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## Season of birth affects the risk of adult-onset asthma in Finland

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## Season of birth affects the risk of adult-onset asthma in Finland

To the Editor,

Previous studies have shown that childhood asthma is associated with season of birth (SOB), namely fall/winter,<sup>1</sup> although the opposite risk has also been detected.<sup>2</sup> There is no previous knowledge of the association between SOB and adult-onset asthma.

We used population-based data from Finnish national registers including 1247 adults over 30 years of age with adult-onset asthma, matched for gender, age, and living region with one or two controls ( $n = 1970$ ) (Figure S1).<sup>3</sup> Information on known risk factors for asthma including parental asthma/allergy, body mass index (BMI), professional training, number of siblings, being the first child, allergic rhinitis (AR), allergic conjunctivitis (AC), and atopic dermatitis (AD) was retrieved from questionnaire and used to form strata (Table S1). The mean (SD, range) age was 54 (12, 31–91) years, with 37% being men (Table S1).

We next evaluated which factors were associated with SOB and detected that of the 16 factors only asthma and severe asthma were associated with those being born between January and June (Table S2). Figure 1 shows the proportion of asthmatics and controls born in different months (Table S3). The proportions remained similar when observing the subgroup with/without at least one allergic disease (AR/AC/AD) (Tables S4 and S5).

In a conditional logistic regression model, those born between January and June were found to be at higher risk for asthma with an overall OR of 1.33 (95% CI 1.11–1.54) (Table S1). Similar association between birth season and asthma was observed when studied by known risk factors of adult-onset asthma (Table 1). The association was consistent in those with and without  $\geq 1$  allergic disease (AR/AC/AD), in those with and without numerous respiratory infections before and/or in school age, in those who spent childhood in farm/countryside but also elsewhere, in those completed primary school (or less) only, and in those with education level exceeding primary school (Table 1). The association was persisted in the 1948–1966 birth cohorts but not in the earlier birth cohorts, in females but not in males, in those with BMI <25 and 25–30, in those having no parental asthma/allergy, having professional training, and  $\geq 2$  siblings or being the first child (Table 1).

Many conditions (such as cardiovascular diseases, diabetes, longevity, academic success/mental health, allergic diseases, birth-weight, pubertal timing, and adult body size) have shown to be associated with SOB.<sup>4,5</sup> We demonstrated here that also adult-onset asthma was positively associated with being born between January and June and was more pronounced in the youngest group, females, being the first child, those with no family history of asthma/

**Abbreviations:** AC, allergic conjunctivitis; AD, atopic dermatitis; AR, allergic rhinitis; BMI, body mass index; CI, confidence interval; FEV1, forced expiratory volume during the first second; OR, odds ratio; PEF, peak expiratory flow; SOB, season of birth.

Anna But and Sanna Toppila-Salmi shared last authorship.

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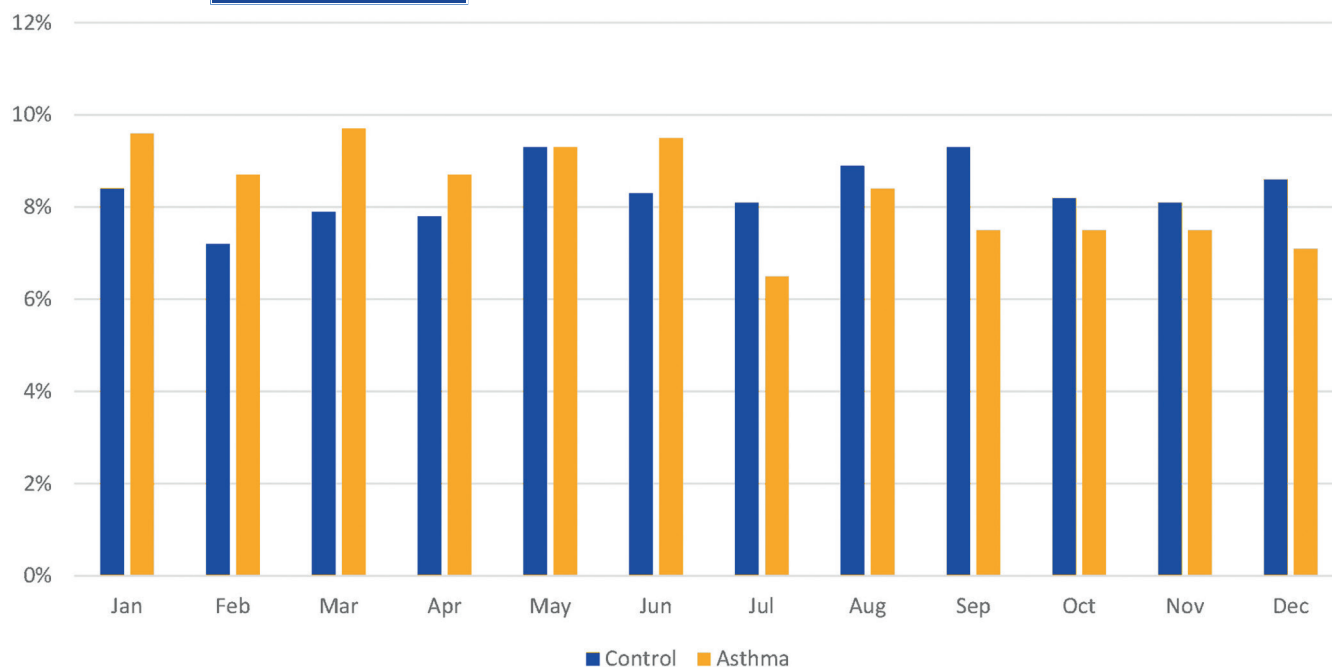


FIGURE 1 Percentage of asthmatics and controls born in different months

TABLE 1 Association of birth season with adult-onset asthma in the population stratified by selected variables

Stratum	Season of birth	Controls, N (%)	Asthmatics, N (%)	OR (95% CI)
<b>Sex</b>				
Female	January–June	620 (49.4)	449 (57.8)	1.40 (1.17–1.68)*
	July–December	636 (50.6)	328 (42.2)	Ref
Male	January–June	342 (47.9)	243 (51.7)	1.16 (0.92–1.47)
	July–December	372 (52.1)	227 (48.3)	Ref
<b>Birth year</b>				
1948–66	January–June	307 (45.5)	249 (57.4)	1.61 (1.23–2.06)*
	July–December	368 (54.5)	185 (42.6)	Ref
1935–47	January–June	351 (49.7)	237 (54.9)	1.23 (0.97–1.56)
	July–December	355 (50.3)	195 (45.1)	Ref
1906–34	January–June	304 (51.6)	206 (54.1)	1.10 (0.85–1.43)
	July–December	285 (48.4)	175 (45.9)	Ref
<b>≥1 allergic disease (AR/AC/AD)<sup>a</sup></b>				
No	January–June	571 (49.8)	233 (56.1)	1.29 (1.03–1.62)*
	July–December	576 (50.2)	182 (43.9)	Ref
Yes	January–June	391 (47.5)	459 (55.2)	1.36 (1.12–1.65)*
	July–December	432 (52.5)	373 (44.8)	Ref
<b>Parental asthma/allergy<sup>b</sup></b>				
No	January–June	785 (48.7)	454 (55.6)	1.32 (1.11–1.56)*
	July–December	826 (51.3)	363 (44.4)	Ref
Yes	January–June	177 (49.3)	238 (55.3)	1.28 (0.96–1.69)
	July–December	182 (50.7)	192 (44.7)	Ref
<b>BMI</b>				
<25	January–June	424 (49.2)	257 (58.5)	1.46 (1.15–1.84)*
	July–December	437 (50.8)	182 (41.5)	Ref

TABLE 1 (Continued)

Stratum	Season of birth	Controls, N (%)	Asthmatics, N (%)	OR (95% CI)
25-30	January-June	363 (48.1)	278 (54.3)	1.28 (1.02-1.61)*
	July-December	392 (51.9)	234 (45.7)	Ref
>30	January-June	137 (46.6)	142 (53.4)	1.31 (0.94-1.83)
	July-December	157 (53.4)	124 (46.6)	Ref
Numerous respiratory infections before and/or in school age				
No	January-June	868 (49.3)	546 (55.3)	1.27 (1.09-1.49)*
	July-December	893 (50.7)	441 (44.7)	Ref
Yes	January-June	94 (45.0)	146 (56.2)	1.57 (1.09-2.26)*
	July-December	115 (55.0)	114 (43.8)	Ref
Childhood in country/farm				
No	January-June	227 (45.2)	180 (58.4)	1.70 (1.28-2.27)*
	July-December	275 (54.8)	128 (41.6)	Ref
Yes	January-June	735 (50.1)	512 (54.5)	1.20 (1.02-1.41)*
	July-December	733 (49.9)	427 (45.5)	Ref
≥2 Siblings				
No	January-June	230 (50.2)	157 (56.9)	1.31(0.97-1.77)
	July-December	228 (49.8)	119 (43.1)	Ref
Yes	January-June	719 (48.3)	527 (55.1)	1.31(1.12-1.55)*
	July-December	771 (51.7)	429 (44.9)	Ref
Birth order = first child				
No	January-June	715 (50.2)	486 (54.2)	1.17(0.99-1.39)
	July-December	708 (49.8)	410 (45.8)	Ref
Yes	January-June	247 (45.2)	206 (58.7)	1.73(1.32-2.26)*
	July-December	300 (54.8)	145 (41.3)	Ref
Primary school or less				
No	January-June	420 (48.5)	271 (56.7)	1.39(1.11-1.74)*
	July-December	446 (51.5)	207 (43.3)	Ref
Yes	January-June	542 (49.1)	420 (54.7)	1.25(1.04-1.51)*
	July-December	562 (50.9)	348 (45.3)	Ref
Lack of professional training				
No	January-June	731 (48.5)	520 (55.3)	1.32(1.12-1.55)*
	July-December	777 51.5)	420 (44.7)	Ref
Yes	January-June	231 (50.0)	172 (56.0)	1.27(0.95-1.70)
	July-December	231 (50.0)	135 (44.0)	Ref

Abbreviations: BMI, body mass index; N, number of cases; OR, odds ratio was calculated using binary logistic regression.

<sup>a</sup>Self-reported allergic disease ever.

<sup>b</sup>Missing value = The subject responded that he/she does not have either of the asked relatives (mother or father).

allergy, no obesity, having several siblings, and professional training. We have previously demonstrated in this cohort that adult-onset asthma was positively associated with the number of allergic comorbidities and that the association was more pronounced in the later birth cohorts and females.<sup>6</sup> Hence, it could be possible that the effect of SOB on increasing asthma risk might be stronger in the subgroup having atopic asthma. The potential connection between birth season and development of chronic inflammatory disease might be related to weight, sun exposure, vitamin D metabolism, and infection risk, although this connection still needs to be proven. This connection was more pronounced in the youngest adult group,

which could in part be related to changes in recommendations concerning sun exposure and vitamin D substitution over time.

Overall, our study was able to demonstrate new evidence of an association between SOB and the adult-onset asthma. Although the lack of data of childbirth and early life events and a possible memory bias might mitigate the findings, our results strengthen the previous findings that early life events have a role in adult-onset asthma<sup>7</sup> and highlight the need to focus also on early life factors in the prevention of asthma burden. Replication in other populations in other countries is, however, necessary, particularly studies related to vitamin D metabolism and its risk effect on adult-onset asthma.

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## KEY WORDS

asthma, adult-onset asthma, epidemiology, season of birth

## CONFLICT OF INTEREST

ST-S report consultancies for ALK-Abelló, AstraZeneca, ERT, GSK, Novartis, Sanofi and Roche Products outside the submitted work, as well as grant of GSK outside the current work. JK reports personal fees for consultancies or lectures from AstraZeneca, Boehringer-Ingelheim, Chiesi Pharma, GSK, MSD, Novartis, Orion Pharma, and SanofiGenzyme outside the current work. HK reports personal fees for consultancies or lectures from AstraZeneca, Boehringer-Ingelheim, Chiesi Pharma, GSK, MSD, Novartis, Orion Pharma, and SanofiGenzyme outside the current work. PI is an employee of GSK. All other authors report no conflicts of interest.

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