METHODS

Participants

Participants were mother-child pairs from the Southampton Women's Survey.[E1] Women aged 20-34 years were recruited during 1998-2002; those who became pregnant were followed through pregnancy and their children visited at 6, 12, 24 and 36 months and 6 years. To exclude effects of prematurity, whilst maximising power, infants born < 35 weeks' gestation were excluded. Children aged six years during 2006-2010 were invited for follow-up; 1485 mother-child pairs were eligible, maternal vitamin status and 6-year follow-up data were available for 860 pairs (Figure 1). Questionnaire data were collected during a home-visit, during this visit spirometry was also attempted. Due to resource limitations clinic-based bronchial provocation testing and exhaled nitric oxide measurements were limited to unselected subsets of participants. Parental consent was obtained and ethical approval was granted by the Southampton and South West Hampshire Local Research Ethics Committee (LREC Number 276/97, 307/97, 089/99 and 06/Q1702/104).

Maternal serum 25-hydroxyvitamin D

Maternal venous blood was sampled at 34 weeks' gestation. To ensure stability samples were centrifuged, separated and stored at -80^{o}C within 24 hours of sampling. 25-hydroxyvitamin D concentrations were measured by a Vitamin D External Quality Assessment Scheme compliant laboratory, with quality control samples in each batch. The radioimmunoassay used (DiaSorin, Minnesota, USA) had a coefficient of variability < 10%.

Maternal vitamin D intake

At 11 and 34 weeks' gestation average frequencies of consumption over the preceding 3 months were recorded using a 100-item food frequency questionnaire (FFQ). The FFQ has

been validated against 4-day food diaries and maternal micronutrient concentrations.[E2] Nutrient intakes were calculated by multiplying frequency of consumption by nutrient content for each food or supplement. Early and late pregnancy intakes were averaged to provide an estimate of pregnancy intake. Energy adjustment can be used to correct for over or underestimation of intake in the FFQ, however, intake data were not automatically adjusted for total energy intake as supplementary intake vitamin D from supplements do not increase in line with energy intake.

Atopy

Skin prick testing was conducted at 1 and 3 years using cat, dog, house dust mite (*Dermatophagoides pteronyssinus*), grass pollens, egg and milk allergens (Hollister-Stier, Spokane, WA); at age 6, tree pollens (ALK Abelló Hørsholm, Denmark) were also tested. For validity a ≥ 3 mm positive and a 0 mm negative control response were required, atopy was defined as any allergen response ≥ 3 mm.

Airway inflammation

Exhaled nitric oxide (eNO) was measured online by trained research nurses according to ERS/ATS recommendations.[E3] Measurements were recorded during controlled expiration at 50 ml/sec using a NIOX® chemiluminescence analyser (Aerocrine, Sweden). A mean value was calculated from three readings where possible. eNO data were normalised using an inverse square root transformation then standardised as a z-score. The sign of the values was reversed so that high untransformed eNO values gave rise to high standardised scores.

Childhood asthma and wheeze

Respiratory assessment was conducted by research nurses using questions from the ISAAC core questionnaire wheezing module.[E4] Specifically, mothers were asked at each visit whether their child had experienced 'episodes of chestiness associated with wheezing or whistling in his/her chest since they were last seen' and at 6 years whether their child had 'ever been diagnosed with asthma by a doctor'. The asthma outcome was refined to current asthma by including only 6-year-old children diagnosed with asthma who had experienced asthma symptoms or received asthma medication within the last year. The wheeze phenotypes were based upon those of the Tuscon Children's Respiratory Study;[E5] questionnaire data from 6, 12, 24 and 36 months and six years were combined to define:

Transient wheeze: wheeze at ages 6, 12, 24 or 36 months but no wheeze and no asthma treatment at 6 years.

Persistent wheeze: wheeze at ages 6, 12, 24 or 36 months and wheeze or asthma treatment at 6 years.

Late-onset wheeze: no wheeze at ages 6, 12, 24 or 36 months but wheeze or asthma treatment at 6 years.

The persistent and late-onset groups were combined because the late-onset group contained few children (Figure1). The persistent/late wheeze group was sub-classified according to atopic status determined by skin prick testing.

Lung function

Spirometry was performed according to ATS/ERS guidelines,[E6] although without noseclips to avoid discomfort. Flow-volume loops were measured for all children by experienced research nurses using a portable Koko spirometer with incentive software (KoKo version 4; PDS Instrumentation; Louisville, USA). Absolute values of FEV_1 and FVC were recorded

with and without standardisation for height[E7] to explore whether any effect of maternal 25-hydroxyvitamin D status upon wheeze risk was mediated by an effect upon child's height.

Bronchial hyperresponsiveness (BHR) was measured by bronchial provocation challenge. Methacholine was administered using a dosimeter (Koko; PDS Instrumentation; Louisville, USA) and a compressed air-driven nebuliser (Sidestream®; Respironics, UK). Challenges were conducted according to ATS/ERS guidelines using incremental methacholine concentrations (0.06 mg/ml to 16 mg/ml).[E8] Challenges were terminated following the 16 mg/ml dose or a 20% fall in FEV_1. BHR was expressed as the inverse of the slope of the regression line through FEV_1 drop and logged methacholine concentration:
Log.slope=100/[regression slope of FEV_1 drop and $\log_{10}$(cumulative methacholine dose) + 10]
The constant removes negative values and the inverse transformation produces a normally distributed variable.[E9] Lower inverse log.slope values indicate increased BHR.

Statistical methods

Poisson regression with robust variance was used to model relative risk for binary outcomes. This is more appropriate than logistic regression for common outcomes where odds ratios cannot be interpreted as relative risks and so are hard to interpret.[E10] Transient and persistent/late wheeze phenotypes were mutually exclusive; children suffering one of these types of wheeze were not at risk of the other so relative risks were calculated by comparing children with transient or persistent/late wheeze to those who had never wheezed. Relative risks for persistent/late wheeze with atopy and persistent/late wheeze without atopy were calculated using non-atopic children who had never wheezed as the comparator group. Relationships between maternal 25-hydroxyvitamin D status and continuous outcome variables were explored using linear regression.

Potential confounders were identified *a priori* and tested for association with each respiratory outcome. Models were developed comprising all the confounding variables listed in Table 1 which were significantly associated with each outcome ($p < 0.1$). Birthweight and gestation were initially excluded from the multivariable models as they may lie on the causal pathway. Similarly, season and year of blood sampling were initially excluded from the multivariable models to preserve variation in the exposure variable which may drive an effect upon outcome. The analyses were repeated including these variables if they were significantly associated with the outcomes. 25-hydroxyvitamin D was analysed as a continuous variable to maximise power, however, the relationship between this exposure and each outcome was checked for linearity by fitting a quadratic term.

As the analyses were designed *a priori* to test a limited number of hypotheses and not all the tests were independent, use of a Bonferroni correction was considered over-conservative.[E11] As a compromise we focused on results with P-values ≤ 0.025 and considered consistency of the findings in our interpretation.

Table E1 Relationship between maternal 25-hydroxyvitamin D status at 34 weeks' pregnancy and offspring asthma and wheeze at age 6 years (adjusted for gestation and birthweight)

	Univariable Model				Final model			
	RR	(95% CI)	P-value	n	RR	(95% CI)	P-value	n
Current doctor-diagnosed asthma at 6 years	0.97	(0.91, 1.04)	0.36	860	0.98	(0.92, 1.04)	0.56	836
Current wheeze at 6 years	0.98	(0.92, 1.03)	0.40	860	0.99	(0.94, 1.05)	0.74	833
Any wheeze at or before 6 years	1.00	(0.98, 1.01)	0.61	856	1.00	(0.98, 1.02)	0.96	832
Transient wheeze	1.00	(0.98, 1.02)	0.85	719	1.00	(0.98, 1.02)	0.88	707
Persistent/late wheeze	0.98	(0.93, 1.03)	0.37	489	0.98	(0.94, 1.03)	0.44	475
Persistent/late wheeze with atopy	0.90	(0.81, 0.99)	0.03	257	0.91	(0.84, 0.99)	0.04	251
Persistent/late wheeze without atopy	0.99	(0.91, 1.06)	0.73	259	1.01	(0.94, 1.09)	0.72	253

Data presented as change in relative risk per 10 nmol/l 25-hydroxyvitamin D.

Adjusted models: asthma - maternal education, maternal asthma, paternal asthma and paternal rhinitis; wheeze at age 6 - maternal education, maternal asthma, paternal rhinitis, pets in the home during the child's infancy, gestation; wheeze at or before 6 years - maternal BMI, child's gender, maternal education, maternal asthma, paternal asthma, maternal rhinitis, gestation; transient wheeze - maternal BMI, child's gender, mother's parity, maternal asthma, maternal rhinitis, gestation; Persistent/late - maternal education, smoking during pregnancy, maternal asthma, paternal asthma, maternal rhinitis, gestation; Persistent/late wheeze with atopy-child's gender, maternal asthma, paternal asthma, paternal rhinitis, pets in the home during infancy; Persistent/late wheeze without atopy-maternal age, smoking during pregnancy, maternal asthma, paternal asthma, pets in the home during infancy, gestation.

Table E2 Relationship between maternal 25-hydroxyvitamin D status at 34 weeks' pregnancy and offspring atopy and airway inflammation (adjusted for gestation and birthweight)

	Univariable Model				Final model			
	RR	(95% CI)	P-value	n	RR	(95% CI)	P-value	n
Atopy age 1 year	0.94	(0.88, 1.01	0.08	773	0.96	(0.90, 1.03	0.24	685
Atopy age 3 years	0.99	(0.94, 1.05)	0.81	676	0.99	(0.94, 1.04)	0.6	661
Atopy age 6 years	0.97	(0.93, 1.02)	0.26	635	0.99	(0.95, 1.04)	0.74	545
	beta	(95% CI)	P-value	n	beta	(95% CI)	P-value	n
Exhaled nitric oxide at 6 years	0.0139	(-0.0441, 0.0163)	0.37	451	-0.0205	(-0.0503, 0.0094)	0.18	434

Data presented as change in relative risk per 10 nmol/l 25-hydroxyvitamin D for binary outcomes and as change in transformed unit of eNO per 10 nmol/l 25-hydroxyvitamin D for exhaled nitric oxide outcome.

Adjusted models: atopy age 1 year - child's gender, gestation, parents' social class, maternal atopy; atopy age 3 years - child's gender, exposure to smoke in infancy, gestation, maternal eczema, atopy age 6 years - child's age at testing, child's gender, gestation, parents social class, maternal asthma, paternal rhinitis, maternal atopy; exhaled nitric oxide - child's age at testing, maternal asthma, paternal rhinitis, maternal height.

Table E3 Relationship between maternal 25-hydroxyvitamin D status at 34 weeks' pregnancy and offspring lung function (adjusted for gestation and birthweight) aged 6 years

	Univariable Model				Final Model			
	beta	(95% CI)	P-value	n	beta	(95% CI)	P-value	n
FEV_1 absolute	-0.0007	(-0.0054, 0.0039)	0.76	739	-0.0002	(-0.0046, 0.0042)	0.93	725
FEV_1 z-score	0.0124	(-0.0078, 0.0326)	0.23	739	0.0109	(-0.0091, 0.0309)	0.28	739
FVC absolute	-0.0011	(-0.0068, 0.0045)	0.69	739	-0.0002	(-0.0055, 0.0051)	0.94	724
FVC z-score	0.0131	(-0.0103, 0.0365)	0.27	739	0.0122	(-0.0112, 0.0356)	0.31	739
BHR slope	-0.0840	(-0.1935, 0.0244)	0.13	216	-0.1020	(-0.2115, 0.0075)	0.07	208

Data presented as change in relative risk per 10 nmol/l 25-hydroxyvitamin D.

Adjusted models: FEV_1 absolute - child's age at testing, child's gender, birthweight, parity, maternal BMI, maternal height; FEV_1 z-score - child's gender; FVC absolute - child's age at testing, child's gender, age at introduction of solid foods, birthweight, maternal BMI, maternal height, FVC z-score - child's gender; BHR - maternal age, smoking in pregnancy, paternal eczema, age at introduction of solid foods

Table E4 Relationship between maternal 25-hydroxyvitamin D at 34 weeks' pregnancy and offspring asthma and wheeze at age 6 years (adjusted for season and year of blood sampling)

	Univariable Model				Final model			
	RR	(95% CI)	P-value	n	RR	(95% CI)	P-value	n
Current doctor-diagnosed asthma at 6 years	0.97	(0.91, 1.04)	0.36	860	0.99	(0.92, 1.06)	0.76	832
Current wheeze at 6 years	0.98	(0.92, 1.03)	0.40	860	1.00	(0.93, 1.07)	0.94	829
Any wheeze at or before 6 years	1.00	(0.98, 1.01)	0.61	856	1.00	(0.98, 1.02)	0.89	828
Transient wheeze	1.00	(0.98, 1.02)	0.85	719	1.00	(0.97, 1.03)	0.95	704
Persistent/late wheeze	0.98	(0.93, 1.03)	0.37	489	0.99	(0.94, 1.05)	0.77	472
Persistent/late wheeze with atopy	0.90	(0.81, 0.99)	0.03	257	0.98	(0.88, 1.09)	0.67	250
Persistent/late wheeze without atopy	0.99	(0.91, 1.06)	0.73	259	0.98	(0.88, 1.09)	0.69	253

Data presented as change in relative risk 10 nmol/l 25-hydroxyvitamin D.

Adjusted models: asthma - maternal education, maternal asthma, paternal asthma and paternal rhinitis, year and season of blood sampling; wheeze at age 6 - maternal education, maternal asthma, paternal rhinitis, pets in the home during the child's infancy, year and season of blood sampling; wheeze at or before 6 years - maternal BMI, child's gender, maternal education, maternal asthma, paternal asthma, maternal rhinitis, year and season of blood sampling; transient wheeze - maternal BMI, child's gender, mother's parity, maternal asthma, maternal rhinitis, year and season of blood sampling; Persistent/late - maternal education, smoking during pregnancy, maternal asthma, paternal asthma, maternal rhinitis, year and season of blood sampling; Persistent/late wheeze with atopy-child's gender, maternal asthma, paternal asthma, paternal rhinitis, pets in the home during infancy, year and season of blood sampling; Persistent/late wheeze without atopy-maternal age, smoking during pregnancy, maternal asthma, paternal asthma, pets in the home during infancy, year and season of blood sampling.

Table E5 Relationship between maternal 25-hydroxyvitamin D status at 34 weeks' pregnancy and offspring atopy and airway inflammation (adjusted for season and year of blood sampling)

	Univariable Model				Final model			
	RR	(95% CI)	P-value	n	RR	(95% CI)	P-value	n
Atopy age 1 year	0.94	(0.88, 1.01)	0.08	773	0.98	(0.90, 1.08)	0.73	681
Atopy age 3 years	0.99	(0.94, 1.05)	0.81	676	1.01	(0.95, 1.08)	0.79	659
Atopy age 6 years	0.97	(0.93, 1.02)	0.26	635	1.01	(0.96, 1.07)	0.75	542
	beta	(95% CI)	P-value	n	beta	(95% CI)	P-value	n
Exhaled nitric oxide age 6 years	0.0139	(-0.0441, 0.0103)	0.37	451	-0.0028	(-0.0561, 0.0146)	0.25	434

Data presented as change in relative risk per 10 nmol/l 25-hydroxyvitamin D for binary outcomes and as change in transformed unit of eNO per 10 nmol/l 25-hydroxyvitamin D for exhaled nitric oxide outcome.

Adjusted models: atopy age 1 year - child's gender, parents' social class, maternal atopy, season and year of blood sampling; atopy age 3 years - child's gender, exposure to smoke in infancy, maternal eczema, season and year of blood sampling; atopy age 6 years - child's age at testing, child's gender, parents social class, maternal asthma, paternal rhinitis, maternal atopy, season and year of blood sampling; exhaled nitric oxide - child's age at testing, maternal asthma, paternal rhinitis, maternal height, season and year of blood sampling.

Table E6 Relationship between maternal 25-hydroxyvitamin D status at 34 weeks' pregnancy and offspring lung function aged 6 years (adjusted for season and year of blood sampling)

	Univariable Model				Final Model			
	beta	(95% CI)	P-value	n	beta	(95% CI)	P-value	n
FEV_1 absolute	-0.0007	(-0.0054,0.0039)	0.76	739	0.0002	(-0.0050, 0.0054)	0.94	728
FEV_1 z-score	0.0112	(-0.0078,0.033)	0.23	739	0.0026	(-0.0209, 0.0261)	0.83	736
FVC absolute	-0.0011	(-0.0068,0.0045)	0.69	739	0.0001	(-0.0061, 0.0064)	0.97	727
FVC z-score	0.0130	(-0.010,0.036)	0.27	739	0.0022	(-0.0253, 0.0297)	0.88	736
BHR slope	-0.084	(-0.194, -0.025)	0.13	216	-0.1898	(-0.3232, -0.0563)	0.006	208

Data presented as change in relative risk per 10 nmol/l 25-hydroxyvitamin D.

Adjusted models: FEV_1 absolute - child's age at testing, child's gender, parity, maternal BMI, maternal height, season and year of blood sampling; FEV_1 z-score - child's gender, season and year of blood sampling; FVC absolute - child's age at testing, child's gender, age at introduction of solid foods, maternal BMI, maternal height, season and year of blood sampling; FVC z-score - child's gender, season and year of blood sampling; BHR - maternal age, smoking in pregnancy, paternal eczema, age at introduction of solid foods, season and year of blood sampling

Table E7 Relationship between maternal average total daily vitamin D intake during pregnancy and offspring asthma and wheeze at age 6 years

	Univariable Model				Final model			
	RR	(95% CI)	P-value	n	RR	(95% CI)	P-value	n
Current doctor-diagnosed asthma at 6 years	1.01	(0.95, 1.07)	0.77	689	1.03	(0.97, 1.09)	0.36	677
Current wheeze at 6 years	1.00	(0.95, 1.06)	0.90	689	1.01	(0.96, 1.07)	0.62	675
Any wheeze at or before 6 years	1.00	(0.98, 1.01)	0.63	685	1.00	(0.98, 1.02)	0.97	674
Transient wheeze	0.99	(0.97, 1.02)	0.51	581	0.99	(0.97, 1.02)	0.66	575
Persistent/late wheeze	1.00	(0.96, 1.05)	0.91	388	1.01	(0.97, 1.06)	0.52	385
Persistent/late wheeze with atopy	1.03	(0.96, 1.11)	0.38	207	1.04	(0.97, 1.11)	0.30	205
Persistent/late wheeze without atopy	0.99	(0.91, 1.08)	0.87	210	0.98	(0.90, 1.07)	0.67	208

Data presented as change in relative risk per mcg/day total intake of vitamin D.

Adjusted models: asthma - maternal education, maternal asthma, paternal asthma and paternal rhinitis; wheeze at age 6 - maternal education, maternal asthma, paternal rhinitis, pets in the home during the child's infancy; wheeze at or before 6 years - maternal BMI, child's gender, maternal education, maternal asthma, paternal asthma, maternal rhinitis; transient wheeze - maternal BMI, child's gender, mother's parity, maternal asthma, maternal rhinitis; Persistent/late - maternal education, smoking during pregnancy, maternal asthma, paternal asthma, maternal rhinitis; Persistent/late wheeze with atopy-child's gender, maternal asthma, paternal asthma, paternal rhinitis, pets in the home during infancy; Persistent/late wheeze without atopy-maternal age, smoking during pregnancy, maternal asthma, paternal asthma, pets in the home during infancy.

Table E8 Relationship between maternal average total daily vitamin D intake during pregnancy and offspring atopy and airway inflammation

	Univariable Model				Final model			
	RR	(95% CI)	P-value	n	RR	(95% CI)	P-value	n
Atopy age 1 year	1.00	(0.95, 1.06)	0.98	623	1.00	(0.95, 1.06)	0.98	556
Atopy age 3 years	1.01	(0.96, 1.06)	0.78	547	1.00	(0.95, 1.05)	0.98	538
Atopy age 6 years	1.03	(0.99, 1.07)	0.09	509	1.03	(0.99, 1.07)	0.20	446
	beta	(95% CI)	P-value	n	beta	(95% CI)	P-value	n
Exhaled nitric oxide 6 years	0.0040	(-0.0252, 0.0332)	0.79	355	0.0042	(-0.0245, 0.0328)	0.77	346

Data presented as change in relative risk per mcg/day total intake of vitamin D for binary outcomes and as change in transformed unit of eNO per mcg/dy of vitamin D intake for exhaled nitric oxide outcome.

Adjusted models: atopy age 1 year - child's gender, parents' social class, maternal atopy; atopy age 3 years - child's gender, exposure to smoke in infancy, maternal eczema, atopy age 6 years - child's age at testing, child's gender, parents social class, maternal asthma, paternal rhinitis, maternal atopy; exhaled nitric oxide - child's age at testing, maternal asthma, paternal rhinitis, maternal height.

Table E9 Relationship between average total daily maternal vitamin D intake during pregnancy and offspring lung function at age 6 years

	Univariable Model				Final Model			
	beta	(95% CI)	P-value	n	beta	(95% CI)	P-value	n
FEV_1 absolute	-0.0016	(-0.0061, 0.0028)	0.48	590	-0.0019	(-0.0061, 0.0024)	0.38	584
FEV_1 z-score	-0.0112	(-0.0304, 0.0080)	0.25	590	-0.0091	(-0.0282, 0.0099)	0.35	590
FVC absolute	-0.0021	(-0.0075, 0.0034)	0.46	590	-0.0022	(-0.0072, 0.0029)	0.40	584
FVC z-score	-0.0130	(-0.0355, 0.0096)	0.26	590	-0.0118	(-0.0343, 0.0107)	0.30	590
BHR slope	-0.0283	(-0.1509, 0.0943)	0.65	169	-0.0189	(-0.1409, 0.1031)	0.76	165

Data presented as change in lung function measure per mcg/kg total intake of vitamin D.

Adjusted models: FEV_1 absolute - child's age at testing, child's gender, parity, maternal BMI, maternal height; FEV_1 z-score - child's gender; FVC absolute - child's age at testing, child's gender, age at introduction of solid foods, maternal BMI, maternal height, FVC z-score - child's gender; BHR - maternal age, smoking in pregnancy, paternal eczema, age at introduction of solid foods

Table E10 Relationship between average maternal daily vitamin D intake from food during pregnancy and offspring asthma and wheeze at age 6 years

	Univariable Model				Final model			
	RR	(95% CI)	P-value	n	RR	(95% CI)	P-value	n
Current doctor-diagnosed asthma at 6 years	1.06	(0.93, 1.21)	0.36	689	1.06	(0.95, 1.19)	0.30	677
Current wheeze at 6 years	1.03	(0.92, 1.14)	0.64	689	1.01	(0.92, 1.11)	0.84	675
Any wheeze at or before 6 years	1.01	(0.98, 1.05)	0.40	685	1.02	(0.99, 1.05)	0.26	674
Transient wheeze	1.01	(0.97, 1.06)	0.54	581	1.02	(0.97, 1.06)	0.49	575
Persistent/late wheeze	1.04	(0.95, 1.14)	0.37	388	1.02	(0.94, 1.10)	0.61	385
Persistent/late wheeze with atopy	1.13	(0.99, 1.30)	0.08	207	1.06	(0.91, 1.23)	0.45	205
Persistent/late wheeze without atopy	0.93	(0.77, 1.11)	0.42	210	0.83	(0.69, 1.00)	0.05	208

Data presented as change in relative risk per mcg/day food intake of vitamin D. Excludes vitamin D intake from supplements.
Adjusted models: asthma - maternal education, maternal asthma, paternal asthma and paternal rhinitis; wheeze at age 6 - maternal education, maternal asthma, paternal rhinitis, pets in the home during the child's infancy; wheeze at or before 6 years - maternal BMI, child's gender, maternal education, maternal asthma, paternal asthma, maternal rhinitis; transient wheeze - maternal BMI, child's gender, mother's parity, maternal asthma, maternal rhinitis; Persistent/late - maternal education, smoking during pregnancy, maternal asthma, paternal asthma, maternal rhinitis; Persistent/late wheeze with atopy-child's gender, maternal asthma, paternal asthma, paternal rhinitis, pets in the home during infancy; Persistent/late wheeze without atopy-maternal age, smoking during pregnancy, maternal asthma, paternal asthma, pets in the home during infancy.

Table E11 Relationship between average maternal daily intake of vitamin D from food during pregnancy and offspring atopy and airway inflammation

	Univariable Model				Final model			
	RR	(95% CI)	P-value	n	RR	(95% CI)	P-value	n
Atopy age 1 year	1.07	(0.96, 1.18)	0.22	623	1.03	(0.93,1.15)	0.53	556
Atopy age 3 years	1.05	(0.95, 1.16)	0.31	547	1.04	(0.94, 1.15)	0.45	538
Atopy age 6 years	1.07	(1.00, 1.14)	0.04	509	1.03	(0.94, 1.12)	0.51	446
	beta	(95% CI)	P-value	n	beta	(95% CI)	P-value	n
Exhaled nitric oxide 6 years	0.0752	(0.0162, 0.1343)	0.01	355	0.0838	(0.0261, 0.1416)	0.004	346

Data presented as change in relative risk per mcg/day total intake of vitamin D for binary outcomes and as change in transformed unit of eNO per mcg/dy of vitamin D intake for exhaled nitric oxide outcome. Excludes vitamin D intake from supplements.

Adjusted models: atopy age 1 year - child's gender, parents' social class, maternal atopy; atopy age 3 years - child's gender, exposure to smoke in infancy, maternal eczema, atopy age 6 years - child's age at testing, child's gender, parents social class, maternal asthma, paternal rhinitis, maternal atopy; exhaled nitric oxide - child's age at testing, maternal asthma, paternal rhinitis, maternal height.

Table E12 Relationship between average maternal daily intake of vitamin D from food during pregnancy intake and offspring lung function aged 6 years

	Univariable Model				Final Model			
	beta	(95% CI)	P-value	n	beta	(95% CI)	P-value	n
FEV_1 absolute	0.0000	(-0.0095, 0.0096)	0.99	590	-0.0009	(-0.0099, 0.0082)	0.85	584
FEV_1 z-score	-0.0049	(-0.0461, 0.0364)	0.82	590	0.0023	(-0.0385, 0.0431)	0.91	590
FVC absolute	0.0037	(-0.0080, 0.0154)	0.53	590	0.0018	(-0.0091, 0.0128)	0.74	584
FVC z-score	0.0150	(-0.0333, 0.0633)	0.54	590	0.0191	(-0.0293, 0.0674)	0.44	590
BHR slope	-0.0067	(-0.2754, 0.2599)	0.96	169	0.0199	(-0.2478, 0.2876)	0.88	165

Data presented as change in unit of lung function measure per mcg/day food intake of vitamin D. Excludes vitamin D intake from supplements. Adjusted models: FEV_1 absolute - child's age at testing, child's gender, parity, maternal BMI, maternal height; FEV_1 z-score - child's gender; FVC absolute - child's age at testing, child's gender, age at introduction of solid foods, maternal BMI, maternal height, FVC z-score - child's gender; BHR - maternal age, smoking in pregnancy, paternal eczema, age at introduction of solid foods.

Table E13 Relationship between total energy-adjusted daily maternal vitamin D intake during pregnancy and offspring asthma and wheeze at age 6 years

	Quartile 1	Quartile 2		Quartile 3		Quartile 4		
	RR	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	P for trend
Current doctor-diagnosed asthma at 6 years	1	1.11	(0.59, 2.09)	0.80	(0.38, 1.66)	1.23	(0.65, 2.33)	0.74
Current wheeze at 6 years	1	0.87	(0.51, 1.47)	0.92	(0.52, 1.61)	0.90	(0.53, 1.52)	0.75
Any wheeze at or before 6 years	1	1.08	(0.91, 1.28)	1.05	(0.88, 1.25)	1.03	(0.86, 1.23)	0.87
Transient wheeze	1	1.12	(0.90, 1.40)	1.08	(0.86, 1.35)	1.03	(0.81, 1.30)	0.93
Persistent/late wheeze	1	0.91	(0.60, 1.39)	0.95	(0.61, 1.49)	1.03	(0.66,1.60)	0.89
Persistent/late wheeze with atopy	1	0.33	(0.12, 0.92)	0.39	(0.15, 0.98)	0.84	(0.40, 1.78)	0.97
Persistent/late wheeze without atopy	1	0.82	(0.38, 1.77)	0.61	(0.28, 1.33)	0.65	(0.28, 1.49)	0.21

Adjusted models: asthma - maternal education, maternal asthma, paternal asthma and paternal rhinitis; wheeze at age 6 - maternal education, maternal asthma, paternal rhinitis, pets in the home during the child's infancy; wheeze at or before 6 years - maternal BMI, child's gender, maternal education, maternal asthma, paternal asthma, maternal rhinitis; transient wheeze - maternal BMI, child's gender, mother's parity, maternal asthma, maternal rhinitis; Persistent/late - maternal education, smoking during pregnancy, maternal asthma, paternal asthma, maternal rhinitis; Persistent/late wheeze with atopy-child's gender, maternal asthma, paternal asthma, paternal rhinitis, pets in the home during infancy; Persistent/late wheeze without atopy-maternal age, smoking during pregnancy, maternal asthma, paternal asthma, pets in the home during infancy.

Table E14 Relationship between daily energy-adjusted maternal vitamin D intake during pregnancy and offspring atopy and airway inflammation

	Quartile 1	Quartile 2		Quartile 3		Quartile 4		
	RR	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	P-trend
Atopy age 1 year	1	1.13	(0.54, 2.38)	1.22	(0.61, 2.46)	1.48	(0.75, 2.89)	0.24
Atopy age 3 years	1	1.21	(0.74, 1.97)	0.88	(0.53, 1.47)	0.93	(0.55, 1.56)	0.51
Atopy age 6 years	1	0.86	(0.53, 1.40)	0.69	(0.43, 1.11)	1.15	(0.76, 1.74)	0.59
		beta	(95% CI)	beta	(95% CI)	beta	(95% CI)	
Exhaled nitric oxide age 6 years	0	-0.127	(-0.422, 0.168)	-0.089	(-0.393, 0.215)	-0.065	(-0.370, 0.239)	0.76

Adjusted models: atopy age 1 year - child's gender, parents' social class, maternal atopy; atopy age 3 years - child's gender, exposure to smoke in infancy, maternal eczema, atopy age 6 years - child's age at testing, child's gender, parents social class, maternal asthma, paternal rhinitis, maternal atopy; exhaled nitric oxide - child's age at testing, maternal asthma, paternal rhinitis, maternal height.

Table E15 Relationship between daily energy-adjusted maternal vitamin D intake during pregnancy and offspring lung function at age 6 years

	Quartile 1	Quartile 2		Quartile 3		Quartile 4		P-trend
	beta	beta	(95% CI)	beta	(95% CI)	beta	(95% CI)	
FEV_1 absolute	0	-0.009	(-0.055, 0.036)	0.022	(-0.023, 0.067)	-0.006	(-0.051, 0.039)	0.87
FEV_1 z-score	0	0.005	(-0.199, 0.209)	0.084	(-0.119, 0.286)	-0.027	(-0.226, 0.173)	0.97
FVC absolute	0	0.019	(-0.035, 0.074)	0.047	(-0.007, 0.102)	0.012	(-0.041, 0.065)	0.50
FVC z-score	0	0.155	(-0.086, 0.397)	0.180	(-0.060, 0.420)	0.039	(-0.197, 0.276)	0.75
BHR slope	0	0.365	(-0.726, 1.457)	0.291	(-0.887, 1.468)	-0.327	(-1.473, 0.818)	0.60

Adjusted models: FEV_1 absolute - child's age at testing, child's gender, parity, maternal BMI, maternal height; FEV_1 z-score - child's gender; FVC absolute - child's age at testing, child's gender, age at introduction of solid foods, maternal BMI, maternal height, FVC z-score - child's gender; BHR - maternal age, smoking in pregnancy, paternal eczema, age at introduction of solid food.

REFERENCES

E1. Inskip HM, Godfrey KM, Robinson SM, Law CM, Barker DJ, Cooper C. Cohort profile: The Southampton Women's Survey. Int J Epidemiol. 2006;35(1):42-8.

E2. Robinson S, Godfrey K, Osmond C, *et al*. Evaluation of a food frequency questionnaire used to assess nutrient intakes in pregnant women. Eur J Clin Nutr. 1996;50(5):302-8.

E3. ATS/ERS. recommendations for standardised procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. European Respiratory Journal. 2005;171(8):912-30.

E4. Asher MI, Keil U, Anderson HR, Beasley R, *et al*. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. Eur Respir J. 1995;8(3):483-91.

E5. Martinez FD, Wright AL, Taussig LM, *et al*. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. N Engl J Med. 1995;332(3):133-8.

E6. Miller MR, Hankinson J, Brusasco V, *et al*. Standardisation of spirometry. Eur Respir J. 2005;26(2):319-38.

E7. Stanojevic S, Wade A, Stocks J, Hankinson J, Coates AL, Pan H, Rosenthal M, Corey M, Lebecque P, Cole TJ. Reference ranges for spirometry across all ages: a new approach. *Am J Respir Crit Care Med*. 2008;177(3):253-60.

E8. Crapo RO, Casaburi R, Coates AL, *et al*. Guidelines for methacholine and exercise challenge testing-1999. Am J Respir Crit Care Med. 2000;161(1):309-29. Epub 2000/01/05.

E9. Chinn S, Arossa WA, Jarvis DL, *et al*. Variation in nebulizer aerosol output and weight output from the Mefar dosimeter: implications for multicentre studies. Eur Respir J. 1997;10(2):452-6.

E10. Barros AJ, Hirakata VN. Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio. BMC medical research methodology. 2003;3:21.

E11. Bland M. An introduction to statistics. Oxford: Oxford University Press; 2000.