Environment International 193 (2024) 109097

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Full length article

Associations of heat with diseases and specific symptoms in Flanders, Belgium: An 8-year retrospective study of general practitioner registration data

Endale Alemayehu Ali [a,*], Bianca Cox [b], Karen Van de Vel [b], Els Verachtert [b], Bert Vaes [a], Simon Gabriel Beerten [a], Elisa Duarte [c], Charlotte Scheerens [a], Raf Aerts [d,e], Gijs Van Pottelbergh [a]

[a] Department of Public Health and Primary Care, KU Leuven, Kapucijnenvoer 33, Leuven, Flanders 3000, Belgium
[b] VITO Health, Flemish Institute for Technological Research (VITO), Mol, Belgium
[c] I-BioStat, Data Science Institute, Hasselt University, Campus Diepenbeek, Diepenbeek, Belgium
[d] Division Ecology, Evolution and Biodiversity Conservation, KU Leuven, Leuven, Belgium
[e] Risk and Health Impact Assessment, Sciensano, Brussels, Belgium

ARTICLE INFO

Keywords:
Disease
General practitioner
Heat
Temperature

ABSTRACT

Introduction: Global temperature rise has become a major health concern. Most previous studies on the impact of heat on morbidity have used hospital data.
Objective: This study aimed to quantify the association between ambient temperature and a variety of potentially heat-related medical conditions and symptoms using general practitioner (GP) data, in Flanders, Belgium.
Methods: We used eight years (2012–2019) of aggregated data of daily GP visits during the Belgian summer period (May-September). A distributed lag nonlinear model (DLNM) with time-stratified conditional quasi-Poisson regression was used to account for the non-linear and delayed effect of temperature indicators (minimum, mean and maximum). We controlled for potential confounders such as particulate matter, humidity, and ozone.
Results: The overall (lag0-14) association between heat and most of the outcomes was J-shaped, with an increased risk of disease observed at higher temperatures. The associations were more pronounced using the minimum temperatures indicator. Comparing the 99th (20 °C) to the minimum morbidity temperature (MMT) of the minimum temperature distribution during summer, the relative risk (RR) was significantly higher for heat-related general symptoms (RR = 1.30 [95 % CI: 1.07, 1.57]), otitis externa (RR = 4.87 [95 % CI:2.98, 7.98]), general heart problems (RR = 2.43 [95 % CI: 1.33, 4.42]), venous problems (RR = 2.48 [95 % CI:1.55, 3.96]), respiratory complaints (RR = 1.97 [95 % CI: 1.25, 3.09]), skin problems (RR = 3.26 [95 % CI: 2.51, 4.25]), and urinary infections (RR = 1.37 [95 % CI: 1.11, 1.69]). However, we did not find evidence for heat-related increases in gastrointestinal problems, cerebrovascular events, cardiovascular events, arrhythmia, mental health problems, upper respiratory problems and lower respiratory problems. An increased risk of allergy was observed when the minimum temperature reached 17.8 °C (RR = 1.50 [95 % CI: 1.23, 1.83]). Acute effects of heat were observed (largest effects at the first few lags).
Summary: Our findings indicated that the occurrence of certain symptoms and illnesses during summer season is associated to high temperature or environmental exposures that are augmented by elevated temperatures. Overall, unlike hospitalization data, GP visits data provide broader population coverage, revealing a more accurate representation of heat-health association.

* Corresponding author.
E-mail address: endalealemayehu.ali@kuleuven.be (E. Alemayehu Ali).

https://doi.org/10.1016/j.envint.2024.109097
Received 20 June 2024; Received in revised form 16 October 2024; Accepted 22 October 2024
Available online 24 October 2024
0160-4120/

1. Introduction

The impact of environmental factors, particularly increasing temperatures, on human health has gained significant attention in both scientific and public health communities. Devastating floods, forest fires and heat waves are mainly due to a rapid increase in global temperature (WMO, 2022). According to the Intergovernmental Panel on Climate Change (IPCC), the global surface temperatures were 1.09 [95 % confidence interval (CI): 0.95 to 1.20] °C higher in 2011–2020 compared to 1850–1900, with higher increases on land (1.59 [95 % CI: 1.34 to 1.83] °C) than over the ocean (0.88 [95 % CI: 0.68 to 1.01] °C) (Nigel et al., 2021) Table 1.

A substantial amount of studies has evidenced an adverse effect of hot weather on human health, with increased exposure to heat being widely accepted to negatively affect human health, resulting in increased mortality and morbidity (Casas et al., 2022; Cheng et al., 2019; De Troeyer et al., 2020; Martinez et al., 2018). Heat impacts on health (mortality and morbidity) are twofold: direct heat illnesses (Faurie et al., 2022; Gifford et al., 2019) and indirect (exacerbation of other diseases: CVD, respiratory, renal, mental disorders diabetes, etc.) (Bunker et al., 2016; Cheng et al., 2019). A large spectrum of direct heat illness, ranging from mild to severe heat stroke, are pathologically associated with high temperature. A *meta*-analysis found that heat was associated with an overall increased risk of direct heat-related illness such as dehydration, heat exhaustion, and heat stroke, which can contribute to morbidity and mortality (Faurie et al., 2022). It has been shown in one systematic review and *meta*-analysis that there was a positive association for cardiovascular morbidity and mortality with high temperatures and heatwaves (Liu et al., 2022). In another *meta*-analysis, heatwaves were not found to be significantly associated with cardiovascular disease or respiratory disease morbidity. However, they reported an association between heatwaves and mortality due to cardiovascular disease (Cheng et al., 2019). It was found in a *meta*-analysis by Thompson et al., (2023) that heat was significantly associated with hospitalization due to mental health problems, and heat waves have been associated with a higher suicide rate (Casas et al., 2022). There is a monotonically increasing mortality risk associated with an increase in temperature during summer period in Europe (Masselot et al., 2023). A study showed that in Belgium, heat is significantly associated with an increase in overall natural mortality and respiratory disease mortality (Demoury et al., 2022a).

Extreme heat exposure has become a major problem and is a risk for everyone, but, some people are more vulnerable than others. Various studies found that the global increase in frequency and intensity of extreme heat spells poses the greatest threat to elderly people (Achebak et al., 2019; Khatana et al., 2022; Saucy et al., 2021) and people with comorbidity (Achebak et al., 2019; Tonelli et al., 2015), as extreme heat may trigger chronic pre-conditions including cardiovascular disease, cerebrovascular disease, and respiratory disease (Cheng et al., 2019; Ebi et al., 2021; Huang et al., 2022; Sohail et al., 2020). Studies indicate that people confined to bed are at a high risk of heat as they are less able to take steps to mitigate the effects of heat. They are also at increased risk due to their dependency on others for care and their potential health vulnerabilities (Kenny et al., 2010; Watts et al., 2015). A *meta*-analysis shows that being confined to bed was significantly associated with deaths during heat wave (Bouchama, 2007).

In many studies, temperature is shown to have a nonlinear association with morbidity, which is often U-shaped with increases in adverse health outcomes at both ends of the temperature distribution. Although it might be that the exact lag with the highest heat effect is slightly different for different conditions (Turner et al., 2012), it is well accepted that heat effects are quite acute (some days) and cold effects more delayed (up to some weeks) (Barnett et al., 2005; Ye et al., 2012).

Most previous studies examined the impact of heat on health, with limited studies based on diagnoses made by General Practitioners (GPs) (Alsaiqali et al., 2022; Hajat et al., 2017; Smith et al., 2016). Primary care is the first point of contact for health problems. Hence, studies using data from GP consultations are essential for reaching a wider population and including mild symptoms and diseases. It also allows us to look at the broader clinical context of disease as it presents to GPs. Thermal stress poses a significant threat to human health and the temperature rise due to climate change is exacerbated by industrialization and urbanization as urban heat islands further increase temperatures (Heaviside et al., 2017). A study in Australia was also showed that heat heatwaves increase GP visits, with the impacts varying between populations (Varghese et al., 2021). Therefore, understanding the association between heat exposure and various morbidities becomes fundamental for effective public health management and intervention strategies. In this study, therefore, we accounted several morbidity outcomes and examined their separate association with heat stress.

The aim of this study was to investigate whether high environmental temperatures were associated with a wide variety of symptoms and diseases as diagnosed and treated by general practitioners during the summer period in Flanders, northern part of Belgium.

2. Methods

2.1. Data

This study used general practitioners (GPs) data between 2012 and 2019 from Flanders, the Dutch- speaking northern part of Belgium. We only used data for the summer seasons, i.e. May to September. Potentially heat-related medical conditions and symptoms were chosen based on literature (Alsaiqali et al., 2022; Bunker et al., 2016; Ebi et al., 2021; Ghazani et al., 2018; Gronlund et al., 2014; Lam and Chan, 2019). We extracted them using their International Classification of Primary Care Code 2 (ICPC-2). Daily numbers of diagnosis associated with specific ICPC, age group (0–14, 15–64, 65+ years) were obtained from INTEGO, a general practice-based morbidity registry managed by the Academic Center for General Practice, KU Leuven. INTEGO receives various information from GPs including diagnoses (ICPC2 and ICD-10 codes), prescriptions (ATC codes), sick leave notes, physiotherapy referrals, laboratory tests, vaccinations, clinical parameters such as height, weight and smoking status. During the study period 2012–2019, the INTEGO

Table 1
Summary statistics (Minimum, 1st percentile (P1), 5th Percentile (P5), Median (50th percentile (P50)), 95th percentile (P95), and 99th percentile (P99)) for meteorological and air pollution variables measured at the station of Uccle, Belgium, in the summer periods (May-September) of 2012–2019.

			Summary statistics				
			Percentiles				
Exposure/covariate	Minimum	P1	P5	Median (P50)	P95	P99	Maximum
Minimum temperature (°C)	−1.3	2.5	5.1	12.2	17.8	20.0	23.7
Mean temperature (°C)	3.4	7.0	10.1	16.8	23.7	27.1	30.8
Maximum temperature (°C)	7.7	11.5	14.8	22.3	30.8	34.3	41.1
Relative humidity (%)	31.5	42.8	51.3	71.5	89.9	95.7	100
Ozone ($\mu g/m^3$)	32.5	39.5	48.5	75.0	122.5	151.0	204.0
Particulate matter 2.5 ($\mu g/m^3$)	2.0	3.0	4.0	9.5	26	36.5	60

project contained data from 134 general practices and involves the participation of, 7884 GPs, covering approximately 786,000 patients. The INTEGO practices were found in 60 of the 300 municipalities of Flanders, with most of the practices in the central-eastern part of the region (Fig. 1, right panel). Since patients often live outside the municipalities where their practices are located, INTEGO patients came from every Flemish municipality except Herstappe, the smallest one (Fig. 1, left panel). We performed analysis for ICPC groups as well as single ICPC codes within each group.

The exposures of interest in this study were daily minimum (Tmin), mean (Tmean), and maxi- mum temperature (Tmax). We also collected data on potential environmental confounders of the association between heat and morbidity, i.e. relative humidity (RH) (Baldwin et al., 2023), and air pollution (Rai et al., 2023). Meteorological data measured in one monitoring station, Uccle weather station were provided by the Royal Meteorological Institute (RMI) of Belgium (RMI, 2024). Ozone (O_3) and particulate matter with aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) in Belgium are measured by the Interregional Environment Agency (IRCEL-CELINE, 2024). We used daily maximum 8-hour average O_3 and daily average $PM_{2.5}$ concentrations measured at the station of Uccle for this analysis.

INTEGO procedures were approved by the Belgian Privacy Commission (no. SCSZG/13/079), and the ethical review board of the Medical School of the KU Leuven (no. ML 1723) (Herestraat 49, 3000 Leuven), waived the requirement of informed consent and approved the INTEGO protocol. Patients who prefer not to have their data included in INTEGO can choose to opt out. In this study, a daily aggregated data was used.

2.2. Data analysis

In this study, we employed a Distributed Lag Non-Linear Model (DLNM) (Gasparrini et al., 2010) integrated with time-stratified conditional quasi-Poisson distribution. We used a time-stratified conditional quasi-Poisson regression to account for seasonal, long-term trends, and the weekly diagnosis cycle, conditioning on the interaction of calendar year, month, and day of the week (Armstrong et al., 2014). DNLMs are widely used in environmental epidemiology to account for the delayed and non-linear effects of various exposures on human health, modelling the exposure-lag-outcome association. A two-dimensional space of functions called DLNM *cross-basis* in which the exposure–response association and the spread effect over the different days (lag-response association) are simultaneously estimated on the basis of non-linear functions. To fully capture the potential lagged effects and to account for possible harvesting effects, we used a maximum lag of two weeks (14 days) (Demoury et al., 2022b). The non-linear exposure-effect association was accounted for using a natural cubic spline (NS) with 3 degrees of freedom (df), placing the spline knots at equally spaced quantiles along the temperature range. The lag structure was modelled using a NS with 4 df, setting the knots at equally-spaced values on the log scale of lags to allow more flexible lag effects at shorter delays (Gasparrini and Armstrong, 2011). Covariates included in the study were relative humidity (RH), $PM_{2.5}$ and O_3, and were corrected for by using a natural spline with 3 df. For RH and air pollutants ($PM_{2.5}$ and O_3), mean values of the current and the previous day (mean of lag0 and lag1) were used. Analyses were done for the total study population (all ages), and by age group (15–64 and 65+ years). Although children (0–14 years) were included in the total population analysis, this group was not analysed separately because of the low number of observations. Total population models were additionally adjusted for age group. In ICPC-specific analyses, we included only those with median N per day greater than zero, while in ICPC groups, all ICPCs were included, regardless of their median N per day. We obtained the minimum mortality temperature (MMT) for each disease groups and specific ICPC separately, and used them as a centering values of the association (Gasparrini and Armstrong, 2013). The MMT was determined based on the first percentile (P1) and 99th percentile (P99), excluding the most extreme temperature to avoid using them as reference values (Fu et al., 2018). Results are presented as relative risks (RR) with 95 % CI estimated at the 95th percentile (P95) and the 99th percentile of the temperature distributions, compared to the corresponding MMT of each health outcome.

In epidemiological analyses, attributable risk measures play an important role, especially in interventions aimed at preventing chronic diseases. We calculated the attributable fraction (AF) as a relative excess measure and the attributable numbers (AN) as an absolute excess measure (Armstrong et al., 2014). The attributable risk was calculated over a range of extreme heat conditions, specifically from the 99th percentile and above of the daily minimum temperature, setting the reference at MMT. Our analysis focuses on this high temperature range to quantify the specific ICPC and diseases caused by heat, providing valuable insight into the public health burden of heat.

A sensitivity analysis for minimum temperature was conducted by applying a Negative-Binomial (NB) model that introduces a shape parameter to directly model the overdispersion instead of quasi-Poisson model.

We used the *dlnm* package (Gasparrini, 2011), *gnm* package (Armstrong et al., 2014), and applied in R studio (R 4.2.1 version) (R Development Core Team, 2010) (R-team, 2022).

3. Result

During the study period, the highest daily minimum, mean and maximum temperatures reached 23.7°C, 30.8 °C and 41.1 °C, respectively, with 99th percentiles (P99) at 20.0 °C, 27.1 °C, and 34.3 °C. The median (50th percentile) minimum, mean and maximum temperatures were 12.2 °C, 16.8 °C and 22.3 °C, respectively. It was found that $PM_{2.5}$ had a minimum value of 2.0 $\mu g/m^3$ and a maximum value of 36.5 $\mu g/m^3$, while RH had a minimum value of 31.5 % and a maximum of 100 %. The minimum Ozone concentration was 32.5 $\mu g/m^3$, and the maximum was 204.0 $\mu g/m^3$. The total number of diagnoses during the study period at INTEGO practices were presented by ICPC groups according to sex and age groups (Appendix S2, Table S2.1).

Table 2 illustrates disease categories (hereafter referred to as ICPC groups) with their specific list of ICPCs, their ICPC code and median number (N) of GP visits per day. Over the entire summer of the study period, the median number of upper respiratory problems per day was

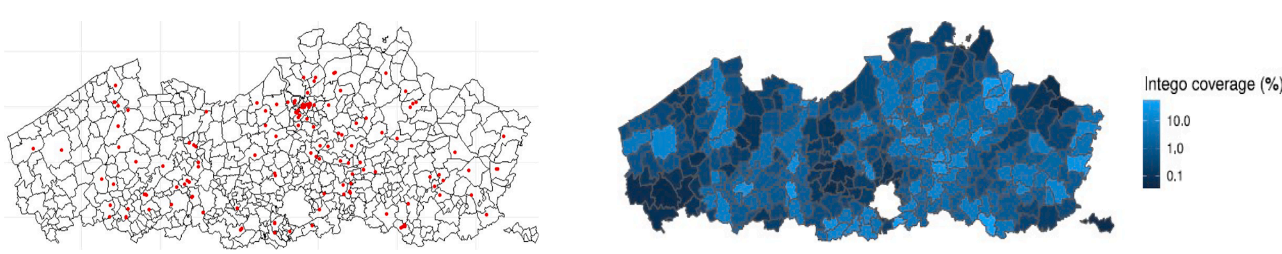

Fig. 1. The distribution of the INTEGO practices across the municipalities in Flanders (left), and INTEGO coverage (in percent) of Flanders' population, with Brussels, which is outside the Flemish Region, represented as an unshaded area (right).

Table 2
The ICPC group (in bold) along with their list of specific ICPCs, their ICPC code, and the median diagnosis per day during summer. *Represents specific ICPC that were considered in a separate ICPC-specific analysis (median N per day > 0).

ICPC categories	ICPC code	Median N per day	ICPC categories	ICPC code	Median N per day
General symptoms		**15**	**Arrhythmia**		**2**
Weakness/tiredness general	A04	4*	Atrial fibrillation/flutter	K78	1*
Feeling ill	A05	0	Paroxysmal tachycardia	K79	0
Fainting/syncope	A06	1*	Cardiac arrhythmia NOS	K80	1*
Adverse effect physical factor	A88	0	**Cerebrovascular event**		**1**
Orthostatic hypotension	K88	1*	Transient cerebral ischemia (TIA)	K89	0
Headache	N01	3*	Stroke/cerebrovascular accident	K90	1*
Vertigo, dizziness	N17	3*	**Mental health problems**		**6**
Decreased appetite	T03	0	Anxious/nervous feeling	P01	0
Dehydration	T11	0	Acute stress response	P02	2*
Other bladder symptoms/complaints	U13	0	Depressed feeling	P03	0
Allergy		**6**	Sleep disorder	P06	2*
Allergy/allergic reaction	A92	1*	Suicide/suicide attempt	P77	0
Other symptom	F29	0	Post-traumatic stress disorder	P82	0
Allergic/unspecified conjunctivitis	F71	0	**Respiratory complaints**		**1**
Allergic rhinitis	R97	2*	Shortness of breath/dyspnoea	R02	1
Urticaria	S98	1*	Wheezing	R03	0
Gastrointestinal problems		**23**	Other breathing problems	R04	0
Nausea	D09	1*	**Upper respiratory problems**		**54**
Diarrhea	D10	1*	Upper respiratory infection acute	R74	31*
Vomiting	D11	0	Sinusitis acute/chronic	R75	7*
Gastrointestinal infection	D70	12*	Tonsillitis acute	R76	5*
Gastroenteritis presumed infection	D73	8*	Laryngitis/tracheitis acute	R77	2*
Ulcerative colitis	D94	0	Influenza	R80	5*
			Lower respiratory problems		**17**
Otitis externa	**H70**	**2**	Acute bronchitis/bronchiolitis	R78	9*
General heart problems		**1**	Pneumonia	R81	2*
Pain attributed to heart	K01	0	Chronical bronchitis	R79	0
Pressure/tightness attributed to heart	K02	0	COPD	R95	1*
Pain cardiovascular system	K03	0	Asthma	R96	3*
Palpitations/awareness of heartbeat	K04	1*	**Skin problems**		**4**
Other irregular heartbeat	K05	0	Skin pain/sensitivity	S01	0
Venous problems		**1**	Pruritus	S02	1*
Swollen veins	K06	0	Locally red skin	S06	0
Swollen ankles/oedema	K07	1*	Bite/sting insect	S12	3*
Cardiovascular event		**1**	**Urinary infection**		**11**
Ischemic heart disease with angina	K74	0	Pyelonephritis/pyelitis	U70	1*
Acute myocardial infarction	K75	0	Cystitis/urinary infection other	U71	10*
Ischemic heart disease without angina	K76	0	Urethritis	U72	0
heart failure (congestive heart failure)	K77	0			

31, followed by gastrointestinal problems and cystitis/other urinary infection with median number per day of 12 and 10 respectively.

Fig. S1.1 (in Appendix) clearly showed that there is an increase in the number of cases in all ICPC groups as of 2018, which can be controlled by the stratum used in the model.

Increases in RRs associated with heat were most pronounced for the minimum temperature indicator. Fig. 2 illustrates the overall cumulative (lag0-14) association between minimum temperature and total population GP consultations for the 15 ICPC groups. Most curves are J-shaped, showing a RR close to 1 for a broad range of minimum temperatures and an increased RR only at the highest temperatures (P95 or even only P99), except for allergies and skin problems, for which the increase in RR is already observed at relatively low temperature (from P5 on wards). Corresponding figures for mean and maximum temperatures are presented in Appendix Fig. S1.4, showing similar curves as observed for minimum temperature. The overall association of minimum temperature and specific symptoms within ICPC groups is presented in Appendix Fig. S1.2.

For all studied ICPC groups and codes, Fig. 3 presents the cumulative (lag 0–14) RR with the 95 % CI at the P95 (17.8 °C) and the P99 (20.0 °C) relative to the MMT, estimated for the total study population.

The estimated RR at the P99 relative to the corresponding MMT was 1.30 [95 % CI: 1.07,1.57] for general symptoms, 4.87 [95 % CI: 2.98, 7.98] for otitis externa, 2.48 [95 % CI: 1.55, 3.96] for venous problems, 3.26 [95 % CI: 2.51, 4.25] for skin problems, 2.43 [95 % CI: 1.33, 4.42] for general heart problems and 1.97 [95 % CI: 1.25, 3.09] for respiratory complaints, 1.37 [95 % CI: 1.11, 1.69] urinary infections. We found an increased risk allergy at P95: RR = 1.60 [95 % CI: 1.23, 1.83], There was also an increased risk for gastrointestinal problems: RR = 1.13 [95 % CI: 0.95, 1.34], cardiovascular events: RR = 1.19 [95 % CI: 0.81, 1.75], cerebrovascular events: RR = 1.12 [95 % CI: 0.55, 2.28], arrhythmia: RR = 1.16 [95 % CI: 0.83, 1.63], upper respiratory problems: RR = 1.00 [95 % CI: 1.01, 1.06] and lower respiratory problems: RR = 1.12 [95 % CI0.95, 1.32], but none of these reached significance. We found a pronounced increase in the allergy risk at P95 (RR = 1.50 [95 % CI: 1.23, 1.83]). For mean temperature (Appendix, Fig. S1.5), RRs at the P99 (27.1 °C) relative to the MMT were often lower and were significant for: otitis externa (9.20 [95 % CI: 2.79, 30.30]), venous problems (2.35 [95 % CI: 1.52, 3.62]), and skin problem (3.08 [95 % CI: 2.37, 4.02]). Similar results were observed for maximum temperature (Appendix, Fig. S1.5), where the same ICPC groups showed significant associations, except an increased risk was found for gastrointestinal problems for maximum temperature.

For individual ICPC codes, the RRs for minimum temperature at P99

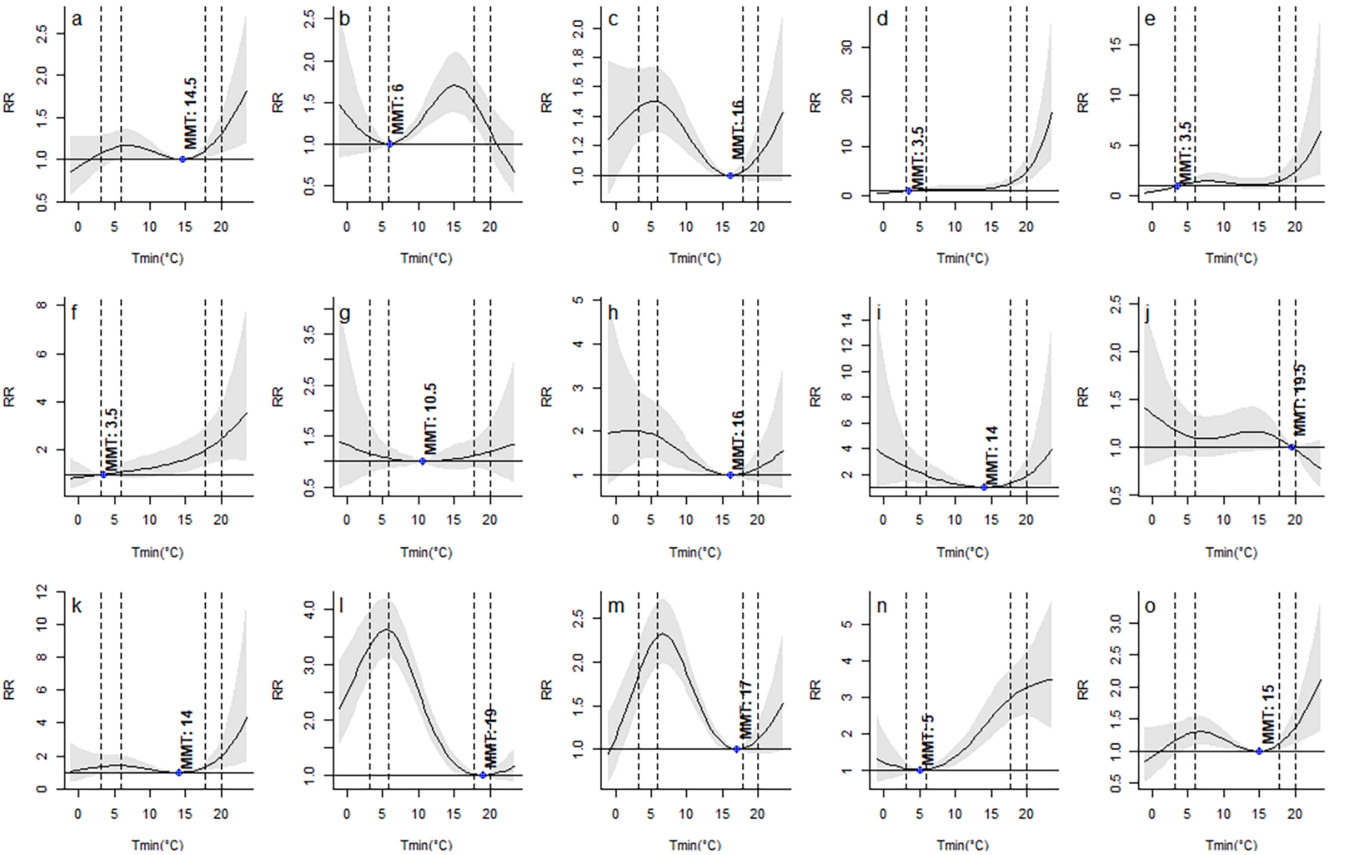

Fig. 2. Cumulative (lag0-14) association of minimum Temperature and total population diagnosis for the following ICPC groups: (a) General symptoms, (b) Allergy, (c) Gastrointestinal problems, (d) Otitis externa, (e) General heart problems, (f) Venous problems, (g) Cardiovascular event, (h) Arrhythmia, (i) Cerebrovascular event, (j) Mental health problems, (k) Respiratory complaints, (l) Upper respiratory problems, (m) Lower respiratory problems, (n) Skin problems and (o) Urinary infections. The solid line represents the relative risk along with its 95% confidence band, while the dashed vertical lines represent the P1, P5, P95 and P99 of minimum temperature. The blue dots indicate the MMT.

relative to corresponding MMT were significantly higher than one for postural hypotension (2.00 [95 % CI: 1.35, 2.99]), allergy/allergic reaction(1.74 [95 % CI: 1.20, 2.51]), nausea (1.72 [95 % CI: 1.04, 2.83]), vomiting (2.51 [95 % CI:1.34, 4.72]) palpitations/awareness of heart (3.33 [95 % CI: 1.80, 6.17]), swollen ankles/oedema (2.40 [95 % CI:1.48, 3.89]), stroke/cerebrovascular accident (RR = 2.38 [95 % CI: 1.28, 4.44]), shortness of breath/dyspnoea (1.93 [95 % CI: 1.14, 3.27]), pruritus (1.65 [95 % CI:1.04, 2.61]),insect bite (8.82 [95 % CI: 5.37, 14.46]) and cystitis/other urinary infection (1.38 [95 % CI:1.11, 1.71]). However, no significant associations were observed for the remaining ICPC codes, except for headache, vertigo/dizziness, urticaria, gastrointestinal infection, gastrointestinal presumed infection, atrial fibrillation/flutter, cardiac arrhythmia, acute stress reaction, influenza, acute bronchitis/bronchiolitis, pneumonia, COPD, asthma and pyelonephritis/pyelitis, which showed positive associations without reaching statistical significance.

Fig. 4 depicts the lag-specific RRs estimated at the P99 of minimum temperature for the ICPC groups. The effect of heat was acute, with the highest RRs often observed at lag1 and lag2, except for allergy, otitis externa, cerebrovascular events, skin problems and urinary infections, showing some delayed heat effects. The lag-response association at the P99 of minimum temperature for individual ICPC codes is presented in Appendix (Fig. S1.3).

Fig. 5 presents the cumulative (lag 0–14) RRs (at P95 and P99 relative to MMT) for minimum temperature estimated for elderly (65+) people. In light of the ICPC groups, heat has a positive association with general symptoms, gastrointestinal problems, otitis externa, general heart problems, venous problems, cardiovascular events, arrhythmia, cerebrovascular event, lower respiratory problems, respiratory complaints, skin problems and urinary infection, but only venous problems: RR = 2.97 [95 % CI: 1.60, 5.49], cerebrovascular events: RR = 2.12 [95 % CI: 1.08, 4.14], respiratory complaints: RR = 2.22 [95 % CI: 1.15, 4.29] and skin problems: RR = 4.04 [95 % CI: 2.57, 6.34] reached significance. In addition, we found a substantial increase in the relative risk of nausea (7.15 [95 % CI: 2.11, 18.27]), swollen ankles/oedema (2.92 [95 % CI: 1.57, 5.45]), stroke/cerebrovascular accident (2.95 [95 % CI: 1.39, 6.22]), acute stress reaction (4.49 [95 % CI: 1.54, 13.11]) and insect bite (13.42 [95 % CI: 7.84, 21.98]). Based on our study, there is a significant increase in gastroenteritis presumed infection among the elderly (3.53 [95 % CI: 1.34, 9.29]), which was not observed when considering all age groups.

For adults aged 15 to 64 (Fig. 6), RRs for minimum temperature (at P99 relative to the corresponding MMT of each health outcome) were significant for Otitis externa (5.80 [95 % CI: 3.11, 10.82]), general heart problems (2.75 [95 % CI: 1.33, 5.70]), venous problems (2.18 [95 % CI: 1.00, 4.75]), respiratory complaints (2.25 [95 % CI: 1.23, 4.11]), skin problems (2.87 [95 % CI: 2.02, 4.08]) and urinary infection (1.35 [95 % CI: 1.02, 1.78). Additionally, heat was associated with general symptoms, allergy, gastrointestinal problems, arrhythmia, cerebrovascular events, and lower respiratory problems, although no statistical significance was reached. Corresponding estimates for individual ICPC codes were significant for postural hypotension (2.52 [95 % CI: 1.43, 4.43]), allergy/allergic reaction NOS (1.65 [95 % CI: 1.06, 2.57]), vomiting (4.30 [95 % CI: 1.69, 10.94]), palpitations/awareness of heart (2.92 [95 % CI: 1.36, 6.26]), shortness of breath/dyspnea (3.34 [95 % CI: 1.36, 8.20]), and insect bite/sting (5.93 [95 % CI: 3.24, 10.87]). RRs estimated at the P99 of mean temperature and maximum temperature for elderly aged 65+ and adults aged 15–64 are presented in (Appendix,

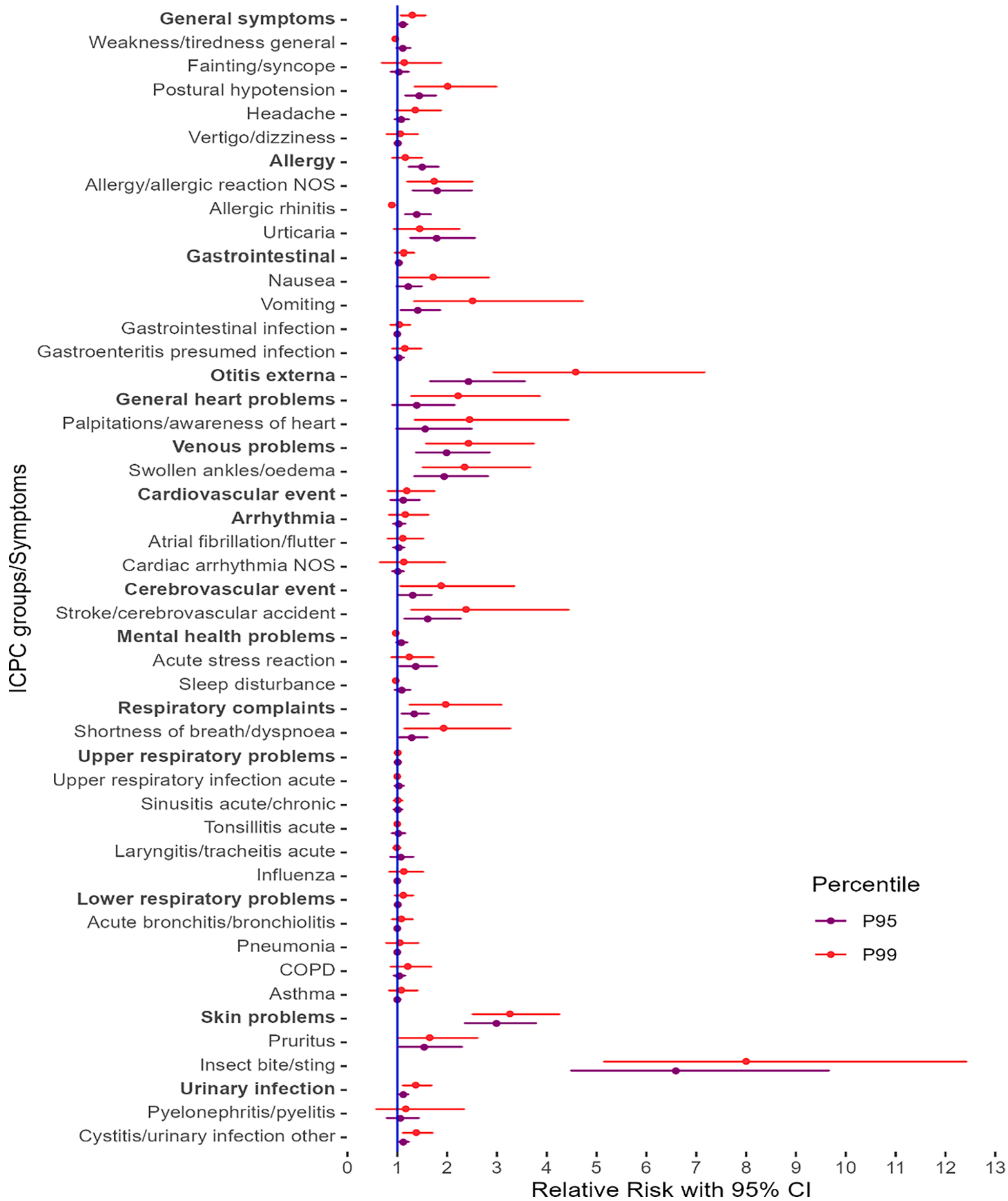

Fig. 3. Cumulative (lag 0–14) relative risk (dot) and 95 % confidence interval (CI: horizontal lines) at the 95th percentile (P95: 17.8°C) and at the 99th percentile (P99: 20.0 °C) compared to corresponding MMT of each health outcome, estimated for the total population and presented for ICPC groups (bold) and individual ICPC codes. Estimates are significant when the 95 % CI does not cross the vertical line (at RR = 1).

Table S2.2).

RRs (at P99) estimated with the quasi-Poisson and negative binomial models are shown in Appendix Fig. S1.6. Results are similar, except that the estimated RR for shortness of breath/dyspnea and pruritus did not reach significance in the negative binomial model.

ANs and AFs (%) with its 95 % CIs for the range of P99 and above, relative to the corresponding MMT for each disease group and specific ICPC code, are presented in Appendix Table S2.3. An increase in ICPC categories attributable to heat was observed for general symptoms (AN: 124, AF: 0.47 [95 % CI: 0.09, 0.84]), otitis externa (AN: 123, AF: 2.80 [95 % CI: 1.43, 3.89]), general heart problems (AN: 35, AF: 1.60 [95 % CI: 0.55, 2.23]), skin problems (AN: 144, AF: 2.34 0 [1.56, 2.95]) and urinary infection (AN: 90, AF: 0.52 [95 % CI: 0.12, 0.88]). An increased GP visits attributable to heat was also found for specific ICPCs, including postural hypotension (AN: 37, AF: 1.39 [95 % CI: 0.42, 2.17, vomiting (AN: 26, AF: 1.62 [95 % CI: 0.70, 2.12]), palpitations/awareness of heart (AN: 31, AF: 1.68 [95 % CI: 0.32, 2.47]), insect bite/sting (AN: 269, AF: 4.08 [95 % CI: 2.31, 5.16]) and cystitis/other urinary infections (AN: 82, AF: 0.52 [95 % CI: 0.09, 0.88]).

4. Discussion

4.1. *Main findings*

In this study, we identified significant association between heat and various ICPC groups including general symptoms, allergy, otitis externa, venous problems, skin problems, general heart problems, respiratory complaints, and urinary infections, as well as specific ICPC codes within the groups such as postural hypotension, allergy/allergic reaction, nausea, vomiting, palpitations/awareness of heart, swollen ankles/oedema, stroke/cerebrovascular accident, shortness of breath/dyspnea, pruritus, insect bite/sting and cystitis/other urinary infection. However, no significant association was found between heat and gastrointestinal problems, cardiovascular event, arrhythmia, cerebrovascular event,

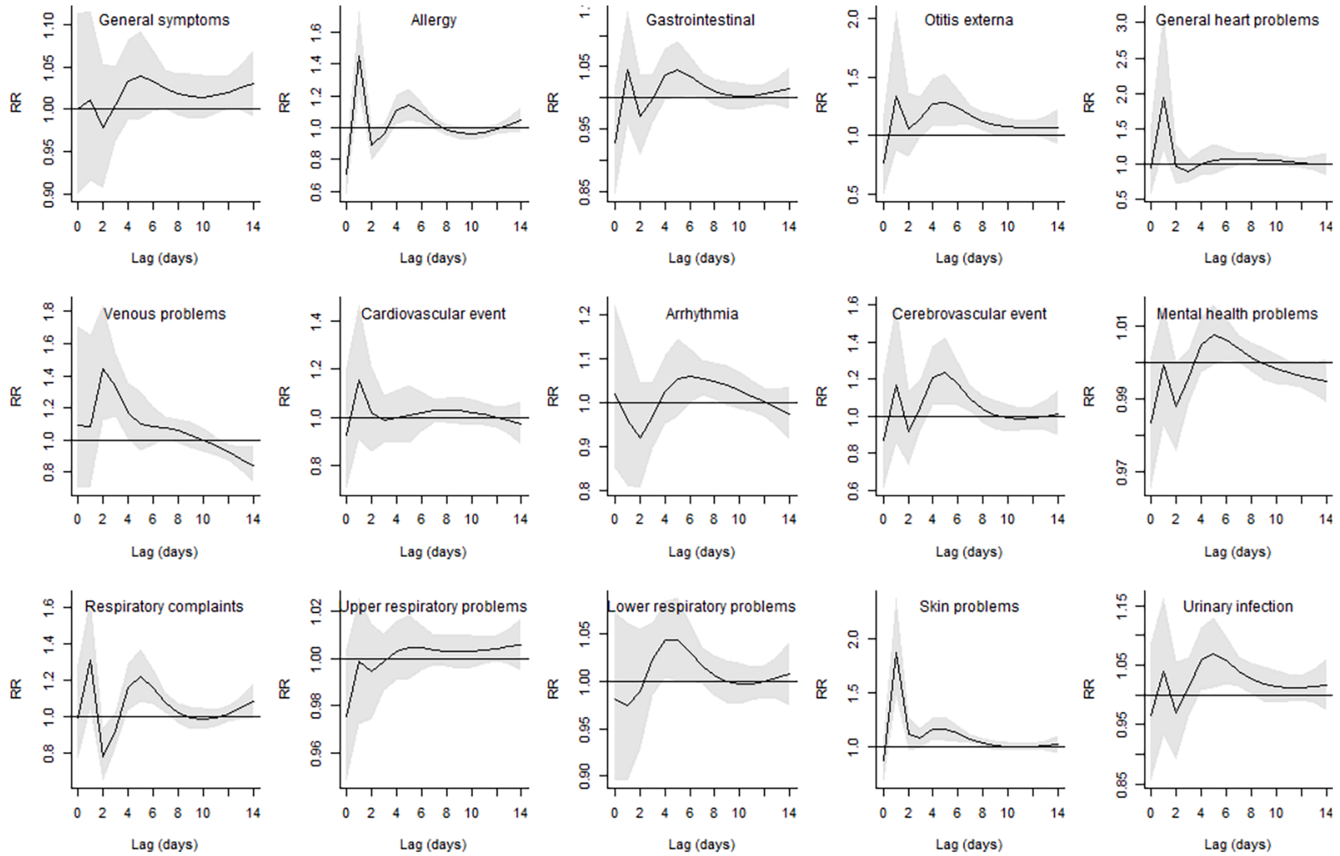

Fig. 4. The lag-response association of minimum temperature (at P99: 20.0 °C) and ICPC groups.

upper respiratory problems, and lower respiratory problems. This may be explained by the following reasons: the broad grouping of diverse conditions, the low numbers of GP visits and the fact that the severity of these conditions lead patients to the hospital emergency, rather than an appointment with their GP. Though the elderly are known to be vulnerable to heat, our study did not show a significant association in most of the ICPC groups, except venous problems and urinary infection, which again might be explained by low statistical power in this small group.

4.2. Comparison to earlier studies

Epidemiological studies have shown that the overall association of ambient temperature and adverse health outcomes are V- or J- or U-shaped (Demoury et al., 2022b). A systematic review of 28 studies also found a non-linear association with a U-, V- or J-shaped, indicating that both extremely hot and cold temperatures are associated with morbidies (Song et al., 2017; Zafeiratou et al., 2021). In this study, we only looked at the summer period (May-September) and we observed J-shaped association for most conditions.

A previous study in Belgium used INTEGO data from 2000 to 2015 to investigate the effect of heat- waves on genera heat-related (ICPC codes A04, A05, A06, A88, T11 and K88, cardiovascular (K74, K75, K76, K78, K79, K80, K89 and K90) and respiratory morbidity (R02, R74, R77, R78, R81, R95, R96) (Alsaiqali et al., 2022). Similar to our findings, they observed an association between heat and general heat-related morbidities, although the included ICPC codes were slightly different (they did not include headache, vertigo, decreased appetite, and other bladder symptoms). Their estimated RR for a heatwave at lag 0 was 1.29 [95 % CI: 1.13, 1.47]. This association seemed to be driven by ICPC codes A88 (adverse effect physical factor), T11 (dehydration), K88 (postural hypotension), whereas we only observed an association for the latter (we did not investigate A88 as individual code because of low numbers). A *meta*-analysis carried out by Faurie et al., (2022) evaluated the impact of hot weather on heat-related, including dehydration, defined as intravascular volume depletion (International Classification of Disease (ICD-10 code E86), heatstroke and heat stress (ICD 10: T67), and direct exposure to heat (ICD 10: X30). They found that for every 1 °C increase in ambient temperature, when measured from study-specific baseline temperatures, there was an 18 % increase in the risk of heat-related illness (ICD-10: E86, T67, X30) morbidity (RR 1.18, 95 %CI 1.16–1.19). Heat-induced headache is common among individuals exposed to excessive temperatures, and it is frequently accompanied by nausea, dizziness, sleep disturbances, or a combination of all three (Mukamal et al., 2009).

In our study, we found increased allergy disease in association to heat, specifically when the minimum temperature was around 17.8°C. Within this group ICPC codes A92 (allergy/allergic reaction), R97 (allergic rhinitis), and S98 (urticaria) showed increased RR and the remaining two codes (F29-other symptom and F71-allergic/unspecified conjunctivitis) were not analysed separately. According to a study in Xinxiang, China (Gao et al., 2021), both mild cold and mild hot temperatures were found to be associated with an increase in hospital outpatient visits for allergic rhinitis (lag 0–3 RR at 75th percentile (25 °C) relative to the median temperature (17 °C): 1.15 [95 % CI: 1.02–1.29]). It is possible that heat may increase the level of pollutants in the air, such as pollen, which can trigger allergic rhinitis (Gao et al., 2021; Small et al., 2018). We also found that people may experience allergy rhinitis when the daily minimum temperature reached its 95th percentile. It has been shown that an increase in temperature can aggravate the symptoms of allergic reactions, as it causes vasodilation and increases blood flow, resulting in discomfort and inflammation (Lam and Chan, 2019). Our findings are in agreement with theirs. The results of our study have shown that the risk of gastrointestinal problems

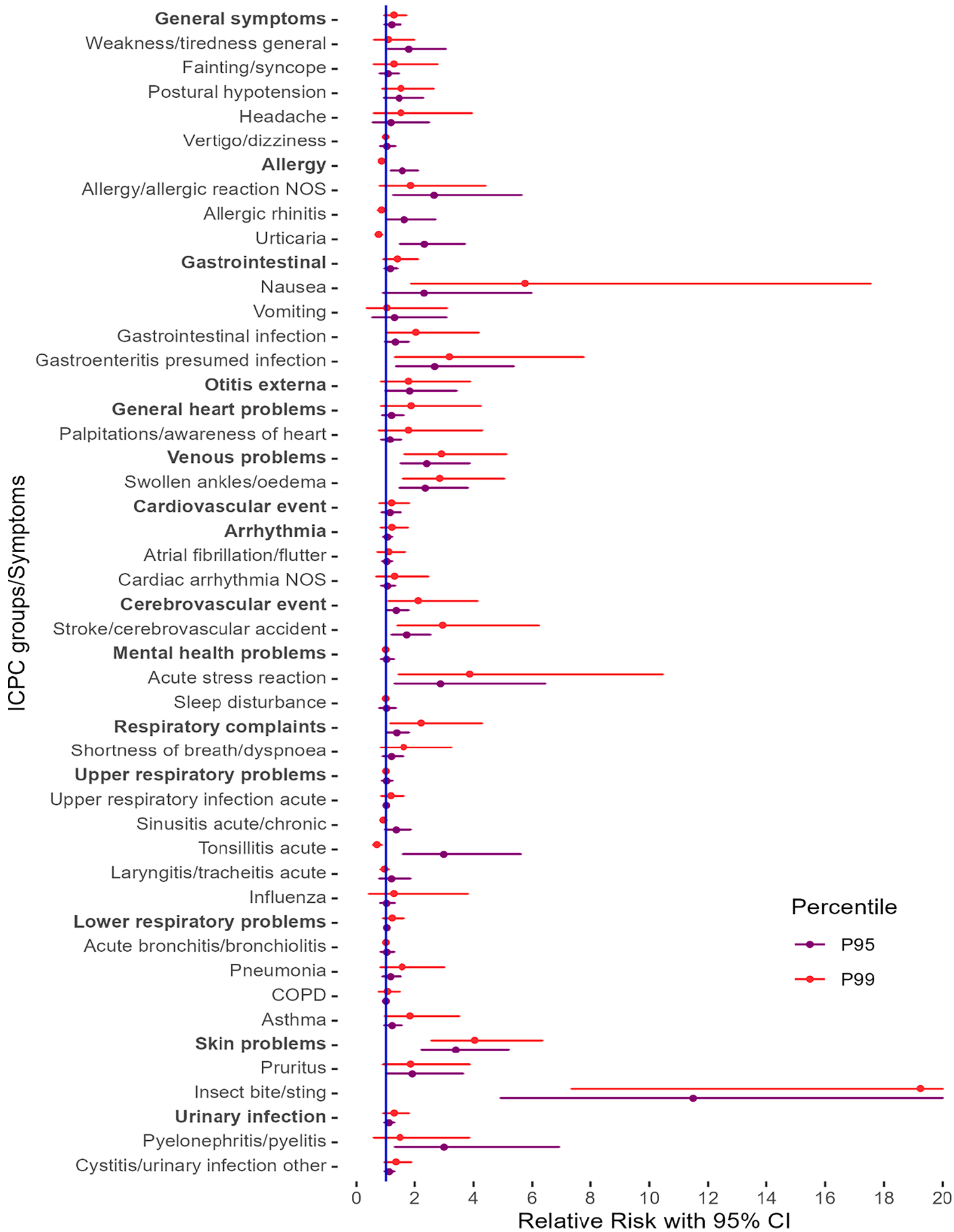

Fig. 5. Cumulative (lag 0–14) relative risk (dot) and 95 % confidence interval (CI: horizontal lines) at the 95th percentile (P95: 17.8 °C) and at the 99th percentile (P99: 20.0 °C) compared to the corresponding MMT of each outcome, estimated for elderly (aged 65+) and presented for ICPC groups (bold) and individual ICPC codes. Estimates are significant when the 95 % CI does not cross the vertical line (at RR = 1).

was not significantly associated with temperature indicators. However, an increased risk of specific symptoms including nausea (ICPC: D09) and vomiting (ICPC: D11) was found. A review of 11 studies on the impact of temperature variability on gastrointestinal infections revealed that an increase in temperature above certain threshold was associated with the diseases, acknowledging the inconsistency of different medical definition and temperature indicators across the studies (Ghazani et al., 2018). A retrospective time series analysis in Spain was explored the association of daily average temperature (°C) and gastrointestinal hospitalization ((ICD-9: codes 001–009) (Morral-Puigmal et al., 2018). It is estimated that extreme heat increases the risk of hospitalization for gastrointestinal conditions by 21 % (cumulative (lag0-28) RR = 1.21 [1.09, 1.34]), with the risk being assessed at P95 of mean temperature compared to the minimum hospitalization temperature (12 °C).

A study in Austria looked at the association of acute otitis externa and daily mean temperature using an emergency department visits during January 1st, 2015, to December 31st, 2018 (Nieratschker et al., 2024). Their study indicated an increase in RR of otitis externa when the daily average temperature reached 27 °C (P95 relative to P50: 1.95 [95 % CI: 1.04, 3.65]). We also found that an increase in minimum

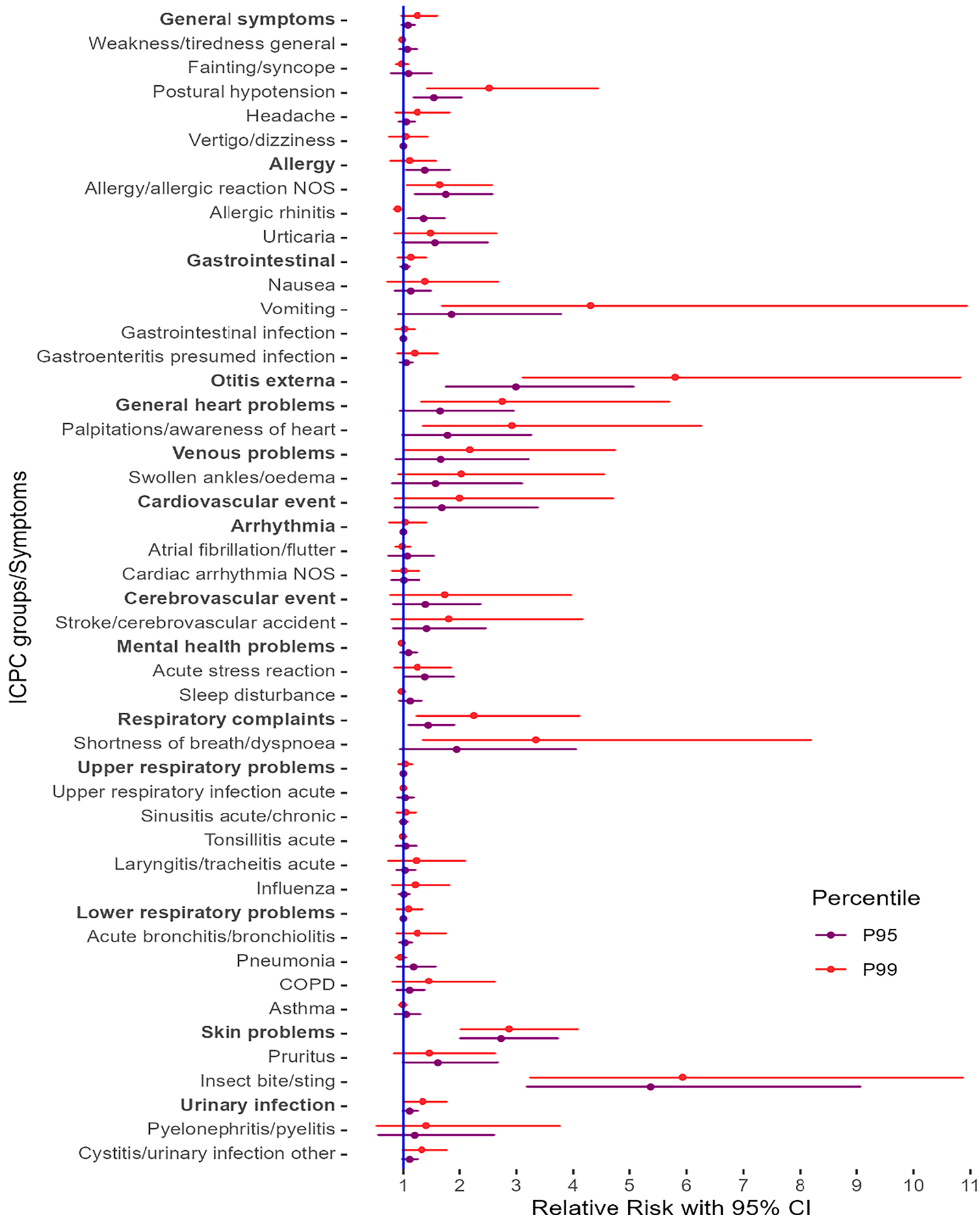

Fig. 6. Cumulative (lag 0–14) relative risk (dot) and 95 % confidence interval (CI: horizontal lines) at the 95th percentile (P95: 17.8°C) and at the 99th percentile (P99: 20.0 °C) compared to the corresponding MMT of each health outcome, estimated for the adults (aged 15–64 years) and presented for ICPC groups (bold) and individual ICPC codes. Estimates are significant when the 95 % CI does not cross the vertical line (at RR = 1).

temperature (at P95 and P99) significantly increases the risk of developing otitis externa, which is consistent with their findings.

In our study, heat stress was not found to significantly impact cardiovascular events. This is in agreement with the study that was conducted in Belgium using GP visit INTEGO data (Alsaiqali et al., 2022). The results of *meta*-analysis based on 266 relevant studies shows that heat was associated with cardiovascular morbidity (RR = 1.005 [95 % CI: 1.003–1.008]). They also found a significant association of heat and mortality (RR = 1.021 [1.020, 1.023]) (Liu et al., 2022). Another *meta*-analysis investigated the effects of high and low temperatures on cause-specific mortality and cardiovascular morbidity, including 31 studies related to the morbidity (Bunker et al., 2016). They included studies that used time-series or case-crossover analysis with any of hospitalization, emergency visits, GP consultations or home visits data. A positive association was found among people aged 65 and older. Cheng et al., (2019), carried out a *meta*-analysis on the impact of heatwave on cardiorespiratory, identifying 18 studies on the heatwave-cardiovascular morbidity associations. The study showed that there was no pronounced effect of heatwave on cardiovascular morbidity. Overall, the heat-related cardiovascular event is not clear, where some study found positive association (Aklilu et al., 2020; Jin et al., 2023) and others showed opposite association (Gronlund et al., 2014; Schulte et al., 2021). In our case, it might be explained by the fact that patients with more serious diseases like cardiovascular disease may instead direct themselves to an emergency department, resulting in their absence from the primary care data set. We also found strong association of heat and general heart problems. This was consistent with a study conducted in Spain, where they found that heart attack and stroke occurred at a 15.3 % higher rate during extreme heat (OR: 1.153 [95 %CI 1.010–1.317]) (Salvador et al., 2023). However, similar to our study for the elderly age group, they did not find any significant effect for a specific age group. In general, variations in study findings can be attributed to the diversity of study population, study design, statistical models, definition of heat events and the consideration of lag effects (Cicci et al., 2022; Dang et al., 2019).

There is inconsistent evidence regarding the effect of heat on cerebrovascular diseases. A *meta*-analysis conducted by Bunker et al., (2016) looked at the impact of extreme temperature (both cold and hot) on cerebrovascular diseases, considering a total of 31 studies, of which 15 studies were only heat-related. They found that heat-related cerebrovascular mortality and morbidity risk was increased for the shorter lags, 0–1 days. However, the overall association with morbidity was not significant. Our study did not show strong association of heat and cerebrovascular events. We also found no association of heat and mental health problems. A systematic review of 35 studies was conducted on the association of high ambient temperatures and heat waves with mental health (Thompson et al., 2018). Admission data from psychiatric hospitals or emergency visits were used in 15 studies. They found an increased risk of mental health-related admission and emergency visits at higher temperatures. They also identified several studies that showed positive association of suicide and increased in temperature. We did not quantify the suicide-heat association due to low number. Overall, the weak association of heat with cerebrovascular and mental health problem in our case might be explained by the fact that patients with serious diseases like cerebrovascular diseases and mental health problems often prefer to go directly to the emergency department instead of visiting their GP.

In our study, temperature indicators showed a significant effect on respiratory complaints. A *meta*-analysis examining the impact of heatwaves on cardiorespiratory morbidity and mortality identified 17 studies focused on the association between heatwaves and respiratory morbidity (Cheng et al., 2019). The study included hospital admissions, emergency department visits, and ambulance attendances data, and outcomes with confirmed ICD codes. Their finding suggested that there was no evidence for the association of heatwave and respiratory morbidity (RR = 1.043 [95 %CI: 0.995, 1.093]). They also carried out the *meta*-analysis per country, which included Australia (7 studies), China (2 studies), South Korea (2 studies), USA (5 studies) and Vietnam (1 study), and observed in significant association except in South Korea (RR:1.07, [95 %CI: 1.05, 1.10]). A time-stratified case-crossover study was carried out based on daily records of hospital outpatient visits of respiratory diseases (ICD-10: J00-J99) during January 1, 2007, to December 31, 2019 (Yang et al., 2022). They reported the RR at P95 of daily mean temperature compared to P5 for different cumulative lag effect (lag0-7, lag0-14 and lag0-14). A slightly increased risk of respiratory diseases was found in their study (lag0-14: 1.014 [95 % CI: 1.002,1.025]). They also found a positive association of heat and upper respiratory tract infection (ICD-10: J00-J06 and J30-J39) (lag0-14: 1.119 [95 % CI: 1.104,1.135]). There was, however, a protective association was found at lag0-21 (0.948 [95 % 0.939,0.957]). In our study, however, the rise in temperature did not appear to be strongly associated with the upper respiratory problems. A previous study of INTEGO data found a protective effect of heat waves on respiratory tract infections in upper and lower respiratory tracts (Alsaiqali et al., 2022).

A study conducted in China analysed hospital admission data to explore the association between temperature indicators (minimum, mean, maximum daily temperature) and skin problems (ICD- 10: *L*00-L99) (Huang et al., 2022). Their multi-city study showed that a 1 °C increase in daily mean temperature during warm season (June-September) increased skin disease risk by 1.25 % (95 % CI: 0.34 %, 2.16 %). In agreement with their findings, we did also find a significant association between heat and skin problems, despite using a different medical code definition (ICPC code instead of an ICD code). In our study, we did also find evidence of an association between heat and urinary infections. A study by examined Borg et al., (2019) the association between heat wave and urinary disease (ICD-10: N00-N39) in Adelaide, South Australia. They used hospital emergency department and inpatient admission data, covering the period 1 July 2003 to 31 March 2014. Their finding revealed that emergency presentations increased during heat waves compared to no-heat wave-days for urinary disease (incidence risk ratio = 1.046 [95 % CI: 1.016, 1.076]). Additionally, a *meta*-analysis based on 82 studies was also found that with a 1 °C increase in temperature, the risk of kidney-related morbidity increased by 1 % (RR = 1.010; 95 % CI: 1.009–1.011), with the greatest risk of urolithiasis (RR = 1.022, 95 % CI:1.016, 1.027)), and an increased risk of urinary tract infections (RR = 1.008, 95 % CI: 1.004–1.012) (Liu et al., 2021). Another single study also found a slightly increased association of daily minimum temperatures and urinary tract infections (RR = 1.004 [95 % CI: 1.00, 1.007] (Borg et al., 2017). Based on our findings, the estimated cumulative effects were higher in models with a minimum temperature than in models with mean or maximum temperatures, suggesting that the lack of cooling during the night is an important risk factor for heat-related deaths. It may also be related to urban heat islands. It has been shown that the risk of indoor heat does not always decrease with a reduction in outdoor temperatures (Buchin et al., 2016). The RRs for minimum temperature were often highest during the first few lags. This is not surprising since the minimum temperature occurs much earlier in the day (early morning) than the maximum temperature (which in summer is sometimes measured only after 4p.m.).

Overall, we found less significant associations for specific age groups. In this analysis, we found more associations with heat in the group of 15–64 year olds than in the over 65 s, which could be explained by a lack of power due to the limited sample size in the over 65 group. On the other hand, it might also be related to the fact that heat effects are often more severe in the elderly and/or they are more likely than younger people to head to the emergency room rather than their GP. There is also a possibility that heat exposure may have a greater impact on young adults, since they tend to be more active outdoors at high temperatures. For example, according to a study conducted in the USA, extreme summer heat events increased asthma hospitalization of youths and adults (Soneja et al., 2016). In the analysis combining all ages, we found the most associations, which may indicate that lower numbers within age groups may explain the insignificant results.

4.3. Strengths and limitations

Our study has several strengths: most studies assessing the association between extreme temperatures and morbidity use data from hospital admissions or emergency services, which often lack information on mild illnesses or symptoms requiring urgent care. Our study, using GP data, extends this type of association to include these conditions. This gives a more complete view of which events may arise more often in situations of extreme temperature. Furthermore, we took into account how heat affected grouped ICPCs and specific symptoms within each individual ICPCs. A comprehensive picture of the association between temperature and morbidities were accounted by using data covering a period of eight years and different temperatures indicators as exposure (minimum, mean, and maximum).

We also acknowledged that there are some limitations in our study. We did not include specific ICPC with daily median GP consultation less than 1. This is to avoid a very wide confidence interval and extremely high RR. However, we included them to the grouped ICPC analysis. When conducting age-specific- analysis, particularly among the elderly (aged 65+), we observed a lower number of GP visits, leading to a loss of statistical power and unclear association. We realized that this is because we used the data only from primary care, but not emergency care. The data for this study were collected primary through opportunistic sampling. This means that patients visited their GPs based on their own availability and how they felt about their illness. This can be seen as a form of self-selection bias, and this may result in an over-representation of people with easy access to GP care (urban populations). We also acknowledge that unmeasured variables such as socioeconomic status, comorbidities, or access to healthcare can confound the relationship between heat exposure and the outcomes. Some patients might have chosen to see their GP for a mild illness immediately, while others may wait for several days until their illness was more severe. This affects the number of lag days to consider. To account longer delay of patients to visit their GPs, we allowed a maximum of 14 days lag effect. We did not examine the trend of association over the entire study periods. The temperature indicators used in this study were measured at a single location, which might have led to exposure miss-classification. Future study may further explore the spatial and temporal variation of heat-health outcomes.

5. Conclusion

In conclusion, our study provides valuable insights into the impact of heat on various health conditions, focusing on GP visits data instead of hospitalization and emergency department data. As primary care data at GP consultation is the first point of contact for most of the patients, our study accounted for large number of patients. We identified various disease groups including heat-related general symptoms, otitis externa, venous problems, and general heart problems, respiratory complaints, skin problems, and urinary infections, and other specific symptoms significantly associated with heat. Future studies might combine data from both GP visits and hospitalizations, allowing a full range of analyses, from mild to severe cases, and utilize additional registries to adjust exposure-outcome models for important SE confounders.

CRediT authorship contribution statement

Endale Alemayehu Ali: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Formal analysis, Data, curation, Conceptualization. **Bianca Cox:** Writing – review & editing, Visualization, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Karen Van de Vel:** Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Els Verachtert:** Writing – review & editing, Data curation. **Bert Vaes:** Writing – review & editing, Project administration. **Simon Gabriel Beerten:** Writing – review & editing, Supervision. **Elisa Duarte:** Writing – review & editing, Supervision. **Charlotte Scheerens:** Writing – review & editing, Supervision. **Raf Aerts:** Writing – review & editing, Supervision. **Gijs Van Pottelbergh:** Writing – review & editing, Supervision, Resources, Project administration, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We would like to thank the Royal Meteorological Institute (RMI) of Belgium for providing envi ronmental data.

Financial support

Bianca Cox and Endale Alemayehu Ali are funded by Partner Organization Environmental Health Care, Department of Health/Flemish Ministry on Welfare, Public Health and Family Matters. INTEGO is also regularly funded by the same organization.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2024.109097.

Data availability

The authors do not have permission to share data.

References

Achebak, H., Devolder, D., Ballester, J., 2019. Trends in temperature-related age-specific and sex-specific mortality from cardiovascular diseases in Spain: a national time-series analysis. The Lancet Planetary Health 3 (7), e297–e306. https://doi.org/10.1016/S2542-5196(19)30090-7.

Aklilu, D., Wang, T., Amsalu, E., Feng, W., Li, Z., Li, X., Tao, L., Luo, Y., Guo, M., Liu, X., et al., 2020. Short-term effects of extreme temperatures on cause specific cardiovascular admissions in Beijing, China. Environ. Res. 186, 109455. https://doi.org/10.1016/j.envres.2020.109455.

Alsaiqali, M., De Troeyer, K., Casas, L., Hamdi, R., Faes, C., Van Pottelbergh, G., 2022. The effects of heatwaves on human morbidity in primary care settings: a case-crossover study. Int. J. Environ. Res. Public Health 19 (2), 832. https://doi.org/10.3390/ijerph19020832.

Armstrong, B., Gasparrini, A., Tobias, A., 2014. Conditional Poisson models: a flexible alternative to conditional logistic case cross-over analysis. BMC Med. Res. Method. 14, 1–6.

Baldwin, J.W., Benmarhnia, T., Ebi, K.L., Jay, O., Lutsko, N.J., Vanos, J.K., 2023. Humidity's role in heat-related health outcomes: a heated debate. Environ. Health Perspect. 131 (5), 55001. https://doi.org/10.1289/EHP11807.

Barnett, A.G., Dobson, A.J., McElduff, P., Salomaa, V., Kuulasmaa, K., Sans, S., 2005. Cold periods and coronary events: an analysis of populations worldwide. J. Epidemiol. Community Health 59 (7), 551–557. https://doi.org/10.1136/jech.2004.028514.

Borg, M., Bi, P., Nitschke, M., Williams, S., McDonald, S., 2017. The impact of daily temperature on renal disease incidence: an ecological study. Environ. Health 16, 1–30.

Borg, M., Nitschke, M., Williams, S., McDonald, S., Nairn, J., Bi, P., 2019. Using the excess heat factor to indicate heatwave-related urinary disease: a case study in Adelaide, South Australia. Int. J. Biometeorol. 63, 435–447. https://doi.org/10.1007/s00484-019-01674-5.

Bouchama, A., 2007. Prognostic Factors in Heat Wave-Related Deaths<subtitle>A Meta-analysis</subtitle>. Arch. Intern. Med. 167 (20), 2170. https://doi.org/10.1001/archinte.167.20.ira70009.

Buchin, O., Hoelscher, M.-T., Meier, F., Nehls, T., Ziegler, F., 2016. Evaluation of the health-risk reduction potential of countermeasures to urban heat islands. Energ. Buildings 114, 27–37. https://doi.org/10.1016/j.enbuild.2015.06.038.

Bunker, A., Wildenhain, J., Vandenbergh, A., Henschke, N., Rocklöv, J., Hajat, S., Sauerborn, R., 2016. Effects of air temperature on climate-sensitive mortality and morbidity outcomes in the elderly; a systematic review and meta-analysis of epidemiological evidence. EBioMedicine 6, 258–268. https://doi.org/10.1016/j.ebiom.2016.02.034.

Casas, L., Cox, B., Nemery, B., Deboosere, P., Nawrot, T.S., 2022. High temperatures trigger suicide mortality in Brussels, Belgium: A case-crossover study (2002–2011). Environ. Res. 207, 112159. https://doi.org/10.1016/j.envres.2021.112159.

Cheng, Z., Xu, H., Bambrick, V., Prescott, N., Wang, Y., Zhang, H., Su, S., Tong, W.H., 2019. Cardiorespiratory effects of heatwaves: A systematic review and meta-analysis of global epidemiological evidence. Environ. Res. 177. https://doi.org/10.1016/j.envres.2019.108610.

Cicci, K.R., Maltby, A., Clemens, K.K., Vicedo-Cabrera, A.M., Gunz, A.C., Lavigne, É., Wilk, P., 2022. High temperatures and cardiovascular-related morbidity: a scoping review. Int. J. Environ. Res. Public Health 19 (18), 11243. https://doi.org/10.3390/ijerph191811243.

Dang, T.A.T., Wraith, D., Bambrick, H., Dung, N., Truc, T.T., Tong, S., Naish, S., Dunne, M.P., 2019. Short-term effects of temperature on hospital admissions for acute myocardial infarction: a comparison between two neighboring climate zones in Vietnam. Environ. Res. 175, 167–177. https://doi.org/10.1016/j.envres.2019.04.023.

De Troeyer, K., Bauwelinck, M., Aerts, R., Profer, D., Berckmans, J., Delcloo, A., Hamdi, R., Van Schaeybroeck, B., Hooyberghs, H., Lauwaet, D., et al., 2020. Heat related mortality in the two largest Belgian urban areas: A time series analysis. Environ. Res. 188, 109848. https://doi.org/10.1016/j.envres.2020.109848.

Demoury, C., De Troeyer, K., Berete, F., Aerts, R., Van Schaeybroeck, B., der Heyden, J., De Clercq, E.M., 2022a. Association between temperature and natural mortality in Belgium: Effect modification by individual characteristics and residential environment. Sci. Total Environ. 851, 158336. https://doi.org/10.1016/j.scitotenv.2022.158336.

Demoury, C., Aerts, R., Vandeninden, B., Van Schaeybroeck, B., De Clercq, E.M., 2022b. Impact of short-term exposure to extreme temperatures on mortality: a multi-city study in Belgium. Int. J. Environ. Res. Public Health 19 (7), 3763. https://doi.org/10.3390/ijerph19073763.

Ebi, K.L., Capon, A., Berry, P., Broderick, C., de Dear, R., Havenith, G., Honda, Y., Kovats, R.S., Ma, W., Malik, A., et al., 2021. Hot weather and heat extremes: health risks. Lancet 398 (10301), 698–708. https://doi.org/10.1016/S0140-6736(21)01208-3.

Faurie, C., Varghese, B.M., Liu, J., Bi, P., 2022. Association between high temperature and heatwaves with heat-related illnesses: A systematic review and meta-analysis. Sci. Total Environ. 852, 158332. https://doi.org/10.1016/j.scitotenv.2022.158332.

Fu, S.H., Gasparrini, A., Rodriguez, P.S., Jha, P., 2018. Mortality attributable to hot and cold ambient temperatures in India: a nationally representative case-crossover study. PLoS Med. 15 (7), e1002619.

Gao, J., Lu, M., Sun, Y., Wang, J., An, Z., Liu, Y., Li, J., Jia, Z., Wu, W., Song, J., 2021. Changes in ambient temperature increase hospital outpatient visits for allergic rhinitis in Xinxiang, China. BMC Public Health 21, 1–9. https://doi.org/10.1186/s12889-021-10671-6.

Gasparrini, A., 2011. Distributed lag linear and non-linear models in R: the package dlnm. J. Stat. Softw. 43 (8), 1.

Gasparrini, A., Armstrong, B., Kenward, M.G., 2010. Distributed lag non-linear models. Stat. Med. 29 (21), 2224–2234. https://doi.org/10.1002/sim.3940.

Gasparrini, A., Armstrong, B., 2011. The impact of heat waves on mortality. Epidimiology 22 (1), 68.

Gasparrini, A., Armstrong, B., 2013. Reducing and meta-analysing estimates from distributed lag non-linear models. BMC Med. Res. Method. 13 (1), 1. https://doi.org/10.1186/1471-2288-13-1.

Ghazani, M., FitzGerald, G., Hu, W., Toloo, G., Xu, Z., 2018. Temperature variability and gastrointestinal infections: a review of impacts and future perspectives. Int. J. Environ. Res. Public Health 15 (4), 766. https://doi.org/10.3390/ijerph15040766.

Gifford, R.M., Todisco, T., Stacey, M., Fujisawa, T., Allerhand, M., Woods, D.R., Reynolds, R.M., 2019. Risk of heat illness in men and women: a systematic review and meta-analysis. Environ. Res. 171, 24–35.

Gronlund, C.J., Zanobetti, A., Schwartz, J.D., Wellenius, G.A., O'Neill, M.S., 2014. Heat, heat waves, and hospital admissions among the elderly in the United States, 1992–2006. Environ. Health Perspect. 122 (11), 1187–1192. https://doi.org/10.1289/ehp.12061.

Hajat, S., Haines, A., Sarran, C., Sharma, A., Bates, C., Fleming, L.E., 2017. The effect of ambient temperature on type-2-diabetes: case-crossover analysis of 4+ million GP consultations across England. Environ. Health 16, 1–8. https://doi.org/10.1186/s12940-017-0284-7.

Heaviside, C., Macintyre, H., Vardoulakis, S., 2017. The urban heat island: implications for health in a changing environment. Current Environmental Health Reports 4, 296–305. https://doi.org/10.1007/s40572-017-0150-3.

Huang, Y., Song, H., Wang, Z., Cheng, Y., Liu, Y., Hao, S., Li, N., Wang, Y., Wang, Y., Zhang, X., & others. (2022). Heat and outpatient visits of skin diseases–A multisite analysis in China, 2014–2018. *Heliyon*, *8*(10). https://doi.org/https://doi.org/10.1016/j.heliyon.2022.e11203.

IRCEL-CELINE. (2024). *Belgian Interregional Environment Agency (IRCEL - CELINE)* . https://www.irceline.be/en.

Jin, J., Meng, X., Wang, D., Han, B., Wu, T., Xie, J., Zhang, Q., Xie, D., Zhang, Z., 2023. Association between ambient temperature and cardiovascular diseases related hospital admissions in Lanzhou, China. Heliyon 9 (1). https://doi.org/10.1016/j.heliyon.2023.e12997.

Kenny, G.P., Yardley, J., Brown, C., Sigal, R.J., Jay, O., 2010. Heat stress in older individuals and patients with common chronic diseases. CMAJ 182 (10), 1053–1060. https://doi.org/10.1503/cmaj.081050.

Khatana, S.A.M., Werner, R.M., Groeneveld, P.W., 2022. Association of extreme heat and cardiovascular mortality in the United States: a county-level longitudinal analysis from 2008 to 2017. Circulation 146 (3), 249–261.

Lam, H.C.Y., Chan, E.Y.Y., 2019. Effects of high temperature on existing allergic symptoms and the effect modification of allergic history on health outcomes during hot days among adults: An exploratory cross-sectional telephone survey study. Environ. Res. 175, 142–147. https://doi.org/10.1016/j.envres.2019.05.017.

Liu, J., Varghese, B., Hansen, A., Borg, M., Zhang, Y., Driscoll, T., Morgan, G., Dear, K., Gourley, M., Capon, A., et al., 2021. Hot weather as a risk factor for kidney disease outcomes: a systematic review and meta-analysis of epidemiological evidence. Sci. Total Environ. 801, 149806.

Liu, J., Varghese, B.M., Hansen, A., Zhang, Y., Driscoll, T., Morgan, G., Dear, K., Gourley, M., Capon, A., Bi, P., 2022. Heat exposure and cardiovascular health outcomes: a systematic review and meta-analysis. e495 The Lancet Planetary Health 6 (6), e484. https://doi.org/10.1016/S2542-5196(22)00117-6.

Martinez, G.S., Diaz, J., Hooyberghs, H., Lauwaet, D., De Ridder, K., Linares, C., Carmona, R., Ortiz, C., Kendrovski, V., Aerts, R., et al., 2018. Heat and health in Antwerp under climate change: Projected impacts and implications for prevention. Environ. Int. 111, 135–143. https://doi.org/10.1016/j.envint.2017.11.012.

Masselot, P., Mistry, M., Vanoli, J., Schneider, R., Iungman, T., Garcia-Leon, D., Ciscar, J.-C., Feyen, L., Orru, H., Urban, A., et al., 2023. Excess mortality attributed to heat and cold: a health impact assessment study in 854 cities in Europe. e281 The Lancet Planetary Health 7 (4), e271. https://doi.org/10.1016/S2542-5196(23)00023-2.

Morral-Puigmal, C., Martinez-Solanas, E., Villanueva, C.M., Basagaña, X., 2018. Weather and gastrointestinal disease in Spain: A retrospective time series regression study. Environ. Int. 121, 649–657. https://doi.org/10.1016/j.envint.2018.10.003.

Mukamal, K.J., Wellenius, G.A., Suh, H.H., Mittleman, M.A., 2009. Weather and air pollution as triggers of severe headaches. Neurology 72 (10), 922–927. https://doi.org/10.1212/01.wnl.0000344152.56020.9.

Nieratschker, M., Haas, M., Lucic, M., Pichler, F., Brkic, F.F., Mueller, C.A., Riss, D., Liu, D.T., 2024. The association between acute otitis externa-related emergency department visits and extreme weather events in a temperate continental climate. Int. J. Hyg. Environ. Health 255, 114274. https://doi.org/10.1016/j.ijheh.2023.114274.

Nigel, A., Erika, C., Faye, A. C., Suraje, D., A.K.M. Saiful, I., Mohammad, R., Daniel, R. C., Jana, S., Mouhamadou, B. S., Claudia, T., Wen, W., & Rashyd, Z. (2021). *Climate Change 2021 The Physical Science Basis Working Group I Contribution to the Sixth Assessment Report of the Intergovernmental Panel on Climate Chan* . https://report.ipcc.ch/ar6/wg1/IPCC_AR6_WGI_FullReport.pdf.

Rai, M., Stafoggia, M., De'Donato, F., Scortichini, M., Zafeiratou, S., Fernandez, L.V., Zhang, S., Katsouyanni, K., Samoli, E., Rao, S., et al., 2023. Heat-related cardiorespiratory mortality: effect modification by air pollution across 482 cities from 24 countries. Environ. Int. 174, 107825. https://doi.org/10.1016/j.envint.2023.107825.

RMI. (2024). *Royal Meteorological Institute of Belgium* . https://www.meteo.be/en/belgium.

R-team. (2022). A Language and Environment for Statistical Computing; R Foundation for Statistical Computing: Vienna, Austria. https://www.r-project.org.

Salvador, C., Gullón, P., Franco, M., Vicedo-Cabrera, A.M., 2023. Heat-related first cardiovascular event incidence in the city of Madrid (Spain): Vulnerability assessment by demographic, socioeconomic, and health indicators. Environ. Res. 226, 115698. https://doi.org/10.1016/j.envres.2023.115698.

Saucy, A., Ragettli, M.S., Vienneau, D., de Hoogh, K., Tangermann, L., Schäffer, B., Wunderli, J.-M., Probst-Hensch, N., Röösli, M., 2021. The role of extreme temperature in cause-specific acute cardiovascular mortality in Switzerland: A case-crossover study. Sci. Total Environ. 790, 147958. https://doi.org/10.1016/j.scitotenv.2021.147958.

Schulte, F., Röösli, M., Ragettli, M.S., 2021. Heat-related cardiovascular morbidity and mortality in Switzerland: a clinical perspective. Swiss Med Wkly 151, w30013. https://doi.org/10.4414/SMW.2021.w30013.

Small, P., Keith, P.K., Kim, H., 2018. Allergic rhinitis. Allergy, Asthma & Clinical Immunology 14, 1–11. https://doi.org/10.1186/s13223-018-0280-7.

Smith, S., Elliot, A.J., Hajat, S., Bone, A., Bates, C., Smith, G.E., Kovats, S., 2016. The impact of heatwaves on community morbidity and healthcare usage: a retrospective observational study using real-time syndromic surveillance. Int. J. Environ. Res. Public Health 13 (1), 132.

Sohail, H., Kollanus, V., Tiittanen, P., Schneider, A., Lanki, T., 2020. Heat, heatwaves and cardiorespiratory hospital admissions in Helsinki, Finland. Int. J. Environ. Res. Public Health 17 (21), 7892. https://doi.org/10.3390/ijerph17217892.

Soneja, S., Jiang, C., Fisher, J., Upperman, C.R., Mitchell, C., Sapkota, A., 2016. Exposure to extreme heat and precipitation events associated with increased risk of hospitalization for asthma in Maryland, USA. Environ. Health 15, 1–7. https://doi.org/10.1186/s12940-016-0142-z.

Song, X., Wang, S., Hu, Y., Yue, M., Zhang, T., Liu, Y., Tian, J., Shang, K., 2017. Impact of ambient temperature on morbidity and mortality: an overview of reviews. Sci. Total Environ. 586, 241–254.

Thompson, R., Hornigold, R., Page, L., Waite, T., 2018. Associations between high ambient temperatures and heat waves with mental health outcomes: a systematic review. Public Health 161, 171–191. https://doi.org/10.1016/j.puhe.2018.06.008.

Thompson, R., Lawrance, E.L., Roberts, L.F., Grailey, K., Ashrafian, H., Maheswaran, H., Toledano, M.B., Darzi, A., 2023. Ambient temperature and mental health: A systematic review and meta-analysis. e589 The Lancet Planetary Health 7 (7), e580. https://doi.org/10.1016/S2542-5196(23)00104-3.

Tonelli, M., Wiebe, N., Guthrie, B., James, M.T., Quan, H., Fortin, M., Klarenbach, S.W., Sargious, P., Straus, S., Lewanczuk, R., et al., 2015. Comorbidity as a driver of adverse outcomes in people with chronic kidney disease. Kidney Int. 88 (4), 859–866. https://doi.org/10.1038/ki.2015.228.

Turner, L.R., Barnett, A.G., Connell, D., Tong, S., 2012. Ambient temperature and cardiorespiratory morbidity: a systematic review and meta-analysis. Epidemiology 23 (4), 594–606. https://doi.org/10.1097/EDE.0b013e3182572795.

Varghese, B., Beaty, M., Bi, P., Nairn, J., 2021. Heatwave-related morbidity in Australia: Effect modification by Individual and Area-level factors. Eur. J. Pub. Health 31 (Supplement_3). https://doi.org/10.1093/eurpub/ckab164.630.

Watts, N., Adger, W.N., Agnolucci, P., Blackstock, J., Byass, P., Cai, W., Chaytor, S., Colbourn, T., Collins, M., Cooper, A., et al., 2015. Health and climate change: policy responses to protect public health. Lancet 386 (10006), 1861–1914. https://doi.org/10.1016/S0140-6736(15)60854-6.

WMO. (2022). *World Meteorological Organization Provisional State of the Global Climate 2022* . https://library.wmo.int/viewer/56335?medianame=Provisional_State_of_the_Climate_2022_en_#page=1&viewer=picture&o=bookmark&n=0&q=.

Yang, R., Wang, Y., Dong, J., Wang, J., Zhang, H., Bao, H., 2022. Association between ambient temperature and cause-specific respiratory outpatient visits: A case-crossover design with a distributed lag nonlinear model in Lanzhou, China. Urban Clim. 46, 101303. https://doi.org/10.1016/j.uclim.2022.101303.

Ye, X., Wolff, R., Yu, W., Vaneckova, P., Pan, X., Tong, S., 2012. Ambient temperature and morbidity: a review of epidemiological evidence. Environ. Health Perspect. 120 (1), 19–28. https://doi.org/10.1289/ehp.10031.

Zafeiratou, S., Samoli, E., Dimakopoulou, K., Rodopoulou, S., Analitis, A., Gasparrini, A., Stafoggia, M., De' Donato, F., Rao, S., Monteiro, A., Rai, M., Zhang, S., Breitner, S., Aunan, K., Schneider, A., Katsouyanni, K., 2021. A systematic review on the association between total and cardiopulmonary mortality/morbidity or cardiovascular risk factors with long-term exposure to increased or decreased ambient temperature. Science of the Total Environment 772, 145383. https://doi.org/10.1016/j.scitotenv.2021.145383.