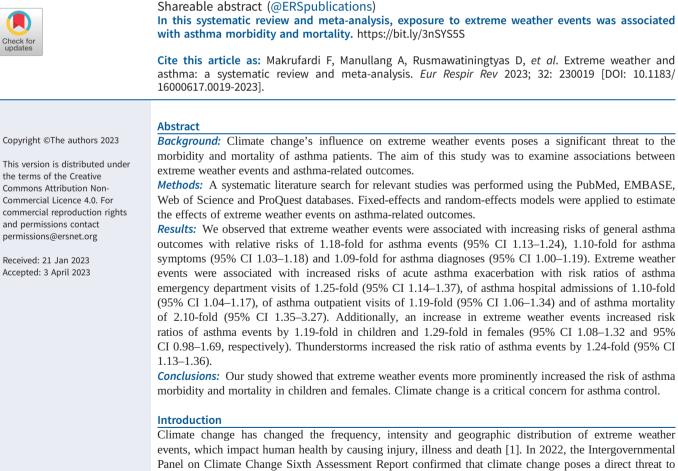


Extreme weather and asthma: a systematic review and meta-analysis

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events, which impact human health by causing injury, illness and death [1]. In 2022, the Intergovernmental Panel on Climate Change Sixth Assessment Report confirmed that climate change poses a direct threat to respiratory health, including asthma [2]. Asthma is the most common chronic lung disease in children and adolescents and is characterised by variable episodes of shortness of breath, chest tightness, wheezing and coughing [3, 4]. Asthma is a consequence of complex genetic–environmental interactions and thus clinical presentations and the type and intensity of airway inflammation and remodelling are heterogeneous [5]. Over the past few decades, research has also revealed a link between exposure to extreme weather events and asthma morbidity and mortality [6, 7]. Accumulating epidemiological evidence indicates that heat

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waves, cold spells, dust storms, hurricanes, floods and storm surges increase asthma-related outcomes [8–10]. This highlights the importance of environmental factors, particularly extreme weather events, in predicting asthma morbidity and mortality.

Extreme weather events aggravate pre-existing respiratory conditions and increase the likelihood of asthma-related events [11]. A time-series study highlighted that hurricanes are an important risk factor for asthma events in the United States [12]. In addition, thunderstorms appear to be an important risk for asthma events in North American and European regions [13-15]. Two studies emphasised the impact of thunderstorm asthma in Australia, which resulted in 10 deaths and approximately 9000 hospital and emergency department (ED) visits for severe and near-fatal asthma [16, 17]. Several studies also emphasised children as being a population at risk for asthma events due to extreme weather occurrences [18-20]. Also, studies in the United States observed that floods are an important risk factor for asthma symptoms with increased risks of 1.86- and 1.04-fold [21, 22]. More wheezing attacks, wheezing that interferes with sleep, severe wheezing that limits speech and wheezing after exercise were observed in females than males under extreme weather events [21]. Several studies also concluded that there are significant associations between extreme weather events and asthma symptoms in children [18, 23]. A study revealed that an increase in floods increased the relative risk of an asthma diagnosis by 2.16-fold [24]. A previous study also observed the importance of extreme weather events, particularly ice storms, with an increased ratio of asthma diagnoses [23]. Those reports demonstrate that extreme weather events result in increasing risks of general asthma outcomes.

Extreme weather events were found to be associated with the risk of asthma ED visits, particularly in females [14]. Extreme heat was also observed to be an important risk factor for asthma hospital admissions in the Asia-Pacific and North American regions [25–27]. A study in the United States observed an increase in the risk of asthma ED visits in children but a decreased risk in the elderly related to extreme weather events [28]. Furthermore, a study conducted in Europe discovered that thunderstorms increased the ratio of asthma symptoms [29]. Extreme temperature events, including cold spells [30, 31] and heat waves [32], were observed to be important risk factors for asthma hospital admissions. Previous reports found increases in the ratio and risk of asthma hospitalisation in children due to thunderstorms and dust storms [7, 33, 34], but a decrease in the risk of asthma outpatient visits [36]. Moreover, extreme weather events were also observed to be an important risk factor for asthma outpatient visits in the European region by increasing the relative risk by 1.26-fold [37]. Studies in Asia observed that an increase in extreme weather events increased the risk of asthma mortality [38, 39]. Taken together, extreme weather events result in increased risks of acute asthma exacerbation events.

Evidence has emerged in epidemiological studies regarding associations between extreme weather events and asthma-related outcomes. However, a systematic review of results between extreme weather events and asthma, particularly in different outcome assessments, is still lacking. The objective of this study was to examine associations between extreme weather events and asthma using a meta-analysis.

Materials and methods

Data sources and search strategy

This systematic review and meta-analysis followed protocols of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [40]. This study also followed the Meta-analysis of Observational Studies in Epidemiology checklist [41]. The study protocol was registered at PROSPERO (registration ID CRD42022370081) before beginning the study. The full checklist and protocol for this study are provided in the supplementary materials. The PubMed, EMBASE, Web of Science and ProQuest databases were searched up to 20 October 2022. Our study had no restriction of date, but it was limited to English-language articles. The search strategy focused on locating studies with estimated coefficients linking extreme weather events to the following asthma-related outcomes: hospital admissions, ED visits, outpatient visits, asthma mortality, asthma symptoms and asthma diagnoses. A combination of the following terms were used to search keywords, titles and abstracts: "asthma", "wheeze", "wheezing", "respiratory allergy", "meteorology", "climate change", "climate", "climat", "dust storm", "hail", "lightning", "tornado", "flood", "hurricane", "cold spell" and "heat wave". Full detailed strategies for each database are shown in supplementary table 1.

Study selection

EndNote bibliographic software was used to import results of the electronic searches. Inclusion criteria consisted of 1) asthma-related outcomes that were induced by extreme weather events (floods, hurricanes,

dust storms, cold spells, blizzards, ice storms, thunderstorms, typhoons and heat waves), 2) studies that presented estimates for asthma-related outcomes, including hospital admissions, ED visits, outpatient visits, asthma mortality, asthma symptoms and asthma diagnoses, 3) the study's outcome was a diagnosis of asthma as defined by the International Classification of Diseases or national/local guidelines, and 4) the study was published in a scientific journal with no date restriction. We excluded studies that 1) were not full-text scientific articles, 2) were review/letters/commentaries, 3) did not present effect estimates, 4) were written in a language other than English and 5) were reassessments of previous and original studies. We only included studies that provided estimates in the form of relative risks or risk ratios and odds ratios (ORs). When detailed estimates were presented only in figures and detailed variables that could be included in the subgroup analysis were not explained, the corresponding authors were contacted to obtain those results. We processed data based on data available in the manuscript when the authors were unable to provide detailed coefficient estimates.

Data extraction

The data we extracted consisted of general study characteristics, including 1) year of publication, 2) first author, 3) location (continent), 4) study period, 5) study design, 6) age of participants in years, 7) sample size, 8) outcome including risk ratios or ORs and 95% confidence intervals, 9) types of outcomes and 10) types of extreme weather events. Details about the types of outcomes, types of extreme weather events and effect estimates that were extracted from the study are presented in supplementary table 2. The Joanna Briggs Institute's critical appraisal checklist was used to assess the risk of bias [42]. The assessment of potential bias using funnel plots was not appropriate in this review due to the small number of studies included in this meta-analysis [43]. The risk of bias assessment is discussed in more detail in supplementary table 3.

Data synthesis and statistical analysis

A qualitative systematic review was conducted using studies that included epidemiological evidence of extreme weather events and asthma-related outcomes. We defined asthma events as a worsening of asthma requiring an unscheduled visit, an ED visit, hospitalisation or occurrence of asthma symptoms. Next, we obtained effect estimates (risk ratios with 95% confidence intervals) for associations between extreme weather events and asthma-related outcomes including asthma events, hospital admissions, ED visits, outpatient visits, asthma mortality, asthma diagnoses and asthma symptoms in the meta-analysis and subgroup analyses. Given the "rare-disease assumption", ORs were equivalent to risk ratios [44]. As a result, in the meta-analysis, we used risk ratio values as measures of associations. Individual risk ratios and pooled risk ratios (risk ratios or ORs) were graphically represented using forest plots. We presented effect estimates from individual studies with the study's size using a funnel plot. We conducted a number of subgroup analyses, including 1) gender (female and male), 2) age (children aged ≤18 years, adults aged from 19–64 years and elderly people aged ≥65 years), 3) region (Australia, Asia, Europe and North America) and 4) type of extreme weather event (hurricanes/typhoons, dust storms, cold spells, floods, heat waves and blizzards/ice storms). Cochran's Q and I^2 statistics were used to assess study heterogeneity. Cochran's Q statistic was considered significant at p<0.10, and I^2 values of >50% were considered to indicate moderate-to-high heterogeneity [45]. Fixed-effects models were used if p>0.1 and $I^2<50\%$, otherwise a random-effects model was used. Sensitivity analyses were also performed to investigate the source of heterogeneity and the robustness of those findings. To assess the stability of the pooled risk ratio, a sensitivity analysis was performed by repeating the main analysis. Review Manager software (RevMan version 5.4.1) was used for all statistical analyses.

Results

Study characteristics

A database search resulted in 6910 studies and then 2720 studies were excluded due to being duplicate publications (figure 1). There were 165 eligible studies recruited for full-text evaluation. We excluded 32 conference abstracts/reviews/commentaries, 35 studies with other exposures, 59 studies that did not report an outcome of interest and eight studies that were not in English. For the qualitative analysis, 31 articles were included in the meta-analysis.

Characteristics of the included studies in the quantitative and descriptive analyses are presented in supplementary table 2. Regions covered by the included studies are presented in supplementary figure 1. In total, 16 studies had a time series study design. Most of the studies were conducted in either North America or Asia. The largest number of studies focused on children, followed by adults and the elderly. 20 studies described thunderstorms, followed by hurricanes/typhoons, dust storms, cold spells, floods, heat waves and blizzards/ice storms.

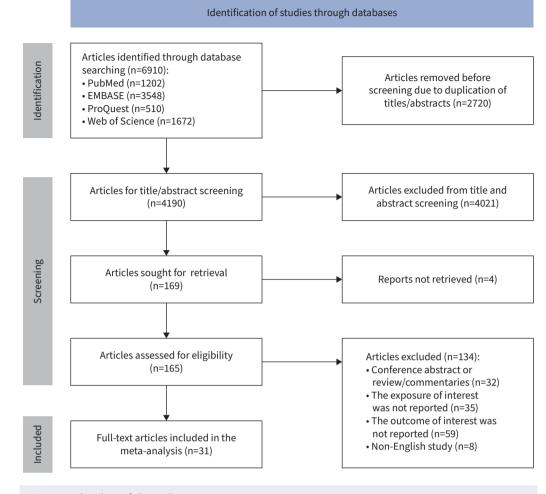


FIGURE 1 Flowchart of the study.

Exposure to extreme weather events associated with increasing risks of general asthma outcomes

We observed that an increase in extreme weather events increased the risk ratio of asthma events by 1.18-fold (95% CI 1.13–1.24; p<0.05) (figure 2a). An increase in extreme weather events increased the risk ratio of asthma symptoms by 1.10-fold (95% CI 1.03–1.18; p<0.05) (figure 2b). Additionally, an increase in extreme weather events increased the risk ratio of asthma diagnoses by 1.09-fold (95% CI 1.00–1.19; p<0.05) (figure 2c). The sensitivity analysis showed there were no differences in increased extreme weather events with increases in asthma events, asthma symptoms or asthma diagnoses (supplementary figures 2A–2C).

Exposure to extreme weather events associated with increasing risks of acute exacerbations of asthma

We observed that an increase in extreme weather events increased the risk ratio of asthma ED visits by 1.25-fold (95% CI 1.14–1.37; p<0.05) (figure 3a). An increase in extreme weather events increased the risk ratio of asthma hospital admissions by 1.10-fold (95% CI 1.04–1.17; p<0.05) (figure 3b). An increase in extreme weather events increased the risk ratio of asthma outpatient visits by 1.19-fold (95% CI 1.06–1.34; p<0.05) (figure 3c). Additionally, an increase in extreme weather events increased the risk ratio of asthma mortality by 2.10-fold (95% CI 1.35–3.27; p<0.05) (figure 3d). The sensitivity analysis showed there were no differences in results of asthma ED visits and asthma hospital admissions (supplementary figures 3A, B), but asthma outpatient visits and asthma mortality showed slight differences in the results (supplementary figures 3C, D).

Subgroup analysis of exposure to extreme weather events on general asthma outcomes

We observed that an increase in extreme weather events increased the risk ratio of asthma events in children by 1.19-fold (95% CI 1.08-1.32; p<0.05) (figure 4a). Consistently, an increase in extreme weather

) Study or subgroup	Log (risk ratio)	SE	Weight (%)	Risk ratio IV, random, 95% CI	IV, r	Risk ratio andom, 95% CI	
Anderson <i>et al.</i> , 2011	0.1035	0.0274	5.3	1.11 (1.05–1.17)		-	
Blindauer et al., 1999	0	0.3537	0.4	1.00 (0.50-2.00)			
CAMPBELL et al., 2019	0.3376	0.2038	1.1	1.40 (0.94-2.09)			
Celenza <i>et al.</i> , 1996	1.1663	0.3395	0.5	3.21 (1.65-6.24)			
Chang <i>et al.</i> , 2021	0.6881	0.2413	0.8	1.99 (1.24-3.19)			
Снем et al., 2021	0.1133	0.0578	4.2	1.12 (1.00-1.25)		T	
Cowan <i>et al.</i> , 2021	0.0198	0.0256	5.3	1.02 (0.97-1.07)			
Fagan <i>et al.</i> , 2001	0.6206	0.1377	2.0	1.86 (1.42-2.44)			
Fanny <i>et al.</i> , 2021	0.5933	0.0891	3.2	1.81 (1.52-2.16)		-	
FIGGS <i>et al.</i> , 2019	0.1722	0.1087	2.6	1.19 (0.96-1.47)		+	
FITZGERALD et al., 2014	-0.0202	0.0052	5.6	0.98 (0.97-0.99)			
Guo et al., 2012	0.1133	0.0527	4.4	1.12 (1.01-1.24)		-	
HASUNUMA et al., 2021	1.6429	0.8281	0.1	5.17 (1.02-26.20)			
Норре <i>et al.</i> , 2012	1.1217	0.2557	0.8	3.07 (1.86-5.07)			
Kontowicz et al., 2022	0.0392	0.0257	5.3	1.04 (0.99-1.09)		•	
Liu et al., 2021	0.1035	0.0274	5.3	1.11 (1.05-1.17)		-	
Lонмus <i>et al.</i> , 2022	0.2316	0.0424	4.8	1.26 (1.16-1.37)		+	
MA et al., 2021	1.1184	0.6261	0.1	3.06 (0.90-10.44)		+	
Merrifield <i>et al.</i> , 2013	0.174	0.0448	4.7	1.19 (1.09-1.30)		+	
Newson <i>et al.</i> , 1997	0.2236	0.0428	4.8	1.25 (1.15-1.36)		T	
Park et al., 2022	0.239	0.0941	3.0	1.27 (1.06-1.53)		-	
Ramesн <i>et al.</i> , 2021	0.1398	0.0562	4.3	1.15 (1.03-1.28)		Ŧ	
RAPPOLD et al., 2011	0.5008	0.1417	1.9	1.65 (1.25-2.18)			
Sмітн et al., 2022	0.0459	0.0173	5.5	1.05 (1.01-1.08)			
SOHAIL et al., 2020	0.1951	0.159	1.6	1.22 (0.89-1.66)			
Son <i>et al.</i> , 2014	0.0839	0.1503	1.7	1.09 (0.81-1.46)			
THALIB <i>et al.</i> , 2012	0.0686	0.0229	5.4	1.07 (1.02-1.12)		-	
TURCOTTE-TREMBLAY et al., 2021	0.0953	0.0335	5.1	1.10 (1.03-1.17)		-	
VILLENEUVE et al., 2005	0.3001	0.143	1.9	1.35 (1.02–1.79)		-	
Yang et al., 2005	0.077	0.0548	4.4	1.08 (0.97-1.20)		-	
YITSHAK SADE et al., 2014	0.0953	0.0642	4.0	1.10 (0.97–1.25)		-	
Total (95% CI)			100.0	1.18 (1.13–1.24)		•	
Heterogeneity: Tau ² =0.01; Chi ² =2	, ,	0001); l ²	=90%	n	.01 0.1	1 10	100
Test for overall effect: z=6.93 (p<0	0.00001)			0	Favours (experimer		
					ravours (experimer	ital) Favours (contro)()

b) Study or subgroup		Log (risk ratio)	SE	Weight (%)	Risk ratio IV, random, 95% CI	l	IV, r	Risk ratio andom, 95		
	Fagan <i>et al.</i> , 2001	0.6206	0.1377	18.5	1.86 (1.42–2.44)			_		
	HASUNUMA et al., 2021	1.6429	0.8281	0.9	5.17 (1.02-26.20)					
	Норре <i>et al.</i> , 2012	0.5596	0.6392	1.5	1.75 (0.50-6.13)					
	Kontowicz et al., 2022	0.0392	0.0257	40.1	1.04 (0.99–1.09)			, in the second se		
	TURCOTTE-TREMBLAY et al., 2021	0.0953	0.0335	39.0	1.10 (1.03–1.17)					
	Total (95% CI)			100.0	1.21 (1.04–1.41)			•		
	Heterogeneity: Tau ² =0.02; Chi ² =22		2); I ² =82	%	С	0.01	0.1	1	10	100
	Test for overall effect: z=2.41 (p=0.	02)				Fav	ours (experime	ntal)	Favours (contro	ol)

c)	Study or subgroup	Log (risk ratio)	SE	Weight (%)	Risk ratio IV, fixed, 95% C	I	IV	Risk rat , fixed, 9		
	Норре <i>et al.</i> , 2012	0.7701	0.6621	0.4	2.16 (0.59–7.91)					
	TURCOTTE-TREMBLAY et al., 2021	0.0862	0.044	99.6	1.09 (1.00-1.19)					
	Total (95% CI)			100.0	1.09 (1.00-1.19))		•		
	Heterogeneity: Chi ² =1.06, df=1 (p= Test for overall effect: z=2.03 (p=0.					0.01	0.1	1	10	100
						Fa	vours (experime	ntal)	Favours (con	trol)

FIGURE 2 Forest plot of extreme weather events with general asthma outcomes: a) asthma events; b) asthma symptoms; c) asthma diagnosis. IV: inverse variance; SE: standard error.

a)					Risk ratio		Risk ratio		
_	Study or subgroup	Log (risk ratio)	SE	Weight (%)	IV, random, 95% C	1	IV, random, 95	% CI	
	Blindauer <i>et al.</i> , 1999	0	0.3537	1.6	1.00 (0.50-2.00)				
	Campbell <i>et al.</i> , 2019	0.3376	0.2038	3.9	1.40 (0.94-2.09)				
	Celenza <i>et al.</i> , 1996	1.1663	0.3395	1.7	3.21 (1.65-6.24)		-		
	Cowan <i>et al.</i> , 2021	0.0198	0.0256	12.9	1.02 (0.97-1.07)		+		
	Fanny <i>et al.</i> , 2021	0.5933	0.0891	9.2	1.81 (1.52–2.16)				
	FIGGS <i>et al.</i> , 2019	0.1722	0.1087	7.9	1.19 (0.96-1.47)				
	Merrifield <i>et al.</i> , 2013	0.207	0.0575	11.3	1.23 (1.10-1.38)		-		
	Park <i>et al.</i> , 2022	0.239	0.0941	8.8	1.27 (1.06–1.53)				
	Ramesн <i>et al.</i> , 2021	0.1398	0.0562	11.3	1.15 (1.03–1.28)		-		
	Rappold <i>et al.</i> , 2011	0.5008	0.1417	6.2	1.65 (1.25–2.18)				
	Sмітн <i>et al.</i> , 2022	0.0459	0.0173	13.2	1.05 (1.01-1.08)		•		
	Son <i>et al.</i> , 2014	0.0839	0.1503	5.8	1.09 (0.81-1.46)		- - -		
	VILLENEUVE <i>et al.</i> , 2005	0.3001	0.143	6.1	1.35 (1.02–1.79)		-		
	Total (95% CI)			100.0	1.25 (1.14–1.37)		•		
	Heterogeneity: Tau ² =0.02; Chi ² =75.2	24, df=12 (p<0.000	001); I ² =	84%		0.01 0.1	1	10	100
	Test for overall effect: z=4.69 (p<0.0	0001)					N		100
						Favours (expe	rimental)	Favours (control)	
b)					Risk ratio		Risk ratio		
,	Study or subgroup	Log (risk ratio)	SE	Weight (%)	IV, random, 95% C	1	IV, random, 95	% CI	

Study or subgroup	Log (risk ratio)	SE	Weight (%)	IV, random, 95% CI		IV, ra	andom, 95%	CI	
Anderson <i>et al.</i> , 2011	0.1035	0.0274	12.3	1.11 (1.05–1.17)			•		
Снем <i>et al.</i> , 2021	0.1133	0.0578	9.3	1.12 (1.00-1.25)			-		
Fitzgerald <i>et al.</i> , 2014	-0.0202	0.0052	13.5	0.98 (0.97-0.99)			4		
Liu <i>et al.</i> , 2021	0.1035	0.0274	12.3	1.11 (1.05-1.17)			-		
Merrifield <i>et al.</i> , 2013	0.1319	0.0719	7.9	1.14 (0.99-1.31)			-		
Newson <i>et al.</i> , 1997	0.2236	0.0428	10.8	1.25 (1.15–1.36)			-		
Sohail <i>et al.</i> , 2020	0.1951	0.159	3.0	1.22 (0.89-1.66)			+		
Тнаlib <i>et al.</i> , 2012	0.0686	0.0229	12.6	1.07 (1.02-1.12)			-		
Yang et al., 2005	0.077	0.0548	9.6	1.08 (0.97-1.20)			-		
Yitshak Sade <i>et al.</i> , 2014	0.0953	0.0642	8.7	1.10 (0.97–1.25)			-		
Total (95% CI)			100.0	1.10 (1.04-1.17)			\$		
Heterogeneity: Tau ² =0.01; Chi ²	² =92.54, df=9 (p<0.000	01); I ² =9	0%		· · · · · ·	I		I	
Test for overall effect: z=3.11 (<i>,</i> , , ,			0	.01	0.1	1	10	100
···· · · · · · · · · · · · · · · · · ·	,				Favou	ırs (experimer	ıtal) Fa	ivours (contro	ol)

c)	Study or subgroup	Log (risk ratio)	SE	Weight (%)	Risk ratio IV, random, 95%	CI	Ri IV, ran	sk rati dom, 9	-	
_	Guo et al., 2012	0.1133	0.0527	46.5	1.12 (1.01-1.24)					
	Lонмus <i>et al.</i> , 2022	0.2316	0.0424	53.5	1.26 (1.16–1.37)					
	Total (95% CI)			100.0	1.19 (1.06-1.34))		•		
	Heterogeneity: Tau ² =0.00; Chi ² =3.0 Test for overall effect: z=2.99 (p=0.0	/ // //	² =67%			0.01	0.1	1	10	100
		,				F	avours (experimenta	l)	Favours (control)	

d)	Study or subgroup	Log (risk ratio)	SE	Weight (%)	Risk ratio IV, fixed, 95% C	I		ľ	Risk ra V, fixed, S			
_	Сналд <i>et al.</i> , 2021	0.6881	0.2413	87.1	1.99 (1.24-3.19)					-		
	Ma et al., 2021	1.1184	0.6261	12.9	3.06 (0.90-10.44))			t	_		
	Total (95% CI)			100.0	2.10 (1.35-3.27))				◆		
	Heterogeneity: Chi ² =0.41, df=1 (p=0 Test for overall effect: z=3.30 (p=0.0					0.01 F	avours (0.1 experim	1 ental)	Favou	10 rs (control)	100

FIGURE 3 Forest plot for extreme weather events with acute exacerbations of asthma. a) Emergency department visits related to asthma. b) Hospital admissions related to asthma. c) Outpatient visits related to asthma. d) Asthma mortality. IV: inverse variance; SE: standard error.

events increased the risk ratio of asthma events by 1.29-fold in females (95% CI 0.98–1.69; p<0.05) and the risk ratio of the asthma events by 1.24-fold in males (95% CI 0.99–1.56; p<0.05). An increase in extreme weather events increased the risk ratio of asthma events by 1.23-fold in Australia (95% CI 1.10–1.38; p<0.05). We identified that an increase in extreme weather events increased the risk ratio of asthma

a) Asthma events

Study or subgroup	n	l² (%)						Relative risk (95% CI)
All	31	90			•			1.18 (1.13-1.24)
Age group								
Adults	6	84			-			1.14 (1.01-1.29)
Children	11	90			-			1.19 (1.08-1.32)
Elderly	5	68			+			1.07 (0.88–1.30)
Gender								
Female	5	96						1.29 (0.98-1.69)
Male	5	97			-			1.24 (0.99–1.56)
Geographical region								
Asia	10	37						1.10 (1.06-1.13)
Australia	3	0			-			1.23 (1.10-1.38)
Europe	5	78			T			1.17 (1.09-1.25)
North America	14	91			-			1.19 (1.11–1.27)
Extreme weather events								
Blizzard/ice storm	2	0						1.10 (1.03-1.17)
Cold spells	5	90			-			1.08 (0.98-1.19)
Dust storm	5	50			•			1.11 (1.04-1.18)
Flood	4	92						1.43 (1.11–1.84)
Heatwave	4	0			-			1.19 (1.04-1.38)
Hurricane/typhoon	3	96						1.50 (0.93-2.43)
Thunderstorm	8	86			•			1.24 (1.13–1.36)
			0.01	0.1	1	10	100	
			0.01	0.1	T	10	100	
) Asthma symptoms		-2 (6/)						
Study or subgroup	n	I ² (%)						Relative risk (95% CI
All	5	82			◆			1.21 (1.04–1.41)
Age group								
Children	2	71						1.91 (0.45-8.18)
Geographical region								
North America	4	84						1.19 (1.02–1.37)
Extreme weather events								
Flood	3	89			+			1.41 (0.84–2.36)

FIGURE 4 Subgroup analyses of extreme weather events with general asthma outcomes. a) Asthma events. b) Asthma symptoms.

events in blizzards/ice storms by 1.10-fold (95% CI 1.03–1.17; p<0.05), 1.11-fold in dust storms (95% CI 1.04–1.18; p<0.05), 1.20-fold in floods (95% CI 1.11–1.84; p<0.05) and 1.24-fold in thunderstorms (95% CI 1.13–1.36; p<0.05). We observed that an increase in extreme weather events increased the risk ratio of asthma symptoms in the North American region by 1.18-fold (95% CI 1.02–1.37; p<0.05) (figure 4b).

Subgroup analysis of exposure to extreme weather events on acute exacerbation of asthma

We observed that an increase in extreme weather events increased the risk ratio of asthma ED visits in children by 1.52-fold (95% CI 1.07–2.15; p<0.05) (figure 5a). An increase in extreme weather events increased the risk ratio of asthma ED visits in females by 1.31-fold (95% CI 1.23–1.40; p<0.05) and the risk ratio in males by 1.29-fold (95% CI 1.21–1.37; p<0.05). An increase in extreme weather events increased the risk ratio of asthma ED visits in Australia by 1.24-fold (95% CI 1.11–1.38; p<0.05). We identified that an increase in extreme weather events increased the risk ratio of asthma ED visits in creased the risk ratio of asthma ED visits in Australia by 1.24-fold (95% CI 1.11–1.38; p<0.05). We identified that an increase in extreme weather events increased the risk ratio of asthma ED visits in heat waves by 1.18-fold (95% CI 1.01–1.39; p<0.05) and by 1.23-fold in thunderstorms (95% CI 1.10–1.38; p<0.05).

We identified that an increase in extreme weather events increased the risk ratio of asthma hospital admissions in adults by 1.16-fold (95% CI 1.01–1.34; p<0.05) (figure 5b). An increase in extreme weather events increased the risk ratio of asthma hospital admissions in females by 1.45-fold (95% CI 1.00–2.09; p<0.05) and by 1.22-fold in males (95% CI 0.95–1.57; p<0.05). An increase in extreme weather events

a) Emergency department visits

a)	Emergency department visits								
_	Study or subgroup	n	l² (%)						Relative risk (95% CI)
	All	13	84			•			1.25 (1.14–1.37)
	Age group								
	Children	2	84						1.52 (1.07–2.15)
	Gender								
	Female	2	0						1.31 (1.23-1.40)
	Male	2	70						1.28 (1.21–1.37)
		-							1120 (1121 1101)
	Geographical region								
	Australia	2	0			-			1.24 (1.11–1.38)
	North America	9	86			-			1.23 (1.11–1.37)
	Extreme weather events								
	Heatwave	3	0			-			1.19 (1.01-1.39)
	Hurricane/typhoon	2	97						1.35 (0.77-2.37)
	Thunderstorm	5	85			•			1.23 (1.10-1.38)
					1		1		
				0.01	0.1	1	10	100	
b)	Hospital admission								
	Study or subgroup	n	l² (%)						Relative risk (95% CI)
	All	10	90			*			1.10 (1.04-1.17)
	Age group								
	Adults	5	87			-			1.16 (1.01–1.34)
	Children	5	90			•			1.10 (0.97-1.23)
	Elderly	4	76			1			1.11 (0.89–1.39)
	Gender								
	Female	4	95						1.45 (1.00-2.09)
	Male	4	87			-			1.22 (0.95–1.57)
	Geographical region								
	Asia	4	19						1.09 (1.04-1.13)
	Australia	2	0						1.12 (1.02–1.23)
	Europe	3	65			-			1.17 (1.02–1.23)
	Extreme weather events	_							
	Cold spells	3	91			t			1.05 (0.93–1.19)
	Dust storm	4	0			L			1.08 (1.04–1.12)
	Thunderstorm	2	82						1.17 (1.04–1.32)
				0.01	0.1	1	10	100	
					0.2	-		200	

FIGURE 5 Subgroup analyses of extreme weather events with acute exacerbations of asthma. a) Asthma emergency department visits. b) Asthma hospital admissions.

increased the risk ratio of asthma hospital admissions in the European region by 1.17-fold (95% CI 1.02– 1.23; p<0.05). We identified that an increase in extreme weather events increased the risk ratio of asthma hospital admissions in dust storms by 1.08-fold (95% CI 1.04–1.12; p<0.05) and by 1.17-fold in thunderstorms (95% CI 1.04–1.32; p<0.05).

Discussion

The novelty of this study is that we investigated the effects of extreme weather events on asthma-related outcomes. Significant findings of this work are that extreme weather events increased the risk of asthma outcomes and stability, especially in children and females, by floods and hurricanes/typhoons, and in the Asia-Pacific region. Our results suggest that climate change and extreme weather events could increase the risk of asthma morbidity and mortality.

We identified that extreme weather events increased the risk of general asthma outcomes. A previous report showed that climate change's influence on extreme weather events increased the risk of asthma events by 1.03-fold (95% CI 1.00–1.07; p<0.05) [46]. A study in the western United States estimated that an increase in extreme weather events increased asthma events at a rate of 25.7–41.9 per 10 000 persons [47]. In our

study, previous reports evidenced that an increase of extreme weather events increased asthma events and asthma symptoms [24, 37]. Hence, we also evaluated the effects of extreme weather events on asthma symptoms and observed that extreme weather events are an important risk factor for asthma symptoms. A previous study showed that with an increase in extreme weather events, 2000 asthma patients complained of shortness of breath and wheezing, which were accompanied by coughing in 45% of patients [48]. A study reported that an increase in extreme weather events increased asthma symptoms in patients who did not have a previous diagnosis [49]. Consistently, we observed that extreme weather events are an important risk factor for an asthma diagnosis. Extreme weather events have the potential to transmit bacterial and viral infections, suggesting a potential impact of extreme weather events is an increase in respiratory diagnoses [50]. Taken together, extreme weather events could be a risk factor for general asthma outcomes.

Next, we emphasised that extreme weather events increased the risk of an acute exacerbation of asthma. Another study showed that ED visits increased by 1.15-fold due to extreme weather events (95% CI 1.01-1.30; p<0.05) [28]. We also found that extreme weather events are an important risk factor for asthma hospital admissions. A previous study reported that asthma hospital admissions increased by 1.09-fold due to extreme weather events (95% CI 0.81–1.46; p<0.05) [26]. Extreme low temperatures were shown in two studies on asthmatic mouse models to aggravate asthmatic airway inflammation [51, 52]. We observed that extreme weather events increased the risk of asthma outpatient visits. A previous study reported that asthma outpatient visits increased by 1.26-fold because of extreme weather events (95% CI 1.16–1.37; p<0.05) [37]. We further identified that extreme weather events are an important risk factor for asthma mortality. Nonoptimal temperatures were responsible for 26.3% of asthma-related deaths, with moderate cold, moderate hot, extreme cold and extreme hot, respectively, accounting for 21.7, 2.4, 2.1 and 0.9% of asthma-related deaths [53]. Additionally, exposure to air pollution was reported to aggravate asthma possibly through the extreme temperature [54]. For example, black carbon can absorb heat, raising temperatures and making the temperature more extreme [54]. The most possible mechanism in asthma aggravation is through transient receptor potential channels, the sensors that provide vital information on environmental temperature, allowing to respond quickly to both noxious heat and cold involved in temperature-induced airway manifestations [55]. Therefore, our findings indicate that extreme weather events can increase the risk of acute exacerbation of asthma.

We next identified populations at risk for general asthma outcomes due to extreme weather events. First, we observed that children are a susceptible group for asthma events due to extreme weather events. A previous study reported that extreme weather events increased the risk of asthma events by 1.11-fold (95% CI 1.02-1.21; p<0.05) [6]. In addition, a study in Turkey revealed that asthma, wheezing and allergic rhinitis were associated with higher mean yearly outdoor humidity levels in schoolchildren [56]. Rain or humidity may induce hydration and fragmentation of pollen grains, which releases allergenic biological aerosols into the atmosphere [57]. We further observed that females had a higher risk of asthma events due to extreme weather events. One study showed higher a prevalence of asthma related to extreme weather events in adult women (a 65% prevalence) compared to adult men [58]. A previous study found that sex hormones are key mediators of the transition of differences in asthma prevalence across sexes [59]. This can be explained by studies that determined DNA methylation of sex hormones (at CpG motifs before and after puberty) due to extreme environmental exposures which were linked to asthma susceptibility [60, 61]. We observed that people who lived in the Australia region had a higher risk of asthma events in response to extreme weather events. A previous study showed that an increase in extreme weather events increased asthma events in Australia [49]. Extreme weather events such as thunderstorms occur in Australia due to a number of factors, including interactions of cold and warm air masses and the presence of low-pressure systems [62]. These storms can bring heavy rain, high winds and lightning, which can aggravate asthma [63]. Thunderstorms are an important risk for asthma events. Studies in 2017 and 2018 showed that an increase of extreme weather events caused an increase of 3365 additional asthma episodes than expected due to thunderstorms [49, 64]. In a thunderstorm, electrical charges within the storm can cause pollen and spores to fracture into smaller particles [65]. Thunderstorm can result in dispersion of pollen, causing severe asthmatic reactions in patients with pollen allergies [10, 66, 67]. Outdoor fungal spores are more diverse and abundant and have been linked to hospitalisations from acute asthma presentations [68]. Extreme weather events are an important risk factor for asthma symptoms in people who live in the North American region. One study revealed that post-hurricane patients reported more asthma or lower respiratory symptoms than pre-hurricane in North America (39% versus 25%, p<0.05) [69]. This can be explained by the topography of North America, which includes mountain ranges and coastlines that are more vulnerable to hurricanes and other severe storms [70]. Taken together, females and children are populations at risk for general asthma outcomes due to extreme weather events.

Populations at risk for acute exacerbations of asthma caused by extreme weather events were observed. Children are the most vulnerable group for asthma ED visits caused by extreme weather events. A previous study reported that extreme weather events increased the risk of asthma ED visits by 1.35-fold (95% CI

1.02–1.77; p<0.05) [19]. Another study observed that the occurrence of fog or liquid precipitation was associated with an increased number of asthma visits by children [19]. Females are a population at risk for asthma ED visits. A previous study showed that extreme weather events increased the risk of asthma ED visits by females by 4.10-fold (95% CI 2.60-5.60; p<0.05) [71]. Stress and anxiety have been linked to asthma ED visits and females may be more likely to experience these during extreme weather events [72]. We identified that extreme weather events increased the risk of asthma ED visits in people who lived in Australia. This result was consistent with studies carried out in Sydney and North Carolina, which reported that ED visits for asthma increased compared to nonextreme weather events [73, 74]. Thunderstorms are an important risk factor for asthma ED visits. A previous study reported that ED visits peaked at 6.3-fold for those with asthma (95% CI 4.10-8.60; p<0.05) [75]. Interestingly, we identified that extreme weather events are an important risk factor for asthma hospital admissions in adults. This finding is consistent with a previous study which showed that an increasing age leads to increased risk of hospital admission in adults by 1.01-fold (95% CI 1.00-1.02; p<0.05) [76]. A study found that adults patients who required hospital admission were patients from the ED with greater severity [77]. Females are a susceptible group for asthma hospital admissions that occur due to extreme weather events. A previous study showed that extreme weather events increased asthma hospital admissions by females by 1.29-fold (95% CI 1.04–1.59; p<0.05). Thunderstorms are an important risk factor for asthma hospital admissions. One study reported that, during a 12-h thunderstorm, asthma-related hospital admissions increased by almost 1000%, an unprecedented number that the health infrastructure was unprepared to handle [78]. During a thunderstorm, dry updrafts transport whole pollen grains to the cloud base's high humidity, which can lead to rupture, and cold downdrafts transport pollen fragments to the ground level, where outflows distribute them. As a consequence, the air contains a high level of respirable allergens [16]. Accordingly, both children and females are populations at risk for general asthma outcomes due to extreme weather events.

There are some limitations in our review. There was a lack of detailed data in the included study, which resulted in some asthma-related outcome variables not being examined in the subgroup analysis. The majority of the exposure assessments were based on meteorological station or remote sensing data, which resulted in incomplete exposure information on crucial asthma risk factors. The included studies were heterogeneous in type, intensity and duration of extreme weather events, which potentially limiting the interpretation of the results. Several studies have not adequately addressed potential sources of bias or methodological weaknesses that may have an impact on the validity of the results. The small number of studies with a particular focus on extreme weather events highlighted the need for further research in order to obtain more robust results.

In conclusion, exposure to extreme weather events was associated with asthma morbidity and mortality. We further identified that children and females are populations at risk for asthma in response to extreme weather events. Our findings suggested that patients with asthma may be more susceptible to poorer outcomes in extreme weather events.

Points for clinical practice

- · Exposure to extreme weather events more prominently increased the risk of asthma morbidity and mortality.
- · Children and females are populations at risk for asthma in response to extreme weather events.
- Climate change poses a direct threat to respiratory health and is a critical concern for asthma control.

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