Ambient air pollution and the development of overweight and obesity in children: a large longitudinal study

Air pollution and childhood overweight and obesity

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Abstract

Background: Ambient air pollution may play a role in childhood obesity development, but evidence is scarce, and the modifying role of socioeconomic status (SES) is unclear. We aimed to examine the association between exposure to air pollution during early childhood and subsequent risk of developing overweight and obesity, and to evaluate whether SES is a modifier of this association.

Methods: This longitudinal study included 416,955 children identified as normal weight between 2-5 years old and registered in an electronic primary healthcare record between 2006-2016 in Catalonia (Spain). Children were followed-up until they developed overweight or obesity, reached 15 years of age, died, transferred out, or end of study period (31/12/2018). Overweight and obesity were defined following the WHO reference obtained from height and weight measures. We estimated annual residential census levels of nitrogen dioxide (NO_2) and particulate matter <10 μm (PM_{10}), <2.5 μm ($PM_{2.5}$) and 2.5-10 μm (PM_{coarse}) at study entry. We estimated the risk of developing overweight and obesity per interquartile range increase in air pollution exposure with Cox proportional hazard models.

Results: 142,590 (34.2%) children developed overweight or obesity. Increased exposure to NO_2, PM_{10}, and PM_{coarse} was associated with a 2-3% increased risk of developing overweight and obesity (hazard ratio [HR] per 21.8μg/m^3 NO_2=1.03 [95%CI: 1.02-1.04]; HR per 6.4μg/m^3 PM_{10}=1.02 [95%CI: 1.02-1.03]; HR per 4.6μg/m^3 PM_{coarse}=1.02, [95%CI: 1.01-1.02]). For all air pollutants, associations were stronger among children living in most compared to least deprived areas.

Conclusions: This study suggests that early life exposure to air pollution may be associated with a small increase in the risk of developing overweight and obesity in childhood, and that this association may be exacerbated in the most deprived areas. Even these small associations are of potential global health importance because air pollution exposure is widespread and the long-term health consequences of childhood obesity are clear.

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Introduction

Ambient air pollution is considered the most harmful environmental risk factor of mortality and morbidity worldwide according to the last Global Burden of Disease study [1]. In adults, air pollution has been associated with adverse respiratory and cardiovascular diseases, decreased lung function, premature mortality, cancer, diabetes, and also with obesity [2–4].

In children, there is growing evidence showing that air pollution may be associated with obesity development [5]. Several mechanisms for this have been postulated, including changes in the basal metabolism inducing inflammation, oxidative stress and hormone disruption [5–7], increases in brain inflammation, including microglial activation and anxiety, leading to increased caloric intake[8], and influences on child behavior such as physical activity levels and eating habits [5,9]. Most epidemiological studies on this topic have reported an increased risk of childhood obesity with increased levels of ambient air pollution exposures during childhood [10–15]. Others, however, have found null association with childhood obesity [5,16,17]. The majority of previous studies evaluated exposure and outcome during mid-childhood (6-11 years) and had a small sample size. However, since the highest incidence rate peak of overweight and obesity falls around 6-7 years of age [18,19], it is important to evaluate longitudinally whether air pollution exposures in earlier stages of life, can affect the development of overweight and obesity in subsequent years.

In Europe, increased levels of childhood obesity have been reported in lower socioeconomic status (SES) areas [19,20], while mixed results have been found regarding the distribution of air pollution by SES areas [21,22]. However, the role of SES in the relation between air pollution and childhood obesity remains unclear [23]. Few studies reported that, even when air pollution levels were similar across SES areas, associations between air pollution and health outcomes were stronger in lower SES areas, suggesting a greater susceptibility among the less advantaged [23,24]. Previous studies on the relationship between air pollution and childhood obesity have considered SES as a confounder, but none have evaluated whether SES modifies this association.

We aimed to evaluate the association between exposure to ambient air pollution before the age of 6 years and subsequent risk of developing overweight and obesity in a large longitudinal study, and to evaluate whether SES is an effect modifier of this association.

Methods

Data was obtained from the Information System for Research in Primary Care (SIDIAP; www.sidiap.org) in Catalonia, Spain [25]. SIDIAP is a de-identified electronic health record dataset from primary care centers of nearly 6 million people, covering around 80% of the population in Catalonia. It has repeated measurements of height and weight from 2006 onwards. The SIDIAP population is highly representative of the entire Catalan region in terms of geographic, age, and sex distributions [26].

This longitudinal study included children (2-5 years) identified as normal weight from January 1st 2006 to December 31st 2016 at the time of the first body mass index (BMI) measurement (date entry). Children with an age- and sex-specific z-scores for body mass index (zBMI, in standard deviation [SD] units) below +2.0 were considered normal weight at baseline [27]. zBMI scores were calculated using the World Health Organization (WHO) growth standard and reference [27,29]. Included children should have at least 2 BMI measurements with minimum 1.5-year difference between the first and last measurement. Children were followed up until they became overweight or obese, or until they reached 15 years of age, transferred out of a SIDIAP primary care centre, or died, or until the end of study period (December 31st 2018). We included only children living in urban areas (areas >10,000 habitants and a population density >150 habitants/km^2). The Clinical Research Ethic Committee of the IDIAPJGol approved this study (code: P16/179).

Body height (nearest 0.1 cm) and weight (nearest 100g) were frequently measured during childhood by health professionals in primary care centers following the same protocol [28]. The protocol recommends measuring child's height and weight at 2 years, 3-4 years, 6 years, 8 years,

10-12 years and 14 years. BMI (kg/m^2) was calculated from height and weight measured during the same visit.

Overweight including obesity (specified as overweight/obesity) and obesity were classified using the same WHO growth standard and reference [27,29]. Children at baseline and <5 year old with a zBMI larger than +2.0 and +3.0 were categorized as having overweight/obesity and obesity, respectively, and were excluded from the study. Children ≥5 years old with a zBMI larger than +1.0 and +2.0 were categorized as having overweight/obesity and obesity, respectively [29]. Extreme values of height, weight and BMI were removed [30,31].

Exposure to air pollution was assessed at census tract level. We estimated annual residential census tract levels of nitrogen dioxide (NO_2), nitrogen oxides (NO_x), particulate matter <10 μm (PM_{10}), <2.5 μm ($PM_{2.5}$), between 10 μm-2.5 μm (PM_{coarse}), and $PM_{2.5}$ light absorption ($PM_{2.5abs}$). Air pollution levels were estimated using a land use regression (LUR) model developed in the ESCAPE framework for Catalonia [32,33]. This LUR model predicted 62-76% of variation in pollutant levels in our study area during 2009. To estimate exposure at census tract level, we created an artificial grid points data set with n random points within each census tract based on its area so increasing the density of points in smaller areas and reducing the number of points in larger areas. We ensured at least 5 observations predicted within each census area. Air pollution was then averaged by census area [34]. We assigned the exposure level of air pollution at the residential census tract location at study entry (first recorded BMI measurement) from 2011 onwards, as information on the residential census tract was only available since 2011. For children entering the study between 2006-2010, we assigned the exposure level of the residential census where the child was living in 2011.

We obtained individual level covariates including sex, age, and child nationality (Spanish/non-Spanish) from SIDIAP. We used a census deprivation index as SES indicator [35]. This indicator was based on 6 indicators (manual and temporary workers, unemployment, insufficient education overall and in young people (aged 16 to 29 years), and dwellings without access to the internet)

obtained from the Spanish national census of 2011 [35]. Additionally, 68% of the children in SIDIAP were previously linked to their mother's electronic health records information [36], which allowed us to obtain information on maternal nationality (Spanish/non-Spanish), smoking (non-smoker/ex-smoker/smoker) and alcohol consumption (yes/no). Further, we estimated green spaces as the areas covered of green spaces within a census tract plus a 300 meter buffer to account for surrounding greenness [34]. Data were obtained from the land cover map of Catalonia from 2009 [37].

Statistical analyses

Cox proportional hazards models were fitted to assess the associations between NO_2, PM_{10}, $PM_{2.5}$, and PM_{coarse} and the development of overweight and obesity during follow-up. We analyzed the air pollutants as continuous variables per interquartile range (IQR) increase and by tertiles of exposure as some of the relationships deviated from linearity, which was assessed through restricted cubic splines with three knot points (Supplemental Fig. S1) [38,39]. Hazard ratios (HR) and 95% confidence intervals (CI) were generated for each exposure. We specified two models: model 1 (basic model) was adjusted for sex and nationality; and model 2 (fully adjusted) was additionally adjusted for the deprivation index so that we were able to specifically evaluate the confounding effect of SES. We evaluated the proportional hazard assumption with graphical and Schoenfeld test approach [40]. We stratified all models by age (1-year category) at index date to reduce the sensitivity to violation of the proportional hazard assumption. We evaluated effect modification by stratifying the analyses by tertiles of the deprivation index, and on a multiplicative scale by introducing interaction terms into the model and evaluating the p-value for interaction with the likelihood ratio test.

To assess the robustness of our results, we performed various sensitivity analyses: we repeated the analyses including only children a) since 2011 as residential census information was only available since 2011; b) who did not change residency during follow-up and who were included in the study since 2011; c) who developed obesity during follow-up compared with children who

were normal or overweight (not including obesity) at baseline; d) we evaluated whether maternal nationality, smoking and alcohol consumption were potential confounders; e) we evaluated the confounding effect of green spaces in multi exposure models as it can partly determine the levels of air pollution in a city and has been considered as a protective exposure against childhood overweight and obesity [41]. All analyses were conducted with R (version 3.6.2), except the restricted cubic splines were performed in STATA version 15.1 (College Station, TX, USA). We followed the RECORD statement for cohort studies using routinely-collected data [42].

Results

We identified 416,955 children who were normal weight at study entry at median age 2.1 (IQR 2.1-2.9) years and who were followed for a median of 5.7 (IQR 3.9-8.7) years (Supplemental Fig. S2, Table 1). During follow-up, the included children had a median of 5 (IQR 3-6) BMI measurements, and 142,590 (34.2%) developed overweight or obesity at a median age of 6.3 (IQR 6.0-8.2) years old. Compared with children who kept normal weight during follow-up, children who developed overweight or obesity were more likely to be boys (50.4% vs. 53.2%, respectively), had more BMI measurements (4 vs. 6 measurements), were more likely to live in the most deprived areas (32.4% vs. 35.1%), and to have Spanish nationality (88.1% vs. 90.8%) (Table 1).

The levels of the air pollutants are shown in table 1. Based on census tract data, more than 50% of the children were exposed to census NO_2 levels that exceeded the WHO guidelines (<40 $\mu g/m^3$), for PM_{10} and $PM_{2.5}$ more than 75% of the children exceed the WHO guidelines (<20 and <10 $\mu g/m^3$, respectively). Levels of the air pollutants were similar across the tertiles of SES (Supplemental Table S1). The air pollutants were highly correlated with each other (r_s = +0.8 to +1.0), and weakly correlated with the deprivation index (r_s = 0.0 to -0.1) (Supplemental Fig. S3). Highly correlated air pollutant indicators (r_s > +0.9) were excluded from the analyses: NO_x and PM_{abs} (correlated with NO_2), and PM_{abs} (correlated with PM_{10}).

In the fully adjusted models, we found that increased levels of NO_2, PM_{10}, and PM_{coarse} were associated with increased risk of developing overweight and obesity during childhood (Table 2). Each 21.8μg/m^3 IQR increase in NO_2 was associated with a 3% increase in the risk of developing childhood overweight and obesity (HR=1.03 [95%CI, 1.02-1.04]). Similar HRs were found for PM_{10} (HR per 6.4μg/m^3=1.02 [95%CI, 1.02-1.03]) and PM_{coarse} (HR per 4.6μg/m^3=1.02 [95%CI, 1.00-1.02]). $PM_{2.5}$ was not associated with the development of overweight and obesity. Models not adjusted for the deprivation index (basic model) gave identical results for all air pollutants (Table 2). When exposures were categorised by tertiles, children exposed to the highest levels (tertile 3, T3) of NO_2, PM_{10} and PM_{coarse} were 5%, 4% and 1%, respectively, more likely to develop overweight and obesity compared with children exposed to the lowest levels (tertile 1, T1) (Table 2).

For all air pollutants, associations with overweight and obesity were stronger among children living in the most deprived areas compared to children living in the least deprived areas (Table 3). For example, for children living in the most deprived areas, the risk of developing overweight and obesity increased by 7% per IQR increase in NO_2 (HR=1.07 [95%CI,1.05-1.08]), whereas for children living in the least deprived areas there was no increase in risk associated with NO_2 (HR=0.99 [95%CI, 0.98-1.00]). Similar trends were observed when air pollutants were analysed in tertiles. All interactions terms between air pollution with SES were statistically significant on a multiplicative scale (p<0.05), with the exception of an interaction term of borderline statistical significance (p=0.08) when we treated PM_{10} in tertiles (Table 3).

In the sensitivity analyses, when we restricted our analyses to 199,245 (47.5% of the original study population) children that entered the study since 2011, we obtained similar HRs for all the air pollutants (Supplemental Table S2). When we removed children who changed residence during follow-up [N = 46,620 (23.3%) of the children that entered the study since 2011], the estimates were mostly similar (Supplemental Table S3). Similar HRs were also obtained when we evaluated the association between air pollution and the risk of developing obesity among children who were normal or overweight (not including obesity) at baseline (Supplemental Table

S4). In the reduced dataset with full data on maternal characteristics (N = 214,578; 51.5% from the original study population), analyses showed that the associations between air pollutants and childhood overweight and obesity risk did not change substantially after adding maternal nationality, maternal smoking and maternal alcohol consumption to the model (Supplemental Table S5). The associations between NO_2 and PM_{10} and childhood overweight and obesity remained similar after adjusting for green spaces, whereas for PM_{coarse} the associations were attenuated (Supplemental Table S6).

Discussion

In this large longitudinal study, we found that exposure to increased levels of NO_2, PM_{10} and PM_{coarse} at early ages (2-5 years) was associated with small increase in risk for subsequent development of childhood overweight and obesity. These associations were stronger among children living in the most deprived areas. Because air pollution exposure is a very widespread exposure and overweight and obesity are very prevalent health outcomes, even these small associations may have important public health consequences. Adjusting by maternal smoking, as a proxy of secondhand smoke of the child, did not affect our results.

While most previous studies reported increased levels of ambient air pollution is associated with increased risk of childhood overweight and obesity [10–15], others have found null association [5,16,17]. Only few studies have evaluated the effect of air pollution during earlier stages of life (0-5 years) on childhood overweight and obesity before the peak increase of overweight and obesity incidence around 6-7 years [18,19]. A cohort in Southern California (United States) followed 2318 children from 6-10 years and observed a positive association between air pollution (estimated during the 1st year of life) and attained BMI at 10 years old [14] A Dutch birth cohort followed 3680 infants until the age of 17 years and reported that the odd of being overweight from age 3-17 years increased with increasing exposure to NO_2 (estimated 1 year before each measurement point) [15]. Similar to our study, this study found that the associations between air pollution and childhood overweight were not confounded by green spaces. Conversely, an Italian

birth cohort including 719 infants did not observe an association between ambient air pollution and childhood obesity at 4 years (N=581) and at 8 years (N = 499) [17]. Air pollution levels were similar across the studies mentioned above, but those with larger sample size reported statistically significant associations. In our study, associations were stronger for NO_2, PM_{10}, PM_{coarse} than for $PM_{2.5}$, even though literature suggests that smaller particles are the more harmful ones [43] This may be explained by the very narrow exposure range of this pollutant in our study (IQR of $PM_{2.5}$ was 1.4 μg/m^3). This is in line with other studies [44–46] and may be explained by high urban background concentrations of $PM_{2.5}$ from other sources than traffic, including sand, Saharan dust, ports, and industrial facilities.

The role of SES in the relationship between air pollution and health outcomes remains unclear in Europe [23]. In the US air pollution levels are consistently higher in more deprived areas,[23] whereas in Europe the evidence is mixed [21,22]. In our study we observed similar levels of air pollution across the different SES areas, but we observed stronger association between air pollution and childhood obesity in the most deprived areas. Several studies have observed stronger associations between air pollution and health outcomes in more deprived populations, but none have studied childhood obesity [23,24]. This environmental inequality could be explained by different reasons. Lower social classes have less resources to protect themselves against air pollution compared with higher social classes [47], and they could be more susceptible to the adverse effects of air pollution as they have generally poorer health outcomes due to poverty, psychosocial stress, and poorer lifestyle behaviors [47,48]. Further, children living in more deprived areas could be also susceptible to other environmental stressors such as noise, second hand tobacco smoke or fear of crime [49]. Thus, the combination of less resources, increased susceptibility and additional exposure to multiple environmental stressors, could result in greater vulnerability to the effects of air pollution. Children living in the least deprived areas would be less exposed to the combined stressors and thus be more resilient to the effects of air pollution, which may explain the null association we observe in this group. Our results highlight the need to aim policies for reduction of air pollution levels at the most disadvantaged populations,

but also a need for more personalized exposure assessment among children from different SES layers to be able to identify the different exposure levels of ambient air pollution among the different micro-environment where the child spend time.

Recently, there has been an increase in studies evaluating the possible biological and behavioral mechanisms underlying the effects of ambient air pollution on childhood overweight and obesity. Experimental studies in mice have shown that air pollution (especially focus on $PM_{2.5}$) may affect metabolic regulation increase weight gain, through alterations in the inflammation/oxidative stress and hormone disruption pathways [6,7,50]. Another animal study suggests that diesel exhaust at early-ages could affect the brain through neuroinflammation, stimulating appetite and increased anxiety diet-induced weight gain [8]. Few epidemiological studies have evaluated the influence of air pollution on lifestyle behaviors that are associated with childhood overweight and obesity. In China and US several studies have shown that air pollution is associated with reduced levels of physical activity, which could lead to increased levels of sedentary behaviors and childhood obesity [51–53] Finally, a recent study found that air pollution may contribute to obesogenic behaviors by increasing the consumption of *trans* fat and fast foods [9].

Major strengths of this study are its longitudinal design, its long follow-up period, its large sample size (>400,000 children), and its representativeness of the urban areas in Catalonia. Further, children were measured frequently during childhood following the same protocol by pediatric health professionals.

Our study also has several limitations. The exposure assessment of air pollution at census tract has less individual variability and is less accurate in comparison to assessment at household level. As air pollution tends to be more local and with higher variability, this may have introduced exposure misclassification. However, we expect this misclassification to be non-differential, which would bias effect estimates towards the null [54]. Further, air pollution levels were estimated from LUR models developed in 2009, whereas study participants entered the study between 2006-2016. We did not temporally adjust the spatial estimates because there were not

enough representative background monitors across all the urban areas of Catalonia. Temporally adjusting the air pollution levels would have introduced more error in the estimates and increased the risk of misclassification bias. However, studies have found that the spatial variation of air pollution levels using LUR model remains largely stable over periods of 10 years, and we may assume that one-year spatial estimates can be considered a good proxy for our study period [55]. In addition, we were unable to account for air pollution exposure in other indoor and outdoor micro-environments where children spend an important amount of time, including the home, school and commuting environment. Focusing on a more personalised exposure assessment, for example combining personal monitoring with GPS-based time activity patterns of the child, would provide a more accurate exposure assessment at the personal level [56,57]. Indoor monitoring or school monitoring would also be relevant in relation to childhood obesity; in separate recent studies we observed higher indoor levels of air pollution to be associated with higher child BMI [58], and higher school levels of ultrafine particles to be associated with childhood obesity risk [12]. However, in large-scale studies, detailed personal or micro-environment level exposure assessments are often not feasible. A combination of large-scale studies, with adequate power to detect small risk increases, and smaller scale studies, with more accurate exposure assessment, will be needed to build up a better evidence base on the obesogenic effects of air pollution during childhood.

Another limitation was that the deprivation index was based at census tract and residual confounding by individual socioeconomic status cannot be ruled out. However, previous studies have found that area-level SES had stronger association with air pollution and health outcomes then individual-level SES [23]. Furthermore, in our sensitivity analyses, maternal nationality, maternal smoking and maternal alcohol consumption, three individual variables as a proxy of individual SES variables, did not confound the observed associations. Finally, we cannot entirely rule out residual confounding by individual behaviors related to obesity, particularly diet and physical activity. Studies with individual-level data on these factors are needed to evaluate their role as mediators or confounders in the association between air pollution and childhood obesity.

Conclusions

This study shows that air pollution is associated with the development of childhood overweight and obesity. The effect of air pollution on childhood overweight and obesity was exacerbated in the most deprived areas. Even these small associations are of potential global health importance because air pollution exposure is widespread and the long-term health consequences of childhood obesity are clear. A greater vulnerability of less advantaged children would be of particular concern.

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Table legend:

- **Table 1:** Population characteristics
- **Table 2:** Association between air pollution (continuous and in tertiles) and the development of childhood overweight and obesity (N = 416,955).
- **Table 3:** Associations between air pollution (continuous and in tertiles) and development of childhood overweight and obesity stratified by deprivation index (N = 416,955).

Table 1: Population characteristics

	Total population **N = 416 955**	**Remained normal weight during follow-up** **N = 274 365 (65.8%)**	**Developed overweight/obesity** **N = 142 590 (34.2%)**
Age at index date, years median (P25-P75)	2.1 (2.1-2.9)	2.1 (2.1-2.7)	2.1 (2.1-3.1)
Girls, N (%)	202 790 (48.6%)	136 076 (49.6%)	66 714 (46.8%)
BMI measurements, median (P25-P75)	5 (3-6)	4 (3-6)	6 (4-7)
Age at case, median (P25-P75)	6.3 (6.0-8.2)	-	6.3 (6.0-8.2)
Time of follow-up, years median (P25-P75)	5.7 (3.9-8.7)	7.1 (4.6-10.2)	4.0 (3.1-5.7)
Deprivation index (tertiles), N (%)			
First (least deprived)	138 985 (33.3%)	94 949 (34.6%)	44 036 (30.9%)
Second	138 985 (33.3%)	90 497 (33.0%)	48 488 (34.0%)
Third (most deprived)	138 985 (33.3%)	88 919 (32.4%)	50 066 (35.1%)
Nationality, N %			
Spain	371 162 (89.0%)	241 702 (88.1%)	129 460 (90.8%)
Foreign	45 793 (11.0%)	32 663 (11.9%)	13 130 (9.2%)
Urban exposures distribution, median (P25-P75)			
Air pollution:			
NO_2 (µg/m³)	42.3 (29.2-51.0)	42.3 (29.2-51.1)	42.1 (29.2-51.0)
PM_{10} (µg/m³)	34.6 (31.4-37.7)	34.6 (31.4-37.7)	34.6 (31.3-37.7)
$PM_{2.5}$ (µg/m³)	14.9 (14.0-15.4)	14.9 (14.0-15.5)	14.9 (14.0-15.4)
PM_{coarse} (µg/m³)	20.3 (17.7-22.3)	20.3 (17.7-22.3)	20.3 (17.6-22.2)
Green spaces:			
% green spaces + 300m	14.2 (1.8-37.0)	14.2 (1.9-36.9)	14.3 (1.6-37.1)

BMI = body mass index, P25 = Percentile 25, P75 = Percentile 75, NO_2 = nitrogen dioxides, PM_{10} = particulate matter (PM) <10 µm, $PM_{2.5}$ = PM <2.5 µm, PM_{coarse} = PM >2.5 µm & < 10 µm. Values are median (P25-P75) for continuous variables, and percentage for categorical variables.

Table 2: Association between air pollution (continuous and in tertiles) and the development of childhood overweight and obesity (N = 416,955).

Air pollution (N = 416,955)	Basic model[a] HR (95% CI)	Adjusted model[b] HR (95% CI)
NO_2		
Per 21.8 µg/m^3	1.03 (1.02-1.03)	1.03 (1.02-1.04)
T2 (<47.6 µg/m^3) vs T1 (<33.7 µg/m^3)	1.01 (1.00-1.03)	1.01 (0.99-1.02)
T3 (≥47.6 µg/m^3) vs T1 (<33.7 µg/m^3)	1.05 (1.04-1.06)	1.05 (1.04-1.07)
PM_{10}		
Per 6.4 µg/m^3	1.02 (1.02-1.03)	1.02 (1.02-1.03)
T2 (<36.6 µg/m^3) vs T1 (<32.5 µg/m^3)	1.01 (1.00-1.03)	1.01 (0.99-1.02)
T3 (≥36.6 µg/m^3) vs T1 (<32.5 µg/m^3)	1.04 (1.03-1.06)	1.04 (1.03-1.06)
$PM_{2.5}$		
Per 1.4 µg/m^3	1.00 (0.99-1.00)	1.00 (1.00-1.00)
T2 (<15.1 µg/m^3) vs T1 (<14.4 µg/m^3)	1.00 (0.99-1.01)	1.00 (0.98-1.01)
T3 (≥15.1 µg/m^3) vs T1 (<14.4 µg/m^3)	0.99 (0.97-1.00)	1.00 (1.00-1.02)
PM_{coarse}		
Per 4.6 µg/m^3	1.02 (1.01-1.03)	1.02 (1.01-1.02)
T2 (<21.6 µg/m^3) vs T1 (<18.7 µg/m^3)	1.00 (0.99-1.02)	1.00 (0.98-1.01)
T3 (≥21.6 µg/m^3) vs T1 (<18.7 µg/m^3)	1.02 (1.00-1.04)	1.01 (1.00-1.03)

Abbreviations: NO_2 = nitrogen dioxides, PM_{10} = particulate matter (PM) <10 µm, $PM_{2.5}$ = PM <2.5 µm, PM_{coarse} = PM >2.5 µm & < 10 µm, T1 = tertile 1, T2 = tertile 2, T3 = tertile 3.

[a] Basic model: adjusted by sex, deprivation index, nationality and had age (1-year categories) in the strata statement.

[b] Adjusted model: adjusted by sex, deprivation index, nationality, deprivation index and had age (1-year categories) in the strata statement.

Table 3: Associations between air pollution (continuous and in tertiles) and development of childhood overweight and obesity stratified by deprivation index (N = 416,955).

Air pollutants (N = 416,955)	Deprivation index (tertiles)	Air pollution		
		Continuous (per IQR)[a] HR (95% CI)	T2 vs T1[b] HR (95% CI)	T3 vs T1[b] HR (95% CI)
NO_2	Tertile 1 (least deprived)	0.99 (0.98-1.00)	1.02 (0.99-1.05)	1.02 (1.00-1.05)
	Tertile 2	1.04 (1.03-1.05)	1.02 (0.99-1.05)	1.06 (1.02-1.09)
	Tertile 3 (most deprived)	1.07 (1.05-1.08)	1.04 (1.02-1.07)	1.09 (1.07-1.12)
	p-interaction[c]	<0.01	0.01	
PM_{10}	Tertile 1 (least deprived)	1.00 (0.99-1.01)	0.98 (0.96-1.01)	1.03 (1.00-1.06)
	Tertile 2	1.03 (1.02-1.04)	1.02 (0.98-1.05)	1.04 (1.00-1.07)
	Tertile 3 (most deprived)	1.06 (1.05-1.07)	1.02 (1.00-1.04)	1.07 (1.05-1.10)
	p-interaction[c]	<0.01	0.08	
$PM_{2.5}$	Tertile 1 (least deprived)	0.99 (0.99-1.00)	0.98 (0.96-1.01)	1.00 (0.97-1.02)
	Tertile 2	1.00 (1.00-1.01)	1.00 (0.96-1.03)	1.02 (0.98-1.05)
	Tertile 3 (most deprived)	1.00 (1.00-1.02)	1.00 (0.99-1.04)	1.05 (1.02-1.07)
	p-interaction[c]	<0.01	0.05	
PM_{coarse}	Tertile 1 (least deprived)	1.00 (1.00-1.02)	1.00 (0.99-1.04)	1.05 (1.02-1.07)
	Tertile 2	1.02 (1.01-1.03)	0.98 (0.95-1.02)	0.97 (0.94-1.01)
	Tertile 3 (most deprived)	1.04 (1.02-1.05)	1.03 (1.00-1.05)	1.04 (1.02-1.07)
	p-interaction[c]	0.01	<0.01	

Abbreviations: NO_2 = nitrogen dioxides, PM_{10} = particulate matter (PM) <10 µm, $PM_{2.5}$ = PM <2.5 µm, PM_{coarse} = PM >2.5 µm & < 10 µm, T1 = tertile 1, T2 = tertile 2, T3 = tertile 3. Models were adjusted for sex, nationality, and had age (1-year categories) in the strata statement.

[a] HR (95% CI) per IQR unit increase (NO_2 per 21.8 µg/m^3, PM_{10} per 6.4 µg/m^3, $PM_{2.5}$ per 1.4 µg/m^3, and PM_{coarse} per 4.6 µg/m^3) pollution in each tertile of the deprivation index.

[b] HR (95% CI) for each tertile increase of air pollution in each tertile of the deprivation index. NO_2 (T1 < 33.7 µg/m^3, T2 < 47.6 µg/m^3, T3 >= 47.6 µg/m^3), PM_{10} (T1 < 32.5 µg/m^3, T2 < 36.6 µg/m^3, T3 >= 36.6 µg/m^3), $PM_{2.5}$ (T1 < 14.4 µg/m^3, T2 < 15.1 µg/m^3, T3 >= 15.1 µg/m^3); PM_{coarse} (T1 < 18.7 µg/m^3, T2 < 21.6 µg/m^3, T3 >= 21.6 µg/m^3).

[c] *p*-values for the multiplicative interaction.