Thorax 2023; 78(9): 850-851. Publisher DOI: 10.1136/thorax-2023-220326

Editorial

Heat-related hospitalisations for asthma – challenges for research

Authors: Eva SL Pedersen[1], Claudia E Kuehni[1,2]

Affiliations:

1 Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland

2 Division of Paediatric Respiratory Medicine and Allergology, Department of Paediatrics, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

Corresponding author:

Eva SL Pedersen, Institute of Social and Preventive Medicine, University of Bern, Switzerland.

Mittelstrasse 43, 3012 Bern, Switzerland. +41 31 684 56 75. Eva.pedersen@unibe.ch

Word count: 1047 of 1000

Figures/tables: 1 of max 2

Citations: 19 of 20

Warm temperatures are associated with health care encounters for asthma and chronic obstructive pulmonary disease (COPD).[1-8] Temperature affects the spread of infectious diseases and increases air pollution levels, pollen counts, and allergenicity—all elevate risks of asthma exacerbations—resulting in hospitalisations.[9] Rising global temperatures possibly escalate effects on respiratory health worldwide. Yet, mapping synergetic effects of daily temperatures, air pollution, allergens, and virus spread is fundamental for understanding causal pathways and mechanisms. Such mapping helps identify vulnerable groups—an essential activity for planning structural and behavioral interventions for minimizing climate change effects on respiratory health.

However, available literature on warmer summer temperature effects on respiratory morbidity remain deficient with many open questions. Some findings suggest higher risk of asthma hospitalisation with higher mean temperatures,[6-8] others disagree;[4, 5] studies differed regarding temperature metrics, confounder selections, mediators, effect modifiers, and outcome definitions.

A large innovative study from the United Kingdom

Konstantinoudis et al.—published in the present issue of Thorax [10]—used sophisticated analyses on a large dataset to investigate effects of daily mean temperature on hospitalisation risks for asthma in the United Kingdom. They analysed national data from more than 260,000 people 5 years and older between 2002–2019; linked residential information with high-resolution daily temperature data and meteorology during summer months (June– August); and used International Classification of Diseases-10th revision (ICD-10) main diagnostic groups J45 (asthma) and J46 (status asthmaticus) as outcome. The case-crossover design—where each person is its own control—accounts for time-stable, individual-level confounders, such as sex and ethnicity. They adjusted for meteorology and national holidays as possible confounders and studied effect modification by age, sex, time period, and region. Since they assumed pollen counts and air pollution levels mediated effects, they excluded these from the model. They found an overall 1.11% increase in risk of asthma hospitalisation for every 1°Celsius increase in ambient summer temperature. The risk was highest among males aged 16–64, while older

adults were not at risk. Also, the risk was largest during 2002–2007 with no effect between 2008–2013 or 2014–2019. They found some spatial variation between regions, yet mainly among males.

What does the study tell us?

The study by Konstantinoudis et al. adds valuable evidence about temperature and asthma morbidity, but some challenges remain, which if addressed in future studies, could help us better design strategies to prevent heat-related asthma hospitalization. These challenges relate to the use of routine outcome data, clarification of mechanisms and pathways, and identification of vulnerable groups.

The outcome: asthma diagnosis as subgroup of lower airway disease

First, in the present study only isolated ICD-10 codes for asthma (J45; J46) are included as outcome. An earlier study from the same group—also published in Thorax [11]—focused only on COPD (J40-44). With rising awareness about asthma-COPD overlap syndrome [12, 13] and billing rules influencing hospital diagnostic code choices, distinctions between asthma and COPD remain ambiguous. The proportion of people receiving either diagnosis varies over time and by patient age, region, and possibly temperature.[14] The same applies to children diagnosed with asthma, acute bronchitis, or viral pneumonia dependent on physician, region, and time period [15, 16]. For future research, we recommend including overall admissions for lower airway disease broken down by all diagnostic groups—asthma, COPD, acute bronchitis, influenza, and pneumonia—and describing how temperature affects broader diagnostic categories.

Selecting single diagnostic subgroups as study outcomes possibly biases results and makes interpretations difficult. For instance, Konstantinoudis et al. found an increase in COPD hospitalisations with rising temperatures during the exact time period when observing no effect for asthma (2007–2018), and they found the strongest effects for COPD among older adults and females—the unaffected subpopulations in the asthma paper.[10, 11] We suggest artificial fluctuations from 1) changes in diagnostic practice over time and by region and 2) different diagnostic labeling for males and females

and by age-group possibly explain the seemingly contradictory results found for asthma and COPD. Analysing all obstructive airway disease diagnoses together could illuminate apparent contradictory findings.

Testing pathways and mechanisms

Second, exploration of mechanisms and pathways could help in the design of interventions. We agree air pollution, pollen counts, and respiratory epidemics can mediate effects from temperature and be on the causal pathway. In fact, the COPD paper found that adjustment for air pollution attenuated effects of temperature on hospitalisations. However, other studies showed effects of pollen and air pollution independent of temperature.[17, 18] Exploring direct effects—and effects of possible mediators—would prepare clinicians and policy makers for translating mechanisms into preventive actions. Further, the authors had analysed maximum temperatures for the COPD analysis and mean temperatures for asthma. Using different exposure metrics in parallel —through sensitivity analyses— within the same study population and for the same outcomes – could teach us whether extreme or rather mean temperatures increase risk, and thus inform counselling and policy more precisely.

Vulnerable groups and effect modifiers

Third, the case-cross-over design is an analysis model that elegantly corrects for confounding by individual characteristics, such as asthma controller treatment or socioeconomic status. Yet systematically exploiting individual characteristics – as effect modifiers rather than as confounders – would help to identify vulnerable groups. For instance, the larger effect on working-age males found in the asthma paper could in future studies be further explored using linked routine data on occupation and thus inform whether males working outdoors are particularly affected. Evidence for effect modification by socioeconomic characteristics—area-based or individual proxies—or ethnicity possibly elucidate pathways leading to extra hospitalisations and promote concise action. For example, some regions have high proportions of inhabitants of South Asian ethnic origin, a population with

increased risk of metabolic and allergic diseases,[19] which could lead to preventative actions. Or, if air pollution was found to be the main mediator, laws could limit traffic flow on warm days.

Conclusions

Konstantinoudis et al. bring us an important step closer to understanding the relationship between heat and respiratory morbidity. Yet we suggest future research digs deeper into understanding pathways (table 1). We recommend curious exploration and close collaboration between environmental epidemiologists and clinicians and analysing large datasets of several diagnostic groups in one paper rather than splitting them up into multiple papers. This could help us reach a higher level of understanding for taking informed actions and reducing future harm.

Acknowledgements

We thank Kristin Bivens for editing this editorial.

Conflict of interest

Both authors declare no conflict of interest

Financial support

This work was supported by the Swiss National Science Foundation, Switzerland (SNSF 320030_212519) and the Swiss Lung Association, Switzerland (2021-08_Pedersen).

Table 1: Suggestions for future research on temperature and respiratory health, to help identifying causal pathways as foundation for designing future preventive strategies.

Study design element	Next step	Knowledge gain
Outcome	Use a unified statistical framework for studying all ICD-10 codes for airway diseases in one model (e.g. asthma, COPD, acute respiratory infections).	Better understanding of combined and disease-specific effects and reduction of effect of possible coding bias; more robust results; larger numbers and improved statistical power and precision.
Exposure	Compute sensitivity analysis of effect of different exposure metrics (e.g. daily minimum, maximum, or mean temperatures, different lag times) within same study population.	Better understanding of effects; easier comparison with results from other studies; elucidation of mechanisms; better information on potential interventions.
Pathways	Conduct mediation analysis of the pathway between temperature, pollen, air pollution, infectious disease epidemics, and hospitalization for lower airway disease.	Understanding whether hospitalisations are triggered directly by the heat itself or mediated via exposures to allergens, air pollution, infectious agents, or other mechanisms.
Effect modifiers	Study how the effect of heat on respiratory hospitalisations is modified by individual-level factors such as health behaviour (e.g. smoking), occupation, treatment, diet, or socioeconomic status.	Better understanding of vulnerable groups to target preventive strategies.
External comparison	Study whether the effect of high temperatures on asthma and COPD hospitalisations decreased over time also in other countries, or whether findings are specific for the UK.	Investigating the causality of the effect and whether the effect—if causal—can be influenced by adaptive mechanisms in individual behavior (e.g. smoking, avoiding heat), public policy (e.g. traffic restrictions on hot days) or changes in health care (better primary care to reduce hospitalisations).

Abbreviations: ICD-10; International Classification of Diseases-10th revision, COPD; Chronic Obstructive Pulmonary Disease

References

1. Deng S, Han A, Jin S, Wang S, Zheng J, Jalaludin BB, Hajat S, Liang W, Huang C. Effect of extreme temperatures on asthma hospital visits: Modification by event characteristics and healthy behaviors. *Environ Res* 2023: 226: 115679.
2. Ma Y, Zhao Y, Zhou J, Jiang Y, Yang S, Yu Z. The relationship between diurnal temperature range and COPD hospital admissions in Changchun, China. *Environ Sci Pollut Res Int* 2018: 25(18): 17942-17949.
3. Wang YC, Lin YK. Temperature effects on outpatient visits of respiratory diseases, asthma, and chronic airway obstruction in Taiwan. *Int J Biometeorol* 2015: 59(7): 815-825.
4. Son JY, Bell ML, Lee JT. The impact of heat, cold, and heat waves on hospital admissions in eight cities in Korea. *Int J Biometeorol* 2014: 58(9): 1893-1903.
5. Zhang Y, Peng L, Kan H, Xu J, Chen R, Liu Y, Wang W. Effects of meteorological factors on daily hospital admissions for asthma in adults: a time-series analysis. *PLoS One* 2014: 9(7): e102475.
6. Lam HC, Li AM, Chan EY, Goggins WB, 3rd. The short-term association between asthma hospitalisations, ambient temperature, other meteorological factors and air pollutants in Hong Kong: a time-series study. *Thorax* 2016: 71(12): 1097-1109.
7. Soneja S, Jiang C, Fisher J, Upperman CR, Mitchell C, Sapkota A. Exposure to extreme heat and precipitation events associated with increased risk of hospitalization for asthma in Maryland, U.S.A. *Environ Health* 2016: 15: 57.
8. Wu Y, Xu R, Wen B, Coelho M, Saldiva PH, Li S, Guo Y. Temperature variability and asthma hospitalisation in Brazil, 2000-2015: a nationwide case-crossover study. *Thorax* 2021: 76(10): 962-969.
9. Bishan C, Bing L, Chixin C, Junxia S, Shulin Z, Cailang L, Siqiao Y, Chuanxiu L. Relationship between airborne pollen assemblages and major meteorological parameters in Zhanjiang, South China. *PLoS One* 2020: 15(10): e0240160.
10. Konstantinoudis G, Minelli C, Lam HCY, Fuertes E, Ballester J, Davies B, Vicedo-Cabrera AM, Gasparrini A, Blangiardo M. Asthma hospitalisations and heat exposure in England: a case-crossover study during 2002-2019. *Thorax* 2023.
11. Konstantinoudis G, Minelli C, Vicedo-Cabrera AM, Ballester J, Gasparrini A, Blangiardo M. Ambient heat exposure and COPD hospitalisations in England: a nationwide case-crossover study during 2007-2018. *Thorax* 2022: 77(11): 1098-1104.
12. de Marco R, Pesce G, Marcon A, Accordini S, Antonicelli L, Bugiani M, Casali L, Ferrari M, Nicolini G, Panico MG, Pirina P, Zanolin ME, Cerveri I, Verlato G. The coexistence of asthma and chronic obstructive pulmonary disease (COPD): prevalence and risk factors in young, middle-aged and elderly people from the general population. *PLoS One* 2013: 8(5): e62985.
13. Hosseini M, Almasi-Hashiani A, Sepidarkish M, Maroufizadeh S. Global prevalence of asthma-COPD overlap (ACO) in the general population: a systematic review and meta-analysis. *Respir Res* 2019: 20(1): 229.
14. Akmatov MK, Ermakova T, Holstiege J, Steffen A, von Stillfried D, Bätzing J. Comorbidity profile of patients with concurrent diagnoses of asthma and COPD in Germany. *Sci Rep* 2020: 10(1): 17945.
15. Mansbach JM, Espinola JA, Macias CG, Ruhlen ME, Sullivan AF, Camargo CA, Jr. Variability in the diagnostic labeling of nonbacterial lower respiratory tract infections: a multicenter study of children who presented to the emergency department. *Pediatrics* 2009: 123(4): e573-581.
16. Porter P, Brisbane J, Tan J, Bear N, Choveaux J, Della P, Abeyratne U. Diagnostic Errors Are Common in Acute Pediatric Respiratory Disease: A Prospective, Single-Blinded Multicenter Diagnostic Accuracy Study in Australian Emergency Departments. *Front Pediatr* 2021: 9: 736018.
17. De Roos AJ, Kenyon CC, Zhao Y, Moore K, Melly S, Hubbard RA, Henrickson SE, Forrest CB, Diez Roux AV, Maltenfort M, Schinasi LH. Ambient daily pollen levels in association with asthma exacerbation among children in Philadelphia, Pennsylvania. *Environ Int* 2020: 145: 106138.

18. Gisler A, Eeftens M, de Hoogh K, Vienneau D, Salem Y, Yammine S, Jakob J, Gorlanova O, Decrue F, Gehrig R, Frey U, Latzin P, Fuchs O, Usemann J. Pollen exposure is associated with risk of respiratory symptoms during the first year of life. *Allergy* 2022: 77(12): 3606-3616.
19. Jones CJ, Paudyal P, West RM, Mansur AH, Jay N, Makwana N, Baker S, Krishna MT. Burden of allergic disease among ethnic minority groups in high-income countries. *Clin Exp Allergy* 2022: 52(5): 604-615.