Supplementary File

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

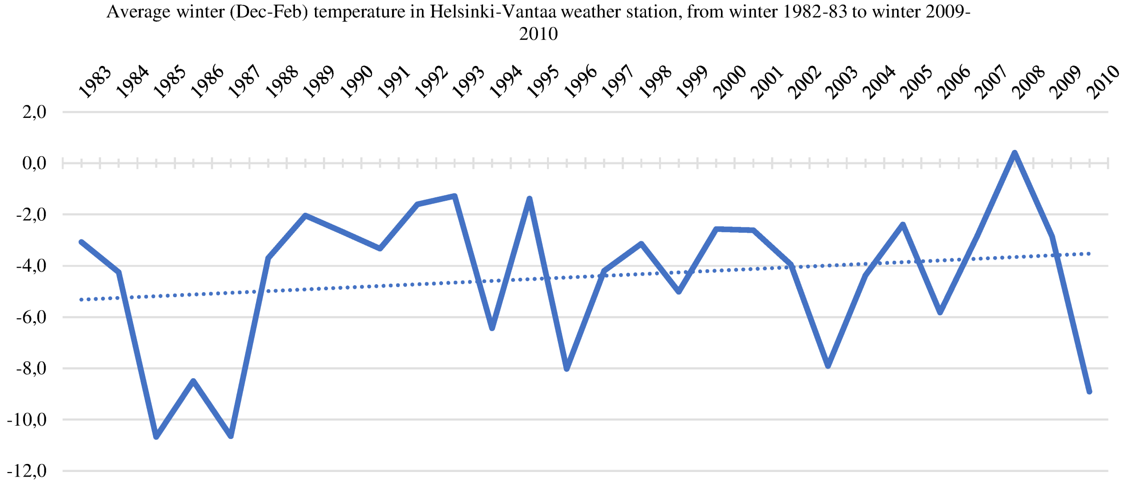
Abate Bekele Belachew, MSc, Aino K. Rantala, MSc, PhD, Maritta S. Jaakkola, MD, PhD, Timo T. Hugg, MSc, PhD, Reija Ruuhela, PhD, Jaakko Kukkonen, PhD, Jouni J.K. Jaakkola, MD, DSc, PhD

Belachew AB, *et al. Occup Environ Med* 2023;0:1–4. doi: 10.1136/oemed-2022-108682

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 i^{th} stratum (subject); β_{0i} is an intercept for i^{th} 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)

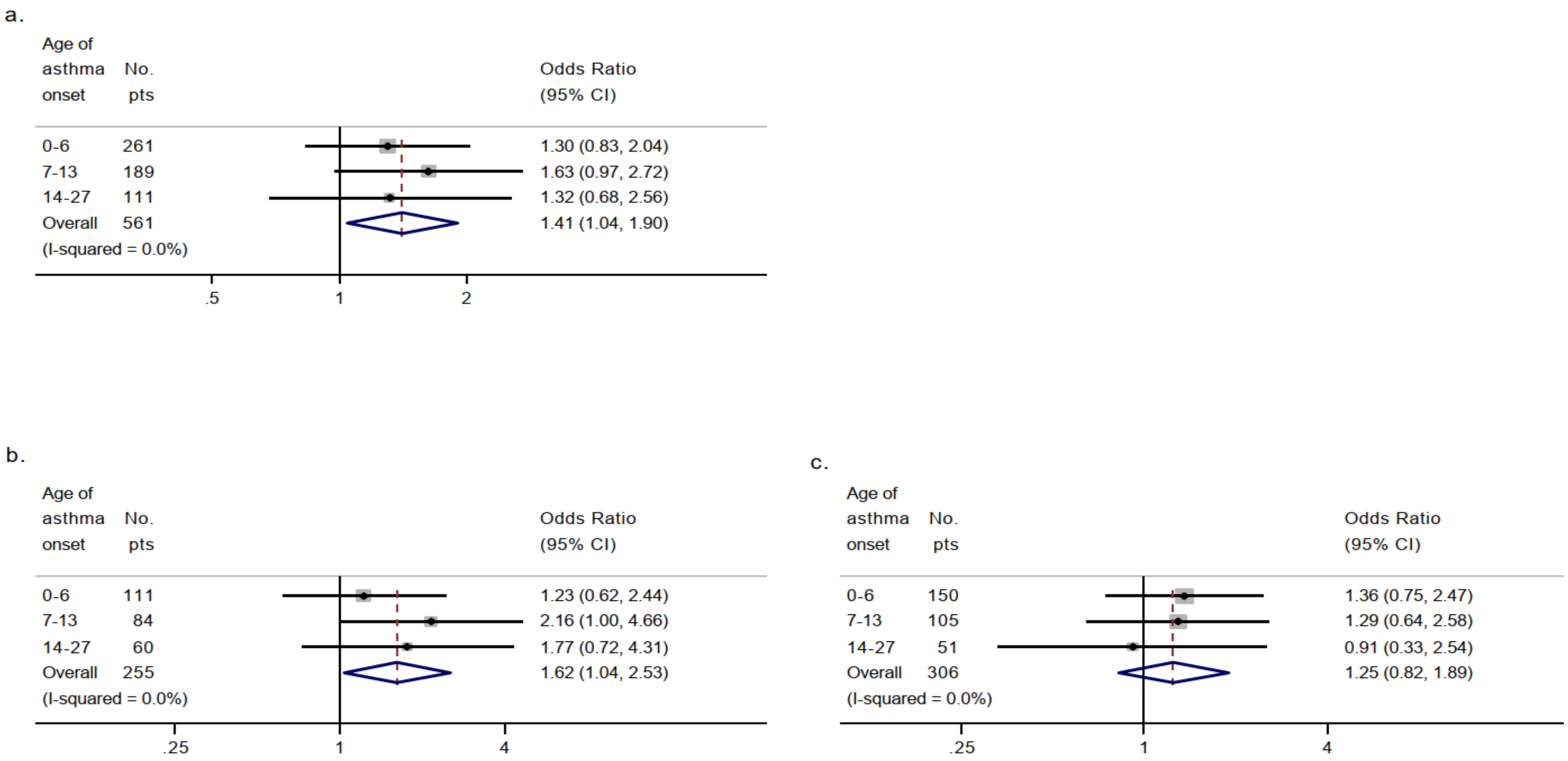
OR: Odds ratio, CI: Confidence interval

Belachew AB, *et al. Occup Environ Med* 2023;0:1–4. doi: 10.1136/oemed-2022-108682

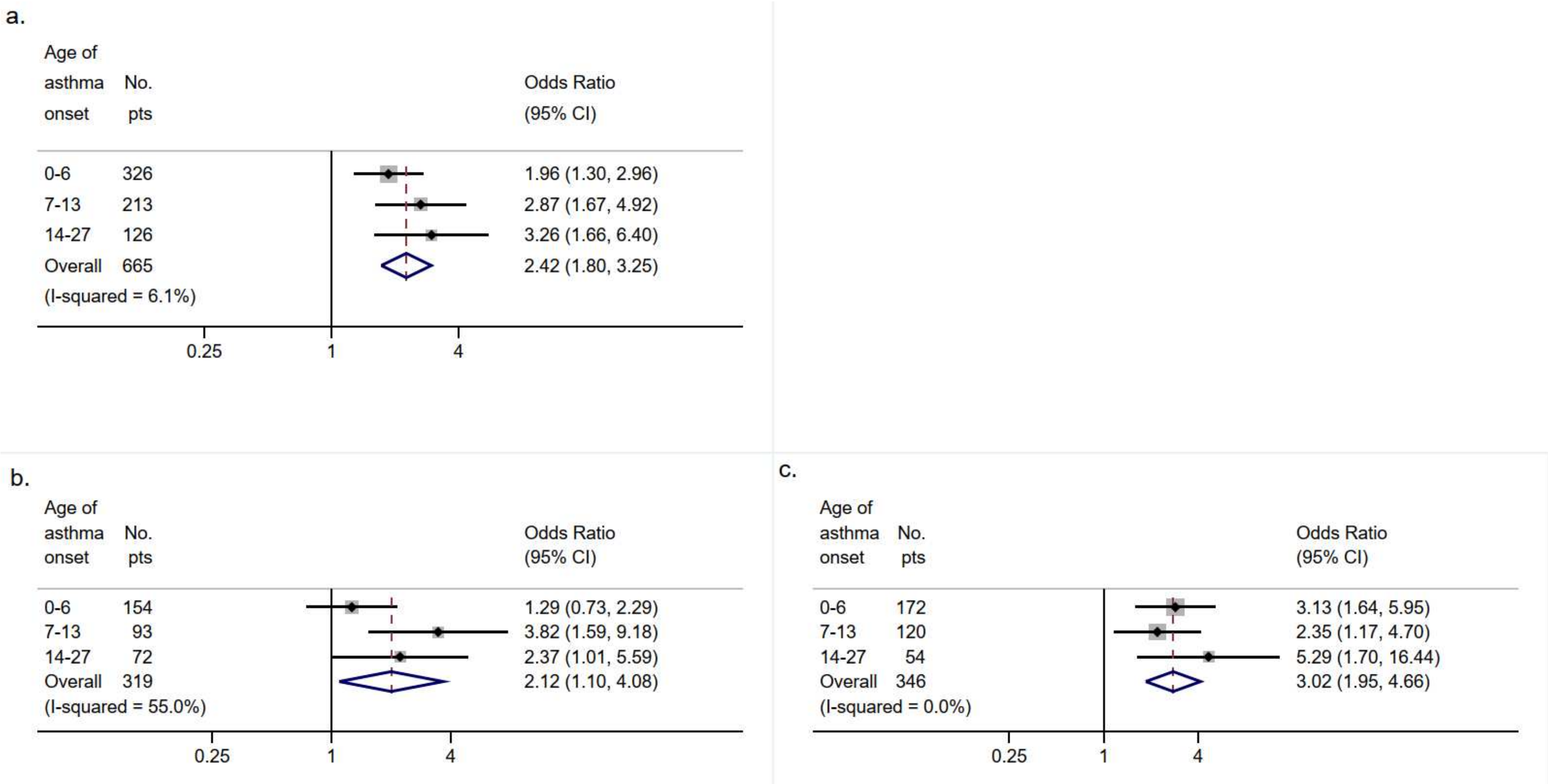
eTable 3 Akaike information criterion (AIC) comparing the fit of various models of average winter temperature (n=945).

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.