



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

*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 at present, as first-birth rates for women aged >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 *et al.* [4] analysing the effect of maternal age on lung function and asthma in adulthood. The authors used data from 10 692 adults aged 25–55 years, 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) and lower risk of asthma and respiratory symptoms in the adult offspring. Both associations were only found 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 sex specific, making a causal association more improbable. Conversely, 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, daycare attendance, living environment in childhood, smoking history and body mass index. However, taking the opportunity from this carefully performed analysis, we would like to open up 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 GÓMEZ REAL *et al.* [4] was obtained through a questionnaire completed by the adult offspring, some of whom were aged >50 years, 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. Caesarean 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 GÓMEZ REAL *et al.* [4] might therefore further decrease 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

 @ERSpublications  
**Adjusting for residual confounding when studying perinatal factors and offspring health can be difficult but it is very important for designing future studies** <http://ow.ly/H78y30kPxMZ>

**Cite this article as:** Ardura-Garcia C, Pedersen ESL, Goutaki M. The limitations of cross-sectional data: perinatal risk factors for asthma. *Eur Respir J* 2018; 52: 1801197 [<https://doi.org/10.1183/13993003.01197-2018>].

inclusion in the analysis would affect the association between maternal age and offspring asthma. Considering this, 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 GÓMEZ REAL *et al.* [4] were born over a broad period of time (nearly 30 years). Both asthma prevalence and maternal age have increased worldwide over past 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 done easily 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.* [4] are highly relevant and novel. The effect of maternal age on lung function in the offspring and the differences observed by sex 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.

Cristina Ardura-Garcia <sup>1</sup>, Eva S.L. Pedersen<sup>1</sup> and Myrofora Goutaki <sup>1,2</sup>

<sup>1</sup>Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland. <sup>2</sup>Paediatric Respiratory Medicine, University Children's Hospital, University of Bern, Bern, Switzerland.

Correspondence: Cristina Ardura-Garcia, Institute of Social and Preventive Medicine, University of Bern, Finkenhubelweg 11, Bern 3012, Switzerland. E-mail: cristina.ardura@ispm.unibe.ch

Received: June 27 2018 | Accepted: June 28 2018

Conflict of interest: None declared.

## References

- 1 Boezen HM, Vonk JM, van Aalderen WM, *et al.* Perinatal predictors of respiratory symptoms and lung function at a young adult age. *Eur Respir J* 2002; 20: 383–390.
- 2 Saloojee H, Coovadia H. Maternal age matters: for a lifetime, or longer. *Lancet Glob Health* 2015; 3: e342–e343.
- 3 Caudri D, Savenije OE, Smit HA, *et al.* Perinatal risk factors for wheezing phenotypes in the first 8 years of life. *Clin Exp Allergy* 2013; 43: 1395–1405.
- 4 Gómez Real F, Burgess JA, Villani S, *et al.* Maternal age at delivery, lung function and asthma in offspring: a population-based survey. *Eur Respir J* 2018; 51: 1601611.
- 5 Herstad L, Klungsoyr K, Skjaerven R, *et al.* Maternal age and elective cesarean section in a low-risk population. *Acta Obstet Gynecol Scand* 2012; 91: 816–823.
- 6 Huang L, Chen Q, Zhao Y, *et al.* Is elective cesarean section associated with a higher risk of asthma? A meta-analysis. *J Asthma* 2015; 52: 16–25.
- 7 Sonnenschein-van der Voort AM, Arends LR, de Jongste JC, *et al.* Preterm birth, infant weight gain, and childhood asthma risk: a meta-analysis of 147,000 European children. *J Allergy Clin Immunol* 2014; 133: 1317–1329.
- 8 Dogaru CM, Nyffenegger D, Pescatore AM, *et al.* Breastfeeding and childhood asthma: systematic review and meta-analysis. *Am J Epidemiol* 2014; 179: 1153–1167.
- 9 Kitano N, Nomura K, Kido M, *et al.* Combined effects of maternal age and parity on successful initiation of exclusive breastfeeding. *Prev Med Rep* 2016; 3: 121–126.
- 10 Forster DA, McLachlan HL, Lumley J. Factors associated with breastfeeding at six months postpartum in a group of Australian women. *Int Breastfeed J* 2006; 1: 18.
- 11 Woolcock AJ, Peat JK. Evidence for the increase in asthma worldwide. *Ciba Found Symp* 1997; 206: 122–134.

Copyright ©ERS 2018