Supplementary Material Chapter 5

Web Appendix 1. Neighbourhood-level crime data description.

Neighbourhood-level crime figures were obtained from Statistics Netherlands data that is based on the Dutch National Police crime figures and is available yearly from 2010 (2010-2015 as National Crime Figures dataset and from 2016 as part of the Neighbourhood characteristics dataset).[1,2] It contains information on types of crime which occurrence can be pinpointed to a geographical location. The types of crime in the dataset correspond to:

Violent crimes: This includes cases of simple and aggravated assault (including domestic violence), threats and stalking, sexual crimes, murder and manslaughter, hostage-taking and human trafficking.

Crimes against property: Includes all forms of theft and burglary.

Crimes against public order: This includes all forms of destruction and crimes against public order and public authority. Some examples of crimes against public order are destruction, vandalism, and participation in a criminal or terrorist organization.

The smallest area-level unit available in the dataset is at neighbourhood level. The dataset gives absolute crime figures per type of crime, e.g., yearly number of registered crimes against property. In addition, the dataset has information on relative figures that correspond to yearly crime rates per 1000 neighbourhood inhabitants.

Web Appendix 2. Assessment of potential confounders and sensitivity analysis.

The underlying models used in the g-formula must be adjusted for factors that confound the exposure-outcome relationship, i.e., covariates that are common causes of neighbourhood SES and birth outcomes. Additionally, the decomposition of the total effect into direct and indirect effects requires the adjustment for factors that confound the neighbourhood SES-neighbourhood crime rates, and the neighbourhood crime rates-birth outcomes relationship. Therefore, the underlying models were adjusted for a first set of variables: maternal age, parity, maternal ethnicity, maternal educational level, equivalised-household income, neighbourhood residential address density, neighbourhood average home value, and percentage of non-western migrants.

At the neighbourhood level, there are other features that might be related to both neighbourhood level crime rates and birth outcomes, and some of these characteristics might be influenced by the exposure as well. Green space, land use characteristics, and social cohesion are potential mediator-outcome confounders that are exposure-dependent. These have been highlighted themselves in the literature as mediators for the relationship between neighbourhood SES and birth outcomes.[3] Since the decomposition into direct and indirect effects requires no exposure-dependent mediator-outcome confounding (i.e., cross-world independence) it is key to assess the influence of these variables. If necessary, the g-formula approach would enable analyses involving exposure-dependent confounders.[4] To assess the relevance of the aforementioned factors we used information from the Statistics Netherlands Neighbourhood Characteristics dataset and the Neighbourhood Livability measurement ('Leefbarometer').[5,6] We fitted models that were additionally adjusted for the following variables: distance to nearest highway (a valid proxy for air pollution[7]), percentage of neighbourhood land area covered by green space, and percentage of neighbourhood land destined to a) restaurants and retail, b) business, and c) semi-built space, along with neighbourhood social context. Maternal lifestyle factors (alcohol consumption, drug use, and smoking) and pre-existent conditions (hypertension and diabetes) were also included in the models. Although maternal lifestyle factors have been recognized in the literature as mediators for the relationship between neighbourhood SES and birth outcomes,[8] some researchers may argue that they could also be confounders.

Tables S1 to S3 show the odds ratios (per outcome) for Model I, which was adjusted for the first set of variables; and Model II, which has been additionally adjusted for the variables mentioned in the previous paragraph. We observed that for none of the outcomes, the adjustment for the additional variables resulted in an attenuation of the estimates for the exposure or mediators. Based on these results, Model I (most parsimonious model) was used for the g-formula underlying models.

As a sensitivity analysis, we assessed the impact of women moving to another neighbourhood during (or shortly prior) their pregnancy, by restricting the underlying models used in the g-formula to women who have been living in the same residential address for at least two years at the time of delivery. Results from this analysis can be found in tables S1 to S3 (Model III).

Table S1. Odds ratios (95% CI) from logistic regression model for the relationship between neighbourhood SES category and low birth weight (model comparison).

	MODEL I	MODEL II	MODEL III
Neighbourhoood SES (quintiles)			
Very high	REF	REF	REF
High	1.02 (0.99;1.05)	1.02 (0.99;1.05)	1.02 (0.99;1.05)
Medium	1.04 (1.01;1.07)	1.05 (1.01;1.07)	1.04 (1.01;1.08)
Low	1.04 (1.01;1.08)	1.04 (1.01;1.08)	1.04 (1.00;1.07)
Very low	1.11 (1.07;1.14)	1.11 (1.07;1.15)	1.11 (1.07;1.14)
Violent crime (quintiles)			
Very low	REF	REF	REF
Low	1.01 (0.97;1.06)	1.01 (0.97;1.06)	1.01 (0.97;1.06)
Medium	1.03 (0.98;1.08)	1.03 (0.98;1.07)	1.03 (0.98;1.08)
High	1.04 (0.99;1.10)	1.04 (0.99;1.10)	1.05 (1.00;1.11)
Very high	1.06 (1.01;1.11)	1.06 (1.01;1.12)	1.06 (0.99;1.12)
Crime against property (quintiles)			
Very low	REF	REF	REF
Low	1.10 (1.05;1.14)	1.10 (1.05;1.14)	1.11 (1.06;1.16)
Medium	1.09 (1.05;1.14)	1.09 (1.05;1.14)	1.09 (1.05;1.15)
High	1.10 (1.04;1.15)	1.10 (1.04;1.15)	1.10 (1.04;1.16)
Very high	1.11 (1.05;1.18)	1.12 (1.06;1.19)	1.11 (1.05;1.2)
Crime against public order and authority (quintiles)			
Very low	REF	REF	REF
Low	1.03 (0.98;1.08)	1.03 (0.98;1.08)	1.03 (0.98;1.08)
Medium	1.02 (0.97;1.07)	1.02 (0.97;1.07)	1.02 (0.97;1.07)
High	1.01 (0.96;1.06)	1.01 (0.96;1.07)	1.01 (0.95;1.06)
Very high	1.03 (0.97;1.09)	1.03 (0.97;1.09)	1.03 (0.96;1.09)

Exposure and mediator variables coded to have the most advantaged category as reference.
Model I: Underlying model used in the g-formula, which includes exposure, mediator variables and confounders (maternal age, parity, maternal ethnicity, maternal educational level, equivalised-household income, neighbourhood residential address density, neighbourhood average home value, and percentage of non-western migrants).
Model II: Same as Model I but additionally accounting for additional neighbourhood-level variables, maternal pre-existent conditions, and maternal lifestyle factors.
Model III: Sensitivity analysis, adjusted as model I but including only women who have lived in the same residential address for at least two years at the moment of delivery.

Table S2. Odds ratios (95% CI) from logistic regression model for the relationship between neighbourhood SES category and small-for-gestational-age (model comparison).

	MODEL I	MODEL II	MODEL III
Neighbourhoood SES (quintiles)			
Very high	REF	REF	REF
High	1.00 (0.98;1.02)	1.00 (0.99;1.03)	1.00 (0.98;1.03)
Medium	1.01 (0.99;1.03)	1.02 (0.99;1.04)	1.01 (0.99;1.03)
Low	1.01 (0.99;1.03)	1.02 (0.99;1.04)	1.01 (0.99;1.03)
Very low	1.06 (1.03;1.08)	1.06 (1.04;1.09)	1.06 (1.04;1.09)
Violent crime (quintiles)			
Very low	REF	REF	REF

Low	0.99 (0.96;1.02)	0.99 (0.96;1.02)	0.99 (0.96;1.02)
Medium	1.00 (0.97;1.03)	1.00 (0.97;1.03)	1.00 (0.97;1.03)
High	1.03 (0.99;1.06)	1.03 (0.99;1.06)	1.03 (0.98;1.06)
Very high	1.06 (1.02;1.10)	1.06 (1.02;1.10)	1.06 (1.01;1.10)
Crime against property (quintiles)			
Very low	REF	REF	REF
Low	1.09 (1.06;1.12)	1.09 (1.01;1.12)	1.09 (1.06;1.13)
Medium	1.13 (1.09;1.16)	1.13 (1.01;1.16)	1.13 (1.10;1.17)
High	1.15 (1.11;1.18)	1.15 (1.01;1.18)	1.15 (1.11;1.19)
Very high	1.16 (1.11;1.20)	1.16 (1.01;1.21)	1.16 (1.11;1.21)
Crime against public order and authority (quintiles)			
Very low	REF	REF	REF
Low	1.04 (1.01;1.07)	1.04 (1.01;1.07)	1.04 (1.01;1.07)
Medium	1.06 (1.02;1.09)	1.06 (1.01;1.09)	1.05 (1.02;1.08)
High	1.07 (1.04;1.10)	1.07 (1.01;1.10)	1.07 (1.03;1.10)
Very high	1.10 (1.07;1.14)	1.10 (1.06;1.14)	1.10 (1.06;1.14)

Exposure and mediator variables coded to have the most advantaged category as reference.
Model I: Underlying model used in the g-formula, which includes exposure, mediator variables and confounders (maternal age, parity, maternal ethnicity, maternal educational level, equivalised-household income, neighbourhood residential address density (quintiles), neighbourhood average home value, and percentage of non-western migrants).
Model II: Same as Model I but additionally accounting for additional neighbourhood-level variables, maternal pre-existent conditions, and maternal lifestyle factors.
Model III: Sensitivity analysis, adjusted as model I but including only women who have lived in the same residential address for at least two years at the moment of delivery.

Table S3. Odds ratios (95% CI) from logistic regression model for the relationship between neighbourhood SES category and preterm birth (model comparison).

	MODEL I	**MODEL II**	**MODEL III**
Neighbourhoood SES (quintiles)			
Very high	REF	REF	REF
High	1.00 (0.98;1.03)	1.00 (0.97;1.03)	1.00 (0.97;1.03)
Medium	1.01 (0.99;1.04)	1.01 (0.98;1.04)	1.01 (0.98;1.04)
Low	1.02 (0.99;1.05)	1.02 (0.99;1.05)	1.02 (0.98;1.04)
Very low	1.07 (1.04;1.10)	1.07 (1.04;1.10)	1.07 (1.03;1.10)
Violent crime (quintiles)			
Very low	REF	REF	REF
Low	1.01 (0.98;1.05)	1.01 (0.97;1.05)	1.02 (0.98;1.06)
Medium	1.03 (0.99;1.07)	1.03 (0.99;1.07)	1.03 (0.99;1.08)
High	1.03 (0.99;1.08)	1.03 (0.99;1.08)	1.04 (1.00;1.09)
Very high	1.04 (1.01;1.08)	1.04 (1.01;1.08)	1.04 (0.98;1.10)
Crime against property (quintiles)			
Very low	REF	REF	REF
Low	1.00 (0.97;1.04)	1.01 (0.98;1.05)	1.00 (0.97;1.05)
Medium	1.03 (0.99;1.07)	1.03 (0.99;1.07)	1.02 (0.97;1.05)
High	1.01 (0.96;1.05)	1.01 (0.96;1.05)	1.01 (0.96;1.05)
Very high	1.04 (1.01;1.07)	1.04 (1.01;1.07)	1.04 (1.01;1.07)

Crime against public order and authority (quintiles)			
Very low	REF	REF	REF
Low	1.02 (0.98;1.06)	1.02 (0.98;1.06)	1.02 (0.98;1.06)
Medium	1.03 (0.99;1.08)	1.03 (0.98;1.07)	1.03 (0.98;1.07)
High	1.01 (0.97;1.06)	1.01 (0.97;1.06)	1.02 (0.97;1.07)
Very high	1.01 (0.96;1.07)	1.01 (0.96;1.07)	1.03 (0.96;1.07)

Exposure and mediator variables coded to have the most advantaged category as reference.
Model I: Underlying model used in the g-formula, which includes exposure, mediator variables and confounders (maternal age, parity, maternal ethnicity, maternal educational level, equivalised-household income, neighbourhood residential address density (quintiles), neighbourhood average home value, and percentage of non-western migrants).
Model II: Same as Model I but additionally accounting for additional neighbourhood-level variables, maternal pre-existent conditions, and maternal lifestyle factors.
Model III: Sensitivity analysis, adjusted as model I but including only women who have lived in the same residential address for at least two years at the moment of delivery.

Web Appendix 3. G-formula step-by-step procedure.

1. The g-formula procedure starts by sampling with replacement the original amount of individuals from the data. In this particular case, instead of sampling individuals, we have sampled clusters (neighbourhoods) in the data to obtain cluster-robust confidence intervals.
2. We use the resampled data to fit suitable models for each mediator and outcome. The models for the mediators included all confounders. The models for the outcomes additionally included all the mediator variables and interaction terms between exposure and mediators.
3. We used the model parameters to predict probabilities for each mediator and outcome. The predicted probabilities were used to draw new values from the distribution used to model the variables to simulate a new dataset without intervention, i.e., the natural course scenario (NC). During this process, the mediator variables were simulated first and then these values were used in the model for the outcome. The comparison between the observed means and the means under the NC (no intervention) scenario was used as a check against gross model misspecification. If the NC predictions are not close to observed values, then models for outcome and/or mediators are likely to be incorrectly specified.
4. Next, using the resampled data set from step 1, we simulated two datasets under two counterfactual (CF) scenarios: Lowest SES CF setting) setting the exposure for all mothers to the lowest neighbourhood SES quintile , and Highest SES CF2 setting) setting the exposure for all mothers to the highest neighbourhood SES quintile. This was done by changing the relevant covariate values (neighbourhood SES quintile) and then following a similar procedure to step 3.
5. Then, we simulated a mediation scenario where neighbourhood SES was intervened as in Lowest SES CF setting but the mediator values will be derived from the Highest SES CF.
6. To examine specific pathways, we let the intervention on neighbourhood SES impact each type of crime one at the time, while holding the other mediators constant at their values under the lowest SES neighbourhood setting.
7. We saved the average values for mediators and outcomes over the simulated scenarios. For binary outcomes, the averages correspond to the proportion of births with a given outcome (or mediator) in each scenario.
8. The simulations and calculation of the average values (steps 3-7) were repeated 30 times and the average of these 30 Monte Carlo iterations was used for the calculation of the mediation parameters. The number of iterations needed is based on the stability of the outcome and mediator averages, which can be checked by plotting the cumulative averages as shown in the Web Appendix Web Appendix 7. Based on this information, 30 MC iterations were considered sufficient to produce stable estimates.
9. The effects were calculated as follows: the absolute total effect (TE) of the exposure on the outcome is estimated by the difference between average values (mediator or

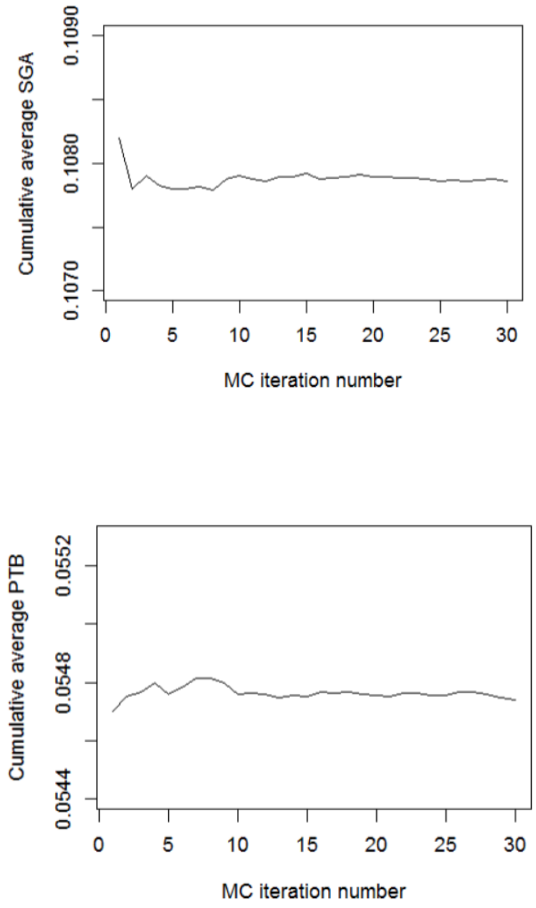
outcome) of the first and second counterfactual scenarios. The mediation scenario is used to obtain the Total Direct Effect (TDE) and the Natural Indirect Effect. The difference in the estimates (average values) between the CF2 and the mediation scenario is the TDE, while the difference in estimates from the TDE and TE is the NIE. The latest can also be obtained by the difference in the estimates from the mediation scenario vs CF1.

10. We repeated the steps above K times to produce (cluster-robust) bootstrap confidence intervals for the effects, and saved all the effects produced in each bootstrap, where K is a large enough value (100+) to produce stable estimates.
11. The final effects were obtained by averaging over the bootstrap iterations, and confidence intervals as the 2.5th and 97.5th quantile of the distribution.

Steps adapted from Pitkänen, et al.[10] A more detailed walkthrough the g-formula procedure applied to mediation analysis can be found elsewhere. Wang, A., Arah, O.A., 2015. G-computation demonstration in causal mediation analysis. Eur J Epidemiol 30, 1119–1127. https://doi.org/10.1007/s10654-015-0100-z

Web Figure 1. Outcome cumulative average plots to assess Monte Carlo stability.

The number of Monte Carlo iterations required is based on the stability of the outcome and mediator averages, which was checked by plotting the cumulative averages as seen below. Based on this information, 30 MC iterations were considered sufficient to produce stable estimates.



Web Figure 1. Monte Carlo (MC) stability for outcome averages.

Web Appendix 4. Absolute effect sizes.

Absolute effect sizes for total effect (TE), total direct effect (TDE) and total indirect effect (NIE). TDE and TIE shown for scenario where all mediators are fixed at the lowest SES neighbourhood setting (general mediation), and for the scenarios where we let the intervention on the exposure impact each mediator one at the time (used to assess the relevance of each pathway).

Table S4. Absolute effect sizes.

TOTAL EFFECT (TE)			
	Mean	**95% CI**	
TE, on SGA	-0.0072554	-0.0083811	-0.0062890
TE, on PTB	-0.0032810	-0.0034984	-0.0032413
TE, on LBW	-0.0042819	-0.0047425	-0.0037579
TE, on violent crime Q1	0.0454185	0.0383388	0.0513573
TE, on violent crime Q2	0.2195786	0.2030835	0.2374659
TE, on violent crime Q3	0.0745673	0.0569701	0.0916063
TE, on violent crime Q4	-0.2387890	-0.2618952	-0.2222673
TE, on violent crime Q5	-0.1007754	-0.1222702	-0.0792183
TE, on crime against property Q1	0.0169041	0.0078304	0.0247199
TE, on crime against property Q2	0.1297942	0.1142611	0.1461172
TE, on crime against property Q3	0.0924222	0.0746375	0.1118857
TE, on crime against property Q4	-0.1137842	-0.1397931	-0.0894360
TE, on crime against property Q5	-0.1253363	-0.1470659	-0.1063525
TE, on crime against public order Q1	0.0296287	0.0243093	0.0351522
TE, on crime against public order Q2	0.1491601	0.1347405	0.1645371
TE, on crime against public order Q3	0.0112305	-0.0091385	0.0296478
TE, on crime against public order Q4	-0.1423549	-0.1578047	-0.1259771
TE, on crime against public order Q5	-0.0476645	-0.0642442	-0.0346077
NATURAL INDIRECT EFFECT (NIE)			
	Mean	**95% CI**	
General mediation, SGA	-0.0020391	-0.0023479	-0.0017460
Violent crime, SGA	-0.0013499	-0.0016766	-0.0009891
Crime against property, SGA	-0.0010779	-0.0013098	-0.0008360
Crime against public order, SGA	-0.0008031	-0.0008310	-0.0007950
General mediation, PTB	-0.0000517	-0.0002298	0.0000964
Violent crime, PTB	-0.0000510	-0.0002870	0.0000907
Crime against property, PTB	-0.0000174	-0.0001940	0.0000057
Crime against public order, PTB	-0.0000088	-0.0001432	0.0000758
General mediation, LBW	-0.0003684	-0.0004906	-0.0002322
Violent crime, LBW	-0.0003735	-0.0005129	-0.0003245
Crime against property, LBW	-0.0000853	-0.0001690	0.0000403

Crime against public order, LBW	-0.0000636	-0.0000634	-0.0000503
TOTAL DIRECT EFFECT (TDE)			
	Mean	**95% CI**	
General mediation, SGA	-0.0053483	-0.0061137	-0.0044931
Violent crime, SGA	-0.0060055	-0.0087750	-0.0040099
Crime against property, SGA	-0.0062774	-0.0072319	-0.0003389
Crime against public order, SGA	-0.0064522	-0.0064244	-0.0064603
General mediation, PTB	-0.0031369	-0.0034602	-0.0029202
Violent crime, PTB	-0.0031376	-0.0029016	-0.0032793
Crime against property, PTB	-0.0031712	-0.0029946	-0.0031943
Crime against public order, PTB	-0.0031798	-0.0030454	-0.0032644
General mediation, LBW	-0.0038860	-0.0044645	-0.0032977
Violent crime, LBW	-0.0039084	-0.0037690	-0.0039574
Crime against property, LBW	-0.0041966	-0.0041129	-0.0043222
Crime against public order, LBW	-0.0042183	-0.0042185	-0.0042316

SGA, small-for-gestational-age; LBW, low birthweight; PTB, preterm birth.

Web Appendix 5. Comparison of observed means vs natural course scenario means.

Table S5. Comparison of observed vs natural course scenario (NC) outcome and mediator means.

	NC mean	95% CI		Observed mean
SGA	0.11	0.11	0.11	0.11
PTB	0.05	0.05	0.05	0.05
LBW	0.04	0.04	0.04	0.04
Violent crime Q1	0.07	0.07	0.07	0.07
Violent crime Q2	0.21	0.21	0.22	0.21
Violent crime Q3	0.25	0.24	0.26	0.25
Violent crime Q4	0.27	0.26	0.28	0.27
Violent crime Q5	0.20	0.19	0.21	0.20
Crime against property Q1	0.08	0.08	0.08	0.08
Crime against property Q2	0.19	0.18	0.19	0.19
Crime against property Q3	0.25	0.24	0.25	0.25
Crime against property Q4	0.28	0.27	0.28	0.28
Crime against property Q5	0.21	0.20	0.21	0.21
Crime against public order Q1	0.06	0.06	0.06	0.06
Crime against public order Q2	0.20	0.19	0.20	0.20
Crime against public order Q3	0.27	0.27	0.28	0.27
Crime against public order Q4	0.29	0.28	0.29	0.29
Crime against public order Q5	0.18	0.17	0.18	0.18

SGA, small-for-gestational-age; LBW, low birthweight; PTB, preterm birth.

Web Appendix 6. Percentage mediated.

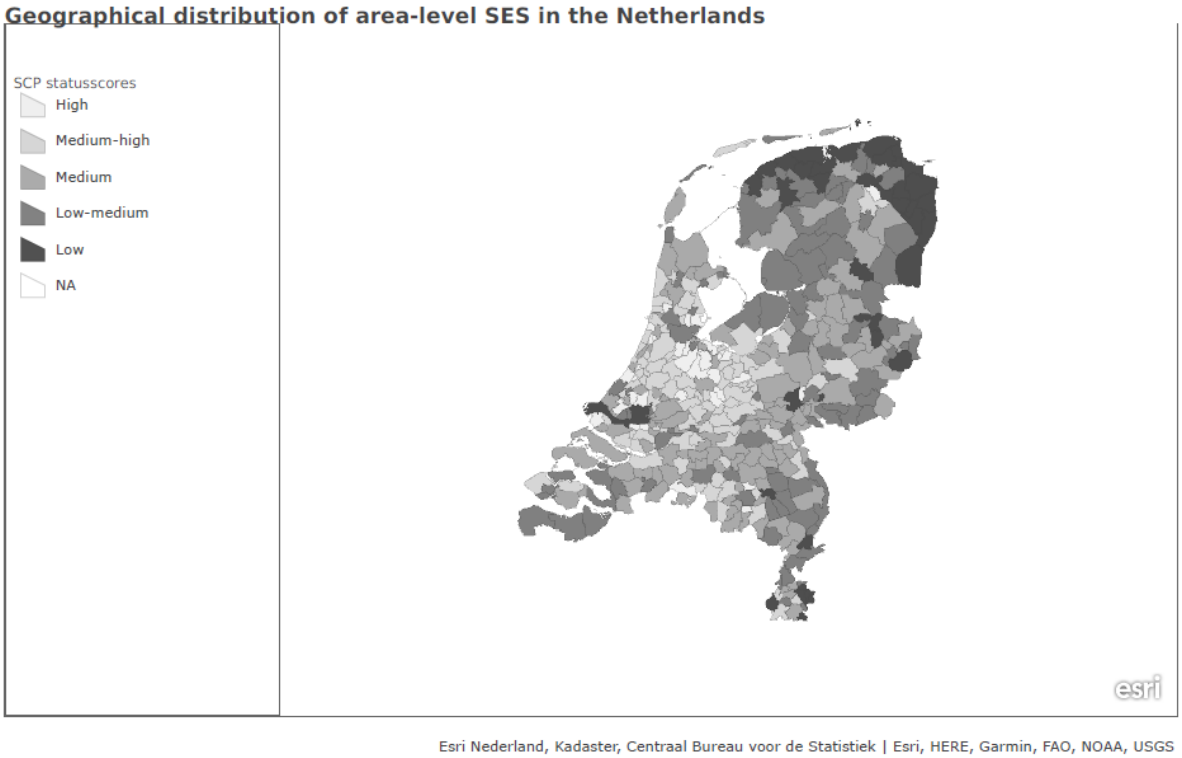
Table S6 shows the percentage mediated via all mediators jointly for the three outcomes. Furthermore, to examine specific pathways, we let the intervention on neighbourhood SES impact each type of crime one at the time, while holding the other mediators constant at their values under the lowest SES neighbourhood setting (step 6 from g-formula procedure, Web Appendix 1). This step is equivalent to including the effect of the chosen mediator in the total direct effect (TDE). Thus, the lower the percentage mediated for each mediator compared to the value with all mediators, the more relevant this pathway is, and the larger its contribution is to the total amount of mediation.[9,10] While the mediation effects are not additive due to the nonlinear nature of the models (logistic regression models), the procedure still gives insight into the specific pathways through which neighbourhood SES is related to birth outcomes.[9]

Table S6. Bootstrapped mean and 95% CI for percentage mediated via all mediators jointly and after adding the effect of each mediator to the TDE.

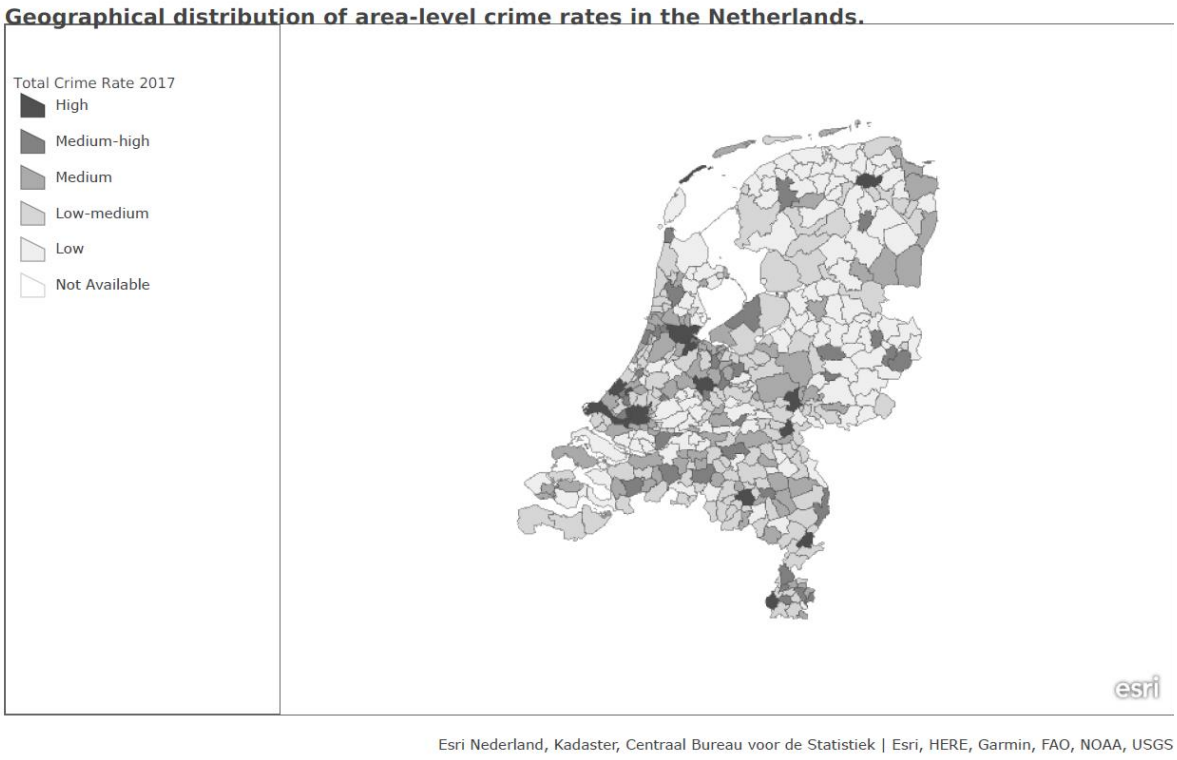
		Mean percentage mediated	95% CI	
SGA	All crime	28.11	24.06	32.36
	Violent crime	18.60	13.63	23.11
	Crime against property	14.86	11.52	18.05
	Crime against public order	11.07	10.96	11.45
PTB	All crime	1.62	-3.02	7.21
	Violent crime	1.60	-2.84	9.00
	Crime against property	0.55	-0.18	6.08
	Crime against public order	0.28	-2.38	4.49
LBW	All crime	8.60	5.42	11.46
	Violent crime	8.72	7.58	11.98
	Crime against property	1.99	-0.94	3.95
	Crime against public order	1.49	1.17	1.48

SGA, small-for-gestational-age; LBW, low birthweight; PTB, preterm birth; TDE, total direct effect.

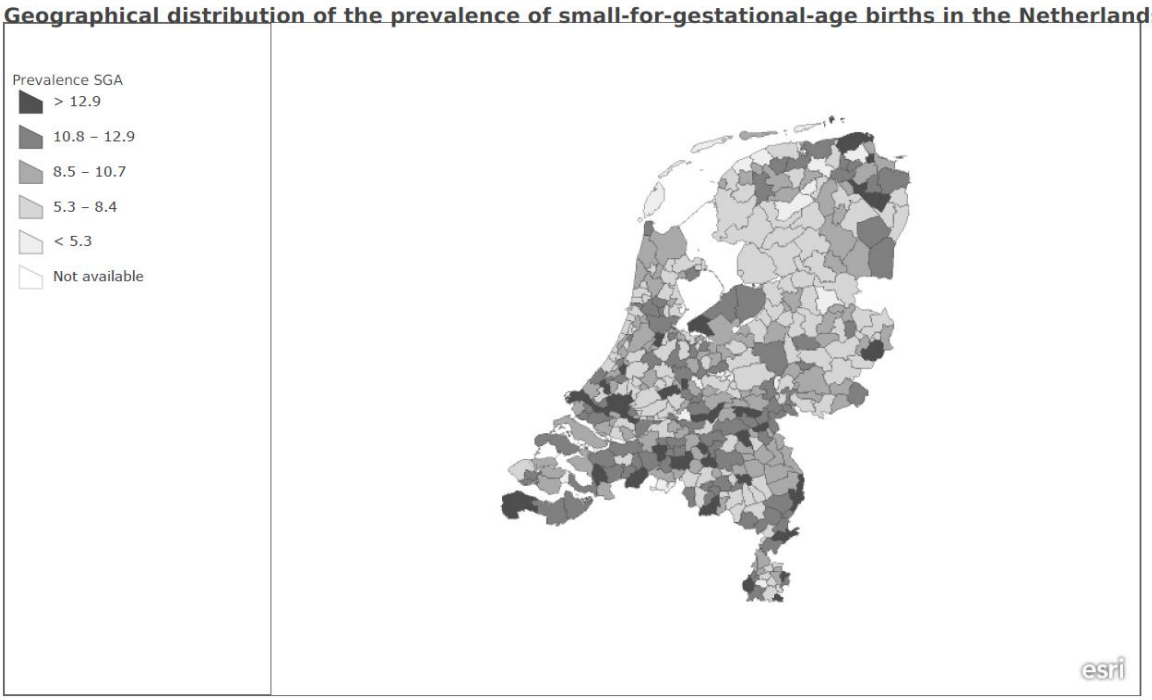
Web Figures 2-6. Geographic distribution of area-level SES, crime rates, and adverse birth outcomes in the Netherlands.



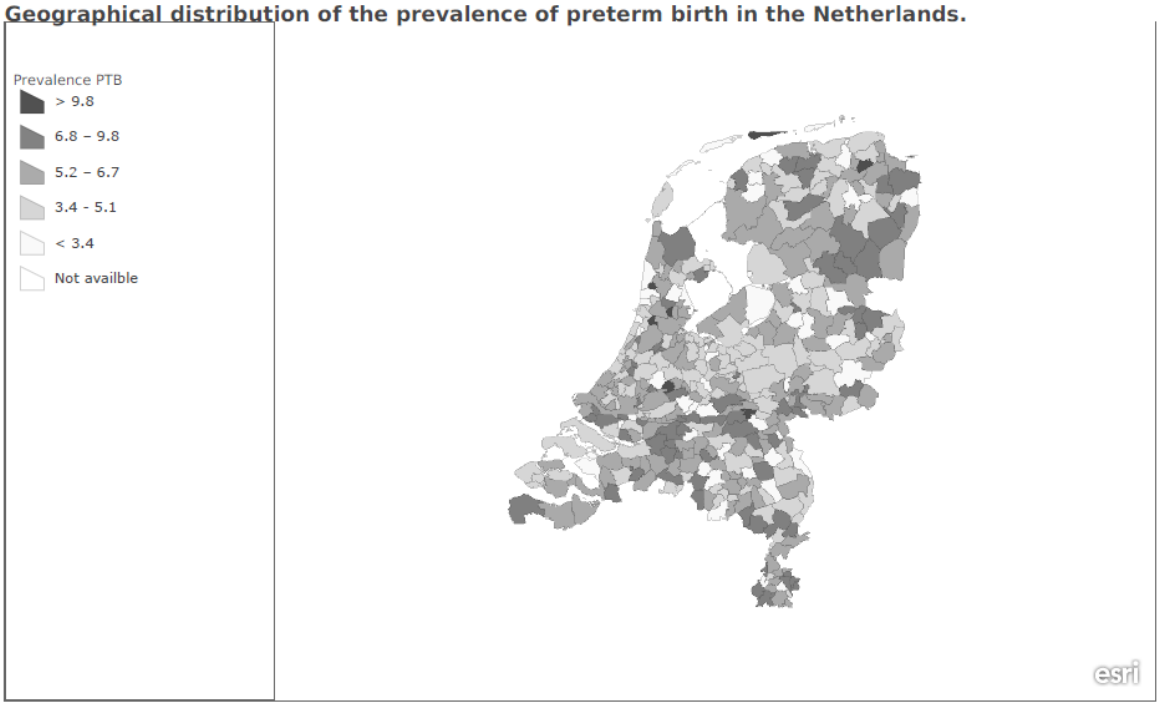
Web Figure 2. Geographical distribution of area-level SES (SCP status scores) in the Netherlands.



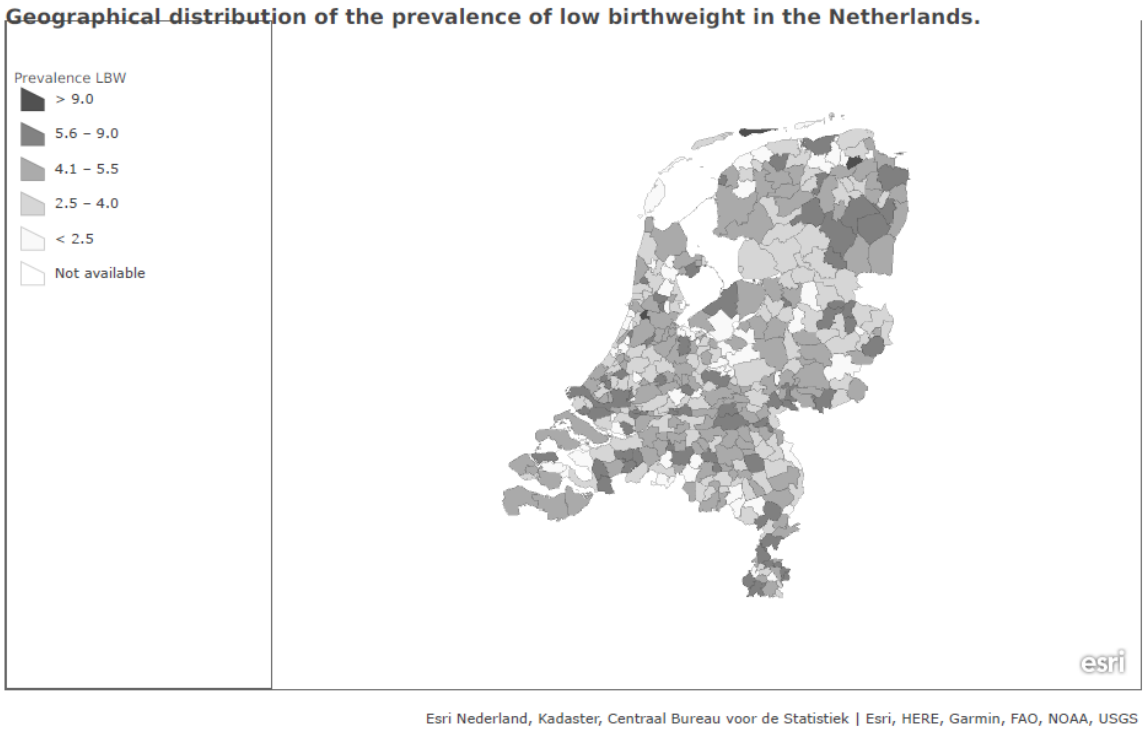
Web Figure 3. Geographical distribution of area-level crime rates (per 1000 inhabitants) in the Netherlands.



Web Figure 4. Geographical distribution of small-for-gestational-age (SGA) rates in the Netherlands.



Web Figure 5. Geographical distribution of preterm birth (PTB) rates in the Netherlands.



Web Figure 6. Geographical distribution of low birthweight (LBW) rates in the Netherlands.

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