Socioeconomic circumstances, health-related behaviours and paediatric infections: a mediation analysis

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ABSTRACT

Objective To examine how the effect of disadvantaged socioeconomic circumstances on the risk of paediatric infections is mediated by pregnancy smoking, excess weight during pregnancy and breast feeding in children under 5 years of age.

Design A population-level, retrospective cohort study. The Swedish Medical Birth Register was combined with the National Patient Register, the longitudinal integration database for health insurance and labour market studies, the Cause of Death Register and a local register held by the Child Health Care Unit in Uppsala Region.

Setting Uppsala Region, Sweden.

Patients 63 216 term and post-term singletons born to women who resided in Uppsala Region, Sweden between 1997 and 2015.

Main outcome measures Number of hospital admissions for infectious diseases. Secondary outcomes were the number of hospitalisations for respiratory and enteric infections, respectively.

Results The effect of disadvantaged socioeconomic circumstances, that is, low maternal education on the overall risk of paediatric infections was mediated to a considerable (33%–64%) proportion by pregnancy smoking, excess weight during pregnancy and breast feeding.

Conclusions Pregnancy smoking, excess weight during pregnancy and breast feeding mediate a considerable proportion of the association between deprived socioeconomic circumstances and paediatric infectious diseases. Therefore, inequalities in paediatric infectious diseases may be reduced by public health policies addressing these health-related behaviours.

WHAT IS KNOWN ABOUT THIS TOPIC

⇒ It is well known that infectious diseases disproportionately affect children living under deprived socioeconomic circumstances.

⇒ Less is known about how the effect of deprived socioeconomic circumstances on paediatric infectious diseases is mediated by health-related behaviours including pregnancy smoking, excess weight during pregnancy and low breast feeding.

WHAT THIS STUDY ADDS

⇒ Pregnancy smoking, excess weight during pregnancy and low breast feeding mediate around half of the association between deprived socioeconomic circumstances and paediatric infectious diseases.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Inequalities in paediatric infectious diseases may be reduced by public health policies targeting these health-related behaviours.

BACKGROUND

Paediatric infections disproportionately affect children living under deprived socioeconomic circumstances. Population-based studies have shown substantial socioeconomic inequalities in common and severe paediatric infections.[1–3] In particular, children born to parents with low socioeconomic position seem to be at a higher risk of gastroenteritis and respiratory tract infections.[1 4 5]

Pregnancy smoking, excess weight during pregnancy and early cessation of exclusive breast feeding are health-related behaviours that may link deprived socioeconomic circumstances to paediatric infectious diseases; they are all associated with both deprived socioeconomic circumstances and paediatric infections.[6–8] Both smoking and excess weight during pregnancy are associated with unfavourable perinatal conditions including low birth weight and congenital malformations.[9 10] Low birth weight and congenital malformations are in turn associated with paediatric infections.[11 12] It is well known that breast feeding reduces the risk of paediatric infections, as breast milk contains IgA antibodies, antibacterial proteins and growth factors that stimulate maturation of the infant's immune system.[13] Both duration and intensity of breast feeding are important, in particular, exclusive breast feeding <4 months seems to increase the risk of paediatric infections.[8]

Previous studies have examined how the effect of disadvantaged socioeconomic circumstances on the risk of paediatric infections is mediated by health-related behaviours using traditional mediation analysis.[14 15] In contrast, counterfactual mediation can decompose the mediation effect into different exposure and different susceptibility.[16] Importantly, this may influence how preventive strategies to tackle health inequalities are designed and implemented.[17]

Therefore, this study aimed to examine how the effect of disadvantaged socioeconomic circumstances on the risk of paediatric infections may be mediated by different exposure and different susceptibility to pregnancy smoking, excess weight during pregnancy and breast feeding in children under 5 years of age.

METHODS

Study design and population

This population-level, retrospective cohort study includes term and post-term singletons born to women who resided in Uppsala Region, Sweden between 1997 and 2015. We linked national and local health and administrative registers using the unique personal identification number assigned to every Swedish resident at birth or immigration. The Swedish Medical Birth Register contains information on prenatal, delivery and neonatal care, with almost complete coverage.[18] The National Patient Register holds information on nearly all hospitalisations in Sweden including International Classification of Disease, Tenth Revision (ICD-10) codes for primary diagnosis.[19] The longitudinal integrated database for health insurance and labour market studies (LISA), contains socioeconomic data including education.[20] The Cause of Death Register holds information on all deaths in Sweden since 1952.[21] The child health service database in Uppsala Region contains information on child health indicators including breast feeding, collected by child health nurses during routine health check-ups. The database holds information on virtually all children under 5 years of age living in Uppsala Region, including children living in deprived families.[22] The data show high concordance with medical records.[23] Registers were linked and subsequently de-identified by the Centre for Epidemiology at the Swedish National Board of Health and Welfare.

Exposures

In our study, socioeconomic circumstances were captured through maternal education level obtained from LISA. Maternal education was categorised as secondary school or less (≤9 years), upper secondary school (10–12 years), short postsecondary education (13–14 years) and long postsecondary education (≥15 years).

Potential mediators and confounders

Information on pregnancy smoking, pregnancy weight, parity, maternal age, maternal country of birth and year of birth was retrieved from the Medical Birth Register. Pregnancy smoking was reported at the first antenatal care visit, normally between 8 and 12 weeks of gestation, and categorised as yes/no.[24] Parity was categorised as 1, 2, 3, 4 and ≥5. Pregnancy maternal body mass index (BMI) was calculated using weight and length obtained at the first antenatal care visit and categorised as excess weight if BMI ≥25 kg/m^2. Maternal age was categorised as ≤25, 25–29, 30–34 and ≥35 years. Maternal country of birth was categorised as Sweden, other high-income countries, upper-middle-income countries, lower-middle-income countries and low-income countries using the World Bank Atlas method.[25] Information on current breast feeding (exclusive, partial breast feeding or no breast feeding) was obtained from the child health service database in Uppsala Region. Breast feeding was categorised as low exclusive breast feeding (exclusive breast feeding <4 months) if partial breast feeding and/or no breast feeding was reported at 1 week, 2 months and/or 4 months. Data on disposable household income were obtained from LISA and divided into annual quintiles (Q1–Q5), with Q1 representing the highest household income quintile.

Outcomes

The main outcome was the overall number of hospitalisations with a principal diagnosis of infectious disease recorded in the National Patient Register. Secondary outcomes were the number of hospitalisations for respiratory and enteric infections, respectively. ICD-10 codes were identified using a previously developed coding scheme. This coding scheme was developed by a panel of infectious disease clinicians, microbiologists and disease coding experts.[2] Online supplemental table A includes a list of ICD-10 codes.

Statistical analysis

We examined associations between maternal education, pregnancy smoking, excess weight during pregnancy and low exclusive breast feeding and number of hospitalisations for paediatric infections using Poisson regression models. Two models were fitted to each outcome (overall, respiratory and enteric infections). In the first model, analyses were adjusted for maternal age, maternal country of birth and year of birth; in the second model, analyses were additionally adjusted for maternal education, pregnancy smoking, excess weight during pregnancy and low exclusive breast feeding. Log follow-up time was used as offset. Results were presented as incidence rate ratios (IRR) with 95% CIs.

In counterfactual mediation analysis, we quantify the effects of maternal education level on paediatric infections acting through health-related behaviours. For each outcome (overall, respiratory and enteric infections), we fitted a natural effect model for the joint mediating effect of pregnancy smoking, excess weight during pregnancy and low exclusive breast feeding. All analyses were adjusted for the potential confounding effect of maternal age, maternal country of birth and year of birth (figure 1). All models used log follow-up time as offset. The natural effect models used robust SEs. In our analysis, the total effect (TE) of maternal education level on childhood infections was decomposed into three components, the pure natural direct effect (PNDE), the pure natural indirect effect (PNIE) and the mediated interactive effect (MIE). The PNDE describes the effect of

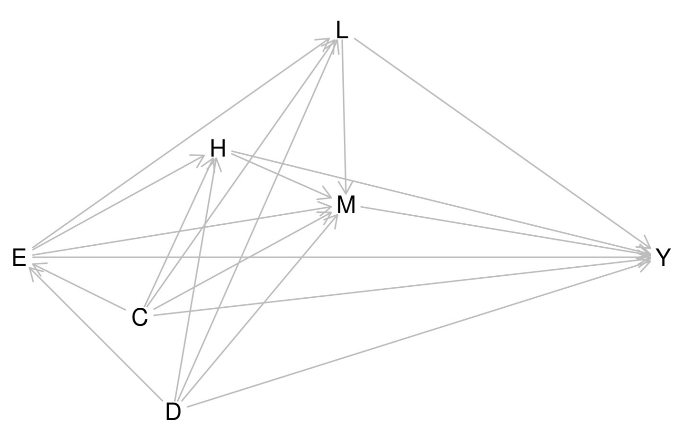

Figure 1 Directed acyclic graph representing the assumed causal structure. E: exposure (maternal education), Y: outcomes (paediatric infections), M: mediators (pregnancy smoking, excess weight during pregnancy and low exclusive breast feeding), C: confounders (maternal age, maternal country of birth and year of birth), L: exposure-induced mediator-outcome confounders (parity and poverty), D: unmeasured confounders (maternal childhood circumstances and genetic factors) and H: unmeasured exposure-induced mediator-outcome confounders (paternal smoking, unhealthy diet, maternal employment, paternal education and paternal employment).

Table 1 Study population characteristics and their association with maternal education level

	≤9 years	10–12 years	13–14 years	≥15 years	All
All	9.7	39.5	12.9	37.8	100.0
Pregnancy smoking					
Yes	24.6	9.3	2.7	0.9	6.8
No	75.4	90.7	97.3	99.1	93.2
Excess weight during pregnancy*					
Yes	46.5	43.0	36.0	28.9	37.1
No	53.5	57.0	64.0	71.1	62.9
Low EBF†					
Yes	50.6	38.5	27.6	23.0	32.4
No	49.4	61.5	72.4	77.0	67.6
Maternal age (years)					
<25	37.9	19.3	9.2	1.8	13.2
25–29	27.8	35.1	30.9	26.1	30.5
30–34	20.5	29.1	35.5	46.3	35.6
>34	13.7	16.5	24.3	25.8	20.7
Maternal country of birth					
Sverige	65.1	85.0	80.9	83.3	81.9
Other HIC	4.0	3.6	5.3	7.8	5.4
UMIC	17.0	5.6	7.3	5.1	6.7
LMIC	4.0	2.9	4.1	3.0	3.2
LIC	10.0	2.8	2.4	0.8	2.7
Year of birth					
Mean	2005.9	2005.9	2005.8	2007.8	2006.6
Household income‡					
Q1	6.2	12.8	21.2	30.6	20.0
Q2	10.1	19.4	19.6	23.3	20.0
Q3	14.1	23.3	18.1	18.7	20.0
Q4	21.9	24.2	20.2	15.0	20.0
Q5	47.7	20.3	20.9	12.2	20.0
Parity					
1	38.3	40.8	44.7	46.2	43.1
2	30.2	37.5	36.6	38.6	37.1
3	16.3	14.8	13.9	12.5	14.0
4	8.3	4.4	3.3	2.2	3.8
≥5	6.8	2.4	1.4	0.6	2.0

Values are percentages unless stated otherwise. Missing data were imputed using multiple imputation. Data were missing on breast feeding for 11% (n=7260), pregnancy overweight for 11% (n=6994), pregnancy smoking for 6% (n=3874), maternal education for 2% (n=1044) and maternal country of birth for 1% (n=331) of children. Proportions and medians were calculated as averages over all imputations. Analyses included all 63 216 children.

*Excess weight during pregnancy was defined as pregnancy BMI ≥25 kg/m^2 at the first antenatal care visit.

†Low EBF was defined as exclusive breast feeding <4 months.

‡Annual quintiles with Q1 representing the highest household income quintile.

BMI, body mass index; HIC, high-income countries; LIC, low-income countries; LMIC, lower-middle-income countries; UMIC, upper-middle-income countries;

maternal education on childhood infections that is neither mediation nor interaction. The PNIE describes the effect of maternal education on childhood infections that is due to just mediation, not interaction (differential exposure). The MIE describes the effect of maternal education on childhood infections that is due to an additive interaction between maternal education level and mediators (differential susceptibility).[26]

Mediation analysis was conducted in two steps. In the first step, we imputed counterfactual outcomes for each potential level of maternal education. The dataset was expanded so it contained four observations per child, one observation for each potential level of maternal education. Mean values for the counterfactual outcomes were then imputed using a Poisson regression model that included maternal education, mediators, confounders and an interaction term between maternal education and mediators. In the second step, we estimated the PNDE, PNIE, TE and MIE. The PNDE, PNIE and a multiplicative interaction term were estimated by fitting a natural effect Poisson regression model to the expanded dataset. The TE was estimated as the linear combinations of PNDE, PNIE and the multiplicative interaction term. The MIE was estimated as the relative excess risk due to interaction (RERI)=$IRR^{TE}-IRR^{PNDE}-IRR^{PINE}+1$. In models with a TE of IRR >1.05, we calculated the overall percentage mediated using the following formula: $((IRR^{PNIE}-1)/(IRR^{TE}-1)+RERI^{MIE}/(IRR^{TE}-1))\times 100$.[26] In sensitivity analysis, we examined if the potential confounding effect of parity by restricting the analysis to the firstborn child and the potential confounding effect of poverty by excluding children born to mothers in the two lowest household income quintiles. Missing data were imputed using multiple imputation. We used a chained-equation approach. The predictive model included all variables including outcomes. Ten imputed datasets were generated. Percentages and medians were calculated as averages over all imputations; regression results were pooled across all imputed datasets using Rubin's rules.

Data preparation was performed in Stata Statistical Software: Release 17 (College Station, Texas, USA). Analyses were conducted using R V.4.2.2, the *medflex* package (V.0.6–7) was used for mediation analysis, the *mice* package (V.3.15.0) was used for multiple imputation and *daggity* (V.0.3–1) was used to illustrate the assumed relationships between variables.[27–29]

RESULTS

Study population

The Medical Birth Register included 63 216 term and post-term (gestational age ≥37 weeks) singletons born alive to mothers who resided in Uppsala Region between 1 January 1997 and 31 December 2015. Children were followed until 5 years of age, death (n=70), emigration (n=1059) or 31 December 2016. The total follow-up was 283 119 person-years. The study included 6977 infectious disease hospitalisations, 3184 admissions for respiratory infections and 1455 admissions for enteric infections. Data were missing on one or more variables for 26% (n=16 219) of children.

Table 1 presents the background characteristics of the study population. In comparison with children born to mothers with long postsecondary education, children born to mothers with shorter education were more likely to be exposed to pregnancy smoking, low exclusive breast feeding and, to a lesser extent, excess weight during pregnancy. Additionally, the mother was more likely to be foreign-born.

Regression analyses

The associations between maternal education and mediators, and overall, respiratory and enteric infections hospitalisations are shown in table 2. Compared with children born to mothers with ≥15 years of education, children born to mothers with shorter education were more likely to be hospitalised for overall infections and respiratory infections; children born to mothers with ≤9 years of education were also more likely to be hospitalised for enteric infections. The association between maternal education and all outcomes decreased considerably when mediators were added to the models. Pregnancy smoking and low exclusive breast feeding were associated with all outcomes. Excess weight during pregnancy was associated with overall and respiratory infections.

Table 2 Associations between maternal education, pregnancy smoking, pregnancy overweight, low exclusive breast feeding and hospitalisations for all respiratory and enteric infections

	All infections		Respiratory infections		Enteric infections	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)
Maternal education (years)						
≥15	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
13–14	1.06 (0.98 to 1.14)	1.03 (0.95 to 1.11)	1.01 (0.90 to 1.14)	0.99 (0.88 to 1.11)	0.93 (0.78 to 1.11)	0.91 (0.76 to 1.08)
10–12	1.11 (1.05 to 1.18)	1.03 (0.97 to 1.10)	1.10 (1.01 to 1.20)	1.03 (0.95 to 1.13)	1.04 (0.91 to 1.18)	0.96 (0.84 to 1.10)
≤9	1.38 (1.26 to 1.51)	1.21 (1.11 to 1.33)	1.37 (1.20 to 1.56)	1.23 (1.07 to 1.41)	1.30 (1.08 to 1.57)	1.13 (0.93 to 1.38)
Pregnancy smoking						
No	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Yes	1.26 (1.15 to 1.37)	1.08 (0.99 to 1.19)	1.22 (1.07 to 1.40)	1.06 (0.92 to 1.22)	1.28 (1.07 to 1.53)	1.09 (0.91 to 1.32)
Excess weight during pregnancy*						
No	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Yes	1.12 (1.06 to 1.18)	1.06 (1.00 to 1.12)	1.11 (1.02 to 1.20)	1.05 (0.97 to 1.14)	1.01 (0.90 to 1.13)	0.95 (0.84 to 1.07)
Low EBF†						
No	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Yes	1.44 (1.37 to 1.51)	1.39 (1.32 to 1.47)	1.37 (1.26 to 1.48)	1.33 (1.22 to 1.44)	1.59 (1.42 to 1.79)	1.58 (1.40 to 1.78)

Model 1 adjusted for maternal age, maternal country of birth and year of birth. Model 2 adjusted for maternal age, maternal country of birth, year of birth, maternal education, pregnancy smoking, excess weight during pregnancy and low exclusive breast feeding. Analyses included all 63 216 children.
*Excess weight during pregnancy was defined as pregnancy BMI ≥25 kg/m^2 at the first antenatal care visit.
†Low EBF was defined as exclusive breast feeding <4 months.
BMI, body mass index; IRR, incidence rate ratio;

Mediation analyses

The total and decomposed effects on paediatric infections due to counterfactual changes in maternal education level are presented in table 3. For overall infections, mediation by health-related behaviours accounted for a large proportion of the TE (total percentage mediated 33%–64%, depending on exposure level). For respiratory and enteric infections, health-related behaviours mediated a substantial proportion of the additional risk observed in the lowest education group (total percentage mediated 57% and 40%, respectively). The mediation effects were due to higher exposure to health-related behaviours and we found no evidence of increased susceptibility. In sensitivity analysis, we

Table 3 Total and decomposed effects on all respiratory and enteric paediatric infections due to counterfactual changes in maternal education level

	All infections	Respiratory infections	Enteric infections
Maternal education level: 13–14 vs ≥15 years			
PNDE*	1.04 (0.94 to 1.14)	1.00 (0.87 to 1.15)	0.93 (0.76 to 1.13)
PNIE*	1.03 (1.02 to 1.05)	1.03 (1.01 to 1.05)	1.05 (1.02 to 1.08)
MIE†	−0.01 (−0.11 to 0.09)	−0.01 (−0.15 to 0.12)	−0.03 (−0.23 to 0.16)
TE*	1.06 (0.96 to 0.15)	1.01 (0.88 to 1.15)	0.93 (0.73 to 1.13)
Total percentage mediated‡	33	–	–
Maternal education level: 10–12 vs ≥15 years			
PNDE*	1.04 (0.97 to 1.13)	1.04 (0.94 to 1.15)	0.97 (0.84 to 1.13)
PNIE*	1.08 (1.03 to 1.13)	1.07 (0.99 to 1.15)	1.17 (1.05 to 1.31)
MIE†	−0.01 (−0.08 to 0.06)	−0.01 (−0.11 to 0.09)	−0.10 (−0.25 to 0.04)
TE*	1.11 (1.04 to 1.19)	1.10 (1.01 to 1.20)	1.04 (0.90 to 1.18)
Total percentage mediated‡	64	60	–
Maternal education level: ≤9 vs ≥15 years			
PNDE*	1.17 (1.03 to 1.32)	1.17 (0.98 to 1.4)	1.18 (0.93 to 1.49)
PNIE*	1.11 (0.99 to 1.25)	1.12 (0.93 to 1.34)	1.32 (1.02 to 1.71)
MIE†	0.10 (−0.02 to 0.22)	0.09 (−0.06 to 0.23)	−0.20 (−0.40 to −0.01)
TE*	1.38 (1.26 to 1.50)	1.37 (1.23 to 1.52)	1.30 (1.10 to 1.51)
Total percentage mediated‡	55	57	40

All models were adjusted for maternal age, maternal country of birth and year of birth. Analyses included all 63 216 children.
*PNDE, PNIE and TE presented as IRR with 95% CI.
†MIE estimated as excess risk due to interaction=$IRR^{TE}-IRR^{PNDE}-IRR^{PINE}+1$.
‡Total percentage mediated estimated as $((IRR^{PNIE}-1)/(IRR^{TE}-1)+RERI^{MIE}/(IRR^{TE}-1))\times 100$ in models with a TE of IRR >1.05.
IRR, incidence rates rations; MIE, mediated interactive effect; PNDE, pure natural direct effect; PNIE, pure natural indirect effect; RERI, relative excess risk due to interaction; TE, total effect.

obtained similar results in an analysis restricted to the firstborn child and in an analysis excluding children born to mothers in the two lowest household income quintiles. This indicates no major confounding effect due to parity or poverty. Online supplemental table B includes results from sensitivity analysis.

DISCUSSION

In this large population-based study, we show that pregnancy smoking, excess weight during pregnancy and breast feeding mediate around half of the association between maternal education level and paediatric infections.

Mediation analyses

We hypothesised that health-related behaviours mediated the relationship between deprived socioeconomic circumstances and paediatric infections, based on previous research; pregnancy smoking, excess weight during pregnancy and low exclusive breast feeding are all associated with paediatric infections and more frequent in deprived groups.[6–8] Similar to our results, a Swedish cohort study reported that pregnancy smoking and family size were important mediators for the effect of social deprivation on respiratory infections in young children.[14] Additionally, an Australian cohort study found that pregnancy smoking and family size mediated the effect of maternal education on a combined measurement of child health that included infectious diseases.[15] In comparison to these studies, we used counterfactual mediation analysis which allowed us to decompose the mediating effect into different exposure and different susceptibility.

Public health policy implications

Inequalities in child health may be reduced by policies that (1) target social stratification, (2) decrease exposure to health-related factors, (3) decreases vulnerability to health-related factors and (4) reduces social consequences of ill-health.[30] In our study, a substantial proportion of the association between maternal education and paediatric infections was mediated by increased exposure to health-related behaviours; we found no evidence of increased susceptibility. Consequently, our findings support strategies that reduce smoking, overweight and obesity and promote breast feeding. Smoking can be reduced by different tobacco control policies, for example, smoke-free legislation, tobacco taxation and smoking cessation programmes; importantly, some evidence suggests that tobacco taxation and smoke-free legislation can reduce absolute socioeconomic inequalities.[31] Overweight and obesity can be addressed by food policies including taxation of unhealthy foods, for example, soft drinks, subsidies of healthy foods and enforcement of understandable nutrition labelling.[32] Currently, Sweden has no specific tax on unhealthy foods. Breast feeding can be promoted by breastfeeding support offered by professionals and lay people together.[33] These policies should be applied universally to ensure that health inequalities are reduced across the entire social gradient.[30]

Strengths and limitations

Our study used high-quality registers with individual-level data and counterfactual mediation analysis. However, a large proportion (26%) of children had missing data on one or more variables. Assuming that data were missing at random, we used multiple imputations to impute missing data thereby reducing the risk of selection bias.[34] Maternal education may induce other factors that in turn may confound the association between health-related behaviours and paediatric infections. In sensitivity analysis, we found no confounding effect of poverty or parity. However, other socioeconomic factors, for example, maternal employment and paternal education may still be confounders. The measured health-related behaviours may be associated with other unmeasured behaviours, for example, pregnancy smoking may be associated with smoking after pregnancy as well as paternal smoking. Therefore, our findings support broad public health policies reaching the whole population over specific interventions targeting, for example, pregnant women. We were unable to adjust for maternal childhood circumstances and genetic factors. Even though we do not expect these factors to be major confounders, they may affect our estimates. Finally, our results may not be generalisable to other settings with different rates of excess weight during pregnancy, pregnancy smoking and breast feeding, at least not without considering the distribution of health-related behaviours by socioeconomic circumstances in these settings.

CONCLUSIONS

We found that pregnancy smoking, excess weight during pregnancy and low breast feeding mediate around half of the association between maternal education level and paediatric infectious diseases. This mediation was due to increased exposure to health-related behaviours in children born to low-educated mothers, we found no evidence of increased susceptibility. Consequently, our results suggest that inequalities in paediatric infectious diseases can be targeted by public health policies addressing exposure to these health-related behaviours.

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Contributors SV conceptualised and designed the study together with PEG and SAS, carried out analyses and drafted the initial manuscript. SAS conceptualised and designed the study together with SV and PEG, coordinated and supervised the database and reviewed and revised the manuscript. PEG designed the study together with SV and SAS, and reviewed and revised the manuscript. SV is guarantor.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study was approved by the Regional Ethics Board in Umeå (reference numbers 2012- 265-31M and 2017-399-32M) and by the Swedish Ethical Review Authority (reference number 2021-06337-02).

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We used anonymous data obtained from third-party sources and some access restrictions may apply. Interested researchers need to obtain data directly from the National Board of Health and Welfare in Sweden (socialstyrelsen@socialstyrelsen.se), Statistics Sweden (scb@scb.se) and the Child Health Service Unit in Uppsala (thomas.wallby@kbh.uu.se).

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Supplemental Table A: Infectious disease categories and associated ICD-10 codes

Category:	Group:	ICD-10 codes:
Enteric infections	Enteric infections	A00, A01, A020, A029, A03, A04, A05, A06, A07,A08
	Enteric symptoms	A09, I880, K528, K529, R11
Respiratory infections	Upper RTI	J00, J01, J02, J03, J04, J05, J06, J32, J340, J36, J37, J390, J391
	Ear infections	H600, H601, H602, H603, H608, H609, H62, H65, H66, H67, H680, H70, H730, H750, H830, H940
	Acute lower RTI	A481, A482, B59, J09, J10, J11, J12, J13, J14, J15, J16, J17, J18, J20, J21, J22
	Chronic lower RTI	J40, J41, J42, J440, J47, J85, J86, J988
	Tuberculosis	A15, A16, A17, A18, A19, N740, N741, J65
Other infections	Kidney infections	N00, N05, N10, N136, N151
	Urinary tract infections	N300, N341, N351, N37, N390
	Reproductive system infections, male	N410, N411, N412, N413, N431, N45, N481, N482, N490, N49, N51
	Reproductive system infections, female	N70, N71, N72, N73, N74, N751, N764, N87
	Sepsis	A391, A392, A393, A394, A395, A398, A399 A40, A41, A483, A021, A327
	HIV/AIDS	B20, B21. B22, B23, B24
	Sexually transmitted infections	A50, A51, A52, A53, A54, A55, A56, A57, A58, A59, A60, A63, A64, N290
	CNS viral infections	A801, A802, A803, A804, A809, A811, A812, A818, A819, A82, A83, A84, A85, A86, A87, A88, A89
	CNS general infections	G00, G01, G02, G030, G039, G04, G05, G06, G07, G08, G09, G610, A321, A390
	Eye infections	B30, H000, H03, H043, H050, H100, H102, H103, H109, H130, H131, H160, H190, H191, H192, H220, H440, H451
	Oral infections	K02, K044, K046, K050, K052, K053, K113, K122
	Heart and Circulatory infections	B332, I00, I01, I02, I05, I06, I07, I08, I09, I301, I33, I38, I39, I400, I410, I411, I412, I430, I716, I790, I791
	Gastrointestinal tract infections	K230, K231, K25, K26, K27, K28, K293, K294, K295, K35, K36, K37, K61, K630, K632, K650, K678, K908, K930

Hepatic infections	K750, K770, K830
Viral Hepatitis	B15, B16, B17, B18, B19
Skin infections, typical	A46, L00, L01, L02, L03, L04, L050, L08
Skin infections, other	B86, T009, T633, T634, T793
Breast infections	N61
Osteomyelitis	M462, M463, M464, M465
Joint infections	M00, M01
Connective tissue infections	M021, M023, M03, M600, M630, M631, M632, M650, M651, M680, M710, M711, M896
Neoplasms from infection	C11, C161, C162, C163, C164, C165, C166, C168, C169, C210, C211, C220, C46, C53, D002, D013, D06
Postoperative infections	T802, T814, T826, T827, T835, T836, T845, T846, T847, T857, T874
Adverse effect of infectious disease treatment	R761, R762, T36, T37, T485, T487, T490, T495, T496, T499, T788, T789, T880, T881, T887
Other Bacterial infections	A20, A21, A22, A23, A24, A25, A26, A27, A28, A30, A31, A320, A328, A329, A33, A34, A35, A36, A37, A38, A42, A43, A44, A480, A484, A488, A49, A65, A66, A67, A68, A69, A70, A71, A74, A75, A77, A78, A79, B95, B96
Other Viral infections	A90, A91, A92, A93, A94, A95, A96, A98, A99, B00, B01, B02, B03, B04, B05, B06, B07, A08, B09, B25, B26, B27, B33, B34, B97
Other Mycoses	B35, B36, B37, B38, B39, B40, B41, B42, B43, B44, B45, B46, B47, B48, B49
Other Protozoan infections	B50, B51, B52, B53, B54, B55, B56, B57, B58, B60, B64
Other infections	B65, B66, B67, B68, B69, B70, B71, B72, B73, B74, B75, B76, B77, B78, B79, B80, B81, B82, B83, B85, B87, B88, B89, B94, B99, E033, E321, F024, F071, I88, T64
Perinatal infections	P002, P027, P23, P35, P36, P37, P38, P39

ICD-10, International Classification of Disease, Tenth Revision. RTI, respiratory tract infections. CNS, central nervous system.

Supplemental Table B: Sensitivity analysis presenting the total and decomposed effects on overall pediatric infections due to counterfactual changes in maternal education level restricted to first born children (model S1) and excluding children born to mothers in the two lowest household income quintiles (model S2)

	S1	S2
Maternal education level: 13–14 vs ≥15 years		
PNDE*	1.05 (0.90–1.22)	1.08 (0.96–1.22)
PNIE*	1.03 (1.01–1.05)	1.03 (1.01–1.05)
MIE†	-0.02 (-0.21–0.16)	-0.01 (-0.13–0.10)
TE*	1.05 (0.90–1.20)	1.10 (0.98–1.22)
Total percentage mediated‡	-	20
Maternal education level: 10–12 vs ≥15 years		
PNDE*	1.03 (0.92–1.17)	1.03 (0.94–1.12)
PNIE*	1.10 (0.99–1.21)	1.07 (1.02–1.13)
MIE†	-0.04 (-0.16–0.07)	-0.02 (-0.11–0.07)
TE*	1.09 (0.97–1.21)	1.08 (0.99–1.17)
Total percentage mediated‡	67	63
Maternal education level: ≤9 vs ≥15 years		
PNDE*	1.14 (0.92–1.40)	1.16 (0.96–1.41)
PNIE*	1.18 (0.91–1.52)	1.12 (0.98–1.27)
MIE†	0.01 (-0.18–0.19)	0.08 (-0.08–0.24)
TE*	1.32 (1.13–1.50)	1.37 (1.20–1.53)
Total percentage mediated‡	59	54

All models were adjusted for maternal age, maternal country of birth and year of birth. Model S1 included all 27 244 children. Model S2 included 37 922 children.

*PNDE, PNIE and TE presented as IRR with 95% CI.

†MIE estimated as excess risk due to interaction = IRR^{TE} - IRR^{PNDE} - IRR^{PINE} +1.

‡Total percentage mediated estimated as $((IRR^{PNIE} - 1)/(IRR^{TE} - 1) + RERI^{MIE}/(IRR^{TE} - 1))*100$.

CI, confidence intervals; IRR, incidence rates rations; MIE, mediated interactive effect; PNDE, pure natural direct effect; PNIE, pure natural indirect effect; TE, total causal effect.