Supplementary material

S1. Formulas and definitions

1. Natural direct effect (NDE): Ya,M(a*)- Ya*,M(a*)

This effect is the contrast between the counterfactual outcome if the individual were exposed at A = a, and the counterfactual outcome if the same individual were exposed at $A = a^*$, with the mediator assuming whatever value it would have taken at the reference value of the exposure $A = a^*$.

2. Natural Indirect Effect (NIE): g (E (Y (aM (a))-Y (aM (a*))))

This effect is the contrast, having set the exposure at level A = a, between the counterfactual outcome if the mediator assumed whatever value it would have taken at a value of the exposure A = a and the counterfactual outcome if the mediator assumed whatever value it would have taken at a reference value of the exposure $A = a^*$.

3. Total Effect (TE): g (E (Y (a)-Y (a*)))

The sum of the NDE and the NIE, even in presence of exposure-mediator interaction.

Table S2. Availability of potential mediators by wave

	Wave available						
Mediators	9 Months	3 years	5 years				
1. Perinatal period characteristics							
Maternal pre-pregnancy body mass index (BMI)	×	n/a	n/a				
Breastfeeding duration	×	n/a	n/a				
Birthweight	×	n/a	n/a				
Gestation	×	n/a	n/a				
Maternal smoking during pregnancy	×	n/a	n/a				
Alcohol use during pregnancy	×	n/a	n/a				
Ever seen a health professional for wheeze	\checkmark	\checkmark	\checkmark				
2. Housing conditions							
Damp/condensation	✓	\checkmark	\checkmark				
Tenure	\checkmark	\checkmark	\checkmark				
Furry pets in household	×	\checkmark	\checkmark				
Environmental tobacco smoke	\checkmark	\checkmark	\checkmark				
Access to garden	\checkmark	\checkmark	\checkmark				
3. Potential exposure to infection							
Sibling number in household	✓	\checkmark	\checkmark				
Informal vs formal childcare	\checkmark	\checkmark	n/aª				
4. Neighbourhood characteristics							
Volume of traffic	×	\checkmark	×				
Housing quality	×	\checkmark	×				
Rubbish on pavement	×	\checkmark	×				
Good area	×	\checkmark	\checkmark				

^a Children are in formal childcare/education by 5 years

Table S3. Characteristics in omitted and analytical samples

	Omitted sample ^a	Analytical sample
Asthma phenotype		
Never	73.8	76.8
Transient	10.0	8.0
Persistent	16.2	15.2
Maternal education qualification		
Degree plus	4.4	6.4
Diploma	25.4	36.4
A levels	14.1	16.7
GCSE A-C	26.9	26.1
GCSE D-G	8.7	6.1
None	20.5	8.3
Child's sex		
Female	48.2	49.4
Maternal age at birth		
14-24 years	32.7	24.2
Maternal ethnicity		
Mixed	2.1	0.7
Indian	2.3	1.8
Pakistani	10.5	3.1
Black	5.8	2.6
Other	2.4	1.3
Maternal atopy		
One	23.1	23.6
Both	7.1	6.8
Maternal pre-pregnancy BMI		
Underweight	5.4	4.4
Overweight	27.8	25.7
Obese	14.5	13.0
Breastfeeding at least 3 months		
Yes	79.3	74.6
Child's birth weight		
Healthy weight	8.6	6.0
Gestational age at birth		
Preterm	7.4	6.7
Maternal Smoking in pregnancy		
Yes	35.8	35.1
Alcohol consumption during pregi		
Any unit per week	7.8	10.3
Wheeze at 9 months		
Yes	4.8	3.6
Damp in the house		
Yes	16.1	14.4

	Omitted sample ^a	Analytical sample
Tenure	•	· · ·
Own mortgage	40.3	60.0
Part rent/mortgage	0.3	0.5
Local authority	30.0	16.3
Housing association	9.7	6.8
Privately rented	11.0	7.9
Living with parents	4.2	4.1
Rent free	0.8	1.0
Furry pets		
Yes	35.6	41.0
Environmental tobacco smoke		
Yes	22.4	17.8
Garden access		
Yes, shared	5.5	3.5
No	19.2	10.1
Sibling number		
1	40.1	47.7
2 or more	38.0	27.5
Childcare		
Formal	7.1	13.9
Condition of buildings		
Fair condition	52.8	38.3
Poor condition	8.2	4.8
Bad condition	0.8	0.4
Volume of traffic		
Light	72.8	75.5
Moderate	17.5	14.8
Heavy	3.4	5.0
Litter in the street		
Some	31.3	21.7
Everywhere	3.8	2.0
Good area		
Good	39.4	38.6
Average	23.0	20.9
Poor	8.2	5.1
Very poor	5.8	2.6

^a Omitted samples were still productive in MCS at age 14 but with item missingness (n=1,710)

sample characteristics (N=7,487)												
	Transient RRR	(95	% CI)	Persistent RRR	(959	% CI)						
Maternal education qua	alification											
Diploma	0.90	0.65	1.24	1.08	0.82	1.44						
A levels	1.00	0.69	1.45	1.14	0.82	1.57						
GCSE A-C	1.09	0.76	1.56	1.29	0.95	1.76						
GCSE D-G	1.43	0.87	2.33	1.65	1.05	2.58						
None	0.92	0.56	1.51	1.73	1.11	2.69						
Child's sex												
Female	0.83	0.69	0.99	0.73	0.63	0.85						
Maternal age at birth												
14-24 years	1.23	0.95	1.59	1.18	0.97	1.43						
Maternal ethnicity												
Mixed	0.50	0 15	1 60	0.76	0 3 2	1 2 1						

Table S4. Univariable relative risk ratios (RRR 95% CI) for transient and persistent asthma by sample characteristics (N=7,487)

14-24 years1.230.951.591.180.971.43Maternal ethnicityMaternal ethnicityNiked0.500.151.690.760.321.81Indian0.510.221.190.930.561.52Pakistani0.540.291.011.130.861.49Black0.550.291.011.130.861.58Other0.830.322.170.590.291.19Maternal atopyU1.141.801.751.482.07Both1.541.062.252.632.033.40Maternal pre-pregnarcy B//Underweight0.940.541.631.591.042.43Overweight1.260.931.701.581.271.96Breastfeeding at least 3NT1.260.931.701.581.271.96Breastfeeding at least 3NT1.260.931.701.581.271.96Gestational age at birthUU1.200.440.330.611.170.981.51Yes1.341.081.661.291.091.541.541.761.43Alchole consumption during pregnarcyUUU1.541.551.573.941.551.57Yes0.960.731.281.451.171.791.591.541.571.541.571.541.571.54 <th>Maternal age at birth</th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th>	Maternal age at birth						
Mixed 0.50 0.15 1.69 0.76 0.32 1.81 Indian 0.51 0.22 1.19 0.93 0.56 1.52 Pakistani 0.54 0.29 1.01 1.13 0.86 1.49 Black 0.55 0.29 1.06 0.96 0.58 1.58 Other 0.83 0.32 2.17 0.59 0.29 1.19 Maternal atopy 0.06 1.43 1.14 1.80 1.75 1.48 2.07 Both 1.54 1.06 2.25 2.63 2.03 3.40 Maternal pre-pregnancy BMI Underweight 0.94 0.54 1.63 1.59 1.04 2.43 Overweight 1.26 0.98 1.61 1.17 0.98 1.39 Obese 1.26 0.98 1.61 1.17 0.98 1.39 Okese 0.82 0.64 1.06 0.82 0.70 0.97 Child's birth weigh	14-24 years	1.23	0.95	1.59	1.18	0.97	1.43
Indian 0.51 0.22 1.19 0.93 0.56 1.52 Pakistani 0.54 0.29 1.01 1.13 0.86 1.49 Black 0.55 0.29 1.06 0.96 0.58 1.58 Other 0.83 0.32 2.17 0.59 0.29 1.19 Maternal atopy	Maternal ethnicity						
Pakistani 0.54 0.29 1.01 1.13 0.86 1.49 Black 0.55 0.29 1.06 0.96 0.58 1.58 Other 0.83 0.32 2.17 0.59 0.29 1.19 Maternal atopy 0.06 1.43 1.14 1.80 1.75 1.48 2.07 Both 1.54 1.06 2.25 2.63 2.03 3.40 Maternal pre-pregnancy BMI 0.94 0.54 1.63 1.59 1.04 2.43 Overweight 0.94 0.54 1.63 1.59 1.04 2.43 Overweight 1.26 0.93 1.61 1.17 0.98 1.39 Obese 1.26 0.93 1.66 0.82 0.70 0.97 Child's birth weight 0.77 0.50 1.20 0.44 0.33 0.60 Gestational age at birth 1.92 1.28 2.88 2.09 1.59 2.74 Maternal S	Mixed	0.50	0.15	1.69	0.76	0.32	1.81
Black 0.55 0.29 1.06 0.96 0.58 1.58 Other 0.83 0.32 2.17 0.59 0.29 1.19 Maternal atopy .	Indian	0.51	0.22	1.19	0.93	0.56	1.52
Other 0.83 0.32 2.17 0.59 0.29 1.19 Maternal atopy 0.94 0.54 1.60 2.57 0.59 0.29 1.99 Both 1.54 1.06 2.25 2.63 2.03 3.40 Maternal pre-pregnancy B/I 0.94 0.54 1.63 1.59 1.04 2.43 Overweight 1.26 0.98 1.61 1.17 0.98 1.39 Obese 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 months 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 months 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 months 1.26 0.82 0.70 0.97 Child's birth weight 0.77 0.50 1.20 0.44 0.33 0.60 Gestational age at birth 1.28 2.88 2.09 1.59 2.74 Maternal Smoking in pregna	Pakistani	0.54	0.29	1.01	1.13	0.86	1.49
Maternal atopy One 1.43 1.14 1.80 1.75 1.48 2.07 Both 1.54 1.06 2.25 2.63 2.03 3.40 Maternal pre-pregnancy BMI 1.04 0.54 1.63 1.59 1.04 2.43 Overweight 1.26 0.98 1.61 1.17 0.98 1.39 Obese 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 morths 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 morths 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 morths 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at best 5 0.82 0.64 1.06 0.82 0.70 0.97 Child's birth weight 0.77 0.50 1.20 0.44 0.33 0.60 Gestational age at birth 1.27 1.28 2.09	Black	0.55	0.29	1.06	0.96	0.58	1.58
One 1.43 1.14 1.80 1.75 1.48 2.07 Both 1.54 1.06 2.25 2.63 2.03 3.40 Maternal pre-pregnancy BMI Underweight 0.94 0.54 1.63 1.59 1.04 2.43 Overweight 1.26 0.98 1.61 1.17 0.98 1.39 Obese 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 months 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 months 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 months 0.82 0.70 0.97 O.17 0.50 1.20 0.44 0.33 0.60 Gestational age at birth 1.92 1.28 2.88 2.09 1.59 2.74 Maternal Smoking in pregnancy 1.49 1.09 1.54 Alcohol consumption during pregnancy 1.09 1.50 Meeze at 9 months	Other	0.83	0.32	2.17	0.59	0.29	1.19
Both 1.54 1.06 2.25 2.63 2.03 3.40 Maternal pre-pregnancy BMU Underweight 0.94 0.54 1.63 1.59 1.04 2.43 Overweight 1.26 0.98 1.61 1.17 0.98 1.39 Obese 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 months 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 months 1.26 0.82 0.70 0.97 0.97 Child's birth weight 0.77 0.50 1.20 0.44 0.33 0.60 Gestational age at birth 1.92 1.28 2.88 2.09 1.59 2.74 Maternal Smoking in pregnancy 1.27 1.66 1.29 1.09 1.54 Alcohol consumption during pregnancy 1.93 1.68 1.27 1.16 0.90 1.50 Yes 0.93 0.68 1.27 1.66 0.90	Maternal atopy						
Maternal pre-pregnancy B/IUnderweight0.940.541.631.591.042.43Overweight1.260.981.611.170.981.39Obese1.260.931.701.581.271.96Breastfeeding at least 3 moths11.060.820.700.97Yes0.820.641.060.820.700.97Child's birth weight0.770.501.200.440.330.60Gestational age at birth1.921.282.882.091.592.74Maternal Smoking in pregmancy1.541.661.291.091.54Alcohol consumption during pregnancy11.661.291.091.54Yes0.930.681.271.160.901.50Ohmp in the house11.553.723.042.104.39Damp in the house11.251.270.861.88Part rent/mortgage2.001.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	One	1.43	1.14	1.80	1.75	1.48	2.07
Underweight 0.94 0.54 1.63 1.59 1.04 2.43 Overweight 1.26 0.98 1.61 1.17 0.98 1.39 Obese 1.26 0.93 1.70 1.58 1.27 1.96 Breastfeeding at least 3 months	Both	1.54	1.06	2.25	2.63	2.03	3.40
Overweight1.260.981.611.170.981.39Obese1.260.931.701.581.271.96Breastfeeding at least 3 morths0.641.060.820.700.97Yes0.820.641.060.820.700.970.110.	Maternal pre-pregnancy B	BMI					
Obese1.260.931.701.581.271.96Breastfeeding at least 3 monthsYes0.820.641.060.820.700.97Child's birth weight0.770.501.200.440.330.60Gestational age at birth1.282.882.091.592.74Preterm1.921.282.882.091.592.74Maternal Smoking in pregnancy1.661.291.091.54Alcohol consumption during pregnancy1.661.291.091.50Mheeze at 9 months0.681.271.160.901.50Pres2.241.353.723.042.104.39Damp in the house1.281.451.171.79Prenure1.093.671.270.861.88Part rent/mortgage2.001.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Underweight	0.94	0.54	1.63	1.59	1.04	2.43
Breastfeeding at least 3 months Yes 0.82 0.64 1.06 0.82 0.70 0.97 Child's birth weight 0.77 0.50 1.20 0.44 0.33 0.60 Gestational age at birth 0.77 0.50 1.20 0.44 0.33 0.60 Gestational age at birth 0.77 0.50 1.28 2.88 2.09 1.59 2.74 Maternal Smoking in pregnancy 1.28 2.88 2.09 1.59 2.74 Alcohol consumption during pregnancy 1.66 1.29 1.09 1.54 Alcohol consumption during pregnancy 1.16 0.90 1.50 Yes 2.24 1.35 3.72 3.04 2.10 4.39 Damp in the house 1.27 1.45 1.17 1.79 Yes 0.96 0.73 1.28 1.45 1.17 1.79 Tenure 1.09 3.67 1.27 0.86 1.88 Part rent/mortgage 2.00 1.09 3.67 3.29 1.33 8.12 Local authority <td< td=""><td>Overweight</td><td>1.26</td><td>0.98</td><td>1.61</td><td>1.17</td><td>0.98</td><td>1.39</td></td<>	Overweight	1.26	0.98	1.61	1.17	0.98	1.39
Yes0.820.641.060.820.700.97Child's birth weight0.770.501.200.440.330.60Gestational age at birthPreterm1.921.282.882.091.592.74Maternal Smoking in pregmarcyYes1.341.081.661.291.091.54Alcohol consumption during pregnancyYes0.930.681.271.160.901.50Wheeze at 9 monthsYes2.241.353.723.042.104.39Damp in the houseYes0.960.731.281.451.171.79TenureOwn mortgage2.001.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Obese	1.26	0.93	1.70	1.58	1.27	1.96
Child's birth weight 0.77 0.50 1.20 0.44 0.33 0.60 Gestational age at birth Preterm 1.92 1.28 2.88 2.09 1.59 2.74 Maternal Smoking in prepency Yes 1.34 1.08 1.66 1.29 1.09 1.54 Alcohol consumption during pregnancy Any unit per week 0.93 0.68 1.27 1.16 0.90 1.50 Wheeze at 9 months	Breastfeeding at least 3 m	onths					
Healthy weight0.770.501.200.440.330.60Gestational age at birthPreterm1.921.282.882.091.592.74Maternal Smoking in pregnancyYes1.341.081.661.291.091.54Alcohol consumption during pregnancyYay0.930.681.271.160.901.50Wheeze at 9 monthsYes2.241.353.723.042.104.39Damp in the houseYes0.960.731.281.451.171.79TenureOwn mortgage2.001.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Yes	0.82	0.64	1.06	0.82	0.70	0.97
Gestational age at birthPreterm1.921.282.882.091.592.74Maternal Smoking in pregnancyYes1.341.081.661.291.091.54Alcohol consumption during pregnancyAny unit per week0.930.681.271.160.901.50Wheeze at 9 monthsYes2.241.353.723.042.104.39Damp in the houseYes0.960.731.281.451.171.79TenureOwn mortgage2.001.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Child's birth weight						
Preterm 1.92 1.28 2.88 2.09 1.59 2.74 Maternal Smoking in pregnancy 1.34 1.08 1.66 1.29 1.09 1.54 Yes 1.34 1.08 1.66 1.29 1.09 1.54 Alcohol consumption during pregnancy 1.16 0.90 1.50 My unit per week 0.93 0.68 1.27 1.16 0.90 1.50 Wheeze at 9 months 1.25 3.72 3.04 2.10 4.39 Damp in the house 1.28 1.45 1.17 1.79 Yes 0.96 0.73 1.28 1.45 1.17 1.79 Tenure 1 1.09 3.67 1.27 0.86 1.88 Part rent/mortgage 2.00 1.09 3.67 1.27 0.86 1.88 Part rent/mortgage 4.93 1.55 15.7 3.29 1.33 8.12 Local authority 2.98 1.50 5.94 2.27 1.47 <td>Healthy weight</td> <td>0.77</td> <td>0.50</td> <td>1.20</td> <td>0.44</td> <td>0.33</td> <td>0.60</td>	Healthy weight	0.77	0.50	1.20	0.44	0.33	0.60
Maternal Smoking in prejertYes1.341.081.661.291.091.54Alcohol consumption durry pregnancy	Gestational age at birth						
Yes1.341.081.661.291.091.54Alcohol consumption during pregnancyAny unit per week0.930.681.271.160.901.50Wheeze at 9 monthsYes2.241.353.723.042.104.39Damp in the houseYes0.960.731.281.451.171.79TenureOwn mortgage2.001.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Preterm	1.92	1.28	2.88	2.09	1.59	2.74
Alcohol consumption during pregnancy Any unit per week 0.93 0.68 1.27 1.16 0.90 1.50 Wheeze at 9 months	Maternal Smoking in preg	nancy					
Any unit per week0.930.681.271.160.901.50Wheeze at 9 months	Yes	1.34	1.08	1.66	1.29	1.09	1.54
Wheeze at 9 monthsYes2.241.353.723.042.104.39Damp in the houseYes0.960.731.281.451.171.79TenureOwn mortgage2.001.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Alcohol consumption duri	ng pregnancy					
Yes2.241.353.723.042.104.39Damp in the houseYes0.960.731.281.451.171.79TenureOwn mortgage2.001.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Any unit per week	0.93	0.68	1.27	1.16	0.90	1.50
Damp in the houseYes0.960.731.281.451.171.79Tenure91.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Wheeze at 9 months						
Yes0.960.731.281.451.171.79Tenure	Yes	2.24	1.35	3.72	3.04	2.10	4.39
TenureOwn mortgage2.001.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Damp in the house						
Own mortgage2.001.093.671.270.861.88Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Yes	0.96	0.73	1.28	1.45	1.17	1.79
Part rent/mortgage4.931.5515.73.291.338.12Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Tenure						
Local authority2.981.505.942.271.473.50Housing association2.951.535.681.590.992.54	Own mortgage	2.00	1.09	3.67	1.27	0.86	1.88
Housing association 2.95 1.53 5.68 1.59 0.99 2.54	Part rent/mortgage	4.93	1.55	15.7	3.29	1.33	8.12
-	Local authority	2.98	1.50	5.94	2.27	1.47	3.50
Privately rented 2.42 1.19 4.91 1.76 1.04 2.96	Housing association	2.95	1.53	5.68	1.59	0.99	2.54
	Privately rented	2.42	1.19	4.91	1.76	1.04	2.96

^A reference category: Never had asthma

Table S4. (continued) Univariable relative risk ratios (RRR 95% CI) for transient and persistent asthma by sample characteristics (N=7,487)

	Transient RRR	(95% CI) F		Persistent RRR	(95% C	CI)
Living with parents	2.44	0.81	7.37	1.21	0.63	2.31
Rent free	2.10	0.59	7.46	1.00	0.33	3.02
Furry pets						
Yes	1.05	0.85	1.30	0.95	0.81	1.12
Environmental tobacco sr	noke					
Yes	1.03	0.78	1.35	1.02	0.81	1.28
Garden access						
Yes, shared	0.87	0.48	1.56	1.17	0.73	1.88
No	1.13	0.80	1.60	1.21	0.92	1.59
Sibling number						
1	1.09	0.85	1.39	0.83	0.70	1.00
2 or more	0.99	0.75	1.31	0.82	0.66	1.02
Childcare						
Formal	0.80	0.59	1.07	0.87	0.72	1.06
Condition of buildings						
Fair condition	1.10	0.86	1.40	1.42	1.22	1.65
Poor condition	1.46	0.87	2.46	1.84	1.20	2.81
Bad condition	3.39	1.07	10.77	1.81	0.35	9.30
Volume of traffic						
Light	1.08	0.66	1.78	1.34	0.86	2.09
Moderate	0.91	0.51	1.60	1.41	0.88	2.26
Heavy	1.04	0.49	2.22	1.72	1.04	2.85
Litter in the street						
Some	1.12	0.84	1.48	1.21	0.99	1.48
Everywhere	1.58	0.90	2.76	0.86	0.47	1.58
Good area						
Good	1.36	1.08	1.72	1.15	0.97	1.38
Average	1.43	1.09	1.88	1.12	0.90	1.40
Poor	1.32	0.77	2.26	1.49	1.05	2.11
Very poor	2.04	1.17	3.57	1.65	1.07	2.53

^A reference category: Never had asthma

Persistent

Total

	Nevel	ITUISICITE	Tersisterit	Total
Maternal education qua	lification			
Degree plus	6.6	6.5	5.4	6.4
Diploma	37.4	33.1	33.0	36.4
A levels	16.9	16.7	15.7	16.7
GCSE A-C	25.6	28.4	27.1	26.1
GCSE D-G	5.6	8.1	7.7	6.1
None	7.9	7.3	11.1	8.3
Child's sex				0.0
Female	50.9	46.5	43.3	49.4
Maternal age at birth	0010			
14-24 years	23.5	27.0	26.8	24.2
Maternal ethnicity	2010	2710	20.0	
Mixed	0.8	0.4	0.6	0.7
Indian	1.9	1.0	1.8	1.8
Pakistani	3.2	1.6	3.7	3.1
Black	2.8	1.6	2.7	2.6
Other	1.4	1.2	0.8	1.3
Maternal atopy				
One	21.8	27.3	30.2	23.6
Both	5.6	8.1	11.8	6.8
Maternal pre-pregnancy	/ BMI			
Underweight	4.2	3.6	5.9	4.4
Overweight	25.3	29.3	26.2	25.7
Obese	12.2	13.9	16.7	13.0
Breastfeeding at least 3	months			
Yes	73.9	76.6	77.4	74.6
Child's birth weight				
Healthy weight	5.0	6.2	10.8	6.0
Gestational age at birth				
Preterm	5.5	10.1	11.0	6.7
Maternal Smoking in pro	egnancy			
Yes	33.6	40.7	39.7	35.1
Alcohol consumption du	iring pregnancy			
Any unit per week	10.1	9.9	11.5	10.3
Wheeze at 9 months				
Yes	2.6	5.7	7.2	3.6
Damp in the house				
Yes	13.6	13.9	18.7	14.4
Tenure				
Own mortgage	61.4	57.8	54.2	60.0
Part rent/mortgage	0.5	0.3	0.7	0.5
Local authority	15.4	18.3	20.1	16.3
Housing association	6.6	8.1	6.7	6.8
Privately rented				
Privately rented	7.5	7.9	10.3	7.9

Table S5. Characteristics of children with transient or persistent asthma in sample (N=7,487)

Transient

Never

	Never	Transient	Persistent	Total
Living with parents	4.0	3.4	5.3	4.1
Rent free	0.9	2.2	1.0	1.0
Furry pets				
Yes	40.9	43.7	40.0	41.0
Environmental tobacco	smoke			
Yes	17.7	18.2	18.0	17.8
Garden access				
Yes, shared	3.4	3.3	3.9	3.5
No	9.7	10.9	11.5	10.1
Sibling number				
1	47.8	50.3	45.8	47.7
2 or more	27.8	26.3	26.3	27.5
Childcare				
Formal	14.3	11.7	12.7	13.9
Condition of buildings				
Fair condition	37.1	38.5	44.1	38.3
Poor condition	4.3	5.9	6.6	4.8
Bad condition	0.3	0.9	0.4	0.4
Volume of traffic				
Light	75.4	77.3	75.0	75.5
Moderate	14.9	12.7	15.3	14.8
Heavy	4.7	5.0	6.0	5.0
Litter in the street				
Some	21.0	22.6	24.6	21.7
Everywhere	1.9	2.9	0.2	2.0
Good area				
Good	38.2	40.6	39.2	38.6
Average	20.6	23.3	20.9	20.9
Poor	4.9	5.0	6.4	5.1
Very poor	2.4	3.8	3.3	2.6

Table S5. (continued) Prevalence of asthma by sample characteristics (N=7,487)

Thorax

Table S6. Relative risk ratios (RRR) for asthma phenotype by SEC adjusted for blocks of mediators including mediators available at all time points (N=7,284)

	Baseline Model			Baseline Model Model 1 Model 2							<u>Model</u>	<u>3</u>	Model 4		
	RRR ^a	95	% CI	RRR	95	% CI	RRR	95% CI		RRR	95	5% CI	RRR	95% CI	
Transient as	sthma														
Diploma	0.85	0.61	1.18	0.79	0.57	1.09	0.78	0.56	1.08	0.78	0.56	1.08	0.77	0.55	1.08
A levels	0.89	0.62	1.28	0.78	0.54	1.14	0.78	0.54	1.15	0.78	0.53	1.14	0.76	0.51	1.12
GCSE A-C	1.00	0.68	1.48	0.83	0.55	1.23	0.80	0.53	1.19	0.80	0.53	1.19	0.77	0.52	1.16
GCSE D-G	1.25	0.72	2.15	1.01	0.59	1.72	1.03	0.60	1.76	1.02	0.59	1.76	0.99	0.58	1.69
None	0.94	0.57	1.57	0.75	0.44	1.30	0.72	0.41	1.27	0.72	0.41	1.28	0.69	0.40	1.21
Persistent a	sthma														
Diploma	1.01	0.77	1.34	0.93	0.66	1.32	0.93	0.66	1.32	0.93	0.66	1.32	0.93	0.66	1.32
A levels	1.04	0.75	1.45	0.93	0.61	1.40	0.92	0.61	1.39	0.93	0.61	1.41	0.93	0.61	1.41
GCSE A-C	1.22	0.89	1.67	1.00	0.68	1.46	1.00	0.69	1.46	1.02	0.69	1.51	1.01	0.69	1.49
GCSE D-G	1.48	0.93	2.35	1.17	0.65	2.11	1.18	0.65	2.14	1.19	0.66	2.16	1.17	0.65	2.12
None	1.73	1.08	2.77	1.45	0.85	2.47	1.43	0.84	2.43	1.48	0.87	2.52	1.46	0.86	2.50

^a All models were adjusted for baseline confounders (child sex, maternal age at birth, maternal ethnicity, and maternal atopy). Degree plus is the reference category. Model 1: Baseline model + perinatal characteristics (maternal pre-pregnancy BMI; breastfeeding duration; birth weight; gestation; maternal smoking during pregnancy; alcohol use during pregnancy; wheeze at 9 months, 3 & 5 years)

Model 2: Model 1 + housing conditions (damp at 9 months, 3 & 5 years; tenure at 9 months, 3 & 5 years; furry pets at 9 months & 3 years; environmental tobacco smoke at 9 months, 3 & 5 years; access to garden at 9 months, 3 & 5 years)

Model 3: Model 2 + potential exposure to infection (sibling number at 9 months, 3 & 5 years; childcare type at 9 months & 3 years)

Model 4: Model 3 + neighbourhood characteristics (volume of traffic; housing quality; rubbish; area rating at 3 & 5 years)

	Baseline Model		Baseline Model Model 1 Model 2			Model 3			Model	4	Model 5		5					
	RRR ^a	959	% CI	RRR	95	% CI	RRR	RRR 95% CI F		RRR	95	5% CI	RRR	RRR 95% CI		RRR	RRR 95% CI	
Transient as	sthma																	
Diploma	0.86	0.62	1.19	0.81	0.58	1.12	0.82	0.59	1.13	0.81	0.58	1.12	0.79	0.56	1.10	0.78	0.55	1.09
A levels	0.93	0.65	1.34	0.83	0.57	1.21	0.84	0.58	1.22	0.82	0.57	1.19	0.79	0.54	1.15	0.76	0.52	1.12
GCSE A-C	1.01	0.69	1.47	0.87	0.59	1.27	0.89	0.60	1.31	0.85	0.57	1.26	0.81	0.55	1.20	0.77	0.52	1.15
GCSE D-G	1.26	0.74	2.14	1.09	0.65	1.85	1.15	0.67	1.96	1.08	0.64	1.83	1.03	0.61	1.74	0.96	0.57	1.63
None	0.92	0.56	1.51	0.73	0.44	1.23	0.77	0.46	1.30	0.71	0.42	1.21	0.68	0.40	1.15	0.63	0.38	1.05
Persistent a	sthma																	
Diploma	1.03	0.78	1.36	0.96	0.72	1.27	0.96	0.73	1.28	0.96	0.73	1.27	0.95	0.72	1.26	0.95	0.72	1.26
A levels	1.08	0.78	1.50	0.96	0.69	1.35	0.98	0.70	1.38	0.97	0.69	1.36	0.96	0.68	1.35	0.95	0.67	1.33
GCSE A-C	1.24	0.91	1.70	1.09	0.79	1.51	1.12	0.82	1.55	1.10	0.80	1.52	1.10	0.79	1.53	1.08	0.78	1.49
GCSE D-G	1.50	0.95	2.35	1.34	0.85	2.12	1.43	0.91	0.25	1.35	0.86	2.13	1.36	0.85	2.15	1.31	0.83	2.07
None	1.71	1.07	2.74	1.35	0.86	2.12	1.44	0.92	2.26	1.35	0.86	2.10	1.37	0.87	2.16	1.31	0.82	2.09
Proportion attenuated (%) ^b		50.70			38.03			50.70			47.89			56.34				

Table S7. Relative risk ratios (RRR) for transient and persistent asthma compared to never by SEC adjusted for blocks of mediators (N=7,487)

^a All models were adjusted for baseline confounders (child sex, maternal age at birth, maternal ethnicity, and maternal atopy). Degree plus is the reference category.

^b Proportion of RRR of persistent asthma attenuated by comparison of baseline model with models 1-4 for lowest SECs (100x (RRR-adjusted RRR)/(RRR-1))

Model 1: Baseline model + perinatal characteristics (maternal pre-pregnancy BMI; breastfeeding duration; birth weight; gestation; maternal smoking during pregnancy; alcohol use during pregnancy; wheeze

Model 2: Model 1 + environmental tobacco smoke

Model 3: Model 2 + housing conditions (damp; tenure; furry pets; access to garden)

Model 4: Model 3 + potential exposure to infection (sibling number; childcare type)

Model 5: Model 4 + neighbourhood characteristics (volume of traffic; housing quality; rubbish; area rating)

	Baseline Model			Model 1			Model 2			Model 3			Model 4		
	RRR ^a	95	5% CI	RRR	95	5% CI	RRR	95	5% CI	RRR	95	5% CI	RRR	95	5% CI
Transient	asthma														
Diploma	0.86	0.62	1.19	0.81	0.58	1.12	0.81	0.58	1.12	0.79	0.56	1.10	0.78	0.55	1.09
A levels	0.93	0.65	1.34	0.83	0.57	1.21	0.82	0.57	1.19	0.79	0.54	1.15	0.76	0.52	1.12
GCSE A-C	1.01	0.69	1.47	0.87	0.59	1.27	0.85	0.58	1.26	0.81	0.55	1.20	0.77	0.52	1.15
GCSE D-G	1.26	0.74	2.14	1.09	0.65	1.85	1.08	0.64	1.83	1.03	0.61	1.74	0.96	0.57	1.63
None	0.92	0.56	1.51	0.73	0.44	1.23	0.71	0.42	1.21	0.68	0.40	1.15	0.63	0.38	1.05
Persistent	asthma	(twice)													
Diploma	0.99	0.68	1.46	0.93	0.63	1.37	0.94	0.64	1.38	0.94	0.64	1.38	0.94	0.64	1.38
A levels	1.01	0.64	1.61	0.94	0.58	1.50	0.95	0.59	1.52	0.96	0.59	1.54	0.94	0.59	1.51
GCSE A-C	1.13	0.73	1.74	1.04	0.67	1.61	1.06	0.69	1.65	1.10	0.70	1.70	1.07	0.69	1.66
GCSE D-G	1.73	1.00	2.99	1.64	0.94	2.87	1.73	0.99	3.03	1.80	1.02	3.17	1.73	0.99	3.05
None	1.57	0.86	2.88	1.32	0.75	2.34	1.40	0.80	2.43	1.48	0.84	2.61	1.42	0.79	2.53
Persistent	asthma	ı (3 time	es)												
Diploma	1.08	0.73	1.59	0.98	0.66	1.46	0.99	0.67	1.46	0.96	0.64	1.44	0.96	0.64	1.45
A levels	1.16	0.74	1.80	0.99	0.63	1.56	0.99	0.63	1.57	0.96	0.60	1.52	0.95	0.59	1.52
GCSE A-C	1.37	0.89	2.10	1.14	0.73	1.79	1.14	0.73	1.77	1.10	0.70	1.75	1.08	0.68	1.72
GCSE D-G	1.20	0.57	2.51	1.00	0.47	2.12	0.96	0.45	2.02	0.93	0.44	1.97	0.90	0.42	1.91
None	1.87	1.05	3.33	1.37	0.76	2.50	1.29	0.71	2.35	1.26	0.69	2.31	1.21	0.65	2.25

Table S8. Relative risk ratios (RRR) for transient and persistent (two and three categorisations) asthma by SEC adjusted for blocks of mediators (N=7,487)

^a All models were adjusted for baseline confounders (child sex, maternal age at birth, maternal ethnicity, and maternal atopy). Degree plus is the reference category. Model 1: Baseline model + perinatal characteristics (maternal pre-pregnancy BMI; breastfeeding duration; birth weight; gestation; maternal smoking during pregnancy; alcohol use during pregnancy; wheeze

Model 2: Model 1 + housing conditions (damp; tenure; furry pets; environmental tobacco smoke; access to garden)

Model 3: Model 2 + potential exposure to infection (sibling number; childcare type)

Model 4: Model 3 + neighbourhood characteristics (volume of traffic; housing quality; rubbish; area rating)

Thorax

	Baseline Model			Model 1			Model 2			Model 3			Model 4		
_	RRR ^a	95	% CI	RRR	95	% CI	RRR	95	% CI	RRR	95	5% CI	RRR	95% CI	
Asthma at 1	L4 years														
Diploma	0.94	0.55	1.60	0.88	0.51	1.51	0.87	0.51	1.49	0.85	0.49	1.49	0.84	0.48	1.47
A levels	0.70	0.36	1.39	0.63	0.31	1.28	0.61	0.30	1.25	0.59	0.28	1.23	0.57	0.27	1.20
GCSE A-C	0.50	0.26	0.96	0.44	0.22	0.88	0.42	0.21	0.84	0.40	0.20	0.82	0.39	0.19	0.80
GCSE D-G	1.19	0.48	2.93	1.07	0.44	2.62	1.04	0.42	2.56	0.98	0.39	2.43	0.93	0.38	2.26
None	0.87	0.41	1.84	0.77	0.36	1.64	0.72	0.32	1.61	0.66	0.29	1.50	0.63	0.28	1.44

Table S9. Odds ratios (OR) for current asthma at 14 years (excluding prior reports) compared to none by SEC adjusted for blocks of mediators (N= 5,930)

^a All models were adjusted for baseline confounders (child sex, maternal age at birth, maternal ethnicity, and maternal atopy). Degree plus is the reference category. ^b Current asthma at 14 years was defined by any report of asthma (yes/no) at 14 years only (excluding [n= 3,099] those who had reported asthma at 7 or 11 years)

Model 1: Baseline model + perinatal characteristics (maternal pre-pregnancy BMI; breastfeeding duration; birth weight; gestation; maternal smoking during pregnancy;

alcohol use during pregnancy; wheeze

Model 2: Model 1 + housing conditions (damp; tenure; furry pets; environmental tobacco smoke; access to garden)

Model 3: Model 2 + potential exposure to infection (sibling number; childcare type)

Model 4: Model 3 + neighbourhood characteristics (volume of traffic; housing quality; rubbish; area rating)

Thorax

Table S10. Longitudinal typlogies of wheeze

0=no wheeze; 1=whee:	ze						
Typology #1 (<u>analysis</u> typology)	Typology #2	9m (taken to health prof. for wheeze)	3y (wheeze in last 12m)	5y (wheeze in last 12m)	7y (wheeze in last 12m)	Frequency	
Never	Never	0	0	0	0	66.0% (7540)	
Early remitting	Gone by seven	1	0	0	0	3.14 (359)	
Early remitting	Gone by seven	1	1	0	0	1.05 (120)	
Early remitting	Gone by seven	1	1	1	0	0.54 (62)	
Early remitting	Gone by seven	0	1	0	0	8.7 (989)	
Early remitting	Gone by seven	0	1	1	0	3.7 (418)	
Persistent/relapsing	Late onset >3	0	0	1	1	2.9 (326)	
Persistent/relapsing	Late onset >3	0	0	0	1	2.9 (336)	
Persistent/relapsing	Always	0	1	1	1	3.82 (436)	
Persistent/relapsing	Always	1	1	1	1	0.56 (64)	
Persistent/relapsing	Relapse by seven	0	1	0	1	1.3 (149)	
Persistent/relapsing	Relapse by seven	1	0	0	1	0.3 (34)	
Persistent/relapsing	Relapse by seven	1	1	0	1	0.2 (26)	
Persistent/relapsing	Relapse by seven	1	0	1	1	0.2 (22)	
Transient/intermittent	Transient	0	0	1	0	4.4 (498)	
Transient/intermittent	Intermittent	1	0	1	0	0.3 (39)	

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4771620/