

Temporal changes in UK birth order and the prevalence of atopy

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Abstract

Background: Many studies have reported an inverse association between birth order and the risk of respiratory allergic disease. In recent decades, the prevalence of atopy has increased alongside reductions in fertility rates.

Aims of the study: To quantitate how much of the increased prevalence of atopy, measured by skin prick test or specific IgE, can be attributed to temporal changes in family size in the United Kingdom.

Methods: Through a systematic literature review (MEDLINE, 1965–2009), five studies of UK populations were identified and their data were included in the calculation of a summary odds ratio for the risk of atopy for each birth order. Information on changes in UK family sizes between 1960 and 2001 was obtained from Eurostat. On this basis, expected increases in the prevalence of atopy were calculated by weighting the proportion in each birth order category for 1960 and 2001 by the summary odds ratio for that category and then calculating the relative risk of atopy in 2001 compared with 1960.

Results: The pooled summary odds ratios for atopy were 0.90, 0.69 and 0.69 for those born second, third and fourth (or higher), respectively. The expected relative increase in the prevalence of atopy resulting from a change in family size between 1960 and 2001 was 3%.

Conclusions: Despite the strong associations between birth order and atopy, reductions in family size in the last 40 years account for little of the increase in atopy.

Over the last half century, the prevalence of allergic disease in most European countries has increased. Many studies have reported an increased risk of respiratory allergies in first born children, an observation with respect to hay fever that gave rise to one of the earliest descriptions of the 'hygiene hypothesis' (1). Over the same time period, the total fertility rate in these countries has fallen; for example, in the UK between 1961 and 2001 fertility rates fell from 2.77 children per woman to 1.63 children (2).

The associations between temporal changes in family size and the prevalence of asthma and hay fever were examined by Wickens et al. (3) who, in 1991, calculated the expected relative increase in the prevalence of asthma resulting from changes in family size over the previous 30 years to be just 1% in England and Wales and 5% in New Zealand. The figure for hay fever (in England) was 4%.

As the relationship between birth order and asthma may be weaker than that between birth order and atopy, we aimed to quantitate how much of the increased prevalence of

atopy in the UK, measured by skin prick test (SPT) response or specific IgE, can be attributed to temporal changes in family size.

Methods

Suitable manuscripts were identified through MEDLINE, searching for the terms 'atopy', 'skin test', 'family size' and 'birth order'. Only papers describing UK populations and using 'objective' measures of atopy (SPT or serum specific IgE) were included. Of 18 identified papers, five (28%) met these criteria. A summary odds ratio for the risk of atopy per birth order category was calculated by combining the data from these studies and weighting them by the inverse variance of the estimates in each study, using the 'metan' command in Stata (College Station, TX, USA). Information on changes in family size in the UK between 1960 and 2001 was obtained from Eurostat (4). Expected increases in the prevalence of atopy on this basis were calculated by weighting the

Table 1 Characteristics of the studies

References	Year	Study design	Area	Age range	N	Allergens tested	Positive test (mm*/ku/l**)	Prevalence of atopy (%)
Jarvis et al. (5)	1997	Cross-Sectional	East Anglia	20–44	907	HDM, cat, grass, birch, Cladosporium	>0.35 ku/l	39.1
Strachan et al. (6)	1997	Birth Cohort	Britain	34–35	2615	HDM, cat, mixed grass pollen	≥3 mm	33.0
Bodner et al. (9)	2000	Case-control	Scotland	39–45	319	HDM, cat, grass pollen	≥3 mm or >0.35 ku/l	54.4
Cullinan et al. (7)	2003	Cohort	Kent	19–63	1050	HDM, cat, grass pollen	≥3 mm	37.0
Harris et al. (8)	2007	Birth Cohort	Kent	8	546	HDM, cat grass pollen	≥2 mm	19.0

HDM, house dust mite.

*Skin prick test mean wheal diameter.

**Specific IgE.

proportion of children in each birth order category for 1960 and for 2001 by the summary odds ratio for that category and then calculating the relative risk for being atopic in 2001 compared with 1960 as a function of birth order.

Results

The five studies included in the analysis are summarized in Table 1. All defined atopy by skin prick or serum responses to extracts of at least house dust mite, grass and cat. One study measured both specific and total IgE and SPT, with atopy defined as a positive result to any of these measurements. These studies included three cohorts, a cross-sectional study and a case control study. All but one study were of adults.

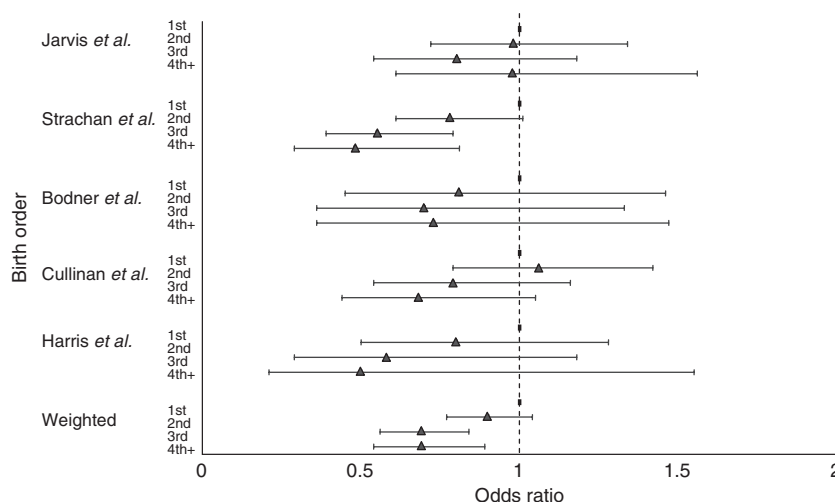
In a cross-sectional survey of adults, Jarvis et al. (5) reported an atopic prevalence of 39.1% finding no association with birth order, although describing a trend toward reduced risk in those with a higher number of siblings. Strachan et al. (6), Cullinan et al. (7) and Harris et al. (8) all reported a trend of decreasing atopy by birth order. Bodner

et al. (9) reported the highest prevalence of atopy (54.4% overall) with a decreasing trend in terms of birth order.

Pooling the five studies provided summary odds ratios for atopy of 0.90 (0.77, 1.04), 0.69 (0.56, 0.84) and 0.69 (0.54, 0.89) for those born second, third and fourth respectively, indicating a trend toward reduced risk of atopy for those who are not first born (Fig. 1).

Between 1960 and 2001, there was a decrease in the mean number of children per family in the UK. In 1960, the percentages of children who were born first, second, third and fourth (or more) were 36.4%, 30.4%, 16.5% and 16.7%, respectively. In 2001, these figures had changed to 40.0%, 37.2%, 14.8% and 8%, respectively.

Weighting these figures by the summary odds ratios above generated an expected relative increase in the prevalence of atopy resulting from smaller family sizes (between 1960 and 2001) of 3%. Analysis by comparison of first and second born children with third and fourth or more, produced similar results. Repeating the analysis with only the results of the three cohort studies resulted in slightly stronger associations between birth order and atopy (OR 0.88, 0.65 and 0.59

**Figure 1** Study-specific odds ratios and weighted summary odds ratios for atopy by order of birth.

respectively) and generated an expected relative increase in the prevalence of atopy (between 1960 and 2001) of 4%.

Discussion

By combining results from a number of studies and obtaining pooled estimates of risk, we confirmed the strong evidence of an association between atopy and birth order. By applying this to national data, we estimated that changes in family size over the past 40 years could account for an increase of 3% in the prevalence of atopy over the same period.

Few studies (10–12) have made objective measures of the temporal increases in atopy. Perhaps, the most relevant in this respect is that of Linneberg et al. (10) who studied persons aged 15–41 in Denmark between 1990 and 1998 using specific IgE to a panel of common aeroallergens. They reported an increase in the prevalence of atopy from 26.5% to 33.9%, a relative increase of 28%. If this figure can be extrapolated to the UK then it would seem that recent reductions in family size account for little of any reported increase in atopy; a conclusion similar to that reached for asthma and hayfever by Wickens et al. (3) over a period of 30 years. Data from UK populations are limited to a single study (11) of businessmen aged between 40 and 64 examined from 1975 to 1998; they suggest a relative increase of 40% in the prevalence of atopy across this period, again indicative that changes in family size have been relatively unimportant.

lence of atopy across this period, again indicative that changes in family size have been relatively unimportant.

We have explored the effects of making several adjustments to our modeling. First, we examined the effect of a greater shift in family structure; for example Italy in 1997 had a much higher proportion of first born children than the UK (4) despite very similar figures in 1960. Repeating our analysis with the birth order rates recorded for Italy in 1997 (50.3%, 36.5%, 9.7%, 2.9% for first, second, third, and fourth or higher respectively) generated only a marginally higher relative increase of about 6%. Second, we tested the effect of a stronger association between atopy and birth order (OR 0.6, 0.4, and 0.2 for second, third and fourth born or more respectively); this too generated a relative increase of only 8%. Finally, as described, we used only cohort-based studies because cross-sectional samples taken during periods when family sizes are decreasing tend, in larger families, to over-represent later born subjects and, in smaller families, to over represent those of low birth order (13). This too made little difference to our final estimate.

In the UK – and in many similar countries – the prevalence of first born children has increased markedly in recent decades. Our findings suggest, however, that this demographic shift explains only up to 3% in the increase of atopy observed over the same period.

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