas could give rise to bias but we found no confounding by response rate. If parents with illness more frequently report their child's illness, and if this difference were more acute in (say) more humid areas, this could give rise to a bias. No evidence of greater observed association between climate and symptoms among children with asthmatic parents was noted.

We have reported all mean estimates, for completeness. Where study specific results vary considerably (significantly inverse and positive), a mean estimate is not necessarily useful. Otherwise, the mean odds ratio serves as a 'best estimate' (its calculation, and that of its confidence interval, taking account of heterogeneity between estimates, as well as their individual uncertainties). The distribution about this mean remains important.

Further studies are needed which integrate more detailed information on meteorological or climate conditions, improved measures of local environmental conditions, atopic phenotypes and physiological factors (e.g. vitamin D) to determine the relevant mechanism(s). Other studies on the impacts of temporal climate variability (seasonality and inter-annual climate variability) will further elucidate the effects of climate on human health respiratory and atopic outcomes.

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Figures and tables

Table 1 Participating studies in PATY dataset.

Table 2. Mean odds ratios and 95% confidence intervals for the association between climate factors and health outcomes. 'H' indicates heterogeneity between country-specific results ($p<0.10$)

Table 3. Mean odds ratios and 95% confidence intervals, with and without adjusting for NO_2 or for PM_{10}

Figure 1. Variation in climate measures across towns, within each country.

Figure 2. Odds ratios adjusted for individual confounders but not for pollutants. Countries are ordered by mean (across towns) of winter temperature.

Table 1 Details of individual research studies contributing to the PATY dataset.

Study	**Number of study areas**	**Data collection**	**Number of children**	**Age range (years)**
Bulgaria, CESAR study	3 areas in 3 towns	Feb-May 1996	3,441	7-11
Germany, Bitterfeldt study	3 areas in 3 towns	Aug 1992-Jul 1993	1,903	6-12
Hungary, CESAR study	5 areas in 5 towns	Feb-May 1996	3,460	7-11
Italy, Sidria study	29 areas in 22 towns	Oct 1994-Mar 1995	9,081	6-10
Poland, CESAR study	4 areas in 4 towns	Feb-May 1996	2,821	7-11
Russia, 10 city study	13 areas in 10 towns	Apr-May 1999	5,453	8-12
Slovakia, CESAR study	4 areas in 3 towns	Feb-May 1996	2,975	7-11
Switzerland, Scarpol study	10 areas in 10 towns	Oct 1992-Mar 1993	2,739	6-12
USA and Canada, 24 city study	24 areas in 24 towns	Sep-Nov in 1988-90	14,937	8-11
Total	95 areas in 84 towns		46,810	6-12

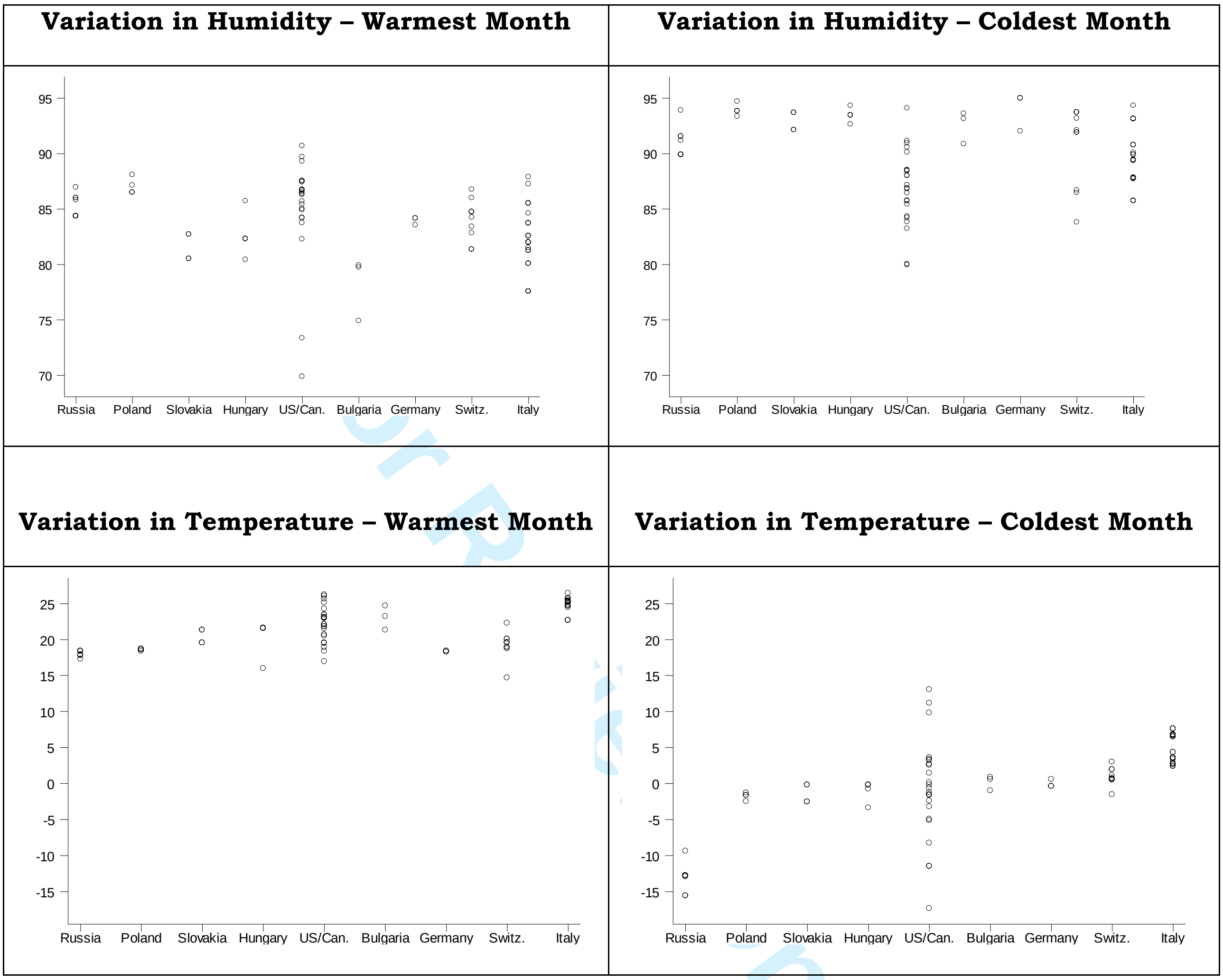
Table 2. Mean odds ratios and 95% confidence intervals for the association between climate factors and health outcomes. 'H' indicates heterogeneity between country-specific results (p<0.10)

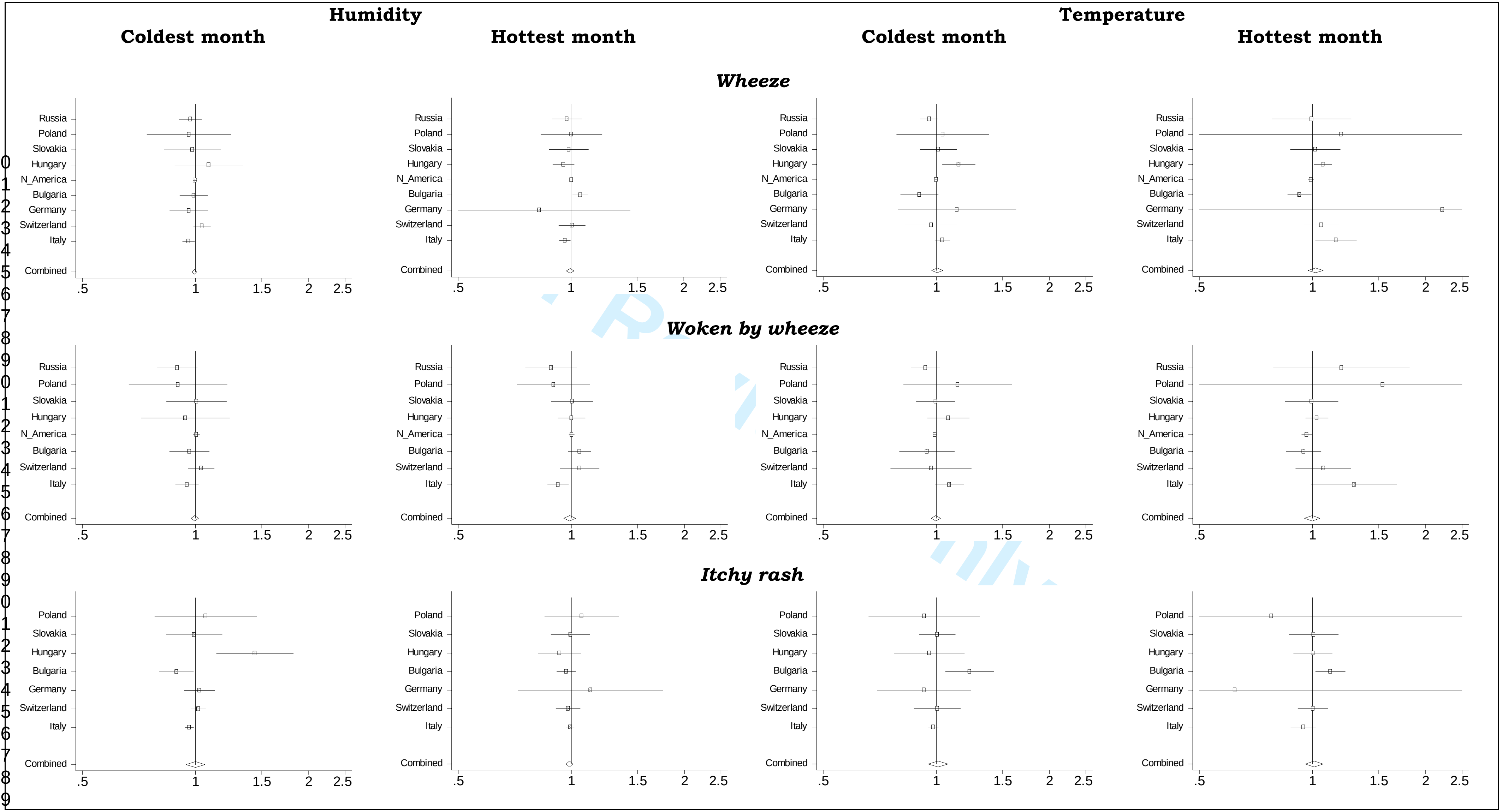
	Mean odds ratio (95% confidence interval)		
	Wheeze	**Woken by wheeze**	**Itchy rash**
Cold month humidity	0.99 (0.98-1.01)	1.00(0.97-1.02)	1.00(0.94-1.06)^{H}
Hot month humidity	1.00 (0.97-1.02)	0.99 (0.95-1.03)	0.99 (0.97-1.01)
Cold month temperature	1.00 (0.97-1.04)^{H}	1.00 (0.97-1.03)	1.01(0.95-1.07)
Hot month temperature	1.02 (0.97-1.07)^{H}	1.00 (0.95-1.05)	1.01(0.96-1.07)

Table 3. Mean odds ratios and 95% confidence intervals, with and without adjusting for NO_2 or for PM_{10}, in those subsets of the data with pollution measures available. All results are adjusted for individual risk factors. 'H' indicates heterogeneity between country-specific results ($p<0.10$)

	With and without controlling for NO_2		**With and without controlling for PM_{10}**	
	without	With	without	with
Wheeze	3 countries		8 countries	
Cold month temperature	0.99(0.93-1.06)^{H}	1.00(0.93-1.08)^{H}	1.00(0.96-1.04)^{H}	1.02(0.97-1.07)^{H}
Hot month temperature	1.08(1.00-1.17)	1.09(1.01-1.19)	1.01(0.97-1.05)	1.04(0.98-1.10)^{H}
Cold month humidity	0.99(0.94-1.04)^{H}	0.99(0.94-1.05)^{H}	1.00(0.99-1.01)	1.00(0.98-1.01)
Hot month humidity	0.97(0.94-1.00)	0.97(0.94-1.00)	1.00(0.99-1.02)	1.00(0.99-1.01)
Woken by Wheeze	3 countries		7 countries	
Cold month temperature	1.00(0.89-1.12)^{H}	1.00(0.87-1.15)^{H}	0.99(0.98-1.00)	1.00(0.98-1.01)
Hot month temperature	1.14(0.99-1.30)	1.13(0.98-1.31)	0.98(0.95-1.01)	1.00(0.95-1.04)
Cold month humidity	0.96(0.89-1.04)^{H}	0.97(0.90-1.04)	1.00(0.97-1.03)	1.00(0.96-1.03)
Hot month humidity	0.95 (0.87-1.04)	0.96(0.87-1.05)	1.00 (0.99-1.02)	1.01(0.99-1.02)
Itchy Rash	2 countries		6 countries	
Cold month temperature	0.98(0.95-1.01)	0.97(0.94-1.01)	1.04(0.93-1.16)^{H}	0.96(0.83-1.12)^{H}
Hot month temperature	0.97(0.91-1.03)	0.95(0.89-1.01)	1.04(0.98-1.12)	0.99(0.86-1.13)^{H}
Cold month humidity	0.99(0.94-1.04)^{H}	0.99(0.94-1.04)^{H}	1.02(0.94-1.11)^{H}	1.07(0.96-1.21)^{H}
Hot month humidity	0.99(0.97-1.01)	0.99(0.97-1.01)	0.98(0.93-1.03)	1.01(0.92-1.11)^{H}

Figure 1. Variation in climate measures across towns, within each country (temperature °C and humidity %).




Humidity
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Poland
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N_America
Bulgaria
Germany
Switzerland
Italy
Combined
Woken by wheeze
Russia
Poland
Slovakia
Hungary
N_America
Bulgaria
Switzerland
Italy
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Itchy rash
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Bulgaria
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Italy
Combined
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1
1.5
2
2.5

Figure 2. Odds ratios adjusted for individual confounders but not for pollutants. Countries are ordered by mean (across towns) of winter temperature.

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