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Long-term exposure to summer specific humidity and cardiovascular disease hospitalizations in the US Medicare population

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Declaration of Competing Interest

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Data sharing statement

Due to restrictions in the data-use agreement with the Centres for Medicare and Services (CMS), the data used in this study cannot be made available publicly or to other researchers. However, other investigators can apply to the CMS for their own data-use agreements to access the Medicare data. We used data from the Gridded Surface Meteorological dataset to assess specific humidity, temperature, NDVI, blue space and precipitation. This data is freely available in Google Earth Engine. A statistical analysis plan is available from the corresponding author (jklompma@hsph.harvard.edu) on reasonable request.

CRedit authorship contribution statement

Jochem O. Klompma: Formal analysis, Methodology, Visualization, Writing – original draft. **Francine Laden:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing. **Peter James:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing. **M. Benjamin Sabath:** Data curation, Resources, Software, Writing – review & editing. **Xiao Wu:** Methodology, Software, Writing – review & editing. **Francesca Dominici:** Funding acquisition, Writing – review & editing. **Antonella Zanobetti:** Funding acquisition, Methodology, Writing – review & editing. **Jaime E. Hart:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2023.108182>.

Abstract

Introduction: Most climate-health studies focus on temperature; however, less is known about health effects of exposure to atmospheric moisture. Humid air limits sweat evaporation from the body and can in turn exert strain on the cardiovascular system. We evaluated associations of long-term exposure to summer specific humidity with cardiovascular disease (CVD), coronary heart disease (CHD) and cerebrovascular disease (CBV) hospitalization.

Methods: We built an open cohort consisting of ~63 million fee-for-service Medicare beneficiaries, aged 65, living in the contiguous US (2000–2016). We assessed zip code level summer average specific humidity and specific humidity variability, based on daily estimates from the Gridded Surface Meteorological dataset (~4km spatial resolution). To estimate associations of summer specific humidity with first CVD, CHD, and CBV hospitalization, we used Cox-equivalent Poisson models adjusted for individual and area-level socioeconomic status indicators, temperature, and winter specific humidity.

Results: Higher summer average specific humidity was associated with an increased risk of CVD, CHD, and CBV hospitalization. We found hazard ratios (HRs) of 1.07 (95% CI: 1.07, 1.08) for CVD hospitalization, 1.08 (95% CI: 1.08, 1.09) for CHD hospitalization, and 1.07 (95% CI: 1.07, 1.08) for CBV hospitalization per IQR increase (4.0 g of water vapor/kg of dry air) in summer average specific humidity. Associations of summer average specific humidity were strongest for beneficiaries eligible for Medicaid and for beneficiaries with an unknown or other race. Higher summer specific humidity variability was also associated with increased risk of CVD, CHD, and CBV hospitalization. Associations were not affected by adjustment for temperature and regions of the US, as well as exclusion of potentially prevalent cases.

Conclusion: Long-term exposure to higher summer average specific humidity and specific humidity variability were positively associated with CVD hospitalization. As global warming could increase humidity levels, our findings are important to assess potential health impacts of climate change.

Keywords

Climate; Humidity; Moisture; Cardiovascular disease

1. Introduction

Projections show that the global surface temperature will continue to increase for the next several decades (Masson-Delmotte et al., 2021). Most studies that evaluate associations of climate on human health focus on temperature, where short- and long-term exposure to high and low temperatures has been associated with several adverse health outcomes (Zanobetti and O'Neill, 2018; Yu et al., 2012; Ye et al., 2012; Zafeiratou et al., 2021). Besides temperature, atmospheric moisture is an important climate component that might affect human health. Studies show that the stress put on the humans by high temperatures is higher when atmospheric moisture levels are higher (Eg and Pw, 2015; McGregor and Vanos, 2018; Davis et al., 2016). As global warming will increase evaporation of water, higher atmospheric moisture levels across much of the globe are expected in the future (Baldwin et al., 2023; Held and Soden, 2006).

There are several ways to assess atmospheric moisture. Relative humidity is the ratio of the amount of moisture in the air compared to the moisture content of moisture-saturated air at the same temperature. In other words, relative humidity levels can change if the air temperature changes but the actual moisture content remains constant (Davis et al., 2016; Baldwin et al., 2023). Mass-based atmospheric moisture variables, such as specific humidity (the mass of moisture per mass of air) and absolute humidity (the mass of moisture per total volume of air), are less sensitive to changing air temperatures. Therefore, mass-based atmospheric moisture variables seem to be more useful indicators to make inferences about health effects of the air's actual amount of moisture (Davis et al., 2016; Baldwin et al., 2023).

Atmospheric moisture is seldom the exposure of interest in environmental health studies (Davis et al., 2016). Most studies include an atmospheric moisture indicator as a confounder or effect modifier, so effect estimates of atmospheric moisture indicators are rarely reported. The few studies that evaluated health effects of atmospheric moisture reported mixed effects of short-term exposure to relative humidity with mortality (Armstrong et al., 2019; Zeng et al., *mdpi.com* 2017;; Rocklöv and Forsberg, 2010). Barreca observed a U-shaped relation of monthly mean specific humidity with all-cause mortality in the US in models adjusted for temperature (Barreca, 2012). Furthermore, a study in the US showed that absolute humidity was the most frequently selected top predictive weather indicator for daily all-cause and cause-specific mortality counts (Zhang et al., 2014). To the best of our knowledge, there are no studies that evaluated associations of long-term exposure to atmospheric moisture with health outcomes.

Specific humidity might be a good indicator of physiologically stressful heat exposure. High specific humidity limits sweat evaporation from the body. Insufficient cooling processes can lead to an increase in the body core temperature which in turn can exert strain on the cardiovascular system (Davis et al., 2016). We hypothesized that long-term exposure to high specific humidity levels might contribute to pathophysiological mechanisms and affect the development of cardiovascular diseases (CVDs). As individuals can to a certain extent acclimatize to their local climate, we hypothesized that higher specific humidity variability may make it harder to acclimatize and that repeated short-term exposures might lead to higher CVD risks.

The aim of our analysis was to evaluate associations of long-term exposure to summer specific humidity with CVD hospitalizations in an American elderly population (~63 million fee-for-service Medicare beneficiaries aged 65 years). We focused on summer average specific humidity and summer specific humidity variability. Furthermore, we evaluated whether associations of exposure to summer specific humidity with CVD hospitalization were modified by individual demographics, temperature, air pollutants, greenness and blue space. We hypothesized that associations of summer specific humidity would be stronger in areas with higher temperatures and air pollutants, or lower levels of greenness and blue space, as these exposures may adversely affect the cardiovascular system, and therefore individuals may become more vulnerable to summer specific humidity exposure.

2. Methods

2.1. Study population

Medicare is the US federal health insurance program for individuals aged 65+ and for younger people with disability status. We built an open cohort by combining data from the Medicare Provider Analysis and Review (MEDPAR) and Medicare denominator files. All fee-for-service Medicare beneficiaries, aged 65+, living in the contiguous US from January 1, 2000 through December 31, 2016 were included in this open cohort. We started follow-up for each beneficiary on January 1, 2000 or January 1 of the year following entry into the cohort. Participants in the cohort were followed until the first CVD hospital admission, or until they reached the end of the follow-up (December 2016), died, or were censored (because they emigrated or switched to Medicare-Health Maintenance Organisations (HMO), private plans).

This study was exempt from informed consent requirements and was approved by the institutional review board at the Harvard T H Chan School of Public Health.

2.2. Outcome definition

We obtained information about CVD hospital admissions from the MEDPAR file. To classify hospital admissions as CVD related, *International Classification of Disease, Ninth Edition* (ICD-9) codes were used from 2000 through the third quarter of 2015, and ICD-10 (from the *Tenth Edition*) codes were used from the fourth quarter of 2015. We looked at first hospital admissions with a primary discharge diagnosis of CVD (ICD-9 codes: 390–459, ICD-10 codes: I00-I99), coronary heart disease (ICD-9 code: 410–414, ICD-10 codes: I20-I25), and cerebrovascular disease (ICD-9 codes: 430–438, ICD-10 codes: I60-I69), hereafter referred to as CVD, CHD, and CBV, respectively. We created separate cohorts for each outcome.

2.3. Exposure assessment

To assess summer (Jun 1–Aug 31) specific humidity, data from the Gridded Surface Meteorological dataset was used (Abatzoglou, 2013). This dataset provides daily average specific humidity estimates at ~4 km spatial resolution covering the contiguous US from 1979 onwards. It is based on a combination of data from the North American Land Data Assimilation System Phase 2 (NLDAS-2) (Mitchell et al., 2004), and of the Parameter-elevation Regressions on Independent Slopes Model (PRISM) (Daly et al., 2008). Detailed information about the development and validation of the dataset can be found elsewhere (Abatzoglou, 2013). As we only had information about the residential zip code of each beneficiary, we calculated spatially weighted daily specific humidity for each zip code, using Google Earth Engine. Next, we calculated summer average daily specific humidity and daily specific humidity variability (standard deviation of within-summer daily specific humidity) for each zip code for each year (2000–2016). In addition, we assessed winter (Dec 1–Feb 28/29) average specific humidity and specific humidity variability to be able to adjust for winter specific humidity. These estimates were linked to participants based on zip code of residence and calendar year.

2.4. Covariates

Information about age at year of Medicare entry, year of entry, sex, race, Medicaid eligibility (an indicator of low socioeconomic status, SES), and zip code of residence was available for all beneficiaries from the Medicare beneficiary file. In addition, we linked several zip code-level variables derived from the US Census and American Community Survey (2000, 2009–2016): population density, percent Hispanic, percent of the population with less than a high school degree, percent Black, median home value, median household income, percent below the poverty level, and percent of owner-occupied housing units. County-level percent of the population that were ever smokers and mean BMI, were derived from the nationwide Behavioural Risk Factor Surveillance System (BRFSS, 2000–2011). We temporally interpolated data for missing years using a moving average algorithm within each zip code, as described previously (Di et al., 2017).

For each zip code for each year (2000–2016), daily maximum air temperature, and daily total precipitation were estimated using data from the Gridded Surface Meteorological dataset (Abatzoglou, 2013). To temporally match the specific humidity exposure estimates, we calculated the spatially weighted summer and winter average maximum temperature and precipitation for each zip code for each year.

We also linked zip code level air pollution, greenness and blue space to each beneficiary based on zip code of residence and calendar year. The spatial variation of these environmental factors is shown in Fig. S1. Annual fine particulate matter (PM_{2.5}), nitrogen dioxide (NO₂) and ozone concentrations across the contiguous US for 2000–2016 were estimated based on predictions from spatio-temporal ensemble models (1 km² spatial resolution) (Requia et al., 2020; Di et al., 2019a, 2019b). For each zip code, the annual average concentrations were estimated by averaging the estimations at grid cells whose centroids fall within the boundary of that ZIP code.

To estimate greenness, we used the Normalized Difference Vegetation Index (NDVI) (NASA, xxxx). To calculate the NDVI, we used Landsat 7 and 8 images for the entire US from June 1, up to August 31 (summer), for each year (2000–2016). Using Google Earth Engine, cloud-free Landsat composites were created for the US. Negative NDVI values were set to zero. We calculated the spatially weighted mean summer NDVI for each zip code for each year.

To estimate blue space we used data from the Joint Research Centre's Global Surface Water Dataset (Pekel et al., 2016). This dataset is based on Landsat 5, 7, and 8 images and contains maps of the location of surface water from 1984 to 2018. We used the "Occurrence" band (the frequency with which water was present) with a 50% threshold to classify each pixel into water or non-water. As zip codes are used for postal services, adjacent water bodies are not always included. Therefore, we calculated spatially weighted mean blue space of zip codes with a 300 m buffer to be able to capture water bodies close to each zip code.

2.5. Statistical analysis

To examine associations between specific humidity and CVD hospitalizations, we used a Cox-equivalent re-parameterized Poisson approach (Shi et al., 2020). In brief, we aggregated

all beneficiaries in our cohort that live within the same zip code in a specific year, with the same sex, race, Medicaid eligibility, 2-year categories of age at study entry and year of follow-up, because they belonged to the same stratum and were treated as a single grid cell in the analysis. Details about this approach can be found elsewhere (Shi et al., 2020).

We used a stratified quasi-Poisson model to estimate associations of time-varying summer average specific humidity and specific humidity variability. The dependent variable was the count of CVD, CHD, or CBV first hospitalizations in each stratum, we used the corresponding total person-time as the offset. Mathematically, this approach is similar to a time-varying Cox proportional hazard model under an Anderson-Gill representation. We applied a bootstrap method using zip code units to calculate statistically robust 95% confidence intervals (CIs).

We included summer average specific humidity and summer specific humidity in the same model. The main models were adjusted for calendar year, US census covariates, BRFSS covariates, winter average specific humidity, winter specific humidity variability, summer and winter average temperature, summer and winter temperature variability, and an offset for total person-time, and strata for all possible combinations of sex, race, Medicaid Eligibility, age at study entry (2-year categories), and follow-up year. The Poisson regression model is specified as $\log(E[\text{hospitalization counts}]) \sim \text{summer average specific humidity} + \text{summer specific humidity variability} + \text{US census covariates} + \text{BRFSS covariates} + \text{calendar year} + \text{winter average specific humidity} + \text{winter specific humidity variability} + \text{summer average temperature} + \text{summer temperature variability} + \text{winter average temperature} + \text{winter temperature variability} + \text{strata}(\text{age, race, gender, Medicaid eligibility, follow-up year}) + \text{offset}(\log[\text{person year}])$. Summer and winter temperature indicators and winter specific humidity indicators were included in our main model to evaluate the independent associations of long-term summer specific humidity exposure with CVD hospitalization. The shape of the exposure–response curves was evaluated by adding natural splines (2 or 3 degrees of freedom) to the specific humidity terms. We performed stratified analyses to assess potential effect modification by sex, age, race, Medicaid eligibility, and blue space (< 75th vs. >75th percentile), and by quartiles of temperature, PM_{2.5}, NO₂, ozone, and greenness.

For sensitivity analyses, we excluded potential prevalent cases by removing individuals who had their first hospital admission within the first year of their follow-up and all records in the year 2000. We ran models with only average summer specific humidity (not adjusted for summer specific humidity variability) or summer specific humidity variability (not adjusted for summer average specific humidity). Further, we additionally included regions of the US (West, East) and summer and winter average daily total precipitation to adjust for regional and meteorological differences. We also ran models without adjusting for average summer and winter temperature and temperature variability or with adjustment for average summer and winter temperature only. All hazard ratios (HRs) were expressed per IQR increase (based on the CVD cohort).

For our analyses, we used R software (R Project for Statistical Computing) version 3.6.1. We conducted the analyses on the Harvard Research Computing Environment, which is supported by the Institute for Quantitative Social Science at Harvard University.

3. Results

About 63 million Medicare beneficiaries living in the contiguous US in 2000–2016 were included in our cohort. We observed 18,610,833 million first CVD hospital admissions (total person years: 401,315,016), 6,607,687 million CHD hospital admissions (total person years: 448,888,035) and 5,551,735 million CBV hospital admissions (total person years: 460,574,345). Of all Medicare beneficiaries, 55.1% were female, 76.6% were between 65 and 74 year of age at study entry, 84.5% were white, and 87.6% were not eligible for Medicaid at study entry (Table 1). For the CVD cohort the median follow-up period was 5 years, for the CHD and CBV cohorts it was 6 years. We found the highest summer average specific humidity levels in the southeastern US and the highest summer specific humidity variability in the Southwestern and Northeastern US (Fig. 1). This is likely due to the high temperatures, warm ocean water (Gulf of Mexico), and moisture advection. Summer average specific humidity and specific humidity variability were higher compared to winter average specific humidity and specific humidity variability (Table 1, Table S1). Summer specific humidity variability was weakly negatively correlated with summer specific humidity variability (Pearson $r = -0.14$, Fig. S2). Correlations between summer average specific humidity and summer average temperature (Pearson $r = 0.36$) and between summer specific humidity variability and summer temperature variability were weakly positive (Pearson $r = 0.36$).

The exposure–response curves showed no or small deviations from linearity for summer average specific humidity and specific humidity variability (Fig. S3) and therefore we show linear associations below. Higher summer average specific humidity and summer specific humidity variability were associated with an increased risk of CVD, CHD and CBV hospitalization (Table 2). For summer average specific humidity, the HR (95% CI) was 1.07 (1.07, 1.08) for CVD hospitalization, 1.08 (1.08, 1.09) for CHD hospitalization and 1.07 (1.07, 1.08) for CBV hospitalization per IQR increase (4.0 g of water vapor/kg of dry air). For summer specific humidity variability, the HRs were weaker, especially for CBV hospitalization.

Effect modification by demographics was most pronounced for Medicaid eligibility and race (Fig. 2). For summer average specific humidity, associations with CVD hospitalization were stronger for beneficiaries eligible for Medicaid (HR = 1.13, 95%CI: 1.12, 1.14 per IQR increase) compared to beneficiaries not eligible (HR = 1.06, 95%CI: 1.06, 1.07 per IQR increase). Analyses stratified by race/ethnicity showed that associations were strongest for beneficiaries with an unknown or other race and weakest for Black beneficiaries. For summer specific humidity variability, associations barely differed between demographic groups. Patterns of effect modification by temperature, air pollution, or blue space were not very clear for summer average specific humidity (Fig. 3). The associations of summer average specific humidity were stronger in areas with lower greenness levels and negative in areas with higher greenness levels. Associations of summer specific humidity variability

were strongest in areas with lower summer average temperatures, ozone concentrations, and higher greenness and blue space levels.

Associations were generally robust to additional adjustment for precipitation, and regions of the US, as well as exclusion of potentially prevalent cases (Table S2). In models including summer average specific humidity but not summer specific humidity variability, associations of summer average specific humidity were slightly stronger compared to associations of our main model. Associations of models without adjustment for temperature variability or average temperature and temperature variability were generally similar to our main models.

4. Discussion

This study showed that long-term exposure to higher summer average specific humidity and specific humidity variability were associated with increased risk of CVD, CHD, and CBV hospitalization. Associations of summer average specific humidity were stronger for Medicaid eligible individuals and for individuals with an unknown or other race. Associations of summer average specific humidity and specific humidity variability were generally similar in single- and two-exposure models and not affected by adjustment for temperature exposures, precipitation or regions of the US.

4.1. Interpretation of findings

There is some evidence that long-term average temperature exposures are associated with a range of adverse health outcomes (Zanobetti and O'Neill, 2018; Zafeiratou et al., 2021). However, the overall heat load experienced by humans depends on various factors in addition to temperature (McGregor and Vanos, 2018). The heat balance of the human body is regulated by increased blood flow to the skin and by sweating (Donaldson et al., 2003). During warm days, high humidity levels limit sweat evaporation from the body and, in turn, the ability to cool down by sweating. This could lead to a rise in body core temperature and can exert strain on the cardiovascular system (Davis et al., 2016; Donaldson et al., 2003; Baker, 2019). Hence, specific humidity might be a good indicator of physiologically stressful heat exposure. We acknowledge that not much is known about biological mechanisms linking long-term exposure to specific humidity (or heat) and cardiovascular diseases.

To the best of our knowledge, there are no studies that have evaluated associations of long-term specific humidity with CVD hospitalization. Barreca reported that low and high monthly mean specific humidity levels were associated with increased all-cause and CVD mortality rates in US counties (Barreca, 2012). In line with our study, Barreca observed that adjusting for temperature barely affected effect estimates (Barreca, 2012). Another study by Zhang et al. evaluated what weather variables were important in predicting daily heat-related mortality counts (Zhang et al., 2014). They reported that absolute humidity, a measure very similar to specific humidity, was most frequently selected as top predictive weather variable for all-cause and cause-specific (e.g., CVD, stroke) mortality (Zhang et al., 2014). We previously reported associations of summer average temperature with CVD in the same population, but observed that associations of summer average temperature substantially

attenuated after adjustment for summer average specific humidity (Klompmaker et al., 2023).

We observed the strongest associations of summer average specific humidity for beneficiaries eligible for Medicaid and for beneficiaries with an unknown or other race. Individuals of low SES may lack air conditioning and may have more underlying health conditions which make them more vulnerable to specific humidity. Further, we note that the percentage of Hispanics (which make up a large part of the unknown or other race individuals) is higher in the Southwest of the US. Hence, differences in associations between white, Black, and individuals with an unknown or other race might be partially due to differences in regional specific humidity effects. For summer average specific humidity, patterns of effect modification by temperature and air pollution were not very clear, indicating that the strength of the associations is not affected by temperature and air pollution levels. Associations of summer specific humidity variability were strongest in areas with lower summer average temperatures. This might be because individuals in these regions might be less acclimatized to heat, and have limited adaptation measures compared to individuals in areas with higher summer average temperatures. Associations of summer specific humidity variability were also stronger in areas with lower ozone concentrations, and higher greenness. We have no clear explanation for this finding.

4.2. Strengths and limitations

A major strength of this analyses is the inclusion of many types of different climates. We assessed specific humidity levels for each zip code in the contiguous US, for each year from 2000 until 2016. Specific humidity data were available at a relatively fine spatial scale. All our models were adjusted for summer and winter average temperature and temperature variability. Further, our results were robust to additional adjustment for precipitation and region, indicating that the observed associations were independent of regional differences. All Medicare fee-for-service beneficiaries aged 65+ years living in the contiguous US were included in our analyses. However, our Medicare fee-for-service population did not include Medicare-HMO (Health Maintenance Organisations, private plans) beneficiaries. A limitation of this study is that we did not have data about individual-level SES (other than Medicaid eligibility), lifestyle factors and air conditioning. Our models were adjusted for several zip code-level SES and lifestyle indicators, but the potential for residual confounding remains. An important limitation of most studies that evaluated associations of climate-related exposures with health is the use of outdoor measurements. In contrast with temperature, outdoor specific humidity is linear and consistently related to indoor specific humidity (Nguyen and Dockery, 2016). Hence, outdoor specific humidity estimates can be more reliably used to represent indoor conditions compared to temperature. Further, we used current year summer specific humidity exposure and some hospitalizations may have preceded the exposure. However, we observed very strong correlations between the specific humidity exposures in consecutive years (Table S3), suggesting that the impact of potential temporal misalignment of exposures would be small. We note that we could not disentangle if associations of long-term summer specific humidity exposures are due to physiological responses of long-term exposures or cumulative effects of short-term exposures.

5. Conclusions

Higher summer average specific humidity and specific humidity variability were positively associated with CVD hospitalizations among this cohort of US Medicare beneficiaries. Our findings are especially important with respect to climate change, as climate change could lead to higher specific humidity levels.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

The data that has been used is confidential.

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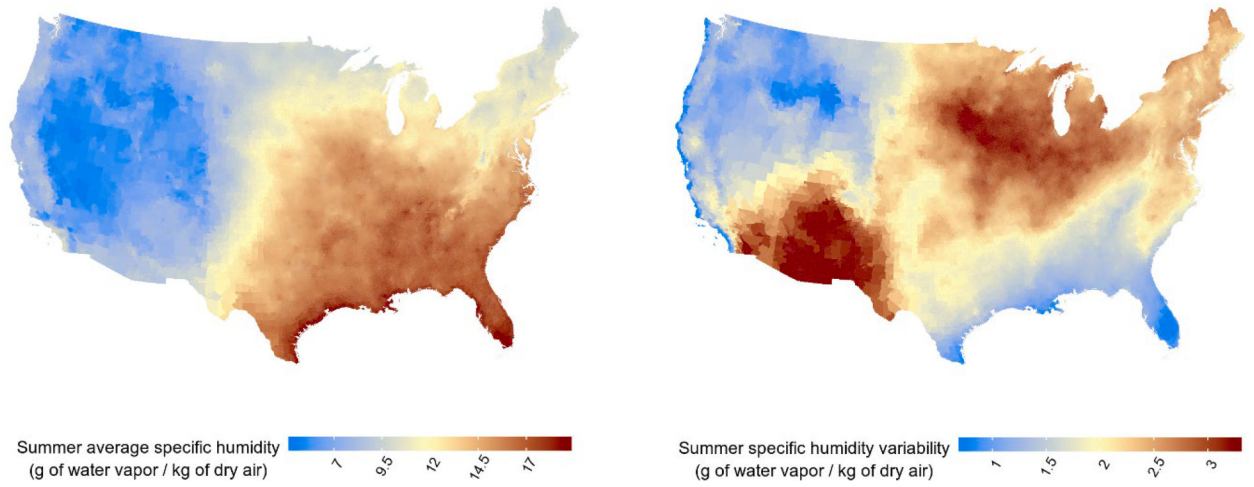


Fig. 1.
 The spatial variation of summer average specific humidity and specific humidity variability per zip code in the contiguous US (year = 2010).

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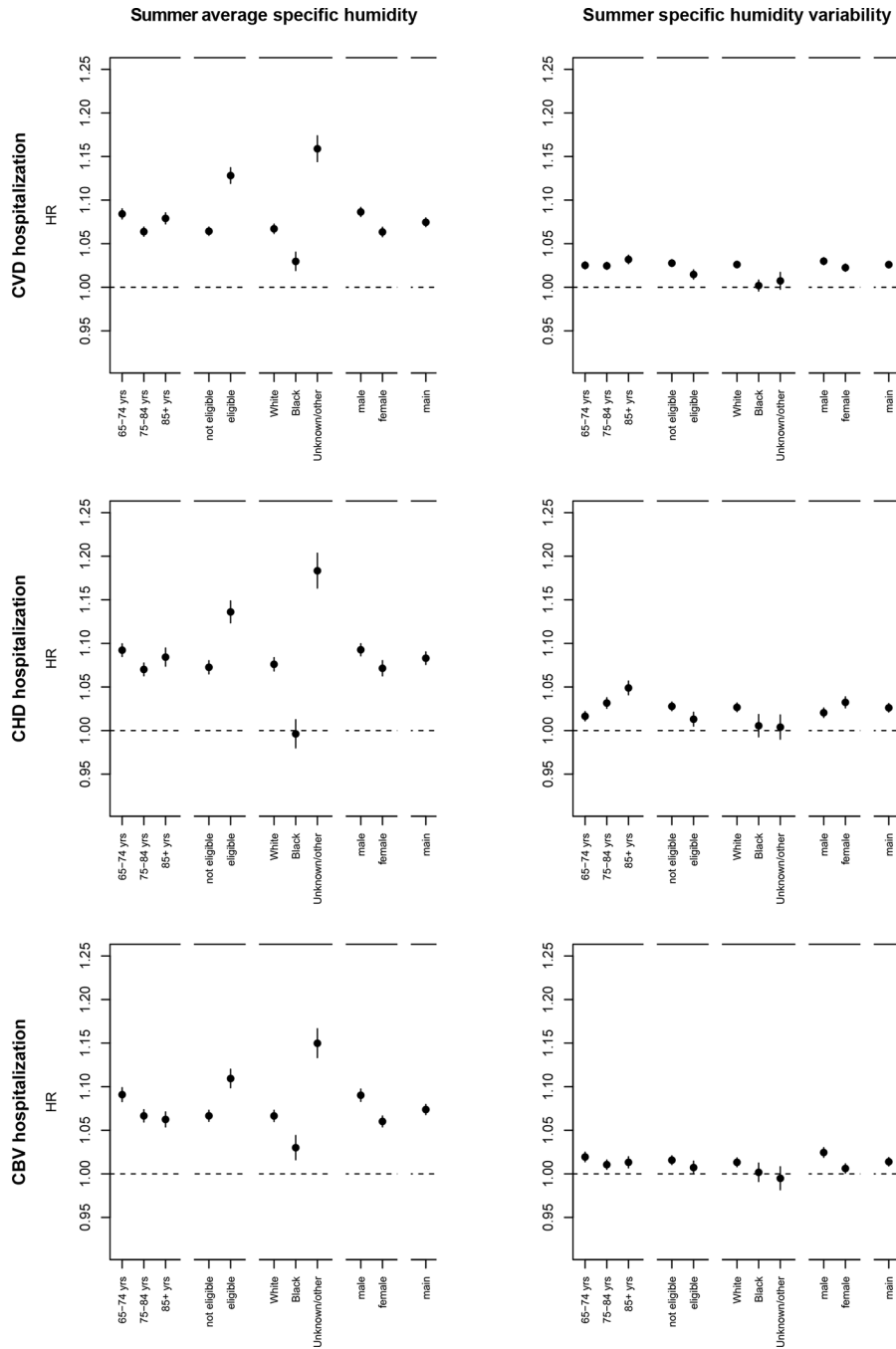


Fig. 2. Associations of summer average specific humidity and specific humidity variability with CVD, CHD and CBV hospitalization in stratified analyses by age (65–74, 75–84, 85 + years), Medicaid eligibility (not eligible, eligible), race (White, Black, unknown/other), and sex (male, female) ^a. ^a Associations are expressed per IQR increase (IQR summer average specific humidity = 4.0 g of water vapor / kg of dry air, IQR summer specific humidity variability = 0.9 g of water vapor / kg of dry air) of the cardiovascular disease hospitalization cohort. Models included summer specific humidity exposures, calendar year, US census

covariates, BRFSS covariates, winter average specific humidity, winter specific humidity variability, summer and winter average temperature, summer and winter temperature variability, an offset for total person-time and strata for all possible combinations of sex, race, Medicaid Eligibility, age at study entry (2-year categories), and follow- up year.

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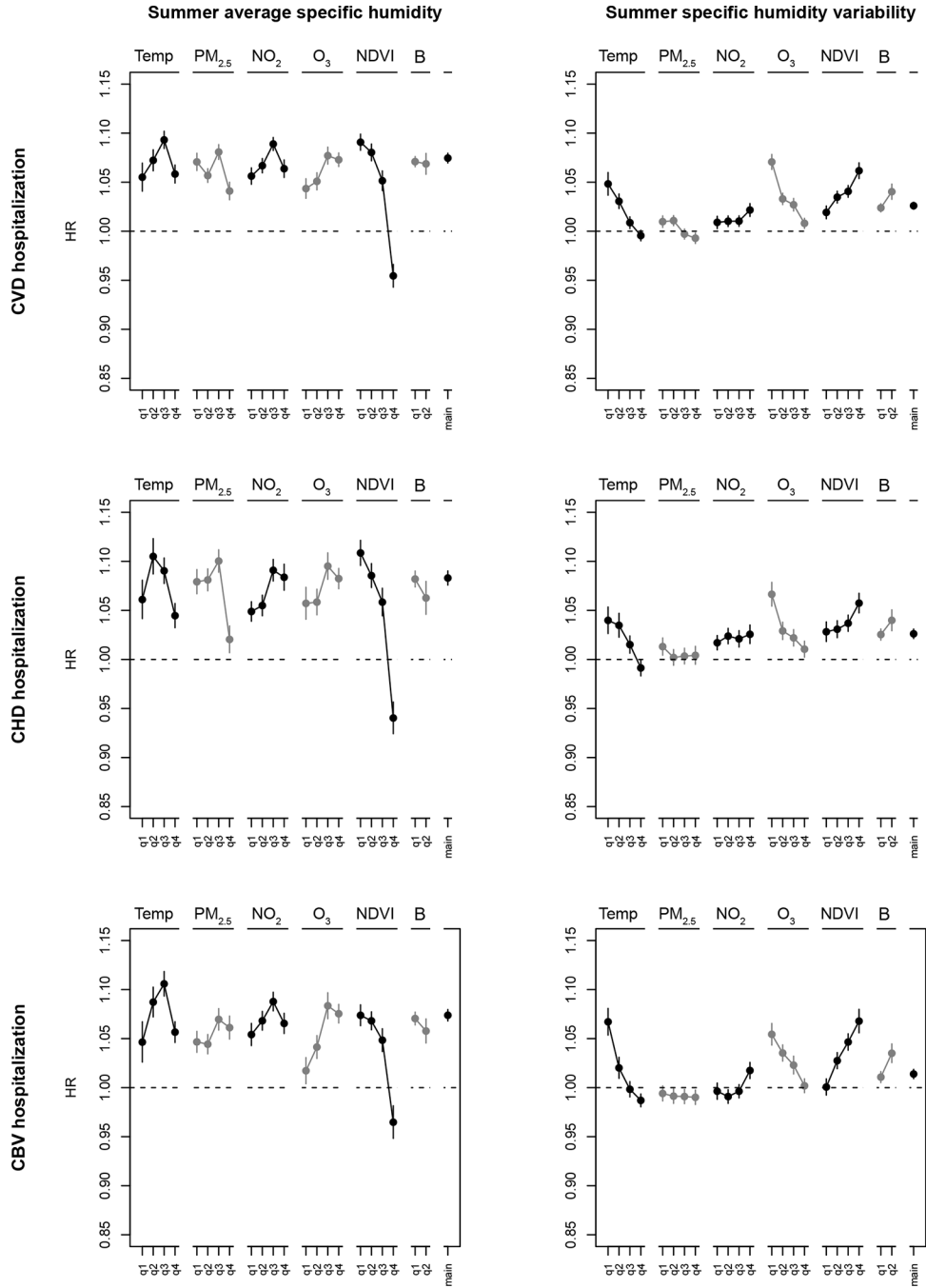


Fig. 3. Associations of summer average specific humidity and specific humidity variability with CVD, CHD and CBV hospitalization in stratified analyses by summer average temperature (Temp), PM_{2.5}, NO₂, ozone (O₃), NDVI and blue space (B) ^{a, b}. ^a Associations are expressed per IQR increase (IQR summer average specific humidity = 4.0 g of water vapor / kg of dry air, IQR summer specific humidity variability = 0.9 g of water vapor / kg of dry air) of the cardiovascular disease hospitalization cohort. Models included summer specific humidity exposures, calendar year, US census covariates, BRFSS covariates, winter

average specific humidity, winter specific humidity variability, summer and winter average temperature, summer and winter temperature variability, an offset for total person-time and strata for all possible combinations of sex, race, Medicaid Eligibility, age at study entry (2-year categories), and follow-up year. ^b To define strata, we used the following quantiles (q25, q50, q75) for the CVD cohort: Summer average temperature (°C): 27.3, 29.9, 32.5; PM_{2.5} (µg/m³): 7.8, 9.7, 11.8; NO₂ (ppb): 10.7, 16.3, 24.6; Ozone (ppb): 36.7, 38.9, 41.1; NDVI: 0.35, 0.52, 0.63; Blue space (% , q75): 2.9. For the CHD cohort: Summer average temperature (°C): 27.3, 29.9, 32.5; PM_{2.5} (µg/m³): 7.8, 9.6, 11.7; NO₂ (ppb): 10.6, 16.1, 24.4; Ozone (ppb): 36.8, 38.9, 41.1; NDVI: 0.36, 0.52, 0.63; Blue space (% , q75): 2.9. For the CBV cohort: Summer average temperature (°C): 27.3, 29.9, 32.5; PM_{2.5} (µg/m³): 7.8, 9.6, 11.7; NO₂ (ppb): 10.6, 16.1, 24.4; Ozone (ppb): 36.8, 38.9, 41.1; NDVI: 0.36, 0.52, 0.63; Blue space (% , q75): 2.9.

Table 1

Descriptive statistics of all US Medicare fee-for-service beneficiaries (n = 63,009,173) during follow-up (2000–2016).

	Individual level data Characteristics at study entry	N (%)
Sex	- Female	34,725,534 (55.1)
Age at study entry	- 65–74 years	48,240,802 (76.6)
	- 75–84 years	10,819,118 (17.2)
	- 85+ years	3,949,253 (6.3)
Race	- White	53,262,938 (84.5)
	- Black	5,511,612 (8.7)
	- Other/unknown	4,234,623 (6.7)
Medicaid eligibility	- Not eligible	55,164,043 (87.5)
	- Eligible	7,845,130 (12.5)
Aggregated data (2000–2016)		
	Zip code level characteristics ^a	Median (IQR)
Summer specific humidity (g of water vapor / kg of dry air)	- Summer average specific humidity	12.0 (4.0)
	- Summer specific humidity variability	2.1 (0.9)
US census covariates	- Population density (persons/mile ²)	517.4 (2919.0)
	- Median home value (\$1,000)	139.4 (145.3)
	- Median household income (\$1,000)	46.0 (24.9)
	- % with less than a high school degree	24.7 (21.6)
	- % below the poverty level	8.6 (8.2)
	- % owner-occupied housing units	71.8 (21.4)
	- % Black	3.7 (13.5)
BRFSS covariates	- % Hispanic	5.0 (14.0)
	- % ever smoked	46.2 (9.1)
Other environmental exposures	- Average BMI	27.4 (1.3)
	- Winter average specific humidity (g of water vapor / kg of dry air)	3.2 (2.2)
	- Winter specific humidity variability (g of water vapor / kg of dry air)	1.3 (0.9)
	- PM2.5 (µg/m ³)	9.7 (4.0)
	- NO ₂ (ppb)	16.3 (13.9)
	- Ozone (ppb)	38.9 (4.4)
	- NDVI (summer)	0.52 (0.27)
	- Blue space (%)	0.4 (2.8)
	- Summer average temperature (°C)	29.9 (5.2)
	- Summer temperature variability (°C)	3.1 (1.2)
- Winter average temperature (°C)	8.4 (11.7)	
- Winter temperature variability (°C)	5.2 (1.9)	
- Summer average precipitation (mm, daily total)	3.1 (2.3)	
- Winter average precipitation (mm, daily total)	2.4 (1.8)	

^aZip code level characteristics are given for the strata (aggregated data based on zip code, year, sex, race, Medicaid eligibility, 2-year categories of age at study entry and year of follow-up) based on the CVD cohort.

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Table 2

HRs of summer average specific humidity and specific humidity variability with CVD (# hospitalizations: 18,610,833, total person years: 401,315,016), CHD (# hospitalizations: 6,607,687, total person years: 448,888,035), and CBV (# hospitalizations: 5,551,735, total person years: 460,574,345) hospitalization in all US Medicare fee-for-service beneficiaries ^a.

Exposure (IQR)	CVD	CHD	CBV
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Summer average specific humidity (4.0 g of water vapor / kg of dry air)	1.07 (1.07, 1.08)	1.08 (1.08, 1.09)	1.07 (1.07, 1.08)
Summer specific humidity variability (0.9 g of water vapor / kg of dry air)	1.03 (1.02, 1.03)	1.03 (1.02, 1.03)	1.01 (1.01, 1.02)

^aAssociations are expressed per IQR increase of the cardiovascular disease hospitalization cohort. Models included summer average specific humidity, summer specific humidity variability and were adjusted for calendar year, US census covariates, BRFSS covariates, winter average specific humidity, winter specific humidity variability, summer and winter average temperature, summer and winter temperature variability, an offset for total person-time and strata for all possible combinations of sex, race, Medicaid Eligibility, age at study entry (2- year categories), and follow-up year.

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