



## Ambient air pollution and low birth weight - are some women more vulnerable than others?



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### ABSTRACT

**Background and objectives:** Ambient air pollution is controllable, and it is one of the greatest environmental threats to human health. Studies conducted worldwide have provided evidence that maternal exposure to ambient air pollution during pregnancy enhances the risk of low birth weight at term (TLBW, < 2500 g among infants born  $\geq 37$  completed weeks of gestation), a maker of intrauterine growth restriction (IUGR), and suggest that some subgroups of pregnant women who are smoking, of low or high body-mass index (BMI), low socioeconomic status (SES) or asthma are more vulnerable towards the effect of ambient air pollution. The aim of this commentary is to review the published literature on the association between ambient air pollution and TLBW regarding increased vulnerability for the above-mentioned subgroups.

**Results:** Although more than fifty epidemiological studies have examined the associations between ambient air pollution and TLBW to date, we only identified six studies that examined the potential effect modification of the association between ambient air pollution and TLBW by the above listed maternal risk factors. Two studies assessed effect modification caused by smoking on the association between ambient air pollution and TLBW. The adjusted odds ratio (OR) for TLBW associated with exposure to ambient air pollution were in one study higher among women who smoked during pregnancy, as compared to the OR of non-smoking women, while in the other study the association was in the opposite direction. The association of ambient air pollution and TLBW were higher among women characterized by extreme BMI (two studies) and low SES compared to non-obese women or women of higher SES (four studies), respectively. Only one study reported the estimated effects among asthmatic and non-asthmatic women and no statistically significant effect modification was evident for the risk of TLBW associated with ambient air pollution.

**Conclusion and recommendations:** The current epidemiologic evidence is scarce, but suggests that pregnant women who are smoking, being underweight, overweight/obese or having lower SES are a vulnerable subpopulation when exposed to ambient air pollution, with an increased risk of having a child with TLBW. The limited evidence precludes for definitive conclusions and further studies are recommended.

### 1. Introduction

The health consequences associated with exposure to ambient air pollution are numerous, observed at all ages and in populations from all over the world, even in areas with relative low exposure levels (World Health Organization, 2016a). During the entire life course we are exposed, but exposure during vulnerable periods of exceptional high rates of development and growth, such as the first nine months of life are generally recognized as more critical than at later time periods (Bearer, 1995; Kim et al., 2016; Makri and Stilianakis, 2008; Rich et al., 2009).

Prenatal exposure to ambient air pollution has been linked with a wide range of adverse birth outcomes although heterogeneity between studies exists (Dadvand et al., 2013; Hannam et al., 2014; Mendola et al., 2015; Pedersen et al., 2013a; Stieb et al., 2012; Tu et al., 2016). The evidence of an association between maternal exposure to ambient air pollution and term low birth weight (TLBW, < 2500 g among infants born  $\geq 37$  completed weeks of gestation) is rather consistent (Dadvand et al., 2013; Habermann and Gouveia, 2014; Lavigne et al., 2016; Pedersen et al., 2013a; Stieb et al., 2016). Another commonly used indicator of intrauterine growth restriction (IUGR), which has

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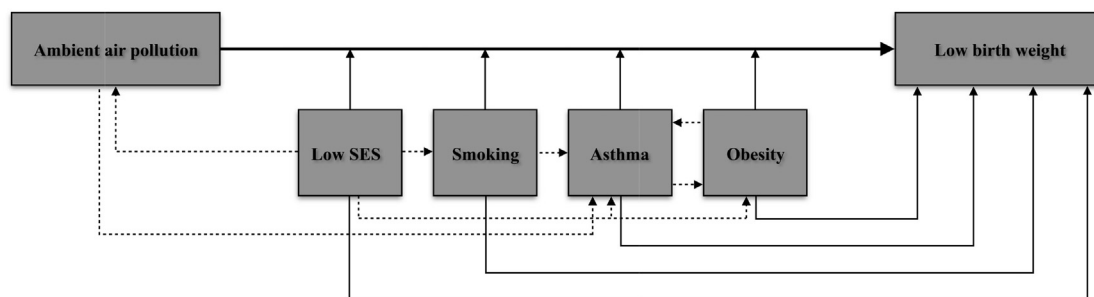


Fig. 1. Effect modifiers of the ambient air pollution - low birth weight relationships.

been associated with ambient air pollution, is small for gestational age (SGA, is often defined as < 10th percentile of the expected gestational age and sex-specific birth weight) (Chernausk, 2012; Gray et al., 2014; Maisonet et al., 2004; World Health Organization, 2012). Recently, ultrasound with Doppler has been used to identify IUGR prenatally and opened new opportunities for studies investigating the impact on early IUGR (Aguilera et al., 2010; Hansen et al., 2008; Iñiguez et al., 2016; Khalil and Thilaganathan, 2016; Malmqvist et al., 2017; Ritz et al., 2014; Roma et al., 2015; Slama et al., 2009; Smarr et al., 2015). Intrauterine growth is influenced by multiple additional factors, which could interact with exposure to ambient air pollution and each other (Valero De Bernab et al., 2004). More than 30 maternal characteristics such as lifestyle factors including overweight/obesity, underweight, diet, physical activity, drugs, alcohol, smoking, residence environment and socioeconomic status (SES) have been associated with an increased risk of TLBW (Valero De Bernab et al., 2004). Some of these risk factors can be hypothesized to modify the association between ambient air pollution and TLBW (Fig. 1). A better understanding of the interplay between known and potential, but yet unknown risk factors, are of importance for prevention of TLBW and development of ambient air quality guidelines. The objective of this commentary is to examine whether pregnant women who were smoking during pregnancy, of low or high body-mass index (BMI), having lower SES or asthma, are a vulnerable subpopulation, with a higher risk of having a child with TLBW, when exposed to ambient air pollution as compared to women, who are not characterized by these risk factors.

2. Materials and methods

Peer-reviewed epidemiological studies available in PubMed and Web Of Science by August 21st 2016 written in English reporting potential effect modification of the association between ambient air pollution and TLBW by a priori selected maternal characteristics (i.e. smoking, obesity, SES and asthma) were identified by carefully checking the full text, tables and results presented in supplemental tables. Keywords used for the literature search and the inclusion/exclusion process are described in (Fig. 2). We selected these maternal characteristics as they are relative common, modifiable and possible contributors to heighten vulnerability towards exposure of ambient air pollution.

3. Results

The characteristics of the six studies that we use as an illustration for this commentary are summarized in (Table 1). Most studies assessed particulate matter with aerodynamic diameter of < 2.5 μm (PM<sub>2.5</sub>) and the results of mean exposure at full pregnancy and effect modification caused by smoking, pre-pregnancy BMI and low SES associated with TLBW are presented in (Table 2). Additional results for other pollutants are summarized in the supplementary appendix (Table S1).

Effect modification by smoking was examined in two studies with inconsistent results (Table 2). The adjusted odds ratio (OR) for TLBW associated with PM<sub>2.5</sub> was higher in smokers than in non-smokers (1.26

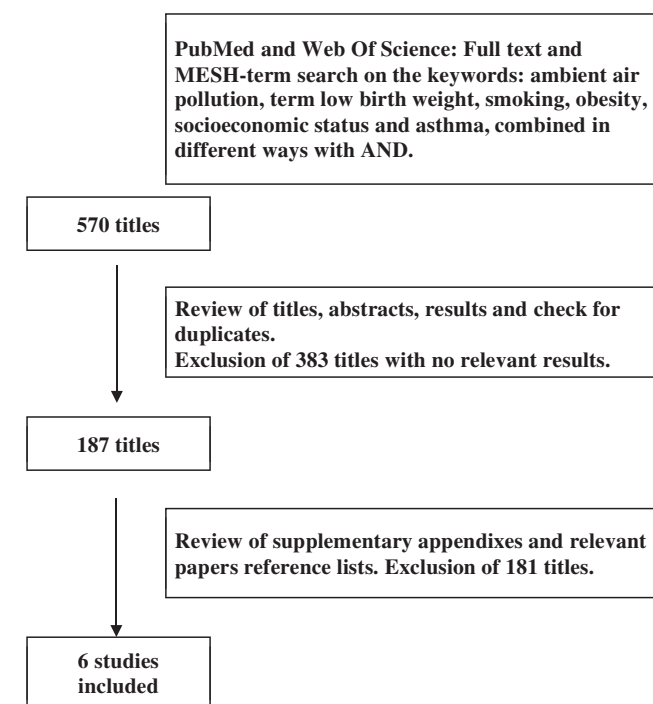


Fig. 2. Literature search and identification of included studies.

vs. 1.14), but the 95% confidence interval (CIs) was overlapping in an European study and the *P*-value for interaction was not statistical significant (*P* = 0.31) (Pedersen et al., 2013a). In a Japanese study, likewise the adjusted OR for TLBW associated with SO<sub>2</sub> was higher in smokers than non-smokers (2.64 vs. 1.55) (Table S1) while for suspended particulate matter (SPM) the adjusted OR was lower in smokers than in non-smokers (0.99 vs. 1.12) (Table 2) (Yorifuji et al., 2015). None of the interactions reached statistical significance.

Results concerning the effect modification by maternal obesity showed the same tendency in the two studies identified (Table 2). Laurent et al. (2014) found that obese women (BMI > 35 kg/m<sup>2</sup>) had a higher OR for TLBW of 1.24 compared to the OR of 1.04 observed among normal weight women (BMI 20–24.9 kg/m<sup>2</sup>) when exposed to PM<sub>2.5</sub>. Pedersen et al. (2013a) likewise found that the OR for TLBW associated with exposure to PM<sub>2.5</sub> was higher in obese women (BMI > 30 kg/m<sup>2</sup>) compared to normal weight women (BMI > 18.5– < 25 kg/m<sup>2</sup>) (1.26 vs. 1.15, (Table 2)). However, underweight women (BMI < 18.5 kg/m<sup>2</sup>) had an OR for the association of TLBW and PM<sub>2.5</sub> of 1.40 while the OR was 1.15 among women with normal pre-pregnancy weight (BMI 20–24.9 kg/m<sup>2</sup>) and the *P*-value for interaction was 0.34 (Pedersen et al., 2013a). Studies evaluating exposure to NO<sub>2</sub> and O<sub>3</sub> also showed a marginally increased risk of TLBW for the obese mothers (BMI > 35 kg/m<sup>2</sup>) as compared with those of normal weight (BMI 20–24.9 kg/m<sup>2</sup>), in this study no risk of TLBW was found for women with underweight (BMI ≤ 19 kg/m<sup>2</sup>) compared to normal

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