Exposure to outdoor residential noise during pregnancy, embryonic size, fetal growth, and birth outcomes

Supplementary Material

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Methods S1. Description of noise exposure assessment.

Total noise levels were calculated by adding up the 4 different noise sources (road traffic, railway, aircraft and industry) in the sound pressure scale by the following formula:

$$Total\ noise = 10lg\left(10^{\frac{Traffic}{10}} + 10^{\frac{Railway}{10}} + 10^{\frac{Aircraft}{10}} + 10^{\frac{Industry}{10}}\right)$$

L_{DEN} was calculated by the following formula:

$$Lden = 10lg\frac{1}{24}\left(12 \times 10\frac{Lday}{10} + 4 \times 10\frac{Levening + 5}{10} + 8 \times 10\frac{Lnight + 10}{10}\right)$$

L_{DAY} and $L_{EVENING}$ were respectively the A-weighted average sound levels assessed during the day (12h: 7a.m.–7p.m.) and the evening (4h: 7p.m.–11p.m.). L_{NIGHT} was the A-weighted average sound level over the night period (8h: 11p.m.-7a.m.)

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Methods S2. Description of ultrasound measurement protocol.

Ultrasound examinations were performed using an Aloka® model SSD-1700 (Tokyo, Japan) or the ATL-Philips® Model HDI 5000 (Seattle, WA, USA). CRL was measured in early pregnancy if the visit was before 13+0 weeks of gestation. Fetal growth measurements, consisting of HC, AC and FL were measured during each ultrasound examination. Standard ultrasound planes for fetal measurements were used.[1-3] In case of limited visibility with abdominal scanning in early pregnancy, transvaginal ultrasound was performed. All sonographers were trained following the guidelines from The Fetal Medicine Foundation to achieve optimal reproducibility. Frequent quality checks were performed to assess the correctness of the fetal growth measurements.[4]

Figure S1. Directed Acyclic Graph (DAG) representing the pathways between noise exposure during pregnancy and embryonic size and fetal growth.
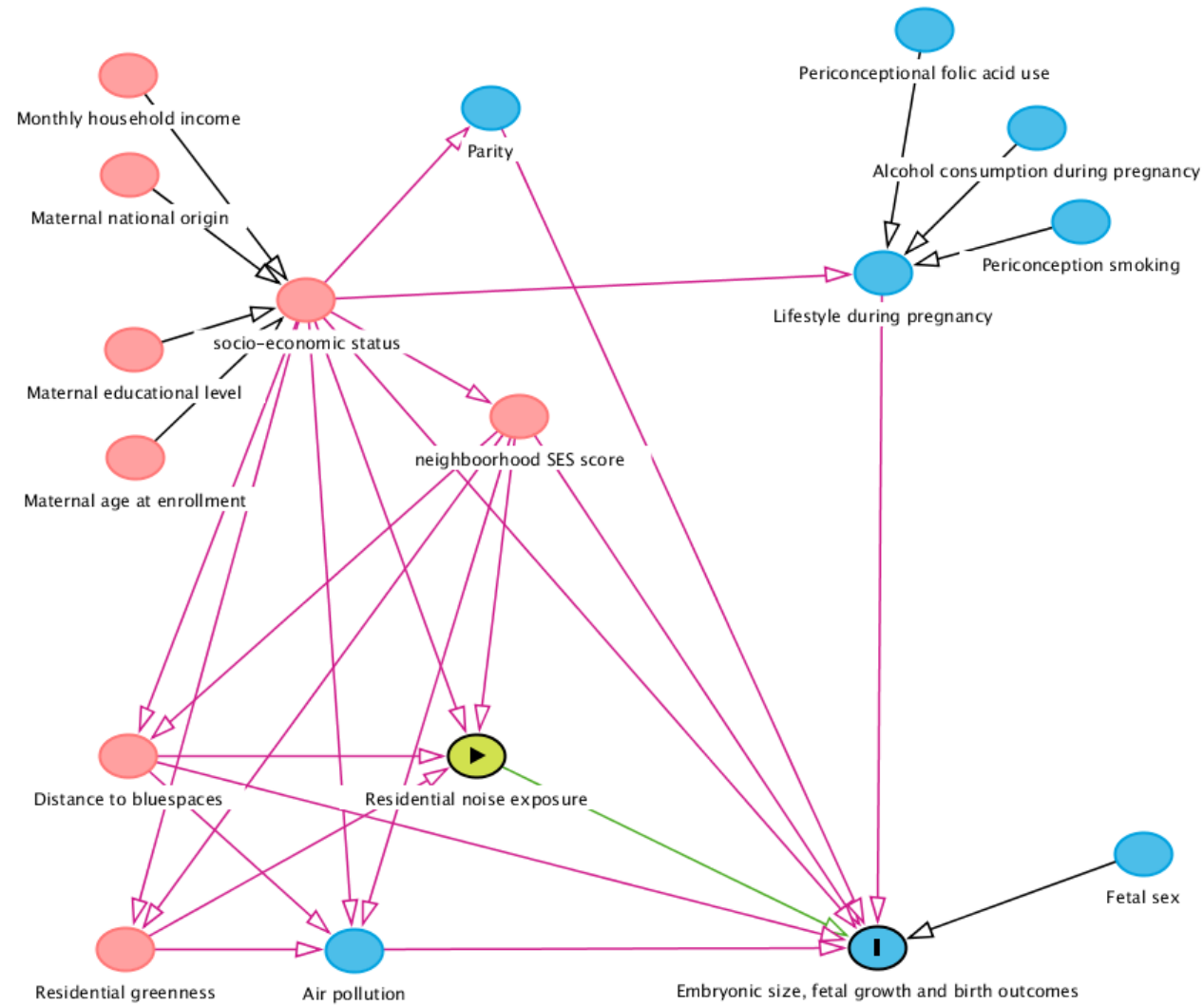
Table S1. Characteristics of the participants in observed and imputed datasets in the study population.

Maternal characteristics	Study population (n=7947) Observed	Imputed	% Imputed
Maternal age at enrollment (years)	29.8 (±5.3)	29.8 (±5.3)	0.0
Maternal national origin			4.9
Dutch	49.9	48.7	
Moroccan	7.1	7.5	
Turkish	9.4	9.8	
Surinamese/Dutch Antilles	12.3	12.5	
Other European	7.6	7.6	
Other non-European	13.8	13.9	
Maternal educational level			8.5
Low	26.9	12.6	
Medium	30.6	46.7	
High	42.5	40.7	
Monthly household income (€)			22.9
<900 euro	12.0	14.7	
900-1600 euro	17.8	21.0	
1600-2200 euro	15.1	15.8	
>2200 euro	55.1	48.5	
Periconceptional smoking (yes *vs.* no)	27.0	27.2	12.4
Alcohol consumption during pregnancy			10.4
Never in pregnancy	47.6	49.0	
Until pregnancy was known	12.7	12.5	
Continued in pregnancy occasionally	32.2	31.3	
Continued in pregnancy frequently	7.5	7.2	
Periconceptional folic acid use (yes *vs.* no)	40.5	38.0	25.5
Parity			1.1
0 children	55.0	55.0	
1 child	30.4	30.4	
2 or more children	14.6	14.6	
Residential greenness	0.37 (±0.1)	0.37 (±0.1)	6.2
Distance to blue space (m)	281.8 (135.2; 484.4)	281.6 (134.8; 482.4)	6.2
Residential neighbourhood SES score	-1.1 (-1.4)	-1.1 (1.4)	0.1
Child characteristics			
Sex (boy *vs.* girl)	50.2	50.2	0.0

Abbreviations: SES, socioeconomic status; dB, decibel. Data are presented as percentage for categorical variables, mean (SD) for continuous variables with a normal distribution, and median (25th; 75th percentile) for continuous variables with a skewed distribution.

Table S2. Characteristics of the participants eligible and non-eligible for inclusion in the analyses of the study population.

	Crown-rump length			Length at birth			Weight at birth		
	Included (N=1527)	Not included (N=7151)	P-value[1]	Included (N=5034)	Not included (N=3644)	P-value[1]	Included (N=7919)	Not included (N=759)	P-value[1]
Maternal age at enrolment (years)	30.9 (4.6)	29.3 (5.4)	<0.01	29.9 (5.2)	29.3 (5.5)	<0.01	29.8(5.3)	28.0 (5.6)	<0.01
Maternal national origin			<0.01			<0.01			<0.01
Dutch	62.0	45.9		53.0	42.7		50.0	35.8	
Moroccan	3.7	7.8		6.4	7.9		7.0	6.8	
Turkish	6.3	9.9		9.0	9.6		9.4	7.7	
Surinamese/Dutch Antilles	8.1	13.6		11.0	14.9		12.2	16.9	
Other European	8.8	7.7		7.8	8.1		7.6	11.5	
Other Non-European	11.0	15.1		12.7	16.8		13.8	21.3	
Maternal educational level			<0.01			<0.01			<0.01
Low	16.6	29.6		25.1	30.3		26.8	31.7	
Medium	28.1	31.6		31.2	30.6		30.6	35.6	
High	55.3	38.7		43.6	39.1		42.6	32.7	
Monthly household income (€)			<0.01			<0.01			<0.01
<900	5.4	14.4		10.8	15.4		11.9	22.0	
900-1600	13.1	19.6		16.4	21.4		17.7	26.6	
1600-2200	13.6	15.4		15.4	14.5		15.1	13.7	
>2200	67.9	50.6		57.4	48.6		55.2	37.7	
Parity			<0.01			<0.01			<0.01
0 children	58.5	55.0		54.5	57.3		55.0	62.7	
1 child	31.7	29.4		31.6	27.4		30.4	23.6	
2 or more children	9.9	15.6		13.9	15.3		14.6	13.7	
Periconceptional smoking			0.12			0.14			0.15
Yes	25.5	27.6		26.6	28.2		27.0	29.7	
No	74.5	72.4		73.4	71.8		73.0	70.3	
Alcohol consumption during pregnancy			<0.01			<0.01			<0.01
Never in pregnancy	37.3	50.5		46.1	50.8		47.6	53.6	
Until pregnancy was known	15.5	12.4		12.7	13.4		12.7	16.2	
Continued in pregnancy occasionally	37.1	30.5		33.5	29.1		32.2	25.6	
Continued in pregnancy frequently	10.1	6.6		7.7	6.7		7.5	4.6	
Periconceptional folic acid use			<0.01			<0.01			<0.01
Yes	53.8	36.0		42.5	34.8		40.6	26.0	
No	46.2	64.0		57.5	65.2		59.5	74.0	
Residential neighbourhood SES score	-0.8 (1.4)	-1.2 (1.4)	<0.01	-1.0 (1.4)	-1.3 (1.4)	<0.01	-1.1 (1.4)	-1.4 (1.3)	0.03
Residential greenness	0.4 (0.1)	0.4 (0.1)	0.12	0.4 (0.1)	0.4 (0.1)	<0.01	0.4 (0.1)	0.4 (0.1)	<0.01
Fetal sex			0.51			0.90			0.19
Boy	49.6	50.6		50.4	50.5		50.2	52.9	
Girl	50.4	49.4		49.6	49.5		49.8	47.1	

Abbreviations: SES, socioeconomic status. Values are percentage for categorical and mean (±SD) for continuous variables with a normal distribution, and median (25th; 75th percentile) for continuous variables with a skewed distribution. [1] χ^2 test was used for categorical variables, two-sample t-test for continuous variables with a normal distribution, and Wilcoxon Rank Sum test for continuous variables with a skewed distribution.

Table S3. List of variables explored in logistic regression model to calculate inverse probability of attrition weights in the study population, and those included in the final calculations.

Variables	Embryonic size Crown-rump length	Fetal growth Length	Fetal growth Head circumference	Fetal growth Weight	Neonatal anthropometrics at birth Length	Neonatal anthropometrics at birth Head circumference	Neonatal anthropometrics at birth Weight
Maternal age at enrollment	x			x	x	x	x
Pre-pregnancy BMI					x		
Maternal national origin	x	x		x	x		
Maternal educational level	x			x			
Monthly household income	x	x	x	x	x	x	x
Periconceptional smoking	x			x		x	
Alcohol consumption during pregnancy	x	x	x	x		x	x
Periconceptional folic acid use	x	x	x	x			x
Parity	x	x	x	x	x	x	x
Residential greenness	x			x	x		
Residential neighbourhood SES score	x	x	x		x	x	

Abbreviations: BMI, body mass index; SES, socioeconomic status

Table S4. Pearson correlations between different noise sources, natural spaces and different air pollutants

	Total noise	Road traffic noise	Railway noise	NDVI 300m	Distance to blue spaces	NO$_2$	PM$_{2.5}$
Total noise	1.00	0.97	0.21	-0.13	-0.01	0.30	0.35
Road traffic noise	0.97	1.00	0.14	-0.14	-0.01	0.36	0.38
Railway noise	0.21	0.14	1.00	0.10	0.16	0.09	0.28
Distance to blue spaces	-0.01	-0.01	0.16	0.18	1.00	-0.04	0.18
NDVI 300m	-0.13	-0.14	0.10	1.00	0.18	-0.28	-0.09
NO$_2$	0.30	0.36	0.09	-0.28	-0.04	1.00	0.67
PM$_{2.5}$	0.35	0.38	0.28	-0.09	-0.01	0.67	1.00

Abbreviations: NDVI 300m, normalized difference vegetation index, 300m buffer ; NO$_2$, nitrogen dioxide; PM2.5, particulate matter with a an aerodynamic diameter less than 2.5μm.

Table S5. Relationship between covariates and total noise exposure and outcomes.

	Study population (n=7947)							
	Total noise exposure (Δ10dB)		Crown-rump length		Length at birth		Weight at birth	
	Mean (SD)/ Correlation	P-value[1]	Mean (SD)/ Correlation	P-value[1]	Mean (SD)/ Correlation	P-value[1]	Mean (SD)/ Correlation	P-value[1]
Maternal age at enrolment (years)	0.0	0.12	0.1	<0.01	0.1	<0.01	0.1	<0.01
Maternal national origin		0.18		0.13		<0.01		<0.01
Dutch	5.6 (0.7)		0.01 (0.9)		50.4 (2.4)		3484.0 (557)	
Moroccan	5.5 (0.7)		0.22 (1.2)		50.3 (2.3)		3527.7 (496)	
Turkish	5.6 (0.7)		0.05 (1.1)		49.9 (2.2)		3418.3 (525)	
Surinamese/Dutch Antilles	5.6 (0.7)		-0.13 (1.1)		49.6 (2.3)		3189.8 (565)	
Other European	5.6 (0.7)		0.06(1.0)		50.2 (2.3)		3431.9 (533)	
Other non-European	5.6 (0.7)		0.14 (1.0)		49.9 (2.4)		3337.6 (549)	
Maternal educational level		0.27		0.27		<0.01		<0.01
Low	5.6 (0.7)		0.07 (1.1)		49.9 (2.3)		3340.3 (565)	
Medium	5.6 (0.7)		-0.03 (1.0)		50.1 (2.4)		3384.0 (545)	
High	5.6 (0.7)		0.045(0.9)		50.5 (2.4)		3502.7 (543)	
Monthly household income (€)		0.68		0.85		<0.01		<0.01
<900	5.6 (0.7)		-0.01 (1.1)		49.6 (2.4)		3285.6 (563)	
900-1600	5.6 (0.7)		0.08 (1.0)		49.9 (2.4)		3367.9 (559)	
1600-2200	5.6 (0.7)		0.04 (1.1)		50.3 (2.3)		3408.6 (548)	
>2200	5.6 (0.7)		0.02 (0.9)		50.5 (2.4)		3486.2 (547)	
Parity		<0.01		0.07		<0.01		<0.01
0 children	5.6 (0.7)		-0.02 (1.0)		50.0 (2.4)		3337.8 (555)	
1 child	5.6 (0.7)		0.11 (1.0)		50.4 (2.3)		3511.4 (530)	
2 or more children	5.5 (0.7)		0.05 (0.9)		50.5 (2.3)		3537.6 (569)	
Periconceptional smoking		<0.01		0.26		<0.01		<0.01
Yes	5.6 (0.7)		-0.02 (1.0)		49.9 (2.4)		3317.2 (563)	
No	5.6 (0.7)		0.04 (1.0)		50.3 (2.4)		3458.4 (550)	
Alcohol consumption during pregnancy		<0.01		0.38		0.01		<0.01
Never in pregnancy	5.6 (0.7)		-0.00 (1.0)		50.1 (2.3)		3402.0 (554)	
Until pregnancy was known	5.6 (0.7)		0.09 (1.0)		50.1 (2.5)		3358.9 (565)	
Continued in pregnancy occasionally	5.6 (0.7)		0.06 (0.9)		50.3 (2.4)		3448.2 (557)	
Continued in pregnancy frequently	5.7 (0.7)		-0.05 (0.9)		50.4 (2.4)		3522.9 (536)	
Periconceptional folic acid use		0.78		0.89		<0.01		<0.01
Yes	5.6 (0.7)		0.03 (0.9)		50.4 (2.4)		3482.5 (551)	
No	5.6 (0.7)		0.03 (1.0)		50.1 (2.4)		3381.6 (557)	
Residential neighbourhood SES score	-0.1	<0.01	0.0	0.50	0.1	<0.01	0.1	<0.01
Residential greenness	-0.1	<0.01	-0.1	0.04	0.0	<0.01	0.0	<0.01
Fetal sex		0.86		<0.01		<0.01		<0.01
Boy	5.6 (0.7)		0.10 (1.0)		50.6 (2.4)		3481.9 (572)	
Girl	5.6 (0.7)		-0.04 (0.9)		49.9 (2.3)		3357.3 (534)	

Abbreviations: SES, socioeconomic status. Values are mean (standard deviation) or correlation coefficients. [1]ANOVA was used for categorical variables or correlation coefficients for the continuous variables (Pearson for variables with a normal distribution and Spearman for variables with a skewed distribution).

Table S6. Associations between a 10 dB increase in total, road traffic and railway noise exposure during pregnancy and embryonic size and fetal growth.

	Crown-rump length (SDS)	Length (SDS)	Head circumference (SDS)	Weight (SDS)
	Coefficient (95% CI)	*Coefficient (95% CI)*	*Coefficient (95% CI)*	*Coefficient (95% CI)*
Total noise exposure				
Unadjusted model	0.07 (0.00 to 0.14)	0.00 (-0.02 to 0.03)	-0.01 (-0.04 to 0.01)	-0.01 (-0.03 to 0.02)
Minimally adjusted model	0.07 (0.00 to 0.14)	0.00 (-0.02 to 0.03)	-0.01 (-0.04 to 0.02)	0.01 (-0.02 to 0.03)
Fully adjusted model	0.07(0.00 to 0.15)	0.01 (-0.01 to 0.04)	-0.00 (-0.03 to 0.02)	0.01 (-0.01 to 0.04)
Road traffic noise exposure				
Unadjusted model	0.06 (0.00 to 0.12)	0.00 (-0.02 to 0.03)	-0.01 (-0.03 to 0.01)	0.00 (-0.02 to 0.02)
Minimally adjusted model	0.06 (0.00 to 0.12)	0.01 (-0.02 to 0.03)	-0.01 (-0.03 to 0.02)	0.01 (-0.02 to 0.03)
Fully adjusted model	0.06 (0.00 to 0.13)	0.02 (-0.01 to 0.04)	-0.00 (-0.03 to 0.02)	0.02 (-0.01 to 0.04)
Railway noise exposure				
Unadjusted model	-0.02 (-0.14 to 0.09)	0.01 (-0.03 to 0.05)	-0.00 (-0.04 to 0.04)	0.01 (-0.03 to 0.05)
Minimally adjusted model	-0.01 (-0.13 to 0.10)	0.01 (-0.03 to 0.05)	0.01 (-0.03 to 0.05)	0.02 (-0.03 to -0.06)
Fully adjusted model	-0.01 (-0.13 to 0.10)	0.02 (-0.03 to 0.06)	0.00 (-0.04 to 0.04)	0.02 (-0.02 to 0.06)

Unadjusted, minimally adjusted and fully adjusted associations between a 10 dB increase in total, road traffic, railway noise exposure during pregnancy and embryonic size and fetal growth.

Coefficients and 95% confidence intervals were obtained by univariate linear regression models and linear mixed models. The minimally adjusted model was adjusted for maternal age at enrollment, maternal national origin, maternal educational level, monthly household income, residential greenness and neighbourhood SES score. The fully adjusted model was additionally adjusted for periconceptional smoking, alcohol consumption during pregnancy, periconceptional folic acid use, parity and fetal sex. Abbreviations: SDS, standard deviation scores; dB, decibel; CI, confidence interval; SES, socioeconomic status.

Table S7. Associations between a 10 dB increase in total noise exposure during pregnancy and per trimester fetal growth

	Mid-pregnancy			Late pregnancy		
	Femur length (SDS)	**Head circumference (SDS)**	**Estimated fetal weight (SDS)**	**Femur length (SDS)**	**Head circumference (SDS)**	**Estimated fetal weight (SDS)**
	Coefficient (95% CI)	*Coefficient (95% CI)*	*Coefficient (95% CI)*	*Coefficient (95% CI)*	*Coefficient (95% CI)*	*Coefficient (95% CI)*
Total noise exposure						
Unadjusted model	-0.00 (-0.04 to 0.03)	-0.02 (-0.05 to 0.01)	-0.00 (-0.03 to 0.03)	0.00 (-0.03 to 0.03)	-0.00 (-0.04 to 0.03)	-0.01 (-0.05 to 0.02)
Minimally adjusted model	-0.00 (-0.03 to 0.03)	-0.02 (-0.05 to 0.01)	0.00 (-0.03 to 0.03)	0.00 (-0.03 to 0.04)	0.00 (-0.03 to 0.03)	-0.01 (-0.04 to 0.03)
Fully adjusted model	0.00 (-0.03 to 0.04)	-0.02 (-0.05 to 0.01)	0.01 (-0.03 to 0.04)	0.01 (-0.02 to 0.05)	0.00 (-0.03 to 0.04)	0.00 (-0.03 to 0.03)

Unadjusted, minimally adjusted and fully adjusted associations between a 10 dB increase in total, road traffic and railway noise exposure during pregnancy and per trimester fetal growth parameters.
Coefficients and 95% confidence intervals were obtained by univariate linear regression models.
In the unadjusted models, models were adjusted for gestational age at birth. The minimally adjusted model was additionally adjusted for maternal age at enrollment, maternal national origin, maternal educational level, monthly household income, residential greenness and neighbourhood SES score. The fully adjusted model was additionally adjusted for periconceptional smoking, alcohol consumption during pregnancy, periconceptional folic acid use, parity and fetal sex. Abbreviations: dB, decibel; SDS, standard deviation score; CI, confidence interval; SES, socioeconomic status.

Table S8. Associations between a 10 dB increase in total, road traffic and railway noise exposure during pregnancy and neonatal anthropometrics at birth.

	Length (cm)	Head circumference (cm)	Weight (grams)
	Coefficient (95% CI)	*Coefficient (95% CI)*	*Coefficient (95% CI)*
Total noise exposure			
Unadjusted model	0.03 (-0.05 to 0.12)	-0.03 (-0.10 to 0.04)	-0.80 (-14.72 to 13.12)
Minimally adjusted model	0.03 (-0.05 to 0.12)	-0.02 (-0.09 to 0.05)	4.41 (-9.46 to 18.29)
Fully adjusted model	0.06 (-0.03 to 0.14)	-0.00 (-0.07 to 0.07)	12.70 (-0.80 to 26.19)
Road traffic noise exposure			
Unadjusted model	0.05 (-0.03 to 0.12)	-0.02 (-0.08 to 0.04)	-0.08 (-12.53 to 12.37)
Minimally adjusted model	0.04 (-0.03 to 0.12)	-0.02 (-0.08 to 0.05)	3.21 (-9.19 to 15.63)
Fully adjusted model	0.06 (-0.02 to 0.13)	0.00 (-0.06 to 0.06)	10.88 (-1.20 to 22.96)
Railway noise exposure			
Unadjusted model	0.06 (-0.08 to 0.20)	-0.02 (-0.12 to 0.08)	19.11 (-3.55 to 41.76)
Minimally adjusted model	0.09 (-0.05 to 0.22)	-0.00 (-0.10 to 0.09)	22.13 (-0.30 to 44.56)
Fully adjusted model	0.07 (-0.07 to 0.20)	-0.01 (-0.11 to 0.09)	21.01 (-0.73 to 42.74)

Unadjusted, minimally adjusted and fully adjusted associations between a 10 dB increase in total, road traffic and railway noise exposure during pregnancy and neonatal anthropometrics at birth.

Coefficients and 95% confidence intervals were obtained by univariate linear regression models.

In the unadjusted models, models were adjusted for gestational age at birth. The minimally adjusted model was additionally adjusted for maternal age at enrollment, maternal national origin, maternal educational level, monthly household income, residential greenness and neighbourhood SES score. The fully adjusted model was additionally adjusted for periconceptional smoking, alcohol consumption during pregnancy, periconceptional folic acid use, parity and fetal sex. Abbreviations: dB, decibel; CI, confidence interval; SES, socioeconomic status.

Table S9. Associations between a 10 dB increase in total, road traffic and railway noise exposure during pregnancy and the risk for adverse birth outcomes.

	Low birthweight	Low birthweight at term	Preterm birth	Small for gestational age
	OR (95% CI)	*OR (95% CI)*	*OR (95% CI)*	*OR (95% CI)*
Total noise exposure				
Unadjusted model	1.12 (0.97 to 1.30)	1.07 (0.85 to 1.34)	1.09 (0.95 to 1.26)	0.97 (0.87 to 1.08)
Minimally adjusted model	1.10 (0.95 to 1.28)	1.06 (0.84 to 1.34)	1.06 (0.92 to 1.23)	0.95 (0.85 to 1.05)
Fully adjusted model	1.07 (0.92 to 1.25)	1.03 (0.82 to 1.31)	1.04 (0.90 to 1.20)	0.92 (0.82 to 1.02)
Road traffic noise exposure				
Unadjusted model	1.11 (0.97 to 1.27)	1.09 (0.89 to 1.34)	1.07 (0.95 to 1.22)	0.96 (0.87 to 1.06)
Minimally adjusted model	1.10 (0.96 to 1.26)	1.09 (0.89 to 1.34)	1.06 (0.93 to 1.20)	0.95 (0.86 to 1.05)
Fully adjusted model	1.07 (0.93 to 1.22)	1.06 (0.86 to 1.31)	1.04 (0.91 to 1.18)	0.92 (0.84 to 1.02)
Railway noise exposure				
Unadjusted model	1.06 (0.84 to 1.34)	1.03 (0.72 to 1.49)	1.06 (0.85 to 1.33)	1.08 (0.91 to 1.28)
Minimally adjusted model	1.06 (0.83 to 1.34)	1.01 (0.69 to 1.46)	1.08 (0.86 to 1.35)	1.06 (0.90 to 1.26)
Fully adjusted model	1.06 (0.83 to 1.34)	1.03 (0.71 to 1.49)	1.07 (0.85 to 1.35)	1.07 (0.90 to 1.27)

Unadjusted, minimally adjusted and fully adjusted associations between a 10 dB increase in total, road traffic and railway noise exposure during pregnancy and the risk for adverse birth outcomes.
Odds ratios and 95% confidence intervals were obtained by logistic regression models. The minimally adjusted model was adjusted for maternal age at enrollment, maternal national origin, maternal educational level, monthly household income, residential greenness and neighbourhood SES score. The fully adjusted model was additionally adjusted for periconceptional smoking, alcohol consumption during pregnancy, periconceptional folic acid use, parity and fetal sex. Abbreviations: dB, decibel; OR, odds ratio; CI, confidence interval; SES, socioeconomic status.

Table S10. Associations between a 10 dB increase in total noise exposure during pregnancy and embryonic size, stratified by maternal age, maternal educational level, national origin and season of birth.

					P-value of interaction
Maternal age					0.06
Total noise exposure	*≤28* Coefficient (95% CI)	*29-32* Coefficient (95% CI)	*≥33* Coefficient (95% CI)		
Unadjusted model	**0.12 (0.03 to 0.29)**	0.03 (-0.08 to 0.13)	0.05 (-0.06 to 0.17)		
Minimally adjusted model	**0.14 (0.04 to 0.31)**	0.02 (-0.08 to 0.13)	0.03 (-0.09 to 0.15)		
Fully adjusted model	**0.15 (0.05 to 0.31)**	0.03 (-0.08 to 0.13)	0.04 (-0.08 to 0.16)		
Educational level					0.81
Total noise exposure	**Low** Coefficient (95% CI)	**Medium** Coefficient (95% CI)	**High** Coefficient (95% CI)		
Unadjusted model	0.05 (-0.15 to 0.25)	0.11 (-0.02 to 0.25)	0.06 (-0.02 to 0.15)		
Minimally adjusted model	0.08 (-0.13 to 0.29)	0.10 (-0.04 to 0.24)	0.06 (-0.03 to 0.15)		
Fully adjusted model	0.10 (-0.12 to 0.31)	0.12 (-0.02 to 0.26)	0.06 (-0.03 to 0.15)		
National origin					0.10
Total noise exposure	**Dutch** Coefficient (95% CI)	**Non-Dutch** Coefficient (95% CI)			
Unadjusted model	0.02 (-0.06 to 0.11)	**0.14 (0.02 to 0.26)**			
Minimally adjusted model	0.01 (-0.07 to 0.09)	**0.14 (0.02 to 0.27)**			
Fully adjusted model	0.01 (-0.07 to 0.09)	**0.17 (0.04 to 0.30)**			
Season of birth					0.07
Total noise exposure	**Winter** Coefficient (95% CI)	**Spring** Coefficient (95% CI)	**Summer** Coefficient (95% CI)	**Autumn** Coefficient (95% CI)	
Unadjusted model	0.07 (-0.08 to 0.22)	**0.21 (0.07 to 0.36)**	-0.07 (-0.21 to 0.07)	0.09 (-0.04 to 0.21)	
Minimally adjusted model	0.06 (-0.09 to 0.21)	**0.18 (0.04 to 0.33)**	-0.05 (-0.20 to 0.09)	0.10 (-0.03 to 0.23)	
Fully adjusted model	0.06 (-0.09 to 0.22)	**0.19 (0.04 to 0.35)**	-0.04 (-0.19 to 0.11)	0.11 (-0.02 to 0.24)	

Unadjusted, minimally adjusted and fully adjusted associations between a 10 dB increase in total noise exposure during pregnancy and embryonic size stratified by maternal age, maternal educational level, national origin and season of birth. Coefficients and 95% confidence intervals were obtained by univariate linear regression models and linear mixed models. [1]χ^2 test was used. The minimally adjusted model was adjusted for maternal age at enrollment, maternal national origin, maternal educational level, monthly household income, residential greenness and neighbourhood SES score. The fully adjusted model was additionally adjusted for periconceptional smoking, alcohol consumption during pregnancy, periconceptional folic acid use, parity and fetal sex. Abbreviations: dB, decibels; CI, confidence interval; SES, socioeconomic status.

Table S11. Associations between an increase in air pollution during pregnancy and embryonic size.

	Crown-rump length (SDS)
	Coefficient (95% CI)
NO$_2$ (Δ 10µm/m^3)	
Unadjusted model	0.06 (-0.05 to 0.17)
Minimally adjusted model	0.01 (-0.10 to 0.13)
Fully adjusted model	0.01 (-0.10 to 0.12)
PM$_{2.5}$ (Δ 5µm/m^3)	
Unadjusted model	0.09 (-0.34 to 0.51)
Minimally adjusted model	-0.04 (-0.48 to 0.40)
Fully adjusted model	-0.04 (-0.48 to 0.40)

Unadjusted, minimally adjusted and fully adjusted associations between an increase in air pollution during pregnancy and embryonic size. Coefficients and 95% confidence intervals were obtained by univariate linear regression models. The minimally adjusted model was adjusted for maternal age at enrollment, maternal national origin, maternal educational level, monthly household income, residential greenness and neighbourhood SES score. The fully adjusted model was additionally adjusted for periconceptional smoking, alcohol consumption during pregnancy, periconceptional folic acid use, parity and fetal sex. Abbreviations: CI, confidence interval; SDS, standard deviation scores; NO$_2$, nitrogen dioxide; PM$_{2.5}$, particulate matter with an aerodynamic diameter of less than 2.5 µm.

Table S12. Associations between a 10 dB increase in total noise exposure during pregnancy and embryonic size, stratified by exposure to air pollutants.

				P-value of interaction
Total noise exposure	**NO$_2$ μm/m^3**			0.41
	≤32.97 μm/m^3 Coefficient (95% CI)	32.98 - 35.73 μm/m^3 Coefficient (95% CI)	≥35.74 μm/m^3 Coefficient (95% CI)	
Unadjusted model	0.11 (-0.03 to 0.25)	0.03 (-0.10 to 0.16)	0.08 (-0.04 to 0.19)	
Minimally adjusted model	0.12 (-0.02 to 0.27)	0.04 (-0.09 to 0.17)	0.07 (-0.04 to 0.19)	
Fully adjusted model	0.14 (-0.00 to 0.29)	0.03 (-0.10 to 0.16)	0.07 (-0.05 to 0.19)	
Total noise exposure	**PM$_{2.5}$ μm/m^3**			0.07
	≤16.61 μm/m^3 Coefficient (95% CI)	16.62 – 17.05 μm/m^3 Coefficient (95% CI)	≥17.06 μm/m^3 Coefficient (95% CI)	
Unadjusted model	0.12 (-0.01 to 0.25)	0.08 (-0.05 to 0.21)	0.01 (-0.11 to 0.13)	
Minimally adjusted model	0.10 (-0.04 to 0.23)	0.07 (-0.06 to 0.20)	0.01 (-0.11 to 0.13)	
Fully adjusted model	0.11 (-0.02 to 0.25)	0.09 (-0.05 to 0.22)	0.03 (-0.09 to 0.16)	

Unadjusted, minimally adjusted, and fully adjusted associations between a 10 dB increase in total noise exposure during pregnancy and embryonic size stratified by exposure to air pollutants. Coefficients and 95% confidence intervals were obtained by univariate linear regression models and linear mixed models. [1]χ^2 test was used. The minimally model was adjusted for maternal age at enrollment, maternal national origin, maternal educational level, monthly household income, residential greenness and neighbourhood SES score. The fully adjusted model was additionally adjusted for periconceptional smoking, alcohol consumption during pregnancy, periconceptional folic acid use, parity and fetal sex. Abbreviations: dB, decibels; CI, confidence interval.

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