Considering the consequences of impaired maternal health and its implications for the child, we would like to emphasise the importance of the study by LEERMAKERS *et al.* [1], which evaluated maternal weight and preschool wheezing, and provides results relevant to society. Currently, weight gain is a worldwide health problem and is of great importance in pregnant females, as the health impacts can be severe, both for the mother and the neonate. We would like to ask the authors and other research groups to include sleep evaluation as a possible confounding factor, as there appears to be relationship between maternal health, obesity, sleep disorders and asthma.

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Sleep should be evaluated during pregnancy as a confounder of maternal health, obesity and asthma
<http://ow.ly/tsWuA>

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References

- 1 Leermakers ET, Sonnenschein-van der Voort AM, Gaillard R, *et al.* Maternal weight, gestational weight gain and preschool wheezing: the Generation R Study. *Eur Respir J* 2013; 42: 1234–1243.
- 2 Zahran H, Bailey C, Garbe P. Vital signs: asthma prevalence, disease characteristics, and self-management education – United States, 2001–2009. *Morb Mortal Wkly Rep* 2011; 60: 547–552.
- 3 Ahmad N, Biswas S, Bae S, *et al.* Association between obesity and asthma in US children and adolescents. *J Asthma* 2009; 46: 642–646.
- 4 Okun ML, Roberts JM, Marsland AL, *et al.* How disturbed sleep may be a risk factor for adverse pregnancy outcomes. *Obstet Gynecol Surv* 2009; 64: 273–280.
- 5 Reutrakul S, Zaidi N, Wroblewski K, *et al.* Interactions between pregnancy, obstructive sleep apnea, and gestational diabetes mellitus. *J Clin Endocrinol Metab* 2013; 98: 4195–4202.
- 6 Izci-Balserak B, Pien GW. Sleep-disordered breathing and pregnancy: potential mechanisms and evidence for maternal and fetal morbidity. *Curr Opin Pulm Med* 2010; 16: 574–582.
- 7 Newburg DS. Innate immunity and human milk. *Journal of Nutrition* 2005; 135: 1308–1312.
- 8 Cohen Engler A, Hadash A, Shehadeh N, *et al.* Breastfeeding may improve nocturnal sleep and reduce infantile colic: potential role of breast milk melatonin. *Eur J Pediatr* 2012; 171: 729–732.
- 9 Mennella JA, Garcia-Gomez PL. Sleep disturbances after acute exposure to alcohol in mothers' milk. *Alcohol* 2001; 25: 153–158.
- 10 Gozal D, Kheirandish-Gozal L. Childhood obesity and sleep: relatives, partners, or both? A critical perspective on the evidence. *Ann NY Acad Sci* 2012; 1264: 135–141.

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From the authors:

We kindly thank K.T. Nozoe and co-workers for their correspondence regarding our recently published article [1]. They suggested that the observed association of maternal body mass index (BMI) with childhood wheezing might be confounded by maternal sleeping problems during pregnancy. We appreciate this interesting suggestion.

As K.T. Nozoe and co-workers mentioned, asthma is a very common chronic disease amongst children. Given its high prevalence and considerable impact on morbidity and healthcare costs, research focused on early risk factors for asthma is important. Identification of causal risk factors and their mechanisms in pregnancy or early childhood, may lead to the development of new preventive strategies focused on the early phase of life. K.T. Nozoe and co-workers suggested that maternal sleep quality during pregnancy could be an important risk factor for childhood asthma, and that maternal sleep problems might be involved in the pathways underlying the association between maternal obesity and the risk of wheezing in offspring. Because of this possible intermediate effect of sleep in the association between maternal BMI and the risk of wheezing in offspring, sleep problems should not be treated as an extraneous confounding factor [2, 3].

In our study, we observed that children of mothers with pre-pregnancy obesity and a history of asthma or atopy, and children of mothers with a higher gestational weight gain had a higher risk of preschool wheezing. We considered growth, infection and atopy as potential underlying mechanisms. Based on the suggestion of K.T. Nozoe and co-workers, we now consider maternal sleep problems as an additional intermediate factor for the association between maternal pre-pregnancy BMI and offspring wheezing. We also consider sleep problems as an intermediate factor for the association between gestational weight gain and wheezing in offspring, since poor sleep quality might be the consequence of high gestational weight gain. We tested whether the results of our previous analysis would change if we added sleep problems to the model.

In our population-based prospective cohort study, we assessed maternal sleep problems with a questionnaire in the third trimester of pregnancy [4]. Respondents were asked how often they had suffered from sleeping badly in the last 3 months (daily; a few days per week; once per week; less than once per week; never). We defined women as having sleep problems when they reported to sleep badly daily or a few days per week. Information about pre-pregnancy BMI, gestational weight gain, sleep problems and offspring wheezing was available in 4014 women. We observed that 48.6% of all pregnant women reported sleeping badly at least a few times per week in the last 3 months. The percentages of sleep problems in underweight, normal weight, overweight and obese women were 46.9%, 46.2%, 53.0% and 61.1%, respectively (Chi-squared $p < 0.001$). In addition, mothers with a history of atopy or asthma experienced more sleep problems than mothers without a history of atopy or asthma (51.4% *versus* 45.1%, Chi-squared $p < 0.001$). Gestational weight gain was not associated with sleep problems.

We examined whether maternal sleep problems during pregnancy could explain part of the association of maternal BMI and gestational weight gain with childhood wheezing. We repeated the analyses of our original model, which was adjusted for many factors (maternal age, parity, ethnicity, education level, distress during pregnancy, smoking during pregnancy, pet keeping, gestational hypertensive disorders, diabetes gravidarum, gestational age at enrolment, gestational age at measurement, gestational weight gain, child's sex, gestational age at birth, birth weight, breastfeeding and daycare attendance), and added maternal sleep problems as a covariate in the model. In table 1, we present the results of the association of pre-pregnancy BMI with offspring wheezing, stratified for maternal history of asthma or atopy. Due to the smaller sample size, the effect estimates of the original model differ slightly to the results presented in the previously published study. Compared with our original model, the effect estimates did not materially change after adjustment for sleep problems. The largest change in effect estimate was seen amongst those with pre-pregnancy obesity and a history of atopy or asthma, but this change was negligible (OR (95% CI) for offspring wheeze in the original analysis: 1.47 (1.09–1.99); model additionally adjusted for sleep problems: 1.44 (1.06–1.94)). In the analysis with gestational weight gain as the exposure, sleep problems did not materially change the effect estimates for risk of wheezing (original model: 1.08 (1.03–1.13); model additionally adjusted for sleep problems: 1.08 (1.03–1.28) per SD increase of gestational weight gain). Thus, additional adjustment for sleep problems did not change our previously published results. This might be

TABLE 1 Pre-pregnancy body mass index (BMI) and wheezing, stratified for maternal history of asthma or atopy (n=4014)

	Original model	Original model adjusted for maternal sleep problems
No maternal history of asthma or atopy		
Underweight	0.93 (0.79–1.10)	0.94 (0.79–1.10)
Normal weight	Reference	Reference
Overweight	1.09 (0.93–1.28)	1.09 (0.93–1.28)
Obese	0.88 (0.67–1.15)	0.87 (0.67–1.14)
Pre-pregnancy BMI [#]	1.01 (0.95–1.08)	1.01 (0.94–1.08)
Maternal history of asthma or atopy		
Underweight	1.13 (0.93–1.39)	1.13 (0.93–1.39)
Normal weight	Reference	Reference
Overweight	0.98 (0.81–1.19)	0.98 (0.81–1.18)
Obese	1.47 (1.09–1.99)*	1.44 (1.06–1.94)*
Pre-pregnancy BMI [#]	1.06 (0.99–1.15)	1.06 (0.98–1.15)

Data are presented as OR (95% CI) and reflect the associations of different pre-pregnancy BMI groups with childhood wheezing, compared with those with a pre-pregnancy BMI of 20–24.9 kg·m⁻², using generalised estimating equation models. [#]: tests for trend were based on generalised estimating equation models with pre-pregnancy BMI (SD scores) as a continuous variable, and reflect the association with wheezing per SD increase of pre-pregnancy BMI. *: $p < 0.05$.

explained by the other factors that were already included in our model. As K.T. Nozoe and co-workers suggest, pregnancy complications such as gestational diabetes and pregnancy-induced hypertension, and nutritional factors in breastfeeding, could also affect the risk of wheezing and might be related to sleep problems. These factors were taken in to account in our previous model.

In conclusion, our additional analysis showed that, independent of maternal sleep problems during pregnancy, children have a higher risk of wheeze if their mothers had pre-pregnancy obesity and a history of atopy or asthma. Higher gestational weight gain is also associated with a higher risk of wheezing in offspring, independent of pre-pregnancy weight gain and sleep problems.

We thank K.T. Nozoe and co-workers for their interesting suggestion. We also encourage future research into maternal sleep quality as a risk factor for wheezing in children and possible biological pathways for this association.

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Maternal sleep quality during pregnancy does not explain the relationship of maternal weight and preschool wheezing <http://ow.ly/u6IuK>

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References

- 1 Leermakers ETM, Sonnenschein-van der Voort AMM, Gaillard R, *et al.* Maternal weight, gestational weight gain and preschool wheezing: the Generation R Study. *Eur Respir J* 2013; 42: 1234–1243.
- 2 Rothman KJ, Greenland S, Lash TL. Modern epidemiology. Philadelphia, Lippincott Williams and Wilkins, 2008.
- 3 Weinberg CR. Toward a clearer definition of confounding. *Am J Epidemiol* 1993; 137: 1–8.
- 4 Jaddoe VW, van Duijn CM, Franco OH, *et al.* The Generation R Study: design and cohort update 2012. *Eur J Epidemiol* 2012; 27: 739–756.

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