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Predictors of lung function in early adulthood: A population-based cohort study

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Abstract

Background and Objective: Lung function reaches a peak/plateau in early adulthood before declining with age. Lower early adult lung function may increase the risk for chronic obstructive pulmonary disease (COPD) in mid-late adult life. Understanding the effects of multiple childhood/adolescent exposures and their potential interactions on plateau lung function would provide insights into the natural history of COPD.

Methods: Longitudinal spirometry data from 688 participants with complete data from a population-based birth cohort (original $n = 1037$) were used to investigate associations between a wide range of childhood/adolescent exposures and repeated measures of FEV_1, FVC and FEV_1/FVC during the early-adult plateau phase. Generalized estimating equations were used to accommodate the multiple timepoints per participant.

Results: FEV_1 reached a peak/plateau between ages 18 and 26 and FVC from 21 to 32 years, whereas FEV_1/FVC declined throughout early adulthood. Childhood asthma and airway hyperresponsiveness were associated with lower early adult FEV_1 and FEV_1/FVC. Smoking by age 18 was associated with lower FEV_1/FVC. Higher BMI during early adulthood was associated with lower FEV_1 and FVC and lower FEV_1/FVC. Physical activity during adolescence was positively associated with FEV_1 and FEV_1/FVC but this was only statistically significant in men. There was no convincing evidence of interactions between exposures.

Conclusion: Childhood asthma and airway hyperresponsiveness are associated with lower lung function in early adulthood. Interventions targeting these may reduce the risk of COPD in mid-late adult life. Promotion of physical activity during adolescence, prevention of cigarette smoking and maintenance of a healthy body weight in early adulthood are also priorities.

KEYWORDS
airway hyperresponsiveness, childhood asthma, Dunedin Multidisciplinary Health and Development Study, lung function development, peak lung function, plateau lung function, population-based cohort study

INTRODUCTION

Lung development starts around 4 weeks of gestation and continues until early adulthood.[1,2] Peak forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) are usually attained between 20 and 25 years in men and a few years earlier in women.[3] These remain stable for several years in a plateau phase, before gradually declining.[2–4]

Maximal attained lung function in early adulthood is partially determined by genetic and prenatal factors,[5] but is also influenced by early life exposures.[6,7] Risk factors for lower plateau lung function include asthma/wheezing,[6,8,9] lower respiratory tract infections,[10] pre- and post-natal exposure to tobacco smoke,[11,12] low birth weight,[13–16] and low socioeconomic status.[17] However, the effects of multiple exposures and their potential interactions on early adult lung function remain poorly understood.

Lower peak lung function is associated with chronic obstructive pulmonary disease (COPD) in mid-late adult life,[18] indicating that COPD can arise from a failure to attain the normal plateau as well as from accelerated lung function decline.[19] Understanding how early life exposures influence early adult lung function would provide insights into the natural history of COPD and may help to guide preventive measures.

We investigated early adult FEV_1 and FVC and FEV_1/FVC in a population-based birth cohort and their childhood/adolescent predictors.

METHODS

Study design and population

The Dunedin Multidisciplinary Health and Development Study (Dunedin Study) investigates health and behaviour in a population-based birth cohort born in 1972/1973 in Dunedin, New Zealand.[20] The cohort was assembled at age 3 years when 1037 individuals were assessed (52% male; 91% of eligible births). The cohort has been assessed at multiple ages from childhood to age 45 years. Each assessment phase was approved by the relevant ethics committee and written informed consent was obtained from participants.

Lung function and respiratory symptoms

Spirometry was measured using a Godart water-sealed spirometer at ages 9, 11, 13, 15 and 21 years, a Morgan rolling-seal spirometer at age 18, and a body plethysmograph (Vmax, Sensormedics, Yorba Linda, CA) at 26, 32, 38 and 45 years according to the standards at the time.[6,21,22] Study members were asked to avoid bronchodilators on the assessment day. Respiratory questionnaires were administered at each assessment as previously described.[23,24]

Definition of variables

Childhood asthma was defined as a parent-reported diagnosis with compatible symptoms or medication use within the previous year at any of the ages 9, 11 or 13.[22] Childhood airway hyperresponsiveness (AHR) was defined as a positive response to a methacholine/salbutamol challenge at 9, 11 or 13 years.[25] Atopy was defined as a positive skin-prick test (weal diameter 2 mm greater than negative control) to one or more of 11 common aeroallergens at age 13.[26] Parental asthma was defined as a history of asthma reported for either biological parent at the age 7 or age 18 assessments.

Exposure to parental smoking was obtained from parents at ages 7, 9 and 11 and the Study member at age 13.[27] Personal smoking was defined as self-reported smoking at least one cigarette per day for at least 1 month during the previous year from age 15 onwards. Maternal smoking during pregnancy was retrospectively collected at age 9 and data were only available for 75% of the cohort: hence, this was only included in a sensitivity analysis. Mean childhood socioeconomic status (SES) was based on parental occupations assessed repeatedly from birth to age 15.[28] Physical activity was assessed using a modification of the Minnesota questionnaire at ages 15 and 18.[29] The annual time spent on physical activity at each age was standardized for age and sex (z-score).

Birth weight was recorded for all Study members. Height and weight were measured in light clothing without shoes at each subsequent assessment to calculate body mass index (BMI) in kg/m^2. Early life weight gain was defined as the change in weight between birth and age 3. Duration of breastfeeding was assessed at age 3 and validated by visiting nurse records.[30] Study members were considered to be breastfed if breastfeeding continued for at least 4 weeks.

SUMMARY AT A GLANCE

Childhood asthma and airway hyperresponsiveness, and higher adult body mass index are associated with lower lung function in early adulthood and may enhance the risk for COPD in later life. Conversely, physical activity is associated with higher adult lung function, especially among boys, and may be protective.

Statistical analysis

Descriptive statistics for men and women were compared using chi-square and *t*-tests. Visual inspection indicated that women and men reached peak FEV_1 around ages 18 and 21, respectively, with little change until age 26. Hence, early adult FEV_1 was defined as occurring from 18 to 26 years for both sexes. FVC peaked at age 32 in women and men, although there was little change since age 21. Consequently, early adult FVC was defined as occurring from 21 to 32 years. FEV_1/FVC declined throughout follow-up with no plateau therefore FEV_1/FVC during the peak/plateau of FEV_1 (18–26 years) was used.

Associations between potential predictors and early adult lung function values were assessed using generalized estimating equations (GEEs) with exchangeable correlation structures to account for the correlations between repeated measures within individuals.[31] Complete-case analyses were performed for the full cohort (with and without sex-interaction terms) and separately for each sex. Potential predictors included childhood asthma, childhood AHR, parental asthma, parental smoking, personal smoking at age 18, childhood SES, physical activity during adolescence, birth weight, breastfeeding and early life weight gain. Based on established predictors of adult lung function, all models included sex (except for sex-specific analyses), and concurrent age, height, and BMI. The choice of predictors and confounders was guided by a directed acyclic graph (Figure S1 in the Supporting Information). We tested interactions between parental asthma and childhood asthma; parental smoking and personal smoking; childhood asthma and personal smoking; childhood AHR and personal smoking; personal smoking and physical activity; childhood asthma and physical activity; maternal smoking during pregnancy and personal smoking; and breastfeeding and parental asthma.[11,32–34]

A sensitivity analysis was conducted using multiple regression to assess associations between exposures and the maximum measured values of FEV_1 and FVC and the FEV_1/FVC ratio at age 18, instead of using values across several ages.

Model assumptions were checked by inspecting histograms of residuals and scatterplots of residuals against continuous predictors and fitted values. One study member with developmental lung abnormalities was excluded. Lung function values from pregnant women were also excluded. Analyses used Stata 15.0 (StataCorp, College Station, TX). Two-sided p-values <0.05 were considered statistically significant.

RESULTS

Characteristics of participants are presented in Table S1 in the Supporting Information. There were no significant differences between those included and missing from the analyses. Men were non-significantly more likely to have childhood asthma and AHR and more likely to have atopy, higher birth weight and early life weight gain. Women were more likely to smoke at age 18 years (Table S2 in the Supporting Information). Men had higher FEV_1 and FVC values, whereas women had higher FEV_1/FVC ratios (Figures 1–3, Table S3 in the Supporting Information).

Six hundred eighty-eight participants had at least one FEV_1 measure between ages 18 and 26 along with complete data for predictors and covariates. The GEE models showed that childhood AHR predicted lower early adult FEV_1 (Table 1). This association was stronger in men (interaction $p = 0.003$). Childhood asthma also predicted lower FEV_1. Physical activity during adolescence was associated with higher early adult FEV_1, whereas concurrent BMI was associated with lower FEV_1 values.

Childhood AHR predicted lower FVC between ages 21 and 32 (Table 2). Early life weight gain predicted higher early adult FVC, whereas concurrent adult BMI was associated with lower FVC. This association was found in both sexes, but was stronger in men (interaction $p = 0.001$).

Childhood AHR, asthma and personal smoking at age 18 were all associated with lower FEV_1/FVC between ages 18 and 26 in both sexes (Table 3). Physical activity during adolescence predicted higher FEV_1/FVC values among men and having been breastfed predicted lower values among women, although neither sex interaction was statistically significant. Higher concurrent BMI was associated with lower FEV_1/FVC overall and among women, with evidence that the association differed between sexes (interaction $p = 0.028$).

Only one of the 24 tested interactions between risk factors was statistically significant (Table S4 in the Supporting Information). This indicated that physical activity was associated with higher FVC in non-smokers (effect 83 mL (95% CI 29 to 136), $p = 0.003$) but not in smokers (effect −38 mL (95% CI −95 to 19), $p = 0.188$).

Adding maternal smoking during pregnancy did not meaningfully affect the results (data not shown). Sensitivity analyses using the maximum measured lung function rather than the plateau showed similar findings except for BMI,

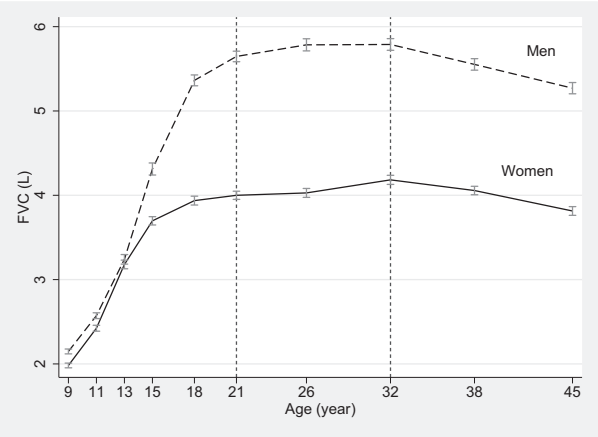

FIGURE 2 Development of FVC from age 9 to 45 years, stratified by sex.

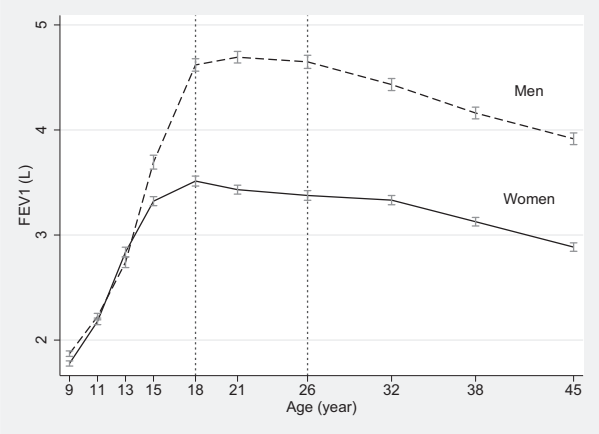

FIGURE 1 Development of FEV_1 from age 9 to 45 years, stratified by sex.

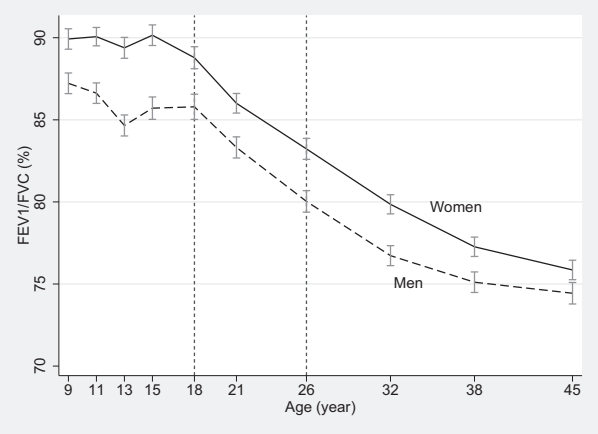

FIGURE 3 Development of FEV_1/FVC from age 9 to 45 years, stratified by sex.

TABLE 1 Predictors of plateau FEV_1 at age 18, 21 and 26 years.[a]

	Full cohort (688 participants, 1945 obs.)			Men (360 participants, 1036 obs.)			Women (328 participants, 909 obs.)			Sex interactions
	Effect (mL)	95% CI	*p*-value	Effect (mL)	95% CI	*p*-value	Effect (mL)	95% CI	*p*-value	*p*-value
Time-invariant variables										
Sex (women is reference)										
Men	662	566 to 759	**<0.001**							
Childhood asthma	−135	−260 to −9	**0.036**	−94	−273 to 85	0.302	−175	−333 to −17	**0.030**	0.503
Childhood AHR	−359	−467 to −250	**<0.001**	−492	−639 to −346	**<0.001**	−183	−328 to −37	**0.014**	**0.003**
Parental asthma	−18	−99 to 63	0.670	22	−113 to 157	0.751	−40	−137 to 57	0.422	0.477
Parental smoking 7–13	17	−56 to 90	0.642	54	−55 to 163	0.329	−31	−121 to 58	0.489	0.236
Personal smoking at 18	−28	−101 to 45	0.455	−73	−187 to 42	0.214	−18	−106 to 70	0.690	0.466
Mean childhood SES (per unit)	−22	−56 to 13	0.215	−17	−71 to 37	0.548	−26	−64 to 13	0.187	0.795
Physical activity at 15 and 18 (z-score)	52	16 to 89	**0.005**	68	23 to 114	**0.003**	20	−34 to 74	0.469	0.184
Birth weight (kg)	56	−10 to 122	0.095	55	−45 to 154	0.282	70	−7 to 147	0.075	0.786
Early life weight gain 0–3 (kg)	18	−5 to 42	0.131	30	−7 to 66	0.115	16	−13 to 45	0.276	0.614
Breastfeeding	0	−69 to 69	0.996	30	−77 to 137	0.582	−29	−113 to 55	0.501	0.400
Time-varying variables										
Age (18 years is reference)										
21 years	−20	−43 to 2	0.075	33	−3 to 69	0.069	−80	−107 to −53	**<0.001**	**<0.001**
26 years	−64	−95 to −33	**<0.001**	−12	−65 to 42	0.672	−119	−153 to −85	**<0.001**	**0.001**
Height (cm)	41	35 to 47	**<0.001**	46	37 to 55	**<0.001**	32	25 to 39	**<0.001**	**0.013**
BMI (kg/m^2)	−11	−17 to −4	**0.001**	−14	−25 to −2	**0.006**	−11	−19 to −3	**0.004**	0.763

Note: Bold *p*-values reflect statistically significant outcomes.
[a]The generalized estimating equations were adjusted for repeated measures of age, height and BMI (time-varying variables in the table).

which was not a significant predictor of peak lung function in this analysis (Table S5 in the Supporting Information).

DISCUSSION

In this population-based birth cohort, we found that childhood asthma and AHR predicted lower early adult FEV_1 and lower FEV_1/FVC. Smoking during adolescence predicted lower FEV_1/FVC. Physical activity during adolescence predicted higher FEV_1 and higher FEV_1/FVC in men, while higher BMI in early adulthood predicted lower FEV_1 and FVC values in both sexes and lower FEV_1/FVC in women.

Our findings highlight the likely impact of childhood AHR and asthma on peak/plateau lung function. Although AHR is characteristic of asthma, making it difficult to separate their independent effects, we found that childhood AHR had strong negative associations with early adult FEV_1 in both sexes, independently of reported asthma, suggesting that this leads to airway remodelling. Previous reports from the Dunedin Study[35] and other cohorts have found that children with AHR have lower growth in FEV_1.[7,8,36] This association was stronger in men, which might be explained by the higher prevalence of AHR among boys (Table S2 in the Supporting Information). Unsurprisingly, childhood asthma and AHR also predicted lower FEV_1/FVC in both sexes, consistent with a previous finding that participants with persistent wheezing had low FEV_1/FVC from childhood to age 26.[6] Similarly, childhood asthma predicted lower FEV_1/FVC ratios that worsened from age 6 to 18 years in two American cohorts.[37]

Childhood AHR also predicted lower early adult FVC. Although the interaction term was not significant, this association also appeared stronger in men. Previous findings regarding this association are inconsistent: AHR predicted lower peak FVC in Dutch cohorts,[7] but not in an Australian cohort.[8] However, childhood asthma and AHR had a greater influence on airway calibre rather than lung size (FVC) as indicated by their association with lower FEV_1/FVC ratios.

Although we identified similar age ranges for the plateaux, women reached peak FEV_1 around age 18, whereas men peaked later around age 21 years (Figure 1). Conversely, FVC peaked around age 32 years in both sexes (Figure 2). Women have been observed to have an earlier peak FEV_1 but later peak FVC in other cohorts.[3,7,38] Men had consistently lower FEV_1/FVC ratios than women

TABLE 2 Predictors of plateau FVC at age 21, 26 and 32 years.[a]

	Full cohort (681 participants, 1928 obs)			Men (356 participants, 1026 obs)			Women (325 participants, 902 obs)			Sex interactions
	Effect (mL)	95% CI	*p*-value	Effect (mL)	95% CI	*p*-value	Effect (mL)	95% CI	*p*-value	*p*-value
Time-invariant variables										
Sex (women is reference)										
Men	1050	934 to 1165	**<0.001**							
Childhood asthma	9	−135 to 153	0.902	61	−148 to 269	0.568	−40	−206 to 127	0.638	0.461
Childhood AHR	−168	−305 to −31	**0.016**	−257	−455 to −59	**0.011**	−58	−212 to 95	0.458	0.120
Parental asthma	−3	−101 to 95	0.955	70	−101 to 242	0.421	−52	−166 to 62	0.374	0.247
Parental smoking 7–13	25	−62 to 112	0.576	23	−113 to 159	0.742	19	−85 to 123	0.716	0.972
Personal smoking at 18	56	−32 to 143	0.213	33	−115 to 182	0.659	44	−54 to 142	0.381	0.914
Mean childhood SES (per unit)	−18	−57 to 21	0.357	8	−52 to 68	0.802	−42	−91 to 6	0.084	0.204
Physical activity at 15 and 18 (z-score)	40	−3 to 82	0.066	50	−5 to 105	0.074	26	−33 to 86	0.387	0.569
Birth weight (kg)	89	6 to 171	**0.035**	118	−15 to 251	0.083	58	−32 to 149	0.204	0.475
Early life weight gain 0–3 (kg)	45	18 to 73	**0.001**	70	29 to 111	**0.001**	24	−11 to 58	0.182	0.094
Breastfeeding	10	−74 to 93	0.822	20	−111 to 151	0.769	3	−98 to 103	0.959	0.841
Time-varying variables										
Age (21 years is reference)										
26 years	95	68 to 122	**<0.001**	150	108 to 192	**<0.001**	36	3 to 68	**0.030**	**<0.001**
32 years	154	127 to 181	**<0.001**	158	115 to 201	**<0.001**	160	129 to 192	**<0.001**	0.935
Height (cm)	46	39 to 54	**<0.001**	51	40 to 62	**<0.001**	41	33 to 50	**<0.001**	0.154
BMI (kg/m^2)	−16	−21 to −10	**<0.001**	−27	−36 to −17	**<0.001**	−8	−15 to −2	**0.010**	**0.001**

Note: Bold *p*-values reflect statistically significant outcomes.
[a]The generalized estimating equations were adjusted for repeated measures of age, height and BMI (time-varying variables in the table).

(Figure 3), but both sexes experienced a similar pattern of decline with age.

Higher birth weight[13–16] and early life weight gain[14,39,40] have been associated with higher lung volumes in early adulthood and we observed similar associations for FVC and non-significant associations for FEV_1. Consistent with a previous report, the positive association between early life weight gain and early adult FVC was observed only in men.[14]

Concurrent adult BMI was associated with lower early adult FEV_1 and FVC in both sexes, and lower FEV_1/FVC in women. This is consistent with earlier findings that BMI at age 32 was associated with lower FEV_1 and FVC and that increases in BMI to age 38 were associated with declines in these values in both sexes and worsening FEV_1/FVC ratios in women.[41] Taken together, these findings confirm that adult obesity has a negative effect on lung volumes. While the effect on lung volumes is generally greater in men than women, the effect of obesity on airflow limitation (FEV_1/FVC) is more pronounced in women. In the sensitivity analysis, however, concurrent BMI was not associated with the highest measured FEV_1 or FVC. Post-hoc analyses of the data to explore this discrepancy indicate that those whose lung function peaked earlier tended to have higher BMI values (Tables S6 and S7 in the Supporting Information), suggesting that those with higher body weight reach peak lung function earlier followed by early adult lung function decline leading to lower values across early adulthood.

Smoking by age 18 predicted lower FEV_1/FVC in early adulthood, suggesting that smoking during late adolescence may impair the final stages of lung development, leading to airflow obstruction in early adulthood. A relationship between smoking and lower FEV_1/FVC was also observed in the Harvard Six Cities cohort, where children aged 10–18 were followed up for 15 years.[42] Unlike some studies, we did not observe any associations between childhood exposure to parental smoking and early adult lung function,[43,44] nor did we find that childhood exposure to parental smoking enhanced the negative effect of adult personal smoking.[11]

Physical activity during adolescence predicted higher FEV_1 and higher FEV_1/FVC. Although the interaction terms were non-significant, these associations appeared stronger among men. By contrast, the ALSPAC study found an association between physical activity and higher lung function only in girls up to age 15.[45] The difference may be because we measured physical activity at 15 and 18 years, by which

TABLE 3 Predictors of FEV_1/FVC at age 18, 21 and 26 years.[a]

	Full cohort (688 participants, 1945 obs.)			Men (360 participants, 1036 obs.)			Women (328 participants, 909 obs.)			Sex interactions
	Effect (%)	95% CI	*p*-value	Effect (%)	95% CI	*p*-value	Effect (%)	95% CI	*p*-value	*p*-value
Time-invariant variables										
Sex (women is reference)										
Men	−2.3	−3.6 to −1.0	**0.001**							
Childhood asthma	−3.4	−5.0 to −1.7	**<0.001**	−3.4	−5.7 to −1.2	**0.003**	−3.5	−5.7 to −1.3	**0.002**	0.948
Childhood AHR	−4.7	−6.2 to −3.2	**<0.001**	−5.2	−7.1 to −3.3	**<0.001**	−3.7	−5.7 to −1.6	**0.001**	0.272
Parental asthma	−0.5	−1.6 to 0.6	0.329	−1.3	−3.1 to 0.6	0.174	0.1	−1.3 to 1.4	0.941	0.240
Parental smoking 7–13	−0.03	−1.0 to 0.9	0.948	0.5	−0.8 to 1.9	0.460	−0.6	−1.9 to 0.7	0.360	0.248
Personal smoking at 18	−1.5	−2.5 to −0.5	**0.004**	−1.7	−3.2 to −0.1	**0.034**	−1.5	−2.9 to −0.2	**0.026**	0.895
Mean childhood SES (per unit)	−0.2	−0.7 to 0.2	0.338	−0.6	−1.3 to 0.1	0.085	0.2	−0.4 to 0.7	0.524	0.074
Physical activity at 15 and 18 (z-score)	0.4	−0.1 to 0.8	0.080	0.5	0.0 to 1.1	**0.045**	−0.1	−0.9 to 0.6	0.714	0.142
Birth weight (kg)	0.3	−0.6 to 1.2	0.471	−0.1	−1.4 to 1.3	0.940	0.8	−0.3 to 2.0	0.152	0.307
Early life weight gain 0–3 (kg)	−0.1	−0.4 to 0.2	0.432	−0.2	−0.7 to 0.2	0.275	−0.1	−0.5 to 0.4	0.749	0.549
Breastfeeding	−0.6	−1.6 to 0.3	0.177	−0.03	−1.4 to 1.3	0.963	−1.4	−2.7 to −0.1	**0.030**	0.150
Time-varying variables										
Age (18 years is reference)										
21 years	−2.4	−2.8 to −2.1	**<0.001**	−2.5	−3.0 to −2.0	**<0.001**	−2.5	−3.0 to −1.9	**<0.001**	0.986
26 years	−5.0	−5.5 to −4.5	**<0.001**	−5.4	−6.1 to −4.7	**<0.001**	−4.8	−5.4 to −4.2	**<0.001**	0.178
Height (cm)	−0.1	−0.1 to 0.0	0.059	−0.1	−0.2 to 0.0	0.135	−0.1	−0.2 to 0.0	0.231	0.924
BMI (kg/m^2)	−0.3	−0.4 to −0.1	**0.001**	−0.1	−0.3 to 0.0	0.067	−0.4	−0.6 to −0.2	**<0.001**	**0.028**

Note: Bold *p*-values reflect statistically significant outcomes.
[a]The generalized estimating equations were adjusted for repeated measures of age, height and BMI (time-varying variables in the table).

time women had nearly completed their FEV_1 development, whereas in men, FEV_1 increased substantially over this period (Figure 1). This is consistent with the earlier finding for associations between aerobic fitness and lung function from the Dunedin Study and a Danish cohort.[46]

The negative association between breastfeeding and early adulthood FEV_1/FVC among women is likely explained by a previous finding that breastfed children were more likely to have atopy and asthma,[30] although the mechanisms for this association are still unclear.

This study has several strengths: the cohort is population-based with high participation rates over multiple ages; although many of the associations that we identified have been reported in other studies, we have more frequent measures of lung function through early adulthood in a population-based cohort as well as detailed data on a wide range of childhood/adolescent and early adulthood risk factors postulated to be important in determining plateau lung function. Several limitations should be acknowledged. First, we identified ages of peak lung function by visual inspection and may have missed individual peak values that fell between assessments. Although lung function in early adulthood is commonly referred to as a 'plateau', this plateau is not well defined and may vary between individuals.[47] We assessed this on a population level, rather for each individual. However, the means of the individual standard deviations for FEV_1 and FVC measurements across the early adult ages were 180 and 211 mL, respectively. These are not much larger than the accepted within-test repeatability criterion of 150 mL. A sensitivity analysis using the highest measured values provided similar findings, except for concurrent BMI as noted above (Table S5 in the Supporting Information). Second, we have limited information on some potential influences, such as early-life lower respiratory tract infections. Third, although we were able to adjust for exposures to maternal smoking during pregnancy and atopy at age 13, there were numerous missing values and these variables were excluded from the main analyses. Sensitivity analyses including these variables suggested that they were not predictors of adult lung function and did not meaningfully affect results. BMI may poorly reflect body composition, although our previous study found little difference between BMI and other measures of adiposity in the prediction of lung function.[41] Finally, based on some of the confidence intervals in Table S2 in the Supporting Information, we may have been underpowered to detect potentially clinically

important interactions. Our single statistically significant interaction (from 24 investigated) is consistent with our nominal Type I error rate of 5% and would not be statistically significant if adjusted for multiple comparisons.

Higher lung function in early adulthood may reduce the risk of chronic lung disease in later life. We have identified several factors that influence this, but it remains to be determined to what extent these are amenable to intervention. For example, we do not yet know how to prevent asthma or AHR and it remains unclear whether better treatment of these in childhood would substantially improve adult lung function. Conversely, some factors, such as obesity, are both preventable and potentially reversible. Reducing obesity is likely to improve lung function, but whether this would fully restore lung function and reduce the risk of COPD is unknown. In the meantime, promoting physical activity is likely to have many health benefits in addition to potentially improving lung function.

In conclusion, childhood asthma and AHR are strongly associated with lower early adult FEV_1, lower FEV_1/FVC and to a lesser extent, lower FVC. Higher adult BMI is also associated with lower values for all three spirometric parameters. Other associations involving physical activity, early life weight gain and breastfeeding were less consistently observed. We need better strategies to manage these predictors of maximal lung function in early adulthood.

AUTHOR CONTRIBUTIONS

Xian Zhang: Conceptualization (equal); formal analysis (lead); investigation (equal); methodology (equal); writing – original draft (lead); writing – review and editing (equal). **Andrew R. Gray:** Conceptualization (equal); formal analysis (supporting); investigation (equal); methodology (equal); supervision (supporting); writing – review and editing (equal). **Robert J. Hancox:** Conceptualization (equal); data curation (lead); funding acquisition (lead); investigation (equal); methodology (equal); supervision (lead); writing – review and editing (equal).

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CONFLICT OF INTEREST STATEMENT

Robert J. Hancox is an Editorial Board member of Respirology and a co-author of this article. He was excluded from all editorial decision-making related to the acceptance of this article for publication.

DATA AVAILABILITY STATEMENT

We do not have ethical approval to make the data publicly available. De-identified data may be available to researchers on reasonable request subject to an approved research proposal.

HUMAN ETHICS APPROVAL DECLARATION

Each assessment was approved by the relevant ethics committee, most recently the New Zealand Health & Disability Ethics Committee 17/STH/25/AM05. Written informed consent was obtained from all participants.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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