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Lifetime exposure to air pollution and academic achievement: A nationwide cohort study in Denmark

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A B S T R A C T

Recent research suggests a link between air pollution and cognitive development in children, and studies on air pollution and academic achievement are emerging. We conducted a nationwide cohort study in Denmark to explore the associations between lifetime exposure to air pollution and academic performance in 9th grade. The study encompassed 785,312 children born in Denmark between 1989 and 2005, all of whom completed 9th-grade exit examinations. Using linear mixed models with a random intercept for each school, we assessed the relationship between 16 years of exposure to $PM_{2.5}$, PM_{10}, and gaseous pollutants and Grade Point Averages (GPA) in exit examinations, covering subjects such as Danish literature, Danish writing, English, mathematics, and natural sciences. The study revealed that a 5 μg/m^3 increase in $PM_{2.5}$ and PM_{10} was associated with a decrease of 0.99 (95 % Confidence Intervals: −1.05, −0.92) and 0.46 (−0.50, −0.41) in GPA, respectively. Notably, these negative associations were more pronounced in mathematics and natural sciences compared to language-related subjects. Additionally, girls and children with non-Danish mothers were found to be particularly susceptible to the adverse effects of air pollution exposure. These results underscore the potential long-term consequences of air pollution on academic achievement, emphasizing the significance of interventions that foster healthier environments for children's cognitive development.

1. Introduction

Air pollution has an enormous impact on health globally, with at least 7 million premature deaths due to cardiovascular, metabolic, and respiratory diseases (Health Effects Institute 2020). An increasing body of evidence suggests that exposure to air pollution impacts neurodevelopment, including cognitive function, in both younger (1–6 years) and older children (7–18 years) (Clifford et al., 2016; Ha, 2021; Margolis et al., 2021; Volk et al., 2021). Although the exact developmental pathways linking prenatal and postnatal air pollution exposure to neurocognitive development remain understudied, one possibility is that air pollutants enter the body during the fetal period and early childhood years and induce neuroinflammation, which contributes to cell loss within the central nervous system, causing cognitive deficits (Brockmeyer and D'Angiulli, 2016) and adverse physical and mental health outcomes in childhood and adolescence (Shonkoff et al., 2012; Stein

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et al., 2002).

Academic achievement is highly correlated with cognitive development and often plays a crucial role in further education, occupation, and income throughout life. Knowledge of negative impacts on academic achievement can be a strong argument for preventive measures reducing children's exposure to air pollution, as a way of improving children's neurocognitive development. Several previous studies suggested that exposure to air pollution may influence academic achievement, although the majority of these studies have been conducted in either an ecological or cross-sectional study design (Berman et al., 2018; Claesen et al., 2021; Clark-Reyna et al., 2016; Gaffron and Niemeier, 2015; Gardin and Requia, 2023; Grineski et al., 2016; Lu et al., 2021). Whereas five of seven studies suggested adverse effects of air pollution on academic achievement (Clark-Reyna et al., 2016; Gaffron and Niemeier, 2015; Gardin and Requia, 2023; Grineski et al., 2016; Lu et al., 2021), the evidence is limited due to the study designs, which do not allow for making causal inferences about these associations. Furthermore, the few longitudinal studies examining the relationship between air pollution and academic achievement employed either a low-resolution or area-aggregated exposure assessment of air pollution (Balalian et al., 2022; Grineski et al., 2020; Marcotte, 2017; Shier et al., 2019; Stingone et al., 2016). Some of these studies relied on birth years (Balalian et al., 2022; Stingone et al., 2016), while others considered a limited timeframe preceding the assessment of academic achievement (Grineski et al., 2020; Marcotte, 2017; Shier et al., 2019). Furthermore, there is a scarcity of consistent findings on sex-specific associations between exposure to air pollution and cognitive development (Chiu et al., 2016; Gardin and Requia, 2023; Shier et al., 2019; Zhang et al., 2018).

In the present study, we hypothesized an inverse association between exposure to air pollution and academic achievement. To address limitations in prior research, we employed a longitudinal study design, enabling an investigation into the temporal relationship between air pollution exposure and academic performance over an extended period. Furthermore, our objective was to identify critical exposure windows, enhancing our understanding of how air pollution affects academic outcomes.

Utilizing unique access to Danish national registers, we conducted a nationwide prospective cohort study to investigate the relationship between lifetime exposure to air pollution from birth until age 15 years and academic achievement in 9th grade. Furthermore, we aimed to identify the most critical exposure windows by pollutants and susceptible adolescents based on their sex, country of origin, maternal parity, birth weight, and socioeconomic status (SES).

2. Materials and methods

2.1. Study population

For our study population, we considered 1,247,831 children born between January 1st, 1989 and December 31st, 2005 identified through the Danish Medical Birth Register. We linked children's identification numbers through the Danish Civil Registration System and created an address history of residence for 16 years from the birth year. We also collected information on birth outcomes (maternal age, gestational age, birth weight, maternal smoking, parity) from the Danish Medical Birth Register, maternal education from the Population's Education Register, and family and maternal disposable income from the Personal Income Register.

Among 1,247,831 children, we included 785,312 students who could be followed up from a year of birth to the completion of exit examinations. Excluded children were depicted in Supplementary Fig. 1.

2.2. Subject-specific school grades

We used the information on compulsory exit examinations in 9th grade in public and private schools in Denmark between the 2005/2006 and 2019/2020 school years from the Academic Achievement Register. The 9th-grade exit examinations consist of five mandatory examination subjects: Danish literature (oral test), Danish writing (reading, spelling, and essay tests), English (oral test), mathematics (written and oral tests before 2006 and calculus and problem-solving in written tests since 2006), and natural sciences (physics/chemistry and biology/geography) (Danish Ministry of Children and Education, 2022). For school years between 2005/2006 and 2006/2007, the test grade was submitted using a 13-point scale and converted to the current 7-point grading scale (−3, 0, 2, 4, 7, 10, and 12) by the Danish Ministry of Education and Children. The grades of exam subjects consisting of two or three tests were computed as a weighted mean of the tests (Danish Ministry of Children and Education, 2022). The GPA in 9th grade was calculated as the mean of the five mandatory subject grades (Danish literature, Danish writing, English, mathematics, and natural sciences) for the students who completed the five mandatory exam subjects. In addition, we categorized the students into two categories: incomplete and complete exam takers of the five mandatory exit examinations.

2.3. Air pollution exposure

We assigned modeled air pollution levels to each child based on their residential addresses. First, the Danish integrated DEHM/UBM model system estimated annual means of air pollution concentration levels in 1979–2019 at 1 × 1 km^2 resolution (Frohn et al., 2022). The annual means were estimated for particulate matter (PM) with an aerodynamic diameter less than 2.5 μm and 10 μm ($PM_{2.5}$, PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO), and ozone (O_3) (see Supplementary Fig. 2). A detailed description of the DEHM/UBM model can be found in Supplementary Text 1. The DEHM/UBM system is regularly being compared with available measurements. These ongoing routine validations ensure the high performance of the air pollution models (Brandt et al., 2003; Brandt et al., 2001; Frohn et al., 2022; Khan et al., 2019); however, they are not published for every model run, but are part of the standard national monitoring reporting on an annual basis (Ellermann et al., 2021). Second, the annual mean levels of air pollutants between 1979 and 2019 were linked to all residential addresses in Denmark with valid geographic coordinates according to the grid of 1 × 1 km^2. We then derived annual weighted mean air pollution levels for each child according to their residential addresses and moving history. We also computed lifetime cumulative exposure levels by taking the mean of yearly exposure levels in the prior years to the exit examinations year. For example, 16-year cumulative exposure was calculated as the mean of yearly exposure levels from birth to the 15th year, whereas 15-year cumulative exposure is the mean of yearly exposure levels from the 1st year to the 15th year after the birth year. The exposure in the birth year was taken as perinatal exposure, whereas subsequent age-specific postnatal exposure levels were calculated as the mean of 5-year annual exposures at age 1–5 years, age 6–10 years, and age 11–15 years.

2.4. Covariates

A priori, we adjusted for sex and school year to enhance precision. In addition, we identified the minimal sufficient covariate adjustment set using a directed acyclic graph (DAG) (Supplementary Fig. 3 and Supplementary Text 2). The covariates included maternal smoking recorded during pregnancy (never, ever), maternal education (≤, > 13 school years), and maternal annual income based on the year when the child turned 15 years old [<, ≥ mean (approximately 242,189 DKK or 36,650 USD after adjusting for Consumer Price Index normalized to the year of 2015 (Danmarks Statistik)]. Maternal education was defined based on mothers' highest completed education updated until the end of the study period (2019) and coded according to the Danish Education Classification (DISCED-15). Maternal education was divided into the low educational level (DISCED-15 = 10–39 or ≤ 13 years of education), which includes primary, secondary, and high school and vocational education, and the high educational level (DISCED-15 = 40–80 or > 13 years of education) which includes academy professions, professional bachelors, bachelor's, master's, and Ph.D. educations.

The abovementioned potential covariates were also examined as effect modifiers, along with other variables, including gestational age (<, ≥ 37 weeks), birth weight (<, ≥ 2500 g), small for gestational age (<, ≥ 10th percentile for gestational age between 23 and 44 weeks), and population density in the parish (the smallest administrative level in Denmark and subject to changes due to mergers or administrative reforms over time), which was measured as the number of persons in all age groups per km^2 in the school years (<, ≥ 1390 population/km^2, mean population density among the students with valid parish information).

2.5. Statistical analysis

For descriptive analyses, T-tests were employed to compare continuous variables, while Chi-square tests were used for categorical variables within subgroups. In correlation analyses involving pollutants and subject-specific grades, Pearson correlation coefficients were utilized.

In the main analysis, we constructed linear mixed-effects models to examine the association between yearly (birth, 1st, …, 15th year) and cumulative (birth-15th, 1st-15th, …, 14th-15th years) exposure to air pollution ($PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, O_3) and GPA. In addition, we compared the associations by certain exposure periods: perinatal, age 1–5 years, age 6–10 years, and age 11–15 years. We controlled for sex and school year in Model 1. We further adjusted for the individual's characteristics: maternal age, country of origin, maternal education and income, and parity in Model 2. In the two models, we included a random intercept for each school to take into account the high correlation of GPA within a school (proportion of the random intercept variance: 10.0 %), and therefore, we did not further adjust for variables of the school characteristics in the model. We also examined subject-specific grades (Danish literature, Danish writing, English, mathematics, and natural sciences) associated with 16-year-long cumulative exposure to air pollution.

We identified susceptible populations to the adverse effects of 16-year-long cumulative exposure to air pollution on academic achievement by investigating effect modification by sex, mother's country of origin (Danish vs. non-Danish mothers), small for gestational age (no vs. yes), parity (0 vs. 1+), maternal education (high vs. low), maternal income (low vs. high), maternal smoking during the pregnancy (never vs. ever), and population density (low vs. high). We added an interaction term for each effect modifier and the air pollutant in Model 2 to test the effect modification on the association between exposure to air pollution and academic achievement using the Wald statistic. Estimated associations were presented as changes in GPA or subject-specific grades with 95 % confidence intervals (CI) per interquartile range (1.8 μg/m^3, 2.0 μg/m^3, 5.9 μg/m^3, 4.1 μg/m^3, 30.0 μg/m^3, 4.7 μg/m^3) and fixed (5 μg/m^3, 5 μg/m^3, 10 μg/m^3, 10 μg/m^3, 50 μg/m^3, and 10 μg/m^3) increases in concentration levels of $PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, and O_3, respectively, to make them comparable to other international studies (Gartland et al., 2022; Strak et al., 2021; World Health, 2021). We compared associations across subject grades by examining the 95 % CI of the point estimates. Non-overlapping CI between the two subject grades indicated significant differences in the associations of exposure to air pollution with the respective subject grades at a significance level of 0.05 (Schenker and Gentleman, 2001).

We conducted a sensitivity analysis and an ad hoc analysis. As we observed that 18.7 % of included students had missing information on maternal smoking status during the pregnancy, we did not include the covariate in the main model. Instead, we adjusted for maternal smoking in a sensitivity analysis and compared the estimates of the associations with those in the main model in a complete dataset (n = 638,599) (Model 2). In an ad hoc analysis, we examined the association between 16-year-long exposure to air pollution and completeness of exit examinations in a conditional logistic regression model, which computed odd ratios (OR) of incomplete exit examinations per fixed increases in air pollution levels, adjusting for sex and school year with strata of schools. We did not adjust for maternal characteristics due to the limited contrast of covariates and exposure levels within schools of incomplete test takers.

We performed statistical analyses using R version 4.0.2 (The Comprehensive R Archive Network, Vienna, Austria; https://cran-r-project.org). A p-value of < 0.05 (two-tailed) was set as the threshold for statistical significance. According to Danish legislation, no ethical permission was required for register-based research; however, this study was approved by the local data protection authorities (University of Copenhagen, 514-0740/22-3000).

3. Results

We included 785,312 children born in Denmark between 1989 and 2005 who completed the exit examinations in 9th grade (mean age of 16) (Supplementary Fig. 1). More boys, children of younger mothers, and children born with low birth weight were either excluded from the study (Supplementary Table 1) or did not complete the exit examinations (Supplementary Table 2).

Among 785,312 complete test takers of the exit examinations, the mean GPA of exit examinations in 9th grade was 7.1 (standard deviation [SD]: 2.5) on a scale from −3 to 12. When we compared the mean GPA by children's characteristics, we observed relatively lower GPA in boys (6.7 for boys vs. 7.4 for girls), children born with low birth weight (6.8 for low vs. 7.1 normal birth weight), and children born as a second or later child (6.9 for ≥ 1 vs. 7.3 for null parity). Depending on maternal characteristics, the mean GPA varied: mothers' age at delivery (6.7 for younger vs. 7.4 for older mothers), maternal education (6.5 for low vs. 8.0 for high education), maternal income (6.5 for low vs. 7.8 for high income), and mothers' country of origin (6.1 for non-Danish vs. 7.1 for Danish mothers) (Table 1).

Mean subject-specific grade was highest in Danish literature (7.6), followed by English (7.5), Mathematics (7.0), natural sciences (6.6), and Danish writing (6.5), showing moderate correlations among the five exam subjects (Pearson's correlation coefficients, 0.5–0.6; Supplementary Table 3).

The spatial distribution of 16-year mean exposure levels of air pollutants by the parish in the year of 9th grade is shown in Supplementary Fig. 2. Cumulative exposure to the pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, and CO) was positively correlated with each other (Pearson correlation coefficients ranging between 0.4 and 0.8), while O_3 was negatively correlated with other pollutants (Supplementary Table 4). Yearly, cumulative, and age-specific exposure levels of most pollutants declined over time, except O_3 (Supplementary Table 5, Supplementary Fig. 4, and Supplementary Table 6, respectively). Cumulative exposure levels were generally higher among children who were born as small for gestational age or the first child, attended a large school, or lived in highly populated areas, or children of mothers who ever smoked or immigrated to Denmark (except PM_{10}) (Supplementary Table 7).

Both yearly and cumulative exposure to $PM_{2.5}$ and PM_{10} showed significantly negative associations with GPA (Supplementary Fig. 5). Cumulative higher exposure to $PM_{2.5}$ and PM_{10} over a sixteen-year period was associated with lower GPA, with estimates of −0.99 (95 % CI: −1.05, −0.92) and −0.46 (−0.50, −0.41) per 5 μg/m^3 increase, respectively (Table 2). Further adjustment for maternal smoking attenuated the associations, but the associations were still significant (Supplementary Table 8). We observed similar strong associations of PM with incomplete school examinations (Supplementary Table 9). In an analysis specific to exposure windows, we observed stronger associations between later childhood (age 11–15 years) exposure to $PM_{2.5}$ and GPA compared to perinatal or earlier childhood (Age 1–10 years) exposure to $PM_{2.5}$ (Table 3).

Table 1
Characteristics of the study population at birth and grade 9 and their Grade Point Average of the exit examinations.

	N (column %), mean ± SD	GPA, mean ± SD
Total	785,312	7.1 ± 2.5
Sex		
Boys	392,524 (50.0)	6.7 ± 2.5
Girls	392,788 (50.0)	7.4 ± 2.5
Maternal age at birth (years)	29.2 ± 4.7	
Younger mothers (<30 years)	427,341 (54.4)	6.7 ± 2.5
Older mothers (≥30 years)	357,971 (45.6)	7.4 ± 2.5
Gestational age (weeks)	39.6 ± 1.9	
Normal (≥37 weeks)	740,990 (94.4)	7.1 ± 2.5
Preterm (<37 weeks)	44,322 (5.6)	7.0 ± 2.5
Birth weight (g)	3493.6 ± 604.1	
Normal (≥2500 g)	748,570 (95.3)	7.1 ± 2.5
Low (<2500 g)	36,742 (4.7)	6.8 ± 2.5
Small for gestational age		
No	715,181 (91.1)	7.1 ± 2.5
Yes	70,072 (8.9)	6.6 ± 2.6
Missing	59	
Maternal smoking		
Never	489,151 (76.6)	7.4 ± 2.5
Ever	149,448 (23.4)	6.3 ± 2.5
Missing	146,713	
Parity		
0	342,990 (43.7)	7.3 ± 2.5
1+	442,322 (56.3)	6.9 ± 2.5
Maternal education		
Higher (>13 years)	293,264 (37.3)	8.0 ± 2.3
Lower (≤13 years)	492,048 (62.7)	6.5 ± 2.5
Maternal income	248.9 ± 269.5	
High (≥242,189DKK)	329,662 (42.0)	7.8 ± 2.3
Low (<242,189DKK)	455,650 (58.0)	6.5 ± 2.5
Country of origin		
Danish	736,376 (93.8)	7.1 ± 2.5
Non-Danish	48,936 (6.2)	6.1 ± 2.6
Age by the end of the school year	16.0 ± 0.4	
< 16 years	401,386 (51.1)	7.2 ± 2.5
≥16 years	383,926 (48.9)	6.9 ± 2.6
Parish-level population density		
Low (<1390 per 1 km^2)	579,286 (76.2)	7.0 ± 2.5
High (≥1390 per 1 km^2)	180,972 (23.8)	7.3 ± 2.6
Missing	25,054	

Negative associations between lifetime exposure to PM and GPA were significantly different by individuals' characteristics, including sex and mothers' country of origin, parity, maternal education, maternal smoking status, and population density (Fig. 1; Supplementary Table 10). In particular, lower GPA associated with 16-year-long exposure to $PM_{2.5}$ was more pronounced in girls (−1.29 [95 % CI: −1.36, −1.21] per 5 μg/m^3 increase in $PM_{2.5}$) than boys −0.69 [95 % CI: −0.76, −0.62]). Children of non-Danish mothers showed greater change in GPA per increase in $PM_{2.5}$ (−1.80 [95 % CI: −1.91, −1.69]) than those of Danish mothers (−0.95 [95 % CI: −1.02, −0.88]) (Fig. 1, Supplementary Table 10).

For the associations of subject-specific grades with lifetime exposure to PM, we observed stronger negative associations with grades in mathematics (−1.67 [95 % CI: −1.76, −1.59] and −0.65 [95 % CI: −0.70, −0.59] per 5 μg/m^3 increase in $PM_{2.5}$ and PM_{10}, respectively) and natural sciences (−1.10 [95 % CI: −1.20, −1.01] and −0.57 [95 % CI: −0.63, −0.50] for $PM_{2.5}$ and PM_{10}, respectively) than in Danish and English ranging between −0.75 and −0.44 for $PM_{2.5}$ and −0.41 and

Table 3
Associations between perinatal and postnatal exposure to air pollution and Grade Point Average (GPA) in 9th grade exit examination (n = 785,312).

Exposure to air pollutants	Per fixed increases in exposure (μg/m^3)	Change in GPA (95 % Confidence Intervals)			
		Perinatal exposure	Postnatal exposure		
			Age 1–5 years	Age 6–10 years	Age 11–15 years
$PM_{2.5}$	5	−0.24 (−0.27, −0.22)	−0.42 (−0.46, −0.37)	−0.55 (−0.61, −0.49)	−1.13 (−1.21, −1.06)
PM_{10}	5	−0.19 (−0.21, −0.17)	−0.27 (−0.30, −0.24)	−0.17 (−0.20, −0.13)	−0.47 (−0.51, −0.42)
NO_2	10	0.12 (0.11, 0.14)	0.05 (0.03, 0.07)	−0.08 (−0.11, −0.06)	−0.26 (−0.29, −0.23)
SO_2	10	−0.01 (−0.01, 0.00)	−0.05 (−0.06, −0.04)	−0.18 (−0.20, −0.16)	−0.37 (−0.41, −0.33)
CO	50	0.09 (0.08, 0.10)	0.02 (0.00, 0.03)	−0.17 (−0.20, −0.15)	−0.38 (−0.41, −0.34)
O_3	10	−0.17 (−0.18, −0.15)	−0.1 (−0.12, −0.08)	0.07 (0.04, 0.10)	0.21 (0.18, 0.25)

$PM_{2.5}$: particulate matter with a diameter less than 2.5 μm; PM_{10}: particulate matter with a diameter less than 10 μm; NO_2: nitrogen dioxide; SO_2: sulfur dioxide; CO: carbon monoxide; O_3: ozone.
Models adjusted for sex, school year, maternal age, mother's country of origin, maternal income, and parity with a random intercept of each school.

Table 2
Associations between 16-year-long cumulative exposure to air pollution and Grade Point Average (GPA) in 9th grade exit examination (n = 785,312).

16-year long cumulative exposure (from birth year to 15 years)	Per IQR increases in exposure (μg/m^3)	Change in GPA (95 % Confidence Intervals)		Per fixed increases in exposure (μg/m^3)	Change in GPA (95 % Confidence Intervals)	
		Model 1	Model 2		Model 1	Model 2
$PM_{2.5}$	1.8	−0.32 (−0.35, −0.30)	−0.36 (−0.38, −0.33)	5	−0.88 (−0.96, −0.81)	−0.99 (−1.05, −0.92)
PM_{10}	2.1	−0.18 (−0.20, −0.16)	−0.19 (−0.21, −0.17)	5	−0.43 (−0.48, −0.39)	−0.46 (−0.50, −0.41)
NO_2	5.9	0.06 (0.04, 0.07)	−0.02 (−0.03, 0.00)	10	0.10 (0.07, 0.12)	−0.03 (−0.05, 0.00)
SO_2	4.2	−0.04 (−0.04, −0.03)	−0.05 (−0.05, −0.04)	10	−0.09 (−0.10, −0.07)	−0.12 (−0.13, −0.10)
CO	30.2	0.07 (0.06, 0.09)	−0.04 (−0.05, −0.02)	50	0.12 (0.10, 0.15)	−0.07 (−0.09, −0.04)
O_3	4.8	−0.08 (−0.09, −0.06)	−0.01 (−0.02, 0.00)	10	−0.16 (−0.19, −0.13)	−0.02 (−0.05, 0.01)

IQR: Interquartile range; $PM_{2.5}$: particulate matter with a diameter less than 2.5 μm; PM_{10}: particulate matter with a diameter less than 10 μm; NO_2: nitrogen dioxide; SO_2: sulfur dioxide; CO: carbon monoxide; O_3: ozone.
Model 1 adjusted for sex and school year with a random intercept of each school; Model 2 additionally adjusted for maternal age, mother's country of origin, maternal income, and parity.

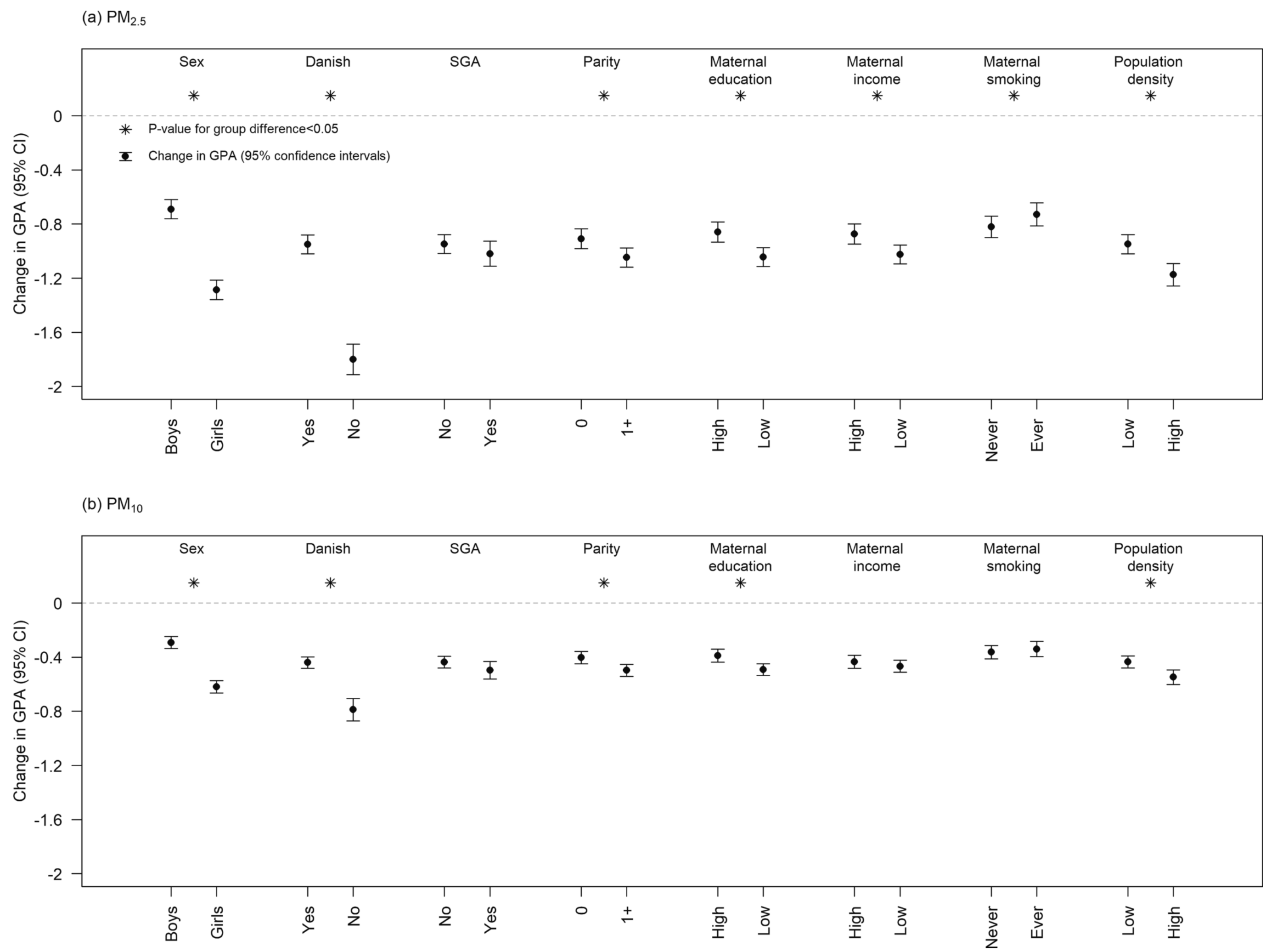

Fig. 1. Associations between 16-year-long exposure to air pollution ($PM_{2.5}$ and PM_{10}) and Grade Point Average (GPA) in 9th grade exit examination by subgroups. $PM_{2.5}$: particulate matter with a diameter less than 2.5 μm (per 5 μg/m^3); PM_{10}: particulate matter with a diameter less than 10 μm (per 10 μg/m^3); SGA: small for gestational age; CI: Confidence Intervals Models were adjusted for sex and school year, maternal age, mother's country of origin, maternal income, and parity with a random intercept of each school.

−0.27 for PM_{10} (Fig. 2, Supplementary Table 10). Confidence intervals of the associations in mathematics and natural sciences did not overlap with those in Danish and English.

While perinatal and postnatal (during both earlier and later childhood) exposure to PM consistently showed negative associations with GPA, only later childhood (≥6 years) exposure to gaseous pollutants such as NO_2, SO_2, and CO exhibited distinctively negative associations with GPA (Table 3, Supplementary Fig. 5). Similar to the associations with PM, we also observed greater negative associations between the gaseous pollutants (NO_2, SO_2, and CO) and GPA among girls and children of non-Danish mothers than corresponding groups (Supplementary Fig. 6).

4. Discussion

In this nationwide cohort study of 785,312 Danish children, higher lifetime exposure to PM showed strong associations with lower GPAs of the mandatory exit examinations in 9th grade. In particular, negative associations were stronger among girls and children of non-Danish mothers. Among the five mandatory subject exams, grades in mathematics and natural sciences were more influenced by air pollution exposure than grades in language-related subjects.

Our study results were generally in line with previous longitudinal studies examining cumulative or yearly exposure to PM (Balalian et al., 2022; Grineski et al., 2020; Shier et al., 2019; Stingone et al., 2016). Shier et al. (2019) found that 4–6 year mean exposure to $PM_{2.5}$ between kindergarten to primary schools was inversely associated with test scores in reading and mathematics in 3rd and 5th grades (approximately 10,000 students for each grade) in a nationally representative survey of the U.S. kindergartners (Shier et al., 2019). Yearly exposure to diesel PM in the birth year was strongly associated with lower math scores but not with reading scores in two longitudinal studies with approximately 200,000 3rd grade students living in New York City, N.Y., U.S. (Balalian et al., 2022; Stingone et al., 2016). However, another longitudinal study found no associations between lifetime (5 years) exposure to $PM_{2.5}$ and mathematics and reading abilities in kindergarten in several states in the U.S. (Marcotte, 2017).

Cumulative exposure to $PM_{2.5}$ and PM_{10} throughout the lifetime as well as in shorter time windows from the birth year, showed negative associations with lower GPA and incomplete school examinations. This may imply that both earlier and later exposure to PM could impact academic achievement via neurocognitive developmental effects (Cserbik et al., 2020) or inflammatory response (Brockmeyer and D'Angiulli, 2016). In contrast to PM, we observed that cumulative exposure to gaseous pollutants was weakly associated with lower GPA and incomplete school examinations, although later childhood exposure to NO_2

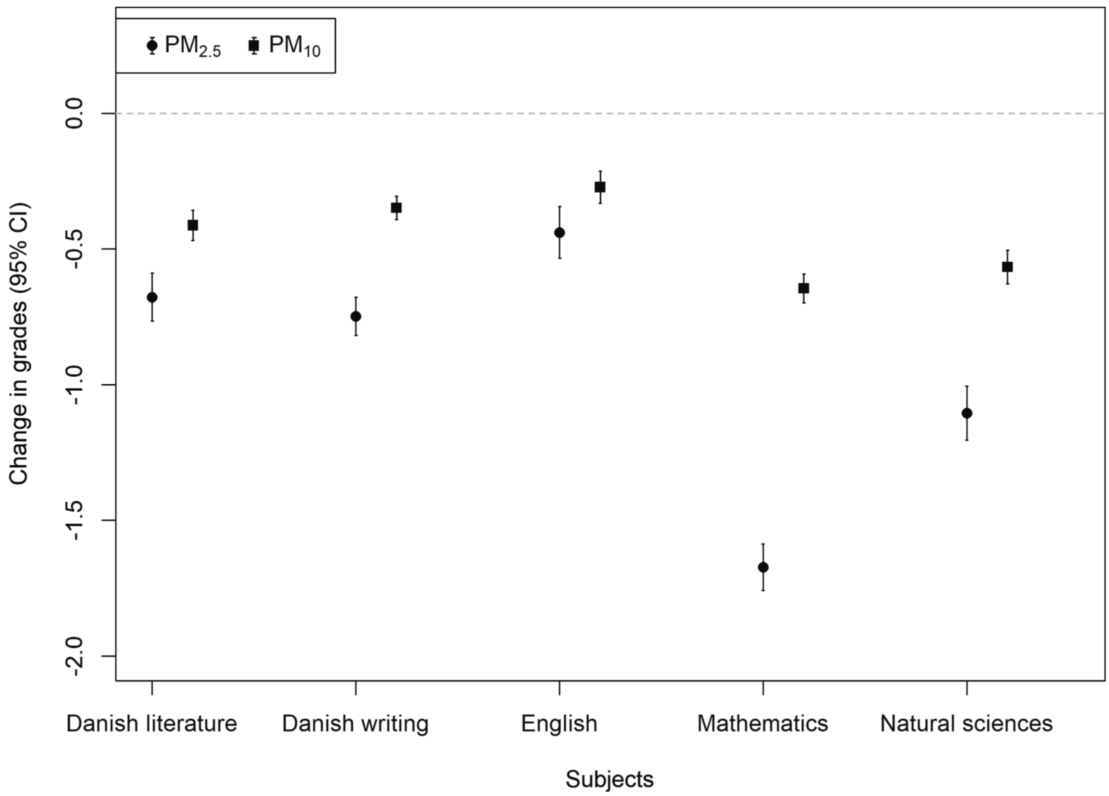

Fig. 2. Associations between 16-year-long exposure to air pollution ($PM_{2.5}$ and PM_{10}) and subject-specific grades in 9th grade exit examination. $PM_{2.5}$: particulate matter with a diameter less than 2.5 μm (per 5 μg/m^3); PM_{10}: particulate matter with a diameter less than 10 μm (per 10 μg/m^3); CI: Confidence Intervals Models were adjusted for sex and school year, maternal age, mother's country of origin, maternal income, and parity with a random intercept of each school.

and CO in recent years (e.g., from the 6th to 15th year) was negatively associated with GPA. As there were no previous studies examining exposure levels of gaseous pollutants (e.g., NO_2) from birth to school years, further studies with lifetime exposure assessment for the gaseous pollutants are needed to gain a comprehensive understanding of critical windows in development and the impacts of different air pollutants on cognitive development.

When comparing the differences in effect sizes of the associations between air pollution and GPA across subgroups, we observed notable distinctions based on sex and the mother's country of origin, as opposed to other effect modifiers. In particular, girls and children of non-Danish mothers showed noticeably lower GPA associated with 16-year-long exposure to air pollution, compared to the corresponding populations. The sex-specific association between air pollution and cognitive development may be dependent on the exposure window (or life stage), hormonal status, and cognitive domain (Chiu et al., 2016; Clougherty, 2010). Our finding of stronger associations among girls in 9th grade was in line with those from a review showing that boys in early childhood and girls in later childhood respond more to air pollution exposure than the opposite sex in the corresponding period (Clougherty, 2010).

Children of non-Danish mothers showed greater reductions in GPA associated with exposure to air pollution even though they already had substantially lower GPA levels compared to children of Danish mothers. Although we do not have a clear explanation for the different associations by mothers' country of origin, we can postulate that non-Danish mothers may speak their mother tongue languages other than Danish at home. Thus, children of non-Danish-speaking mothers might not only be exposed to high air pollution levels but also be more susceptible to adverse effects on their already-lower academic achievement because of having fewer native Danish relations, parental Danish language proficiency, and information on learning support compared to children of Danish mothers.

While the five subject grades were strongly associated with $PM_{2.5}$ and PM_{10}, the negative associations were greater with grades in mathematics and natural sciences than in Danish (literature and writing) and English in the present study. Similar to our findings, four of five U.S. studies showed that students' test scores in mathematics, science, and reading were significantly associated with air pollution. Among the subject exams, test scores in mathematics or science were lower than in reading (English) associated with exposure to air pollution (Balalian et al., 2022; Grineski et al., 2020; Lu et al., 2021; Stingone et al., 2016). Mathematics and science are primarily linked to fluid intelligence, which pertains to the capacity for problem-solving and logical reasoning (Green et al., 2017). Specifically, the frontal region of the brain is closely related to fluid intelligence (Cattell 1987). While we do not have a definitive explanation for the negative impact of air pollution on specific subjects, it can thus be suggested that air pollution affects particular areas of neurocognitive development, particularly the frontal domain, where reasoning, learning, and creativity converge (Collins and Koechlin 2012). However, other studies pointed to associations between pollution and the hippocampus, which is also connected to mathematical thinking (Margolis et al., 2022; Tseng et al., 2019; Woodward et al., 2018). Therefore, more research is needed to draw firm conclusions.

This study has several strengths. First, the study is based on almost 800,000 children followed from birth to 15 years. Moreover, using historical residential data for each student for 16 years, we assessed individuals' lifetime exposure to air pollution with high spatial and temporal resolution and investigated the association with academic achievement in 9th grade. Second, we were able to consider maternal and child characteristics in the model and were able to eliminate some confounding effects, such as socioeconomic factors that are associated with lifetime exposure to air pollution and students' academic achievement. Moreover, other potential confounders or effect modifiers, including maternal smoking, were addressed in sensitivity and stratified analyses. Third, although the population had a relatively small proportion of minorities in a homogenous ethnic country, we still had the statistical power to detect the susceptible population to the adverse effects of air pollution on academic achievement.

This study also has several limitations. First, we were not able to assess their time spent at home or school, including physical activities, which, to some extent, may have led to exposure misclassification. Second, we could not rule out the possibility of residual confounding, such as child adversity, other than maternal income or education. Further studies need to consider integrated factors of children's social and home environments. Third, we did not consider other spatially varying factors. For example, road traffic noise and green space are spatially correlated with air pollution exposure levels and associated with neurocognitive development or school performance. Synergistic and independent effects of air pollution with noise and greenness should be examined in future studies. Fourth, the main analysis included students who attended a school and completed the five mandatory exit examinations. However, the included students had socially and academically better positions than the excluded students, and the risk of incomplete examinations was greater among children with higher exposure levels than those with lower exposure levels (Supplementary Table 9). Therefore, our study may have a selection bias, resulting in underestimated associations. Thus, caution must be exercised in the interpretation of the results. Fifth, while GPA and subject grades provide quantifiable data that measures and compares students' cognitive skills, including critical thinking, problem-solving, and information processing, the use of the exit examinations as a marker for neurocognitive development has a potential limitation because the grades of the exit examinations are not solely affected by students' cognition but also by other factors, such as the learning environment at home or school. Moreover, exit examinations may not measure the full spectrum of cognitive abilities, be inherent to cultural biases, focus on memorization, and not reflect individual differences in students' learning styles or learning rates. Therefore, a holistic approach that includes various assessment forms, consideration of individual differences, and an understanding of diverse cognitive abilities is essential. Sixth, GPA was calculated as the mean of the weighted exam subject grades, reflecting the weighted average of 7-point scale test scores. Although students who passed the exam with grades between 2 and 12 followed a normal distribution (Haastrup, 2004), the unit intervals are not equal, and the range is bounded. Consequently, the data used in the linear mixed models and correlation analysis may not conform to the linearity assumption, resulting in potentially inaccurate estimates and confidence intervals, especially at the higher and lower ends of the GPA spectrum. Seventh, in comparing associations across subject grades, we assessed the 95 % CI of the estimates, considering the intricate computation of covariance structure in two distinct linear mixed models. While we refrain from speculating on substantial changes in result interpretation, it is crucial to exercise caution when considering this comparison. Eighth, in contrast to PM, exposure to gaseous pollutants only in later childhood was negatively associated with GPA. While this phenomenon implies strong effects of exposure to gaseous pollutants, mainly from traffic, in later childhood on academic achievement, it may reflect the close time proximity between the measurements of exposure and outcome. Hence, caution is warranted in interpreting the results. Finally, we conducted our research in a homogeneous ethnic country. As a result, the findings of our study cannot be generalized to other populations with different racial/ethnic backgrounds or educational systems.

5. Conclusions

Lifetime exposure to fine particles and later childhood exposure to gaseous pollutants were strongly associated with children's academic achievement in 9th grade. The negative associations of exposure to fine particles with academic achievement were stronger in mathematics and natural sciences than in language-related subjects. Moreover, exposure to high levels of fine particles and gaseous pollutants was more strongly associated with students' academic achievement among girls and children of non-Danish mothers than among boys and children of Danish mothers. These findings provide evidence for the need for pollution control and urban planning to protect biologically and socially disadvantaged populations from the potential adverse effects of air pollution on neurocognitive development.

CRediT authorship contribution statement

Youn-Hee Lim: Writing – original draft, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Josephine Funck Bilsteen:** Writing – review & editing, Investigation, Conceptualization. **Laust Hvas Mortensen:** Writing – review & editing, Data curation, Conceptualization. **Linnea Ranja Mignon Lanzky:** Writing – review & editing, Data curation. **Jiawei Zhang:** Writing – review & editing, Formal analysis. **Stéphane Tuffier:** Writing – review & editing, Data curation. **Jørgen Brandt:** Writing – review & editing, Data curation. **Matthias Ketzel:** Writing – review & editing, Data curation. **Trine Flensborg-Madsen:** Writing – review & editing, Conceptualization. **Cathrine Lawaetz Wimmelmann:** Writing – review & editing, Conceptualization. **Gunhild Tidemann Okholm:** Writing – review & editing, Conceptualization. **Emilie Rune Hegelund:** Writing – review & editing, Formal analysis, Conceptualization. **George Maria Napolitano:** Writing – review & editing, Formal analysis, Conceptualization. **Zorana Jovanovic Andersen:** Writing – review & editing, Funding acquisition. **Steffen Loft:** Writing – review & editing, Writing – original draft, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary data

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