Influence of Daily Individual Meteorological Parameters on the Incidence of Acute Coronary Syndrome

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Abstract: Background: A nationwide study was conducted to explore the short term association between daily individual meteorological parameters and the incidence of acute coronary syndrome (ACS) treated with coronary emergency catheter interventions in the Republic of Slovenia, a south-central European country. Method: We linked meteorological data with daily ACS incidence for the entire population of Slovenia, for the population over 65 years of age and for the population under 65 years of age. Data were collected daily for a period of 4 years from 1 January 2008 to 31 December 2011. In line with existing studies, we used a main effect generalized linear model with a log-link-function and a Poisson distribution of ACS. Results and Conclusions: Three of the studied meteorological factors (daily average temperature, atmospheric pressure and relative humidity) all have relevant and significant influences on ACS incidences for the entire population. However, the ACS incidence for the population over 65 is only affected by
daily average temperature, while the ACS incidence for the population under 65 is affected by daily average pressure and humidity. In terms of ambient temperature, the overall findings of our study are in line with the findings of the majority of contemporary European studies, which also note a negative correlation. The results regarding atmospheric pressure and humidity are less in line, due to considerable variations in results. Additionally, the number of available European studies on atmospheric pressure and humidity is relatively low. The fourth studied variable—season—does not influence ACS incidence in a statistically significant way.

**Keywords:** cardiovascular disease; meteorological factors; atmospheric pressure; humidity; temperature; myocardial infarction; weather; Europe

1. **Introduction**

Since Rosahn in 1937 [1], a number of studies on almost all continents [2–9] have indicated that weather plays an important role in the onset of cardiovascular (CV) disease. The short-term effect on both CV morbidity and mortality has been evaluated through various analyses [10–22].

Several researchers have focused their attention on acute myocardial infarction (AMI), which is a common CV disease that requires emergency medical treatment. The impact of ambient temperature on AMI morbidity has received less attention in the past [23], while the influence of seasonal variations on the incidence of AMI has been well examined. However, these seasonal variations do not seem to be universal [24–32]. It is possible that there is geographical variation in the seasonal distribution of AMI [33]. Fewer studies are available on the influence of individual meteorological parameters on AMI [34,35] although a statistically significant effect of ambient temperature on AMI risk has been consistently reported [36–38]. Only a minority of them have been nationwide [39] as in our study.

Our study included patients who in the research period had received emergency treatment in catheterisation laboratories, with primary and rescue percutaneous coronary emergency catheter intervention. The population is suitable for investigation because the danger of the leading symptom of ACS, angina pectoris, is well known in Slovenia. We also have a good national survey of diagnoses leading to hospitalisation and the “door-to-balloon time”—a critical element in reperfusion therapy worldwide—is short. By focusing on the chosen group of patients, we wished to ensure a minimum time gap between the patient’s exposure to individual meteorological conditions, the onset of symptoms and the diagnostics and therapy applied.

The aim of the study was to examine the influence of daily individual meteorological parameters on the incidence of ACS in Slovenia and to compare the findings with other European studies. Additionally, we hope that the study results can improve hospital material and work schedule planning, as well as provide relevant weather alerts for people with heart-related conditions.
2. Materials and Methods

Slovenia, a country with a population of two million people, is a central European country with an area of 20,000 km², situated between Italy, Hungary, Austria and Croatia. The air temperature in Slovenia has a distinctive daily and yearly course and differences between seasons are pronounced.

Data on the incidence of ACS were obtained from all hospitals in Slovenia that have catheterization laboratories with 24-h medical teams for emergency treatment of patients. They are located in the three largest cities—Ljubljana, Maribor and Celje. Ambulance or helicopter emergency transport is used for transporting patients from remote locations directly to an interventional cardiac catheterization facility. Data were collected daily for a period of 4 years from 1 January 2008 to 31 December 2011. During the study, 6434 patients received emergency treatment in catheterisation laboratories, of which there were 4412 (69%) men and 2022 (31%) women; 2494 men (39%) and 612 (10%) women were younger than 65 years of age. Data on daily ambient temperatures, humidity and atmospheric pressure (meteorological data) were obtained from 32 meteorological stations of the Slovenian Environment Agency (Figure 1).

Figure 1. Meteorological stations in Slovenia [40].

Distance and altitude of a town were considered in choosing the appropriate station in terms of the patient’s address of permanent residence. The stations cover one or more municipalities in the three major geographical regions of Slovenia. To gain representative meteorological data for Slovenia, we summed the weighted station data. The weighted station data was computed by multiplying each station data by the percentage of the population that live in the municipalities covered by a specific station. The climatological data thus represents the climatological conditions for the population in Slovenia as accurately as possible.
Since not all of the 32 climatological stations used the same data format, special care had to be taken to ensure data consistency. Furthermore, in order to pair the climatological data with the incidence of ACS data properly, appropriate data handling and calculation techniques and tools had to be used. For merging and aggregating data R 3.0.0 (The R Foundation for Statistical Computing, Vienna, Austria) [41] with its basic packages was used while statistical analysis was done with SPSS 20.0 (IBM Corporation, Armonk, New York, NY, USA) [42].

To link data on the incidence of ACS and climatological data, we followed the well-established approach of a multivariate analysis based on a main effect generalized linear model, assuming a log-link function with a Poisson distribution (GLM-LL model) [7,37,43,44]. The Poisson distribution is a discrete distribution and is appropriate for counts of observations (number of acute coronary syndromes per day).

3. Results

In this section, the results of GLM-LL models are presented linking climatological data with the following: daily ACS incidence for the entire population, daily ACS incidence for the population over 65 years of age and daily ACS incidence for the population under 65 years of age. In order to investigate the seasonal effect of warm and cold periods on ACS incidence, we introduced a season variable into the model. The warm period (Season = 1) was defined as the period from April to September and the cold period (Season = 0) was defined as the period from October to March.

Tests of over-dispersion confirmed the Poisson model assumptions for the three fitted models. In all three cases, the ratio of deviance to degrees of freedom, the ratio of the Pearson Chi-Square to degrees of freedom and the variance to mean ratio did not surpass 1.3. Additionally, statistical tests of the GLM-LL models showed statistically significant goodness of fit. In all three models, the $p$-value of the Omnibus test (Likelihood Ratio Chi-Square) was below 0.05. Such results indicate a relevant improvement of the fitted model over the intercept-only model.

The results for daily ACS incidence for the entire population presented in Table 1 show that all the beta coefficients of the fitted model were statistically significantly different from 0, except the beta coefficient of the season variable. The per mille change of the beta coefficient is computed according to the formula $\text{Exp}(B) - 1 = 0.993 - 1 = -0.007$. The same formula is used to compute the 95% confidence intervals (95% CI). The Exp function is used because the interpretation of beta coefficients of the GLM-LL model has to take into account their exponential nature. Thus, if the average daily temperature increases by 1 °C, the daily incidence of ACS decreases by approximately 7‰, with a 95% CI (−12‰, −2‰). If the daily average humidity increases by 1%, the daily incidence of ACS decreases by approximately 3‰, 95% CI (−6‰, −1‰). If the daily average pressure increases by 1 mbar, the daily incidence of ACS decreases by approximately 4‰, 95% CI (−7‰, −1‰).
Table 1. Daily ACS incidence for the entire population.

| Parameter          | B     | 95% Confidence Interval | Hypothesis Test | Exp(B) | 95% Confidence Interval for Exp(B) |
|--------------------|-------|-------------------------|-----------------|--------|-----------------------------------|
|                    |       | Lower | Upper | Wald Chi-Square | Sig.   | Lower | Upper |
| (Intercept)        | 5.9309| 2.640 | 9.222 | 12.478 | 0.000 | 376.504 | 14.015 | 10,114.4 |
| Average daily T (°C) | −0.0071 | −0.012 | −0.002 | 7.484 | 0.006 | 0.993 | 0.988 | 0.998 |
| Average daily H (%) | −0.0031 | −0.006 | −0.001 | 5.854 | 0.016 | 0.997 | 0.994 | 0.999 |
| Average daily P (mbar) | −0.0042 | −0.007 | −0.001 | 6.363 | 0.012 | 0.996 | 0.993 | 0.999 |
| Season             | 0.0222 | −0.062 | 0.106 | 0.268 | 0.605 | 1.022 | 0.940 | 1.112 |

Notes: Dependent variable: ACS incidence for the entire population; model: (intercept), average daily temperature (T) (°C), average humidity (H) (%), average pressure (P) (mbar), and season (warm period: April–September, cold period: October–March); Sig.: significance probability.

The results of daily ACS incidence for the population under 65 presented in Table 2 show that all the beta coefficients of the fitted model were statistically significantly different from 0, except the beta coefficient of average daily temperature and the beta coefficient of the season variable. If the daily average humidity increases by 1%, the daily incidence of ACS decreases by approximately 4‰, 95% CI (−7‰, −0.2‰). If the daily average pressure increases by 1 mbar, the daily incidence of ACS decreases by approximately 7‰, 95% CI (−11‰, −2‰).

Table 2. Daily ACS incidence for population under 65.

| Parameter          | B     | 95% Confidence Interval | Hypothesis Test | Exp(B) | 95% Confidence Interval for Exp(B) |
|--------------------|-------|-------------------------|-----------------|--------|-----------------------------------|
|                    |       | Lower | Upper | Wald Chi-Square | Sig.   | Lower | Upper |
| (Intercept)        | 7.7627 | 3.050 | 12.476 | 10.422 | 0.001 | 2351.29 | 21.112 | 261,867.6 |
| Average daily T (°C) | −0.0050 | −0.012 | 0.002 | 1.770 | 0.183 | 0.995 | 0.988 | 1.002 |
| Average daily H (%) | −0.0037 | −0.007 | 0.000 | 4.198 | 0.040 | 0.996 | 0.993 | 0.9998 |
| Average daily P (mbar) | −0.0068 | −0.011 | −0.002 | 8.011 | 0.005 | 0.993 | 0.989 | 0.998 |
| Season             | −0.0027 | −0.123 | 0.118 | 0.002 | 0.965 | 0.997 | 0.884 | 1.125 |

Notes: Dependent variable: ACS incidence for population under 65 years of age; model: (intercept), average daily temperature (T) (°C), average humidity (H) (%), average pressure (P) (mbar), season (warm period: April–September, cold period: October–March); Sig.: significance probability.

The results of daily ACS incidence for the population over 65 presented in Table 3 show that the model’s intercepts, as well as the influences of average daily humidity, average daily pressure and season on daily ACS incidence for patients older than 65 years, were not statistically significant.

The only statistically significant beta coefficient is thus average daily temperature. If the average daily temperature increases by 1 °C, the daily incidence of ACS decreases by approximately 9‰, 95% CI (−16‰, −2‰). Based on the three GLM-LL models presented, it appears that daily average temperature has an impact on ACS incidence for the entire population as well as the population over 65. Humidity and pressure, on the other hand, impact on the ACS incidence of the entire population and the population of people under 65.
Table 3. Daily ACS incidence for population over than 65 years.

| Parameter | B       | 95% Confidence Interval | Hypothesis Test | Exp(B)  | 95% Confidence Interval for Exp(B) |
|-----------|---------|-------------------------|-----------------|---------|----------------------------------|
|           | Lower   | Upper                   | Wald Chi-Square | Sig.    | Lower   | Upper                           |
| (Intercept) | 2.8726  | −1.724                  | 7.469           | 1.501   | 0.221   | 17.682                          |
| Average daily T (°C) | −0.0091 | −0.016                  | −0.002          | 6.311   | 0.012   | 0.991                           |
| Average daily H (%) | −0.0024 | −0.006                  | 0.001           | 1.911   | 0.167   | 0.998                           |
| Average daily P (mbar) | −0.0018 | −0.006                  | 0.003           | 0.607   | 0.436   | 0.998                           |
| Season    | 0.0455  | −0.071                  | 0.162           | 0.582   | 0.445   | 1.047                           |

Notes: Dependent variable: ACS incidence for population over 65; model: (intercept), average daily temperature (T) (°C), average humidity (H) (%), average pressure (P) (mbar), season (warm period: April–September, cold period: October–March); Sig.: significance probability.

4. Discussion

The discussion is organised into four main parts, each presenting one of the key variables of our model. Our findings regarding each variable are compared to contemporary studies. Most studies focus on temperature while only a few consider other meteorological variables.

Contemporary European studies conducted in France [36], Germany [45], Italy [43], Hungary [39], England [46] and Denmark [23] report a negative correlation between average daily temperature and the incidence of AMI, as in our study. In Portugal Vasconcelos et al. [47] also reported a negative correlation, although they used various indices rather than individual meteorological variables. On the other hand, Wijnbergen et al. from The Netherlands [48] and Goerre et al. from Switzerland [35] report that incidences of AMI do not statistically significantly differ between colder days and warmer days. Similarly, a study of hospitals in a Turkish city and patients over the age of 65 did not confirm any connection between incidence and low temperatures [49]. Many recent studies have also established differences in terms of age [4,36,45,46,50] regarding the incidence of AMI at low temperatures. Our study also confirmed the effect of cold temperatures being more pronounced among the older population.

The few European studies that included pressure in their analysis found contradicting results. Some did not find any relation between pressure and the incidence of AMI [43,48,51,52] or the relationship was not statistically significant [52]. Others describe either a positive correlation [35,36] or, as in our study, a negative correlation [36,47].

There are also not many studies evaluating the influence of humidity on the incidence of AMI. Ruhenstroth-Bauer et al. [3] from Germany established a similarly negative correlation as our study. On the other hand, Panagiotakos et al. [50] from Greece, Abrignani et al. [43] from Italy and Ezekowitz et al. [53] in an international study report positive correlations. Barnett et al. [54] and Wijnbergen et al. [48] reported that the effect of humidity was not statistically significant. The results in relation to humidity are less comparable because some authors use maximal ambient humidity and others use relative humidity in their research.

Many studies studying the seasonal effects on AMI incidences found statistically significant influences [24,27,28,30], while some studies found only partial influences [25,26] and others do not
report statistically significant seasonal effects [4,29,31,55]. Our results also show that the season does not statistically significantly influence ACS incidences. Our findings are aligned with the findings of Marchant et al. [56], who report that AMI was more common on colder days, independent of the season. Moreover, Slovenia doesn’t experience extreme cold and warm seasons, which agrees with Ku et al. [55], who also found no variations in a region lacking temperature extremes.

5. Conclusions

The overall findings of our study correspond to the findings of other European studies in terms of temperature. In light of the proven major effect of lower temperatures on the risk of the onset of ACS, even more attention and preventive measures should be directed into this field. While there are some major differences in relation to humidity and pressure among published European studies, there have also been far fewer studies that analyse this effect. It has also been established that the incidence rate differs among different countries. This probably cannot be explained only by conventional risk factors and temperature, since there are also other factors, including other meteorological variables, which may play an important part. Further research should also include an analysis of the time that individuals actually spend outdoors.

The results of our study suggest that more attention should be focused on the negative effect of low temperatures, low pressure and low humidity. Warning systems considering all these variables should be developed similarly to existing hot weather warning systems [57]. Our future work will focus on the potential of developing a mobile application with a corresponding back-end system providing relevant alerts for people with heart-related conditions. Another avenue of further work is the improvement of hospital material and work schedule planning through the integration of meteorological data.

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Author Contributions

Mirjam Ravljen wrote the main part of the paper, carried out a survey of the literature, gathered the data and contributed to the interpretation of the results. Marjan Bilban supervised the research, reviewed the manuscript and helped write the paper. Lučka Kajfež-Bogataj contributed to the choice of meteorological variables, to the interpretation of the results and reviewed the manuscript. Damjan Vavpotič and Tomaž Hovelja designed the research methodology, analyzed the data and helped write the paper. Damjan Vavpotič was the research leader.

Conflicts of Interest

The authors declare no conflict of interest.
References

1. Rosahn, P.D. Incidence of coronary thrombosis in relation to climate. *JAMA* 1937, 109, doi: 10.1001/jama.1937.02780420054021.

2. Sarna, S.; Romo, M.; Siltanen, P. Myocardial-infarction and weather. *Ann. Clin. Res.* 1977, 9, 222–232.

3. Ruhenstroth-Bauer, G.; Baumer, H.; Burkel, E.M.; Sönning, W.; Filipiak, B. Myocardial infarction and the weather: A significant positive correlation between the onset of heart infarct and 28 khz atmospherics—A pilot study. *Clin. Cardiol.* 1985, 8, 149–151.

4. Ebi, K.L.; Exuzides, K.A.; Lau, E.; Kelsh, M.; Barnston, A. Weather changes associated with hospitalizations for cardiovascular diseases and stroke in california, 1983–1998. *Int. J. Biometeorol.* 2004, 49, 48–58.

5. Turner, R.M.; Muscatello, D.J.; Zheng, W.; Willmore, A.; Arendts, G. An outbreak of cardiovascular syndromes requiring urgent medical treatment and its association with environmental factors: An ecological study. *Environ. Health* 2007, 6, doi:10.1186/1476-069X-6-37.

6. Amiya, S.; Nuruki, N.; Tanaka, Y.; Tofuku, K.; Fukuoka, Y.; Sata, N.; Kashima, K.; Tsubouchi, H. Relationship between weather and onset of acute myocardial infarction: Can days of frequent onset be predicted? *J. Cardiol.* 2009, 54, 231–237.

7. Lee, J.H.; Chae, S.C.; Yang, D.H.; Park, H.S.; Cho, Y.; Jun, J.E.; Park, W.H.; Kam, S.; Lee, W.K.; Kim, Y.J.; *et al.* Influence of weather on daily hospital admissions for acute myocardial infarction (from the korea acute myocardial infarction registry). *Int. J. Cardiol.* 2010, 144, 16–21.

8. Fong, T.; Ma, E. Effects of meteorological parameters on hospital admission for respiratory and cardiovascular diseases. *J. Public Health* 2013, 21,175–182.

9. Fink, R.; Eržen, I.; Medved, S.; Kastelec, D. Experimental research on physiological response of elderly with cardiovascular disease during heat wave period. *Indoor Built. Environ.* 2014, doi:10.1177/1420326X13519348.

10. Braga, A.L.; Zanobetti, A.; Schwartz, J. The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities. *Environ. Health Perspect.* 2002, 110, 859–863.

11. Koken, P.J.M.; Piver, W.T.; Ye, F.; Elixhauser, A.; Olsen, L.M.; Portier, C.J. Temperature, air pollution, and hospitalization for cardiovascular diseases among elderly people in Denver. *Environ. Health Perspect.* 2003, 111, 1312–1317.

12. Dilaveris, P.; Synetos, A.; Giannopoulos, G.; Gialafos, E.; Pantazis, A.; Stefanadis, C. Climate impacts on myocardial infarction deaths in the athens territory: The climate study. *Heart* 2006, 92, 1747–1751.

13. Gerber, Y.; Jacobsen, S.J.; Weston, S.A.; Killian, J.M.; Roger, V.L. Seasonality and daily weather conditions in relation to myocardial infarction and sudden cardiac death in olmsted county, Minnesota. *Circulation* 2006, 113, 287–292.

14. Michelozzi, P.; Kirchmayer, U.; Katsouyanni, K.; Biggeri, A.; McGregor, G.; Menne, B.; Kassomenos, P.; Anderson, H.R.; Baccini, M.; Accetta, G.; *et al.* Assessment and prevention of acute health effects of weather conditions in Europe, the phewe project: Background, objectives, design. *Environ. Health* 2007, 6, doi:10.1186/1476-069X-6-12.
15. Analitis, A.; Katsouyanni, K.; Biggeri, A.; Baccini, M.; Forsberg, B.; Bisanti, L.; Kirchmayer, U.; Ballester, F.; Cadum, E.; Goodman, P.G.; et al. Effects of cold weather on mortality: Results from 15 European cities within the phewe project. *Amer. J. Epidemiol.* 2008, 168, 1397–1408.

16. Baccini, M.; Biggeri, A.; Accetta, G.; Kosatsky, T.; Katsouyanni, K.; Analitis, A.; Anderson, H.; Bisanti, L.; D’Ippoliti, D.; Danova, J.; et al. Heat effects on mortality in 15 European cities. *Epidemiology* 2008, 19, 711–719.

17. Kriszbacher, I.; Jozsef, B.; Koppan, A.; Imre, B.; Miklos, K. The effect of climate on heart attack mortality. *Int. J. Cardiol.* 2010, 139, 92–93.

18. Törö, K.; Bartholy, J.; Pongrácz, R.; Kis, Z.; Keller, É.; Dunay, G. Evaluation of meteorological factors on sudden cardiovascular death. *J. Forensic Leg. Med.* 2010, 17, 236–242.

19. Hopstock, L.A.; Fors, A.S.; Bonaa, K.H.; Mannsverk, J.; Njolstad, I.; Wilsgaard, T. The effect of daily weather conditions on myocardial infarction incidence in a subarctic population: The Tromso study 1974–2004. *J. Epidemiol. Community Health* 2012, 66, 815–820.

20. Xu, B.; Liu, H.; Su, N.; Kong, G.; Bao, X.; Li, J.; Wang, J.; Li, Y.; Ma, X.; Zhang, J.; et al. Association between winter season and risk of death from cardiovascular diseases: A study in more than half a million inpatients in Beijing, China. *BMC Cardiovasc. Disord.* 2013, 13, doi:10.1186/1471-2261-13-93.

21. Gómez-Acebo, I.; Llorca, J.; Dierssen, T. Cold-related mortality due to cardiovascular diseases, respiratory diseases and cancer: A case-crossover study. *Public Health* 2013, 127, 252–258.

22. Gasparini, A.; Armstrong, B.; Kovats, S.; Wilkinson, P. The effect of high temperatures on cause-specific mortality in England and Wales. *Occup. Environ. Med.* 2012, 69, 56–61.

23. Wichmann, J.; Ketzel, M.; Ellermann, T.; Loft, S. Apparent temperature and acute myocardial infarction hospital admissions in copenhagen, denmark: A case-crossover study. *Environ. Health* 2012, 11, doi:10.1186/1476-069X-11-19.

24. Spencer, F.A.; Goldberg, R.J.; Becker, R.C.; Gore, J.M. Seasonal distribution of acute myocardial infarction in the second national registry of myocardial infarction. *J. Amer. Coll. Cardiol.* 1998, 31, 1226–1233.

25. Fischer, T.; Lundbye-Christensen, S.; Johnsen, S.P.; Schönheyder, H.C.; Sørensen, H.T. Secular trends and seasonality in first-time hospitalization for acute myocardial infarction—A Danish population-based study. *Int. J. Cardiol.* 2004, 97, 425–431.

26. Leibowitz, D.; Planer, D.; Weiss, T.; Rott, D. Seasonal variation in myocardial infarction is limited to patients with st-elevations on admission. *Chronobiol. Int.* 2007, 24, 1241–1247.

27. Loughnan, M.E.; Nicholls, N.; Tapper, N.J. Demographic, seasonal, and spatial differences in acute myocardial infarction admissions to hospital in Melbourne, Australia. *Int. J. Health Geogr.* 2008, 7, doi:10.1186/1476-072X-7-42.

28. Turin, T.C.; Rumana, N.; Kita, Y.; Nakamura, Y.; Miura, K.; Ueshima, H. Ambient weather conditions and the onset of acute myocardial infarction: The consociation between triggering factors and conventional risk factors. *J. Cardiol.* 2010, 55, 283–284.

29. Cheng, T. Seasonal variation in acute myocardial infarction. *Int. J. Cardiol.* 2009, 135, 277–279.

30. Li, Y.; Du, T.; Lewin, M.R.; Wang, H.; Ji, X.; Zhang, Y.; Xu, T.; Xu, L.; Wu, J.S. The seasonality of acute coronary syndrome and its relations with climatic parameters. *Amer. J. Emerg. Med.* 2011, 29, 768–774.
31. Pell, J.P.; Cobbe, S.M. Seasonal variations in coronary heart disease. *QJM* **1999**, *92*, 689–696.
32. Houck, P.; Lethen, J.; Riggs, M.; Gantt, D.; Dehmer, G. Relation of atmospheric pressure changes and the occurrences of acute myocardial infarction and stroke. *Amer. J. Cardiol.* **2005**, *96*, 45–51.
33. Savopoulos, C.; Ntaios, G.; Hatzitolios, A. Is there a geographic variation in the seasonal distribution of acute myocardial infarction and sudden cardiac death? *Int. J. Cardiol.* **2009**, *135*, 253–254.
34. Cheng, T. Mechanism of seasonal variation in acute myocardial infarction. *Int. J. Cardiol.* **2005**, *100*, 163–164.
35. Goerre, S.; Egli, C.; Gerber, S.; Defila, C.; Minder, C.; Richner, H.; Meier, B. Impact of weather and climate on the incidence of acute coronary syndromes. *Int. J. Cardiol.* **2007**, *118*, 36–40.
36. Danet, S.; Richard, F.; Montaye, M.; Beauchant, S.; Lemaire, B.; Graux, C.; Cottel, D.; Marécaux, N.; Amouyel, P. Unhealthy effects of atmospheric temperature and pressure on the occurrence of myocardial infarction and coronary deaths. A 10-year survey: The lille-world health organization monica project (monitoring trends and determinants in cardiovascular disease). *Circulation* **1999**, *100*, 1–7.
37. Liang, W.M.; Liu, W.P.; Chou, S.Y.; Kuo, H.W. Ambient temperature and emergency room admissions for acute coronary syndrome in Taiwan. *Int. J. Biometeorol.* **2008**, *52*, 223–229.
38. Bhaskaran, K.; Hajat, S.; Haines, A.; Herrett, E.; Wilkinson, P.; Smeeth, L. Effects of ambient temperature on the incidence of myocardial infarction. *Heart* **2009**, *95*, 1760–1769.
39. Ildiko, K.; Jozsef, B.; Ildiko, C.; Imre, B. The occurrence of acute myocardial infarction in relation to weather conditions. *Int. J. Cardiol.* **2009**, *135*, 136–138.
40. Zorko, V. *Meteorological Stations in Slovenia*; Slovenian Environment Agency: Ljubljana, Slovenia, 2014.
41. Team, R.D.C. The R Project for Statistical Computing. Available online: [http://www.r-project.org/](http://www.r-project.org/) (accessed on 15 October 2014).
42. IBM. SPSS Software, Predictive Analytics Software and Solutions. Available online: [http://www-01.ibm.com/software/analytics/spss/](http://www-01.ibm.com/software/analytics/spss/) (accessed on 15 October 2014).
43. Abrignani, M.G.; Corrao, S.; Biondo, G.B.; Renda, N.; Braschi, A.; Novo, G.; Di Girolamo, A.; Braschi, G.B.; Novo, S. Influence of climatic variables on acute myocardial infarction hospital admissions. *Int. J. Cardiol.* **2009**, *137*, 123–129.
44. Abrignani, M.G.; Corrao, S.; Biondo, G.B.; Lombardo, R.M.; di Girolamo, P.; Braschi, A.; di Girolamo, A.; Novo, S. Effects of ambient temperature, humidity, and other meteorological variables on hospital admissions for *Angina pectoris*. *Eur. J. Prev. Cardiol.* **2012**, *19*, 342–348.
45. Wolf, K.; Schneider, A.; Breitner, S.; von Klot, S.; Meisinger, C.; Cyrys, J.; Hymer, H.; Wichmann, H.E.; Peters, A.; Cooperative Health Research in the Region of Augsburg Study. Air temperature and the occurrence of myocardial infarction in Augsburg, Germany. *Circulation* **2009**, *120*, 735–742.
46. Bhaskaran, K.; Hajat, S.; Haines, A.; Herrett, E.; Wilkinson, P.; Smeeth, L. Short term effects of temperature on risk of myocardial infarction in england and wales: Time series regression analysis of the myocardial ischaemia national audit project (minap) registry. *Brit. Med. J.* **2010**, *341*, doi:10.1136/bmj.c3823.
47. Vasconcelos, J.; Freire, E.; Almendra, R.; Silva, G.L.; Santana, P. The impact of winter cold weather on acute myocardial infarctions in Portugal. *Environ. Pollut.* **2013**, *183*, 14–18.

48. Wijnbergen, I.; van’t Veer, M.; Pijls, N.H.; Tijssen, J. Circadian and weekly variation and the influence of environmental variables in acute myocardial infarction. *Neth. Heart J.* **2012**, *20*, 354–359.

49. Ünsal, A.; Metintaş, S.; Ayranci, Ü.; Çevik, A.A. Effective variations on acute myocardial infarction in the elderly in a city in west of Turkey. *Eur. J. Gen. Med.* **2006**, *3*, 152–158.

50. Panagiotakos, D.B.; Chrysohoou, C.; Pitsavos, C.; Nastos, P.; Anadiotis, A.; Tentolouris, C.; Stefanadis, C.; Toutouzas, P.; Paliatsos, A. Climatological variations in daily hospital admissions for acute coronary syndromes. *Int. J. Cardiol.* **2004**, *94*, 229–233.

51. Verberkmoes, N.J.; Hamad, M.A.S.; ter Woorst, J.F.; Tan, M.; Peels, C.H.; van Straten, A.H.M. Impact of temperature and atmospheric pressure on the incidence of major acute cardiovascular events. *Neth. Heart J.* **2012**, *20*, 193–196.

52. Wanitschek, M.; Ulmer, H.; Süssenbacher, A.; Dörler, J.; Pachinger, O.; Alber, H.F. Warm winter is associated with low incidence of ST elevation myocardial infarctions and less frequent acute coronary angiographies in an alpine country. *Herz* **2013**, *38*, 163–170.

53. Ezekowitz, J.A.; Bakal, J.A.; Westerhout, C.M.; Giugliano, R.P.; White, H.; Keltai, M.; Prabhakaran, D.; Tricoci, P.; Van de Werf, F.; Califf, R.M.; *et al.* The relationship between meteorological conditions and index acute coronary events in a global clinical trial. *Int. J. Cardiol.* **2013**, *168*, 2315–2321.

54. Barnett, A.; Dobson, A.; McElduff, P.; Salomaa, V.; Kuulasmaa, K.; Sans, S.; WHO MONICA Project. Cold periods and coronary events: An analysis of populations worldwide. *J. Epidemiol. Community Health* **2005**, *59*, 551–557.

55. Ku, C.S.; Yang, C.Y.; Lee, W.J.; Chiang, H.T.; Liu, C.P.; Lin, S.L. Absence of a seasonal variation in myocardial infarction onset in a region without temperature extremes. *Cardiology* **1998**, *89*, 277–282.

56. Marchant, B.; Ranjadayalan, K.; Stevenson, R.; Wilkinson, P.; Timmis, A. Circadian and seasonal factors in the pathogenesis of acute myocardial infarction—The influence of environmental-temperature. *Brit. Heart J.* **1993**, *69*, 385–387.

57. Morabito, M.; Crisci, A.; Moriondo, M.; Profili, F.; Francesconi, P.; Trombi, G.; Bindi, M.; Gensini, G.F.; Orlandini, S. Air temperature-related human health outcomes: Current impact and estimations of future risks in central Italy. *Sci. Total Environ.* **2012**, *441*, 28–40.

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