

Supplement to: Patterns of atopic eczema disease activity from birth through mid-adulthood in two British birth cohorts

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eMethods

For the imputation analysis, thirty imputed datasets were generated. All of the eczema variables used to generate the latent classes and all early life factors were used to impute the missing variables. Auxilliary variables were also used to impute missing variables. For 1958, we included asthma, hayfever/rhinitis, contact dermatitis, adulthood social class, smoking during adulthood, mother's age at birth, father's age at birth, maternal education at birth, number of people living per room at birth, number of people mother cooked for when pregnant, antenatal visits, and parity. For 1970, we included asthma, hayfever/rhinitis, parent atopy, contact dermatitis, adulthood social class, smoking during adulthood, marital status at birth, mother's age at completion of education at birth, premarital conception, method of labor, and lactation.

eFigure 1: Subtype interpretations by model

Each column contains a description of the phenotypes resulting from latent class analyses (LCAs) with the indicated number of classes. Arrows indicate when >8% of individuals within a phenotype move to a new phenotype when an additional class is allowed into the LCA.

1958 Cohort

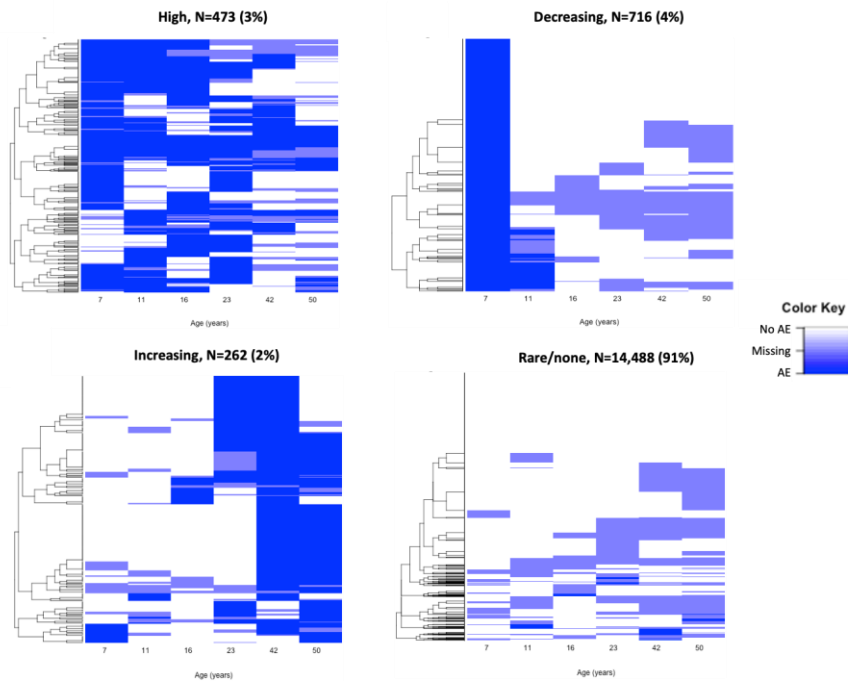
2 classes	3 classes	4 classes	5 classes
Rare/ No AE (87%)	Rare/ No AE (87%)	Rare/ No AE (91%)	Rare/ No AE (83%)
Atopic eczema (13%)	Increasing (10%)	Increasing (2%)	Increasing high (1%)
			Increasing low (9%)
	Decreasing (3%)	Decreasing (4%)	Decreasing (5%)
		High (3%)	High (2%)

1970 Cohort

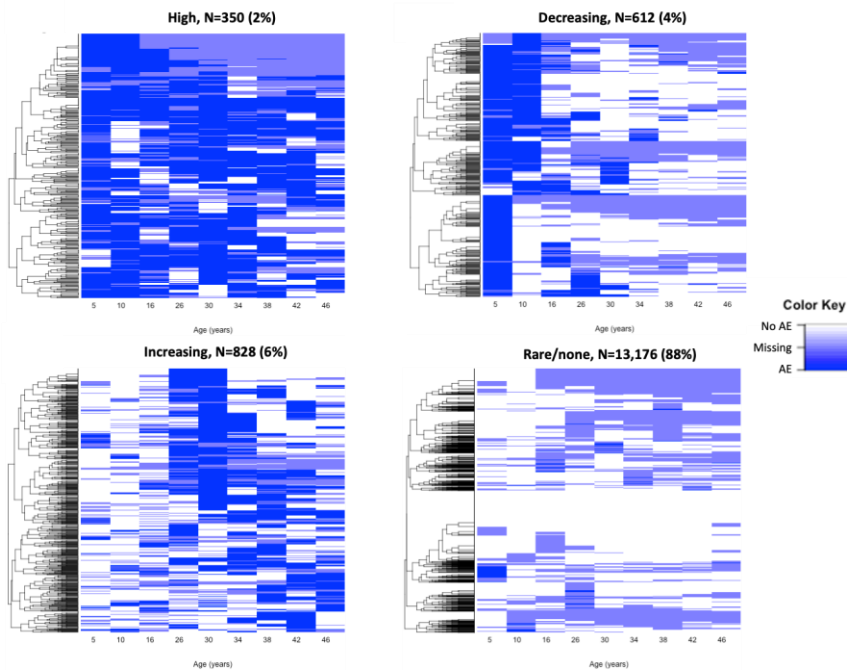
2 classes	3 classes	4 classes	5 classes
Rare/ No AE (90%)	Rare/ No AE (90%)	Rare/ No AE (88%)	Rare/ No AE (88%)
Atopic eczema (10%)	Increasing (6%)	Increasing (6%)	Increasing high (1%)
			Increasing low (5%)
	Decreasing (4%)	Decreasing (4%)	Decreasing (4%)
		High (2%)	High (2%)

eFigure 2. Heat maps of individual participant disease patterns across ages, organized by subgroup from the latent class analysis

1958 Cohort



1970 Cohort



eTable 1. Questions about atopic eczema, asthma, and rhinitis by year and by cohort

Eczema questions

1958 Cohort					1970 Cohort				
Age	Question	Missing (N=17,196 at birth)	Positive responses (% of total responses at that wave)		Age	Question	Missing (N=17,415 at birth)	Positive responses (% of total responses at that wave)	
Age 7	Eczema during or prior to past year?	3,385	1,100	8%	Age 5	Eczema during or prior to past year?	5,013	1,495	12%
Age 11	Eczema during past year?	4,432	652	5%	Age 10	Eczema during past year?	4,823	887	7%
Age 16	Eczema in the past year?	3,714	470	3%	Age 16	Eczema during past year?	8,296	668	8%
Age 23	Eczema in the past year?	5,577	634	5%	Age 26	Eczema during past year?	8,863	963	12%
					Age 30	Eczema during past year?	6,802	978	9%
					Age 34	Eczema since last survey?	8,242	662	7%
					Age 38	Eczema currently?	8,992	604	7%
Age 42	Eczema in the past year?	6,627	812	8%	Age 42	Eczema since last survey?	8,103	566	6%
					Age 46	Eczema since last survey	9,246	410	5%
Age 50	Eczema currently?	8,165	442	5%					

*Note that shaded questions are most similar across cohorts and included in the sensitivity analyses.

Asthma questions

1958 Cohort		1970 Cohort	
Age	Question	Age	Question
Age 7	Ever had asthma attack?		
Age 11	Ever had asthma or wheezy bronchitis?	Age 10	Asthma during past year?
Age 16	Ever had asthma or wheezy bronchitis?	Age 16	Had asthma during past year?
Age 23	Asthma or bronchitis in the past year?	Age 26	Suffered from asthma during past year?
		Age 30	Had asthma during past year?
		Age 34	Asthma attacks in the last 12 months?
		Age 38	Suffers from asthma or wheezy bronchitis currently?
Age 42	Asthma in the past year?	Age 42	Asthma or wheezy bronchitis since last survey?
		Age 46	Asthma or wheezy bronchitis since last survey?
Age 50	Suffers from asthma or wheezy bronchitis currently?		

Hay fever/rhinitis questions

1958 Cohort		1970 Cohort	
Age	Question	Age	Question
Age 7	Ever hay fever or sneezing attacks?	Age 5	Hay fever and sneezing during or prior to past year?
Age 11	Hay fever/rhinitis during past year?	Age 10	Hay fever during past year?
Age 16	Hay fever in the past year?	Age 16	Had hay fever/allergic rhinitis during past year?
Age 23	Hay fever in the past year?	Age 26	Suffered from hay fever during past year?
		Age 30	Had hay fever/allergic rhinitis during past year?
		Age 34	Hay fever during past year?
		Age 38	Suffers from hay fever/sneeze/runny nose currently?
Age 42	Hay fever/allergic rhinitis in the past year?	Age 42	Hay fever since last survey?
		Age 46	Hay fever since last survey?
Age 50	Suffers from hay fever currently?		

eTable 2. Latent class fit statistics

1958 Cohort

Model fit statistics				
	2 Class Model	3 Class Model	4 Class Model	5 Class Model
Log likelihood	-14371.63	-13974.91	-13886.37	-13846.54
Degrees Freedom	5	8	11	14
BIC	28799.22	28039.37	27895.86	27849.77
Sample size-adjusted BIC	28783.33	28013.94	27860.90	27805.28
Entropy	0.78	0.73	0.89	0.79
Distribution of individuals among subgroups				
	N (%)	N (%)	N (%)	N (%)
Rare/none	13,807 (87)	13,879 (87)	14,488 (91)	13,278 (83)
Decreasing	-	510 (3)	716 (4)	725 (5)
Increasing high	-	-	-	151 (1)
Increasing low	2,132 (13)	1,550 (10)	262 (2)	1,430 (9)
High	-	-	473 (3)	355 (2)

1970 Cohort

Model fit statistics				
	2 Class Model	3 Class Model	4 Class Model	5 Class Model
Log likelihood	-22788.98	-22461.98	-22196.70	-22159.75
Degrees Freedom	5	8	11	14
BIC	45635.45	45015.95	44519.89	44480.48
Sample size-adjusted BIC	45619.56	44990.52	44484.92	44435.99
Entropy	0.93	0.93	0.92	0.91
Distribution of individuals among subgroups				
	N (%)	N (%)	N (%)	N (%)
Rare/none	13,495 (90)	13,426 (90)	13,176 (88)	13,106 (88)
Decreasing	-	614 (4)	612 (4)	545 (4)
Increasing high	-	-	-	134 (1)
Increasing low	1,471 (10)	926 (6)	828 (6)	816 (5)
High	-	-	350 (2)	365 (2)

1958 Cohort (using only five comparable data inputs across cohorts)

Model fit statistics				
	2 Class Model	3 Class Model	4 Class Model	5 Class Model
Log likelihood	-12784.14	-12387.77	-12330.09	-12324.42
Degrees Freedom	5	8	11	13
BIC	25623.56	24863.99	24781.80	24792.58
Sample size-adjusted BIC	25607.67	24838.57	24746.84	24751.26
Entropy	0.77	0.69	0.75	0.79
Distribution of individuals among subgroups				
	N (%)	N (%)	N (%)	N (%)
Rare/none	13,975 (88)	14,197 (89)	14,049 (88)	14,049 (88)
Decreasing high	-	558 (4)	-	188 (1)
Decreasing low	-	-	171 (1)	117 (1)
Increasing	1,951 (12)	1,171 (7)	1,388 (9)	1,403 (9)
High	-	-	318 (2)	169 (1)

1970 Cohort (using only five comparable data inputs across cohorts)

Model fit statistics				
	2 Class Model	3 Class Model	4 Class Model	5 Class Model
Log likelihood	-15547.25	-15463.6	-15326.87	-15321.36
Degrees Freedom	5	8	11	14
BIC	31149.76	31015.62	30775.31	30797.44
Sample size-adjusted BIC	31133.87	30990.19	30740.35	30752.96
Entropy	0.92	0.94	0.94	0.75
Distribution of individuals among subgroups				
	N (%)	N (%)	N (%)	N (%)
Rare/none	13,801 (93)	13,752 (92)	13,168 (88)	5,642 (38)
Decreasing	1,084 (7)	109 (1)	659 (4)	671 (5)
Increasing high	-	1,024 (7)	109 (1)	111 (1)
Increasing low	-	-	-	7,612 (51)
High	-	-	949 (6)	849 (6)

Notes: Lower log likelihood and BIC indicate better model fit. Higher entropy score indicates better class discrimination

eTable 3: Average classification probabilities by most likely disease trajectory subtype for the four-class solution

1958 Cohort

Most likely subtype (assigned class)	Subtype			
	Prob (High)	Prob (Decreasing)	Prob (Increasing)	Prob (Rare/No disease)
High	0.832	0.031	0.076	0.062
Decreasing	0.075	0.658	0.018	0.250
Increasing	0.090	0.000	0.791	0.119
Rare/No disease	0.004	0.019	0.027	0.950

1970 Cohort

Most likely subtype (assigned class)	Subtype			
	Prob (High)	Prob (Decreasing)	Prob (Increasing)	Prob (Rare/No disease)
High	0.804	0.102	0.093	0.001
Decreasing	0.078	0.753	0.071	0.097
Increasing	0.050	0.052	0.791	0.107
Rare/No disease	0.001	0.021	0.035	0.943

Notes: Average probabilities of subtype membership, according to their most likely subtype (rows). Numbers close to 1 indicate high confidence in the classification.

eTable 4. Association between early life factors and atopic eczema activity subtypes by cohort

Panel A: 1958 Cohort (Total N across all classes = 15,939)

	High vs Rare/no AE	Decreasing vs Rare/no AE	Increasing vs Rare/no AE	High vs Decreasing AE	Increasing vs Decreasing AE
	Odds Ratio (95% CI)				
Sex					
Male	Reference	Reference	Reference	Reference	Reference
Female	1.63 (1.35, 1.97)	0.81 (0.70, 0.95)	1.73 (1.34, 2.22)	2.01 (1.58, 2.55)	2.12 (1.58, 2.84)
Ethnicity					
European, Caucasian	Reference	Reference	Reference	Reference	Reference
Other	0.56 (0.17, 1.82)	0.83 (0.39, 1.76)	1.43 (0.53, 3.85)	0.67 (0.17, 2.71)	1.72 (0.50, 5.94)
Region of early childhood residence					
Southern England	Reference	Reference	Reference	Reference	Reference
Central England/Wales	1.11 (0.89, 1.39)	0.89 (0.74, 1.07)	1.06 (0.78, 1.44)	1.24 (0.93, 1.66)	1.19 (0.83, 1.69)
N. England/Scotland	0.78 (0.62, 0.98)	0.78 (0.65, 0.93)	0.86 (0.64, 1.16)	1.00 (0.75, 1.33)	1.10 (0.78, 1.56)
Highest social class in childhood^a					
I/II	Reference	Reference	Reference	Reference	Reference
III	0.74 (0.61, 0.91)	0.82 (0.69, 0.97)	0.86 (0.66, 1.14)	0.90 (0.70, 1.17)	1.06 (0.77, 1.45)
IV/V	0.59 (0.41, 0.85)	0.53 (0.38, 0.73)	0.72 (0.45, 1.16)	1.12 (0.69, 1.81)	1.37 (0.78, 2.41)
Household size in early childhood					
<=3 persons	Reference	Reference	Reference	Reference	Reference
4+ persons	1.15 (0.80, 1.65)	0.85 (0.66, 1.10)	0.92 (0.59, 1.42)	1.35 (0.87, 2.08)	1.07 (0.65, 1.77)
In utero smoke exposure					
No	Reference	Reference	Reference	Reference	Reference
Any	0.89 (0.71, 1.12)	1.03 (0.86, 1.24)	1.01 (0.76, 1.35)	0.86 (0.65, 1.14)	0.98 (0.70, 1.37)

Childhood smoke exposure					
No	Reference	Reference	Reference	Reference	Reference
Any	0.90 (0.71, 1.13)	0.91 (0.73, 1.14)	0.90 (0.66, 1.22)	0.98 (0.72, 1.33)	0.98 (0.68, 1.42)
Birth weight					
Per kg increase	1.09 (0.91, 1.32)	1.04 (0.90, 1.21)	1.06 (0.83, 1.36)	1.05 (0.83, 1.32)	1.02 (0.76, 1.36)
Breastfeeding					
No	Reference	Reference	Reference	Reference	Reference
Any	1.38 (1.10, 1.73)	1.27 (1.06, 1.51)	1.42 (1.05, 1.93)	1.09 (0.83, 1.44)	1.12 (0.80, 1.59)

^aRegistrar General's social class: I Professional, II Managerial and technical; III Skilled; IV Partly-skilled; V Unskilled.

Panel B: 1970 Cohort (Total N across all classes = 14,966)

	High vs Rare/no AE	Decreasing vs Rare/no AE	Increasing vs Rare/no AE	High vs Decreasing AE	Increasing vs Decreasing AE
	Odds Ratio (95% CI)				
Sex					
Male	Reference	Reference	Reference	Reference	Reference
Female	1.97 (1.58, 2.46)	0.99 (0.84, 1.17)	1.80 (1.56, 2.08)	1.99 (1.52, 2.61)	1.82 (1.47, 2.25)
Ethnicity					
European, Caucasian	Reference	Reference	Reference	Reference	Reference
Other	1.12 (0.63, 1.99)	1.16 (0.78, 1.74)	0.82 (0.55, 1.22)	0.97 (0.49, 1.89)	0.70 (0.41, 1.21)
Region of early childhood residence					
Southern England	Reference	Reference	Reference	Reference	Reference
Central England/Wales	1.03 (0.77, 1.38)	0.83 (0.68, 1.02)	0.90 (0.74, 1.08)	1.24 (0.88, 1.75)	1.08 (0.82, 1.41)
N. England/Scotland	0.94 (0.71, 1.23)	0.65 (0.52, 0.79)	0.83 (0.69, 0.99)	1.45 (1.04, 2.02)	1.28 (0.98, 1.67)
Highest social class in childhood ^a					
I/II	Reference	Reference	Reference	Reference	Reference
III	0.67 (0.54, 0.84)	0.83 (0.70, 0.99)	0.94 (0.81, 1.10)	0.81 (0.61, 1.07)	1.13 (0.90, 1.42)

IV/V	0.41 (0.23, 0.71)	0.66 (0.46, 0.94)	0.97 (0.73, 1.28)	0.62 (0.32, 1.20)	1.47 (0.94, 2.30)
Household size in early childhood					
<=3 persons	Reference	Reference	Reference	Reference	Reference
4+ persons	0.89 (0.62, 1.28)	1.05 (0.79, 1.40)	0.93 (0.73, 1.20)	0.85 (0.54, 1.33)	0.89 (0.62, 1.27)
In utero smoke exposure					
No	Reference	Reference	Reference	Reference	Reference
Any	0.78 (0.61, 1.01)	0.99 (0.82, 1.19)	0.88 (0.75, 1.04)	0.79 (0.58, 1.08)	0.89 (0.70, 1.14)
Childhood smoke exposure					
No	Reference	Reference	Reference	Reference	Reference
Any	1.03 (0.79, 1.34)	1.03 (0.84, 1.25)	0.94 (0.79, 1.11)	1.00 (0.73, 1.39)	0.91 (0.71, 1.18)
Parent atopy					
No	Reference	Reference	Reference	Reference	Reference
Any	2.54 (2.00, 3.23)	2.52 (2.11, 3.01)	1.38 (1.16, 1.65)	1.01 (0.75, 1.35)	0.55 (0.43, 0.70)
Birth weight					
Per kg increase	1.06 (0.85, 1.31)	0.95 (0.81, 1.11)	0.89 (0.77, 1.02)	1.11 (0.86, 1.44)	0.93 (0.76, 1.15)
Breastfeeding					
No	Reference	Reference	Reference	Reference	Reference
Any	1.36 (1.09, 1.71)	1.12 (0.94, 1.33)	1.12 (0.96, 1.30)	1.21 (0.92, 1.60)	1.00 (0.80, 1.25)

^aRegistrar General's social class: I Professional, II Managerial and technical; III Skilled; IV Partly-skilled; V Unskilled.

eTable 5: Proportions of individuals with atopic eczema, asthma, and rhinitis within each disease trajectory subtype with by cohort

1958 Cohort		Atopic eczema subclass				
		Overall	High	Decreasing	Increasing	Rare/None
Age 7	Eczema	8%	80%	100%	8%	0.1%
	Asthma	3%	15%	13%	3%	2%
	Rhinitis	6%	18%	12%	7%	5%
Age 11	Eczema	5%	69%	19%	5%	2%
	Asthma	12%	33%	24%	12%	11%
	Rhinitis	8%	27%	17%	9%	7%
Age 16	Eczema	3%	69%	0%	10%	1%
	Asthma	12%	32%	21%	11%	11%
	Rhinitis	12%	34%	22%	15%	11%
Age 23	Eczema	5%	74%	0%	48%	2%
	Asthma	4%	14%	8%	8%	4%
	Rhinitis	17%	39%	23%	30%	15%
Age 42	Eczema	8%	46%	0%	92%	4%
	Asthma	6%	17%	9%	14%	5%
	Rhinitis	16%	32%	19%	27%	15%
Age 50	Eczema	5%	29%	0%	74%	2%
	Asthma	10%	24%	13%	20%	9%
	Rhinitis	14%	27%	15%	26%	13%

1970 Cohort		Atopic eczema subclass				
		Overall	High	Decreasing	Increasing	Rare/None
Age 5	Eczema	12%	93%	96%	10%	6%
	Asthma	-	-	-	-	-
	Rhinitis	4%	15%	14%	6%	4%
Age 10	Eczema	7%	83%	59%	11%	2%
	Asthma	3%	14%	12%	4%	2%
	Rhinitis	11%	34%	25%	16%	10%
Age 16	Eczema	8%	84%	38%	18%	3%
	Asthma	9%	34%	16%	14%	7%
	Rhinitis	25%	46%	42%	32%	23%
Age 26	Eczema	12%	86%	29%	58%	4%
	Asthma	8%	24%	16%	15%	6%
	Rhinitis	21%	40%	29%	29%	19%
Age 30	Eczema	9%	87%	15%	65%	2%
	Asthma	7%	21%	14%	13%	6%
	Rhinitis	20%	39%	27%	29%	18%
Age 34	Eczema	7%	83%	9%	52%	1%
	Asthma	4%	8%	6%	8%	3%
	Rhinitis	22%	40%	30%	32%	20%
Age 38	Eczema	7%	77%	4%	55%	1%
	Asthma	10%	29%	16%	20%	9%
	Rhinitis	20%	41%	28%	30%	18%
Age 42	Eczema	6%	68%	2%	49%	1%
	Asthma	9%	24%	11%	15%	8%
	Rhinitis	20%	42%	28%	28%	18%
Age 46	Eczema	5%	61%	1%	37%	1%
	Asthma	12%	30%	17%	18%	10%
	Rhinitis	20%	42%	27%	29%	19%

eTable 6. Complete case analysis: Association between early life factors and atopic eczema activity subtypes from for 1958 and 1970 meta-analysis (Total N across all classes = 19,888)

	High vs Rare/no AE	Decreasing vs Rare/no AE	Increasing vs Rare/no AE	High vs Decreasing AE	Increasing vs Decreasing AE
	Odds Ratio (95% CI)				
Sex					
Male	Reference	Reference	Reference	Reference	Reference
Female	1.76 (1.48, 2.10)	0.96 (0.84, 1.09)	1.82 (1.58, 2.11)	1.84 (1.49, 2.29)	1.91 (1.57, 2.31)
Ethnicity					
European, Caucasian	Reference	Reference	Reference	Reference	Reference
Other	0.83 (0.47, 1.46)	1.02 (0.68, 1.52)	0.64 (0.41, 1.01)	0.81 (0.41, 1.61)	0.63 (0.35, 1.14)
Region of early childhood residence					
Southern England	Reference	Reference	Reference	Reference	Reference
Central England/Wales	1.05 (0.86, 1.30)	0.83 (0.71, 0.98)	0.90 (0.76, 1.08)	1.27 (0.98, 1.64)	1.08 (0.86, 1.37)
N. England/Scotland	0.78 (0.63, 0.96)	0.63 (0.54, 0.74)	0.78 (0.66, 0.92)	1.24 (0.96, 1.61)	1.24 (0.99, 1.56)
Highest social class in childhood^a					
I/II	Reference	Reference	Reference	Reference	Reference
III	0.76 (0.64, 0.91)	0.79 (0.69, 0.91)	0.90 (0.78, 1.05)	0.97 (0.77, 1.21)	1.15 (0.94, 1.40)
IV/V	0.52 (0.35, 0.78)	0.65 (0.48, 0.87)	0.85 (0.63, 1.14)	0.80 (0.49, 1.32)	1.30 (0.86, 1.96)
Household size in early childhood					
<=3 persons	Reference	Reference	Reference	Reference	Reference
4+ persons	0.94 (0.70, 1.25)	1.00 (0.79, 1.26)	0.96 (0.76, 1.21)	0.94 (0.65, 1.35)	0.96 (0.70, 1.33)
In utero smoke exposure					
No	Reference	Reference	Reference	Reference	Reference
Any	0.76 (0.62, 0.93)	0.98 (0.84, 1.14)	0.92 (0.78, 1.08)	0.77 (0.60, 0.99)	0.93 (0.75, 1.16)
Childhood smoke exposure					
No	Reference	Reference	Reference	Reference	Reference

Any	0.99 (0.82, 1.20)	0.98 (0.84, 1.14)	0.95 (0.81, 1.12)	1.01 (0.79, 1.28)	0.97 (0.78, 1.20)
Birth weight					
Per kg increase	1.02 (0.86, 1.20)	0.95 (0.83, 1.08)	0.94 (0.82, 1.08)	1.07 (0.87, 1.32)	1.00 (0.83, 1.20)
Breastfeeding					
No	Reference	Reference	Reference	Reference	Reference
Any	1.37 (1.14, 1.65)	1.13 (0.98, 1.31)	1.14 (0.98, 1.32)	1.21 (0.96, 1.53)	1.01 (0.82, 1.23)
Cohort					
1970	Reference	Reference	Reference	Reference	Reference
1958	1.29 (1.08, 1.55)	1.13 (0.97, 1.30)	0.33 (0.27, 0.39)	1.15 (0.91, 1.44)	0.29 (0.23, 0.37)

^aRegistrar General's social class: I Professional, II Managerial and technical; III Skilled; IV Partly-skilled; V Unskilled

