

## Letter to the Editor

**Breast-feeding and risk of asthma, hay fever, and eczema***To the Editor:*

The World Health Organization recommends breast-feeding for at least 6 months after delivery because of general health benefits for the child.<sup>1</sup> However, studies on breast-feeding have yielded inconsistent results regarding its association with the risks for developing asthma, hay fever, and eczema.<sup>2-4</sup> A large homogeneous population-based cohort, such as the one used in this study (UK Biobank; N = 502,682), provides statistical power to fill in unaddressed gaps in the knowledge on the effects of breast-feeding on the risks of developing asthma, hay fever, and eczema. A total of 336,364 Caucasian participants, born between 1937 and 1969, with self-reported information about being breast-fed or not were included in this study. Information on length and exclusivity of breast-feeding was not available. Baseline characteristics and prevalences are presented in [Table E1](#) in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org).

In the main analysis we included all 336,364 participants. We compared the odds of self-reported asthma, hay fever, and eczema diagnosis separately and hay fever/eczema combined, depending on breast-feeding using logistic regression. When not adjusting for possible confounders, a decreased risk of asthma (odds ratio [OR] = 0.88;  $P < 2.10 \times 10^{-16}$ ; [Fig 1, A](#)) and hay fever/eczema (OR = 0.94;  $P = 1.89 \times 10^{-10}$ ; [Fig 1, B](#)) was found for the breast-fed population. We then reanalyzed all disease phenotypes and included covariates that we identified to be associated with these phenotypes (see [Table E2](#) in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)). To evaluate the effect of the covariates, each covariate was first included in the model separately (see [Table E3](#) in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)). By including year of birth in the model we can see that breast-feeding changes from having a protective effect on hay fever and/or eczema, to increasing the risk for disease. This suggests that year of birth operates as a strong qualitative confounder in the unadjusted analyses, that is, change the effect in the opposite direction. This suggests that the opposite directions of the secular trends of breast-feeding and hay fever/eczema represent an ecologic fallacy (see [Fig E1](#) in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)), which might be resolved by adjustment for year of birth. Therefore, not adjusting for year of birth will give a negative association (as seen in the univariate analysis). The full model, adjusting for all covariates, showed that the effect of breast-feeding on the odds of being diagnosed with asthma was no longer significant (OR = 0.99;  $P = .96$ ; [Fig 1, A](#)), while associated with higher odds for hay fever/eczema (OR = 1.06;  $P = 7.80 \times 10^{-6}$ ) ([Fig 1, B](#)). Breast-feeding also increased the odds for eczema and hay fever diagnosed separately (see [Fig E2, A and B](#), in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)).

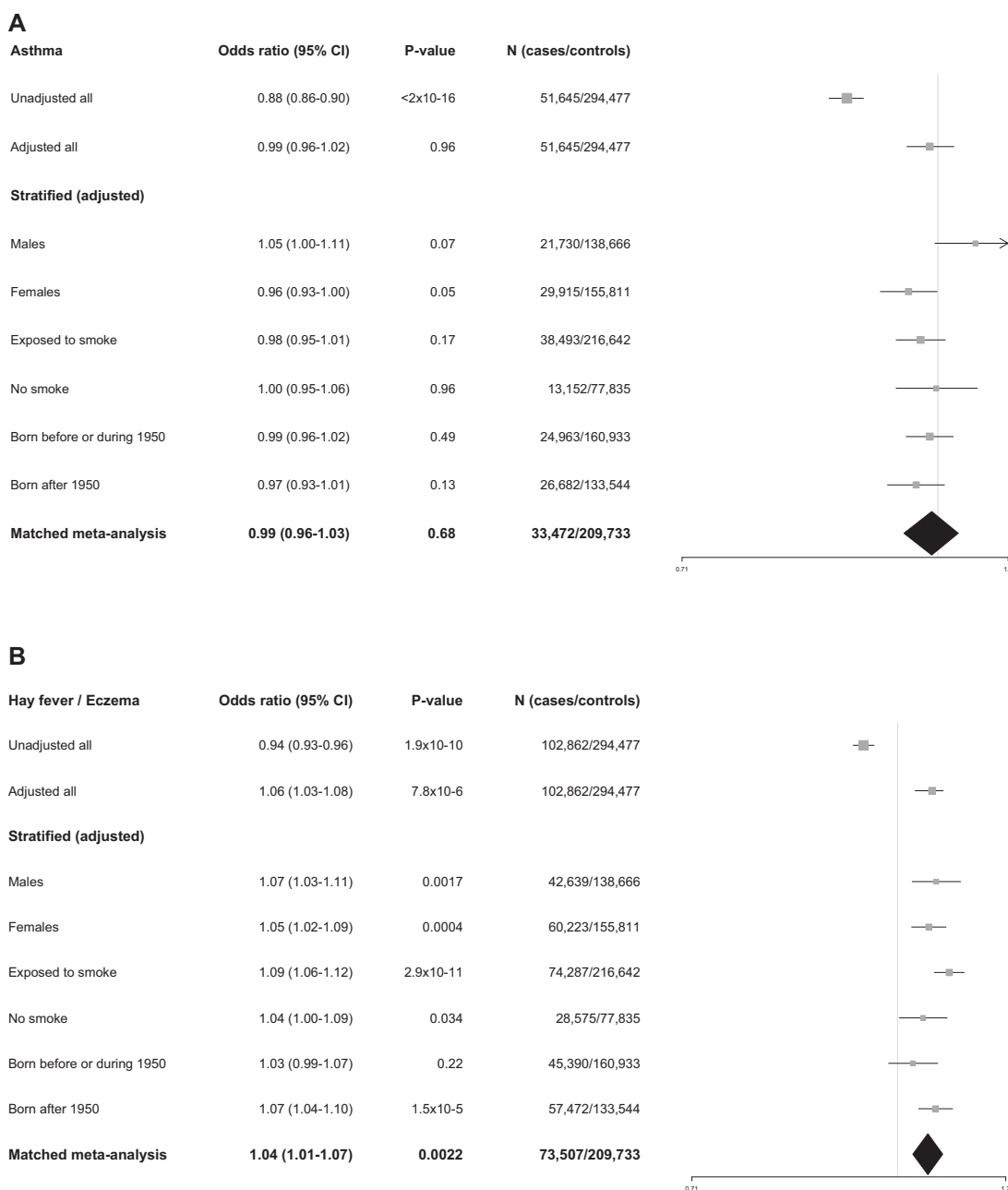
We could see an effect of socioeconomic status (for which Townsend deprivation index [TDI] is used as a proxy) on asthma and hay fever in the full model. Higher TDI (lower socioeconomic status) was associated with increased odds for asthma (OR = 1.02;  $P = 9.01 \times 10^{-11}$ ) while associated with lower odds for hay fever (OR = 0.098;  $P = 7.46 \times 10^{-8}$ ). Note that the effect size denotes the change in OR per unit of TDI

( $-6 < \text{TDI} < 10$ ). By comparing the groups with lowest and highest TDI, the effect would be larger. The decreased odds for hay fever are in line with the "hygiene hypothesis," which suggests that a lack of endemic infections increases the risk of being diagnosed with allergies due to a lack of early childhood exposure to, for example, microorganisms.<sup>5</sup> Endemic infections might be related to socioeconomic status indirectly (eg, by crowding). Maternal smoking around birth and smoking in house seem to be risk factors for developing asthma (OR = 1.03;  $P = .047$ ), while having a protective effect on hay fever and eczema (OR = 0.94;  $P = 3.54 \times 10^{-6}$ ). High body mass index was significantly associated with increased odds for asthma (OR = 1.04;  $P < 2 \times 10^{-16}$ ) and hay fever/eczema (OR = 1.004;  $P = .00024$ ). Higher birth weight lowered the odds for asthma (OR = 0.93;  $P = 3.13 \times 10^{-11}$ ) and hay fever/eczema (OR = 0.97;  $P = .0039$ ).

To measure the robustness of these links between asthma, hay fever, and eczema with being breast-fed, we did additional subgroup analyses of all 336,364 participants, which confirmed the same results as the full model ([Fig 1, A and B](#); see [Fig E2, A and B](#)). Interestingly, females showed a significant association between breast-feeding and decreased odds for asthma in the subgroup analysis ( $P = .046$ ), with an opposite effect as compared with males ([Fig 1, A](#)). This might be due to a difference between atopic asthma (more common in males) and nonatopic asthma (more common in females). When analyzing participants with asthma without hay fever/eczema (proxy for nonatopic asthma), breast-feeding is significantly protective (OR = 0.95;  $P = .02$ ) against asthma. Also, no difference ( $P$  value for interaction = .52) was seen between males and females. When analyzing breast-feeding with participants with asthma with hay fever/eczema (proxy for atopic asthma), we see increased odds for disease associated with breast-feeding (OR = 1.053;  $P = .018$ ). Even though the  $P$  values would not hold for multiple testing, it indicates that breast-feeding may have a different direction of effect on nonatopic asthma compared with atopic asthma.

Identifying the actual effect of breast-feeding on disease outcome is a challenge because there may be unknown or unobserved differences between breast-fed and non-breast-fed participants. For example, nonlinear effects and interactions between covariates could mask or distort the effect of breast-feeding. To overcome such problems, and to strengthen the results from our main analysis, we matched breast-fed and non-breast-fed participants for suspected confounders (see [Fig E3](#) in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)). We matched breast-fed and non-breast-fed individuals in 16 subgroups. To make the groups as homogeneous as possible, we excluded individuals with extreme body mass index values (obese and underweight) and low birth weights (<2.5 kg). After meta-analyzing the results from the matched subgroups, the results were still significant with the same direction of effect as in the main adjusted analysis. This strengthens our conclusion that breast-feeding is associated with increased odds of being diagnosed with hay fever and eczema (see [Table E4](#) in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)).

Observational studies do not allow for clinical recommendations because residual confounding might still be an issue.



**FIG 1.** Forest plots for the effect of breast-feeding for asthma (A) and hay fever/eczema (B) for the unadjusted model, the adjusted model, the adjusted subgroup analysis, and the matched meta-analysis. The matched meta-analysis is adjusted for body mass index, birth weight, TDI, home area, and year of birth.

Observed effects might also be due to reversed causality, that is, that individuals with a known risk of developing disease may not have been breast-fed or had a higher chance of being breast-fed due to recommendations. Today, women with higher socioeconomic status and high education level seem to breast-feed more often.<sup>6</sup> If TDI does not fully cover socioeconomic status, and because we did not have information on maternal education, socioeconomic status and education might drive the association between breast-feeding and the increased risk for hay fever and eczema. However, during the period 1950 to 1960 this trend seems to have been the opposite,

that is, that breast-feeding rates were lower for women with a high school education than for those with less education,<sup>7</sup> and so the use of TDI and the lack of maternal education in the regression model would rather have a diminishing effect on the estimates.

In summary, this study reports evidence that breast-feeding is associated with an increased risk for hay fever and eczema. Because of the high power achieved by the large sample size and the rigorous information on confounding variables, we conclude that breast-feeding is not likely to have a large effect on the risk of developing asthma.

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