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Exposure to climate change-related extreme events in the first year of life and occurrence of infant wheezing

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ABSTRACT

Introduction: Climate change increases the intensity and frequency of extreme events, which will most impact younger generations. Within the NINFEA birth cohort, we investigated the relationship between exposure to such events during the first year of life and infant respiratory health.
Methods: The NINFEA cohort study recruited pregnant women across 11 years in Italy, allowing for climatic variability exploitation by birth place and time. We combined geocoded addresses with climate data, to derive children's cumulative exposure to the following extreme events during their first year: (i) heatwaves (i.e. 3 + consecutive days, with maximum temperature > 35 °C); (ii) days with wildfire $PM_{2.5}$ >15 μg/m3 and (iii) daily precipitation > 100 mm; (iv) months with exceptional drought. Logistic regression models estimated the relationship between each exposure and wheezing at 6–18 months, adjusting for individual and contextual factors.
Results: Wheezing prevalence in the cohort was 17.6%. The exposure to each additional heatwave in the first year of life increased wheezing risk by 16%, with an odds ratio (OR) of 1.16 and a 95% Confidence Interval (CI) of 1.00;1.35. The OR for each month of extreme drought exposure was 1.10, 95%CI 0.95; 1.26. Results for wildfire $PM_{2.5}$ were unclear with wider confidence intervals (OR for each high exposure day:1.36, 95% CI 0.85; 2.16). Wheezing was not associated with extreme precipitation.
Conclusions: Exposure to multiple extreme events, especially heatwaves, in the first year of life is associated with later infant respiratory health suggesting the need to implement climate change mitigation policies to protect long-term health.

1. Introduction

Human-caused climate change (CC) affects the frequency and intensity of extreme events, such as heatwaves, drought, floods, and wildfires around the globe (Lee et al., 2023), which have potential acute and long-term health consequences. Among them, CC-related extreme events have been linked to a higher risk of overall mortality, acute injuries, and hospital admissions in the following days and weeks (Perera and Nadeau, 2022; Costello et al., 2009). Nevertheless, estimating the health burden of exposure to CC-related extreme events is complex since they can cumulate over the life course, leading to a greater burden of exposure and possibly long-term health threats (Costello et al., 2009). In addition, the occurrence of CC-related extreme events varies widely over space, time, and generations. The most vulnerable populations disproportionately feel the health consequences of such exposures. Those include infants and children, pregnant women, the elderly, individuals with underlying diseases, and those living in poverty, disadvantaged circumstances, or vulnerable regions (Organization WH. Climate Change: World Health Organization;, 2023). Some areas of the world are considered particularly vulnerable to CC. The Mediterranean Basin is warming 20 % faster than the global average. Its mean temperature is projected to increase by 2.2 °C when the world exceeds 1.5 °C above pre-industrial levels (Bleu UMaP, 2020). Significant climatic shifts are underway in the region, leading to a rising frequency and intensity of extreme weather events, including episodes of storms and floods alternating with heatwaves and droughts, which consequently amplify the

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susceptibility to wildfires (Bleu UMaP, 2020). An increasing body of evidence suggests that children's respiratory health might be affected by CC-related events (Helldén et al., 2021; Perera and Nadeau, 2022). Heatwaves, wildfires, and extreme precipitation have been linked to increased hospitalization for respiratory diseases in young children (Perera and Nadeau, 2022; Kline and Prunicki, 2023; Makrufardi et al., 2023). Nevertheless, several studies addressing these associations concentrate on single exposure types and investigate their short-term effects on acute outcomes (Perera and Nadeau, 2022; Helldén et al., 2021; Kline and Prunicki, 2023; Makrufardi et al., 2023). Limited information is available on the long-term respiratory health trajectories and/or early signs of impaired respiratory health resulting from cumulative exposure to multiple extreme events (Kline and Prunicki, 2023). Even less is known about the consequences of exposures occurring in specific windows of susceptibility, despite being established that early life events can affect the health status later in life (Jaddoe et al., 2020). Implementing a life-course approach could prove beneficial in bridging these knowledge gaps (Burrows and Fussell, 2022).

We focused on the potential chronic and long-term impacts of CC-related extreme events, hypothesizing that such exposures may impact the development of the immature adaptive immune system as well as airway structure and function during this critical early period. Infant wheezing was identified as the outcome of interest since early childhood wheezing episodes, particularly if recurrent, predict asthma development and lung function in later life (Melén et al., 2024). In this study, we leveraged geo-referenced data from the Italian NINFEA (Nascita e Infanzia: gli Effetti dell'Ambiente) birth cohort (Richiardi et al., 2007), which enrolled participants from rural and urban areas of most Italian Regions over eleven years, to assess the effects of early life exposures to CC-related extreme events, on later infant respiratory health. Specifically, this study aimed to investigate the association between cumulative exposure to different extreme events occurring in the first year of life, namely high temperatures, drought, extreme precipitations, and wildfire-related Particular Matter $PM_{2.5}$ (i.e. all the suspended Particular Matter with a diameter lower than 2.5 μm), and self-reported infant wheezing occurrence, taking advantage of the variability of climatic conditions given the time and place of birth of the cohort's children.

2. Methods

2.1. Study population

The study population is part of the Italian NINFEA birth cohort. The project enrolled approximately 7500 mothers during pregnancy across the whole country for 11 years (2005–2016). To be included in the study women needed to have sufficient knowledge of the Italian language and Internet access availability. Women who were aware of the project and volunteered to participate completed the baseline questionnaire (Q1) at enrolment, which could have occurred at any time during pregnancy, and are followed up with their children through questionnaires 6 (Q2) and 18 (Q3) months after delivery and when the children turn 4 (Q4), 7 (Q7), 10 (Q10), 13 (Q13) and 16 (Q16) years of age. Information on the follow-up response proportion at each questionnaire is available as a technical report on the project website (NINFEA, 2005). Further information on the study design has been published previously (Richiardi et al., 2007).

As for this study we were interested in early wheezing episodes we only used information from the Q1 and Q3 questionnaires of the NINFEA database (version 2022.11). All children for whom information on wheezing between 6 and 18 months of age was available in Q3 were included in the current study.

The Ethical Committee of the San Giovanni Battista Hospital and CTO/CRF/Maria Adelaide Hospital of Turin approved the NINFEA study (approval No. 45 and following amendments) and written informed consent was obtained from all the participants.

2.2. Exposure definition

We considered exposure to extreme temperatures and precipitations, drought, and wildfires. The frequency and intensity of these extreme events can vary over space and time and are directly affected by CC. We geo-referenced through Google Maps Application Programming Interface (API) service the addresses of mothers during pregnancy assessed in Q1 and matched them with spatio-temporal gridded data extracted from the following datasets: (i) the ERA5 reanalysis dataset (Hersbach et al., 1940); (ii) the Global SPEI (Standardised Precipitation Evapotranspiration Index) database v. 2.9 (Serrano et al., 2010) and (iii) the SILAM (System for Integrated Modeling of Atmospheric Composition model) (Toll et al., 2015). We provide more specific information on the datasets used to derive the indicators, such as units of measurement and grid resolution in **the** Appendix**, Table A1**. For all children in the study, we derived their exposure history from the day of birth until the first birthday for the four CC-related extreme events listed above. We considered a one-year window, i.e. the first year of life, to ensure that all children were exposed to all four seasons, thus accounting for the seasonality of the exposures. We applied multiple definitions of extreme events, using multiple cutoff points supported by relevant literature (Sherwood and Huber, 2010; Tusting, 2020). Additionally, indices recommended by the Expert Team on Climate Change Detection and Indices (ETCCDI) (Karl et al., 1999) were used as a reference whenever possible.

We computed the following indicators referred to each child's first year of life: (i) the number of days with maximum temperature above 35 °C hereafter defined as SU35, or (ii) 30 °C (SU30); (iii) the number of heatwaves (HW), defined as more than three consecutive days with maximum temperature above 35 °C; (iv) the number of months with a SPEI index lower than −2.0, defined as exceptional drought, (v) − 1.6, extreme drought and (vi) − 1.3, severe drought, following the drought severity definition adopted in the Lancet Countdown Report of 2023 (Romanello et al., 2023); (vii) the number of days with maximum daily precipitation above 50 mm ((PR50), or (viii) 100 mm (PR100); (ix) the number of days with PM 2.5 from wildfires concentration above the WHO daily 15 μg/m^3 and annual (x) 5 μg/m^3 threshold limits. For additional information on the indicators and their data sources refer to **Supplementary Material**, **Table S1**.

2.3. Outcome assessment

The main outcome of interest was wheezing between 6 and 18 months of life, as assessed in Q3 when the child turned 18 months of age. All questions on wheezing present in the questionnaires were based on the standardized questionnaire of the International Study of Asthma and Allergies in Childhood (ISAAC) study (Solé et al., 1998). Specifically, we considered infant wheezing as a binary outcome based on whether the mother indicated wheezing among the conditions listed in the following question: "Indicate which of the following episodes did your child have between the 6th and 18th month of life [..] Wheezing or whistling in the chest".

We also considered, as a secondary outcome, whether a physician had diagnosed the wheezing episodes that children experienced between the ages of 6 and 18 months. The question was worded as follows: "Have the episodes of wheezing/whistling in the chest that your child experienced between the 6th and 18th month of age ever been diagnosed by a pediatrician at least once?".

2.4. Statistical analysis

We fitted three logistic regression models, considering increasing sets of potential confounders, and adopting a complete case approach. Since some mothers joined the NINFEA cohort with more than one child we adopted robust standard errors, clustered by the maternal ID. Model 1 was the crude unadjusted model. In Model 2 we adjusted for the following individual-level variables, based on the information provided by the mothers during the baseline assessment (Q1): pre-pregnancy maternal smoke (yes vs. no), maternal education (divided into three levels: no/primary; secondary school; graduation or postgraduate degree); parity as a continuous variable; maternal age at delivery, and maternal ever asthma (yes vs. no). Model 3 was adjusted for the same individual-level variables considered in Model 2 and for additional contextual factors (i.e. depending on their residence address): the climatic zone of residence according to the Köppen-Geiger climate classification at a 1-km resolution for the 1980–2016 period (Beck et al., 2018), degree of urbanization (rural vs. urban), according to the GHS Settlement Model layers (GHS-SMOD) indicator (Florczyk et al., 2019); and the Italian macro-area of residence (north, center and south/islands).

2.5. Sensitivity analyses

First, to address the potential over-reporting of wheezing by the mothers and as a proxy of severity and recurrence of wheezing episodes, we conducted a sensitivity analysis on the cohort participants who had the information on whether a physician had diagnosed the wheezing episodes between 6 and 18 months of age. Second, given the partial overlap between the periods of the exposure (i.e. first year of life) and the outcome assessment (i.e. 6–18 months of life), we conducted a sensitivity analysis focusing exclusively on exposures occurring within the first 6 months of life. We adopted Models 1, the crude model, and Model 3, further adjusted for the month of birth to account for the seasonality of exposure. Lastly, since participants might have moved between the baseline assessment (Q1) and the period of the outcome assessment (Q3) we performed a sensitivity analysis by restricting the analysis to participants who did not change their residence address between Q1 and Q3.

2.6. Stratified analyses

We conducted some stratified analyses to investigate whether the relationship between exposure to extreme events and infant wheezing was different according to socioeconomic status (Pizzi et al., 2024) (SES), degree of urbanization (Schröder et al., 2015), and child sex (Mandhane et al., 2005), as assigned at birth. We used maternal education as a proxy of the SES and explored its role in potentially mitigating the consequences of extreme events exposure on health. We conducted a stratified analysis dividing the cohort into two subsets based on the maternal level of education, dichotomized in high school (or lower) and university (or higher). Due to the possible differences in the exposure occurrences and their consequences according to the degree of urbanization, we conducted a stratified analysis on the urban and rural/*peri*-urban groups according to the corresponding GHS-SMOD classification of the residence area (Commission et al., 2019). The analyses were also stratified according to child sex as assigned at birth (male and female) and assessed through questionnaires.

All the analyses were carried out using R software (version 4.3.1.) (Team RC, 2013).

3. Results

3.1. Study population

The study population included 5704 children for whom we had information on wheezing between 6 and 18 months. A flow diagram describing the progression from the initially enrolled mother–child pairs to the ultimate study composition is reported in the Appendix, **Fig. A1**. Table 1 summarises the distribution of the outcome and all the variables used as covariates in the analysis of the study population.

Due to missing information about residence or residence outside the Italian territory, we could not calculate exposures for 411 subjects. The complete case approach led us to exclude individuals with missing covariate information. Missingness however did not exceed 6.9 % for all the variables included in the models, resulting in a final sample of 4916 children for the main analysis. Fig. 1 summarises the distribution of individual exposure to extreme events in the first year of life.

Table 1
The main characteristics of the study population (n = 5704).

Variable	mean (SD[1]); n° (%)	missing n° (%)
Maternal smoke during pregnancy		41 (0.7 %)
no	4951 (86.8 %)	
yes	712 (12.5 %)	
Maternal education		42 (0.7 %)
high school or lower	2032 (35.7 %)	
university or more	3630 (63.6 %)	
Parity		275 (4.8 %)
nulliparous	3960 (69.4 %)	
multiparous	1469 (25.8 %)	
Maternal asthma		146 (2.6 %)
no	5187 (90.9 %)	
yes	371 (6.5 %)	
Maternal age at delivery (years)	33.3 (4.23)	–
Climatic zone of residence[3]		381 (6.8 %)
Temperate, dry summer	1461 (25.6 %)	
Temperate, no dry season	3785 (66.4 %)	
Arid	41 (0.7 %)	
Cold	26 (0.4 %)	
Degree of urbanization		392 (6.9 %)
rural/periurban	2420 (42.2 %)	
urban	2902 (50.9 %)	
Infant wheezing[4]		
no	4698 (82.4 %)	
yes	1006 (17.6 %)	
Physician-diagnosed wheezing[5]		112 (2.0 %)
no	4701 (82.4 %)	
Yes	891 (15.6 %)	
Italian macro-area of residency		25 (0.4 %)
north	3845 (67.4 %)	
center	1280 (22.5 %)	
south and islands	554 (9.7 %)	

[1]SD: Standard Deviation
[2]EHII: Equivalised Household Income Indicator, categorized in high and middle-low according to the tertiles of the 2011 EUSILC- Italian distribution of the equivalized total disposable household income.
[3]Climatic zone according to the Köppen-Geiger climate classification, defined as follows:
Temperate, dry summer: Temperate climate with dry and warm/hot summer.
Temperate, no dry season: Temperate climate, no dry season, warm/hot summer.
Arid: Arid climate, steppe, cold.
Cold: Cold climate, no dry season, warm summer.
[4]Wheezing occurrence between 6 and 18 months as reported by the mothers in the questionnaire compiled when the child turned 18 months of age.
[5]Reported diagnosis by a physician of wheezing between 6 and 18 months, assessed in the questionnaire compiled when the child turned 18 months of age.

3.2. Exposure to extreme events and wheezing occurrence

As reported in Table 2, we found an increased risk of infant wheezing for exposure to extreme temperatures. Specifically, the risk of wheezing increased by 4 % for each additional day of exposure to temperatures exceeding 35°C (SU35) in all the models adopted with an odds ratio (OR) of 1.04, and a 95 % confidence interval (CI) from 1.01 to 1.07. The 95 % percentile for the SU35 indicator in our cohort corresponded to 4 days, while the median level of exposure corresponded to 0 days (results not shown). The OR comparing the 5 % of children with the highest exposure to days with temperatures exceeding 35°C with the median level of exposure would be 0.13 (95 %CI 0.04; 0.24), corresponding to 13 (95 % CI from 4 to 24) extra cases of wheezing every 100 children, as the estimated prevalence of wheezing predicted by model 3 at the median level of exposure was 14.7 %.

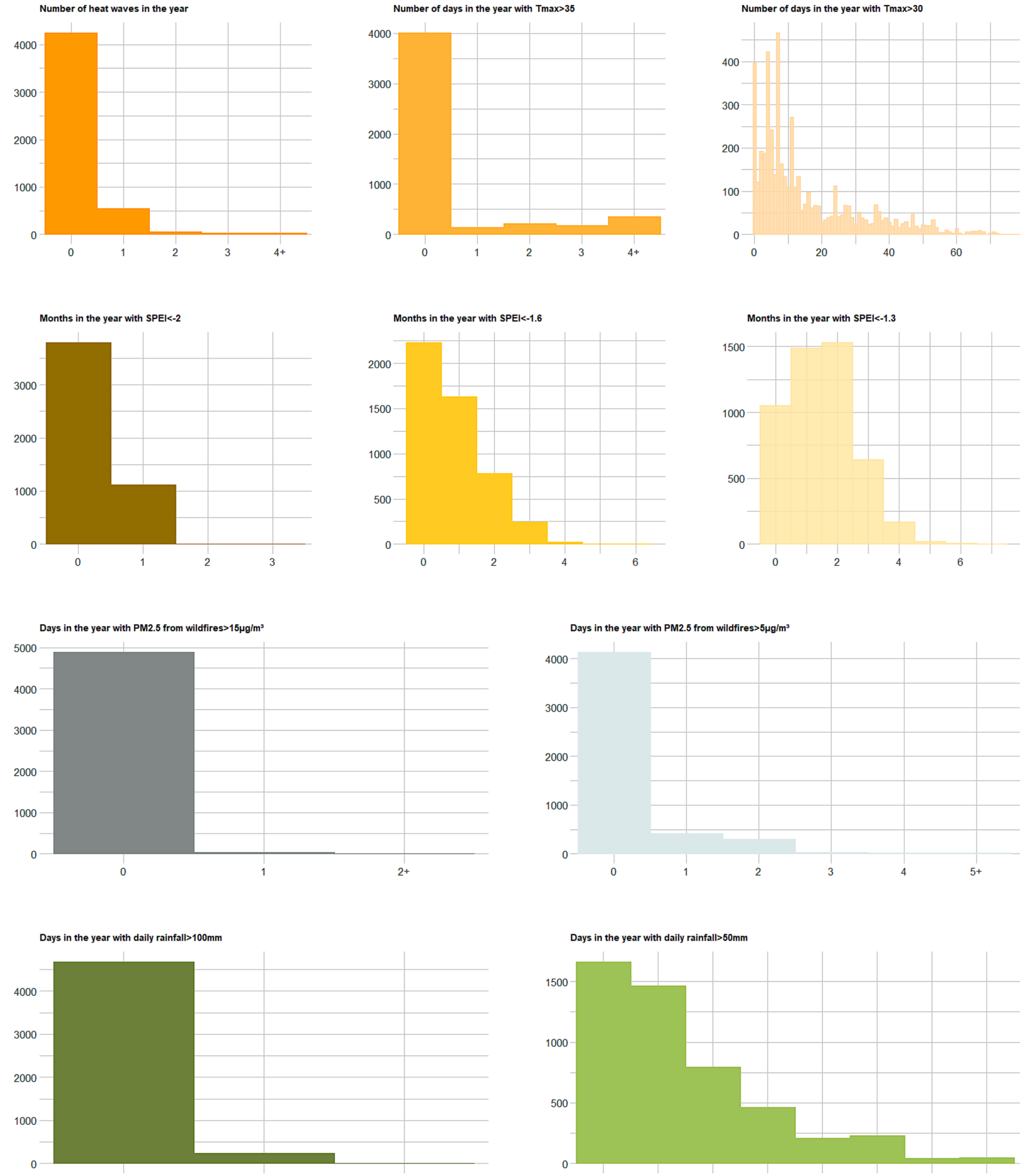

Fig. 1. Exposure to CC-related events in the study population: Histograms represent the absolute frequency of exposure to episodes of high temperatures, months of drought, and days of exposure to high $PM_{2.5}$ from wildfire concentrations and extreme rainfall over the first year of life of children included in the main analysis sample (n = 4916).

Table 2
Odd Ratios (ORs) and corresponding 95 % Confidence Interval (CI) of wheezing between 6–18 months for indicators of CC-related extreme events (n = 4916).

	Scale[1]	Model 1[2] OR (95 % CI)	Model 2[3] OR (95 % CI)	Model 3[4] OR (95 % CI)
SU35[5]	Number of days	1.04 (1.01; 1.07)	1.04 (1.01; 1.07)	1.04 (1.01; 1.07)
SU30[5]	Number of days	1.01 (1.00; 1.01)	1.01 (1.00; 1.01)	1.01 (1.00; 1.01)
HW[5]	Number of events	1.16 (1.00; 1.35)	1.16 (1.00; 1.35)	1.16 (1.00; 1.35)
Exceptional drought[5]	Number of months	1.13 (0.99; 1.29)	1.13 (0.98; 1.29)	1.10 (0.95; 1.26)
Extreme drought[5]	Number of months	1.05 (1.01; 1.06)	1.04 (1.01; 1.08)	1.03 (0.99.; 1.08)
Severe drought[5]	Number of months	1.03 (1.00; 1.06)	1.03 (1.00; 1.07)	1.03 (1.00; 1.06)
PR50[5]	Number of days	1.01 (0.97; 1.06)	1.01 (0.97; 1.06)	1.03 (0.98; 1.08)
PR100[5]	Number of days	0.97 (0.74; 1.28)	0.97 (0.74; 1.27)	1.02 (0.77; 1.34)
$PM_{2.5}$ >15 μg/m3[5]	Number of days	1.37 (0.89; 2.10)	1.38 (0.87; 2.18)	1.36 (0.85; 2.16)
$PM_{2.5}$ >5 μg/m3[5]	Number of days	1.07 (0.98; 1.16)	1.07 (0.98; 1.16)	(0.98; 1.17)

[1]The exposure scale of the unitary increment to which each ORs refers. i.e. the increase of one day/month/event of exposure during the first year of life.
[2]Model 1: the crude model.
[3]Model 2: model adjusted for pre-pregnancy maternal smoke; maternal education; parity; maternal age at delivery; and maternal asthma.
[4]Model 3: model adjusted for all the variables considered in Model 2; area of residence in Italy, Climatic zone according to the Köppen-Geiger climate classification, and degree of urbanization.
[5]The indicators are defined as follows:
SU35: Number of days in the first year of life with maximum temperature above 35 °C.
SU30: Number of days in the first year of life with maximum temperature above 30 °C.
HW: Number of times in the first year of life with more than three consecutive days with maximum temperature above 35 °C.
Exceptional drought: Number of months in the first year of life with Standardized Precipitation and Evapotranspiration Index (SPEI) below −2.0.
Extreme drought: Number of months in the first year of life with Standardized Precipitation and Evapotranspiration Index (SPEI) below −1.6.
Severe drought: Number of months in the first year of life with Standardized Precipitation and Evapotranspiration Index (SPEI) below −1.3.
PR50: Number of days in the first year of life with total daily precipitation above 50 mm.
PR100: Number of days in the first year of life with total daily precipitation above 100 mm.
PM > 15 μg/m3: Number of days in the first year of life with PM 2.5 concentration above 15 $\mu g/m^3$.
PM > 5 μg/m3: Number of days in the first year of life with PM 2.5 concentration above 5 $\mu g/m^3$.

Similarly, wheezing risk increased by 16 % for each heatwave event, OR: 1.16 (95 % CI: 1.00; 1.35) in all the models adopted. We found weaker evidence indicating an increased wheezing risk associated with being exposed to excessively dry months. Model 3 showed odds increased by 10 % (95 %CI: 0.95; 1.26) for each month of exposure to exceptional drought, while ORs for extreme and severe drought exposures were slightly lower but with narrower CIs. Results were weaker and less consistent for each additional day of exposure to $PM_{2.5}$ levels above 15 $\mu g/m^3$, model 3 OR was 1.36 (95 % CI: 0.85–2.13). Exposure to extreme precipitation was not associated with infant wheezing.

3.3. Sensitivity analyses

In the Appendix, **Table A2** we present the analysis results for the 4828 subjects for whom we had data on physician-diagnosed wheezing episodes between 6 and 18 months of age. These results align with those for self-reported wheezing. The results of the analyses focusing exclusively on 6 months of life exposures are reported in the Appendix, **Table A3** In this case, the results were similar to the main analysis although most estimates had larger confidence intervals. However, we did not find an association of extreme drought exposure with wheezing in this analysis, while the estimates for exposure to high PM2.5 from wildfires were higher. The results of the analyses conducted on the subgroup of children who did not change their address between Q1 and Q3 are reported in Appendix, **Table A4.** Minor changes were observed, with slightly stronger estimates noted for heat and heatwave exposure. In the subgroup of this analysis, model 3 showed an OR for heatwaves exposure of 1.21 (95 %CI 1.04—1.42) compared with 1.16 (95 %CI 1.00–1.35) in the main analysis.

3.4. Stratified analyses

Exposure to CC-related extreme events was similarly frequent among children of mother with low–high school education and those with mother with high education.. Results of the analyses stratified according to the maternal education l, degree of urbanization, and sex are reported in the Appendix, **Table A5-A7.** The associations between exposure to extreme events and the risk of infant wheezing did not vary substantially by maternal education strata (**Table A5**). Living in urban areas was instead associated with a higher frequency of exceptional droughts and a lower frequency of exposure to extreme precipitations and PM2.5 from wildfires. The estimates slightly changed according to the degree of urbanization, with a higher wheezing risk for exposure to high temperatures and heatwaves in children living in urban environments (**Table A6**). Similarly, we did not find relevant differences according to child sex (**Table A7**) but a slightly higher wheezing risk for exposure to heatwaves and exceptional drought in males.

4. Discussion

We found a positive association between the exposure to multiple CC-related extreme events −specifically, high temperatures and drought during the first year of life and the occurrence of infant wheezing between 6 and 18 months of age. Results for the exposure to $PM_{2.5}$ from wildfires were weak and non-consistent while no association was observed for extreme precipitations.

Acute respiratory health outcomes have been previously linked to CC-related extreme events exposures and children have been identified as a particularly vulnerable population (Makrufardi et al., 2023). This susceptibility to external environmental stressors might be attributed to a respiratory system still under development (Schittny, 2017). However, those previous studies mainly evaluated short-term outcomes such as hospitalization rates or symptom exacerbations (Makrufardi et al., 2023). Here, we focused on the potential medium- and long-term effects of early-life exposure to CC-related extreme events by evaluating their impact on infant wheezing over an extended timeframe, encompassing several months. Infant wheezing is a good predictor of future respiratory health especially, but not solely, when recurrent (Melén et al., 2024). As a proxy of symptom severity and recurrence, we repeated the analyses on doctor-diagnosed wheezing episodes, which confirmed our results.

We were interested in understanding whether cumulative exposure to extreme CC-related events in early life may potentially have long-term health effects. While we did not investigate the specific mechanisms involved, we can speculate on possible explanations. The positive association found between exposure to extreme temperatures and wheezing might be due to increased exposure to proinflammatory airway stressors associated with extreme heat. High temperatures can prolong pollen seasons and increase pollen production, leading to airway sensitization and more severe allergic respiratory disorders (Wright, 2020). Urban heat also raises ground-level ozone concentrations, a pro-inflammatory and oxidative compound linked to increased asthma risk (Sheffield et al., 2011). Additionally, higher temperatures may encourage children to spend more indoor time (Nguyen et al., 2021), increasing exposure to indoor pollutants like tobacco smoke and moulds. The increased risk of wheezing associated with drought may be attributed to elevated air pollution levels from dust, smoke, and suspended particulate matter during prolonged droughts (Brand et al., 2008). The cumulative pollutant exposure can irritate the respiratory system and impair lung development, raising the risk of respiratory conditions such as asthma and bronchitis. This mechanism might partially explain the lack of effect for drought that we found when considering exposures over 6 months, which might not have been long enough to translate into respiratory consequences. Additionally, drought episodes can lead to high concentrations of airborne allergens like pollen, exacerbating respiratory issues in susceptible individuals. Our results were less clear for what concerns the exposure to $PM_{2.5}$ linked to wildfire smoke, which is a direct airway irritant, and infant wheezing risk. Although estimates for wildfire-related $PM_{2.5}$ exposure were positive, confidence intervals were wide, likely due to the limited number of participants exposed to $PM_{2.5}$ levels exceeding WHO thresholds. We did not find associations between extreme precipitation events and respiratory health.

While the current study is exploratory, our findings underscore the potential public health implications of early-life exposure to climate-related risk factors, particularly for extreme heat and droughts. The observed association between extreme heat exposure and wheezing risk reinforces the need for strategies to protect children from extreme weather events, especially during critical developmental periods. Incorporating these findings into clinical practice should encourage healthcare providers to consider environmental factors when managing at-risk pediatric patients. The absolute risk of wheezing increase in the population might be high, around 13 % (95 %CI: 4 %; 24 %) for highly exposed children (i.e. those exposed to 4 + days of temperature exceeding 35 °C in their first year of life) compared to the non-exposed ones. Since CC is expected to lead to a rise in the number of hot days and heatwaves, the percentage of the population facing extreme heat exposures in the first year of life is projected to grow. Moreover, since early-life wheezing is a known predictor of future respiratory health, our results raise the possibility that CC-related extreme events exposure in infancy may have long-lasting effects on respiratory outcomes. Further research is needed to fully quantify the magnitude and clinical significance of these long-term impacts.

To our knowledge, this is the first study that used individual data to explore the relationship between exposure to multiple CC-related extreme events and possible mid and long-term respiratory health in childhood. We took advantage of conducting our study in the NINFEA birth cohort which recruited participants across 11 years and living in both urban and rural areas of the entire Italian territory. These characteristics and the possibility to account for seasonality through exposure definition enabled us to exploit the wide exposure variability due to children's date and place of birth. Ultimately, the adoption of a life-course framework, allowed us to analyze the potentially long-term effect of the cumulative exposure to CC-related extreme events over the first year of life and to adjust for multiple individual and contextual potential confounders.

This study has some limitations. First, as the wheezing occurrence was assessed at 18 months of age, covering the 12 months between 6 and 18 months of age, in some cases, it might have preceded the exposures (i.e. wheezing episodes occurring between 7 and 12 months of the child). We used 12-month exposure and outcome windows to avoid confounding by seasonality, which cannot be completely controlled for. Results of the sensitivity analyses, focusing on the first six months of exposure only, are consistent with those of the main analysis, even if there was a diluted effect for drought. On the other hand, although commonly employed in epidemiological investigations, self-reported wheezing could potentially lead to misclassification, as parents might label isolated instances of audible breathing as wheezing (Al-Shamrani et al., 2019). However, our results were supported by those of the sensitivity analyses on physician-confirmed wheezing, which might also represent, among the wheezing episodes, those with greater and more frequent symptoms. Additionally, although we had information on maternal asthma, which had a small confounding effect in our analysis, we lacked information on paternal asthma, which might be a potential confounder. Another limitation concerns the relatively low exposure resolution, which ranged from 0.1x0.1 (for PM 2.5) to 0.5x0.5 degrees (for SPEI), corresponding in Italy to around 8x8 to 41x41 km respectively, did not allow us to account for small-scale weather variability. However, our study's large temporal and spatial coverage allowed for sufficient exposure heterogeneity. As our exposure assessment is based on residential addresses, potential misclassification arises from not accounting for children's mobility or time spent outside their home location during the study period. Future studies incorporating individual-level mobility tracking could refine exposure estimates. We also lacked data on certain specific variables, such as overall PM levels and indoor air pollution, which could have impacted the outcome. However, we adjusted Model 3 for the degree of urbanization, climatic zone of residency, and Italian macro-area, which we think could capture the distribution of environmental-related confounders.

5. Conclusions

The positive association between the exposure to multiple CC-related extreme events, mainly high temperatures and drought, during the first year of life and infant wheezing occurrence suggest that the study of the mid and long-term health impacts of CC-related exposures and their underlying mechanisms warrants consideration in future investigations. It is important to delineate the direct and indirect health impacts of exposure to CC-related extreme events and to identify vulnerable populations and exposure windows. Recurrent wheezing episodes, due to their elevated prevalence, impact on later respiratory health, and sensitivity to environmental exposures, serve as a case study (Mathiarasan and Hüls, 2021). While many environmental exposures disproportionally affect children living in socio-economic disadvantage [37], our analyses stratified for maternal education, used here as a proxy for socioeconomic context, revealed no significant variations in the associations between exposure to CC-related extreme events and wheezing across different socio-economic strata. This suggests that living in a more advantaged context alone might not be enough to prevent the adverse effects of extreme events at an early age. Therefore, focusing solely on adaptation capacity may be insufficient, if not adequately supported by strong CC mitigation strategies. These observed early-life implications suggest that climate change is already impacting population health. Policymakers need to acknowledge these effects and take urgent action to safeguard the health of present and future generations.

Contributors

Silvia Maritano: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data Curation, Writing – Original Draft, Visualization; Lorenzo Richiardi: Conceptualization, Methodology, Validation, Resources, Writing – Review & Editing, Supervision, Project administration, Funding acquisition; Sofia Quaglia: Conceptualization, Formal analysis; Franca Rusconi: Resources, Writing – Review & Editing, Project administration; Milena Maule: Methodology, Resources, Writing – Review & Editing, Supervision; Giovenale Moirano: Conceptualization, Methodology, Software, Validation, Formal analysis, Data Curation, Writing – Review & Editing, Supervision.

Data Sharing

Due to the sensitive nature of the questions asked in this study, the NINFEA project respondents were assured raw data would remain confidential and would not be shared. We used publicly available datasets for the exposure assessment which can be accessed at the following links:

1. Copernicus ERA5 reanalysis- https://cds.climate.copernicus.eu/cdsapp#!/dataset/reanalysis-era5-single-levels?tab=overview
2. SPEIbase v 2.9- https://spei.csic.es/database.html
3. SILAM model for PM 2.5 from wildfires dispersion- https://silam.fmi.fi/fires.html?parameter=fireFRPfcst&region=Europe&height=0&sldsize=71&startpos=0

CRediT authorship contribution statement

Silvia Maritano: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Lorenzo Richiardi:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Funding acquisition, Conceptualization. **Sofia Quaglia:** Formal analysis, Conceptualization. **Franca Rusconi:** Writing – review & editing, Resources, Project administration. **Milena Maule:** Writing – review & editing, Supervision, Resources, Methodology. **Giovenale Moirano:** Writing – review & editing, Validation, Supervision, Software, Methodology, Formal analysis, Data curation, 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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2025.109303.

Data availability

The authors do not have permission to share data.

References

Al-Shamrani, A., Bagais, K., Alenazi, A., Alqwaiee, M., Al-Harbi, A.S., 2019. Wheezing in children: Approaches to diagnosis and management. Int J Pediatr Adolesc Med. 6 (2), 68–73.

Beck, H.E., Zimmermann, N.E., McVicar, T.R., Vergopolan, N., Berg, A., Wood, E.F., 2018. Present and future Köppen-Geiger climate classification maps at 1-km resolution. Scientific Data. 5 (1), 180214.

Bleu UMaP, 2020. State of the Environment and Development in the Mediterranean. United Nations Environment Programme and Mediterranean. Action Plan and Plan Bleu.

Brand, P.L.P., Baraldi, E., Bisgaard, H., Boner, A.L., Castro-Rodriguez, J.A., Custovic, A., et al., 2008. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. European Respiratory Journal. 32 (4), 1096–1110.

Burrows, K., Fussell, E., 2022. A life course epidemiology approach to climate extremes and human health. The Lancet Planetary Health. 6 (7), e549–e550.

Commission, E., Centre, J.R., Freire, S., Corbane, C., Zanchetta, L., Schiavina, M., et al., 2019. GHSL data package 2019 – Public release GHS P2019: Publications. Office.

Costello, A., Abbas, M., Allen, A., Ball, S., Bell, S., Bellamy, R., et al., 2009. Managing the health effects of climate change: Lancet and University College London Institute for Global Health Commission. The Lancet. 373 (9676), 1693–1733.

Florczyk, A.J., Corbane, C., Ehrlich, D., Freire, S., Kemper, T., Maffenini, L., et al., 2019. GHSL data package 2019. Luxembourg, Eur. 29788 (10.2760), 290498.

Helldén, D., Andersson, C., Nilsson, M., Ebi, K.L., Friberg, P., Alfvén, T., 2021. Climate change and child health: a scoping review and an expanded conceptual framework. Lancet Planet Health. 5 (3), e164–e175.

Hersbach H, Bell, B., Berrisford, P., Biavati, G., Horányi, A., Muñoz Sabater, J., Nicolas, J., Peubey, C., Radu, R., Rozum, I., Schepers, D., Simmons, A., Soci, C., Dee, D., Thépaut, J-N. ERA5 hourly data on single levels from 1940 to present. Copernicus Climate Change Service (C3S) =. In: (CDS) CDS, editor. 2023.

Jaddoe, V.W.V., Felix, J.F., Andersen, A.N., Charles, M.A., Chatzi, L., Corpeleijn, E., et al., 2020. The LifeCycle Project-EU Child Cohort Network: a federated analysis infrastructure and harmonized data of more than 250,000 children and parents. Eur J Epidemiol. 35 (7), 709–724.

Karl, T.R., Nicholls, N., Ghazi, A., 1999. Clivar/GCOS/WMO Workshop on Indices and Indicators for Climate Extremes Workshop Summary. Climatic Change. 42 (1), 3–7.

Kline, O., Prunicki, M., 2023. Climate change impacts on children's respiratory health. Current Opinion in Pediatrics. 35 (3).

Lee H, Calvin K, Dasgupta D, Krinner G, Mukherji A, Thorne P, et al. IPCC, 2023: Climate Change 2023: Synthesis Report, Summary for Policymakers. Contribution of Working Groups I, II and III to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change [Core Writing Team, H. Lee and J. Romero (eds.)]. IPCC, Geneva, Switzerland. 2023.

Makrufardi, F., Manullang, A., Rusmawatiningtyas, D., et al., 2023. Extreme weather and asthma: a systematic review and meta-analysis. Eur Respir Rev 32, 230019.

Makrufardi, F., Manullang, A., Rusmawatiningtyas, D., Chung, K.F., Lin, S.C., Chuang, H. C., 2023. Extreme weather and asthma: a systematic review and meta-analysis. Eur Respir Rev. 32 (168).

Mandhane, P.J., Greene, J.M., Cowan, J.O., Taylor, D.R., Sears, M.R., 2005. Sex differences in factors associated with childhood- and adolescent-onset wheeze. *Am J Respir Crit Care Med.* 172 (1), 45–54.

Mathiarasan, S., Hüls, A., 2021. Impact of Environmental Injustice on Children's Health-Interaction between Air Pollution and Socioeconomic Status. Int J Environ Res Public Health. 18 (2).

Melén, E., Zar, H.J., Siroux, V., et al., 2024. Asthma Inception: Epidemiologic Risk Factors and Natural History Across the Life Course. Am J Respir Crit Care Med. 210 (6), 737–754. https://doi.org/10.1164/rccm.202312-2249SO.

Nguyen, H.T., Le, H.T., Connelly, L.B., 2021. Weather and children's time allocation. *Health Economics* 30 (7), 1559–1579.

NINFEA P. Il progetto NINFEA: Nascita e INFanzia: gli Effetti dell'Ambiente Pubblicazioni- technical reports 2005 [Available from: https://www.progettoninfea.it/publications.

Organization WH. Climate Change: World Health Organization; 2023 [Available from: https://www.who.int/news-room/fact-sheets/detail/climate-change-and-health.

Perera, F., Nadeau, K., 2022. Climate Change, Fossil-Fuel Pollution, and Children's Health. New England Journal of Medicine. 386 (24), 2303–2314.

Pizzi, C., Moirano, G., Moccia, C., et al., 2024. Socioeconomic position during pregnancy and pre-school exposome in children from eight European birth cohort studies. *Soc Sci Med.* 359, 117275.

Richiardi, L., Baussano, I., Vizzini, L., Douwes, J., Pearce, N., Merletti, F., 2007. Feasibility of recruiting a birth cohort through the Internet: The experience of the NINFEA cohort. European Journal of Epidemiology. 22 (12), 831–837.

Romanello, M., Di Napoli, C., Green, C., Kennard, H., Lampard, P., Scamman, D., 2023. The 2023 report of the Lancet Countdown on health and climate change: the imperative for a health-centred response in a world facing irreversible harms. The Lancet 402 (10419), 2346–2394.

Schittny, J.C., 2017. Development of the lung. Cell and Tissue Research. 367, 427–444.

Schröder, P.C., Li, J., Wong, G.W., Schaub, B., 2015. The rural-urban enigma of allergy: what can we learn from studies around the world? *Pediatr Allergy Immunol.* 26 (2), 95–102.

Serrano SMV, Beguería S, López-Moreno JI, Angulo-Martínez M, Kenawy AME. A new global 0.5° gridded dataset (1901-2006) of a multiscalar drought index: comparison with current drought index datasets based on the Palmer Drought Severity Index. American Meteorological Society; 2010.

Sheffield, P.E., Knowlton, K., Carr, J.L., Kinney, P.L., 2011. Modeling of Regional Climate Change Effects on Ground-Level Ozone and Childhood Asthma. American Journal of Preventive Medicine. 41 (3), 251–257.

Sherwood, S.C., Huber, M., 2010. An adaptability limit to climate change due to heat stress. Proceedings of the National Academy of Sciences 107 (21), 9552–9555.

Solé, D., Vanna, A.T., Yamada, E., Rizzo, M.C., Naspitz, C.K., 1998. International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire: validation of the asthma component among Brazilian children. J Investig Allergol Clin Immunol. 8 (6), 376–382.

Team RC. R, 2013. A language and environment for statistical computing. R Foundation for Statistical Computing. (no Title).

Toll, V., Reis, K., Ots, R., Kaasik, M., Männik, A., Prank, M., et al., 2015. SILAM and MACC reanalysis aerosol data used for simulating the aerosol direct radiative effect

with the NWP model HARMONIE for summer 2010 wildfire case in Russia. Atmospheric Environment. 121, 75–85.
Tusting, L.S., et al., 2020. "Environmental temperature and growth faltering in African children: a cross-sectional study." The. Lancet Planetary Health 4 (3), e116–e123.
Wright, R.J., 2020. Influences of climate change on childhood asthma and allergy risk. The Lancet Child & Adolescent Health. 4 (12), 859–860.