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ORIGINAL RESEARCH

EMERGING TECHNOLOGIES AND INNOVATIONS

Association Between the Incidence of Hospitalizations for Acute Cardiovascular Events, Weather, and Air Pollution

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ABSTRACT

BACKGROUND The incidence of hospitalizations for cardiovascular events has been associated with specific weather conditions and air pollution. A comprehensive model including the interactions between various environmental factors remains to be developed.

OBJECTIVES The purpose of this study was to develop a comprehensive model of the association between weather patterns and the incidence of cardiovascular events and use this model to forecast near-term spatiotemporal risk.

METHODS We present a spatiotemporal analysis of the association between atmospheric data and the incidence rate of hospital admissions related to heart failure (922,132 episodes), myocardial infarction (521,988 episodes), and ischemic stroke (263,529 episodes) in ∼24 million people in Canada between 2007 and 2017. Our hierarchical Bayesian model captured the spatiotemporal distribution of hospitalizations and identified weather and air pollution-related factors that could partially explain fluctuations in incidence.

RESULTS Models that included weather and air pollution variables outperformed models without those covariates for most event types. Our results suggest that environmental factors may interact in complex ways on human physiology. The impact of environmental factors was magnified with increasing age. The weather and air pollution variables included in our models were predictive of the future incidence of heart failure, myocardial infarction, and ischemic strokes.

CONCLUSIONS The increasing importance of environmental factors on cardiovascular events with increasing age raises the need for the development of educational materials for older patients to recognize environmental conditions where exacerbations are more likely. This model could be the basis of a forecasting system used for local, short-term clinical resource planning based on the anticipated incidence of events. (JACC Adv 2023;2:100334) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

CO = carbon monoxide

HF = heart failure

IS = ischemic stroke

MI = myocardial infarction

NO_2 = nitrogen dioxide

O_3 = ozone

PM <2.5 = particulate matter <2.5 μm

SO_2 = sulfur dioxide

Understanding how weather and air pollution levels influence the incidence of acute cardiovascular events could have significant implications for public health, including the timing of weather warnings and allocation of hospital resources. Changes in environmental factors at a regional or a national level have been linked to the incidence of hospitalizations, especially for acute cardiovascular events such as heart failure (HF) decompensation,[1,2] myocardial infarction (MI),[3,4] and ischemic stroke (IS),[5,6] as have air pollutants.[7-9] There are many challenges in establishing an association between weather and cardiovascular risk. One of the reasons for this is that many patient-level factors are also associated with hospitalizations for cardiovascular disease.[10,11] In addition, the impact of weather could be relatively small to be identified in an insufficiently powered study. In order to obtain reliable results, the assessment of a large number of patients with cardiovascular disease and a long observation period are necessary. In this study, we used an extensive data set that spans a broad time period and geography, combined with advanced data analytic methods to determine the granular spatiotemporal association between air pollution and complex atmospheric patterns and the incidence rate of hospital admissions related to HF, MI, and IS. Furthermore, we used the selected air pollutants and weather variables to create a prediction model in order to assess the possibility of using these variables for a short-term forecasting system for adverse cardiovascular events.

METHODS

This population-based cross-sectional study was approved by the Research Ethics Board of the University Health Network (Toronto, Ontario, Canada) and by the Canadian Institute of Health Information. The requirement for patient consent was waived for this study because of the retrospective nature of the study.

STUDY POPULATION. Hospital admissions and mortality related HF, MI, and IS for a 10-year period (April 1, 2007 to February 27, 2017) were obtained from the discharge abstract database maintained by the Canadian Institute for Health Information. Submission of administrative data to the Canadian Institute for Health Information is legally mandated for all hospitals in Canada except for those in Quebec. In Canada, the entire population is covered by a single-payer universal health plan. A universal provincial health number was provided in an encrypted format for each case, which allowed us to identify hospital transfers and multiple admissions.

We included deidentified patient data from hospital admissions where the primary diagnosis was HF (International Statistical Classification of Diseases and Related Health Problems-10th Revision, Canada, standard code I50.0-I50.9), MI (I21.0-I21.9), ischemic and other strokes (I63.0-I63.0, I64), hemorrhagic stroke (I60.0-I60.9, I61.0-I61.0), and ventricular tachycardia and supraventricular tachycardia (I47.1-I47.2, Y71.2). There were some modifications of the International Classification of Diseases definitions for strokes in ∼2014 which increased the measured incidence after the change. For hospitalizations related to hemorrhagic stroke ($n = 58{,}593$) and supraventricular tachycardia ($n = 100{,}459$), the sample size was too small and as such, the results were inconsistent and therefore not reported here.

In order to define episodes of care, multiple admissions of the same patient were considered as separate incident cases only if the discharge date of the previous admission was at least 30 days from the following admission. The first admission of an episode was referred to as the index admission, and any subsequent admissions within the same episode were considered readmissions associated with the index admission.

We identified 2,401,764 discharge records for 1,344,142 unique patients of at least 18 years of age diagnosed and hospitalized with an acute cardiovascular event between April 1, 2007, and February 27, 2017. A total of 1,192,601 patients who underwent 1,747,869 hospitalizations were included in the study. A flowchart depicting the number of discharge patient records, the number of patients diagnosed with 1 of the 3 acute cardiovascular event types, the number of hospital admissions related to an acute

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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cardiovascular event as well as the exclusion criteria is presented in Supplemental Figure 1. Patients with a place of residence in Quebec who were admitted in a hospital outside of Quebec were excluded since the Canadian Institute for Health Information does not release data for this province, and patients from Northern Canada (Northwest Territories, Nunavut and Yukon) were excluded due to a very low population density.

SPATIOTEMPORAL MODELING AND PREDICTION MODELS. The number of hospitalization episodes was analyzed using the Besag-York-Mollie model[12] with a spatial, temporal, and spatiotemporal effect. The model was adjusted for gender and age distribution. The initial set of 17 weather and pollution variables were obtained from the European Centre for Medium-Range Weather Forecasts products ERA (ECMWF is the European Centre for Medium-Range Weather Forecasts)-Interim,[13] ERA-5,[14] and CAMS (Copernicus Atmosphere Monitoring Services).[15] Initial selection of variables consisted of those environmental variables that are known or have been reported to affect human health and were available in the European Centre for Medium-Range Weather Forecasts data sets for the study period. We also included variables derived from the original weather variables, their interactions, lags, and changes within the last week. They were added to the model in a step-wise procedure, and variables or variable pairs were selected based on the Watanabe-Akaike information criterion which is an estimate of the out of sample prediction accuracy[16] and a measure for goodness of fit. The posteriors of the models were estimated using an Integrated Nested Laplace Approximation through the R-Package R-INLA, version 20.03.17. In order to test the predictive ability of our final multivariate Bayesian model, we used the data from March 2016 to February 2017 as test data set (unlabeled) and the rest as training data and compared the observed and predicted outcomes of the period used as holdout set. In order to facilitate the comparison of model results with observations, standardized incidence rates, which represent the observed vs expected number of hospitalization and are obtained from the model's posterior distribution, were transformed into event rate.

Details of the development and parametrization of the spatiotemporal models are provided in the Supplemental Material. All analyses were performed using the R Project for Statistical Computing v4.0.2.

RESULTS

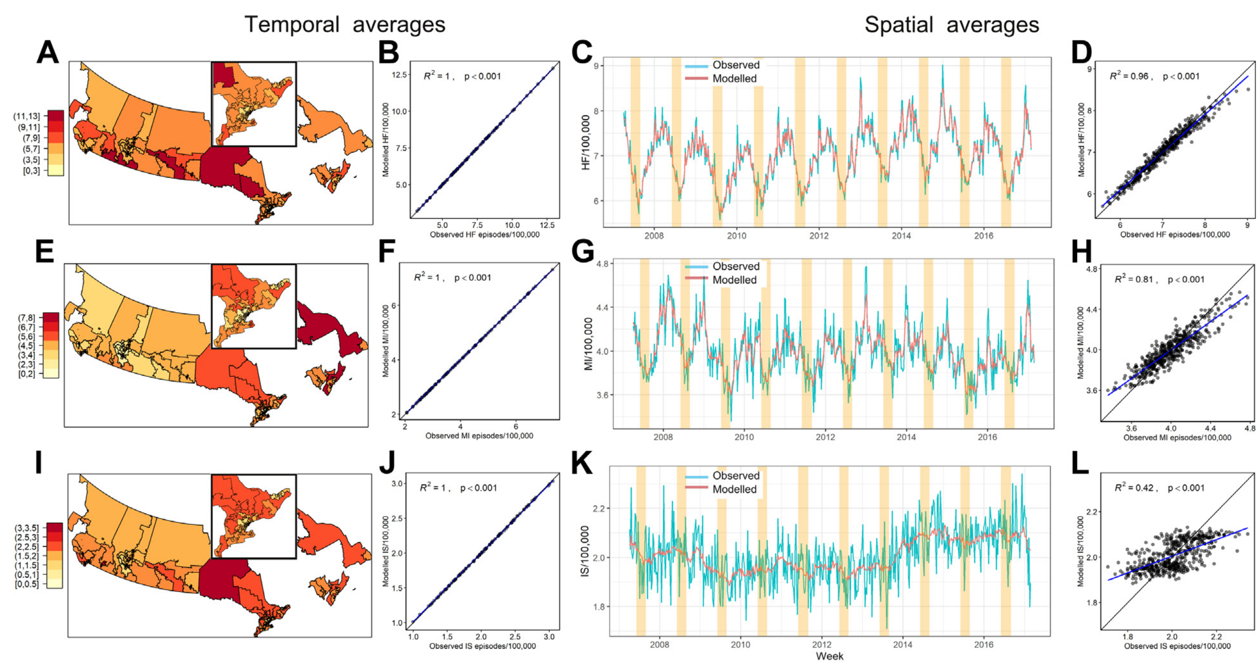
INCIDENCE OF HEART FAILURE, MYOCARDIAL INFARCTION, AND ISCHEMIC STROKE. This population-based study includes a Canadian population from 2007 to 2017 (24 out of 35 million people). We studied 922,132 hospitalization episodes related to HF, 521,988 related to MI, and 263,529 related to IS (Supplemental Figure 1). The annual incidence of hospital admissions per 100,000 adults were 366 for HF, 208 for MI, and 105 for IS.

MODELED AND OBSERVED HOSPITALIZATION RATES. The rate of hospital admissions was elevated in the mid to western part of Ontario for all 3 acute cardiovascular event types, in the most eastern parts of Canada for MI and IS, and in British Columbia for HF (**Figure 1**). The rates were generally reduced around large cities such as Vancouver, Edmonton, and Toronto. The correlation between modeled and observed weekly episode rates across the study region was above 0.97 for all 3 acute cardiovascular event types (**Figures 1B**, **1F**, and **1J**).

There was no clear temporal trend for hospital admissions related to HF and MI, whereas for IS, an unusually high incidence was observed around 2014 to 2016 (**Figure 1K**). The time series show a clear seasonal pattern for hospital admissions related to HF and MI with high levels in winter and low levels in summer months (**Figures 1C** and **1G**), as also seen in the linear and nondynamic temporal trend of the models (Supplemental Appendix). The modeled rates also correspond reasonably well to the observed rates across time, with correlations of 0.96 for HF, 0.81 for MI, and 0.42, for IS (**Figure 1**, last column).

ENVIRONMENTAL FACTORS ASSOCIATED WITH THE INCIDENCE OF HEART FAILURE, MYOCARDIAL INFARCTION, AND ISCHEMIC STROKE. All weather and air pollution variables considered in the model building process are listed in the Supplemental Table 1. Since environmental factors might affect people of different ages differently, we modeled hospital admissions for the entire population and for 5 age groups (18-39, 40-49, 50-59, 60-69, and 70 years and older) separately. The models that included covariates related to weather and air pollution showed a better performance (lower Watanabe-Akaike information criterion) compared to models without covariates for all 3 acute cardiovascular event types for the total population (**Table 1**) and age-specific subgroups, with the exceptions of ages 40 to 49 years and ages ≥60 years for MI (**Central Illustration**).

FIGURE 1 **Comparison of Modeled and Observed Cardiovascular Event Rates**



(Top to bottom) Heart failure, myocardial infarction, and ischemic stroke. **(First column)** Map of study region showing multi-year average of weekly observed episodes **(A, E, I)**. White areas do not belong to the study region. The area around Toronto is inserted with enlargement onto the map for better visibility. **(Second column)** Scatterplots of observed and modeled episodes **(B, F, J)** corresponding to maps. Multi-year averages consist of averages of 517 weeks and are therefore relatively smooth. The maps of the modeled multi-year averages, which look identical to the maps of observed values, are not shown. **(Third column)** Time series of observed (blue) and modeled (red) hospitalizations rates, averaged over 100 study regions **(C, G, K)**. The summer season (June-August) is highlighted with orange and shows reduced heart failure and myocardial infarction rates. **(Last column)** Scatterplots of observed vs modeled episodes **(D, H, L)** corresponding to time series. **Blue line** represent the linear regression of the scatterplot of the observed vs modeled incidence. HF = heart failure; IS = ischemic stroke; MI = myocardial infarction.

For different age groups, the variable selection process resulted in different numbers of variables and interactions that influenced hospitalizations (Supplemental Figure 2). The models for all types of acute cardiovascular events selected the smallest number of influential covariates in people under the age of 39 years—mostly UV radiation for IS (**Figure 2**), wind interacting with carbon monoxide (CO) for HF, with sulfur dioxide (SO_2) for MI, and with air pressure (labeled ‘surface pressure’) for IS (interactions shown in Supplemental Appendix). The largest numbers of influential covariates—including low temperatures, high/low wind speeds, high/low air pressures, wet/dryness, as well as many air pollutants—were found in individuals 60 to 69 years of age for HF, 50 to 59 years of age for MI, and over 70 years of age for IS, suggesting that environmental covariates and their interactions became increasingly important as patients aged.

In the overall population as well as with increasing age, the risk for HF hospitalizations is especially increased in conditions with low air pressure (Supplemental Appendix). The risk for MI depends on high air pressure (surface pressure lag) and increased precipitation (**Figure 2**) as well as SO_2 in interaction with temperature (Supplemental Appendix). The risk for IS is higher with high air pressure, low evaporation, and increased SO_2 (**Figure 2**). In general, our models found a large number of influential variables and interactions.

The incidences of hospitalizations resulting from a model with the covariates described above and for all ages were compared to observations unseen by the model (out-of-sample validation). The results demonstrate a good predictive ability of the model for HF and MI and a lower ability for IS (Figure 3).

DISCUSSION

COMPARISON TO PREVIOUS STUDIES. Spatiotemporal models have been used for analyzing environmental variables and health associations for the last 2 decades in North America.[17,18] However, the analytic approach used in the present study, made to explore the spatiotemporal association between environmental factors and the incidence of hospital admissions related to cardiovascular events, both at a granular level and by using the interaction between the various factors, is novel. Previous studies have used Canadian data to investigate the relations between environmental variables and acute cardiovascular events, but often considered a single or a few environmental variables at a time (vs 18 original and 4 derived variables in this study), and explored the associations with mortality and not hospitalizations.[19-22] Furthermore, we purposefully decided to use a data-driven approach to identify the variables and interactions that were contributing to the model as opposed to using a hypothesis-driven variable selection. This approach allowed us, not only to confirm that previously described and hypothesized associations remained valid but also to identify novel associations.

While low temperatures have been shown to be associated with an increased risk of hospital admissions related to HF, MI, and IS in several previous studies[1-8,23-30] (see also Supplemental Table 2), other variables such as air pressure, wind velocity, humidity, and air pollutants have been infrequently studied and yielded inconsistent results. This might partly be because of the complex interactions with other environmental variables, smaller sample sizes, and the heterogeneity of the geographic regions among the studies. Previous studies have partially explored the interaction between environmental factors and age, most often in a dichotomous manner as opposed to in a progressive manner.[2,5,23-28,31] By analyzing age as a multilevel categorical variable, we were able to show a progressive increase in the importance of environmental factors in relation to hospital admissions for acute cardiovascular events as one ages. More specifically, we showed that in the youngest ages, hospital admissions were related to wind speed and air pollutants (type of air pollutants depended on the specific acute cardiovascular event). As one ages, low temperature, high/low wind speed, high/low pressure, wet/dryness, and air pollutants also became associated with the incidence of cardiovascular events. The increased importance of environmental factors with increasing age might be explained by impaired thermoregulatory control in the elderly, as well as an increased burden of cardiovascular risk factors as one ages.[32,33]

TABLE 1 Number, Incidence Rate per 100,000 People in the Respective Age Group and Model Performance With and Without Weather and Pollution-Related Covariates for Each Acute Cardiovascular Event Type

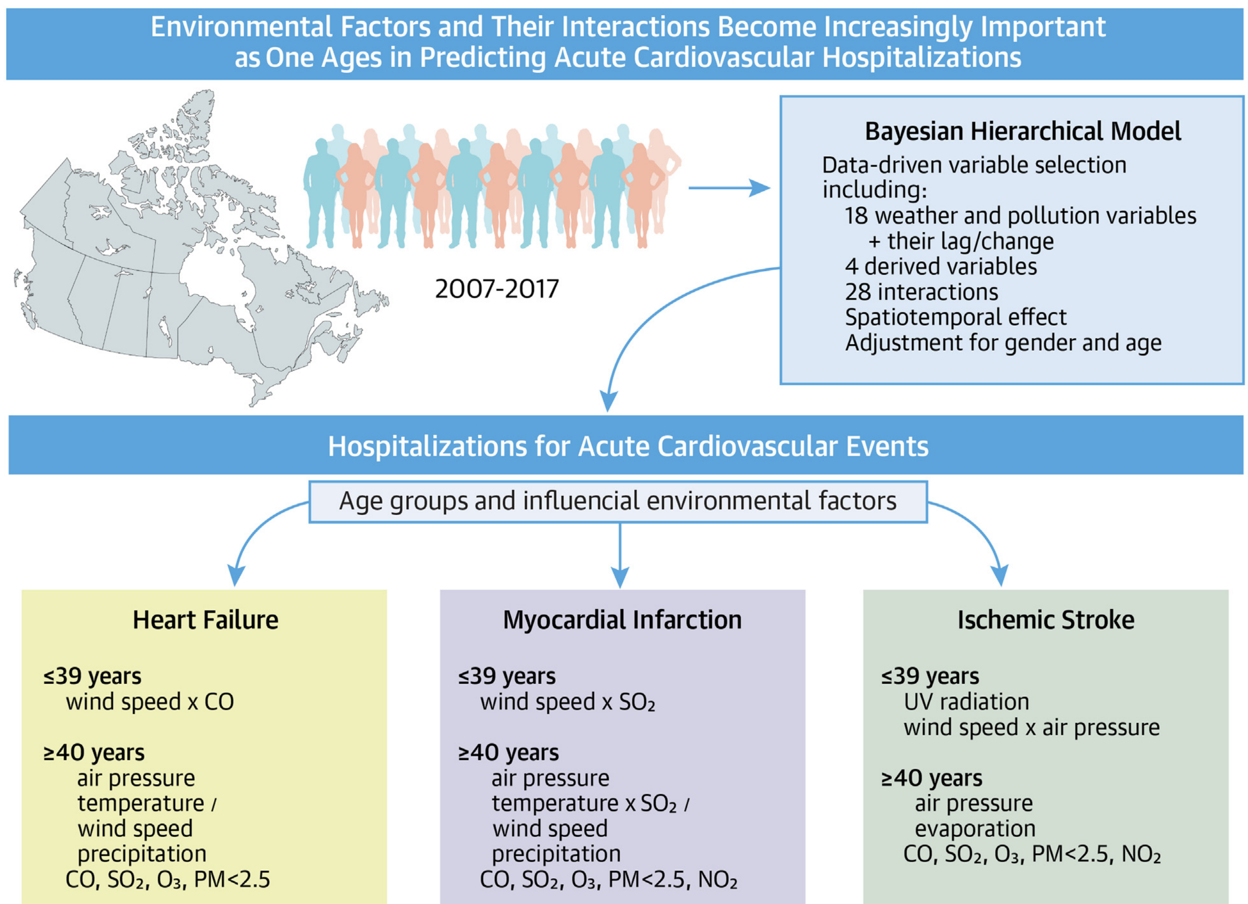
	Total Number of Episodes	Annual Incidence Rate	WAIC[a] Without Covariates[b]	WAIC With Covariates[c]
Heart failure				
Total population	922,132	366.1	296496.8	296288.3[d]
Age 18-49 y	7,588	11.7	44207.8	44204.5[d]
Age 40-49 y	15,998	43.2	70833.6	70820.5[d]
Age 50-59 y	53,772	145.8	132813.9	132793.4[d]
Age 60-69 y	128,547	492.1	184813.7	184788.0[d]
Over age 70 y	716,227	2,785.0	282736.1	282580.6[d]
Myocardial infarction				
Total population	521,988	208.1	265167.8	265161.7[d]
Age 18-49 y	7,829	12.2	45065.2	45065.1[d]
Age 40-49 y	38,559	103.9	115148.5	115149.0
Age 50-59 y	93,682	252.8	167219.6	167218.1[d]
Age 60-69 y	118,200	446.8	179988.3	180018.2
Over age 70 y	263,718	1,016.5	227169.6	227171.2
Ischemic stroke				
Total population	263,529	104.7	226652.7	226650.9[d]
Age 18-49 y	4,398	6.7	30213.7	30194.2[d]
Age 40-49 y	10,084	27.2	53710.8	53698.8[d]
Age 50-59 y	26,431	71.4	95086.3	95073.8[d]
Age 60-69 y	46,939	178.6	126336.5	126333.8[d]
Over age 70 y	175,677	678.8	203267.6	203259.2[d]

A lower WAIC value indicates a better estimated predictive ability. Models with environmental covariates have lower WAIC values, except for MI in individuals 40 to 49 years of age and 60+ years of age. [a]Watanabe-Akaike information criterion. [b]Models with spatial, temporal, and spatiotemporal effect that were only adjusted for age and gender distribution. [c]Models with spatial, temporal, and spatiotemporal effect that were adjusted for age and gender distribution as well as the weather and pollution-related covariates that were selected by the variable-selection procedure, also referred to as 'final model.' [d]Cardiac events and age-groups for which adding covariates improved the model performance, indicating that weather and pollution variables explain part of the distribution of the hospitalization episodes.

MI = myocardial infarction; WAIC = Watanabe-Akaike information criterion.

HEART FAILURE. Hospitalizations related to HF have been linked to high-pressure systems[1] and the air pollutants SO_2 and nitrogen dioxide (NO_2) but not ozone (O_3),[34,35] whereas associations with humidity[1,2] and the air pollutants particulate matter <2.5 μm (PM <2.5)[34-36] and CO,[29,34-36] have been inconsistent. Our results showed that in younger individuals, HF related hospitalizations were especially associated with the interaction between wind speed and CO. As one ages, low-pressure systems as well as low temperatures, along with both high and low wind speeds, wetness, and the air pollutants CO, SO_2, O_3, and

CENTRAL ILLUSTRATION **Association Between Weather, Air Pollution and Acute Cardiac Hospitalizations**



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The main outcome of this study is the standardized incidence rate for hospitalization for acute cardiovascular events in Canada over a 10-year period. We evaluated the association between these outcomes and environmental factors using a Bayesian hierarchical model. This study shows that the association between environmental factors and hospitalization rate is age-dependent both in the number and type of environmental factors associated with various types of acute events. CO = carbon monoxide; NO_2 = nitrogen dioxide; O_3 = ozone; PM <2.5 = particulate matter <2.5 μm; SO_2 = sulfur dioxide.

PM <2.5 became important. In contrast to previous work, we did not find an association with NO_2. Novel findings were the relation between age-specific HF hospitalizations and wind speed, low-pressure systems, and the air pollutant O_3. A previous study[1] that found an association between high atmospheric pressure and hospitalizations related to HF differed in several ways from the present study. For instance, it only included 112,793 individuals, and they were all 65 years of age or above and from a specific region. Furthermore, only few environmental variables were investigated, and the endpoint was a combination of HF related hospitalizations and deaths.

MYOCARDIAL INFARCTION. Hospitalizations related to MI have been linked to humidity,[26] high wind speed,[3,26,28] PM <2.5,[37] and CO,[29,37] whereas associations with pressure,[3,26,28] SO_2,[37,38] NO_2,[37,39] and O_3,[37,39] have been inconsistent. Our results showed that in younger individuals, MI related hospitalizations were associated with the interaction between wind speed and SO_2. As one ages, high-pressure systems as well as the interaction between low temperatures and high SO_2, along with high and low wind speeds, wetness, and all 5 air pollutants became important. Similar to our study, Radisauskas et al[28] showed that in 6,753 patients with MI, there was an

FIGURE 2 Summary of Final Models

Variable abbreviations:
Inst. north.: Instantaneous northward
Inst. eastw.: Instantaneous eastward

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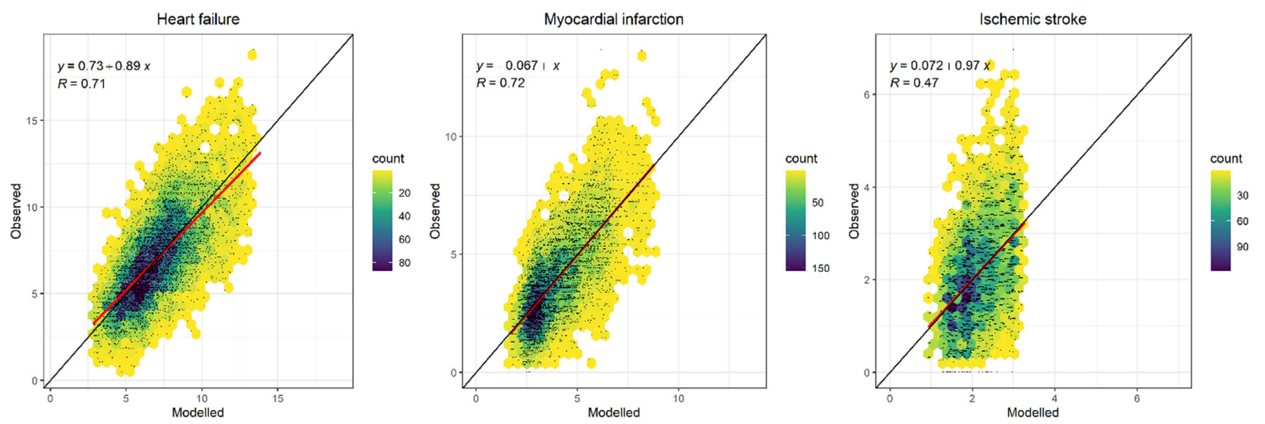
FIGURE 3 Predictive Ability of Final Models



Scatterplots of predicted and observed hospitalization rates per 100,000 people for heart failure, myocardial infarction, and ischemic stroke, with Pearson correlation and regression equation and line **(red)**. Predictions were produced with the final multivariate Bayesian models on a hold-out data set covering March 2016 to February 2017. Each **dot** represents a 1-week period after March 2016. To facilitate interpretation, the plot region was divided into regular hexagons, and the **dots** in each hexagon counted **(color)**.

association, albeit weak, between high atmospheric pressure and hospitalizations related to MI in especially older patients aged 65 to 84 years. In contrast, 2 other studies[3,26] showed either an inverse or no relation between atmospheric pressure and MI related hospitalizations, respectively. In the former study,[3] which investigated the association of weather with day-to-day incidence of MI in 274,029 patients using the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) registry, the authors found that low air temperature, low atmospheric air pressure, high wind velocity, and shorter sunshine duration were associated with increased risk of MI. However, there was no significant difference between patients above and below 75 years of age. It is possible that the authors had seen an age-effect had they used more than 2 age categories. For the latter study,[26] which included 6,499 patients with acute cardiovascular diseases, the diagnosis of MI was not separated from the acute cardiovascular diseases and thus results for hospitalizations alone cannot be derived. For SO_2, many studies have shown an association with MI related hospitalizations.[37,38] However, to our knowledge, no study has examined the interactions between SO_2 and environmental variables in different age-groups. Overall, our results not only replicated previous findings but also extended them by showing that interactions with SO_2 play an important role for

FIGURE 2 Continued

Model coefficients expressed as probabilities of standardized incidence rates being larger **(red)** or smaller **(blue)**. Probabilities <50% are not shown because the sum of the probability for standardized incidence rate >1 and that for standardized incidence rates <1 is equal to 100%. Probabilities for standardized incidence rate >1 indicate a positive association, while those for standardized incidence rate <1 indicate a negative association. The size of the points is proportional to the probabilities. Probabilities were obtained directly from the posterior distributions. Coefficients for all variables, derived variables, lags, and 1-week changes that were selected by the final multivariable model are shown for each age-group as indicated by the numbers on the x-axis. If a variable's coefficient is not shown here, it means that either the variable was not selected in the final model or that it was part of a selected interaction and therefore only shown in the Supplemental Appendix where coefficients for all interactions are presented. CO = carbon monoxide; NO_2 = nitrogen dioxide; SIR = standardized incidence rate; SO_2 = sulfur dioxide.

MI related hospitalizations and that different environmental variables and their interactions were important in different age-groups.

ISCHEMIC STROKE. For IS, hospital admissions have been linked to all 5 air pollutants,[40] variability in pressure,[5,6,31] and low UV radiation,[41] whereas associations with pressure,[31,42] humidity,[5,30,42] and wind speed[5,30] were inconsistent. Our results showed that in younger individuals, hospitalizations related to IS were associated with increased UV radiation, and the interaction between wind speed and pressure. As one ages, high-pressure systems and dryness became important, as did all air pollutants but especially SO_2. In accordance with our study, Quemei et al[31] found that in 946 patients with IS, hospitalizations were related to increased pressure and that this relation was more pronounced in the elderly. In contrast, a recent systematic review and meta-analysis[42] of 11 studies containing 314,385 patients found that although the effect of pressure varied across studies, the overall pooled effect estimate indicated no relation between pressure and hospital admissions related to ischemic and hemorrhagic stroke. However, as the authors pointed out, the studies were inconsistent in study design, had small sample sizes, and the results were not adjusted for confounders.

The evidence for the association between UV radiation and hospitalization due to IS is very scarce. One study[41] found that in 16,606 patients aged 45 years of age or above, lower levels of sunlight radiation were associated with higher stroke incidence, both on short- and long-term basis. A direct comparison with our study is difficult due to different study designs. For instance, in the study by Kent et al,[41] the patients were followed up after 1, 2, 5, 10, and 15 years of exposure to sunlight radiation, whereas our study had a cross-sectional design. Novel findings of the present study were the relation between IS hospitalizations and UV radiation and the interaction between wind speed and pressure in the youngest age-group. One should, however, be more careful in drawing conclusions regarding IS as the predictions for that event type were less good than for MI and HF, which could be due to the lower event rate or because strokes can occur due to nonenvironmental causes that are missing in our model.

PHYSIOLOGICAL EFFECTS OF WEATHER AND AIR POLLUTION. Results from this study suggest that air pollutants and weather interact in complex ways to influence the body's physiological mechanisms that can potentially increase the risk of an acute cardiovascular event. Hospital admissions related to HF, MI, and IS were particularly associated with air pollutants, wind velocity, and their interactions. The air pollutants SO_2, PM <2.5, and O_3 are known respiratory irritants. They can cause lung inflammation[35] or—along with CO—hyperviscosity, which can both lead to systemic inflammatory responses[43] or enhanced coagulation/thrombosis.[43,44] The pathophysiological changes that result from systemic inflammation include oxidative stress, endothelial dysfunction, and platelet activation, which can eventually result in a thrombotic reaction, or progression of atherosclerosis with plaque instability or plaque rupture. In addition, PM <2.5 and O_3 are known to cause peripheral arterial vasoconstriction which can elevate blood pressure and lead to increased cardiac demand.[45]

Cold temperatures were found to play a role in the incidence rates for hospital admissions due to most acute cardiovascular event categories. Cold temperatures cause several pathophysiological changes such as upregulation of the sympathetic nervous system, leading to increased cardiac contractility, heart rate, rate of relaxation, and impulse conduction through the atrioventricular node.[46] These changes increase the levels of plasma catecholamine and vasopressin, which then intensifies the activity of the renin angiotensin system, leading to salt and water retention and volume overload.[47] This cascade of reactions causes peripheral vasoconstriction and increases cardiac demand by increasing blood pressure, thus making it more difficult for oxygen to be extracted from red blood cells and consequently leading to acute decompensation.[48-51] Exposure to the cold has also been shown to exert negative effects on inflammation and hemostasis through the activation of specific molecules, leading to an inflammatory and hypercoagulable status, with a higher risk of developing thromboembolism.[49,52,53]

We further found that low-pressure systems and atmospheric humidity were associated with increased hospitalizations for HF in the overall population as well as in the elderly. Low-pressure systems are accompanied by a decrease in the partial pressure of inspired oxygen, a reduction of alveolar CO_2 pressure, and an increase in air humidity. All of these cause a decrease in blood pressure and blood flow velocity.[54] Hypotension and decreased oxygen extraction could lead to HF decompensation in patients who have a limited cardiac reserve. On the other hand, high-pressure systems, which were found to be associated with MI and IS, increase cardiac demand by increasing blood pressure and causing tachycardia, both of which can result in decreased cardiac output.[55] Moreover, increased water in the air, which could increase risk either via drops of moisture that can create a surface of condensation when the vapor is inhaled, triggering a coagulation cascade through hyperviscosity, or droplets of water that carry air pollutants, raising the risk of thromboembolism,[56,57] was related to MI and IS.

STUDY LIMITATIONS. This study is an ecological study and as such, results only represent associations; none of the conclusions of this study should be construed as representing causal relationships. Furthermore, this study used administrative data, which are known to have limited accuracy, and it is possible that some hospitalizations have been misclassified (either false positive or false negative). In addition, there could be unmeasured confounders in the association between environmental factors and acute cardiovascular hospitalizations such as socioeconomic status. Specifically, low socioeconomic status has been linked to both poor health outcomes and environmental risk factors such as rural areas and some but not all air pollutants.[58-61] Further investigations should be carried out to determine how socioeconomic factors mediate changes in the effects of environmental factors and hospitalization for acute cardiovascular events.

CONCLUSIONS

We derived a mathematical model of the spatiotemporal association between complex atmospheric data and the incidence rate of hospital admissions related to HF, MI, and IS. This population-based study of 24 million people covers a broad geography span and a recent 10-year time frame. It is unique in both the size of the population studied and the analytical approach used which allows to model multiple risk factors together as opposed to look at them in isolation. By analyzing 5 progressive age groups, we were able to explore the associations across different age groups and found that environmental factors become more important as people age. The clinical implication of these findings is that patients, particularly older ones, should be provided with educational materials and resources to recognize the types of environmental conditions associated with higher risk of exacerbations. These conditions, as identified in our study, include lower temperatures, high wind speed, atmospheric pressure, high precipitation, and high degrees of pollution, and could eventually be combined into local short-term environmental risk indices. Patients could then be counseled to avoid going outside and pay particular attention to manageable risk factors during periods of high risks.

Moreover, we showed that accounting for environmental factors and their interactions improves our ability to model the spatiotemporal incidence of hospitalization for acute cardiovascular events. By using the first 9 years of data as a training set, we were able to accurately predict the spatiotemporal incidence of hospitalizations for HF and MI, and to a somewhat lower degree of IS in the last year of the data. Our prediction models showed good concordance of the observed and predicted spatiotemporal incidences, which means that establishing a forecasting system for acute cardiovascular events might be possible. Such a system would eventually allow health care systems to more efficiently allocate health care resources in period of high expected incidence.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In this large population-based study of 24 million people constituting 0.9, 0.5 and 0.3 million hospital admissions related to HF, MI, and IS, respectively, and covering a broad geography span and a recent 10-year time frame, we showed that acute cardiovascular events and environmental factors interact in complex ways, with increasing complexity in the older population. More specifically, hospital admissions for acute cardiovascular events were related to wind speed and air pollutants in the youngest ages, whereas low temperature, high/low wind speed, high/low pressure, wet/dryness, and air pollutants, became increasingly important as one ages. By accounting for these environmental factors and their interactions, we were able to accurately predict the spatiotemporal incidence of hospitalizations for HF and MI, and to a somewhat lower degree of IS.

TRANSLATIONAL OUTLOOK: Patients at high risk of cardiovascular events, particularly older ones, should be educated on the environmental circumstances associated with increased risk of exacerbations and subsequent hospitalization. The environmental factors along with their interactions, as identified in our study, could eventually be combined into a forecasting system to be used for local short-term forecasting of the incidence of cardiovascular events which in turn could be used for local resource planning during high-risk periods. For example, patients could be counseled to avoid going outside and pay particular attention to manageable risk factors during periods of high-risk environmental factors.

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KEY WORDS acute cardiac events, heart failure, hospital admissions, pollution, spatiotemporal patterns, weather

APPENDIX For supplemental tables, figures, and Methods, please see the online version of this paper.