MODESTUM

Research Article

The effects of temperature and humidity on mortality in acute medical admissions

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ARTICLE INFO	ABSTRACT
	The full effects of meteorological variables on mortality have not yet been elucidated. This study's aim was to investigate whether 30-day in-hospital mortality in emergency hospital admissions for non-respiratory diseases were sensitive to the effects of humidity and ambient temperature on the day of admission. We studied all emergency medical admissions to St. James's Hospital, Dublin, during 2002-2018 (n=113,807) and investigated temperature and humidity on day of admission. We employed multivariable logistic regression to identify temperature and humidity mortality predictors, adjusting for underlying comorbidities. Lower temperatures on day of admission predicted higher 30-day in-hospital mortality (adjusted OR: 1.12, 95% CI: 1.06-1.17), but lower humidity levels did not (adjusted OR: 0.97, 95% CI: 0.91-1.03). There was no interaction between meteorological variables and comorbidities on mortality. In conclusion, temperature may be a more significant predictor of in-hospital mortality than humidity for non-respiratory patients.
	Keywords: temperature, humidity, comorbidity, mortality outcomes

INTRODUCTION

Studies on the effects of environmental factors on human health have increased in recent decades due in part to the growing acknowledgement of the deleterious health effects of climate change. The effects of air pollution on a range of different morbidity and mortality outcomes have been extensively investigated (Abelsohn and Stieb, 2011; Chen and Hoek, 2020; Manisalidis et al., 2020). The effects of other environmental factors that might influence morbidity and mortality, such as humidity and air temperature at time of an acute medical event, have received less attention. While it is recognized that non-optimum temperatures, at temperature extremes and even moderately high or low temperatures, can affect mortality (Gasparrini et al., 2015), the overall impact of humidity on mortality has not been clearly established epidemiologically.

The effect of humidity on human health is exerted via heat stress (impaired thermoregulation with high humidity due to reduced evaporative capacity in the environment) and dehydration, either of which could exacerbate cardiovascular morbidity (Donaldson et al., 2003; Watso and Farquhar, 2019). It has previously demonstrated that, in the case of emergency respiratory admissions, conditionally dependent on the level of particulate matter (PM10), higher humidity levels on the day of admission were associated with improved survival compared with lower humidity levels (Akasheh et al., 2018). It is unclear as to whether this observation would apply to all admitted patients, particularly for those without respiratory disease.

Although all of the pathophysiological mechanisms by which temperature influences morbidity and mortality are not yet fully understood (Gasparrini et al., 2015), non-optimum temperature has been associated with a wide range of adverse morbidity and mortality outcomes (Bunker et al., 2016; Ryti et al., 2016; Song et al., 2017; Turner et al., 2012). The relationship between temperature and mortality is typically U-shaped and demonstrates significant geographical heterogeneity (D'Ippoliti et al., 2010; Hajat and Kosatky, 2010).

To what extent humidity modifies the effect of temperature on health is unclear and indeed the individual effects of humidity on human health are not yet fully understood (Davis et al., 2016). The aim of this study, was to investigate whether humidity and temperature on day of admission predicted 30-day in-hospital mortality outcomes in emergency medical admissions to a large teaching hospital in Dublin, Ireland. Furthermore, we sought to determine whether patients admitted with a higher comorbidity burden were more susceptible to such environmental influences.

MATERIALS AND METHODS

Background

St James's Hospital, Dublin, is the largest acute academic teaching hospital in Ireland and serves as a secondary care center for emergency admissions in a catchment area with a population of 270,000 adults. All emergency medical admissions are admitted from the emergency department (ED) to an Acute Medical Admission Unit, the operation and outcome of which have been described elsewhere (Conway et al., 2014, 2018). As a city center hospital, St James's admits person's resident elsewhere but working in the capital, in addition to visitors to Dublin who become acutely ill. During the study period, residents in the catchment area accounted for 74.5% of all emergency medical admissions; this compares with a proportion of 59% of ED presentations accounted for by local residents in two London hospitals, where the social influences on ED visitations have been examined (Beeknoo and Jones, 2016).

Data Collection

An anonymous patient database was employed, collating core information of clinical episodes spanning 17 years (2002-2018) from the patient administration system (PAS), the national hospital in-patient enquiry (HIPE) scheme, the patient electronic record, the emergency room and laboratory systems. HIPE is a national database of coded discharge summaries from acute public hospitals in Ireland (O'Callaghan et al., 2012; O'Loughlin et al., 2005). International classification of diseases, ninth revision, clinical modification (ICD-9-CM) has been used for both diagnosis and procedure coding from 1990 to 2005, with ICD-10-CM used since then. Data included parameters such as the unique hospital number, admitting consultant, date of birth, gender, area of residence, principal and up to nine additional secondary diagnoses, principal and up to nine additional secondary procedures, and admission and discharge dates. Additional information cross-linked and automatically uploaded to the database included physiological, hematological and biochemical parameters. Only patients who were admitted to the hospital for non-respiratory medical emergencies were included in this analysis.

Daily air temperature and humidity data were obtained from Met Éireann, the Irish Meteorological Service. Daily air temperature was measured by maximum daily temperature (°C) and humidity was measured by mean daily relative humidity (percentage). These meteorological measurements were recorded at the Dublin Airport weather station, a manned weather station situated north of Dublin City Center.

This study had no interventional component, used anonymized routinely collected data, complied with data protection legislation, and was undertaken with the approval of hospital authorities; hence the study did not require approval from our institutional ethics committee.

Comorbidity Score

Patient comorbidity was assessed by a comorbidity score (Conway et al., 2020a) published in 2014, which was further adjusted by additional information collected by our information system since. To devise the score, we searched ICD-9 hospital episode discharge codes (back-mapping ICD-10 codes to ICD-9 as appropriate) based on the definition for chronic physical or mental health disorders proposed by the US Department of Health and Human Services in Chapter III of their document "Private payers serving individuals with disabilities and chronic conditions" (Ozminkowski, 2000). These ICD codes were similar to those proposed by the Canadian group for multi-morbidity (Tonelli et al., 2015) and the work of Quan et al. (2005). ICD codes that captured chronic physical or mental health disorders that limit people in activities that they generally would be expected to be able to perform were grouped according to the following ten systems:

1. cardiovascular,
2. respiratory,
3. neurological,
4. gastrointestinal,
5. diabetes,
6. renal,
7. neoplastic disease,
8. others (including rheumatological disabilities),
9. ventilatory assistance required, and
10. transfusion requirement.

In addition, we searched our hospital's other databases for evidence of diabetes (diamond database) (Kopelman and Sanderson, 1996), respiratory insufficiency (FEV1<2L), troponin status (high sensitivity troponin>25 ng/L) (Courtney et al., 2014), low albumin (<35 G/dL) and anemia (hemoglobin levels<10 g/dL) or chronic renal insufficiency–modification of diet in renal disease (MDRD)<60 mL/min*1.73 m^2 (Chin et al., 2011). Each component of the score was then weighted according to 30-day in-hospital mortality. The comorbidity score showed a curvilinear relationship to 30-day in-hospital episode mortality ranging from 2.4% (95% confidence interval (CI): 2.2%, 2.5%) at six points to 23.0% (95% CI: 21.8%, 24.2%) at 16 points.

Other Predictor Variables

The acute illness severity score (AISS) is an age-adjusted aggregate score derived from admission laboratory parameters (Courtney et al., 2014; O'Sullivan et al., 2012; Silke et al., 2010). The AISS is exponentially related to 30-day in-hospital mortality ranging from 2.5% (95%CI 2.3%, 2.6%) to 32.1% (95%CI 30.4%, 33.8%) (Conway et al., 2015; Silke et al., 2010). Sepsis status categorisation was based on

1. no blood culture performed,
2. blood culture performed with a negative result, and
3. blood culture performed with a positive result (Conway et al., 2020b).

The 30-day in-hospital mortality rates for these categories was and 3.1%, 9.6% and 17.8%, respectively.

Statistical Methods

Descriptive statistics were calculated for demographic data, including means/standard deviations (SD), medians/interquartile ranges (IQR), or percentages. We examined 30-day in-hospital mortality as the primary outcome. We performed comparisons between categorical variables and 30-day in hospital mortality using Chi-squared

tests; multiple comparisons were adjusted for multiplicity using Scheffe's comparison statistic. Logistic regression analysis was employed to examine significant potential mortality predictors (p<0.10 by Wald test from the univariate analysis) of 30-day in-hospital mortality to ensure that the model included all variables with predictive power. Adjusted odds ratios (OR) and 95% CIs were calculated for those significant model predictors. A stepwise logistic regression analysis examined the association between 30-day mortality and the following predictor variables: AISS (Froom and Shimoni, 2006; O'Sullivan et al., 2012; Prytherch et al., 2005), Comorbidity score (Conway et al., 2020a), Charlson index (Charlson et al., 1987), and sepsis status (Conway et al., 2020b). Of course, over a prolonged observation period of 15 years, many patients were admitted more than once. For example, those admitted more than once, twice or three times was 48.8%, 31.2%, and 22.2%, respectively, with 5.3% admitted>10 times each. Clearly there will be a difference in mortality rates if calculated by episode or by patient; calculated mortality is therefore explicitly stated as per admission or as per patient and only a patient's last admission was considered if they were admitted more than once. We employed a logistic model with robust estimate to allow for clustering; the correlation matrix thereby reflected the average discrete risk attributable to each of these predictor variables (Silke et al., 2010).

We used the margins command in Stata to estimate and interpret adjusted predictions for sub-groups, while controlling for other variables such as time, using computations of average marginal effects. Margins are statistics calculated from predictions of a previously fitted model at fixed values of some covariates and averaging or otherwise over the remaining covariates. In the multivariable logistic regression model we adjusted univariate estimates of effect, using the previously described outcome predictor

variables. The model parameters were stored; post-estimation intra-model and cross-model hypotheses could thereby be tested.

Statistical significance at p<0.05 was assumed throughout. Stata v.15 (Stata Corporation, College Station, TX, USA) statistical software was used for analysis.

RESULTS

Patient Demographics

There were a total of 113,807 emergency medical admissions in 58,126 patients over the 17-year study period (2002-2018). This included patients admitted directly into the Intensive Care Unit or High Dependency Unit. The proportion of males was 48.8%. The median (IQR) length of stay (LOS) was 5.0 (2.1, 9.7) days. The median (IQR) age was 63.3 (43.3, 77.8) years, with the 90th percentile boundary at 85.3 years.

We set a cut-point for the comorbidity score of ⩾10 points representing high versus (vs.) low comorbidity burden. Patients with high comorbidity score were older with a median (IQR) age of 75.1 years (64.4, 82.6) vs. 60.8 years (41.2, 76.6). They were more likely to be male (53.4% vs. 46.7%) and had a longer median (IQR) LOS of 9.1 days (5.1, 16.0) vs. 4.6 days (1.9, 8.7).

The demographic characteristics shown in **Table 1** are outlined with a division of relative humidity levels at the time of admission (lower/higher cut at quartile (Q) 3). Humidity cut-points per quintile were at 77%, 82%, 86%, and 91% values; high humidity was taken to be at Q3 or above (⩾89%). The patient group characteristics at time of presentation are tabulated by comorbidity score, Charlson index (Charlson et al., 1987), and sepsis status. At baseline, there were no major differences between the groups in terms of median age at time

Table 1. Characteristics of emergency medical admission episodes by humidity levels

		Low (N=45,471)	High (N=57,013)	p-value
Age (years)	Mean (SD)	60.2 (20.7)	60.2 (20.7)	0.840
	Median (Q1, Q3)	63.3 (43.4, 77.8)	63.3 (43.3, 77.8)	
LOS (days)	Mean (SD)	6.9 (6.4)	7.1 (6.5)	<0.001
	Median (Q1, Q3)	4.9 (2.0, 9.5)	5.0 (2.1, 9.8)	
Gender	Male	22,286 (49.0%)	27,860 (48.9%)	0.64
	Female	23,185 (51.0%)	29,153 (51.1%)	
30-day in-hospital mortality	Alive	43,474 (95.6%)	54,431 (95.5%)	0.29
	Dead	1,997 (4.4%)	2,582 (4.5%)	
Illness severity	1	1,332 (3.5%)	1,736 (3.3%)	0.21
	2	2,825 (7.4%)	3,915 (7.5%)	
	3	4,755 (12.4%)	6,500 (12.5%)	
	4	6,438 (16.9%)	8,617 (16.6%)	
	5	7,522 (19.7%)	10,037 (19.3%)	
	6	15,330 (40.1%)	21,212 (40.8%)	
Comorbidity score	<6	9,771 (31.3%)	12,001 (29.9%)	<0.001
	⩾6<8	10,015 (32.1%)	12,789 (31.9%)	
	⩾8<12	9,458 (30.3%)	12,608 (31.4%)	
	⩾12<20	1,935 (6.2%)	2,731 (6.8%)	
Charlson index	0	17,858 (46.1%)	26,137 (45.9%)	0.11
	1	10,355 (26.7%)	15,532 (27.3%)	
	2	10,553 (27.2%)	15,260 (26.8%)	
Sepsis group	1 (no blood culture performed)	35,158 (77.3%)	43,529 (76.3%)	<0.001
	2 (blood culture negative)	8,803 (19.4%)	11,580 (20.3%)	
	3 (blood culture positive)	1,510 (3.3%)	1,904 (3.3%)	

of admission (63.3 years vs 63.3 years, p=0.084, IQR: 43.3, 77.8), median LOS (5.0 days, IQR: 2.1, 9.7), or per episode 30-day hospital mortality (4.5%, 95% CI: 4.3%, 4.6%). From an overall clinical perspective, one therefore could regard the groups, relating to admission on days of low or of high humidity, as essentially equivalent in risk profile and complexity or comorbidity status.

Temperature and Humidity Variation with Season

The median temperature in our temperate climate was 11.0°C (IQR: 7.1, 13.1) with respective 10 and 90 percentile values at 4.2°C and 15.6°C. The variation by season range from a median of 13.1°C (IQR: 11.2, 15.3) in summer to a winter median of 7.1°C (IQR: 4.7, 9.9). The corresponding relative humidity levels were 83% (IQR: 77%, 91%) with respective 10 and 90 percentile values at 70 % and 91%. The variation by season range from a summer median of 79% (IQR: 73%, 86%) to a winter median of 87% (IQR: 82%, 91%) (**Figure 1**).
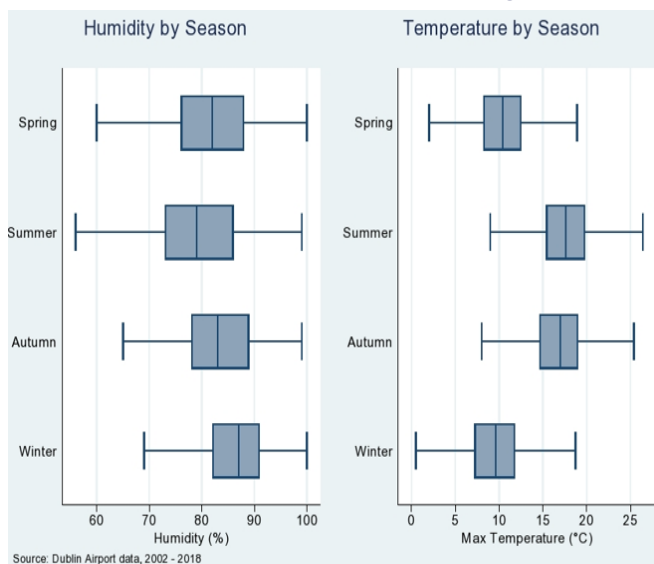

Figure 1. Relative humidity and maximal daily temperature from the daily Dublin Airport weather station records between 2002 and 2018. The box & whisker plots indicate the median (line subdividing the box) and the IQR. The upper and lower extremes (fence) are the smallest and largest values that are not outliers

Multivariable Logistic Regression Predictor Model Including Comorbidity Score, Temperature or Humidity on Admission Day & Subsequent 30-day in-hospital Mortality Outcome

In the univariate analysis, higher humidity levels on day of hospital admission were a non-significant predictor of increased 30-day in-hospital mortality (OR 1.03, 95% CI: 0.98, 1.08). Conversely, lower humidity levels on day of admission trended towards increased 30-day in-hospital mortality in the multivariable analysis, but this finding was also non-significant (adjusted OR 0.97, 95% CI: 0.91, 1.03). The 30-day in-hospital mortality (model-predicted) rates reflected this with a mortality rate of 10.4% (95% CI: 9.7%, 11.0%) at humidity levels of 50-70%, compared with 9.7% (95% CI: 9.1%, 10.4%) at humidity levels >95% (**Figure 2** and **Figure 3**).
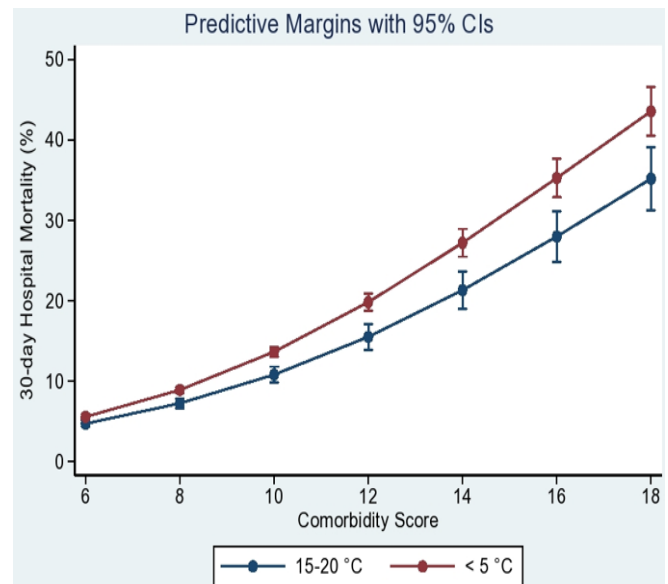

Figure 2. The risk of 30-day in-hospital mortality per episode increased essentially as a linear function of the underlying, after adjustment for other predictive variables including acute illness severity, Charlson index, comorbidity score, & sepsis status. Lower temperature levels on day of admission independently predicted worse outcomes
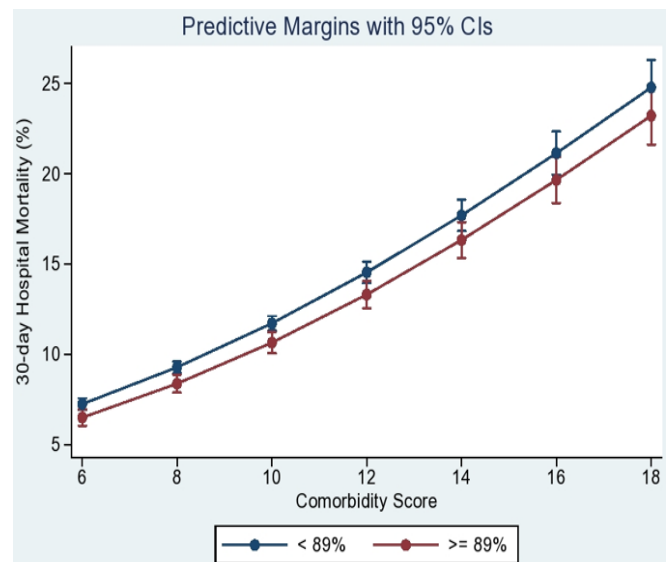

Figure 3. The risk of a death by the 30-day of a hospital episode increased essentially as a linear function of the underlying, even after adjustment for other predictive variables including acute illness severity, Charlson index, comorbidity score, and sepsis status. Trends to increased mortality at higher humidity levels (>75th percentile) on day of admission, did not achieve significance

The mortality outcomes were worse at lower prevailing temperatures on day of hospital admission. Lower temperature on day of admission predicted increased 30-day in-hospital mortality on univariate analysis (OR 1.13, 95% CI: 1.08, 1.17) and in multivariable analysis (adjusted OR 1.12, 95% CI: 1.06, 1.17). The 30-day in-hospital mortality (model-predicted) rates progressively increased with decreasing temperature on day of admission with a mortality rate of 10.6% (95% CI: 10.3%, 11.0%) at temperatures <5°C compared with 8.6% (95% CI: 7.9%, 9.2%) at temperatures >15 °C.

The frequency of admissions with comorbidity scores of 0-6, 6-10 and >10 were 51.6%, 36.4%, and 11.9%; the median (IQR) comorbidity score was 8.4 (6.0, 10.4). The 30-day in-hospital mortality (model predicted) rates progressively increased with rising comorbidity scores and were 5.3%, 12.9%, and 33.3% at scores of 6, 10, and 16 points, respectively. Comorbidity score predicted 30-day in-hospital mortality on univariate analysis (OR 1.47, 95% CI: 1.46, 1.48) and in the multivariable analysis (adjusted OR 1.31, 95% CI: 1.29, 1.33). Essentially the rate of increase of 30-day hospital rates, for the temperature or humidity modelling functions, increased as a linear or near linear function, with little evidence of dependency of the outcome on any temperature or humidity actions on the underlying comorbidity score.

DISCUSSION

These data suggested, in contrast to previous research in patients admitted with a primary respiratory indication, that the admission day level of humidity has little impact on non-respiratory emergency medical admissions. We demonstrated, however, that temperature on day of admission may predict 30-day in-hospital mortality for non-respiratory medical admissions, with higher risk of mortality in admissions on days with lower temperatures compared with admissions on days with higher temperatures. Furthermore, underlying comorbidity burden, represented by comorbidity scores ≥10 points, was also an important predictor of 30-day in-hospital mortality for non-respiratory medical admissions and did not modify the effects of humidity or temperature on mortality.

The finding of humidity having limited impact on 30-day in-hospital mortality is in accordance with other studies that have demonstrated little evidence of humidity effects on mortality and morbidity. A multi-country study examined the effect of humidity on all-cause mortality in 24 countries with mostly temperate climates, including Ireland, and found a very small negative association of humidity with mortality, with a 23% increase in relative humidity being associated with 1.1% (95% CI: 0.8, 1.3) decrease in mortality after adjusting for temperature (Armstrong et al., 2019). Similarly, a time series analysis in 12 U.S. cities examining the acute and lagged effects of humidity on respiratory or cardiovascular mortality found no consistent effect (Braga et al., 2002). The absence of humidity effects on mortality is further supported by studies which have compared heat indices (biometeorological measures combining temperature and humidity) with that of dry bulb temperature (a measure of temperature only) in their respective abilities to predict mortality and have found no consistent advantage in one over the other (Barnett et al., 2010; Ragettli et al., 2017). On the other hand, a number of studies have demonstrated an association between humidity and mortality, including cardiovascular mortality and mortality in the elderly (de Barros et al., 2021; Dilaveris et al., 2006; Ou et al., 2014; Qi et al., 2020). Indeed, we previously demonstrated the effect of humidity on respiratory mortality (Akasheh et al., 2018). The inconsistent findings on the effects of humidity on health outcomes may be due to the inconsistency with which humidity is incorporated into studies: as the humidity variable chosen may be highly

correlated with other meteorological variables, it may be challenging to isolate the individual effects of humidity (Davis et al., 2016). Furthermore, similar to the geographical heterogeneity seen in temperature-mortality associations, humidity-mortality associations may also be subject to regional variation, with humidity having a greater influence on mortality in particular populations or in particular climates (Davis et al., 2016).

The temperature effects were consistent with falling admission day temperature predicting worse 30-day in-hospital mortality outcomes. This is consistent with numerous other studies that have demonstrated an association between cold temperatures and cardiovascular, cerebrovascular, and all-cause mortality (Atsumi et al., 2013; Rodrigues et al., 2019; Zeka et al., 2014). It is noteworthy that an increased in-hospital mortality risk was not observed after admission on days with high temperatures. Previous studies have demonstrated an increased risk of all-cause mortality on the day of, and on the days immediately following, high temperatures, even in temperate climates (Armstrong et al., 2011; Gasparrini et al., 2015). Our finding of no heat effect on mortality is consistent, however, with a large multi-country study that examined temperature-mortality associations in a number of locations globally and found that Dublin was unique in that high temperature had no effect on mortality outcomes (Baccini et al., 2008). A later study ascribed this finding to the limited variation in summertime temperatures in Dublin (Hajat and Kosatky, 2010).

Predictably, increased comorbidity burden, as measured by a comorbidity score ≥10 points, was an independent predictor of 30-day in-hospital mortality. It is interesting, however, that underlying comorbidity did not modify the effect of temperature or humidity on mortality outcomes. There has been somewhat contradictory evidence on whether comorbidities modify the effect of temperature on mortality. There is some evidence that individuals with particular underlying comorbidities, such as diabetes, cardiovascular or cerebrovascular disease, may be more susceptible to the effects of temperature (Basu, 2009; Medina-Ramón et al., 2006). A large systematic review which sought to determine the individual- and community-level factors which affect vulnerability to temperature-mortality associations, however, found only limited or suggestive evidence of effect modification by chronic conditions (Son et al., 2019). The reason for the latter study's finding, and the finding from our own analysis, may be because only certain comorbidities modify the effect of temperature on mortality, whereas others do not; analyses assessing interaction between all comorbidities and temperature on mortality, therefore, may not identify any interaction between the two variables.

One of the strengths of this study is the use of a database that had rich, anonymised data from thousands of patients over 17 years, which allowed us to explore the potential modifying effects of comorbidities on temperature-mortality and humidity-mortality associations. The data came from the five separate sources, including electronic hospital records, and were sufficiently detailed to reduce the risk of significant errors or misclassification being introduced into our dataset. Secondly, we explored and isolated the individual effects of humidity on mortality, which is an underexplored topic within

environmental epidemiology. Many other studies that have explored the effects of meteorological variables on mortality have either excluded humidity from their studies or treated it as a confounder (Armstrong et al., 2019; Davis et al., 2016).

This study had a number of limitations which must be considered. Firstly, the temperature measure used in this analysis was maximum daily temperature, which is prone to measurement error more than mean daily temperature, as the former is based on a single measurement, while the latter is based on repeated measurements taken throughout the day (Barnett et al., 2010). Nonetheless, it has been previously shown that different temperatures measures have, on average, the same predictive abilities (Barnett et al., 2010). Secondly, while we adjusted for a significant number of covariates in our models, we did not adjust for long-term trend in mortality, seasonality or day of the week on admission, which may have acted as time-varying confounders in our analysis. Thirdly, we examined the effect of humidity and temperature on 30-day all-cause mortality; there may have been certain conditions upon which humidity and temperature had a more pronounced effect and would not have been captured in our analysis.

Although we did not find a humidity effect on non-respiratory mortality in our analysis, further research is needed to explore the effects of humidity on more specific causes of mortality and in a variety of locations, as humidity-mortality associations likely demonstrate geographical heterogeneity. As part of a climate change adaptation strategy, it is imperative that models are developed to project future morbidity and mortality due to all meteorological variables across different populations, climates and locations (Schwartz et al., 2004).

In conclusion, our data demonstrated that temperature was a more significant predictor of 30-day in-hospital mortality than humidity in non-respiratory medical admissions and that humidity had little impact on predicting 30-day in-hospital mortality for this group. Lower temperatures were associated with increased 30-day in-hospital mortality and higher temperatures had little effect. Underlying comorbidities were an independent predictor of 30-day in-hospital mortality and did not modify the effects of temperature or humidity on mortality.

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