

Letter to the editor:

Title: The limitations of cross-sectional data: perinatal risk factors for asthma.

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To the editor:

The relationship between perinatal factors and lung function or development of asthma has been studied for decades and we have increasing evidence for the importance of early life factors for respiratory health in adulthood [1]. Pregnancies in adolescent and older women have implications for maternal and child health. The topic is relevant in our days, as first-birth rates for women older than 35 years have increased exponentially [2]. A number of studies showed an association between maternal age and respiratory symptoms and asthma in childhood, suggesting that lung development might differ between children born to very young or very old mothers [3]. However, the evidence for longer-lasting effects is scarce.

We read with great interest the paper by Gómez Real and colleagues analysing the effect of maternal age on lung function and asthma in adulthood [4]. The authors used data from 10692 adults aged 25-55 years old, participating in the European Community Respiratory Health Survey (ECRHS) II. They found that maternal age at delivery was associated with better lung function (forced expiratory volume in 1 s (FEV1)) and lower risk of asthma and respiratory symptoms in the adult offspring. Both associations were found only in female offspring. The authors concluded that results were unchanged after adjustment for a range of potential confounders.

The authors proposed pathophysiological mechanisms to explain their findings. However, the effect observed is relatively small for such a large cohort and gender specific, making a causal association more improbable. On the other hand, the effect of maternal age on offspring asthma may be mediated through other intermediate factors. We commend the authors for adjusting their findings for as many confounders as were available from the data, including birth order, birthweight, maternal smoking during pregnancy, maternal education, maternal asthma, day care attendance, living environment in childhood, smoking history and body mass index (BMI). However, taking the opportunity from this carefully performed analysis, we would like to open the discussion on factors that are relevant when designing future studies on the association of perinatal factors with asthma in the offspring.

Most of the information on confounders in the study by Gomez Real et al. were obtained through a questionnaire completed by the adult offspring, some of whom were more than 50

years old, which could lead to recall and reporting bias. The authors acknowledged the risk of bias concerning self-reported asthma outcomes and maternal smoking, the latter being differential in those with a very young mother. However, there is little discussion about whether reporting bias might be different in those who developed asthma compared to those who did not. It is easy to imagine how mothers of asthmatic adults are more prone to conceal their smoking habits during pregnancy compared to mothers of healthy adults.

There are several other perinatal factors that influence asthma risk, such as birth modality and gestational age. C-sections and low gestational age are more common among older mothers [5] and have been shown to increase the risk of asthma in the child [6,7]. Including these factors as confounders in the study by Gomez et al. might therefore decrease even further the odds ratio reported for the association between maternal age and offspring asthma. Irrespective of the effect, these factors should be taken into account when studying the effect of maternal age.

Another potential confounder or effect modifier is breastfeeding. It has been shown that breastfed children have a lower risk of developing asthma and better lung function [8]. Studies on maternal age and initiation and duration of breastfeeding showed controversial results [9,10] and it is difficult to ascertain how its inclusion in the analysis would affect the association between maternal age and offspring asthma. Considering, breastfeeding is an important factor to be taken into account when studying perinatal factors associated with asthma.

A methodological issue to consider in similar future studies is that the participants in the study by Gomez et al. were born over a broad period of time (nearly 30 years). Both asthma prevalence and maternal age have increased worldwide over the last decades [11]. Therefore, we should also consider the generational effect when analysing factors related to asthma risk. Adjusting the results for the year in which the offspring was born could have been easily done with the available data, removing this potential source of confounding.

To conclude, while residual confounding should be thoroughly studied before drawing firm conclusions on the effect of maternal age on lung function and asthma in the offspring, the findings from the study by Gómez Real et al. are highly relevant and novel. The effect of maternal age on lung function in the offspring and the differences observed by gender should now be studied in the existing birth cohorts studying asthma, to see if findings can be reproduced. Prospective studies with a broad range of objectively recorded perinatal factors may be able to shed more light on this important matter, given the current trend of delayed motherhood.

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