

**ONLINE REPOSITORY MATERIAL**

eTables 1-7

Prospective association of 25-hydroxyvitamin D<sub>3</sub> and D<sub>2</sub> with childhood lung function, asthma, wheezing and flexural dermatitis

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**eTable 1.** Univariable associations between confounders and age- and sex-adjusted serum 25(OH)D<sub>3</sub>, 25(OH)D<sub>2</sub>, PTH and calcium concentrations. Data are given as SD change per SD/category change (95% CI).

	Season-adjusted 25(OH)D <sub>3</sub>	25(OH)D <sub>2</sub>	Phosphate	Albumin-adjusted calcium	Parathyroid hormone
BMI (kg/m <sup>2</sup> )	-0.01 (-0.01 to 0.00)	-0.01 (-0.02 to 0.00)	0.00 (-0.01 to 0.01)	0.00 (-0.01 to 0.00)	0.01 (0.01 to 0.02)
Non-white ethnicity	-0.67 (-0.78 to -0.57)	-0.08 (-0.19 to 0.03)	0.02 (-0.09 to 0.12)	-0.02 (-0.12 to 0.09)	0.35 (0.24 to 0.45)
Head of household social class					
i (highest)	0.02 (-0.04 to 0.08)	-0.06 (-0.12 to 0.00)	0.03 (-0.04 to 0.09)	-0.05 (-0.12 to 0.01)	-0.02 (-0.08 to 0.05)
ii	0.03 (-0.04 to 0.10)	0.04 (-0.03 to 0.11)	0.00 (-0.07 to 0.07)	0.05 (-0.02 to 0.13)	0.02 (-0.05 to 0.09)
iii non-manual	0.00 (-0.07 to 0.08)	0.06 (-0.02 to 0.14)	-0.06 (-0.14 to 0.02)	0.10 (0.02 to 0.18)	-0.04 (-0.12 to 0.04)
iii manual	-0.12 (-0.21 to -0.03)	0.18 (0.09 to 0.28)	-0.07 (-0.17 to 0.02)	0.03 (-0.06 to 0.13)	0.06 (-0.03 to 0.16)
iv/v (lowest)	-0.12 (-0.25 to 0.02)	0.14 (0.01 to 0.27)	-0.01 (-0.14 to 0.12)	0.10 (-0.03 to 0.24)	0.06 (-0.07 to 0.19)
Paternal education					
None/CSE	-0.07 (-0.12 to -0.02)	0.08 (0.03 to 0.14)	-0.01 (-0.06 to 0.05)	0.08 (0.03 to 0.13)	0.00 (-0.06 to 0.05)
Vocational	0.11 (0.01 to 0.20)	-0.15 (-0.25 to -0.05)	0.00 (-0.10 to 0.10)	-0.08 (-0.18 to 0.01)	-0.02 (-0.12 to 0.08)
Ordinary level	0.12 (0.05 to 0.20)	-0.09 (-0.16 to -0.02)	0.01 (-0.07 to 0.08)	-0.06 (-0.13 to 0.01)	0.02 (-0.05 to 0.09)
Advanced level	0.14 (0.07 to 0.21)	-0.08 (-0.15 to -0.01)	-0.01 (-0.08 to 0.06)	-0.07 (-0.14 to 0.00)	-0.01 (-0.08 to 0.06)
University degree	0.08 (0.01 to 0.15)	-0.15 (-0.22 to -0.07)	0.04 (-0.03 to 0.12)	-0.15 (-0.23 to -0.08)	-0.02 (-0.09 to 0.06)
Maternal education					

None/CSE	-0.08 (-0.14 to -0.02)	0.09 (0.03 to 0.16)	-0.03 (-0.09 to 0.03)	0.06 (-0.01 to 0.12)	0.03 (-0.03 to 0.10)
Vocational	0.12 (0.01 to 0.22)	-0.11 (-0.21 to 0.00)	0.09 (-0.02 to 0.19)	0.02 (-0.09 to 0.12)	-0.11 (-0.22 to -0.01)
Ordinary level	0.14 (0.06 to 0.21)	-0.07 (-0.15 to 0.00)	-0.01 (-0.09 to 0.06)	-0.04 (-0.11 to 0.04)	-0.06 (-0.14 to 0.01)
Advanced level	0.08 (0.00 to 0.15)	-0.15 (-0.22 to -0.07)	0.04 (-0.04 to 0.11)	-0.06 (-0.14 to 0.01)	-0.02 (-0.10 to 0.05)
University degree	0.08 (0.00 to 0.17)	-0.15 (-0.23 to -0.06)	0.08 (0.00 to 0.17)	-0.14 (-0.23 to -0.06)	-0.02 (-0.11 to 0.07)
Ultraviolet B protection score	0.01 (0.00 to 0.02)	0.00 (-0.01 to 0.01)	-0.01 (-0.02 to 0.00)	0.01 (0.00 to 0.02)	-0.01 (-0.02 to 0.00)
Average h/day spent outdoors during summer	0.06 (0.03 to 0.08)	0.02 (0.00 to 0.05)	0.01 (-0.01 to 0.04)	0.02 (-0.01 to 0.04)	-0.02 (-0.04 to 0.01)
Maternal history of asthma	-0.04 (-0.12 to 0.03)	0.03 (-0.04 to 0.11)	0.00 (-0.07 to 0.08)	-0.05 (-0.12 to 0.03)	0.05 (-0.03 to 0.12)
Maternal history of allergy	0.02 (-0.03 to 0.07)	0.00 (-0.04 to 0.05)	0.01 (-0.04 to 0.06)	0.01 (-0.04 to 0.06)	-0.01 (-0.06 to 0.04)
Puberty stage at spirometry assessment					
1-3	0.05 (0.02 to 0.09)	0.00 (-0.04 to 0.04)	-0.03 (-0.07 to 0.01)	-0.02 (-0.06 to 0.01)	-0.04 (-0.08 to 0.00)
4	0.04 (-0.23 to 0.31)	-0.10 (-0.38 to 0.18)	0.27 (-0.02 to 0.55)	0.03 (-0.24 to 0.30)	-0.15 (-0.43 to 0.13)
5	-0.03 (-0.30 to 0.24)	-0.12 (-0.40 to 0.16)	0.26 (-0.02 to 0.55)	0.00 (-0.27 to 0.27)	-0.13 (-0.41 to 0.15)

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**eTable 2.** Univariable associations between confounders and asthma, wheezing and flexural dermatitis. Data are given as odds ratio per SD/category change (95% CI)-

	Asthma	Wheezing	Flexural dermatitis
BMI (kg/m <sup>2</sup> )	1.03 (1.01 to 1.04)	1.01 (0.99 to 1.03)	1.01 (0.99 to 1.03)
Non-white ethnicity	1.22 (1.00 to 1.49)	1.19 (0.87 to 1.65)	1.15 (0.84 to 1.60)
Head of household social class			
i (highest)	1 (reference)	1 (reference)	1 (reference)
ii	1.31 (1.13 to 1.51)	1.30 (1.04 to 1.62)	1.13 (0.91 to 1.41)
iii non-manual	1.20 (1.02 to 1.40)	1.01 (0.78 to 1.29)	1.10 (0.86 to 1.40)
iii manual	1.32 (1.09 to 1.59)	0.96 (0.70 to 1.32)	1.14 (0.85 to 1.53)
iv/v (lowest)	1.72 (1.35 to 2.19)	1.14 (0.76 to 1.73)	0.53 (0.32 to 0.89)
Paternal education			
None/CSE	1 (reference)	1 (reference)	1 (reference)
Vocational	0.81 (0.67 to 0.97)	1.04 (0.75 to 1.44)	0.88 (0.64 to 1.20)
Ordinary level	0.79 (0.69 to 0.91)	1.13 (0.89 to 1.44)	0.79 (0.62 to 1.00)
Advanced level	0.77 (0.67 to 0.87)	1.32 (1.06 to 1.65)	1.12 (0.91 to 1.38)
University degree	0.70 (0.60 to 0.80)	1.19 (0.94 to 1.51)	1.17 (0.94 to 1.46)
Maternal education			
None/CSE	1 (reference)	1 (reference)	1 (reference)
Vocational	0.72 (0.59 to 0.87)	1.00 (0.71 to 1.41)	0.91 (0.66 to 1.25)
Ordinary level	0.79 (0.69 to 0.90)	1.20 (0.95 to 1.54)	0.92 (0.73 to 1.16)
Advanced level	0.70 (0.60 to 0.81)	1.11 (0.86 to 1.43)	0.98 (0.77 to 1.24)
University degree	0.67 (0.57 to 0.79)	1.39 (1.06 to 1.82)	1.12 (0.87 to 1.46)
Ultraviolet B protection score	1.05 (1.02 to 1.07)	1.01 (0.98 to 1.05)	1.02 (0.99 to 1.06)
Average h/day spent outdoors during summer	1.03 (0.98 to 1.08)	0.99 (0.92 to 1.07)	1.04 (0.97 to 1.12)
Maternal history of asthma	78.24 (60.91 to 100.50)	2.16 (1.78 to 2.61)	1.26 (1.01 to 1.56)
Maternal history of allergy	0.39 (0.35 to 0.43)	0.59 (0.51 to 0.69)	0.82 (0.71 to 0.95)

**eTable 3.** Univariable associations between confounders, exposures and age, height and sex-standardized spirometry results (FVC, FEV<sub>1</sub> and FEF<sub>25-75</sub> are for post-salbutamol measurements).

	SD change per SD/category change (95%CI)			Odds ratio per SD/category change (95%CI)
	FVC	FEV <sub>1</sub>	FEF <sub>25-75</sub>	Increase in post- salbutamol FEV <sub>1</sub> ≥12%
BMI (kg/m <sup>2</sup> )	0.04 (0.00 to 0.09)	0.04 (-0.01 to 0.09)	0.00 (0.00 to 0.01)	1.01 (0.98 to 1.05)
Non-white ethnicity	-0.86 (-1.56 to -0.16)	-0.89 (-1.64 to -0.14)	0.10 (-0.22 to 0.01)	1.24 (0.82 to 1.88)
Head of household social class				
i (highest)	-2.07 (-2.44 to -1.71)	-2.32 (-2.71 to -1.93)	-0.33 (-0.39 to -0.27)	1 (reference)
ii	0.24 (-0.19 to 0.66)	0.26 (-0.20 to 0.71)	-0.03 (-0.04 to 0.10)	0.82 (0.60 to 1.12)
iii non-manual	-0.09 (-0.57 to 0.39)	-0.09 (-0.60 to 0.42)	-0.01 (-0.09 to 0.07)	0.76 (0.54 to 1.07)
iii manual	-0.62 (-1.24 to 0.00)	-0.68 (-1.34 to -0.01)	-0.10 (-0.20 to 0.00)	0.49 (0.31 to 0.77)
iv/v (lowest)	-0.51 (-1.34 to 0.33)	-0.57 (-1.46 to 0.32)	-0.09 (-0.23 to 0.05)	0.27 (0.12 to 0.59)
Paternal education				
None/CSE	-2.52 (-2.87 to -2.17)	-2.83 (-3.20 to -2.46)	-0.40 (-0.46 to -0.35)	1 (reference)
Vocational	0.35 (-0.29 to 1.00)	0.41 (-0.28 to 1.09)	0.06 (-0.04 to 0.17)	1.13 (0.70 to 1.81)
Ordinary level	0.62 (0.14 to 1.09)	0.70 (0.19 to 1.20)	0.11 (0.03 to 0.18)	1.31 (0.93 to 1.84)
Advanced level	0.56 (0.11 to 1.01)	0.64 (0.16 to 1.12)	0.09 (0.02 to 0.16)	1.41 (1.03 to 1.94)
University degree	0.54 (0.07 to 1.00)	0.64 (0.14 to 1.14)	0.09 (0.01 to 0.16)	1.77 (1.27 to 2.46)
Maternal education				
None/CSE	- 2.58 (-3.02 to -2.14)	-2.88 (-3.34 to -2.41)	-0.43 (-0.50 to -0.36)	1 (reference)
Vocational	0.50 (-0.19 to 1.19)	0.44 (-0.30 to 1.17)	0.10 (-0.01 to 0.21)	1.0 (0.57 to 1.76)
Ordinary level	0.54 (0.04 to 1.05)	0.60 (0.06 to 1.14)	0.11 (0.03 to 0.20)	1.75 (1.20 to 2.55)
Advanced level	0.67 (0.15 to 1.19)	0.74 (0.19 to 1.30)	0.12 (0.04 to 0.21)	2.61 (1.79 to 3.82)
University degree	0.49 (-0.07 to 1.06)	0.56 (-0.04 to 1.15)	0.10 (0.01 to 0.19)	3.10 (2.08 to 4.64)
Ultraviolet B protection score	0.00 (-0.01 to 0.02)	0.00 (-0.02 to 0.01)	0.00 (-0.01 to 0.00)	0.98 (0.93 to 1.04)
Average h/day spent outdoors during	0.02 (-0.01 to 0.05)	0.01 (-0.02 to 0.05)	0.00 (-0.01 to 0.01)	1.08 (0.96 to 1.22)

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summer					
Maternal history of asthma		-0.14 (-0.61 to 0.33)	-0.25 (-0.75 to 0.26)	-0.06 (-0.13 to 0.02)	1.03 (0.74 to 1.44)
Maternal history of allergy		0.13 (-0.17 to 0.43)	0.19 (-0.13 to 0.51)	0.03 (-0.02 to 0.07)	0.83 (0.67 to 1.04)
Ever had asthma		0.38 (-0.02 to 0.77)	0.31 (-0.11 to 0.72)	0.01 (-0.04 to 0.06)	1.52 (1.23 to 1.88)
Puberty stage at spirometry assessment					
	1-3	-2.08 (-2.32 to -1.83)	-2.29 (-2.55 to -2.02)	-0.33 (-0.37 to -0.29)	1 (reference)
	4	1.23 (-0.12 to 2.57)	1.52 (0.08 to 2.95)	0.25 (0.03 to 0.47)	1.43 (0.44 to 4.59)
	5	1.64 (0.29 to 3.00)	1.94 (0.49 to 3.38)	0.32 (0.09 to 0.54)	1.41 (0.44 to 4.57)

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**eTable 4.** Prospective association of unadjusted (for season) 25(OH)D<sub>3</sub> concentrations, assessed at mean age 9.8 years) with asthma, wheezing (N=3,323 n of asthma cases=464;14.0% and n of wheezing cases=141; 4.2% ) and flexural dermatitis (N=3,748, n of cases= 300; 8.0%), assessed a minimum of one year after the exposure. Data are given as odds ratio per doubling of exposure (95%CI).

	Model 1	Model 2	Model 3
Wheezing	1.11 (0.99 to 1.24)	1.13 (1.00 to 1.27)	1.12 (1.00 to 1.26)
Asthma	0.99 (0.92 to 1.06)	1.02 (0.93 to 1.12)	1.00 (0.91 to 1.11)
Flexural dermatitis	1.00 (0.92 to 1.09)	1.00 (0.91 to 1.08)	1.01 (0.92 to 1.10)

Model 1 is unadjusted (25(OH)D<sub>3</sub> is standardized by age and sex)

Model 2 is adjusted for ethnicity, maternal history of asthma and allergy, head of household social class, mothers and partners education, time spent outdoors during summer, protection from ultraviolet B and BMI

Model 3 is adjusted for Model 2 plus serum concentrations of 25(OH)D<sub>2</sub>, phosphate, albumin-adjusted calcium and parathyroid hormone)

**eTable 5.** Prospective association of unadjusted (for season) 25(OH)D<sub>3</sub> concentrations, assessed at mean age 9.8 years) with lung function after 400µg salbutamol dose (assessed at age 15 years, n=2,259)

Outcome	Model 1	Model 2	Model 3
SD change in outcome per doubling of exposure (95%CI)			
FVC	0.01 (-0.02 to 0.04)	0.01 (-0.02 to 0.04)	0.01 (-0.02 to 0.04)
FEV <sub>1</sub>	0.02 (-0.01 to 0.05)	0.02 (-0.01 to 0.05)	0.02 (-0.01 to 0.05)
FEF <sub>25-75</sub>	-0.01 (-0.01 to 0.00)	-0.01 (-0.01 to 0.00)	-0.01 (-0.01 to 0.00)
Odds ratio per doubling of exposure (95%CI)			
≥12% increase in FEV <sub>1</sub>	1.08 (0.97 to 1.19)	1.07 (0.97 to 1.20)	1.07 (0.95 to 1.20)

Model 1 is unadjusted (25(OH)D<sub>3</sub> is standardized by age and sex)

Model 2 is adjusted for ethnicity, maternal history of asthma and allergy, head of household social class, mothers and partners education, time spent outdoors during summer, protection from ultraviolet B, BMI, asthma, pubertal stage at 15 years

Model 3 is adjusted for Model 2 plus serum concentrations of 25(OH)D<sub>2</sub>, phosphate, albumin-adjusted calcium and parathyroid hormone)



**eTable 6.** Prospective association of total 25(OH)D concentrations ( assessed at mean age 9.8 years) with asthma, wheezing (N=3,323 n of asthma cases=464;14.0% and n of wheezing cases=141; 4.2% ) and flexural dermatitis (N=3,748, n of cases= 300; 8.0%), assessed a minimum of one year after the exposure. Data are given as odds ratio per doubling of exposure (95%CI).

	Model 1	Model 2	Model 3
Wheezing	1.13 (1.01 to 1.27)	1.14 (1.02 to 1.29)	1.13 (1.00 to 1.26)
Asthma	0.98 (0.91 to 1.05)	1.01 (0.91 to 1.10)	0.99 (0.90 to 1.10)
Flexural dermatitis	1.02 (0.93 to 1.11)	1.02 (0.94 to 1.12)	1.02 (0.94 to 1.12)

Model 1 is unadjusted (25(OH)D<sub>3</sub> is standardized by age and sex)

Model 2 is adjusted for ethnicity, maternal history of asthma and allergy, head of household social class, mothers and partners education, time spent outdoors during summer, protection from ultraviolet B and BMI

Model 3 is adjusted for Model 2 plus serum concentrations of phosphate, albumin-adjusted calcium and parathyroid hormone)

**eTable 7.** Prospective association of total 25(OH)D concentrations (assessed at mean age 9.8 years) with lung function after 400µg salbutamol dose (assessed at age 15 years, n=2,259)

Outcome	Model 1	Model 2	Model 3
SD change in outcome per doubling of exposure (95%CI)			
FVC	0.01 (-0.02 to 0.04)	0.01 (-0.02 to 0.04)	0.01 (-0.02 to 0.04)
FEV <sub>1</sub>	0.01 (-0.02 to 0.05)	0.01 (-0.02 to 0.04)	0.01 (-0.02 to 0.05)
FEF <sub>25-75</sub>	-0.01 (-0.01 to 0.00)	0.00 (-0.01 to 0.00)	-0.01 (-0.01 to 0.00)
Odds ratio per doubling of exposure (95%CI)			
≥12% increase in FEV <sub>1</sub>	1.06 (0.95 to 1.17)	1.04 (0.94 to 1.17)	1.03 (0.93 to 1.16)

Model 1 is unadjusted (25(OH)D<sub>3</sub> is standardized by age and sex)

Model 2 is adjusted for ethnicity, maternal history of asthma and allergy, head of household social class, mothers and partners education, time spent outdoors during summer, protection from ultraviolet B, BMI, asthma, pubertal stage at 15 years

Model 3 is adjusted for Model 2 plus serum concentrations of phosphate, albumin-adjusted calcium and parathyroid hormone)