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BRIEF COMMUNICATION

Parental allergic disease before and after child birth poses similar risk for childhood allergies

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Abstract

Whether the strength of associations between parental and child allergic diseases differs by whether the first onset of the parental disease is before or after a child's birth has never been examined and is the aim of this study. Yearly childhood asthma, allergic rhinitis, and eczema diagnoses were longitudinally regressed against the effect of a parental disease (pre- *vs* post-child birth) of the same type separately for each parent using generalized estimation equations. Both a maternal and paternal history of asthma were associated with childhood asthma prevalence up to 15 years of age. Effect estimates were similar for parental asthma with first onset before and after the birth of the child. The results for allergic rhinitis and eczema were less consistent. Parental allergic diseases with first onsets before and after the birth of a child both pose risks to childhood allergic disease in the offspring, especially for asthma.

A positive family history of allergic disease in a first-degree relative is a well-established risk factor for childhood allergic diseases. In birth cohort studies, information on family history is nearly always collected at the time of recruitment to reduce biased reporting. However, this strategy does not permit the identification of parental allergic diseases that develop after the birth of the child. To date, no study has reported on the extent to which this underreporting of family history occurs, and how the strength of associations between parental and child allergic diseases may be affected. The aim of this study was to address these two research gaps.

The recently completed 15-year follow-ups of the German GINIplus and LISAplus birth cohort studies offer the opportunity to address these questions (1–3). From the data collected using repeatedly administered parent-completed questionnaires, yearly doctor diagnoses of childhood asthma (3–15 years), allergic rhinitis (3–15 years), and eczema (birth-15 years) were calculated. Maternal and paternal asthma, allergic rhinitis, and eczema (self-reported ever disease occurrence) were also determined using the data collected for the biological parents at the time of birth of the child and when the child was 15 years old. At this later follow-up, the age of onset of each parental allergic condition (first occurrence of self-reported disease) was also available and used to determine whether the first onset of parental disease was before or after the birth of the child. If parental health information was given at one time point but missing at the other, the missing data were coded as being a report of no disease. Further details of the study design and outcome definitions are provided in Table S1. Local ethics committees approved both studies and written consent was obtained from parents of participants.

All analyses were conducted using the program R, version 3.1.1.: Vienna, Austria. For each childhood clinical manifestation (asthma, allergic rhinitis, and eczema), the effect of a parental disease of the same type was longitudi-

nally analyzed separately for the mother and father using generalized estimation equations with a logit link and autocorrelation structure of order 1 (geeglm function from the geepack package). Models were adjusted for child sex and age, older siblings, parental education (based on the highest number of years of education of either parent: low <10 years, medium = 10 years, high >10 years), maternal smoking during pregnancy, secondhand smoke exposure in the home (between birth and 4 years), cohort (GINIplus observation group, GINIplus intervention group, and LISAplus), and region (Munich, Wesel, Leipzig, and Bad Honnef).

In total, 7641 children (84.1% of the original cohorts) had information on at least one health outcome at one time point and the health status of their biological mother or father could be determined (population characteristics provided in Table 1). The childhood prevalence of asthma and allergic rhinitis increased with age and that for eczema decreased (Fig. S1). Maternal allergic conditions were slightly more prevalent than paternal ones, and allergic diseases with first onset before the birth of the child were much more prevalent than those with first onset after the birth of the child (Table S2). Of the 4430 children ultimately identified as having a positive parental history of allergic disease, 275 (6.6%) would not have been captured using only parental history data collected at baseline.

Both a maternal and paternal history of asthma were associated with childhood asthma prevalence up to 15 years of age (Fig. 1). Effect estimates for asthma were similar when associations were stratified by whether the first onset of parental asthma was before or after the birth of the child. The post-birth results were less consistent for allergic rhinitis and eczema as only the association between childhood eczema and maternal eczema post-birth was significant. Associations for asthma remained similar when stratified by the sex of the child. Effect estimates for post-birth paternal allergic rhinitis and eczema were elevated only among males. Only the interaction term between post-birth paternal allergic rhinitis and the sex of the child was significant (P-value = 0.02).

We are the first study to report that parental allergic diseases with first onsets before and after the birth of a child both increase the risk of childhood allergic diseases, especially for asthma. Furthermore, our study suggests that a reasonable proportion of participants (6.6% in the current study) in longitudinal studies are misclassified with respect to their family history of allergic disease when this history is only assessed at baseline. Although we acknowledge that this is likely true for all potentially time-varying covariates, a positive family history is one of the strongest risk factors for childhood allergic diseases. We recommend that family history be repeatedly assessed in longitudinal studies. Our results are also important for public health policy as they suggest that a proportion of high-risk children are missed at birth and may not receive counseling regarding potential preventive measures (4).

Associations with asthma did not consistently differ by the sex of the parent or child. Our results thus highlight the importance of considering both maternal and paternal allergic diseases as risk factors and argue against the existence of parent-of-origin effects or differences in associations based on the sex of the child. The literature on these topics is currently conflicting (e.g., 5–9).

The strengths of this study are the longitudinal outcome data from birth to 15 years and the information on several host and (early life) environmental factors, which may confound genetic associations. However, as with all longitudinal cohort studies, selection bias is likely present. Participants in this study differed from the original cohorts in several respects, including that they were more likely to have a parental history of allergic disease, which may have influenced the risk estimates. However, further adjustments for

Table 1 Characteristics of study participants

Characteristics	*n*/*N*	%
Males	3941/7641	51.6
Older siblings	3482/7623	45.7
Parental education		
<10 years	644/7602	8.5
=10 years	2223/7602	29.2
>10 years	4735/7602	62.3
Smoking		
During pregnancy	1160/7416	15.6
Ever in home (1–4 years)	2930/6713	43.6
Ever in home (6–15 years)	1878/4827	38.9
Ever owned a pet	3626/5544	65.4
Gas used in home during first year of life	537/7422	7.2
Mold/dampness in home during first year of life	1777/7411	24.0
Cohort		
GINIplus observation group	2811/7641	36.8
GINIplus intervention group	2038/7641	26.7
LISAplus	2792/7641	36.5
City		
Munich	3686/7641	48.2
Wesel	2829/7641	37.0
Leipzig	845/7641	11.1
Bad Honnef	281/7641	3.7
Maternal asthma		
Before birth of participant	664/7609	8.7
After birth of participant	139/7609	1.8
Paternal asthma		
Before birth of participant	567/7501	7.6
After birth of participant	83/7501	1.1
Maternal allergic rhinitis		
Before birth of participant	2321/7590	30.6
After birth of participant	271/7590	3.6
Paternal allergic rhinitis		
Before birth of participant	2065/7427	27.8
After birth of participant	143/7427	1.9
Maternal eczema		
Before birth of participant	932/7610	12.2
After birth of participant	73/7610	1.0
Paternal eczema		
Before birth of the participant	507/7466	6.8
After birth of the participant	38/7466	0.5

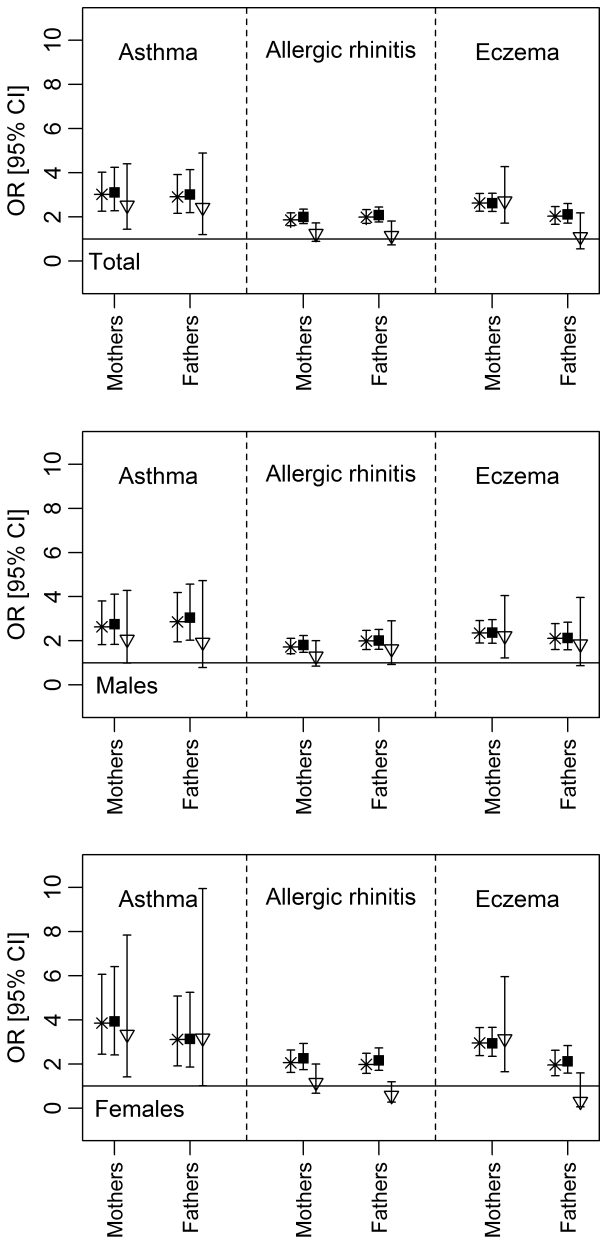

Figure 1 Adjusted disease-specific longitudinal associations between maternal and paternal allergic diseases (ever [stars], with first onset before [filled squares], and after [empty triangles] the birth of the child) and childhood allergic disease prevalences up to 15 years. Odds ratios and 95% confidence intervals are presented for the total population (top), and for male (middle) and female (bottom) participants.

secondhand smoke exposure between six and 15 years, mold exposure during the first year of life, use of gas stove during the first year of life and pet ownership (birth to 15 years) did not largely alter the main results (not shown). The long-time span (15 years) between the collection of the two sets of parental health data also required a careful examination of potential data inconsistencies/uncertainties. Associations remained stable when parents with inconsistent results (e.g., report of ever asthma at baseline but not at 15-year follow-up) and subsequently with missing data at either time point were excluded (Table S3). Furthermore, parental health data were only available for the age of onset of self-reported disease for all three parental health outcomes, and not when or whether these diseases were confirmed by a physician. The results with parental eczema need also be interpreted with caution as, in contrast to early-life eczema which is commonly associated with atopy, later-life (adult) eczema is often related to occupational exposures.

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Author contributions

EF designed and carried out the analyses, interpreted the data, drafted the initial manuscript, revised the manuscript, and approved the final manuscript as submitted. MS and JH also contributed to the design of the analysis. MS, AvB, IL, BH, C-PB, SK, DB, and JH contributed to the data collection, interpreted the data, reviewed and revised the manuscript, and approved the final manuscript as submitted. All authors agree to be accountable for this work.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Period prevalence of childhood doctor diagnosed asthma, allergic rhinitis and eczema.

Table S1. Cohort characteristics and outcome definitions.

Table S2. Maternal and paternal allergic disease prevalences.

Table S3. Disease-specific adjusted associations between a parental history of asthma, allergic rhinitis and eczema, respectively, and the corresponding childhood health outcome.

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