Assessment of the Health Modifying Effects of Weather on COPD Patients

Doctoral (PhD) Thesis

Gergely Péter Márovics

Doctoral School of Clinical Medical Sciences

Leader of Doctoral School: Lajos Bogár PhD, DSc

Progam Leader: István Kiss PhD, DSc

Supervisor: János Girán, PhD

University of Pécs

Medical School

Department of Public Health Medicine

Pécs

2024

Table of Contents

1. Introduction

The climate and weather of the Earth have a significant impact on the biological functions and health of the human body. Today, we are facing the wide-ranging effects of global climate change, which is increasing the importance of their impact on human health. Climate change affects weather and weather patterns, which may be directly related to both communicable and non-communicable diseases.

In the last 20 years, we have seen a surge in human biometeorological research investigating the effects of meteorological factors on human health. Much of this work has investigated the links between various cardiovascular diseases and temperature increases associated with global climate change, particularly heatwaves. These types of studies have mostly focused on mortality, including excess mortality caused by heat waves, which have helped to develop different heat action plans in Europe and worldwide. However, another major aspect, morbidity, in particular hospital or emergency department admissions related to respiratory diseases, has received considerably less attention.

Chronic obstructive pulmonary disease (COPD) is a heterogeneous lung disease that affects more than 200 million people worldwide, with around 16 million new cases each year and more than 3 million deaths, making it the third leading cause of death globally. Smoking is the number one risk factor for COPD, but indoor and outdoor air pollution cannot be neglected. In addition, there is evidence of higher risk from different types of occupations, such as mining, agriculture, construction, respiratory infections, and different weather conditions.

COPD-related mortality shows seasonal variation, with significantly higher mortality in the winter months. Cold spells, cold waves, and low daily mean temperatures all increase the risk of COPD-related mortality. The frequency of COPD-related hospitalizations is also inversely related to temperature, with typically higher morbidity during winter. Extremely cold and hot temperatures can both increase COPD morbidity, which can also lead to a worsening of the symptoms of the disease. Both daily heat exposure and diurnal temperature variation also pose a risk for both morbidity and mortality because of COPD. The limited evidence suggests that extremely low dew point may also increase the number of COPD-related emergency visits. Reasons include an increased risk of cold-weather-induced airway inflammation and respiratory tract infections and an increase in cold-weather-induced respiratory exacerbations. It is important to note that weather effects on COPD can vary from individual to individual, depending on the age, sex, and other factors of the patient.

2. Aims

There is limited information available on COPD-related hospital and emergency department admissions, so my research aimed to investigate the following aspects:

- What impact do extreme weather conditions have on COPD-related emergency department visits?
- Is there any relationship between diurnal variability in weather and COPD-related emergency department visits?
- If so, provide an answer to whether significant changes or stable conditions are riskier for COPD patients.
- In parallel, determine whether the length of those periods has an impact on COPD-related emergency department visits.

Answering these questions is key to a better understanding of the environmental risk factors for people diagnosed with COPD. However, these results alone do not reveal much about who are most vulnerable in the COPD population. Therefore, my aim was also:

- To stratify the analysis by age and sex to identify groups that are particularly vulnerable to weather conditions.
- to use the results to raise awareness among emergency department staff about periods of risk and vulnerable groups so that they can deliver care more effectively.

3. Materials and Methods

The database created during my research covers two large data sets: on the one hand, I had to use weather data of the city of Pécs, and on the other hand, I needed clinical patient data for the analyses. Both data sets were collected for the period from 1 January 2010 to 31 December 2019 and organized in a common database. The data on meteorological parameters included daily minimum, maximum and mean temperatures in degrees Celsius (°C); daily precipitation in millimeters (mm); daily mean dew point in degrees Celsius (°C); daily mean station-level air pressure in hectopascals (hPa); daily mean wind speed in meters per second (m/s); and daily mean relative humidity in percent (%). The data source was the Pécs-Pogány Airport meteorological station and the meteorological station operated by the Department of Physical and Environmental Geography (DPEG), Institute of Geography and Earth Sciences, University of Pécs Faculty of Sciences (UP FS IGES). Data on patients were extracted from the e-MedSolution database of the Clinical Centre of the University of Pécs (UP CC). I collected the following data for those registered by the Emergency Department (EB) in outpatient care aged 18 years and older: sex; date of birth; date of admission and discharge to the department; and post-admission diagnoses.

The daily data of Pécs-Pogány Airport were first converted from the British system to the metric system. This was followed by the processing of the DPEG meteorological data, where I created daily summaries of minute-by-minute data. After preparing the data, the extremes derived from them had to be determined, which was solved by dichotomization: each weather variable was split into two groups according to the 1^{st}, 5^{th}, 10^{th}, 90^{th}, 95^{th}, and 99^{th} percentile values. In the case of 1^{st}, 5^{th}, and 10^{th} percentiles, values less than or equal to the cut-off value were coded 1, and the others 2. In the case of 90^{th}, 95^{th}, and 99^{th} percentiles, values greater than or equal to the cut-off value were coded 1, the others were coded 2 in the database. In the next step, the weather variations for consecutive days were determined by calculating the difference between the measured values for each day and the parameters for the previous day. The diurnal temperature range was also added to the database which was calculated by the difference between the daily maximum and minimum temperatures. To define significant and non-significant daily changes, the standard deviations of each parameter was used: when the daily change was within one standard deviation, I considered the day as non-significant and changes outside one standard deviation as significant. The length of the intervals to these periods (significant and non-significant change) was also assigned.

To group the patient data, the patients who visited the ED for COPD-related emergency care were sorted according to the BNO-10 codes as defined in the international literature: patients with a code J4400, J4410, J4480, or J4490 were assigned a code 1 in the database, the others a code 2. I then aggregated the data on COPD presentations based on daily averages, where days with above-average COPD-related ED visits were assigned a code 1, and days with equal than or below average were assigned a code 2. The study population was split by sex and age groups. In terms of sex, males were assigned a code 1 and females a code 2, and in terms of age, two groups were formed based on the mean age of COPD patients: those under 67 years (group 1) and those over 67 years (group 2).

Statistical analyses were performed using IBM SPSS 28 and Jamovi 2.3.28 software. The descriptive statistics included climatological characteristics of the city of Pécs, the observed weather extremes and the characteristics of the daily changes in the weather, as well as the demographic characteristics of the patients registered at the ED, especially COPD-related visits. Demographic characteristics were tested using the Mann-Whitney U test to show the difference in various attributes between sex and age groups. The associations between extreme values of weather parameters and extreme changes in weather parameters (independent variables) and an above-average number of COPD-related benefits (dependent variable) were examined using contingency (2×2 table) tables to generate risk estimates between dependent and independent variables. Stratified analyses by age groups and sex and Mantel-Hanszel odds ratio calculations were also performed. The effects of the magnitude and duration of diurnal changes in weather on COPD case rates were determined by ordinal logistic regression analysis with a pretest using collinearity analysis. The ordinal logistic regression analysis was performed stratified by sex and age groups as well. The significance levels were set at $p<0.05$, so the confidence interval (CI) was 95% in all cases.

4. Results

4.1. Weather Parameters and COPD-related ED visits

Extremely low daily mean temperatures were identified as a risk factor, with a 27.5%-58.3% increased chance of having a higher-than-average number of daily COPD-related ED visits. Similar associations were also observed with extremely low values of daily minimum and maximum temperatures, which indicated an increased chance of a higher-than-average number of daily COPD-related ED visits by 35.8%-47.6%. Extremely low values of dew point were associated with significantly higher odds (76.2%-95%) of a higher-than-average number of daily COPD-related ED visits on those days. Extremely low values of relative humidity were associated with a 25.6%-57.5% chance of a higher-than-average number of daily COPD-related ED visits. However, the most significant risk factor was identified as days with a maximum pressure above 1013 hPa, which increased the odds of a higher-than-average number of daily COPD-related ED visits by 136.5% (Figure 1).

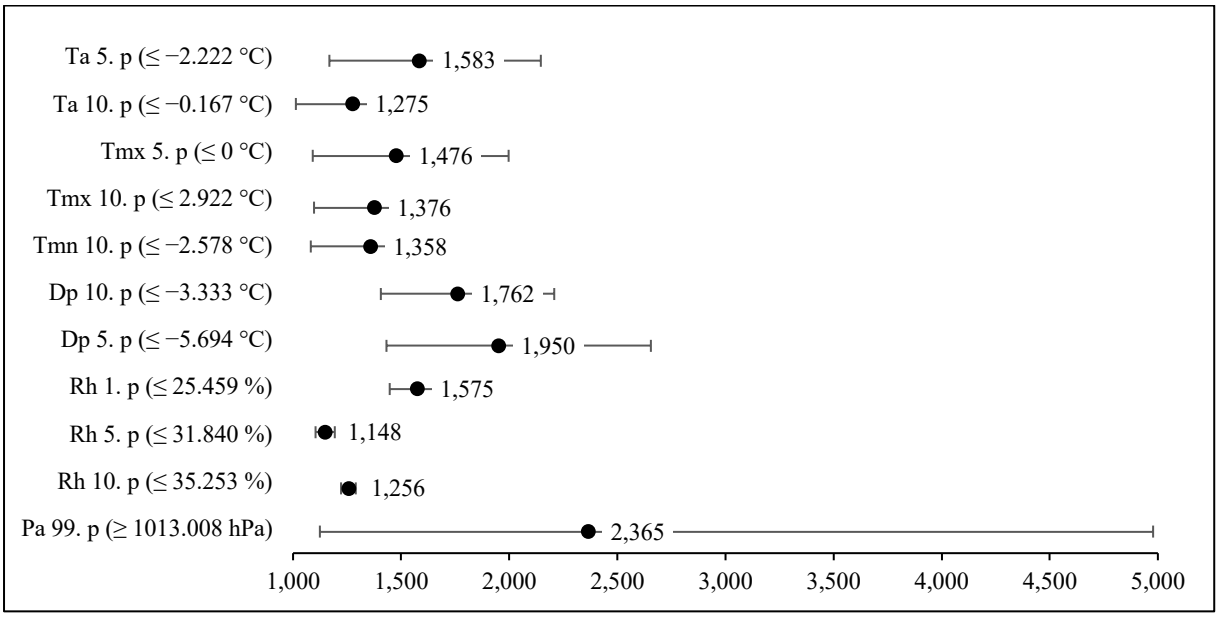

Figure 1. The odds ratios (OR) and their corresponding 95% confidence intervals (95%CI) for extremes of meteorological parameters and the higher-than-average number of daily COPD-related ED.

The daily mean, maximum, and minimum temperature extremes were identified as protective factors, which reduced the odds of a higher-than-average number of daily COPD-related ED visits by 23.4%-55.3%. In addition, extremely high values of dew point were found to be a protective factor, reducing the odds of a higher-than-average number of daily COPD-

related ED visits by 29.1% (Figure 2). There was no sign that either sex or age acted as a confounder or an effect modifier.

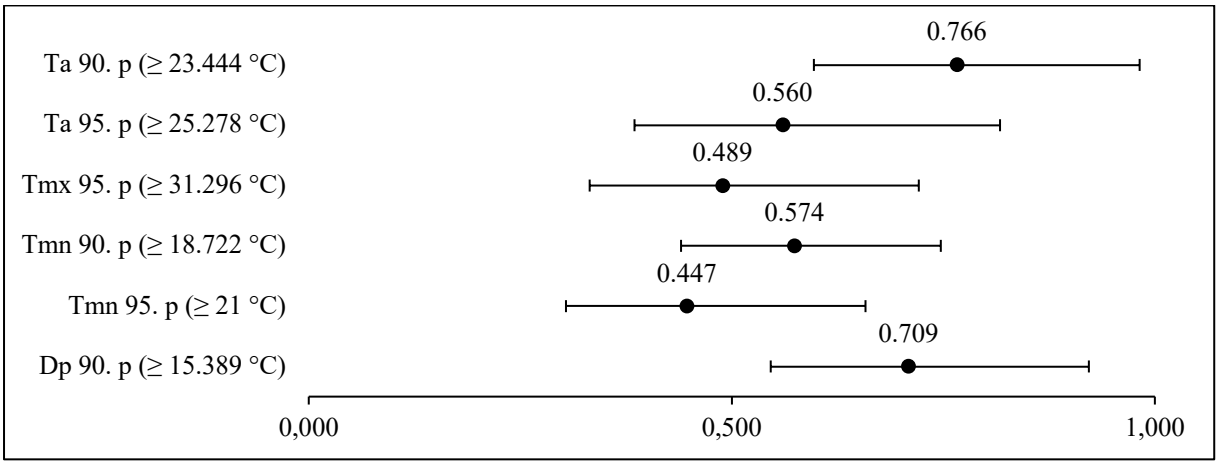

Figure 2. The odds ratios (OR) and their corresponding 95% confidence intervals (95%CI) for extremes of meteorological parameters and the higher-than-average number of daily COPD-related ED.

4.2. The Extremes of Daily Weather Variations and COPD-related ED-visits

The extremes of daily weather variations are associated with COPD-related ED visits. While the picture is mixed for mean temperature variability - both a large decrease (38.5% higher chance) and a large increase (49.1%-66.9% higher chance) can be considered as a risk factor - for the other meteorological parameters studied, it is established that extreme decreases or increases in their values negatively influence the higher-than-average number of daily COPD-related ED visits. A decrease of more than 9.111°C in maximum temperature increased the odds of a higher-than-average number of daily COPD-related ED visits by 91.5%. On consecutive days with a greater than 3.722°C difference in minimum temperature, the odds of having a higher-than-average number of daily COPD-related ED visits increased by 30.6%. For differences in dew point changes, on days with a 2.722°C increase from the previous day, the odds of having a higher-than-average number of daily COPD-related ED visits increased by 30.6%. For air pressure difference and wind speed difference, days, when these parameters decreased, were more likely to have a higher-than-average number of daily COPD-related ED visits: a decrease in air pressure difference of at least 5.1 hPa increased this chance by 42.3%-50.1%; for wind speed difference, a decrease of at least 5.741 m/s was required for a higher-than-average number of daily COPD-related ED visits to occur with a 34.1%-66.1% chance (Figure 3). There was no sign that either sex or age acted as a confounder or an effect modifier.

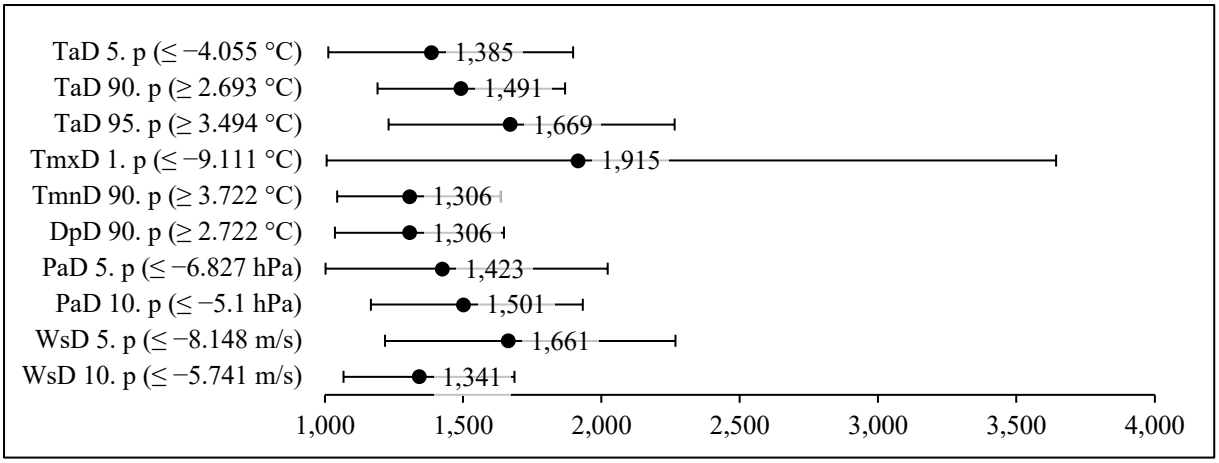

Figure 3. The odds ratios (OR) and their corresponding 95% confidence intervals (95%CI) for extremes of meteorological parameters' variability and the higher-than-average number of daily COPD-related ED visits.

4.3. The Duration and Magnitude of Weather Variability and COPD-related Emergency Visits

Three parameters were identified that influence COPD case rates by their variability over time. These were the variability of diurnal temperature range, air pressure, and relative humidity. When examining the duration of each period, I found that the shorter the period of stable conditions, the higher the chance of an increase in COPD case rates. Despite the low odds of an increase in COPD case rates under these conditions (0.3%-1.9%), the results indicate a statistically significant association (Figure 4). When stratified by sex, I found that the shorter the period of stable air pressure, the higher the odds of an increase in male COPD case rates (1.7%) (Figure 5). In the female population, no statistically significant results were observed for any of the parameters examined. Similar to the female population, my stratified analysis did not indicate a statistically significant association for age groups either.

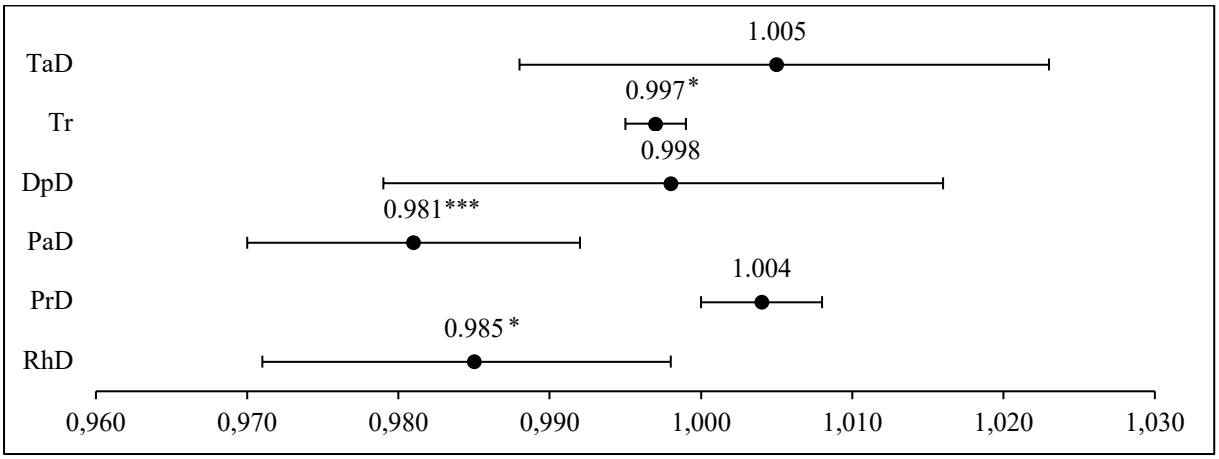

*Figure 4. The odds ratios (OR) and their corresponding 95% confidence intervals (95%CI) for the daily variation of meteorological parameters and the COPD case rates (***p<0.001, *p<0.05).*

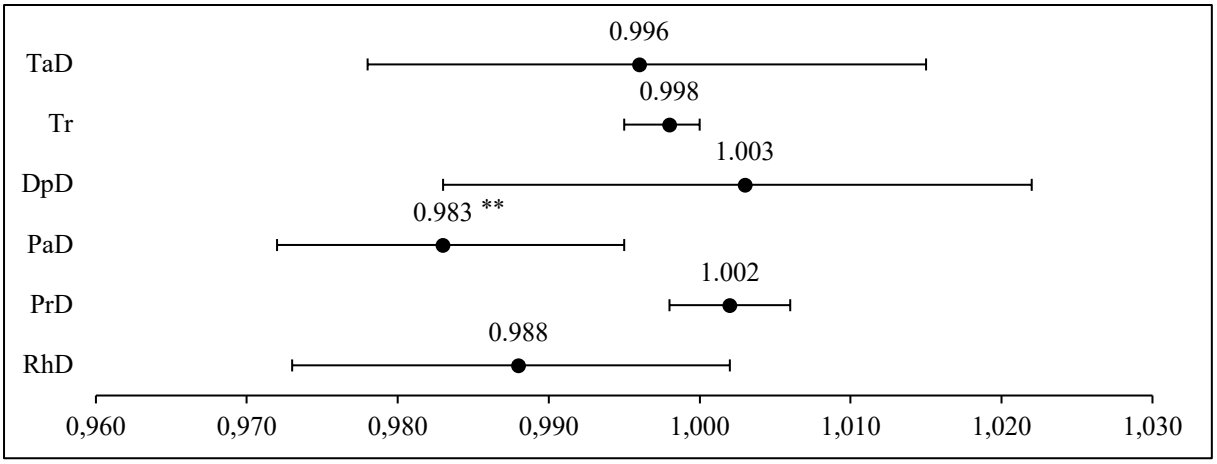

*Figure 5. The odds ratios (OR) and their corresponding 95% confidence intervals (95%CI) for the daily variation of meteorological parameters and the male COPD case rates (***p<0.001).*

The analysis of the magnitude and duration of weather variability and its effects on COPD case rates was also conducted. Looking at the whole population, I found associations for four parameters. Changes in the diurnal temperature range of more than 3.618°C in a short period increased the odds of an increase in COPD case rates by 0.5%. Changes in air pressure and relative humidity increased the chance of higher COPD case rates by 2.7% and 2.8%, respectively, when the magnitude of their change did not exceed one standard deviation and the intervals of change were short. Associations in opposite directions were observed for changes in precipitation. When the change in precipitation was within one standard deviation and the interval was long, the chance of having more COPD cases increased by 0.6% (Figure 6). The analysis did not indicate a statistically significant association for variability of daily mean-, maximum-, and minimum temperatures.

Using stratified analysis, I attempted to determine whether there are differences in the effects of variability in weather parameters between sex and age groups. For diurnal temperature range variability, the analysis revealed a fundamental difference: while changes of more than one standard deviation (3.618°C) over a short period increased the odds of higher female and male COPD case rates by 0.3% and 0.4%, respectively, changes of less than one standard deviation over a short period increased the odds of higher male COPD case rates by 19.6%. For changes in air pressure and relative humidity, COPD case rates for both sexes increased with similar odds compared to the whole population: when the magnitude of change did not exceed one standard deviation and these intervals were shorter, the odds of higher female COPD case rates were 1.6% and 1.8%, respectively, and the odds of higher male COPD case rates were 2.6% and 2.5%, respectively. For precipitation variation, the opposite direction

was seen for sex, and to a similar extent: when a difference in precipitation was observed over a long period, the odds of having a higher number of female COPD cases increased by 0.4%, compared with 0.5% for male COPD cases (Figure 6). The results did not indicate that there was a significant difference in COPD case rates for the young or elderly population compared with COPD case rates for the overall population.

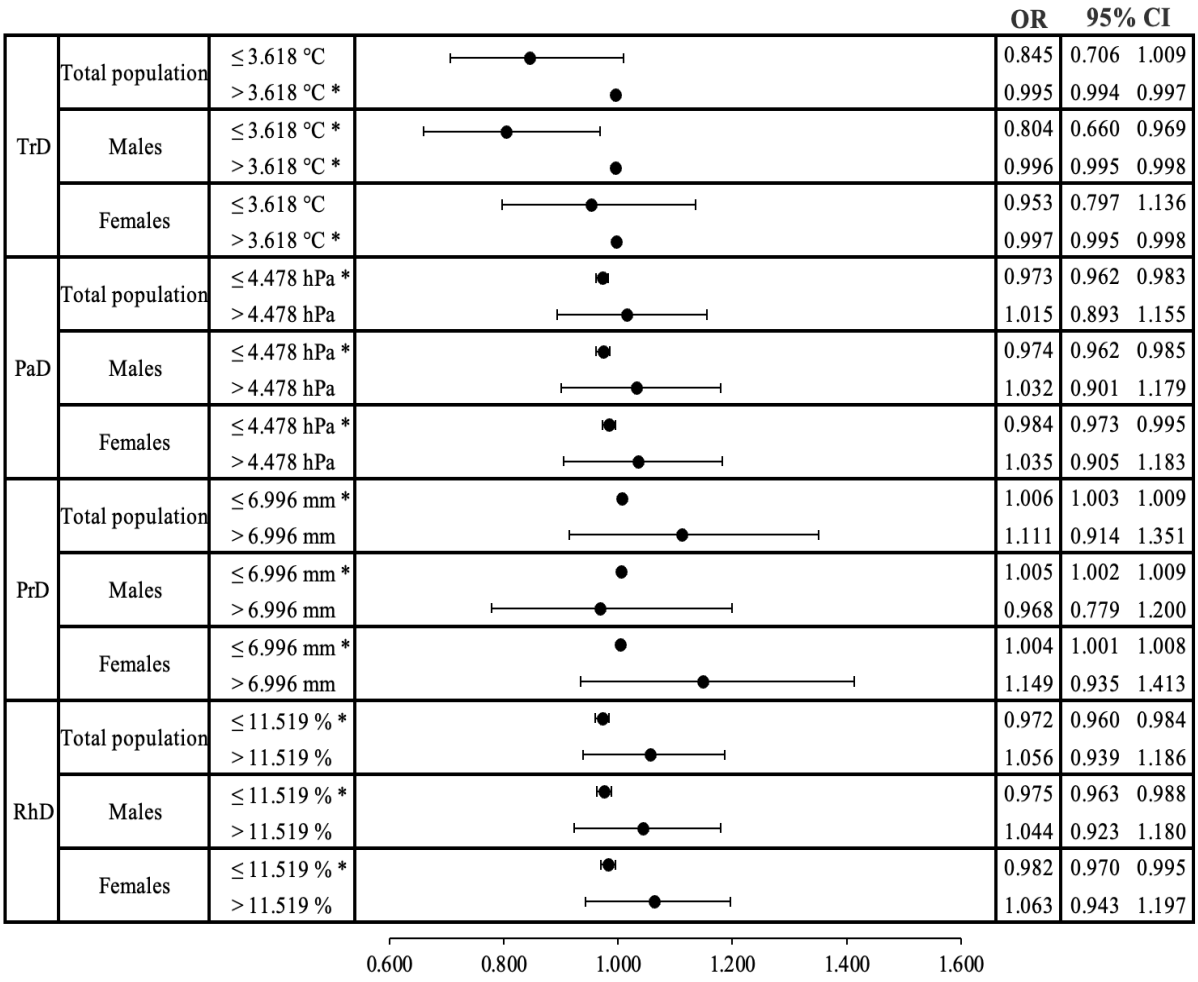

*Figure 6. The odds ratios (OR) and their corresponding 95% confidence intervals (95%CI) for the duration and magnitude of weather variability and COPD case rates of the total, male, and female population (*p<0.05).*

5. Discussion

5.1. Weather Parameters and COPD-related ED visits

I found statistically significant associations between extremely low daily mean (below -0.167°C), maximum (below 2.922°C), and minimum (below −2.578°C) temperatures and higher-than-average numberr daily of COPD-related ED visits. These weather conditions increased the risk of a higher-than-average number daily of COPD-related ED visits by 27.5%-58.3%. In addition, a statistically significant association has been found between extremely low values of dew point (below −3.333°C) and relative humidity (below 35.253%) and higher-than-average numbers daily of COPD-related ED visits. The results suggest that there was a 14.8%-95% chance of a higher-than-average number daily of COPD-related ED visits occurring on a given day. The highest risk was associated with extremely high air pressure (above 1013.008 hPa): the risk of a higher-than-average number daily of COPD-related ED visits increased by 136.5% when such air pressure conditions existed (Figure 1). Our results are consistent with other studies investigating the association between cold temperature events and the frequency of respiratory disease and COPD-related emergency visits. However, there is limited research available on the dew point, my previous work has already revealed a link between extremely low dew point and a higher-than-average number of COPD-related ED visits.

In parallel, my research also found that high daily mean (above 23.444°C), maximum (above 31.296°C) and minimum temperatures (above 18.722°C) and high dew point (above 15.389°C) were identified as protective factors for above average COPD-related emergency care. These weather conditions can reduce the odds of having a higher-than-average number of COPD-related ED visits by 23.4%-55.3% (Figure 2).

A stratified analysis by sex and age groups was performed to see whether these attributes have a confounding effect or possibly modify the effect of the meteorological parameters on the association between COPD-related emergency care. The data revealed that the majority of COPD-related ED visits were made by older patients compared with patients admitted with non-COPD-related visits. There was also a female predominance among COPD patients, just as there was among patients admitted with non-COPD-related visits. However, my results do not establish that the association between weather factors associated with extreme cold weather and higher-than-average number of COPD-related ED visits is influenced by sex or age.

In summary, extreme cold atmospheric conditions significantly increase the chances of a higher-than-average number of COPD-related ED visits, and extreme warm weather reduces this type of risk. The reasons can be attributed to an increased risk of cold weather-induced

airway inflammation and respiratory tract infections and an increase in cold weather-induced respiratory exacerbations.

5.2. The Extremes of Daily Weather Variations and COPD-related ED-visits

In my research, I found that extreme daily mean temperature changes (at least 4.055°C cooling, 2.693°C warming), maximum temperature changes (at least 9.111°C cooling), and minimum temperature changes (at least 3.722°C warming) were significantly associated with a higher-than-average number of COPD-related ED visits. These temperature changes increased the odds of a higher-than-average number of COPD-related ED visits by 30.6% and 91.5%, respectively. In addition, a statistically significant association was found between dew point change (at least 2.722°C increase), air pressure change (at least 5.1 hPa decrease) and mean wind speed change (at least 5.741 m/s decrease), and a higher-than-average number of COPD-related ED visits. These changes increased the odds of a higher-than-average number of COPD-related emergency visits by 30.6% and 66.1% on the days of interest (Figure 3). The results of my thesis confirm the conclusions of other studies, including our own earlier study, which came to similar conclusions. Sudden temperature changes can cause stress on the respiratory system, leading to inflammation and airway constriction. This can cause breathing difficulties and exacerbations in people with COPD.

In summary, extreme diurnal temperature range, dew point, air pressure, and wind speed changes significantly increase the risk of a higher-than-average number of COPD-related ED visits.

5.3. The Duration and Magnitude of Weather Variability and COPD-related Emergency Visits

COPD case rates are influenced by three factors that can be relevant to the temporal variability of changes: the variability of diurnal temperature range, changes in air pressure, and changes in relative humidity. Examination of each period showed that the shorter the period of stable atmospheric conditions - i.e. the more variable the weather pattern - the more likely it is that COPD case rates will increase. Despite the low odds (0.3%-1.9%) of an increase in COPD case rates under these conditions, the results suggest a statistically significant association (Figure 4). I also stratified the analysis to identify the effect of sex on the duration of variability of weather and the association between COPD-related ED visits. When examining the different periods, I found that the shorter the duration of stable air pressure, the more likely the increase in COPD case rates among males (1.7%) (Figure 5). For the female population, I did not find a

statistically significant association for any of the parameters examined. These results are in line with other studies exploring the association between respiratory disease and diurnal temperature range, demonstrating the role of this parameter in respiratory hospitalizations, including COPD-related ED visits.

COPD case rates are influenced by three factors that can be relevant to the temporal variability of changes: the variability of diurnal temperature range, changes in air pressure, and changes in relative humidity. Examination of each period showed that the shorter the period of stable atmospheric conditions – i.e. the more variable the weather pattern – the more likely it is that COPD case rates will increase. Despite the low odds (0.3%-1.9%) of an increase in COPD case rates under these conditions, the results suggest a statistically significant association (Figure 4). I also stratified the analysis to identify the effect of sex on the duration of variability of weather and the association between COPD-related ED visits. When examining the different periods, I found that the shorter the duration of stable air pressure conditions, the more likely the increase in COPD case rates among men (1.7%) (Figure 5). For the female population, I did not find a statistically significant association for any of the parameters examined. These results are in line with other studies exploring the association between respiratory disease and daily heat intake, demonstrating the role of the diurnal temperature range in respiratory hospitalizations, including COPD-related ED visits.

In stratified analyses, the effects of variability in weather parameters on COPD case rates were examined for sexes. I found significant differences between sexes for diurnal temperature variability. While changes of more than one standard deviation (3.618°C) over a short period increased the odds of higher COPD case rates in females and males by 0.3% and 0.4%, respectively, changes of less than one standard deviation over a short period increased the odds of higher COPD case rates in males by 19.6%. For changes in air pressure and relative humidity, the increase in COPD case rates for each sex was similar to the increase observed in the overall population. For the short-term, one standard deviation changes, the odds of higher COPD case rates increased by 1.6% for females and 2.6% for males. For relative humidity changes, the risk increased by 1.8% in females and 2.5% in males. For precipitation changes, the sex-specific associations were consistent with those observed in the overall population. Long-lasting precipitation variation within one standard deviation increased the odds of higher COPD case rates by 0.4% in females and by 0.5% in males. My results are consistent with previous studies that have reported greater susceptibility to diurnal temperature ranges in male COPD patients. However, it should be noted that these studies show a male predominance, which may result in

men appearing more sensitive to these weather changes, in contrast to the population studied in this thesis.

6. Conclusions

- Days with an extremely low dew point of below -3.333°C had a 76.2%-95% chance of resulting in a higher-than-average number of daily COPD-related ED visits.
- Days with extremely high barometric pressure values above 1013.008 hPa had up to 136.5% higher odds of a higher-than-average number of daily COPD-related ED visits.

- When the daily dew point increase was extreme, at least 2.722 °C, there was a 30.6% chance of a higher-than-average number of daily COPD-related ED visits.
- On days when the air pressure decreased day by day and this decrease was greater than 5.1 hPa, the odds of having a higher-than-average number of daily COPD-related ED visits ranged from 42.3% to 50.1%.
- When the average wind speed decreased by at least 5.741 m/s from one day to the next, the odds of having a higher-than-average number of daily COPD-related ED visits varied between 34.1% and 66.1%.

- When the magnitude of the change in air pressure and relative humidity change did not exceed one standard deviation and the intervals were short, the odds of having a higher COPD case rate in the emergency department were 2.7%-2.8%.
- A change in temperature of up to 3.618°C within a short interval increased the odds of registering more COPD-related emergency department visits among males by 19.6%.

7. List of publications

Publications related to the present PhD Thesis:

Kiss, T.; Leitol, C.; **Márovics, G. P.**; Zentai, T.; Baczur, R.; Girán, J. The First Steps to Develop a Monitoring-Based Method to Support the Sustainable Mosquito Control in an Urban Environment in Hungary. SUSTAINABILITY 2020, 12. https://doi.org/10.3390/su12125013. [**IF: 3,251; Q2**]

Márovics, G. P.; Girán, J. A szélsőséges időjárás-változás és a COPD-vel kapcsolatos sürgősségi ellátások kapcsolata. Egészségtudomány 2024, 1. Accepted for publication: 30.12.2023.

Márovics, G. P.; Pozsgai, É.; Németh, B.; Czigány, S.; Németh-Simon, S.; Girán, J. How Vulnerable Are Patients with COPD to Weather Extremities? – A Pilot Study from Hungary. Healthcare (Basel) 2022, 10 (11), 2309. https://doi.org/10.3390/healthcare10112309. [**IF: 2,8; Q2**]

Márovics, G. P.; Pozsgai, É.; Németh, B.; Czigány, S.; Soós, S.; Németh-Simon, S.; Girán, J. Weather Variability and COPD: A Risk Estimation Identified a Vulnerable Sub-population in Hungary. In Vivo 2024, Vol. 38 Issue 2. Accepted for publication: 25.03.2024. [**IF: 2,406; Q2**]

Molnár, F. J.; Rendeki, M.; Rendeki, S.; Nagy, B.; Bacher, V.; Bogár, P. Z.; Schlégl, Á. T.; Koltai, A.; Maróti, P.; **Márovics, G. P.** Validation of 3D Printed MAYO Tubes and Stethoscope in Simulated Medical Environment – Tools Fabricated with Additive Manufacturing for Emergency Care. HELIYON 2023, 9. https://doi.org/10.1016/j.heliyon.2023.e20866. [**IF: 4,0; Q1**]

Cumulative impact factor related to the present PhD Thesis: 12,851

Presentations related to the present PhD Thesis:

Márovics, G. P.; Girán, J. Az időjárás egészségmódosító hatásainak vizsgálata Pécs példáján. XIV. NKE Konferencia Szeged, 26-27.08.2021.

Márovics, G. P.; Girán, J. The Effects of Daily Air Pressure Change on COPD Patients of Department of Emergency Medicine. 10th Jubilee Interdisciplinary Doctoral Conference. Pécs, Magyarország, 12-13.11.2021.

Márovics, G. P.; Girán, J. Az időjárás néhány paraméterének hatása a COPD morbiditásra. V. Orvosmeteorológiai Konferencia Budapest, 09-10.12.2021.

Publications not related to the present PhD Thesis:

Girán, J.; **Márovics, G. P.** Település-egészségtan. In *Megelőző orvostan és népegészségtan*; Ádány, R., Kiss, I., Paulik, E., Sándor, J., Ungvári, Z. I., Eds.; Medicina Könyvkiadó Zrt.: Budapest, 2023; pp 405–409.

Kecskes, G.; Szabo, A.; Sutori, D.; Maróti, P.; **Márovics, G. P.**; Molnár, F. T. Pneumothorax/Pneumomediastinum and Pre-Existing Lung Pathology in Ventilated COVID-19 Patients: A Cohort Study. JOURNAL OF THORACIC DISEASE 2022, 14, 4733–4740. https://doi.org/10.21037/jtd-22-817.

Márovics, G. P. Az Egészségtervezés És Az Egészségfejlesztési Tervezés Módszereinek Közös Pontjai És Különbségei. EGÉSZSÉGFEJLESZTÉS 2019, 1, 4–8.

Nemeth, M.; Ternák, G.; Rozanovic, M.; **Márovics, G. P.**; Bogar, L. Antibiotic Consumption Patterns in European Countries Show Association with Obesity Prevalence; A Possible Clue to the Origin of the Obesity Pandemic, 2022. https://m2.mtmt.hu/api/publication/33591421.

Rozanovic, M.; Domokos, K.; **Márovics, G. P.**; Rohonczi, M.; Csontos, C.; Bogár, L.; Rendeki, S.; Kiss, T.; Rozanovic, M. N.; Loibl, C. Can We Predict Critical Care Mortality with Non-Conventional Inflammatory Markers in SARS-CoV-2 Infected Patients? CLINICAL HEMORHEOLOGY AND MICROCIRCULATION 2023, 84, 71–82. https://doi.org/10.3233/CH-231697.

Sándor-Bajusz, K. A.; Kraut, A.; Baasan, O.; **Márovics, G. P.**; Berényi, K.; Lohner, S. Publication of Clinical Trials on Medicinal Products: Follow-up on Trials Authorized in Hungary. TRIALS 2022, 23. https://doi.org/10.1186/s13063-022-06268-y.

Ternák, G.; Berényi, K.; **Márovics, G. P.**; Sümegi, A.; Fodor, B.; Németh, B.; Kiss, I. Dominant Antibiotic Consumption Patterns Might Be Associated With the Prevalence of Multiple Sclerosis in European Countries. IN VIVO 2020, 34, 3467–3472. https://doi.org/10.21873/invivo.12186.

Ternák, G.; Berényi, K.; Németh, B.; Szenczi, Á. I.; **Márovics, G. P.**; Kiss, I. Association of Antibiotic-Consumption Patterns with the Prevalence of Hematological Malignancies in European Countries. SCIENTIFIC REPORTS 2022, 12. https://doi.org/10.1038/s41598-022-11569-y.

Ternák, G.; **Márovics, G. P.**; Sümegi, K.; Bánfai, Z.; Büki, G.; Magyari, L.; Szabó, A.; Melegh, B. Down-Syndrome-Related Maternal Dysbiosis Might Be Triggered by Certain Classes of Antibiotics: A New Insight into the Possible Pathomechanisms. ANTIBIOTICS 2023, 12. https://doi.org/10.3390/antibiotics12061029.

Ternák, G.; Németh, M. F.; Rozanovic, M.; **Márovics, G. P.**; Bogár, L. Antibiotic Consumption Patterns in European Countries Are Associated with the Prevalence of Parkinson's Disease; the Possible Augmenting Role of the Narrow-Spectrum Penicillin. ANTIBIOTICS 2022, 11. https://doi.org/10.3390/antibiotics11091145.

Ternák, G.; Németh, M. F.; Rozanovic, M.; **Márovics, G. P.**; Bogár, L. "Growth-Promoting Effect" of Antibiotic Use Could Explain the Global Obesity Pandemic: A European Survey. ANTIBIOTICS 2022, 11. https://doi.org/10.3390/antibiotics11101321.

Cumulative impact factor: 41,106
Number of independent citations: 9

8. Acknowledgments

I would like to take this opportunity to thank my supervisor, Dr. János Girán, for his professional guidance, help, and conscientious work during my PhD studies, and for always providing me with excellent advice.

I am grateful to Prof. Dr. István Kiss for the trust he has placed in me, for allowing me to develop my professional career, and for being a credible role model for me on a human, scientific, and professional level.

I am thankful to all the staff of the Department of Public Health Medicine, especially Dr. Balázs Németh and Dr. Károly Berényi, who helped me with their ideas and insights, and I could rely on them in many matters. I would also like to thank Dr. Éva Pozsgai for her help in proofreading and Dr. Edit Bőszné Murányi for her support.

I would also like to thank my colleagues Dr. Szilvia Németh-Simon, Dr. Szilvia Soós, and Dr. Szabolcs Czigány for their contributions to the publications on which my thesis is based. Special thanks to Dr. Péter Kanizsai and the staff of the Institute of Geography and Earth Sciences for their support.

I cannot be grateful enough to my wife, Fatima Faisal, who has supported me with endless patience over the years, standing by me in every situation, helping me, encouraging me, and never letting me give up in the most difficult moments. Thank you to my mother Andrea Paluska, my father László Márovics, my brother Ádám Márovics and my grandmother Gizella Horváth for supporting me throughout my life and for always being there for me, they have laid the foundations for my studies. I am also grateful to all the members of my family, including Dr. Zelma Faisal and Erzsébet Györgyi.

Last but not least, many thanks to my friends, especially Zsolt Horváth, Levente Major, Péter Hatvani, Dániel Homlok, and Dr. Péter Maróti, who, in addition to his professional support, has been a friend next to me.

The projects TUDFO/51757-1/2019-ITM (Tématerületi Kiválóság Program) and 2021-2-HU01-KA220-HED-000050972 (ClimateMed Erasmus+ Project) contributed greatly to the preparation of this thesis.