Short report

Effect of cold winters on the risk of new asthma: a case-crossover study in Finland

Abate Bekele Belachew,[1,2] Aino K Rantala,[1] Maritta S Jaakkola ,[1] Timo T Hugg,[1] Reija Ruuhela,[3] Jaakko Kukkonen,[3,4] Jouni J K Jaakkola [1,3]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/oemed-2022-108682).

[1]Center for Environmental and Respiratory Health Research, Population Health Reserach Unit, University of Oulu, Oulu, Finland
[2]School of Public Health, College of Medicine and Health Sciences, Arba Minch University, Arba Minch, Ethiopia
[3]Air Quality Research, Finnish Meteorological Institute, Helsinki, Finland
[4]University of Hertfordshire, Hatfield, UK

Correspondence to
Professor Jouni J K Jaakkola, Center for Environmental and Respiratory Health Research, University of Oulu, Oulu 90570, Finland; jouni.jaakkola@oulu.fi

Received 7 October 2022
Accepted 29 August 2023

To cite: Belachew AB, Rantala AK, Jaakkola MS, *et al*. *Occup Environ Med* Epub ahead of print: [please include Day Month Year]. doi:10.1136/oemed-2022-108682

ABSTRACT

Background Cold weather increases respiratory symptoms and provokes exacerbations of asthma, but there are no previous studies on its role in the aetiology of asthma.

Objective We tested the hypothesis that a cold winter increases the risk of developing asthma during the following 1 to 2 years.

Methods We conducted a case-crossover study of 315 newly diagnosed cases of asthma from the population-based Espoo Cohort Study from birth to the age of 27 years. The hazard period constituted 3 winter months preceding the onset of asthma and bidirectional reference periods of 1 year before hazard period and 1 year after onset of asthma. Exposure constituted average ambient temperature during the winter months of December, January and February. The outcome of interest was new doctor-diagnosed asthma. The measure of effect was OR of asthma estimated by conditional logistic regression analysis.

Results The average winter temperature for the study period from winter 1983 to 2010 was −4.4°C (range −10.7 to 0.4). A 1°C decrease in the average winter temperature predicted a 7% increase in the risk of new asthma (OR=1.07, 95% CI 1.02 to 1.13). A cold winter with an average temperature below the climate normal value (−4.5°C; period 1981–2010) increased the risk of new asthma by 41% during the following year (OR: 1.41; 95% CI 1.04 to 1.90).

Conclusions This case-crossover study provides original evidence that a cold winter with below normal average temperatures increases the risk of developing new asthma during the following 1 to 2 years.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Short-term and long-term exposure to cold may damage the airway epithelium.
⇒ Though previous studies have showed the effect of cold temperature on asthma exacerbation, evidence about potential role of cold temperature on asthma inception is lacking.

WHAT THIS STUDY ADDS

⇒ A population-based case-crossover study of 315 subjects with new asthma provided evidence that cold winter predicts a significant increase in the onset of asthma during the following 1–2 years.
⇒ This observation was present in males and females in preschool and school children and young adults.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings support the hypothesis that cold weather causes asthma. Clinicians should take this observation into account in their clinical practice. For example, air ways protection during cold winter weather may reduce the risk of asthma among subjects with cold weather-related symptoms and hereditary burden of asthma.

INTRODUCTION

Environmental exposures, such as cold air or air pollution, may trigger symptoms or exacerbation of asthma.[1] There is also evidence that long-term exposure to air pollution increases the risk of developing new asthma.[2] Based on a systematic literature search, there are no previous studies on the potential role of long-term exposure to cold weather in the aetiology of asthma. We hypothesised that a cold winter increases the risk of developing asthma during the following year. We studied the population-based Espoo Cohort Study in Southern Finland by using the cold winter temperature as the exposure and applying a case-crossover study design.

METHODS

Study design and population

We applied a case-crossover design to estimate the relation between average winter temperature and the onset of asthma. In a case-crossover design, the study subjects are selected from cases, here those who have experienced an onset of asthma. The inference is based on a comparison of each subject's exposure, here the average temperature, during a time period relevant for the causation of the outcome, here the winter preceding the onset, which is referred to as a hazard period, and during one or more reference (control) periods.[3] We decided to apply a bidirectional selection of reference periods, one before the hazard period and the other after the onset of asthma. This design has been previously proposed appropriate for studying the effects of varying short-term air pollution exposures on health outcomes with an abrupt onset, such as asthma attack.[3 4] The timing of the onset of asthma is difficult to measure exactly due to usually a longer induction period needed for the diagnosis. We postulate that the health outcome in the case-crossover study does not necessarily need to be abrupt if the hazard period is sufficiently long for the studied relation. In the present study on the onset of asthma, we used the three winter months, December, January and February, as the hazard period and the three winter months a year before hazard period and after onset of asthma as two bidirectional reference periods.

The study population comprised all the 315 subjects of the Espoo Cohort Study,[5 6] born between 1 January 1984 and 31 March 1990 who developed asthma during the first 27 years of their life.

Health outcome

The outcome of interest was the development of asthma during the study period. The information on doctor-diagnosed asthma and the age of onset, as well as on its potential determinants, was collected at the baseline survey in 1991 and at a 6-year and 20-year follow-up surveys,[5 6] which were conducted at the ages of 0–6, 7–13 and 20–27 years. Questionnaire information on asthma was verified and complemented by a telephone survey and register data from the National Hospital Discharge Register and the Finnish Care Register (HILMO).[5 6]

Exposure assessment

We used 3 month (December–February) average temperature (°C) at the Helsinki-Vantaa weather station to define characteristics of the winters from the winter 1982–1983 to winter 2009–2010 (online supplemental eFigure 1). In this study, we defined winter as cold when the average temperature was lower than the climate normal value (−4.5°C) in the 30 year climate normal period 1981–2010. Temperature data were obtained from the Finnish Meteorological Institute (FMI). Helsinki-Vantaa weather station, located 15 km from Espoo, which is the nearest station from which homogenous long time series of the meteorological parameters are available, can be considered meteorologically representative for the Helsinki Metropolitan Area including Espoo.

Hourly or daily temperatures may differ between the location of the weather station and the other parts of the metropolitan area, but the 3 month averages are similar across this area.

The winters are defined as deviations from statistical normal temperature values, and these do not depend on absolute values.

Statistical analysis

We used OR as the measure of effect of a cold winter on the onset of asthma. We applied conditional logistic regression analysis to estimate the ORs with their corresponding 95% CIs. Sex and age may modify the effect of temperature on the onset of asthma.[7] Therefore, we conducted a priori subgroup analyses by gender and age. Heterogeneity between stratified estimates was assessed using the Breslow-Day test.[8] We compared models and conducted sensitivity analyses (online supplemental eMethod in the Supplement). All statistical analyses were conducted using Stata V.16 (StataCorp).

RESULTS

Characteristics of the study population

Exposure distributions are presented in online supplemental eTable 1. The average winter temperature was −4.5°C (±3.0) during the hazard period and −4.0°C (±2.7) during reference periods. The study population included 150 females (48.6%) and 165 males (52.4%). Most cases (53.7%) developed asthma during the first 6 years (online supplemental eTable 2).

Winter temperature and the onset of asthma

Figure 1 illustrates that the relation between average winter temperature (x-axis) and the risk of asthma (y-axis) during the following calendar year appears linear. In conditional logistic regression, a 1°C decrease in the average winter temperature predicted a 7% increase in the asthma risk (OR=1.07, 95% CI 1.02 to 1.13). The risk of asthma was 41% (OR: 1.41; 95% CI 1.04 to 1.90) higher after exposure to colder than average preceding winter compared with control periods (online supplemental eFigure 2). We conducted a sensitivity analysis with a

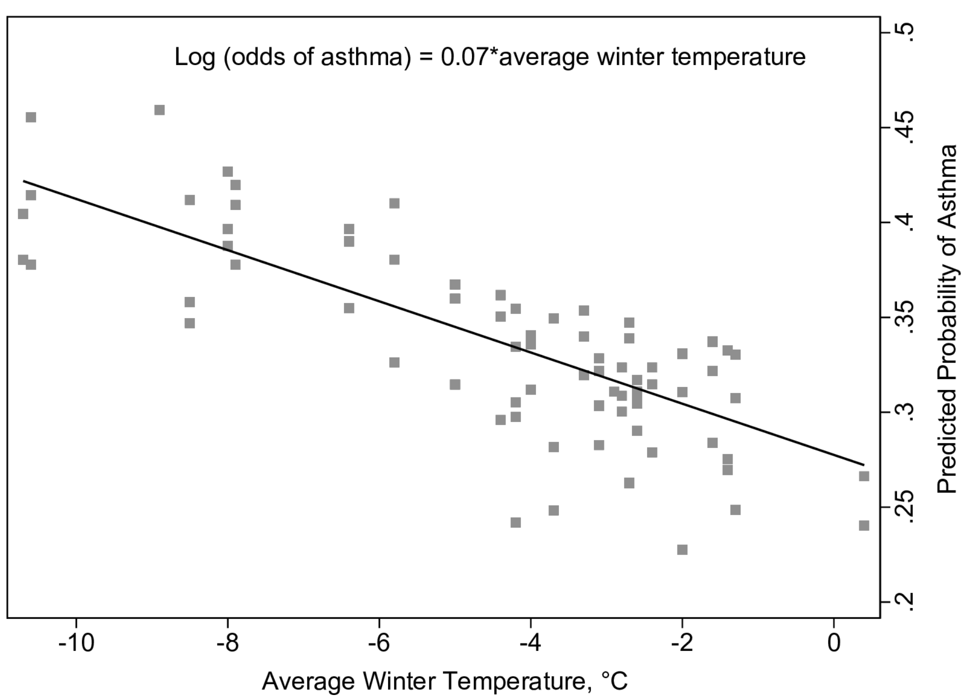


Figure 1 Predicted probability of asthma by average temperature of the previous winter.

hazard period of two winters. The results were robust (online supplemental eFigure 3). We also assessed potential influence of age and sex on the association between cold temperature and asthma onset but based on test of homogeneity of OR across the categories of age (X^2=0.89, df=2, p=0.642) and sex (X^2=0.75, df=1, p=0.388), the effect estimates were homogeneous (online supplemental eTable 3).

DISCUSSION

Our case-crossover study from Espoo, Finland, showed that low average winter temperature (December–February) predicts the onset of asthma during the following 2-year-long period during the first 27 years of life. The relation between average winter temperature and asthma risk was linear: a 1°C decrease in average winter temperature predicted a 7% increase in the odds of asthma in the winter average temperature range of −10.7 to 0.4°C. A cold winter increased the risk of developing asthma by 41% (95% CI 4% to 90%) during the following calendar year. This association was present in males and females in all age groups.

We calculated the average ambient temperature during the 3 winter months based on the FMI's weather monitoring data at the Helsinki-Vantaa weather station that can be considered representative for Espoo. The outcome assessment was based on self-reported doctor-diagnosed asthma. Finland has an affordable public healthcare system complemented by private sector healthcare and a high coverage of occupational health service. The costs are subsidised up to 60% by public funds and these are often all covered by private insurance, resulting in easy access to medical consultation. Furthermore, the National Social Insurance Institute covers all residents of Finland and provides 75% reimbursement of asthma medications for those with asthma fulfilling their diagnostic criteria. This is a strong financial incentive for getting a doctor's diagnosis of asthma. The diagnoses are approved centrally by the National Social Insurance Institution when applying for subsidies, which reduces heterogeneity in diagnostic practices. The diagnoses are based on national guidelines.

We used a bidirectional referent selection strategy that can take into account trends in both exposures and outcomes.[4] Following this strategy, for a hazard period of 3 winter months during the preceding winter in relation to the onset of asthma, and corresponding winter-month periods 1 year before the hazard period and 1 year after the onset of asthma were used as reference periods (n=2). This strategy also limits the possibility of selection bias due to long time interval between the hazard and referent periods and allows us to select the reference (control) periods from the study period where the cases have already occurred.[9]

This is the first study that provides evidence that the risk of developing asthma is related to cold winter conditions during the preceding winter. There is compelling evidence that short-term exposure to low temperatures increases respiratory symptoms, especially among subjects with asthma.[10] Controlled experiments have provided evidence that nasal breathing in cold air causes short-term nasal responses such as rhinorrhoea, congestion and sneezing.[11] Long-term exposure causes damage to the airway epithelium and even changes in the airway wall structure and function.[12] It is biologically plausible that these damages may further lead to the development of airway inflammation and clinical symptoms and signs of asthma. Although long-term exposure to cold weather is a biologically plausible cause of asthma, we cannot exclude the possibility that other environmental exposures related to a cold winter, such as an increase in ambient and indoor air pollution due increased heating using fossil fuels, could contribute to the increased risk of asthma. Thus, the overall effect of cold winters on asthma may constitute both low temperatures and changes in environmental exposures and behaviour.

CONCLUSION

This population-based case-crossover study provides new evidence that a cold winter increases the risk of developing new asthma during the following 1 to 2 years.

Twitter Jouni J K Jaakkola @jouni_jaakkola

Contributors JJKJ had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: JJKJ. Acquisition of data: AKR, MJ, TTH, RR and JJKJ. Analysis and interpretation of data: all authors. Drafting of the manuscript: ABB and JJKJ. Critical revision of the manuscript for important intellectual content: AKR, MJ, TTH, RR and JK. Statistical analysis: ABB, AKR, RR and JJKJ. Obtained funding: JJKJ, MJ and JK. Study supervision: JJKJ.

Funding This study was supported by the Academy of Finland (grant numbers 310371 and 310372 (GLORIA Consortium)), the Yrjö Jahnsson Foundation, and the University of Oulu strategic funds and the Biocenter Oulu grant.

Disclaimer Sponsors did not participate in the design and conduct of the study, in the collection, analysis and interpretation of the data, or in the preparation, review, or approval of the manuscript.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval The study protocol was approved by the Ethics Committee of Oulu University Hospital, Oulu, Finland (EETTMK: 75/2013). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets generated and/or analysed during the current study are not publicly available due to issues of confidentiality, but are available from the corresponding author on reasonable request.

ORCID iDs

Maritta S Jaakkola http://orcid.org/0000-0003-1373-7784
Jouni J K Jaakkola http://orcid.org/0000-0003-4168-4683

REFERENCES

1 Dick S, Doust E, Cowie H, *et al*. Associations between environmental exposures and asthma control and exacerbations in young children: a systematic review. *BMJ Open* 2014;4:e003827.
2 Gehring U, Wijga AH, Koppelman GH, *et al*. Air pollution and the development of asthma from birth until young adulthood. *Eur Respir J* 2020;56:2000147.
3 Jaakkola JJK. Case-crossover design in air pollution epidemiology. *Eur Respir J* 2003;21:81S–85s.
4 Mostofsky E, Coull BA, Mittleman MA. Analysis of observational self-matched data to examine acute triggers of outcome events with abrupt onset. *Epidemiology* 2018;29:804–16.
5 Jaakkola JJK, Hwang BF, Jaakkola N. Home dampness and molds, parental atopy, and asthma in childhood: a six-year population-based cohort study. *Environ Health Perspect* 2005;113:357–61.

6 Rantala AK, Jaakkola MS, Mäkikyrö EMS, *et al*. Early respiratory infections and the development of asthma in the first 27 years of life. *Am J Epidemiol* 2015;182:615–23.
7 Liu X, He Y, Tang C, *et al*. Association between cold spells and childhood asthma in Hefei, an analysis based on different definitions and characteristics. *Environ Res* 2021;195:110738.
8 Breslow NE, Day NE. Statistical methods in cancer research. The analysis of case-control studies, 1. IARC; 1980.
9 Bateson TF, Schwartz J. Selection bias and confounding in case-crossover analyses of environmental time-series data. *Epidemiology* 2001;12:654–61.
10 Hyrkäs H, Ikäheimo TM, Jaakkola JJK, *et al*. Asthma control and cold weather-related respiratory symptoms. *Respir Med* 2016;113:1–7.
11 Koskela HO. Cold air-provoked respiratory symptoms: the mechanisms and management. *Int J Circumpolar Health* 2007;66:91–100.
12 Sue-Chu M. Winter sports athletes: long-term effects of cold air exposure. *Br J Sports Med* 2012;46:397–401.

Supplementary File

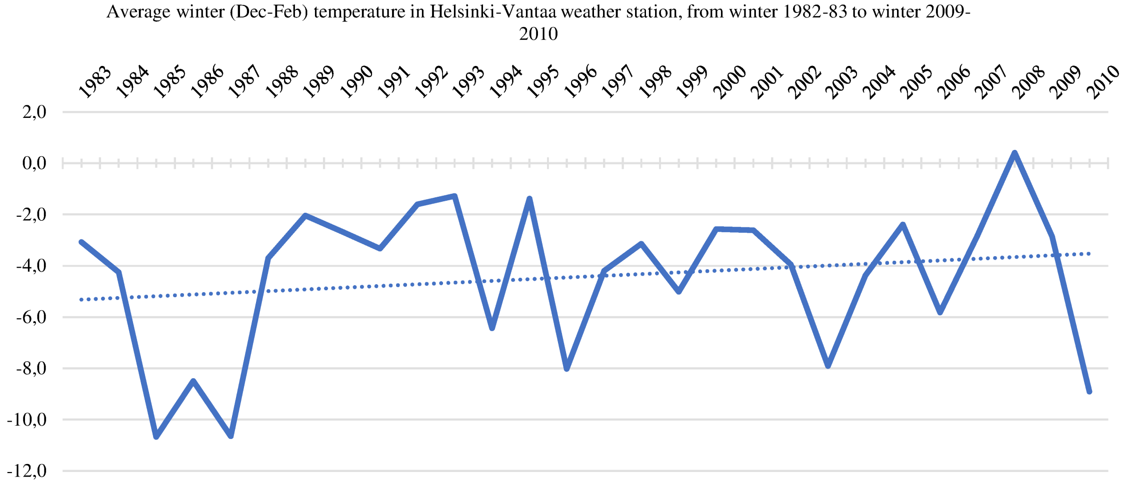
The effect of cold winters on the risk of new asthma: a case-crossover study in Finland

Abate Bekele Belachew, MSc, Aino K. Rantala, MSc, PhD, Maritta S. Jaakkola, MD, PhD, Timo T. Hugg, MSc, PhD, Reija Ruuhela, PhD, Jaakko Kukkonen, PhD, Jouni J.K. Jaakkola, MD, DSc, PhD

eTable 1 Characteristics of the hazard and reference periods, The Espoo Cohort Study 1984-2011

Exposure	**Hazard period (previous winter) (n=315)**	**Bidirectional reference periods (n=630)**
	% (95 % CI)	% (95 % CI)
Average winter temperature (°C)		
≥ -4.5	68.3 (62.9, 73.2)	75.1 (71.5, 78.3)
< -4.5	31.7 (26.8, 37.1)	24.9 (21.7, 28.5)
Quartiles	No. (%)	No. (%)
Q_1 (-5)	88 (27.9)	136 (21.6)
Q_2 (-3.3)	57 (18.1)	118 (18.7)
Q3 (-2)	89 (28.3)	186 (29.5)
Q_4 (-1.3)	81 (25.7)	190 (30.2)
Minimum, Maximum	-10.7, 0.4	-10.7, 0.4
Mean (±SD)	-4.5 (±3.0)	-4.0 (±2.7)

SD: Standard deviation



eFigure 1 Time series of the winter average temperature during the study period from winter 1982-1983 to winter 2009-2010. Winters 1984-1985 and 1986-1987 were unusually cold.

eMethod: Modeling the average winter temperature and the onset of asthma

The relation between the average winter temperature and the onset of asthma was modeled using the conditional logit model according to the following formula:

logit(P(Case=1| Temperature, i stratum))= β_{0i}+ β_1Temperature,

where the left side of the equation is the logit of probability of asthma (i.e., case=1) given preceding winter's average temperature for an ith stratum (subject); β_{0i} is an intercept for ith stratum or subject, β_1 is the slope for a 1°C decrease in the average winter temperature.

The odds of asthma onset was 7% higher (aOR=1.07, 95%CI: 1.02, 1.13, *P*=0.009) for a unit decrease in the average winter temperature. In other words, the colder the winter temperature was, the higher was the risk of asthma. This relationship was found to be homogeneous across the sex and age strata (eTable2). To ensure the validity of our results, we used first various scenarios for the nature of the relationship between the average winter temperature and asthma onset. The relationship between the average winter temperature and the asthma onset appeared to be linear (Figure 1, in the main report). We further modeled the average winter temperature (°C) by using both linear and cubic splines in conditional logistic regression. We compared our ordinary regression model (i.e., a model assuming a linear relationship between log odds of asthma onset and average winter temperature) with linear or cubic spline models using Akaike Information Criteria (AIC). Our ordinary model had the lowest AIC, indicating the best fit for our data (eTable3). Thus, it is reasonable to assume a linear relationship.

In the analyses, we used the average winter temperature of -4.5 degrees Celsius, which corresponds to the 30 years' average temperature in the previous climate normal period (1981-2010) for the area where the Espoo Cohort study cases were residing. The result is presented in eFigure 2. These results show that the odds of asthma is higher after a preceding cold winter in comparison to a warmer winter. Sensitivity analysis was conducted including two preceding cold winters as the hazard period, and the results were found to be robust (eFigure 3).

eTable 2 Increase in the risk of asthma related to 1°C decrease in the average winter temperature by sex and age of asthma onset, The Espoo Cohort Study 1984-2011.

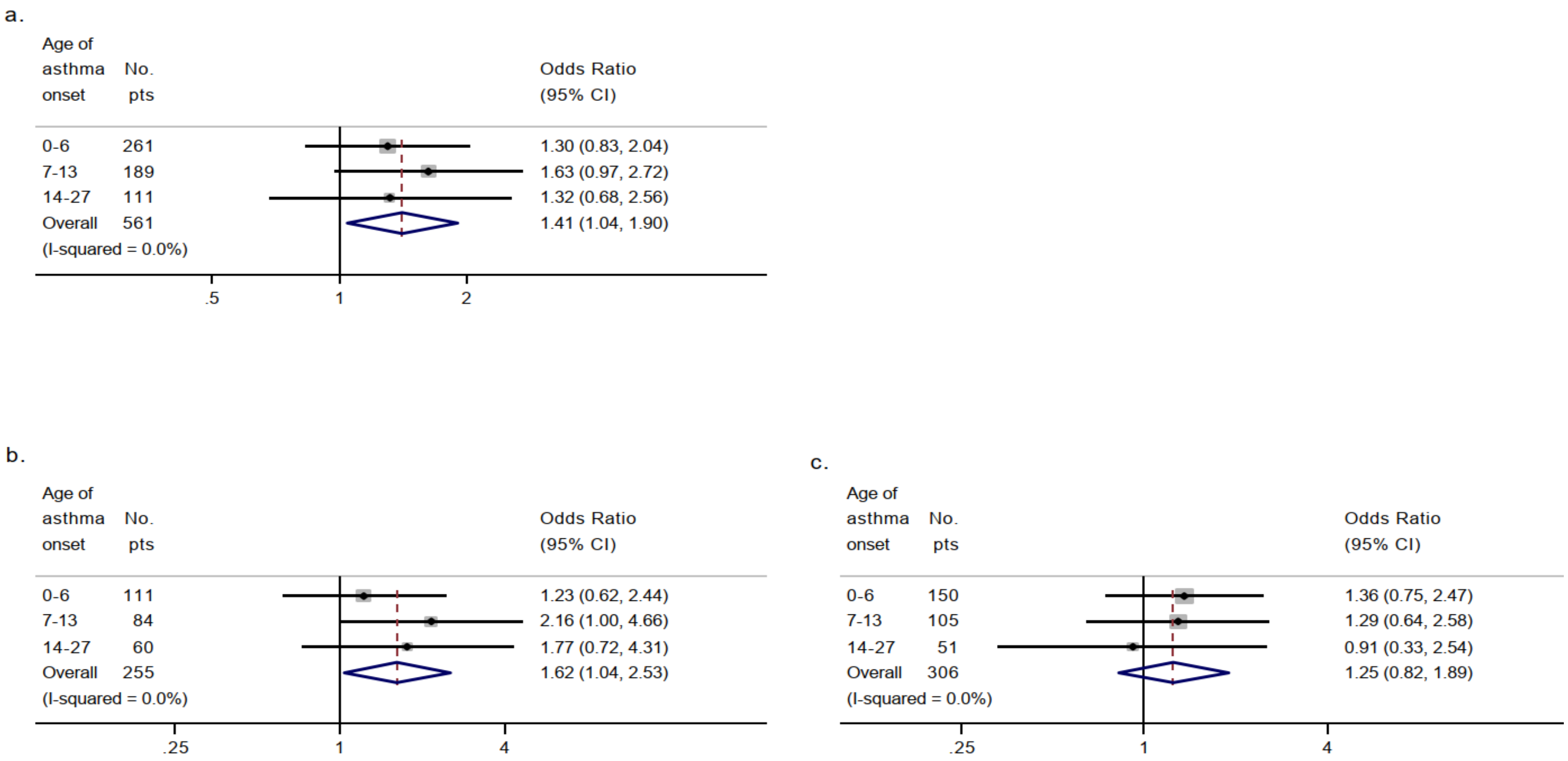
	Age of asthma onset (in yrs)	No. (%)	Increase in the risk of asthma (OR) per 1ºC decrease (95% CI)
All	**0-27**	**315**	**1.07 (1.02, 1.13)**
	0–6	169 (53.7)	1.08 (1.01, 1.15)
	7–13	92 (29.2)	1.09 (0.98, 1.21)
	14–27	54 (17.1)	1.00 (0.86, 1.16)
Women	**0-27**	**150 (47.6)**	**1.07 (0.99, 1.16)**
	0–6	82 (54.7)	1.06 (0.96, 1.18)
	7–13	37 (24.7)	1.15 (0.99, 1.35)
	14–27	31 (16.6)	1.01 (0.84, 1.21)
Men	**0-27**	**165 (52.4)**	**1.07 (0.99, 1.15)**
	0–6	87 (52.7)	1.09 (0.99, 1.18)
	7–13	55 (33.3)	1.04 (0.91, 1.20)
	14–27	23 (13.9)	0.98 (0.75, 1.28)

OR: Odds ratio, CI: Confidence interval

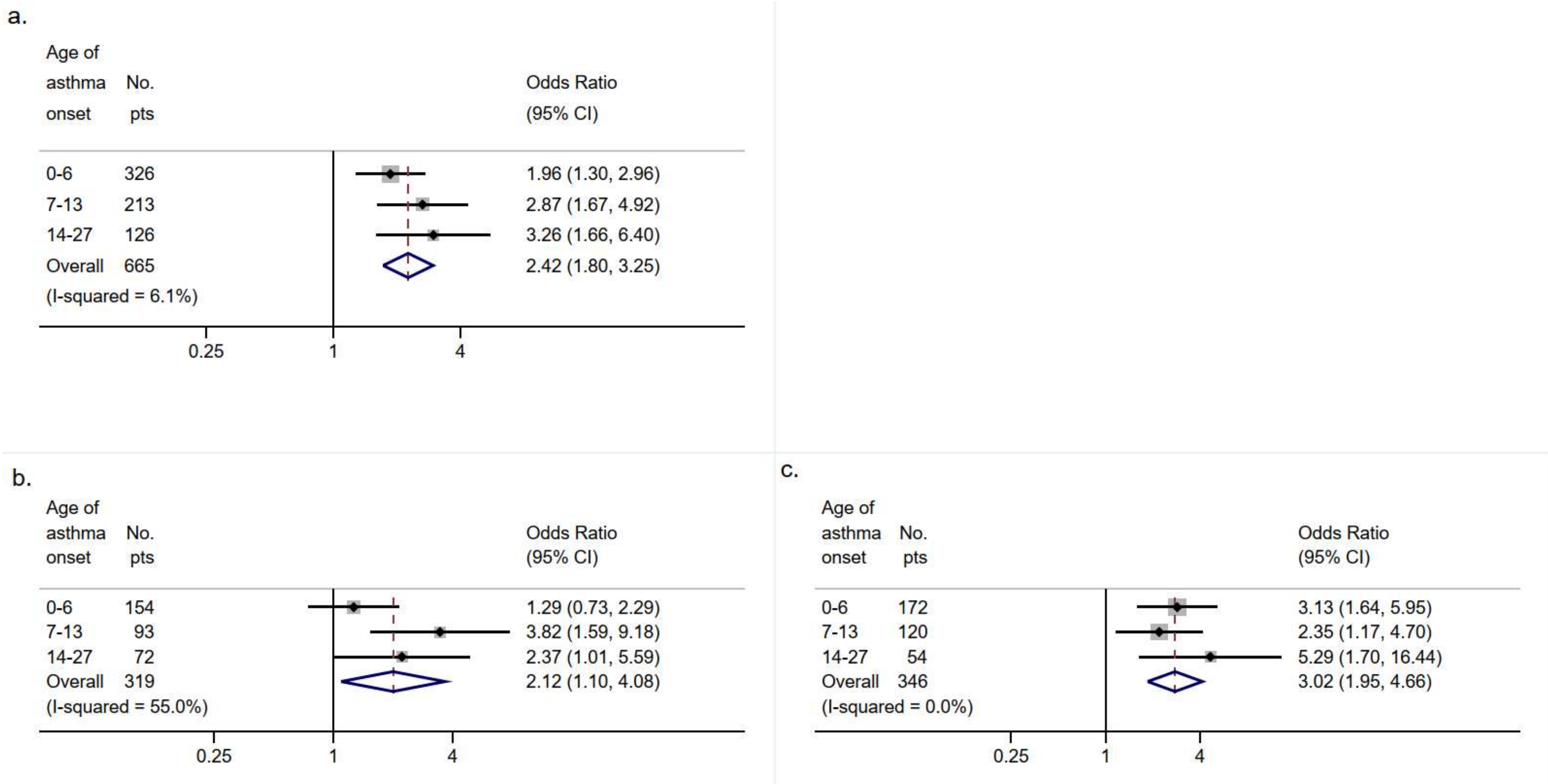
eTable 3 Akaike information criterion (AIC) comparing the fit of various models of average winter temperature (n=945).

Contrast	AIC	Cut points
Model 1[a]	687.2	
Model 2[b]	691.5	-5, -3.3, -2
Model 3[c]	691.2	-10.6, -4, -2.7, -1.3
Model 4[d]	691.6	-10.6, -4.4, -3.3, -2.4, -1.3

[a] linear relationship was assumed
[b] linear spline with knots at quartiles
[c] Cubic spline with 4 knots
[d] Cubic spline with 5 knots



eFigure 2 Age-stratified analysis of the association between exposure to cold temperature (< -4.5 °C coded as 1 else 0) and the onset of asthma. Panel (a) shows an overall association, and panels (b) and (c) show associations for females and males, respectively. Note: age of onset category 21-27 included only a few cases and was merged with the age category 14-20. No. pts – the number of participants with cases (n=315) to controls ratio of 1:2. This gives a total of 945 observations. It should be noted that 128 cases (including 65 girls and 63 boys) making up 384 observations did not contribute to the analysis because they had concordant exposure status during the hazard and control periods. CI – Confidence interval



eFigure 3 Age-stratified analysis of the association between exposure to cold winter (average temperature < -4.5 °C coded as 1 else 0) and the onset of asthma considering two subsequent winters as the hazard period. Panel (a) shows the overall associations, and panels (b) and (c) associations for girls and boys separately, respectively. Note: age of onset category 21-27 included only a few cases and was merged to age category 14-20. No. pts – the number of participants with cases (n=315) to controls ratio of 1:2, giving a total of 945 observations. Altogether 92 cases (276 observations) did not contribute to the analysis, because they had concordant exposure status during the comparison periods. In addition, 4 cases had missing values in the control period.