S1. Formulas and definitions

1. Natural direct effect (NDE): $Y_{a,M(a^*)} - Y_{a^*,M(a^*)}$
   
   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

| Mediators                                      | Wave available |
|-----------------------------------------------|----------------|
|                                               | 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    | ✓         | ✓       | ✓       |
| **2. Housing conditions**                     |           |         |         |
| Damp/condensation                             | ✓         | ✓       | ✓       |
| Tenure                                        | ✓         | ✓       | ✓       |
| Furry pets in household                       | ×         | ✓       | ✓       |
| Environmental tobacco smoke                   | ✓         | ✓       | ✓       |
| Access to garden                              | ✓         | ✓       | ✓       |
| **3. Potential exposure to infection**         |           |         |         |
| Sibling number in household                   | ✓         | ✓       | ✓       |
| Informal vs formal childcare                  | ✓         | ✓       | n/a³    |
| **4. Neighbourhood characteristics**          |           |         |         |
| Volume of traffic                             | ×         | ✓       | ×       |
| Housing quality                               | ×         | ✓       | ×       |
| Rubbish on pavement                           | ×         | ✓       | ×       |
| Good area                                     | ×         | ✓       | ✓       |

³ Children are in formal childcare/education by 5 years
|                                | Omitted sample | 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 pregnancy** |    |                   |
| 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              |
Table S3. (continued) Characteristics in omitted and analytical samples

| Characteristics                        | Omitted sample | 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               |

*Omitted samples were still productive in MCS at age 14 but with item missingness (n=1,710)
Table S4. Univariable relative risk ratios (RRR 95% CI) for transient and persistent asthma by sample characteristics (N=7,487)

| Maternal education qualification | Transient RRR | (95% CI) | Persistent RRR | (95% CI) |
|----------------------------------|--------------|----------|----------------|----------|
| Diploma                          | 0.90         | 0.65     | 1.24           | 0.82     |
| A levels                         | 1.00         | 0.69     | 1.45           | 0.82     |
| GCSE A-C                         | 1.09         | 0.76     | 1.56           | 0.95     |
| GCSE D-G                         | 1.43         | 0.87     | 2.33           | 1.05     |
| None                             | 0.92         | 0.56     | 1.51           | 1.11     |
| Child's sex                      | Female       | 0.83     | 0.69           | 0.73     |
| Maternal age at birth            | 14-24 years  | 1.23     | 0.95           | 1.18     |
| Maternal ethnicity               | Mixed        | 0.50     | 0.15           | 0.76     |
|                                  | Indian       | 0.51     | 0.22           | 0.93     |
|                                  | Pakistani    | 0.54     | 0.29           | 1.13     |
|                                  | Black        | 0.55     | 0.29           | 0.96     |
|                                  | Other        | 0.83     | 0.32           | 0.59     |
| Maternal atopy                   | One          | 1.43     | 1.14           | 1.75     |
|                                  | Both         | 1.54     | 1.06           | 2.63     |
| Maternal pre-pregnancy BMI       | Underweight  | 0.94     | 0.54           | 1.59     |
|                                  | Overweight   | 1.26     | 0.98           | 1.17     |
|                                  | Obese        | 1.26     | 0.93           | 1.58     |
| Breastfeeding at least 3 months  | Yes          | 0.82     | 0.64           | 0.82     |
|                                  | Child's birth weight | 0.77 | 0.50     | 0.44     |
|                                  | Healthy weight | 0.77 | 0.50     | 0.44     |
|                                  | Gestational age at birth | 1.92 | 1.28     | 2.09     |
| Maternal Smoking in pregnancy    | Yes          | 1.34     | 1.08           | 1.29     |
| Alcohol consumption during pregnancy | Any unit per week | 0.93 | 0.68     | 1.16     |
|                                  | Wheeze at 9 months | Yes  | 2.24     | 1.35     |
|                                  | Damp in the house | Yes  | 0.96     | 0.73     |
| Tenure                           | Own mortgage | 2.00     | 1.09           | 1.27     |
|                                  | Part rent/mortgage | 4.93 | 1.55     | 1.57     |
|                                  | Local authority | 2.98 | 1.50     | 2.27     |
|                                  | Housing association | 2.95 | 1.53     | 1.59     |
|                                  | Privately rented | 2.42 | 1.19     | 1.76     |

*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)

| Sample Characteristics         | Transient RRR (95% CI) | Persistent RRR (95% 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)      | 0.81 (1.12)             |
| Environmental tobacco smoke    |                        |                         |
| Yes                            | 1.03 (0.78, 1.35)      | 0.81 (1.28)             |
| Garden access                  |                        |                         |
| Yes, shared                    | 0.87 (0.48, 1.56)      | 0.73 (1.88)             |
| No                             | 1.13 (0.80, 1.60)      | 0.92 (1.59)             |
| Sibling number                 |                        |                         |
| 1                              | 1.09 (0.85, 1.39)      | 0.83 (1.00)             |
| 2 or more                      | 0.99 (0.75, 1.31)      | 0.82 (1.02)             |
| Childcare                      |                        |                         |
| Formal                         | 0.80 (0.59, 1.07)      | 0.72 (1.06)             |
| Condition of buildings         |                        |                         |
| Fair condition                 | 1.10 (0.86, 1.40)      | 1.22 (1.65)             |
| Poor condition                 | 1.46 (0.87, 2.46)      | 1.20 (2.81)             |
| Bad condition                  | 3.39 (1.07, 10.77)     | 0.35 (9.30)             |
| Volume of traffic              |                        |                         |
| Light                          | 1.08 (0.66, 1.78)      | 0.86 (2.09)             |
| Moderate                       | 0.91 (0.51, 1.60)      | 0.88 (2.26)             |
| Heavy                          | 1.04 (0.49, 2.22)      | 1.04 (2.85)             |
| Litter in the street           |                        |                         |
| Some                           | 1.12 (0.84, 1.48)      | 0.99 (1.48)             |
| Everywhere                     | 1.58 (0.90, 2.76)      | 0.47 (1.58)             |
| Good area                      |                        |                         |
| Good                           | 1.36 (1.08, 1.72)      | 0.97 (1.38)             |
| Average                        | 1.43 (1.09, 1.88)      | 0.90 (1.40)             |
| Poor                           | 1.32 (0.77, 2.26)      | 1.05 (2.11)             |
| Very poor                      | 2.04 (1.17, 3.57)      | 1.07 (2.53)             |

*Reference category: Never had asthma*
Table S5. Characteristics of children with transient or persistent asthma in sample (N=7,487)

|                                | Never | Transient | Persistent | Total |
|--------------------------------|-------|-----------|------------|-------|
| Maternal education qualification |       |           |            |       |
| 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                     |       |           |            |       |
| Female                          | 50.9  | 46.5      | 43.3       | 49.4  |
| Maternal age at birth           |       |           |            |       |
| 14-24 years                     | 23.5  | 27.0      | 26.8       | 24.2  |
| Maternal ethnicity              |       |           |            |       |
| 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 pregnancy   |       |           |            |       |
| Yes                             | 33.6  | 40.7      | 39.7       | 35.1  |
| Alcohol consumption during 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                | 7.5   | 7.9       | 10.3       | 7.9   |
Table S5. (continued) Prevalence of asthma by sample characteristics (N=7,487)

|                                | 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 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)

| Phenotype        | SEC | Baseline Model | Model 1 | Model 2 | Model 3 | Model 4 |
|------------------|-----|----------------|---------|---------|---------|---------|
|                  | RRR | 95% CI         | RRR     | 95% CI  | RRR     | 95% CI  | RRR     | 95% CI  | RRR     | 95% CI  |
| Transient asthma |      |                |         |         |         |         |         |         |         |         |
| Diploma          | 0.85| 0.61 1.18      | 0.79    | 0.57    | 1.09    | 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    |
| 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    |
| 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    |
| 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    |
| Persistent asthma|      |                |         |         |         |         |         |         |         |         |         |
| 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    |
| 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    |
| 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    |
| 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    |
| 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    |

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

|                | Baseline Model | Model 1     | Model 2     | Model 3     | Model 4     | Model 5     |
|----------------|----------------|-------------|-------------|-------------|-------------|-------------|
|                | RRR            | 95% CI      | RRR         | 95% CI      | RRR         | 95% CI      | RRR         | 95% CI      | RRR         | 95% CI      | RRR         | 95% CI      |
| Transient asthma |                |             |             |             |             |             |             |             |             |             |             |             |
| Diploma        | 0.86           | 0.62 - 1.19 | 0.81        | 0.58 - 1.12 | 0.82        | 0.59 - 1.13 | 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 | 0.79        | 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 | 0.81        | 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 | 1.03        | 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 asthma |              |             |             |             |             |             |             |             |             |             |             |             |
| Diploma        | 1.03           | 0.78 - 1.36 | 0.96        | 0.72 - 1.27 | 0.96        | 0.73 - 1.28 | 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        | 0.79 - 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 - 2.05 | 1.35        | 0.86 - 2.14 | 1.36        | 0.85 - 2.17 | 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 |

*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)
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)

|                          | Baseline Model | Model 1 | Model 2 | Model 3 | Model 4 |
|--------------------------|----------------|---------|---------|---------|---------|
|                          | RRR | 95% CI | RRR | 95% CI | RRR | 95% CI | RRR | 95% CI | RRR | 95% 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 (3 times)|     |       |     |       |     |       |
| 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 |

*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)
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)

| Asthma at 14 years | Baseline Model | Model 1 | Model 2 | Model 3 | Model 4 |
|-------------------|----------------|---------|---------|---------|---------|
|                   | RRR  95% CI    | RRR  95% CI | RRR  95% CI | RRR  95% CI | RRR  95% CI |
| Diploma           | 0.94 0.55 1.60 | 0.88 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 |

*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)
### Table S10. Longitudinal typologies of wheeze

| Typology #1 (baseline 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                      | 98.0%     |
| Early remitting                | Gone by seven | 1                                     | 0                       | 0                      | 0                      | 3.14%     |
| Early remitting                | Gone by seven | 1                                     | 1                       | 0                      | 0                      | 1.06%     |
| Early remitting                | Gone by seven | 1                                     | 1                       | 1                      | 0                      | 0.54%     |
| Early remitting                | Gone by seven | 0                                     | 1                       | 0                      | 0                      | 8.7%      |
| Persistent/relapsing           | Late onset >3 | 0                                     | 0                       | 1                      | 1                      | 2.9%      |
| Persistent/relapsing           | Late onset >3 | 0                                     | 0                       | 0                      | 0                      | 2.9%      |
| Persistent/relapsing           | Always       | 0                                     | 1                       | 1                      | 1                      | 3.62%     |
| Persistent/relapsing           | Always       | 1                                     | 1                       | 1                      | 1                      | 0.56%     |
| Persistent/relapsing           | Relapse by seven | 0                                     | 1                       | 0                      | 1                      | 1.3%      |
| Persistent/relapsing           | Relapse by seven | 1                                     | 0                       | 0                      | 1                      | 0.3%      |
| Persistent/relapsing           | Relapse by seven | 1                                     | 1                       | 0                      | 1                      | 0.2%      |
| Persistent/relapsing           | Relapse by seven | 1                                     | 0                       | 1                      | 1                      | 0.2%      |
| Transient/intermittent         | Transient    | 0                                     | 0                       | 1                      | 0                      | 4.4%      |
| Transient/intermittent         | Intermittent | 1                                     | 0                       | 1                      | 0                      | 0.3%      |

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