Title: Valve disease and hypotension hospital admissions peaked at physically equivalent temperature 0°C in Germany in 2009-2011

Article Type: Letter to the Editor

Keywords: hospital admission, weather, risk factor, biometeorology, pulmonary heart disease, pulmonary embolism

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Dearest Editor,

Please find attached a Letter entitled “Valve disease and hypotension hospital admissions peaked at physically equivalent temperature 0°C in Germany in 2009-2011”, which we would like to submit for publication in International Journal of Cardiology.

This manuscript has not been published or under consideration by other scientific journals elsewhere. The research was funded by the EU FP7 (n° 262608) The authors have read and approved the final manuscript.

The authors are also very happy to provide analysis scripts (i.e. in STATA; DO file), and results outputs anytime upon request since the data are institutional/publicly available. Moreover, the authors would like to consider modifying the manuscript to suit other categories (such as Research Article, Short Report, Rapid Communication, Case Study, Technical Note, new Development, Viewpoint, Letter..) in the present Journal, if this were more appropriate for the Journal readers.

Your consideration of this article is greatly appreciated indeed!

Yours sincerely,

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This statement is to certify that all Authors have seen and approved the manuscript being submitted. We warrant that the article is the Authors' original work. We warrant that the article has not received prior publication and is not under consideration for publication elsewhere. On behalf of all Co-Authors, the corresponding Author shall bear full responsibility for the submission.

This research has not been submitted for publication nor has it been published in whole or in part elsewhere. We attest to the fact that all Authors listed on the title page have contributed significantly to the work, have read the manuscript, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission to the International Journal of Cardiology.
Valve disease and hypotension hospital admissions peaked at physically equivalent temperature 0°C in Germany in 2009-2011

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Conflict of interest
None.

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Valve disease and hypotension hospital admissions peaked at physically equivalent temperature 0°C in Germany in 2009-2011

Cover title: Weather and hospital admissions

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Keywords: hospital admission, weather, risk factor, biometeorology, pulmonary heart disease, pulmonary embolism
Environmental factors have been central to many human chronic diseases and the weather is of no exception. The effect of the weather has been noted in scientific literature since the 1930s as increased hospital admissions due to coronary occlusion and heart failure were firstly observed in low temperature which has prompted the concern on the influence of the seasonality effect. However, overall across the globe, conflicting results on the effect of the weather on health outcomes have been presented in literature. While there could have exhibited a complex interactions between the weather and health outcomes, methodological concerns on previous research have been brought up recently. Therefore, we aimed to provide epidemiological evidence on the relationship of the weather as biometeorological, and hospital admissions due to valve disease and hypotension that could have been less studied in a national setting in Germany in the recent years.

Daily historical meteorological data including air temperature, humidity, wind speed, radiation flux, cloud cover, and vapour pressure between 1 January, 2009 and 31 December, 2011 (3 full calendar years) were obtained from Federal Ministry of Transport, Building, and Urban Development (more details via: http://www.dwd.de/). Daily hospital admissions with all diagnoses including emergency admissions in the same study period were extracted from the database held in Statistisches Bundesamt (more details via: https://www.destatis.de/EN/Homepage.html), Wiesbaden, Germany. Statistisches Bundesamt randomly select 10% of hospital admissions from each German hospital at the end of each year and store the data for research purpose. Currently, there are 1,618 hospitals in their record list. The admission ('primary diagnosis') is coded using the International Classification of
In this study, we identified hospital admissions due to I08-Valve disease \( n=1,092 \) or I95-Hypotension \( n=12,211 \) as the study outcomes.

In the first phase, to handle study exposures we firstly used Geographic Information System to map out the included weather stations \( 64 \) out of \( 78 \) representative stations across Germany based on the completeness of weather data and their validity) from each State of Germany (see Supplementary Figure 1). There are \( 16 \) States in total. In each weather station, we generated all the included meteorological parameters mentioned above into a single index called physically equivalent temperature (PET) as the main study exposure to be correlated with hospital admissions. We then averaged daily PETs from each weather station for each German State. PET, with a widely known unit °C, which has been known to be used to consider a heat balance of the human body under the standard conditions in an outdoor setting and initially created to characterize and evaluate the thermal bioclimate in a physiologically setting. The application of PET assessment can be carried out by a RayMan model (more details via: http://www.mif.uni-freiburg.de/rayman/intro.htm). In the current analysis, \( 64 \) weather stations from \( 13 \) States with complete weather data were included for the statistical analysis. This has excluded \( 3 \) States containing Berlin, Saarland, and Saxony-Anhalt without any of meteorological parameters that would be needed for PET calculation. Hospital admissions from these \( 3 \) States were also excluded when being correlated with PETs. During the second phase, to correlate PETs with hospital admissions, we plotted both PETs and hospital admissions into figures. Statistical software STATA 12.0 version (STATA, College Station, Texas, USA) was used for all the analyses.
This study was approved and funded by the EU FP-7 Data without Boundaries project (grant number: n° 262608).

In Figure 1 and 2, relationships of PETs and hospital admissions due to valve disease and hypotension are displayed, respectively. Although more hospital admissions were observed in days with lower PETs, the highest amount seemed to be when PET was close to 0°C but not below. In Japan, it was observed more outpatient visits for hypotension in single clinic in Tokyo in the spring time of 2010 when the weather changed. Animal research also indicated that during rewarming in rats, after 1-week long cold exposure at air temperature 4°C, all measures normalized quickly except mean arterial blood pressure, which fell below baseline (hypotension) for the first few days. Similar observations were made in vivo. The potential mechanism could be via venoconstriction since temperature could affect the venoconstriction induced by Ruscus. Literature in the relationship of the weather and valve disease or hypotension using large human samples is still scarce.

There are a few strengths in conducting this study. First, our data are limited to very recent years to ensure that we don’t find strong associations by chance alone through pooling decades of data. Second, we have drawn clear study catchments across Germany to ensure that both medical data and meteorological data can be matched geographically to rule out the potential ecological bias (i.e. 1 weather station plus numerous hospitals from other sub-regions). We also ensured that in each German state, there would be at least one weather station to provide valid weather data to be correlated with hospital admissions within the State. On the other hand, there were still some limitations. First, we were unable to link with other population
surveys to have proper covariates to be adjusted. Therefore, no causation could be drawn. Moreover, we did not include air pollution data due in part to the fact that by adjusting for air pollution in the epidemiological and statistical modelling, the effects could be stronger and easily reach the statistical significance. The other practical reason was that the level of air pollution in Germany has been low in the recent years (details via: http://www.umweltbundesamt.de/en/data/current-concentrations-of-air-pollutants-in-germany). Therefore, the effect from air pollution would be minimal. By examining the correlations between the weather as biometeorologic and hospital admissions at the State/population level, it is to indicate how much additional medical and social resources, such as medical professional-time and hospital facilities, might be anticipated across each German State and/or nationally.

In sum, valve disease and hypotension hospital admissions peaked at physically equivalent temperature 0°C in Germany in 2009-2011. Nationally, while preparing reallocation of medical and social resources in response to the change of weather, adaptation to the weather, in particular at 0°C, would seem to be imperative.
References


Supplementary Figure 1 The included weather stations in Germany
Figure 1 Relationships of PETs and hospital admissions due to I08-Valve disease
Figure 2 Relationships of PETs and hospital admissions due to I95-Hypotension