Original research

Distinct trajectories of lung function from childhood to mid-adulthood

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ABSTRACT

Rationale Life course trajectories of lung function development and decline influence the risk for lung disease but are poorly documented.

Objective To document lung function trajectories from childhood to mid-adult life.

Methods We modelled forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and FEV_1/FVC at ages 9, 11, 13, 15, 18, 21, 26, 32, 38 and 45 years from a population-based cohort using latent profile analysis to identify distinct subgroups of participants with similar lung function trajectories. Regression analyses were used to assess associations between the trajectories, early life factors and postbronchodilator airflow obstruction at age 45.

Results Among 865 participants with ≥6 measures of lung function, we identified 10 distinct FEV_1 trajectories. Most were approximately parallel except for a childhood airway hyper-responsiveness-related persistently low trajectory (3% of study population); two accelerated-decline trajectories, one of which (8%) was associated with smoking and higher adult body mass index (BMI) and a catch-up trajectory (8%). Findings for FEV_1/FVC trajectories were similar. Nine trajectories were identified for FVC: most were also approximately parallel except for a higher BMI-related accelerated-decline trajectory. The three FEV_1 trajectories leading to the lowest FEV_1 values comprised 19% of the cohort but contributed 55% of airflow obstruction at age 45.

Conclusions Lung function trajectories to mid-adult life are largely established before adolescence, with a few exceptions: a childhood airway hyper-responsiveness-related persistently low trajectory, which starts low and gets worse with age, and accelerated adult decline trajectories associated with smoking and obesity. Adverse trajectories are associated with a high risk of airflow obstruction in mid-adult life.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Trajectories of lung function throughout life may influence the risk for lung disease in older adulthood. Failure to attain a normal peak lung function in early adult life may be as important as accelerated decline.

WHAT THIS STUDY ADDS

⇒ For most people, lung function trajectories are established early in childhood. Asthma and airways hyper-responsiveness are associated with life course-persistent adverse trajectories.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Efforts to maximise lung function throughout life and prevent lung disease in older adulthood need to focus on early childhood.

INTRODUCTION

Life course trajectories of lung function are related to health and longevity and influence the risk for chronic lung disease in older adulthood.[1] The main identified risk factor for chronic obstructive pulmonary disease (COPD) is accelerated forced expiratory volume in 1 s (FEV_1) decline due to smoking in adulthood,[2] but COPD can also follow failure to attain a normal peak lung function in early adulthood.[3] Moreover, low lung function in early adulthood also predicts non-respiratory comorbidities and higher all-cause mortality.[4 5]

Recent cohort studies suggest there are several distinct lung function trajectories in the general population.[6–10] However, most of these only captured either lung function growth[6 8 9] or decline phase.[10] Only the Tasmanian Longitudinal Health Study (TAHS) reported data from both phases, using up to six repeated assessments of lung function from ages 7 to 53 years, but did not measure lung function between ages 18 and 45.[7] Including measurements from early adulthood when spirometry usually reaches a peak is important to provide insights into the natural history of lung function development. Furthermore, most studies only report trajectories for FEV_1: trajectories of other lung function parameters have received little attention.[11]

We identified trajectories for FEV_1, forced vital capacity (FVC) and FEV_1/FVC in the Dunedin Multidisciplinary Health and Development Study (Dunedin Study), a population-based cohort with 10 lung function assessments from ages 9 to 45 years. We then investigated plausible predictors of these trajectories (online supplemental figure S1) and examined associations between lung function trajectories and airflow obstruction at age 45.

METHODS

Cohort

The Dunedin Study investigates health and behaviour in a population-based cohort born in Dunedin in 1972/1973.[12 13] The cohort was formed at age 3 years when 1037 individuals (52% male; 91% of eligible births) attended the first follow-up. The cohort has been further assessed at ages 5, 7, 9,

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11, 13, 15, 18, 21, 26, 32, 38 and 45 years (see online supplement for additional methods).

Measurements

Height and weight were measured at each assessment. Spirometry was performed at each assessment since age 9.[14 15] At age 45, spirometry was repeated after inhaling 200 µg salbutamol via a large-volume spacer.[16] Predicted values for FEV_1, FVC and FEV_1/FVC at each age were generated using multiple linear regression models for non-smoking, non-asthmatic, non-pregnant men and women adjusting for height and height squared. Airflow obstruction was defined as a postbronchodilator FEV_1/FVC ratio <0.7 at age 45.[17]

Definition of variables

Childhood asthma was defined as a parent/self-reported diagnosis with compatible symptoms or asthma medication use within the previous year at ages 9, 11 or 13 years.[18 19] Childhood airway hyper-responsiveness (AHR) was defined as a positive response to methacholine/salbutamol challenge at ages 9, 11 or 13 years.[20]

Participants were considered to be breastfed if breastfeeding continued for at least 4 weeks.[21] Preschool attendance was reported at age 3. Household overcrowding at age 3 was defined as fewer than two rooms (excluding kitchen and bathroom) per child.[22] Childhood cat and dog ownership was defined as having lived with cat and dog by age 9.[22] Parental smoking was ascertained at ages 7, 9, 11 and 13 years.[22] At 3 years, parents were asked about the number of coughs and colds the participant had had in the previous year.

Childhood socioeconomic status was assessed throughout childhood based on the education and income associated with their parents' occupation.[18] Parental history of asthma or hay fever was ascertained when participants were aged 7 and 18.

Atopy was assessed at ages 13, 21 and 32 years by skin prick tests for common aeroallergens. Atopy was defined as a weal diameter 2 mm greater than the negative control to one or more allergens.[23]

Cumulative smoking was calculated from the reported number of cigarettes smoked up to age 18 years and the number smoked between each subsequent assessment (one pack-year=20 cigarettes/day for 1 year).[16]

Statistical analysis

We analysed FEV_1 at each age (from 9 to 45 years) using latent profile analysis (LPA) to identify distinct subgroups of study participants whose FEV_1 measurements followed a similar pattern over time. LPA is described extensively elsewhere.[24] Briefly, it identifies unobserved subgroups of individuals who share similar characteristics, based on a series of continuous variables. We used estimated posterior probabilities to assign individuals to the trajectory that they were most likely to belong to.

Based on previous studies,[7 8] we hypothesised at least four FEV_1 trajectories. LPA models with 4–12 trajectories were fitted to the data. After excluding models with trajectories with <2% of the cohort, the model with the lowest Bayesian information criterion (BIC) value was selected.[25] Descriptive labels were assigned to the identified trajectories. The primary analysis included study members with at least six spirometry measures between ages 9 and 45, including at least one measure from each of childhood (ages 9–15), early adulthood (ages 18–32) and mid-adulthood (ages 38–45). Baseline/early childhood characteristics were compared between those included and not included in these models. Missing data were assumed to be mostly missing completely at random. A sensitivity analysis included those with at least two spirometry measures at any ages from 9 to 45 years.

Associations between childhood and adult factors (exposures) and trajectories were examined using multivariable binary logistic regression where the outcome belonged to that particular trajectory vs belonging to any other trajectory. Further analyses compared each trajectory with the 'average' trajectory. The choice of plausible exposures was informed by a directed acyclic graph (online supplemental figure S1). Initially, all exposures were included in each model, followed by univariable models for exploratory purposes. Firth logistic regression was used when the size of the trajectory of interest was below 50.[26] Statistical significance was determined using the Bonferroni-Holm method (per variable, separately for univariable and multivariable models). This controls the family-wise error rate without requiring assumptions about the (in)dependence of the hypotheses being tested.[27] This analysis was repeated for each identified FEV_1 trajectory.

The same approach was used for FVC and FEV_1/FVC. One participant with developmental abnormalities affecting lung function was excluded from all analyses. Measurements were excluded at ages when pregnancy was reported. Two-sided p values <0.05 were considered statistically significant. Analyses used Stata V.15.0 (StataCorp).

Table 1 Characteristics of study population included in main analysis

Characteristic	
Sex—male	442/865 (51%)
Birth weight (mean kg±SD)	3.4±0.5
Breastfed for ≥4 weeks	431/863 (50%)
Childhood asthma ages 9–13	124/807 (15%)
Childhood AHR ages 9–13	153/798 (19%)
BMI at age 9 (mean kg/m^2±SD)	16.4±1.6
Childhood SES (mean±SD)*	3.2±1.1
Exposure to parental smoking	534/852 (63%)
Atopy at 21	520/796 (65%)
BMI at age 45 (mean kg/m^2±SD)	28.5±5.8
Ever smokers by age 45	450/865 (52%)
Tobacco smoked by age 45 (mean pack years±SD)	7.1±10.4

865 study members with at least 6 spirometry measures between ages 9 and 45 were included in the main analysis. The numbers for each characteristic vary depending on the number providing data at that assessment.
*Higher scores indicate lower socioeconomic status on a scale of 1–6.
AHR, airway hyper-responsiveness; BMI, body mass index; SES, socioeconomic status.

RESULTS

Trajectories of FEV_1

The primary analyses included 865 study members with at least six spirometry measures from ages 9 to 45 (table 1). Comparisons with those excluded from this analysis are shown in online supplemental table S1). The LPA model with the lowest BIC identified 10 distinct FEV_1 trajectories (online supplemental table S2). Most, but not all, trajectories were approximately parallel throughout follow-up (figure 1). Exceptions included two accelerated decline trajectories and a persistently low trajectory that started low and declined further over time.

Participant characteristics according to identified FEV_1 trajectories are shown in online supplemental table S3. The

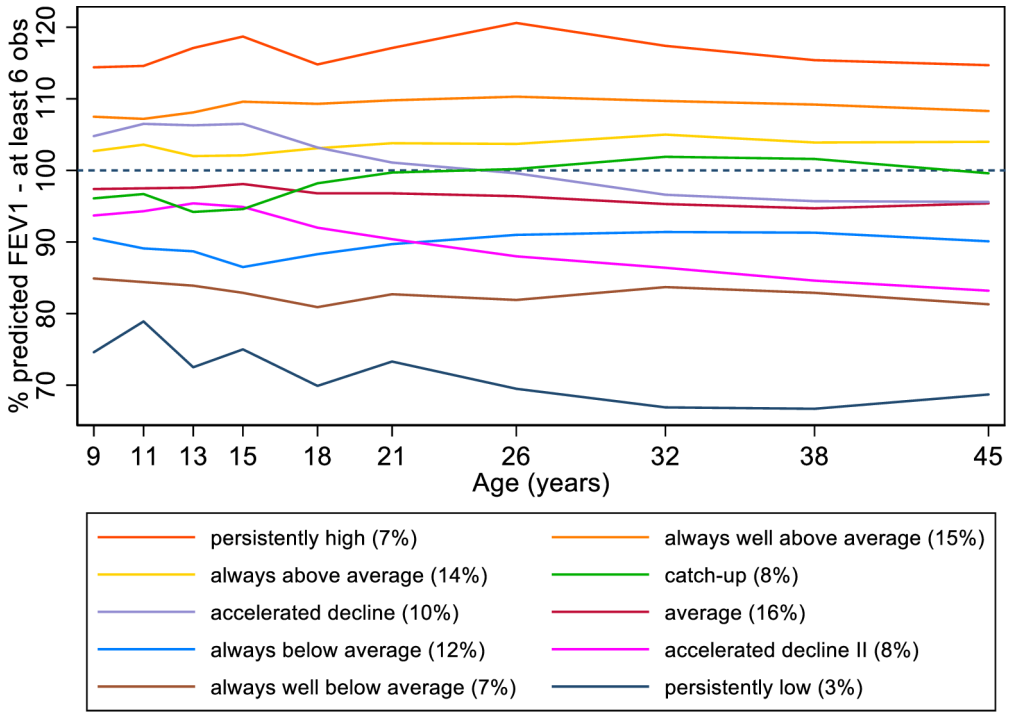

Figure 1 Distinct trajectories of FEV_1 from ages 9 to 45 years. FEV_1, forced expiratory volume in 1 s.

persistently low FEV_1 trajectory had the highest prevalence of childhood asthma and AHR and the highest prevalence of atopy. The accelerated-decline-II trajectory had the highest cumulative tobacco pack-years by age 45.

Pairwise comparisons showed that participants in the persistently low trajectory were more likely to have childhood AHR compared with all other trajectories combined (statistically significant associations are summarised in table 2: for full results, see online supplemental tables S4 and S5). Childhood AHR was also associated with the always-well-below-average trajectory. The accelerated-decline-II trajectory was associated with tobacco pack-years by age 45 and body mass index (BMI) at age 45. BMI at age 9 was positively associated with the persistently high trajectory. Overall, BMI at age 9 was also associated with lower odds of belonging to the always-below-average trajectory. However, there was evidence of a U-shaped association with higher odds of belonging to this trajectory among those with high BMI values ($\geq$18.9 kg/m^2 (top 6.6%)) at age 9.

At age 45, participants in the persistently low FEV_1 trajectory had the highest prevalence of postbronchodilator airflow obstruction (59%), followed by accelerated-decline-II (23%) and always-well-below-average (16%) trajectories. By comparison, the overall prevalence of postbronchodilator airflow obstruction among the other 7 trajectories was 5%.

Trajectories of FVC

The LPA model with the lowest BIC identified 11 distinct FVC trajectories but one of these was very small (n=11, 1.3%). Therefore, the model with the second lowest BIC which had nine trajectories was selected (online supplemental table S2). Most of the identified FVC trajectories were approximately parallel during follow-up (figure 2). The persistently low FVC trajectory had the highest prevalence of childhood AHR and atopy over the ages (online supplemental table S6). Pairwise comparisons showed that BMI at age 45 was positively associated with the accelerated-decline trajectory compared with all others and negatively associated with the catch-up trajectory (table 2, online supplemental tables S7 and S8).

Trajectories of FEV_1/FVC

The LPA model with the lowest BIC identified 10 distinct FEV_1/FVC trajectories (online supplemental table S2). Most were approximately parallel throughout follow-up (figure 3). Participants in the persistently low FEV_1/FVC trajectory had the highest prevalence of childhood asthma and AHR (online supplemental table S9). This trajectory also had the highest prevalence of atopy: all trajectory members were atopic at ages 21 and 32. The accelerated-decline trajectory had the highest tobacco pack-years by age 45.

Pairwise comparisons showed that participants in the persistently low trajectory were more likely to have childhood AHR compared with all others (table 2, online supplemental tables S10 and S11). Childhood AHR was also associated with the always-well-below-average trajectory and negatively associated with the always-well-above-average trajectory. Cumulative smoking was associated with accelerated-decline and above-average-but-with-decline trajectories, and negatively associated with the always-well-above-average trajectory. BMI at age 45 was negatively associated with the persistently high trajectory. Participants in the always-below-average trajectory were more likely to have attended preschool at age 3 years.

At age 45, participants in the persistently low FEV_1/FVC trajectory had the highest prevalence of postbronchodilator airflow obstruction (74%), followed by the always-well-below-average (43%) and accelerated-decline (37%) trajectories. The overall prevalence of postbronchodilator airflow obstruction among the other 7 trajectories was 2%.

The sensitivity analysis, including those with at least two spirometry measures from 9 to 45 years, is shown in online supplemental figure S2.

Table 2 Summary of statistically significant predictors of lung function trajectories

Parameter	Predictor	Trajectory	OR (95% CI)
FEV_1	Childhood AHR	Always above average	0.17 (0.06 to 0.49)
		Always well below average	3.57 (1.60 to 7.95)
		Persistently low	12.90 (3.45 to 47.9)
	Tobacco by age 45	Accelerated decline II	1.06 (1.03 to 1.08)
	BMI at age 9	Always below average	0.66 (0.54 to 0.81)
		Persistently high	1.31 (1.09 to 1.58)
	BMI at age 45	Accelerated decline II	1.08 (1.03 to 1.13)
FVC	BMI at age 45	Catch-up	0.90 (0.84 to 0.97)
		Accelerated decline	1.15 (1.10 to 1.20)
FEV_1/FVC	Childhood AHR	Always well above average	0.23 (0.08 to 0.64)
		Always well below average	7.79 (3.61 to 16.9)
		Persistently low	12.40 (2.60 to 58.5)
	Tobacco by age 45	Always well above average	0.96 (0.93 to 0.99)
		Above average but with decline	1.04 (1.02 to 1.06)
		Accelerated decline	1.06 (1.03 to 1.09)
	BMI at age 45	Persistently high	0.89 (0.82 to 0.96)
	Preschool attendance	Always below average	2.78 (1.38 to 5.61)

Summary of full results in online supplemental tables S4, S7 and S10. Statistical significance defined as p<0.05 after adjustment for multiple comparisons using Bonferroni-Holm method. ORs show the association of each unit of the predictor with membership of that trajectory compared with all other trajectories. Childhood AHR and preschool attendance are binary (yes/no). Units of tobacco smoked are pack-years. BMI units are kg/m^2.

AHR, airway hyper-responsiveness; BMI, body mass index; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity.

DISCUSSION

Using up to 10 assessments of spirometry in a large prospective population-based cohort followed from ages 9 to 45 years, we identified distinct trajectories of FEV_1, FVC and FEV_1/FVC. A striking observation is that most, but not all, of the identified trajectories were approximately parallel, demonstrating that, for most people, their lung function trajectory into mid-adult life was already established before adolescence. Notable exceptions included childhood AHR-associated persistently low trajectories, which started low and diverged further from the others over time, and accelerated-decline trajectories associated with smoking and higher adult BMI. We also identified catch-up trajectories for FEV_1 and FVC, which, for FVC, were associated with lower adult BMI values. Importantly, we found that the three FEV_1 and three FEV_1/FVC trajectories leading to the lowest values at age 45 contributed most of the airflow obstruction at age 45 despite representing small proportions of the cohort.

The FEV_1 trajectories that we identified are broadly consistent with those reported in other cohorts. The only other study to cover a similar age range from childhood to mid-adulthood (ages 7–53), identified 6 distinct FEV_1 trajectories among 2438 Australian participants.[7] Using a similar statistical approach to ours, a study of two British population-based cohorts identified four FEV_1 trajectories based on three or four spirometry measures from ages 5 to 24.[8] Another British cohort observed high and low FEV_1 trajectories from ages 10 to 26.[9] Among asthmatics, the Childhood Asthma Management Programme classified 684 participants into four FEV_1 trajectories based on spirometry measures from ages 7 to 26.[28] Looking at changes after peak adult lung function, an American study identified five FEV_1 trajectories from ages 25 to 55.[10]

We identified more distinct FEV_1 trajectories than all these studies.[7–10 28] This is likely because we selected the model with the best empirical fit (lowest BIC), whereas other studies either limited the maximum number of trajectories or merged similar-looking trajectories. However, even if we were to merge similar trajectories, the combined evidence suggests that there are at least five FEV_1 trajectories in the general population: persistently high, average, below average, accelerated decline and persistently low. In addition, an early below average with catch-up during adolescence FEV_1 trajectory was observed in both our study (8%) and the TAHS (8%).[7] None of the other cohorts had sufficient data to identify this. For comparison with earlier studies, graphs with fewer trajectory classes are shown in online supplemental figure S3.

We also identified 10 distinct FEV_1/FVC trajectories. Two studies found normal/high and persistently low trajectories from ages 11 to 32 and 10 to 26 years.[6 9] Only the recent TAHS study investigated FEV_1/FVC trajectories beyond early adulthood, reporting six trajectories.[11] Although they used a different statistical approach and had fewer ages of assessment with few lung function measurements in early adulthood, the patterns of trajectories were broadly consistent with our findings. In particular, the adverse trajectories leading to airflow obstruction in mid-adult life ('early low-rapid decline', 'early normal-rapid decline', 'early low-normal decline') were similar to the persistently low, accelerated-decline and always-well-below-average trajectories that we have identified. Graphs with fewer FEV_1/FVC classes are shown in online supplemental figure S4.

In our study FEV_1/FVC trajectories and FEV_1 trajectories had similar associations with AHR: for both parameters, persistently low (both 3% of the cohort) and always-well-below-average (7% and 8%, respectively) trajectories were associated with childhood AHR, whereas those in the always-well-above-average FEV_1/FVC trajectory (15%) and always-above-average FEV_1 (14%) trajectories were less likely to have childhood AHR. Other studies have found that asthma is associated with persistently low FEV_1 trajectories.[7 8] AHR is a hallmark of asthma and these findings indicate that childhood asthma plays a key role in the impaired development of FEV_1 and airflow obstruction. Although parental asthma has been reported to be associated with impaired lung function among offspring,[6 29] we did not find any direct association between parental asthma and lung function trajectories, after accounting for the potential mediator of childhood asthma in the participants. The TAHS study found an association between parental asthma and low FEV_1/FVC (but not FEV_1) trajectories but did not report whether this association persisted after adjusting for childhood asthma.[7 11] All participants in the persistently low FEV_1/FVC trajectory were atopic, although this was not a statistically significant independent predictor of this trajectory once adjusted for the other variables including AHR.

Unsurprisingly, accelerated-decline-II FEV_1 and accelerated-decline and above-average-but-with-decline FEV_1/FVC trajectories were all associated with cumulative smoking. Although smoking was not a statistically significant predictor of the

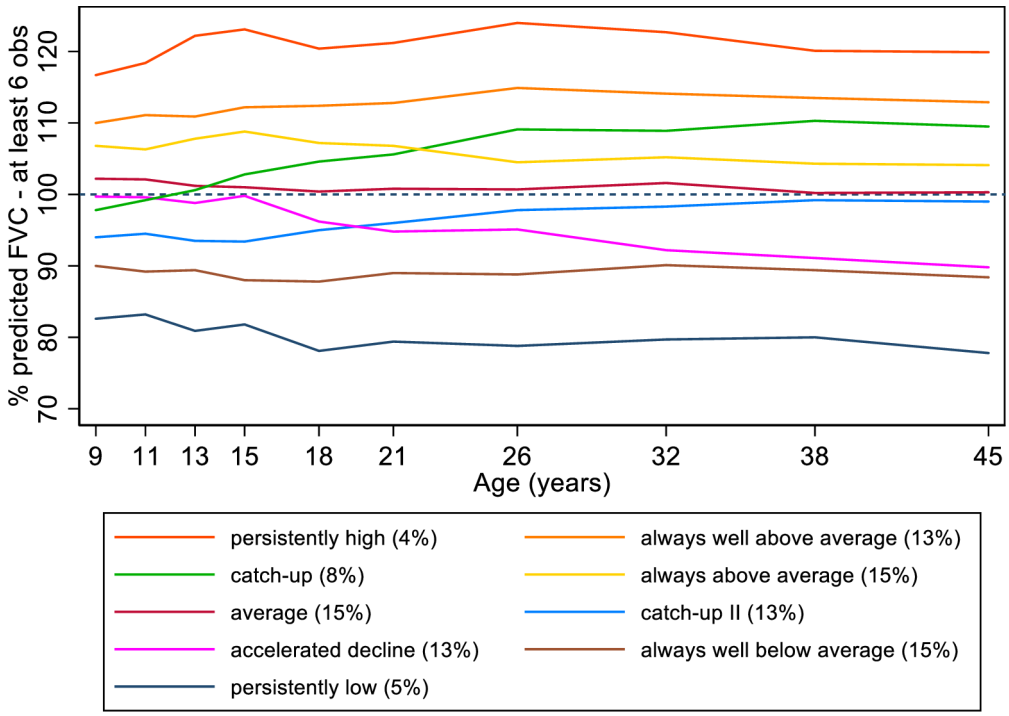

Figure 2 Distinct trajectories of FVC from ages 9 to 45 years. FVC, forced vital capacity.

accelerated decline FEV_1 trajectory in TAHS, this trajectory had the highest prevalence of smoking,[7] and smoking was associated with the FEV_1/FVC trajectories leading to adult airflow obstruction.[11]

We identified nine distinct trajectories for FVC. To our knowledge, only two previous studies have investigated FVC trajectories. A high and a low FVC trajectories were identified in the Isle of Wight cohort, based on three measures at ages 10, 18 and 26 years.[9] The TAHS study identified five FVC trajectories.[11] Although fewer in number, several of these trajectories appear consistent with the trajectories that we identified, with persistently low, persistently high and catch-up trajectories. However, they did not identify an accelerated decline FVC trajectory. Graphs with fewer FVC classes are shown in online supplemental figure S5.

We found a high degree of overlap between identified FEV_1 and FVC trajectories (figure 4), for example, 68% of participants in the persistently low FEV_1 trajectory were assigned to either the

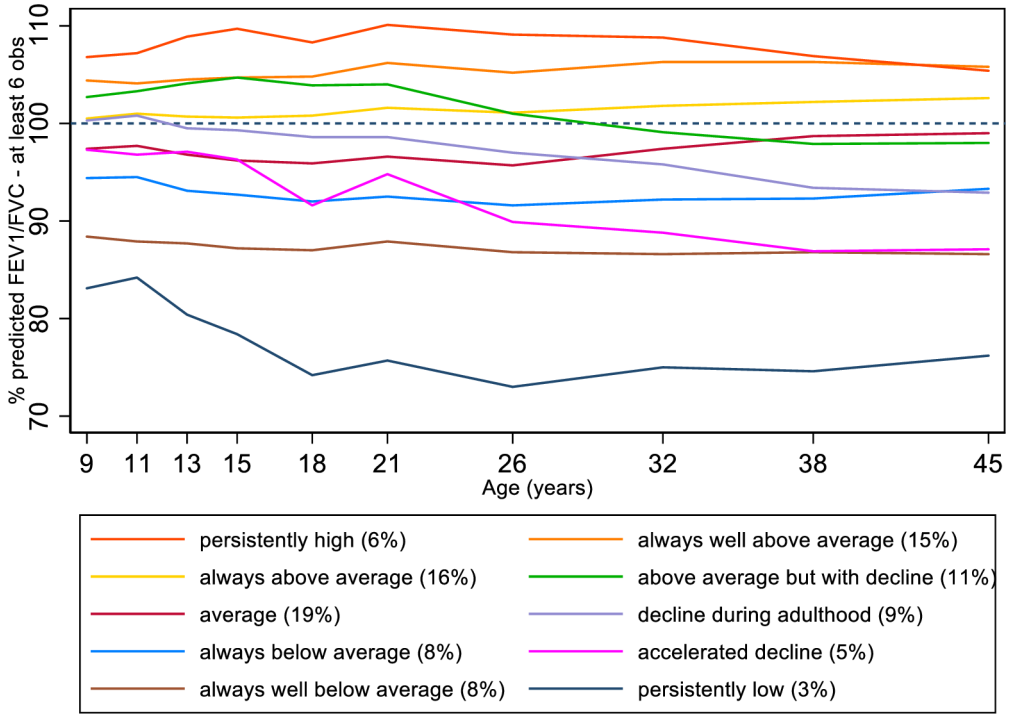

Figure 3 Distinct trajectories of FEV_1/FVC from ages 9 to 45 years. FEV_1/FVC, forced expiratory volume in 1 s/forced vital capacity.

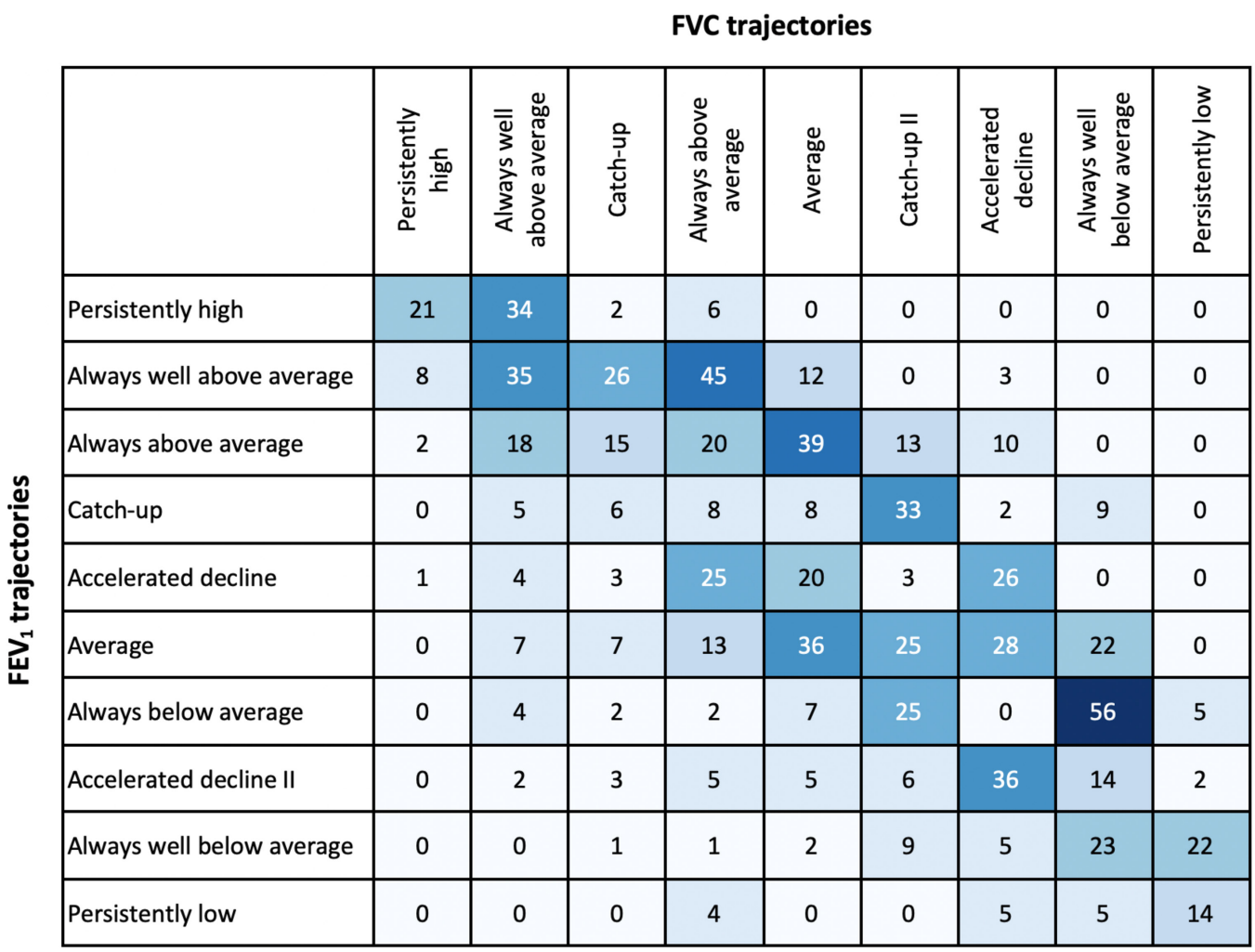

Figure 4 Heatmap showing overlap between trajectories of FEV_1 (rows) and FVC (columns) with darker shades for higher counts. Numbers indicate number of participants. FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity.

persistently low or always-well-below-average FVC trajectory, and 87% of those in the persistently high FEV_1 trajectory were assigned to either the persistently high or always-well-above-average FVC trajectory. We also found considerable overlap between the FEV_1 and FEV_1/FVC ratio trajectories but there was less overlap between the FVC and FEV_1/FVC trajectories (online supplemental figures S6 and S7). The extent to which FVC and FEV_1/FVC trajectories provide additional health information to FEV_1 trajectories remains unclear and needs further investigation: although TAHS found that trajectories leading to obstructive, restrictive and mixed patterns of lung function disorder had different predictors and health associations, these classifications were based on the lung function outcomes at age 53 rather than the trajectories themselves.[11]

We identified few associations between our potential exposures and the better than average lung function trajectories. BMI at age 9 was positively associated with the persistently high FEV_1 trajectory and negatively associated with the always-below-average trajectory, suggesting that early childhood growth may have a long-term protective effect on adult FEV_1, although there was also evidence that overweight children may be more likely to have always-below-average trajectories. By contrast, BMI at age 45 was associated with accelerated decline FEV_1 and FVC trajectories, and a lower likelihood of the catch-up FVC trajectory, confirming the detrimental impact of increasing body weight in adolescence and adulthood on lung function.

Collectively, the three trajectories leading to the lowest FEV_1 values (persistently low, always-well-below-average and accelerated-decline-II) represented 19% of the cohort and 55% of postbronchodilator airflow obstruction (meeting GOLD spirometric criteria for COPD) at age 45. Moreover, the three FEV_1 trajectories that did not reach the normal peak in early adulthood (persistently low, always-well-below-average and always-below-average) represented 22% of the cohort and 44% of airflow obstruction at age 45. This is consistent with an analysis of three cohorts in which half of the participants with spirometric COPD had lower lung function in early adulthood, followed by a normal rate of lung function decline.[3] It is also supported by our observations for the FEV_1/FVC trajectories: the persistently low and always-well-below-average trajectories represented only 11% of study cohort, but contributed 60% of postbronchodilator airflow obstruction at age 45, indicating that over half of mid-adulthood spirometric COPD has childhood origins.

Our finding that most of the identified trajectories were approximately parallel suggests that, for most people, these trajectories are already established by adolescence. This raises important issues. First, it remains unclear how to maximise

lung growth in early life to set people on beneficial trajectories. Second, it is unclear whether interventions involving better management of childhood asthma/AHR, avoiding smoking and maintaining healthy body weight could 'correct' the adverse lung function trajectories, or at what age(s) these interventions could be effective. Third, the underlying mechanisms of persistently high and catch-up lung function trajectories are unknown: understanding these would provide important insights into promotion of healthy lung function development in the general population. Finally, the long-term consequences of different lung function trajectories for health and longevity are not yet established, for example, we do not know whether low lung function in late adulthood from persistently low trajectories has similar consequences to low lung function due to accelerated decline.

To our knowledge, these are the most complete longitudinal data on lung function from childhood to mid-adulthood currently available, and this is only the second study to characterise lung function trajectories in terms of all three main spirometric parameters. Strengths of the study include the prospective population-based design, large sample size, high retention rates during follow-up, assessments of lung function at up to 10 time points and an objective approach to model selection. Although 17% of the original cohort was excluded from the main analysis due to insufficient lung function measures, findings were very similar in the sensitivity analysis which included participants with at least two spirometry measures (n=1008; 97% of the original cohort; online supplemental figure S2). Furthermore, those included in and excluded from the main analysis had similar baseline characteristics (online supplemental table S1). We chose to analyse the data using LPA because this allows each individual to be assigned to the most likely trajectory. In our study, the posterior probabilities of belonging to the trajectories were very high (online supplemental table S12), indicating a good model fit. The trajectories for each individual participant associated with the identified FEV_1, FVC and FEV_1/FVC trajectory classes are shown in online supplemental figures S8–S10. The LPA approach has been used by several previous studies[30] and is conceptually similar, but mathematically different, to group-based trajectory modelling that has been used by some others.[7 11]

Several limitations should be acknowledged. We do not have lung function data before age 9, when the trajectories of lung function may be largely determined,[31 32] and we do not yet have lung function measures in later adulthood to complete the trajectories across the life course. Our definition of postbronchodilator airflow obstruction at age 45 does not necessarily indicate clinical COPD. However, in our cohort at this age, the lower limit of normal for FEV_1/FVC ratio (0.69) is very similar to the GOLD criterion of FEV_1/FVC ratio <0.7 that we used. Although we have reports of coughs and colds at age 3, we may have missed early life exposures such as severe lower respiratory tract infections.[33 34] We also compared exposures for each trajectory to all other trajectories combined, whereas previous reports have tended to use the 'average' trajectory as the reference group. Our approach risks diluting risk factors that might be shared by more than one trajectory. On the other hand, the 'average' group may simply have a mix of beneficial and adverse factors and may not necessarily represent ideal lung health. To facilitate comparisons with previous studies, multivariable analyses using the 'average' trajectories as the reference groups are shown in online supplemental tables S13–S15. Overall, there were few differences with the main analyses, although some of the associations changed statistical significance—mostly becoming non-significant, which is likely because of the lower power due to the smaller size of the reference category. Finally, the precision of our estimated associations for some exposure–trajectory combinations is limited by the size of the less common trajectories along with the collinearity between some exposures, such as AHR, asthma and atopy.

CONCLUSIONS

We identified distinct trajectories of lung function from childhood to age 45 years in a prospective population-based cohort. Most of these trajectories were approximately parallel, demonstrating that, for most people, their lung function trajectories appear to be established before adolescence. However, we observed a few exceptions: childhood asthma/AHR-associated persistently low trajectories, which started low and diverged further from the other trajectories over time, and accelerated decline trajectories associated with smoking and higher adult BMI.

Despite representing a minority of the cohort, the three trajectories leading to the lowest FEV_1 values contributed most of the postbronchodilator airflow obstruction at age 45. To promote healthy adult lung function trajectories and reduce the risk of COPD, we need strategies to maximise lung growth in early life and minimise childhood asthma-related lung function impairment.

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Contributors All authors contributed to the study concept and design. RJH acquired data. XZ and ARG conducted the statistical analysis. RJH, ARG and XZ interpreted the data. XZ drafted the manuscript. All authors critically revised the manuscript for important intellectual content. RJH is the guarantor of the paper.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by New Zealand Health and Disability Ethics Committee (17/STH/25/AM05). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. We do not have ethical approval to make the data publicly available. Deidentified data may be available to researchers on reasonable request subject to an approved research proposal.

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Distinct trajectories of lung function from childhood to mid-adulthood

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Online Supplement

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Supplementary Methods

The Dunedin Study is a longitudinal investigation of health and behaviour in a population-based cohort born between April 1972 and March 1973 in Dunedin, New Zealand.[1, 2] The cohort was formed at age 3 years when 1,037 individuals still living in the Otago province (52% male; 91% of eligible births) attended the first follow-up. The cohort has been further assessed at ages 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, 38, and 45 years. Each assessment was approved by the relevant ethics committee and consent was obtained from all participants.

Height and weight in light clothing without shoes were measured at each assessment. Spirometry was performed at each assessment since age 9 years according to the standards at the time.[3, 4] At age 45, spirometry was repeated after inhaling salbutamol 200mcg via a large-volume spacer.[5] The primary outcome was pre-bronchodilator FEV_1 at each age from age 9 to 45 years expressed as percentage of predicted value. Secondary outcomes were percent-predicted pre-bronchodilator FVC and FEV_1/FVC. To generate predicted values, male and female reference equations were derived from the Dunedin Study using multiple linear regression models at each assessment age, adjusting for height and height squared, excluding those with any history of asthma or smoking, or currently pregnant**.** Airflow obstruction was defined as a post-bronchodilator FEV_1/FVC ratio <0.7 at age 45.[6]

Respiratory questionnaires were administered at each assessment since age 9.[7] Childhood asthma was defined as a parent/self-reported diagnosis with compatible symptoms or asthma medication use within the previous 12 months at age 9, 11, or 13 years.[7, 8] Childhood airway hyperresponsiveness (AHR) was defined as a positive response to

methacholine/salbutamol challenge at age 9, 11, or 13 years. A positive response to methacholine was defined as a a fall in FEV_1 of ≥20% after inhaling up to 25mg/mL methacholine using an abbreviated, validated protocol. For children with baseline obstruction (symptomatic children with FEV_1/FVC ratio <0.75 or asymptomatic children with FEV_1/FVC <0.70), for whom methacholine challenge was deemed unsafe, 0.5% salbutamol was administered undiluted through a Hudson nebuliser at an airflow rate of 6 L/min for 1.5 minutes. An improvement in FEV1 of ≥10% 5 minutes after nebulisation was considered to indicate significant AHR. [9]

The duration of breastfeeding was ascertained at age 3 years and for most participants this was validated by visiting nurse records.[10] Participants were considered to be breastfed if breastfeeding continued for at least four weeks.

Preschool attendance was reported at age 3. Household overcrowding at age 3 was defined as fewer than two rooms (excluding kitchen and bathroom) per child.[11] Childhood cat and dog ownership was defined as having lived with cat and dog by age 9 years.[11] Parental smoking was obtained from the parents at ages 7, 9, and 11 years and participants themselves at age 13. Participants were regarded as being exposed to parental smoking if either parent smoked at any of these ages.[11] At 3 years, parents were asked about the number of coughs and colds the participant had had in the previous 12 months.

Childhood socioeconomic status (SES) was assessed repeatedly from birth to age 15 years based on the occupation of their parents. Each occupation was assigned to a SES value (1 = professional, 6 = unskilled) based on the income and education associated with that occupation in New Zealand. The highest (most professional) of the parents value was used

for each age and the average of these values across the assessments at birth, 3, 5, 7, 9, 11, 13, and 15 years was calculated.[7]

At age 7 years, parents were asked whether the participant's biological mother or father had a history of asthma or hay fever. This information was also obtained directly from the participant at age 18. A parental history of asthma or hay fever was defined as a positive response for either parent at either age.

Atopy was assessed at ages 13 and 21 years by standardised skin prick tests for 11 common aeroallergens including house dust mite (*Dermatophagoides pteronyssinus;* Bencard, Brentford, UK), rye grass, cat, dog, horse, kapok, wool, *Aspergillus fumigatus*, *Alternaria*, *Penicillium*, *Cladosporum* (Hollister-Stier, Spokane, WA). Cockroach allergen was added at age 21. The same allergen tests were repeated at age 32, using allergens supplied by ALK (Allergy Canada, Thornhill, Ontario, Canada). Atopy was defined as a weal diameter 2 mm greater than the negative control to one or more allergens.[12]

Cumulative tobacco exposure was calculated from the reported number of cigarettes smoked per day up to 18 years, and between each of the assessments up to age 45 years. One pack-year is defined as the equivalent of 20 cigarettes a day for one year. Where tobacco data were missing for an assessment, the amount reported at the next assessment was used to calculate cumulative exposure.[5]

Statistical analysis

We analysed FEV_1 at each age (from 9 to 45 years) using latent profile analysis (LPA) to identify distinct subgroups of study participants whose FEV_1 measurements followed a similar pattern over time. LPA is described extensively elsewhere.[13] Briefly, it identifies

unobserved subgroups of individuals who share similar characteristics, based on a series of continuous variables. Based on estimated posterior probabilities, individuals were assigned to the trajectory that they were most likely to belong to. The analysis was informed by the GRoLTS-checklist, which is provided below (Supplement Table S1).[14]

Based on previous studies [15, 16], we hypothesized at least four FEV_1 trajectories. LPA models with 4 to 12 trajectories from were fitted to the data. After excluding models with trajectories with <2% of the cohort, the model with the lowest BIC value was selected.[17] We used the BIC approach to model selection because we wanted this to be data-driven and objective rather than based on prior assumptions (with the caveat that we excluded models with very small groups). This approach is used elsewhere and suggests that BIC is preferred to the AIC.[18]

Descriptive labels were assigned to the identified trajectories. The primary analysis included Study members with at least six spirometry measures between age 9 and 45, including at least one measure from each of childhood (age 9 to 15), early adulthood (age 18 to 32), and mid-adulthood (age 38 and 45). Baseline/early childhood characteristics were compared between those included and not included in these models. Missing data were assumed to be mostly missing completely at random. A sensitivity analysis included those with at least two spirometry measures at any ages from 9 to 45 years.

Associations between childhood and adult factors (exposures) and each FEV_1 trajectory (outcome) were examined using multivariable binary logistic regression where the outcome was belonging to that particular trajectory versus belonging to any other trajectory. At the request of a reviewer, further analyses compared each trajectory to the identified “average”

trajectory. The choice of plausible exposures was informed by a Directed Acyclic Graph (Supplement Figure S1). Initially, all exposures were included in each model, followed by univariable models for exploratory purposes. When the size of the trajectory of interest was below 50, Firth logistic regression was used instead of the maximum likelihood estimator.[19] Statistical significance was determined using the Bonferroni-Holm method (per variable, separately for univariable and multivariable models). This controls the family-wise error rate without requiring assumptions about the (in)dependence of the hypotheses being tested.[20] This analysis was repeated for each identified FEV_1 trajectory.

The prevalence of post-bronchodilator airflow obstruction at age 45 was calculated for each FEV_1 trajectory.

The same approach was used for FVC and FEV_1/FVC. One participant with developmental abnormalities affecting lung function was excluded from all analyses. Measurements were excluded at ages when pregnancy was reported. Two-sided p-values <0.05 were considered statistically significant. Analyses used Stata 15.0 (StataCorp, College Station, TX).

At the request of a reviewer, the trajectories with smaller numbers of classes for FEV_1, FEV_1/FVC, and FVC are shown in Figures S3, S4 and S5 respectively. These analyses were unplanned because the models are not the best fit for the data (using our *a priori* criterion of BIC) and should therefore be interpreted with caution.

The trajectories for each individual participant associated with the identified FEV_1, FVC, and FEV_1/FVC trajectory classes are shown in Supplementary Figures S8, S9, and S10 respectively below.

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Table S1. Comparison of baseline characteristics between participants included in and excluded from the main analysis

	Included [a] n=865	Excluded n=171	P-value [b]
Sex - male	442/865 (51%)	93/171 (54%)	0.432
Birth weight (kg)	3.4±0.54	3.34±0.54	0.332
Breastfeeding	431/863 (50%)	71/171 (42%)	**0.044**
Childhood asthma 9-13	124/807 (15%)	5/62 (8%)	0.119
Childhood AHR 9-13	153/798 (19%)	11/57 (19%)	0.981
Atopy at 13	307/685 (45%)	21/39 (54%)	0.271
BMI at 9	16.4±1.6	16.6±2.2	0.235
Childhood SES [c]	3.2±1.1	3.4±1.3	**0.028**
Exposure to parental smoking	534/852 (63%)	82/119 (69%)	0.186
Number of coughs/colds at age 3	2.7±2.0	2.8±2.0	0.389
Preschool attendance	141/857 (16%)	32/170 (19%)	0.451
Household crowding	357/865 (41%)	74/171 (43%)	0.627
Dog/Cat ownership	305/756 (40%)	27/58 (47%)	0.354

[a] Study members with at least six spirometry measures between age 9 and 45 were included in the main analysis. One person with developmental abnormalities was excluded.
[b] P-values were from Chi-square test for categorical variables and t-test for continuous variables.
[C] The higher the SES score, the lower the socioeconomic status (on a scale of 1 to 6).

Table S2 – BIC values for latent profile analysis models with different number of classes

FEV_1 – models with 4-class to 12-class (n=865)

Number of classes	df	BIC
4	83	54555.41
5	104	54075.85
6	125	54000.51
7	146	53880.43
8	167	53852.08
9	188	53853.33
10	209	53774.32
11	230	53838.88
12	251	53837.63

The 10-class model had the smallest BIC value.

FVC – models with 4-class to 12-class (n-865)

Number of classes	df	BIC
4	83	53665.13
5	104	53297.07
6	125	53061.12
7	146	52937.27
8	167	52892.09
9	188	52849.42
10	209	52892.54
11	230	52834.18
12	251	52877.58

The 11-class model had the lowest BIC value, however, one of its class was too small (n=11), therefore, the 9-class model with the 2nd lowest BIC value was selected instead.

FEV_1/FVC – models with 4-class to 12-class (N=865)

Number of classes	df	BIC
4	83	47962.71
5	104	47621.66
6	125	47464.50
7	146	47484.60
8	167	47277.04
9	188	47287.96
10	209	47208.05
11	230	47210.29
12	251	47290.15

The 10-class model had the smallest BIC value.

Table S3. Characteristics of participants according to identified FEV_1 trajectories

	Persistently high n=63	Always well above average n=129	Always above average n=117	Catch-up n=71	Accelerated decline n=82	Average n=138	Always below average n=101	Accelerated decline II n=73	Always well below average n=63	Persistently low n=28	Overall n=865
Female	30/63 (48%)	63/129 (49%)	65/117 (56%)	28/71 (39%)	32/82 (39%)	80/138 (58%)	51/101 (50%)	33/73 (45%)	32/63 (51%)	9/28 (32%)	423 (49%)
Male	33/63 (52%)	66/129 (51%)	52/117 (44%)	43/71 (61%)	50/82 (61%)	58/138 (42%)	50/101 (50%)	40/73 (55%)	31/63 (49%)	19/28 (68%)	442 (51%)
Childhood asthma	7/58 (12%)	10/117 (9%)	9/109 (8%)	12/68 (18%)	10/78 (13%)	14/127 (11%)	16/97 (16%)	12/69 (17%)	16/57 (28%)	18/27 (67%)	124/807 (15%)
Childhood AHR	3/58 (5%)	14/116 (12%)	5/107 (5%)	17/67 (25%)	13/78 (17%)	15/126 (12%)	25/95 (26%)	14/68 (21%)	24/56 (43%)	23/27 (85%)	153/798 (19%)
Atopy at 13	18/49 (37%)	41/94 (44%)	30/88 (34%)	36/62 (58%)	34/65 (52%)	44/114 (39%)	33/81 (41%)	30/60 (50%)	22/48 (46%)	19/24 (79%)	307/685 (45%)
Atopy at 21	37/60 (62%)	69/121 (57%)	70/114 (61%)	49/64 (77%)	46/75 (61%)	80/125 (64%)	64/92 (70%)	44/64 (69%)	37/56 (66%)	24/25 (96%)	520/796 (65%)
Atopy at 32	34/61 (56%)	68/128 (53%)	67/113 (59%)	49/70 (70%)	46/81 (57%)	73/136 (54%)	62/100 (62%)	46/68 (68%)	42/62 (68%)	26/28 (93%)	513/847 (61%)
BMI at 9	16.9±1.7	16.4±1.4	16.4±1.7	16.1±1.5	16.5±1.4	16.5±1.6	15.8±1.7	16.8±1.7	15.8±1.4	16.5±1.5	16.4±1.6
BMI at 45	28.3±4.9	28.0±5.2	27.3±5.1	27.5±4.9	30.2±5.6	28.5±6.8	28.1±5.2	30.6±7.2	27.6±5.6	30.7±6.9	28.5±5.8
Parental smoking	38/61 (62%)	75/126 (60%)	68/116 (59%)	44/71 (62%)	53/81 (65%)	93/136 (68%)	68/100 (68%)	43/71 (61%)	38/62 (61%)	14/28 (50%)	534/852 (63%)
Tobacco smoked by 45	7.2±10.9	6.3±9.3	4.2±8.7	6.7±8.9	9.5±12.3	7.1±9.7	6.3±9.6	12.0±13.3	7.8±11.1	4.4±9.4	7.1±10.4
Parental asthma	12/61 (20%)	23/122 (19%)	21/117 (18%)	8/71 (11%)	23/78 (29%)	31/134 (23%)	21/99 (21%)	18/69 (26%)	18/62 (29%)	4/28 (14%)	179/841 (21%)
Parental atopy	27/61 (44%)	54/122 (44%)	49/117 (42%)	30/71 (42%)	37/79 (47%)	61/134 (46%)	42/99 (42%)	30/70 (43%)	36/62 (58%)	16/28 (57%)	382/843 (45%)
Birth weight	3.498±0.504	3.349±0.478	3.474±0.539	3.434±0.543	3.360±0.495	3.346±0.493	3.407±0.499	3.289±0.666	3.332±0.525	3.300±0.383	3.383±0.520
Breastfeeding	32/63 (51%)	64/129 (50%)	60/116 (52%)	45/71 (63%)	38/82 (46%)	59/137 (43%)	52/101 (51%)	36/73 (49%)	30/63 (48%)	15/28 (54%)	431/863 (50%)
Coughs/colds at 3	2.6±2.0	2.6±2.0	2.5±1.7	2.7±2.1	2.8±2.1	2.7±1.9	2.8±2.1	2.6±2.2	3.3±2.3	2.5±2.4	2.7±2.0
Preschool attendance	11/61 (18%)	18/127 (14%)	17/116 (15%)	10/71 (14%)	19/81 (23%)	20/138 (14%)	17/100 (17%)	11/73 (15%)	15/62 (24%)	3/28 (11%)	141/857 (16%)
Household crowding	28/63 (44%)	63/129 (49%)	54/117 (46%)	27/71 (38%)	31/82 (38%)	54/138 (39%)	38/101 (38%)	30/73 (41%)	23/63 (37%)	9/28 (32%)	357/865 (41%)
Dog/Cat ownership	33/56 (59%)	47/106 (44%)	32/101 (32%)	23/64 (36%)	30/73 (41%)	50/121 (41%)	37/92 (40%)	22/62 (35%)	22/55 (40%)	9/26 (35%)	305/756 (40%)
Childhood SES	3.2±1.2	3.3±1.0	3.0±1.1	3.0±1.1	3.2±1.1	3.1±1.1	3.2±1.1	3.5±1.1	3.3±1.1	3.5±1.1	3.2±1.1
Airflow obstruction at 45	4/57 (7%)	4/127 (3%)	2/113 (2%)	1/66 (2%)	8/72 (11%)	7/125 (6%)	8/97 (8%)	16/71 (23%)	9/58 (16%)	16/27 (59%)	75/813 (9%)

Data are n/N (%) or mean±SD. Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high).

Table S4. Predictors of identified FEV_1 trajectories – multivariable models

	Persistently high n=63	Always well above average n=129	Always above average n=117	Catch-up n=71	Accelerated decline n=82	Average n=138	Always below average n=101	Accelerated decline II n=73	Always well below average n=63	Persistently low n=28
Female (ref)										
Male	1.04 (0.56-1.95)	1.26 (0.79-2.00)	0.78 (0.49-1.24)	1.26 (0.70-2.27)	1.60 (0.91-2.80)	0.74 (0.47-1.18)	0.87 (0.53-1.44)	0.99 (0.53-1.86)	0.93 (0.49-1.75)	1.23 (0.47-3.23)
Childhood asthma	1.93 (0.69-5.34)	0.57 (0.24-1.39)	1.25 (0.54-2.90)	0.49 (0.19-1.27)	1.03 (0.43-2.46)	0.95 (0.41-2.20)	0.73 (0.33-1.62)	1.48 (0.59-3.76)	1.08 (0.44-2.64)	3.25 (1.10-9.58)
Childhood AHR	0.12 (0.03-0.59)	0.93 (0.44-1.93)	**0.17 (0.06-0.49)**	1.84 (0.85-4.02)	0.95 (0.42-2.13)	0.43 (0.19-0.96)	1.61 (0.80-3.22)	0.81 (0.33-1.99)	**3.57 (1.60-7.95)**	**12.9 (3.45-47.9)**
Atopy at 21	0.98 (0.51-1.87)	0.70 (0.43-1.14)	1.01 (0.62-1.65)	1.77 (0.88-3.56)	0.77 (0.43-1.38)	0.92 (0.57-1.48)	1.40 (0.79-2.47)	1.30 (0.64-2.62)	0.73 (0.36-1.49)	2.56 (0.41-16.1)
Parental asthma	1.05 (0.49-2.25)	0.92 (0.51-1.65)	0.86 (0.47-1.58)	0.40 (0.15-1.04)	1.59 (0.85-2.97)	0.95 (0.53-1.69)	1.13 (0.61-2.10)	1.22 (0.60-2.49)	1.48 (0.72-3.02)	0.40 (0.12-1.35)
Parental smoking	0.97 (0.50-1.85)	0.71 (0.44-1.14)	1.01 (0.62-1.63)	1.12 (0.61-2.04)	1.23 (0.69-2.20)	1.24 (0.76-2.02)	1.53 (0.89-2.65)	0.71 (0.38-1.35)	1.01 (0.52-1.95)	0.53 (0.20-1.37)
Tobacco smoked by 45	0.99 (0.96-1.02)	0.97 (0.95-1.00)	0.96 (0.93-0.99)	0.99 (0.96-1.03)	1.02 (1.00-1.05)	1.00 (0.98-1.02)	1.01 (0.98-1.03)	**1.06 (1.03-1.08)**	1.00 (0.96-1.03)	0.99 (0.94-1.04)
Childhood SES	0.96 (0.71-1.29)	1.18 (0.95-1.48)	0.86 (0.69-1.07)	0.88 (0.66-1.16)	0.83 (0.64-1.07)	0.98 (0.79-1.22)	1.04 (0.81-1.33)	1.27 (0.94-1.72)	1.02 (0.74-1.39)	1.63 (0.95-2.81)
Birth weight	1.05 (0.57-1.94)	0.91 (0.58-1.43)	1.81 (1.13-2.90)	1.17 (0.65-2.10)	1.04 (0.62-1.74)	0.72 (0.46-1.12)	1.34 (0.81-2.23)	0.77 (0.42-1.41)	0.60 (0.33-1.11)	0.42 (0.15-1.18)
BMI at 9	**1.31 (1.09-1.58)**	1.09 (0.94-1.27)	1.02 (0.87-1.18)	0.86 (0.70-1.07)	0.97 (0.81-1.15)	1.16 (1.00-1.34)	**0.66 (0.54-0.81)**	1.02 (0.85-1.23)	0.80 (0.62-1.02)	1.20 (0.89-1.62)
BMI at 45	0.97 (0.91-1.03)	0.98 (0.94-1.03)	0.96 (0.91-1.00)	1.00 (0.94-1.06)	1.04 (0.99-1.09)	0.97 (0.93-1.02)	1.01 (0.97-1.06)	**1.08 (1.03-1.13)**	0.99 (0.94-1.05)	1.05 (0.98-1.12)
Breastfeeding	1.27 (0.67-2.38)	1.10 (0.68-1.76)	0.72 (0.44-1.15)	1.78 (0.96-3.30)	0.82 (0.47-1.42)	0.75 (0.47-1.20)	1.14 (0.68-1.90)	1.32 (0.71-2.49)	0.91 (0.47-1.75)	0.83 (0.32-2.17)
Household crowding	0.79 (0.41-1.50)	1.72 (1.08-2.72)	1.22 (0.76-1.94)	0.99 (0.55-1.79)	0.88 (0.50-1.54)	0.75 (0.47-1.21)	0.98 (0.58-1.63)	0.87 (0.46-1.64)	0.83 (0.43-1.63)	0.91 (0.34-2.49)
Preschool attendance	1.36 (0.63-2.91)	0.84 (0.44-1.62)	0.88 (0.45-1.69)	0.89 (0.38-2.07)	1.71 (0.88-3.31)	0.65 (0.33-1.28)	0.65 (0.31-1.40)	1.00 (0.44-2.30)	1.97 (0.92-4.20)	1.22 (0.27-5.48)
Dog and cat exposure	1.98 (1.05-3.73)	1.24 (0.77-1.99)	0.66 (0.40-1.09)	1.05 (0.57-1.95)	1.03 (0.59-1.80)	0.93 (0.58-1.50)	1.16 (0.69-1.94)	0.74 (0.39-1.41)	1.05 (0.54-2.06)	0.69 (0.23-2.02)

Pairwise comparisons (each trajectory versus all other trajectories) with Bonferroni-Holm method were performed. Analyses adjust for all the other factors (exposures) in the table. Odds ratio (OR) and 95% confidence intervals are reported in the table. Statistically significant associations are shown in bold ($p<0.05$ after Bonferroni-Holm method). See text for definitions. Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high). Odds ratios for BMI (and other continuous variables) are for a one-unit increase in these variables.

Table S5. Predictors of identified FEV_1 trajectories – univariable models

	Persistently high n=50	Always well above average n=128	Always above average n=142	Above average but with decline n=93	Average n=162	Decline during adulthood n=74	Always below average n=72	Accelerated decline n=46	Always well below average n=73	Persistently low n=25
Female (ref)										
Male	1.23 (0.69-2.19)	1.23 (0.84-1.79)	1.09 (0.76-1.56)	0.84 (0.55-1.30)	0.72 (0.51-1.02)	0.80 (0.49-1.29)	0.84 (0.52-1.37)	1.14 (0.63-2.06)	1.33 (0.82-2.16)	2.01 (0.88-4.61)
Childhood asthma	0.35 (0.11-1.15)	**0.25 (0.11-0.59)**	**0.36 (0.18-0.72)**	0.60 (0.29-1.23)	0.86 (0.52-1.43)	0.70 (0.33-1.51)	1.78 (0.96-3.29)	2.16 (1.09-4.26)	**3.48 (2.01-6.02)**	**18.1 (7.2-45.2)**
Childhood AHR	0.27 (0.08-0.89)	**0.20 (0.08-0.46)**	**0.45 (0.25-0.82)**	0.39 (0.18-0.82)	0.80 (0.50-1.28)	0.91 (0.48-1.75)	1.11 (0.58-2.09)	**2.88 (1.54-5.40)**	**5.66 (3.35-9.56)**	**29.8 (9.5-93.6)**
Atopy at 21	1.37 (0.71-2.65)	0.83 (0.55-1.25)	0.69 (0.47-1.01)	0.81 (0.51-1.28)	1.06 (0.73-1.55)	1.02 (0.60-1.72)	1.15 (0.67-1.97)	0.69 (0.37-1.28)	1.62 (0.92-2.87)	26.1 (1.6-431.7)
Parental asthma	0.51 (0.21-1.22)	0.65 (0.39-1.09)	0.83 (0.53-1.33)	1.11 (0.66-1.86)	1.34 (0.89-2.01)	0.99 (0.55-1.80)	0.96 (0.52-1.76)	1.89 (1.00-3.55)	1.03 (0.57-1.87)	1.51 (0.64-3.60)
Parental smoking	0.78 (0.44-1.40)	0.79 (0.54-1.16)	1.14 (0.78-1.67)	1.09 (0.70-1.71)	1.33 (0.92-1.91)	0.77 (0.47-1.26)	0.83 (0.50-1.36)	1.01 (0.55-1.85)	1.27 (0.75-2.13)	0.74 (0.34-1.64)
Tobacco smoked by 45	1.01 (0.98-1.03)	**0.97 (0.95-0.99)**	0.97 (0.95-0.99)	1.02 (1.01-1.04)	0.99 (0.97-1.00)	1.03 (1.01-1.05)	0.98 (0.95-1.01)	**1.06 (1.04-1.09)**	1.01 (0.99-1.03)	0.98 (0.94-1.03)
Childhood SES	0.98 (0.76-1.27)	0.90 (0.76-1.06)	0.93 (0.79-1.10)	1.13 (0.93-1.37)	1.03 (0.88-1.20)	0.97 (0.78-1.20)	0.93 (0.75-1.15)	1.34 (1.01-1.77)	0.94 (0.75-1.16)	1.31 (0.90-1.90)
Birth weight	1.43 (0.82-2.50)	1.15 (0.80-1.66)	1.09 (0.77-1.54)	0.80 (0.53-1.20)	0.92 (0.66-1.28)	0.78 (0.50-1.23)	0.68 (0.43-1.07)	1.01 (0.57-1.80)	1.55 (0.97-2.49)	1.03 (0.48-2.22)
BMI at 9	0.89 (0.73-1.08)	1.03 (0.92-1.17)	1.06 (0.95-1.19)	0.86 (0.73-1.00)	**1.19 (1.07-1.32)**	0.82 (0.69-0.98)	1.00 (0.85-1.19)	0.81 (0.64-1.01)	1.01 (0.86-1.19)	1.07 (0.85-1.36)
BMI at 45	0.93 (0.88-0.99)	1.01 (0.98-1.04)	1.03 (0.99-1.06)	0.99 (0.95-1.03)	**1.05 (1.02-1.08)**	0.95 (0.91-1.00)	1.00 (0.96-1.04)	**0.91 (0.85-0.97)**	0.96 (0.92-1.01)	1.07 (1.01-1.13)
Breastfeeding	1.19 (0.67-2.11)	0.93 (0.64-1.36)	1.19 (0.83-1.70)	0.89 (0.58-1.37)	1.08 (0.77-1.52)	1.00 (0.62-1.61)	0.61 (0.37-1.00)	0.70 (0.38-1.27)	1.20 (0.74-1.95)	1.77 (0.79-3.98)
Household crowding	1.23 (0.69-2.18)	1.31 (0.90-1.91)	0.91 (0.63-1.32)	1.38 (0.90-2.13)	0.83 (0.58-1.18)	1.39 (0.86-2.24)	0.65 (0.39-1.08)	1.21 (0.67-2.19)	0.72 (0.44-1.19)	0.57 (0.24-1.34)
Preschool attendance	0.68 (0.28-1.62)	1.38 (0.86-2.21)	0.62 (0.35-1.08)	0.82 (0.44-1.52)	0.97 (0.61-1.55)	1.11 (0.59-2.08)	2.11 (1.22-3.66)	1.15 (0.54-2.49)	0.79 (0.40-1.58)	0.78 (0.25-2.44)
Dog and cat exposure	1.16 (0.64-2.09)	1.16 (0.77-1.73)	0.83 (0.56-1.23)	1.39 (0.88-2.20)	0.84 (0.57-1.22)	0.60 (0.35-1.04)	1.41 (0.82-2.44)	0.82 (0.43-1.56)	1.14 (0.67-1.95)	1.27 (0.57-2.82)

Pairwise comparisons (each trajectory versus all other trajectories) with Bonferroni-Holm method were performed. Odds ratio (OR) and 95% confidence intervals are reported in the table. Statistically significant associations are shown in bold ($p<0.05$ after Bonferroni-Holm method). See text for definitions. Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high). Odds ratios for BMI (and other continuous variables) are for a one-unit increase in these variables.

Table S6. Characteristics of participants according to identified FVC trajectories

	Persistently high n=32	Always well above average n=109	Catch-up n=65	Always above average n=129	Average n=129	Catch-up II n=114	Accelerated decline n=115	Always well below average n=129	Persistently low n=43	Overall n=865
Female	16/32 (50%)	54/109 (50%)	29/65 (45%)	63/129 (49%)	72/129 (56%)	48/114 (42%)	48/115 (42%)	72/129 (56%)	21/43 (49%)	423 (49%)
Male	16/32 (50%)	55/109 (50%)	36/65 (55%)	66/129 (51%)	57/129 (44%)	66/114 (58%)	67/115 (58%)	57/129 (44%)	22/43 (51%)	442 (51%)
Childhood asthma	6/31 (19%)	17/94 (18%)	9/60 (15%)	17/122 (14%)	14/119 (12%)	13/112 (12%)	19/107 (18%)	18/122 (15%)	11/40 (28%)	124/807 (15%)
Childhood AHR	2/31 (6%)	21/94 (22%)	10/59 (17%)	21/121 (17%)	16/118 (14%)	21/111 (19%)	18/106 (17%)	27/118 (23%)	17/40 (43%)	153/798 (19%)
Atopy at 13	9/26 (35%)	32/80 (40%)	22/52 (42%)	52/100 (52%)	43/101 (43%)	49/100 (49%)	46/89 (52%)	34/100 (34%)	20/37 (54%)	307/685 (45%)
Atopy at 21	19/32 (59%)	63/103 (61%)	39/58 (67%)	73/122 (60%)	81/120 (68%)	71/105 (68%)	69/103 (67%)	76/114 (67%)	29/39 (74%)	520/796 (65%)
Atopy at 32	19/31 (61%)	61/107 (57%)	39/64 (61%)	72/125 (58%)	75/128 (59%)	71/112 (63%)	69/109 (63%)	76/128 (59%)	31/43 (72%)	513/847 (61%)
BMI at 9	16.6±1.2	16.4±1.5	16.1±1.4	16.7±1.6	16.6±1.7	16.0±1.5	16.8±1.8	15.9±1.6	15.9±1.4	16.4±1.6
BMI at 45	27.3±5.2	28.0±4.9	26.0±3.7	29.4±6.2	27.9±5.5	26.8±4.3	32.6±7.1	27.8±5.5	28.1±5.7	28.5±5.8
Parental smoking	20/32 (63%)	63/104 (61%)	40/64 (63%)	83/129 (64%)	86/127 (68%)	71/114 (62%)	68/112 (61%)	76/127 (60%)	27/43 (63%)	534/852 (63%)
Tobacco smoked by 45	6.9±10.4	7.6±10.9	8.6±11.4	5.9±9.6	5.6±9.1	8.4±10.6	8.7±11.9	7.1±10.2	4.2±8.5	7.1±10.4
Parental asthma	5/31 (16%)	30/103 (29%)	12/64 (19%)	22/125 (18%)	24/127 (19%)	22/114 (19%)	26/108 (24%)	28/126 (22%)	10/43 (23%)	179/841 (21%)
Parental atopy	12/31 (39%)	56/103 (54%)	31/64 (48%)	51/125 (41%)	55/127 (43%)	49/114 (43%)	48/110 (44%)	54/126 (43%)	26/43 (60%)	382/843 (45%)
Birth weight	3.503±0.545	3.430±0.513	3.364±0.523	3.310±0.532	3.445±0.469	3.399±0.534	3.381±0.596	3.371±0.468	3.238±0.511	3.383±0.520
Breastfeeding	19/32 (59%)	51/107 (48%)	39/65 (60%)	59/129 (46%)	55/129 (43%)	56/114 (49%)	70/115 (61%)	62/129 (48%)	20/43 (47%)	431/863 (50%)
Coughs/colds at 3	2.9±2.3	2.5±2.0	2.5±2.1	2.6±2.0	2.4±1.7	3.0±2.1	2.9±2.0	2.7±2.0	3.3±2.7	2.7±2.0
Preschool attendance	8/32 (25%)	18/107 (17%)	6/63 (10%)	20/128 (16%)	18/129 (14%)	21/113 (19%)	20/114 (18%)	22/128 (17%)	8/43 (19%)	141/857 (16%)
Household crowding	14/32 (44%)	45/109 (41%)	19/65 (29%)	56/129 (43%)	58/129 (45%)	43/114 (38%)	55/115 (48%)	49/129 (38%)	18/43 (42%)	357/865 (41%)
Dog/Cat ownership	17/30 (57%)	40/86 (47%)	23/53 (43%)	48/116 (41%)	41/110 (37%)	38/109 (35%)	37/99 (37%)	48/114 (42%)	13/39 (33%)	305/756 (40%)
Childhood SES	3.3±1.3	3.1±1.1	3.1±1.0	3.2±1.1	3.2±1.0	3.3±1.2	3.3±1.2	3.2±1.1	3.2±1.1	3.2±1.1
Airflow obstruction at 45	6/29 (21%)	13/100 (13%)	6/62 (10%)	12/122 (10%)	5/119 (4%)	6/108 (6%)	13/109 (12%)	8/124 (6%)	6/40 (15%)	75/813 (9%)

Data are n/N (%) or mean±SD. Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high).

Table S7. Predictors of identified FVC trajectories – multivariable models

	Persistently high n=32	Always well above average n=109	Catch-up n=65	Always above average n=129	Average n=129	Catch-up II n=114	Accelerated decline n=115	Always well below average n=129	Persistently low n=43
Female (ref)									
Male	1.02 (0.47-2.22)	0.97 (0.58-1.61)	1.17 (0.61-2.21)	1.18 (0.76-1.83)	0.85 (0.54-1.34)	1.54 (0.95-2.48)	1.24 (0.74-2.09)	0.66 (0.42-1.05)	0.82 (0.41-1.65)
Childhood asthma	2.70 (0.89-8.19)	1.00 (0.45-2.21)	1.34 (0.49-3.64)	1.00 (0.49-2.05)	0.92 (0.42-2.02)	0.62 (0.27-1.42)	1.35 (0.61-2.99)	0.84 (0.40-1.75)	1.13 (0.41-3.07)
Childhood AHR	0.24 (0.05-1.12)	1.34 (0.65-2.76)	0.86 (0.33-2.23)	1.14 (0.60-2.19)	0.68 (0.32-1.40)	0.82 (0.40-1.67)	0.65 (0.29-1.46)	1.44 (0.75-2.75)	2.30 (0.94-5.65)
Atopy at 21	0.95 (0.42-2.13)	0.83 (0.48-1.45)	0.88 (0.45-1.73)	0.61 (0.38-0.98)	1.23 (0.75-2.01)	1.29 (0.77-2.15)	1.13 (0.64-2.01)	1.21 (0.73-2.00)	1.04 (0.47-2.32)
Parental asthma	0.73 (0.26-2.06)	1.93 (1.10-3.39)	0.65 (0.26-1.60)	0.92 (0.53-1.60)	0.78 (0.43-1.41)	1.20 (0.68-2.14)	0.74 (0.38-1.44)	0.86 (0.49-1.54)	1.46 (0.66-3.24)
Parental smoking	1.00 (0.44-2.25)	1.07 (0.63-1.83)	1.44 (0.73-2.86)	0.89 (0.57-1.40)	1.37 (0.84-2.23)	0.88 (0.54-1.43)	0.86 (0.51-1.47)	0.84 (0.52-1.34)	1.11 (0.53-2.31)
Tobacco smoked by 45	1.00 (0.96-1.04)	0.99 (0.97-1.02)	1.00 (0.97-1.03)	0.99 (0.96-1.01)	0.98 (0.95-1.00)	1.02 (1.00-1.04)	1.03 (1.01-1.05)	0.99 (0.97-1.02)	0.99 (0.95-1.03)
Childhood SES	0.97 (0.66-1.41)	0.90 (0.70-1.14)	0.98 (0.72-1.33)	1.03 (0.83-1.27)	0.96 (0.77-1.20)	1.18 (0.94-1.48)	0.95 (0.75-1.22)	1.02 (0.82-1.27)	0.98 (0.69-1.38)
Birth weight	1.26 (0.58-2.70)	1.21 (0.73-2.02)	0.73 (0.39-1.36)	0.75 (0.49-1.15)	1.20 (0.77-1.88)	1.11 (0.70-1.75)	1.22 (0.73-2.03)	1.05 (0.67-1.65)	0.55 (0.28-1.08)
BMI at 9	1.16 (0.91-1.49)	1.02 (0.87-1.21)	1.07 (0.86-1.33)	1.16 (1.01-1.33)	1.16 (1.00-1.34)	0.82 (0.69-0.97)	0.97 (0.83-1.14)	0.84 (0.71-0.99)	0.81 (0.62-1.06)
BMI at 45	0.95 (0.87-1.03)	0.99 (0.94-1.03)	**0.90 (0.84-0.97)**	1.01 (0.98-1.05)	0.97 (0.93-1.01)	0.95 (0.90-1.00)	**1.15 (1.10-1.20)**	0.99 (0.95-1.03)	1.01 (0.94-1.07)
Breastfeeding	1.43 (0.64-3.19)	1.08 (0.64-1.82)	1.39 (0.72-2.67)	0.96 (0.62-1.51)	0.54 (0.34-0.86)	0.99 (0.61-1.60)	2.06 (1.20-3.54)	0.86 (0.54-1.37)	0.94 (0.45-1.93)
Household crowding	0.95 (0.43-2.10)	1.06 (0.63-1.78)	0.58 (0.29-1.15)	1.04 (0.67-1.62)	1.23 (0.78-1.94)	0.87 (0.54-1.41)	1.43 (0.85-2.39)	0.76 (0.48-1.22)	1.39 (0.68-2.85)
Preschool attendance	1.80 (0.76-4.29)	0.83 (0.41-1.72)	0.63 (0.24-1.67)	0.93 (0.51-1.72)	0.88 (0.46-1.69)	1.19 (0.64-2.20)	0.98 (0.48-1.98)	0.93 (0.50-1.75)	1.45 (0.59-3.57)
Dog and cat exposure	1.87 (0.85-4.08)	1.22 (0.72-2.05)	1.21 (0.62-2.34)	1.01 (0.64-1.58)	0.95 (0.60-1.52)	0.71 (0.43-1.17)	0.80 (0.47-1.37)	1.40 (0.87-2.23)	0.63 (0.29-1.37)

Pairwise comparisons (each trajectory versus all other trajectories) with Bonferroni-Holm method were performed. Analyses adjust for all the other factors (exposures) in the table. Odds ratio (OR) and 95% confidence interval are reported in the table. Statistically significant associations are shown in bold ($p<0.05$ after Bonferroni-Holm method). Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high). Odds ratios for BMI (and other continuous variables) are for a one-unit increase in these variables.

Table S8. Predictors of identified FVC trajectories – univariable models

	Persistently high n=32	Always well above average n=109	Catch-up n=65	Always above average n=129	Average n=129	Catch-up II n=114	Accelerated decline n=115	Always well below average n=129	Persistently low n=43
Female (ref)									
Male	0.96 (0.48-1.92)	0.97 (0.65-1.45)	1.20 (0.72-2.00)	1.00 (0.69-1.46)	0.72 (0.50-1.05)	1.37 (0.92-2.04)	1.40 (0.94-2.08)	0.72 (0.50-1.05)	1.00 (0.55-1.84)
Childhood asthma	1.42 (0.59-3.43)	1.25 (0.71-2.20)	0.97 (0.46-2.02)	0.87 (0.50-1.52)	0.70 (0.39-1.27)	0.69 (0.37-1.28)	1.22 (0.71-2.09)	0.95 (0.55-1.62)	2.25 (1.11-4.57)
Childhood AHR	0.34 (0.09-1.27)	1.25 (0.74-2.10)	0.85 (0.42-1.72)	0.87 (0.52-1.44)	0.62 (0.36-1.09)	0.98 (0.59-1.64)	0.84 (0.49-1.45)	1.30 (0.81-2.09)	**3.40 (1.78-6.48)**
Atopy at 21	0.76 (0.37-1.54)	0.81 (0.53-1.25)	1.10 (0.62-1.94)	0.76 (0.51-1.12)	1.12 (0.74-1.70)	1.13 (0.73-1.74)	1.09 (0.70-1.69)	1.07 (0.70-1.63)	1.52 (0.74-3.13)
Parental asthma	0.76 (0.30-1.93)	1.62 (1.02-2.58)	0.84 (0.44-1.62)	0.76 (0.46-1.25)	0.84 (0.52-1.36)	0.87 (0.53-1.43)	1.20 (0.75-1.93)	1.07 (0.68-1.69)	1.16 (0.57-2.38)
Parental smoking	0.98 (0.48-2.00)	0.90 (0.59-1.38)	0.99 (0.59-1.68)	1.09 (0.74-1.61)	1.30 (0.87-1.94)	0.98 (0.65-1.47)	0.91 (0.60-1.37)	0.87 (0.59-1.28)	0.99 (0.53-1.86)
Tobacco smoked by 45	1.00 (0.97-1.04)	1.00 (0.99-1.02)	1.01 (0.99-1.04)	0.99 (0.97-1.01)	0.98 (0.96-1.00)	1.01 (1.00-1.03)	1.02 (1.00-1.03)	1.00 (0.98-1.02)	0.97 (0.93-1.00)
Childhood SES	1.07 (0.78-1.47)	0.93 (0.78-1.12)	0.89 (0.71-1.12)	1.01 (0.85-1.19)	0.98 (0.83-1.17)	1.06 (0.89-1.27)	1.07 (0.89-1.28)	1.00 (0.84-1.18)	1.01 (0.77-1.33)
Birth weight	1.59 (0.79-3.20)	1.22 (0.83-1.80)	0.93 (0.57-1.51)	0.73 (0.51-1.04)	1.32 (0.91-1.90)	1.07 (0.73-1.56)	0.99 (0.68-1.45)	0.95 (0.66-1.36)	0.58 (0.33-1.02)
BMI at 9	1.09 (0.88-1.35)	1.03 (0.90-1.18)	0.90 (0.75-1.08)	1.14 (1.01-1.27)	1.12 (0.99-1.26)	0.84 (0.73-0.97)	**1.19 (1.05-1.34)**	**0.80 (0.69-0.92)**	0.80 (0.63-1.01)
BMI at 45	0.97 (0.90-1.04)	0.98 (0.95-1.02)	**0.91 (0.86-0.96)**	1.03 (1.00-1.06)	0.98 (0.95-1.01)	**0.93 (0.90-0.97)**	**1.13 (1.09-1.17)**	0.98 (0.94-1.01)	0.99 (0.94-1.05)
Breastfeeding	1.47 (0.72-2.98)	0.90 (0.60-1.35)	1.55 (0.93-2.60)	0.82 (0.56-1.19)	0.71 (0.49-1.03)	0.96 (0.65-1.43)	1.67 (1.12-2.49)	0.92 (0.63-1.33)	0.87 (0.47-1.59)
Household crowding	1.12 (0.56-2.26)	1.00 (0.67-1.50)	0.56 (0.32-0.98)	1.11 (0.76-1.62)	1.19 (0.82-1.74)	0.84 (0.56-1.26)	1.36 (0.92-2.02)	0.85 (0.58-1.25)	1.03 (0.56-1.91)
Preschool attendance	1.80 (0.81-4.01)	1.03 (0.60-1.77)	0.51 (0.22-1.22)	0.93 (0.56-1.56)	0.80 (0.47-1.36)	1.19 (0.71-1.98)	1.09 (0.65-1.84)	1.06 (0.65-1.75)	1.22 (0.57-2.64)
Dog and cat exposure	1.97 (0.95-4.07)	1.33 (0.85-2.09)	1.14 (0.65-2.01)	1.05 (0.70-1.57)	0.86 (0.57-1.30)	0.76 (0.50-1.16)	0.87 (0.56-1.34)	1.09 (0.73-1.63)	0.74 (0.38-1.45)

Pairwise comparisons (each trajectory versus all other trajectories) with Bonferroni-Holm method were performed. Odds ratio (OR) and 95% confidence intervals are reported in the table. Statistically significant associations are shown in bold ($p<0.05$ after Bonferroni-Holm method). See text for definitions. Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high). Odds ratios for BMI (and other continuous variables) are for a one-unit increase in these variables.

Table S9. Characteristics of participants according to identified FEV_1/FVC trajectories

Data are n/N (%) or mean±SD. Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high)

	Persistently high n=50	Always well above average n=128	Always above average n=142	Above average but with decline n=93	Average n=162	Decline during adulthood n=74	Always below average n=72	Accelerated decline n=46	Always well below average n=73	Persistently low n=25	Overall n=865
Female	22/50 (44%)	57/128 (45%)	67/142 (47%)	49/93 (53%)	90/162 (56%)	40/74 (54%)	38/72 (53%)	21/46 (46%)	31/73 (42%)	8/25 (32%)	423 (49%)
Male	28/50 (56%)	71/128 (55%)	75/142 (53%)	44/93 (47%)	72/162 (44%)	34/74 (46%)	34/72 (47%)	25/46 (54%)	42/73 (58%)	17/25 (68%)	442 (51%)
Childhood asthma	3/48 (6%)	6/120 (5%)	9/132 (7%)	9/88 (10%)	21/152 (14%)	8/69 (12%)	15/64 (23%)	12/45 (27%)	23/65 (35%)	18/24 (75%)	124/807 (15%)
Childhood AHR	3/47 (6%)	6/117 (5%)	14/131 (11%)	8/88 (9%)	25/152 (16%)	12/67 (18%)	13/63 (21%)	17/44 (39%)	34/65 (52%)	21/24 (88%)	153/798 (19%)
Atopy at 13	20/39 (51%)	43/100 (43%)	39/114 (34%)	24/70 (34%)	60/128 (47%)	29/64 (45%)	22/49 (45%)	21/42 (50%)	28/56 (50%)	21/23 (91%)	307/685 (45%)
Atopy at 21	33/46 (72%)	71/115 (62%)	78/134 (58%)	53/87 (61%)	99/149 (66%)	44/67 (66%)	45/66 (68%)	24/42 (57%)	50/67 (75%)	23/23 (100%)	520/796 (65%)
Atopy at 32	35/49 (71%)	66/126 (52%)	75/140 (54%)	51/91 (56%)	87/157 (55%)	47/72 (65%)	52/72 (72%)	25/45 (56%)	50/70 (71%)	25/25 (100%)	513/847 (61%)
BMI at 9	16.1±1.6	16.4±1.8	16.5±1.7	16.0±1.5	16.7±1.6	15.9±1.5	16.4±1.7	15.9±1.4	16.4±1.7	16.5±1.0	16.4±1.6
BMI at 45	26.6±4.5	28.7±5.5	29.2±5.5	28.0±5.4	29.9±6.8	27.1±4.6	28.4±5.6	26.0±5.2	27.3±4.8	31.0±9.4	28.5±5.8
Parental smoking	28/49 (57%)	73/126 (58%)	92/141 (65%)	60/93 (65%)	108/159 (68%)	41/72 (57%)	41/70 (59%)	29/46 (63%)	48/71 (68%)	14/25 (56%)	534/852 (63%)
Tobacco smoked by 45	7.8±11.0	4.6±8.1	5.0±8.1	9.8±12.2	5.9±9.6	10.3±11.9	5.3±8.5	15.6±14.4	7.9±11.3	5.3±7.8	7.1±10.4
Parental asthma	6/48 (13%)	20/127 (16%)	26/138 (19%)	21/92 (23%)	40/157 (25%)	15/71 (21%)	14/68 (21%)	15/46 (33%)	15/69 (22%)	7/25 (28%)	179/841 (21%)
Parental atopy	18/48 (38%)	56/128 (44%)	58/138 (42%)	38/92 (41%)	74/157 (47%)	30/71 (42%)	34/69 (49%)	23/46 (50%)	36/69 (52%)	15/25 (60%)	382/843 (45%)
Birth weight	3.472±0.466	3.416±0.548	3.403±0.438	3.327±0.528	3.365±0.528	3.322±0.543	3.286±0.569	3.388±0.581	3.489±0.555	3.393±0.361	3.383±0.520
Breastfeeding	27/50 (54%)	62/128 (48%)	76/142 (54%)	44/93 (47%)	83/161 (52%)	37/74 (50%)	28/72 (39%)	19/46 (41%)	39/72 (54%)	16/25 (64%)	431/863 (50%)
Coughs/colds at 3	3.3±2.3	2.6±1.8	2.7±2.0	2.8±1.9	2.5±1.9	2.6±1.9	2.9±2.0	2.6±2.3	2.8±2.2	3.1±2.8	2.7±2.0
Preschool attendance	6/50 (12%)	26/127 (20%)	16/139 (12%)	13/92 (14%)	26/161 (16%)	13/73 (18%)	20/72 (28%)	8/45 (18%)	10/73 (14%)	3/25 (12%)	141/857 (16%)
Household crowding	23/50 (46%)	60/128 (47%)	56/142 (39%)	45/93 (48%)	61/162 (38%)	36/74 (49%)	23/72 (32%)	21/46 (46%)	25/73 (34%)	7/25 (28%)	357/865 (41%)
Dog/Cat ownership	21/48 (44%)	49/113 (43%)	45/123 (37%)	39/82 (48%)	52/141 (37%)	20/67 (30%)	27/56 (48%)	15/42 (36%)	26/60 (43%)	11/24 (46%)	305/756 (40%)
Childhood SES	3.2±1.2	3.1±1.1	3.1±1.1	3.3±1.0	3.2±1.2	3.2±1.1	3.1±1.0	3.5±1.2	3.1±1.1	3.5±1.3	3.2±1.1
Airflow obstruction at 45	1/48 (2%)	1/122 (1%)	0/136 (0%)	2/84 (2%)	0/153 (0%)	7/69 (10%)	3/70 (4%)	16/43 (37%)	28/65 (43%)	17/23 (74%)	75/813 (9%)

Table S10. Predictors of identified FEV_1/FVC trajectories – multivariable models

	Persistently high n=50	Always well above average n=128	Always above average n=142	Above average but with decline n=93	Average n=162	Decline during adulthood n=74	Always below average n=72	Accelerated decline n=46	Always well below average n=73	Persistently low n=25
Female (ref)										
Male	1.40 (0.71-2.75)	1.27 (0.80-2.00)	1.31 (0.85-2.01)	0.95 (0.56-1.61)	0.69 (0.45-1.05)	0.71 (0.40-1.28)	0.96 (0.51-1.81)	0.86 (0.42-1.78)	1.25 (0.66-2.39)	2.25 (0.76-6.61)
Childhood asthma	0.46 (0.10-2.22)	0.61 (0.23-1.59)	0.49 (0.21-1.15)	1.37 (0.55-3.43)	0.79 (0.40-1.59)	0.92 (0.34-2.47)	2.42 (0.95-6.15)	1.47 (0.51-4.22)	1.14 (0.51-2.57)	3.07 (0.98-9.65)
Childhood AHR	0.21 (0.04-0.98)	**0.23 (0.08-0.64)**	0.62 (0.30-1.29)	0.32 (0.12-0.88)	1.04 (0.55-1.94)	0.80 (0.33-1.96)	0.61 (0.23-1.65)	2.31 (0.92-5.80)	**7.79 (3.61-16.9)**	**12.4 (2.6-58.5)**
Atopy at 21	1.78 (0.87-3.66)	1.02 (0.64-1.65)	0.72 (0.46-1.12)	0.90 (0.52-1.56)	1.33 (0.83-2.15)	1.31 (0.69-2.47)	0.98 (0.50-1.93)	0.67 (0.31-1.46)	0.68 (0.32-1.44)	5.07 (0.29-88.0)
Parental asthma	0.45 (0.15-1.30)	0.62 (0.33-1.16)	0.92 (0.53-1.62)	1.17 (0.62-2.21)	1.54 (0.94-2.52)	1.06 (0.52-2.18)	0.85 (0.39-1.88)	1.62 (0.74-3.53)	0.63 (0.27-1.49)	0.99 (0.33-3.0)
Parental smoking	0.79 (0.40-1.56)	0.70 (0.44-1.12)	1.18 (0.75-1.86)	0.98 (0.56-1.71)	1.46 (0.92-2.31)	1.06 (0.58-1.96)	0.71 (0.37-1.36)	0.87 (0.42-1.82)	1.54 (0.79-3.01)	0.68 (0.25-1.84)
Tobacco smoked by 45	1.00 (0.96-1.03)	**0.96 (0.93-0.99)**	0.97 (0.94-0.99)	**1.04 (1.02-1.06)**	0.98 (0.96-1.00)	1.02 (0.99-1.05)	0.99 (0.95-1.02)	**1.06 (1.03-1.09)**	1.02 (0.99-1.05)	1.00 (0.95-1.06)
Childhood SES	1.21 (0.88-1.66)	0.88 (0.71-1.09)	0.99 (0.81-1.21)	0.99 (0.76-1.27)	1.02 (0.83-1.25)	0.94 (0.71-1.25)	0.85 (0.63-1.15)	1.30 (0.90-1.87)	1.00 (0.73-1.36)	1.70 (0.98-2.96)
Birth weight	1.24 (0.65-2.36)	1.29 (0.83-2.01)	1.04 (0.68-1.59)	0.82 (0.50-1.36)	0.96 (0.63-1.47)	0.80 (0.46-1.41)	0.67 (0.37-1.21)	1.01 (0.49-2.06)	1.45 (0.76-2.77)	1.05 (0.35-3.19)
BMI at 9	0.94 (0.74-1.19)	1.04 (0.89-1.20)	1.06 (0.92-1.21)	0.83 (0.68-1.00)	1.15 (1.01-1.31)	0.83 (0.67-1.03)	0.98 (0.79-1.22)	0.83 (0.63-1.09)	1.11 (0.90-1.37)	1.12 (0.81-1.55)
BMI at 45	**0.89 (0.82-0.96)**	1.01 (0.97-1.06)	1.02 (0.98-1.06)	1.00 (0.95-1.05)	1.05 (1.01-1.08)	0.96 (0.91-1.02)	1.01 (0.95-1.07)	0.95 (0.89-1.03)	0.94 (0.88-1.00)	1.04 (0.97-1.12)
Breastfeeding	1.38 (0.70-2.73)	0.93 (0.59-1.49)	1.02 (0.66-1.58)	1.26 (0.73-2.17)	0.91 (0.59-1.40)	1.05 (0.57-1.92)	0.48 (0.25-0.92)	0.80 (0.38-1.70)	1.27 (0.66-2.44)	1.58 (0.56-4.49)
Household crowding	0.87 (0.44-1.71)	1.41 (0.89-2.21)	0.85 (0.55-1.32)	1.60 (0.94-2.72)	0.80 (0.51-1.24)	1.30 (0.72-2.34)	0.70 (0.36-1.35)	0.90 (0.42-1.92)	0.67 (0.34-1.32)	0.77 (0.27-2.20)
Preschool attendance	0.89 (0.35-2.23)	1.28 (0.70-2.33)	0.72 (0.38-1.37)	0.78 (0.38-1.63)	1.19 (0.67-2.10)	0.77 (0.33-1.80)	**2.78 (1.38-5.61)**	1.00 (0.39-2.58)	0.31 (0.09-1.07)	0.95 (0.20-4.55)
Dog and cat exposure	1.44 (0.73-2.84)	1.25 (0.79-2.00)	0.84 (0.53-1.32)	1.29 (0.76-2.19)	0.86 (0.55-1.34)	0.66 (0.35-1.24)	1.38 (0.72-2.62)	0.66 (0.30-1.43)	1.16 (0.59-2.25)	1.44 (0.51-4.08)

Pairwise comparisons (each trajectory versus all other trajectories) with Bonferroni-Holm method were performed. Analyses adjust for all the other factors (exposures) in the table. Odds ratio (OR) and 95% confidence interval are reported in the table. Statistically significant associations are shown in bold ($p<0.05$ after Bonferroni-Holm method). Odds ratios adjust for all other variables. Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high). Odds ratios for BMI (and other continuous variables) are for a one-unit increase in these variables.

Table S11. Predictors of identified FEV_1 trajectories – univariable analyses

	Persistently high n=50	Always well above average n=128	Always above average n=142	Above average but with decline n=93	Average n=162	Decline during adulthood n=74	Always below average n=72	Accelerated decline n=46	Always well below average n=73	Persistently low n=25
Female (ref)										
Male	1.23 (0.69-2.19)	1.23 (0.84-1.79)	1.09 (0.76-1.56)	0.84 (0.55-1.30)	0.72 (0.51-1.02)	0.80 (0.49-1.29)	0.84 (0.52-1.37)	1.14 (0.63-2.06)	1.33 (0.82-2.16)	2.01 (0.88-4.61)
Childhood asthma	0.35 (0.11-1.15)	**0.25 (0.11-0.59)**	**0.36 (0.18-0.72)**	0.60 (0.29-1.23)	0.86 (0.52-1.43)	0.70 (0.33-1.51)	1.78 (0.96-3.29)	2.16 (1.09-4.26)	**3.48 (2.01-6.02)**	**18.1 (7.2-45.3)**
Childhood AHR	0.27 (0.08-0.89)	**0.20 (0.08-0.46)**	**0.45 (0.25-0.82)**	0.39 (0.18-0.82)	0.80 (0.50-1.28)	0.91 (0.48-1.75)	1.11 (0.58-2.09)	**2.88 (1.54-5.40)**	**5.66 (3.35-9.56)**	**29.8 (9.5-93.6)**
Atopy at 21	1.37 (0.71-2.65)	0.83 (0.55-1.25)	0.69 (0.47-1.01)	0.81 (0.51-1.28)	1.06 (0.73-1.55)	1.02 (0.60-1.72)	1.15 (0.67-1.97)	0.69 (0.37-1.28)	1.62 (0.92-2.87)	26.1 (1.6-432.7)
Parental asthma	0.51 (0.21-1.22)	0.65 (0.39-1.09)	0.83 (0.53-1.33)	1.11 (0.66-1.86)	1.34 (0.89-2.01)	0.99 (0.55-1.80)	0.96 (0.52-1.76)	1.89 (1.00-3.55)	1.03 (0.57-1.87)	1.51 (0.64-3.60)
Parental smoking	0.78 (0.44-1.40)	0.79 (0.54-1.16)	1.14 (0.78-1.67)	1.09 (0.70-1.71)	1.33 (0.92-1.91)	0.77 (0.47-1.26)	0.83 (0.50-1.36)	1.01 (0.55-1.85)	1.27 (0.75-2.13)	0.74 (0.34-1.64)
Tobacco smoked by 45	1.01 (0.98-1.03)	**0.97 (0.95-0.99)**	0.97 (0.95-0.99)	1.02 (1.01-1.04)	0.99 (0.97-1.00)	1.03 (1.01-1.05)	0.98 (0.95-1.01)	**1.06 (1.04-1.09)**	1.01 (0.99-1.03)	0.98 (0.94-1.03)
Childhood SES	0.98 (0.76-1.27)	0.90 (0.76-1.06)	0.93 (0.79-1.10)	1.13 (0.93-1.37)	1.03 (0.88-1.20)	0.97 (0.78-1.20)	0.93 (0.75-1.15)	1.34 (1.01-1.77)	0.94 (0.75-1.16)	1.31 (0.90-1.90)
Birth weight	1.43 (0.82-2.50)	1.15 (0.80-1.66)	1.09 (0.77-1.54)	0.80 (0.53-1.20)	0.92 (0.66-1.28)	0.78 (0.50-1.23)	0.68 (0.43-1.07)	1.01 (0.57-1.80)	1.55 (0.97-2.49)	1.03 (0.48-2.22)
BMI at 9	0.89 (0.73-1.08)	1.03 (0.92-1.17)	1.06 (0.95-1.19)	0.86 (0.73-1.00)	**1.19 (1.07-1.32)**	0.82 (0.69-0.98)	1.00 (0.85-1.19)	0.81 (0.64-1.01)	1.01 (0.86-1.19)	1.07 (0.85-1.36)
BMI at 45	0.93 (0.88-0.99)	1.01 (0.98-1.04)	1.03 (0.99-1.06)	0.99 (0.95-1.03)	**1.05 (1.02-1.08)**	0.95 (0.91-1.00)	1.00 (0.96-1.04)	**0.91 (0.85-0.97)**	0.96 (0.92-1.01)	1.07 (1.01-1.13)
Breastfeeding	1.19 (0.67-2.11)	0.93 (0.64-1.36)	1.19 (0.83-1.70)	0.89 (0.58-1.37)	1.08 (0.77-1.52)	1.00 (0.62-1.61)	0.61 (0.37-1.00)	0.70 (0.38-1.27)	1.20 (0.74-1.95)	1.77 (0.79-3.98)
Household crowding	1.23 (0.69-2.18)	1.31 (0.90-1.91)	0.91 (0.63-1.32)	1.38 (0.90-2.13)	0.83 (0.58-1.18)	1.39 (0.86-2.24)	0.65 (0.39-1.08)	1.21 (0.67-2.19)	0.72 (0.44-1.19)	0.57 (0.24-1.34)
Preschool attendance	0.68 (0.28-1.62)	1.38 (0.86-2.21)	0.62 (0.35-1.08)	0.82 (0.44-1.52)	0.97 (0.61-1.55)	1.11 (0.59-2.08)	2.11 (1.22-3.66)	1.15 (0.54-2.49)	0.79 (0.40-1.58)	0.78 (0.25-2.44)
Dog and cat exposure	1.16 (0.64-2.09)	1.16 (0.77-1.73)	0.83 (0.56-1.23)	1.39 (0.88-2.20)	0.84 (0.57-1.22)	0.60 (0.35-1.04)	1.41 (0.82-2.44)	0.82 (0.43-1.56)	1.14 (0.67-1.95)	1.27 (0.57-2.82)

Pairwise comparisons (each trajectory versus all other trajectories) with Bonferroni-Holm method were performed. Odds ratio (OR) and 95% confidence intervals are reported in the table. Statistically significant associations are shown in bold ($p<0.05$ after Bonferroni-Holm method). See text for definitions. Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high). Odds ratios for BMI (and other continuous variables) are for a one-unit increase in these variables.

Table S12. Mean and range of posterior probabilities for each identified lung function trajectory

FEV_1	**Persistently high n=63**	**Always well above average n=129**	**Always above average n=117**	**Catch-up n=71**	**Accelerated decline n=82**	**Average n=138**	**Always below average n=101**	**Accelerated decline II n=73**	**Always well below average n=63**	**Persistently low n=28**
Mean posterior probability	0.96	0.93	0.84	0.85	0.83	0.87	0.89	0.88	0.93	0.99
Range of posterior probability	0.53-1.00	0.50-1.00	0.39-1.00	0.38-1.00	0.39-1.00	0.40-1.00	0.50-1.00	0.46-1.00	0.48-1.00	0.97-1.00
% with probability <75%	8% (5/63)	10% (13/129)	24% (28/117)	25% (18/71)	35% (29/82)	19% (26/138)	20% (20/101)	22% (16/73)	11% (7/63)	0% (0/28)
% with probability <50%	0% (0/63)	1% (1/129)	5% (6/117)	4% (3/71)	7% (6/82)	4% (6/138)	1% (1/101)	1% (1/73)	2% (1/63)	0% (0/28)
FVC	**Persistently high n=32**	**Always well above average n=109**	**Catch-up n=65**	**Always above average n=129**	**Average n=129**	**Catch-up II n=114**	**Accelerated decline n=115**	**Always well below average n=129**	**Persistently low n=43**	
Mean posterior probability	0.95	0.92	0.86	0.9	0.89	0.88	0.88	0.93	0.98	
Range of posterior probability	0.54-1.00	0.50-1.00	0.43-1.00	0.52-1.00	0.46-1.00	0.44-1.00	0.35-1.00	0.47-1.00	0.59-1.00	
% with probability <75%	6% (2/32)	15% (16/109)	23% (15/65)	18% (23/129)	16% (20/129)	20% (23/114)	23% (26/115)	11% (14/129)	2% (1/43)	
% with probability <50%	0% (0/32)	0% (0/109)	5% (3/65)	0% (0/129)	1% (1/129)	4% (5/114)	2% (2/115)	1% (1/129)	0% (0/43)	
FEV_1/FVC	**Persistently high n=50**	**Always well above average n=128**	**Always above average n=142**	**Above average but with decline n=93**	**Average n=162**	**Decline during adulthood n=74**	**Always below average n=72**	**Accelerated decline n=46**	**Always well below average n=73**	**Persistently low n=25**
Mean posterior probability	0.92	0.92	0.88	0.85	0.88	0.87	0.90	0.93	0.94	0.99
Range of posterior probability	0.45-1.00	0.34-1.00	0.48-1.00	0.38-1.00	0.43-1.00	0.48-1.00	0.42-1.00	0.55-1.00	0.54-1.00	0.90-1.00
% with probability <75%	14% (7/50)	13% (17/128)	20% (29/142)	25% (23/93)	23% (37/162)	23% (17/74)	15% (11/72)	15% (7/46)	8% (6/73)	0% (0/25)
% with probability <50%	2% (1/50)	2% (2/128)	1% (2/142)	6% (6/93)	4% (6/162)	1% (1/74)	3% (2/72)	0% (0/46)	0% (0/73)	0% (0/25)

Table S13. Predictors of identified FEV_1 trajectories – multivariable models using the average trajectory as the reference group

	Persistently high n=63	Always well above average n=129	Always above average n=117	Catch-up n=71	Accelerated decline n=82	Average n=138	Always below average n=101	Accelerated decline II n=73	Always well below average n=63	Persistently low n=28
Female (ref)										
Male	1.25 (0.58-2.70)	1.64 (0.88-3.05)	1.19 (0.64-2.22)	1.72 (0.78-3.80)	1.93 (0.95-3.92)	Reference	1.14 (0.58-2.23)	1.45 (0.64-3.28)	1.07 (0.45-2.52)	2.12 (0.46-9.78)
Childhood asthma	1.88 (0.52-6.79)	0.57 (0.16-2.01)	1.21 (0.40-3.69)	1.09 (0.31-3.90)	1.44 (0.44-4.75)	Reference	1.16 (0.35-3.92)	1.38 (0.39-4.89)	1.27 (0.34-4.82)	2.16 (0.34-13.6)
Childhood AHR	0.34 (0.06-1.88)	2.36 (0.81-6.83)	0.55 (0.16-1.94)	2.54 (0.87-7.43)	2.15 (0.70-6.61)	Reference	3.10 (1.09-8.80)	2.19 (0.64-7.48)	**6.96 (2.24-21.6)**	**22.0 (3.8-127.5)**
Atopy at 21	1.00 (0.44-2.30)	0.85 (0.44-1.63)	1.15 (0.60-2.21)	2.07 (0.87-4.92)	0.73 (0.34-1.56)	Reference	1.50 (0.72-3.14)	1.48 (0.60-3.66)	0.67 (0.26-1.68)	1.89 (0.19-19.1)
Parental asthma	1.03 (0.39-2.71)	0.86 (0.37-1.99)	0.88 (0.39-2.00)	0.52 (0.16-1.68)	1.39 (0.58-3.31)	Reference	1.18 (0.50-2.80)	1.35 (0.51-3.54)	1.34 (0.49-3.65)	0.41 (0.05-3.20)
Parental smoking	0.61 (0.27-1.38)	0.62 (0.32-1.18)	0.95 (0.49-1.82)	1.01 (0.43-2.34)	0.90 (0.41-2.00)	Reference	1.44 (0.66-3.16)	0.65 (0.27-1.54)	0.86 (0.34-2.15)	0.33 (0.06-1.90)
Tobacco smoked by 45	0.99 (0.96-1.04)	0.97 (0.93-1.00)	0.97 (0.93-1.00)	0.98 (0.94-1.02)	1.02 (0.99-1.06)	Reference	1.01 (0.98-1.05)	1.05 (1.01-1.09)	1.00 (0.96-1.05)	1.01 (0.93-1.10)
Childhood SES	0.99 (0.67-1.45)	1.18 (0.87-1.61)	0.91 (0.67-1.23)	1.00 (0.67-1.51)	0.91 (0.64-1.31)	Reference	1.06 (0.76-1.47)	1.33 (0.87-2.03)	1.01 (0.66-1.55)	1.40 (0.62-3.17)
Birth weight	1.64 (0.72-3.73)	1.57 (0.82-3.02)	2.10 (1.11-3.99)	1.65 (0.77-3.54)	1.35 (0.64-2.83)	Reference	1.82 (0.90-3.67)	0.99 (0.47-2.08)	0.57 (0.24-1.33)	0.37 (0.06-2.24)
BMI at 9	1.13 (0.88-1.45)	0.89 (0.71-1.10)	0.89 (0.73-1.09)	0.69 (0.51-0.94)	0.79 (0.60-1.03)	Reference	**0.61 (0.48-0.79)**	0.96 (0.74-1.24)	0.74 (0.54-1.01)	0.87 (0.52-1.47)
BMI at 45	1.00 (0.93-1.07)	1.02 (0.96-1.08)	1.00 (0.94-1.06)	1.03 (0.96-1.11)	1.09 (1.01-1.17)	Reference	1.03 (0.97-1.10)	1.07 (1.00-1.14)	1.02 (0.95-1.10)	1.10 (0.97-1.25)
Breastfeeding	1.80 (0.83-3.94)	1.45 (0.77-2.71)	1.12 (0.60-2.10)	2.15 (0.99-4.68)	1.18 (0.58-2.41)	Reference	1.38 (0.69-2.73)	1.54 (0.70-3.37)	1.23 (0.53-2.86)	2.01 (0.44-9.13)
Household crowding	1.24 (0.56-2.75)	2.07 (1.10-3.90)	1.42 (0.75-2.70)	1.32 (0.59-2.94)	0.94 (0.44-2.03)	Reference	1.11 (0.56-2.19)	1.06 (0.47-2.42)	0.92 (0.38-2.21)	1.39 (0.31-6.19)
Preschool attendance	1.80 (0.65-4.96)	1.14 (0.44-2.92)	1.03 (0.42-2.56)	1.53 (0.50-4.74)	2.30 (0.88-5.97)	Reference	1.01 (0.36-2.82)	1.38 (0.45-4.19)	2.56 (0.86-7.65)	3.45 (0.38-31.0
Dog and cat exposure	2.49 (1.12-5.51)	1.42 (0.74-2.74)	0.84 (0.43-1.62)	1.16 (0.52-2.59)	1.13 (0.53-2.43)	Reference	1.11 (0.55-2.25)	0.81 (0.34-1.91)	0.87 (0.36-2.10)	0.38 (0.05-2.79)

Pairwise comparisons (each trajectory versus all the "average" trajectory) with Bonferroni-Holm method were performed. Analyses adjust for all the other factors (exposures) in the table. Odds ratio (OR) and 95% confidence intervals are reported in the table. Statistically significant associations are shown in bold ($p<0.05$ after Bonferroni-Holm method). See text for definitions. Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high). Odds ratios for BMI (and other continuous variables) are for a one-unit increase in these variables.

Table S14 Predictors of identified FVC trajectories – multivariable models using the average trajectory as the reference group

	Persistently high n=32	Always well above average n=109	Catch-up n=65	Always above average n=129	Average n=129	Catch-up II n=114	Accelerated decline n=115	Always well below average n=129	Persistently low n=43
Female (ref)									
Male	1.04 (0.44-2.47)	1.13 (0.58-2.19)	1.23 (0.54-2.80)	1.30 (0.71-2.37)	Reference	1.69 (0.88-3.24)	1.64 (0.79-3.41)	0.81 (0.43-1.51)	0.81 (0.35-1.89)
Childhood asthma	1.89 (0.52-6.87)	0.77 (0.22-2.74)	1.49 (0.43-5.21)	1.16 (0.43-3.16)	Reference	0.78 (0.24-2.50)	1.21 (0.36-4.10)	0.96 (0.33-2.79)	0.85 (0.23-3.20)
Childhood AHR	0.46 (0.10-2.19)	2.17 (0.69-6.84)	1.04 (0.31-3.49)	1.76 (0.70-4.45)	Reference	1.14 (0.39-3.30)	1.05 (0.31-3.54)	2.04 (0.77-5.42)	3.56 (1.11-11.4)
Atopy at 21	0.87 (0.34-2.22)	0.70 (0.34-1.43)	0.85 (0.37-1.94)	0.49 (0.25-0.95)	Reference	0.92 (0.45-1.88)	0.83 (0.37-1.84)	0.87 (0.43-1.73)	0.79 (0.31-2.02)
Parental asthma	0.92 (0.29-2.95)	2.40 (1.08-5.33)	0.84 (0.27-2.57)	1.14 (0.53-2.47)	Reference	1.27 (0.56-2.88)	1.19 (0.46-3.08)	1.21 (0.54-2.71)	1.29 (0.48-3.42)
Parental smoking	0.82 (0.32-2.11)	0.74 (0.36-1.51)	1.09 (0.45-2.66)	0.67 (0.35-1.25)	Reference	0.59 (0.29-1.20)	0.64 (0.29-1.40)	0.65 (0.33-1.26)	0.72 (0.29-1.79)
Tobacco smoked by 45	1.02 (0.97-1.07)	1.00 (0.96-1.04)	1.01 (0.97-1.06)	1.01 (0.98-1.04)	Reference	1.03 (1.00-1.07)	1.05 (1.01-1.09)	1.02 (0.99-1.05)	1.00 (0.95-1.05)
Childhood SES	1.05 (0.66-1.66)	0.97 (0.70-1.35)	1.06 (0.70-1.60)	1.09 (0.80-1.49)	Reference	1.21 (0.87-1.70)	0.90 (0.63-1.29)	1.08 (0.78-1.48)	1.01 (0.66-1.55)
Birth weight	1.23 (0.50-3.02)	1.07 (0.52-2.19)	0.71 (0.33-1.55)	0.70 (0.39-1.28)	Reference	1.06 (0.55-2.02)	1.42 (0.69-2.92)	0.87 (0.45-1.67)	0.47 (0.20-1.10)
BMI at 9	1.05 (0.77-1.43)	0.89 (0.70-1.13)	0.98 (0.74-1.29)	1.01 (0.83-1.22)	Reference	0.72 (0.56-0.92)	0.83 (0.66-1.05)	0.79 (0.64-0.97)	0.78 (0.57-1.05)
BMI at 45	0.97 (0.89-1.06)	1.01 (0.94-1.08)	0.92 (0.85-1.01)	1.05 (0.99-1.11)	Reference	1.00 (0.93-1.07)	**1.18 (1.10-1.26)**	1.01 (0.95-1.08)	1.03 (0.95-1.12)
Breastfeeding	2.43 (0.98-6.00)	1.76 (0.87-3.54)	2.19 (0.98-4.90)	1.76 (0.95-3.25)	Reference	1.62 (0.86-3.08)	**3.33 (1.62-6.84)**	1.34 (0.69-2.57)	1.51 (0.62-3.67)
Household crowding	0.77 (0.30-2.01)	0.91 (0.45-1.84)	0.52 (0.22-1.22)	0.92 (0.49-1.71)	Reference	0.84 (0.43-1.67)	1.19 (0.57-2.47)	0.64 (0.34-1.19)	1.25 (0.52-2.99)
Preschool attendance	1.91 (0.69-5.32)	1.20 (0.46-3.13)	1.01 (0.31-3.24)	0.94 (0.39-2.22)	Reference	1.45 (0.59-3.57)	1.26 (0.47-3.41)	1.20 (0.50-2.84)	1.69 (0.56-5.09)
Dog and cat exposure	2.07 (0.83-5.18)	1.12 (0.57-2.23)	1.24 (0.54-2.84)	1.09 (0.57-2.06)	Reference	0.69 (0.35-1.36)	0.85 (0.40-1.78)	1.36 (0.73-2.55)	0.72 (0.29-1.79)

Pairwise comparisons (each trajectory versus all the "average" trajectory) with Bonferroni-Holm method were performed. Analyses adjust for all the other factors (exposures) in the table. Odds ratio (OR) and 95% confidence interval are reported in the table. Statistically significant associations are shown in bold ($p<0.05$ after Bonferroni-Holm method). Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high). Odds ratios for BMI (and other continuous variables) are for a one-unit increase in these variables.

Table S15. Predictors of identified FEV_1/FVC trajectories – multivariable models using the average trajectory as the reference group

	Persistently high n=50	Always well above average n=128	Always above average n=142	Above average but with decline n=93	Average n=162	Decline during adulthood n=74	Always below average n=72	Accelerated decline n=46	Always well below average n=73	Persistently low n=25
Female (ref)										
Male	1.54 (0.63-3.76)	1.74 (0.95-3.19)	1.66 (0.93-2.95)	1.30 (0.62-2.70)	Reference	0.93 (0.43-2.00)	1.53 (0.69-3.40)	1.19 (0.45-3.14)	1.71 (0.74-3.96)	1.45 (0.33-6.29)
Childhood asthma	0.52 (0.09-3.12)	0.62 (0.20-1.91)	0.58 (0.21-1.60)	1.45 (0.45-4.66)	Reference	0.76 (0.22-2.70)	3.15 (0.99-10.0)	1.42 (0.40-4.98)	1.36 (0.45-4.08)	3.05 (0.87-10.7)
Childhood AHR	0.19 (0.03-1.12)	0.26 (0.09-0.80)	0.58 (0.24-1.40)	0.37 (0.11-1.29)	Reference	1.04 (0.34-3.25)	0.51 (0.16-1.69)	3.50 (1.09-11.2)	**8.58 (2.97-24.8)**	8.34 (1.81-38.6
Atopy at 21	1.67 (0.66-4.27)	0.87 (0.45-1.66)	0.67 (0.37-1.23)	0.72 (0.34-1.53)	Reference	1.06 (0.46-2.40)	0.85 (0.36-2.02)	0.34 (0.12-1.00)	0.42 (0.16-1.10)	2.08 (0.11-39.3)
Parental asthma	0.29 (0.08-1.04)	0.43 (0.20-0.91)	0.61 (0.30-1.21)	0.82 (0.37-1.85)	Reference	0.76 (0.31-1.84)	0.51 (0.20-1.34)	0.69 (0.23-2.01)	0.65 (0.23-1.87)	0.98 (0.26-3.66)
Parental smoking	0.67 (0.27-1.64)	0.57 (0.30-1.09)	0.86 (0.47-1.58)	0.65 (0.29-1.42)	Reference	0.68 (0.30-1.54)	0.40 (0.17-0.93)	0.52 (0.19-1.42)	1.26 (0.51-3.10)	0.62 (0.19-2.00)
Tobacco smoked by 45	1.03 (0.98-1.08)	0.99 (0.95-1.03)	0.99 (0.96-1.03)	**1.05 (1.02-1.09)**	Reference	1.05 (1.01-1.09)	1.00 (0.96-1.05)	**1.07 (1.03-1.12)**	1.03 (1.00-1.07)	1.00 (0.94-1.06)
Childhood SES	0.96 (0.66-1.40)	0.82 (0.61-1.10)	0.96 (0.75-1.23)	0.96 (0.69-1.35)	Reference	0.86 (0.59-1.25)	0.81 (0.56-1.17)	1.24 (0.77-2.01)	1.12 (0.72-1.72)	1.38 (0.79-2.43)
Birth weight	1.34 (0.52-3.47)	1.15 (0.62-2.12)	1.04 (0.56-1.94)	0.74 (0.36-1.52)	Reference	0.97 (0.49-1.94)	0.67 (0.31-1.45)	1.46 (0.57-3.75)	1.45 (0.63-3.34)	1.71 (0.39-7.50)
BMI at 9	0.74 (0.54-1.02)	0.89 (0.74-1.08)	0.90 (0.74-1.08)	0.73 (0.57-0.95)	Reference	0.72 (0.55-0.94)	0.83 (0.63-1.10)	0.69 (0.48-1.01)	0.93 (0.71-1.22)	1.10 (0.70-1.72)
BMI at 45	**0.86 (0.78-0.95)**	0.99 (0.94-1.04)	0.98 (0.94-1.03)	0.95 (0.89-1.01)	Reference	0.91 (0.85-0.98)	0.99 (0.92-1.06)	0.92 (0.85-1.00)	0.89 (0.82-0.97)	0.99 (0.92-1.07)
Breastfeeding	1.79 (0.70-4.60)	0.99 (0.53-1.86)	1.00 (0.57-1.77)	1.17 (0.55-2.46)	Reference	1.24 (0.56-2.76)	0.37 (0.15-0.91)	0.60 (0.21-1.75)	1.34 (0.56-3.19)	1.73 (0.47-6.38)
Household crowding	1.15 (0.45-2.93)	1.50 (0.79-2.83)	0.97 (0.54-1.76)	1.93 (0.91-4.08)	Reference	1.67 (0.74-3.79)	0.83 (0.36-1.94)	0.68 (0.23-2.03)	0.60 (0.24-1.52)	0.87 (0.20-3.74)
Preschool attendance	0.62 (0.19-2.02)	1.07 (0.48-2.41)	0.67 (0.30-1.53)	0.74 (0.28-1.91)	Reference	0.67 (0.23-1.94)	2.18 (0.87-5.47)	0.65 (0.18-2.36)	0.15 (0.03-0.78)	0.40 (0.04-3.80)
Dog and cat exposure	2.14 (0.86-5.29)	1.55 (0.81-2.96)	1.14 (0.62-2.08)	1.53 (0.73-3.18)	Reference	0.81 (0.35-1.90)	1.90 (0.82-4.38)	0.64 (0.23-1.76)	1.15 (0.48-2.78)	1.01 (0.27-3.71)

Pairwise comparisons (each trajectory versus all the "average" trajectory) with Bonferroni-Holm method were performed. Analyses adjust for all the other factors (exposures) in the table. Odds ratio (OR) and 95% confidence interval are reported in the table. Statistically significant associations are shown in bold ($p<0.05$ after Bonferroni-Holm method). Odds ratios adjust for all other variables. Birth weight in kg. BMI in kg/m^2. Tobacco smoked in pack-years. Childhood SES on a 6-point scale (1=high). Odds ratios for BMI (and other continuous variables) are for a one-unit increase in these variables.

Figure S1 Directed Acyclic Graph

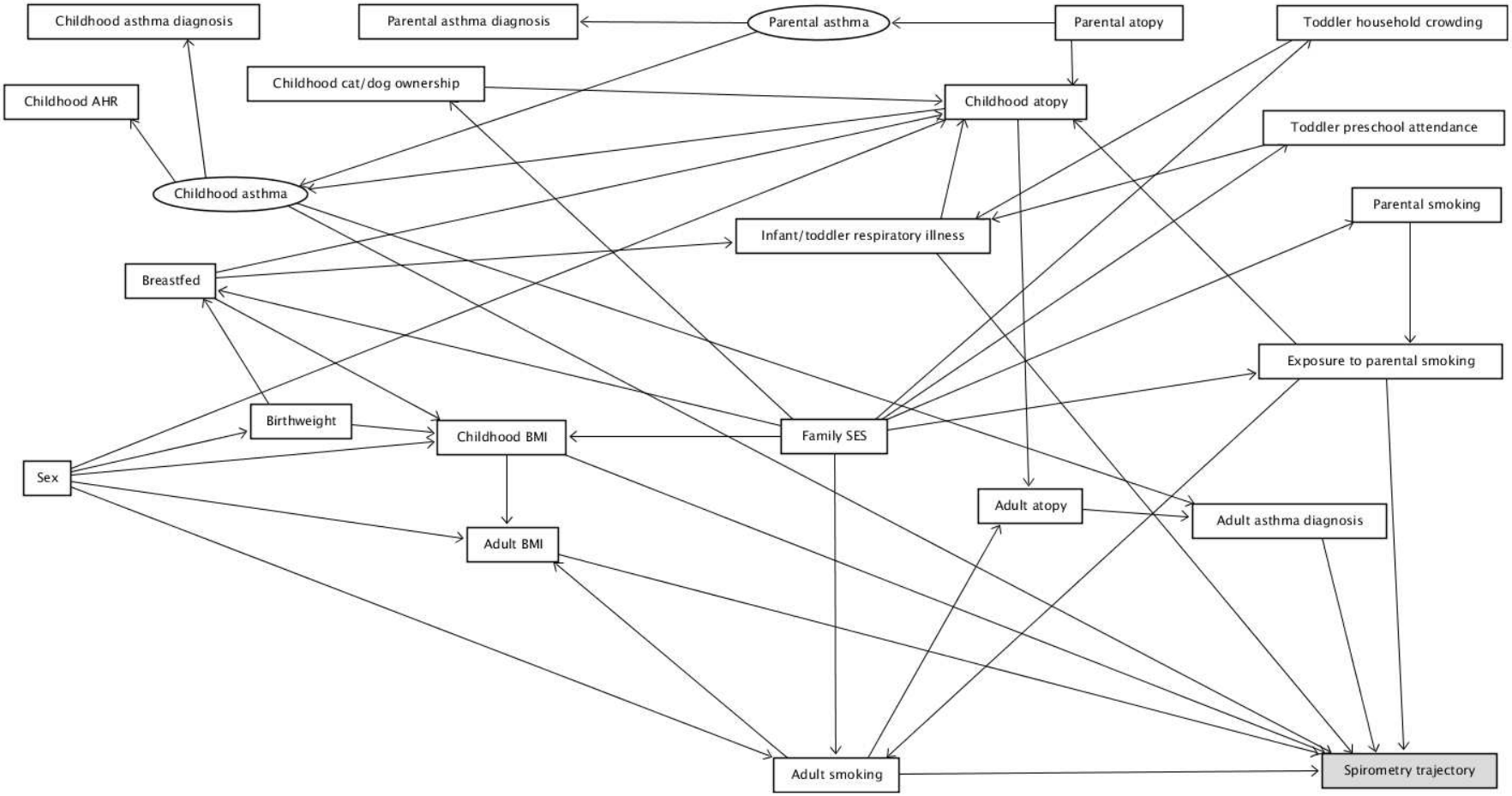
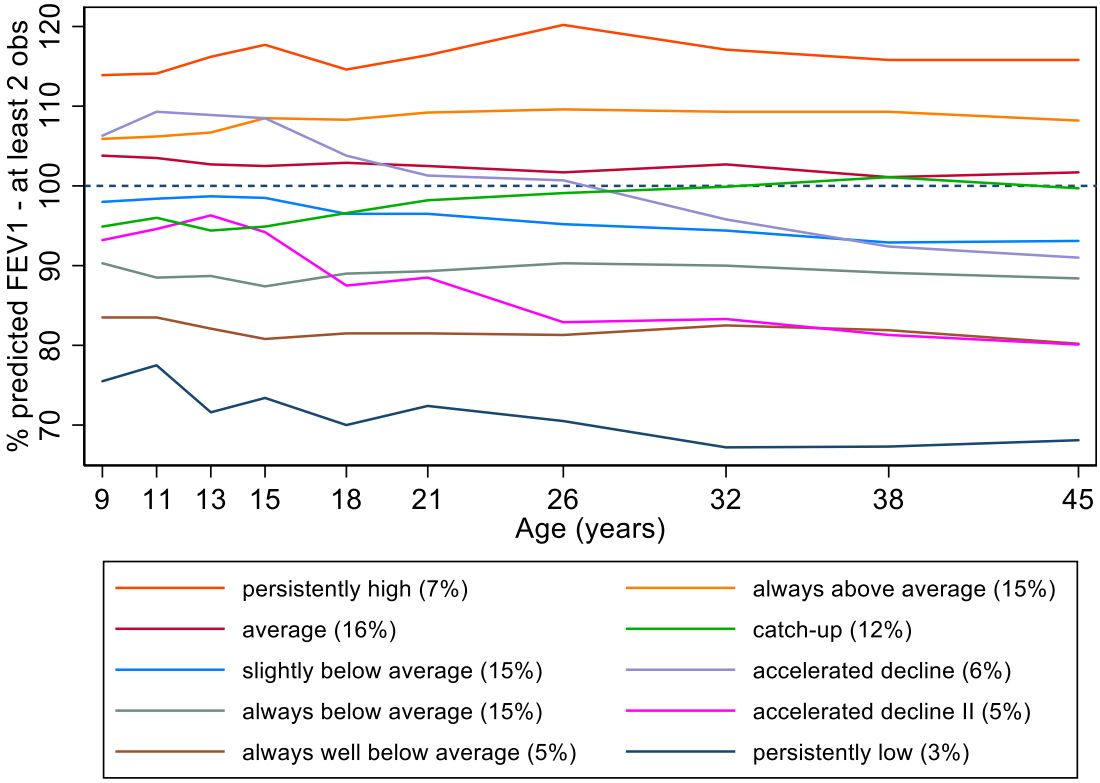
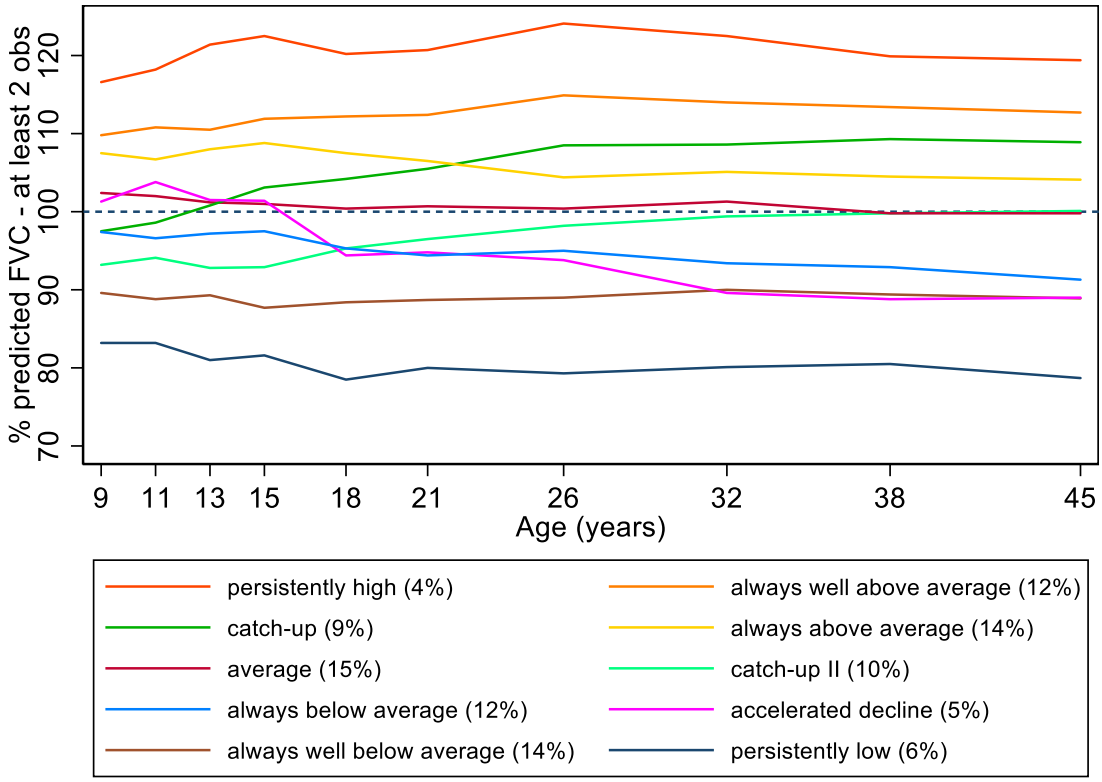


Figure S2 – Distinct trajectories of lung function from age 9 to 45 years based on participants (n=1,008) with at least two spirometry measures over the period




% predicted FVC - at least 2 obs
70
80
90
100
110
120
9
11
13
15
18
21
26
32
38
45
Age (years)
persistently high (4%)
always well above average (12%)
catch-up (9%)
always above average (14%)
average (15%)
catch-up II (10%)
always below average (12%)
accelerated decline (5%)
always well below average (14%)
persistently low (6%)

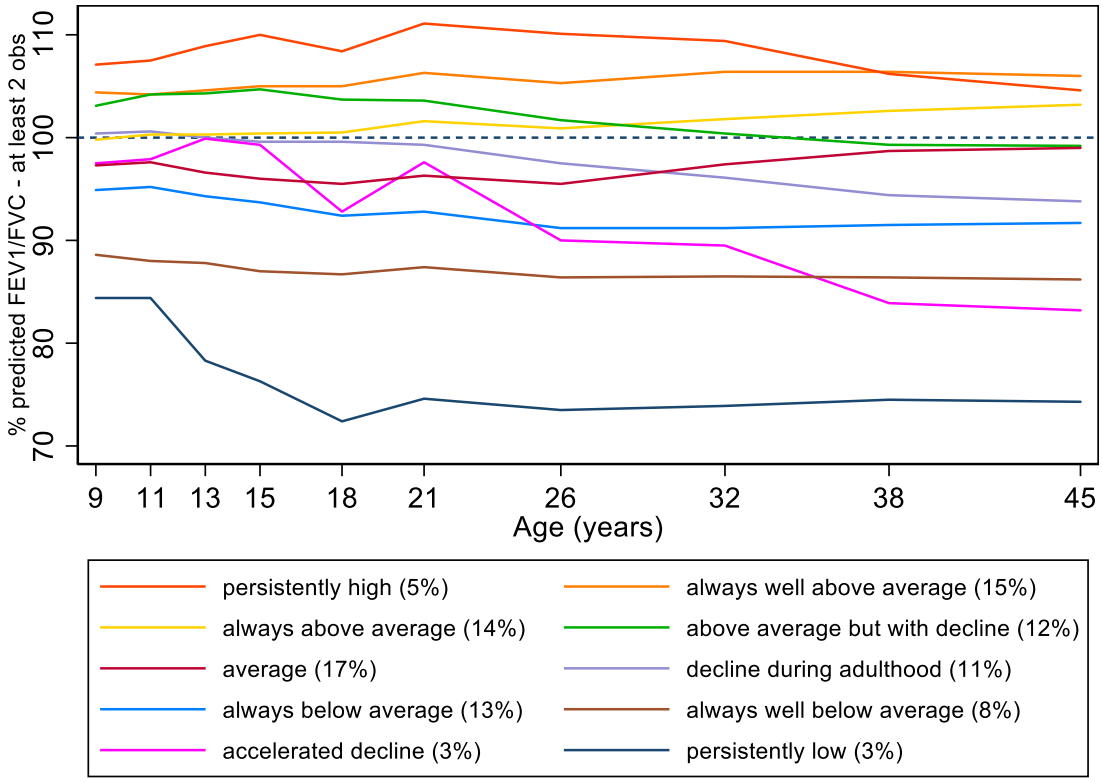
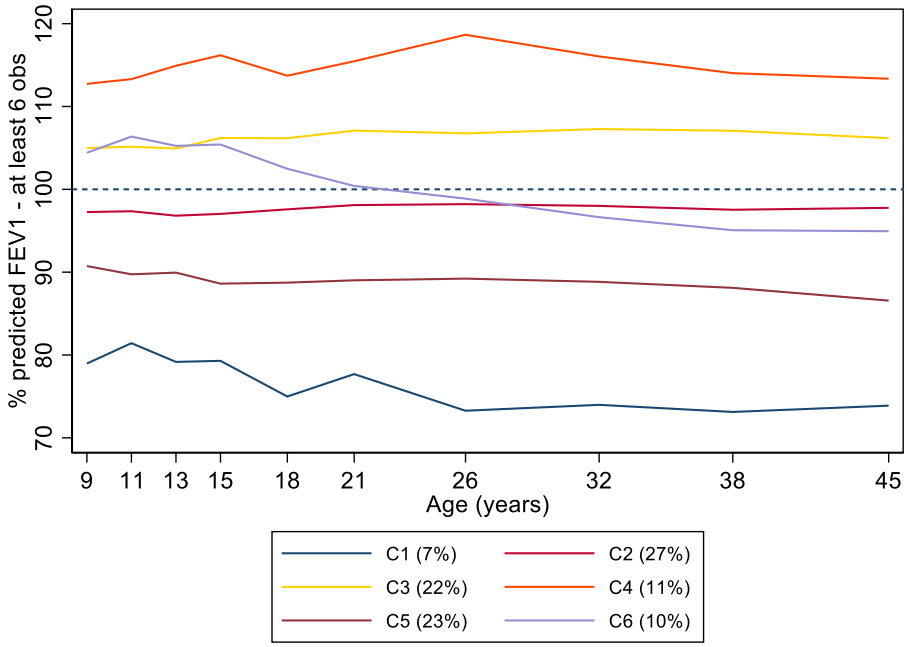
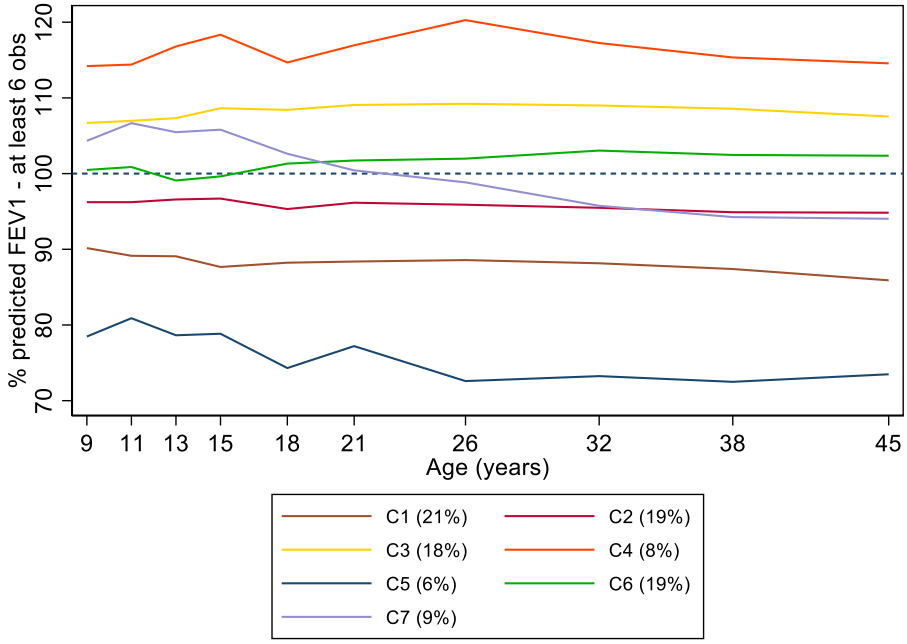

% predicted FEV1/FVC - at least 2 obs
70
80
90
100
110
9
11
13
15
18
21
26
32
38
45
Age (years)
persistently high (5%)
always well above average (15%)
always above average (14%)
above average but with decline (12%)
average (17%)
decline during adulthood (11%)
always below average (13%)
always well below average (8%)
accelerated decline (3%)
persistently low (3%)

Figure S3 – Distinct trajectories of FEV_1 from age 9 to 45 years, for models with fewer classes

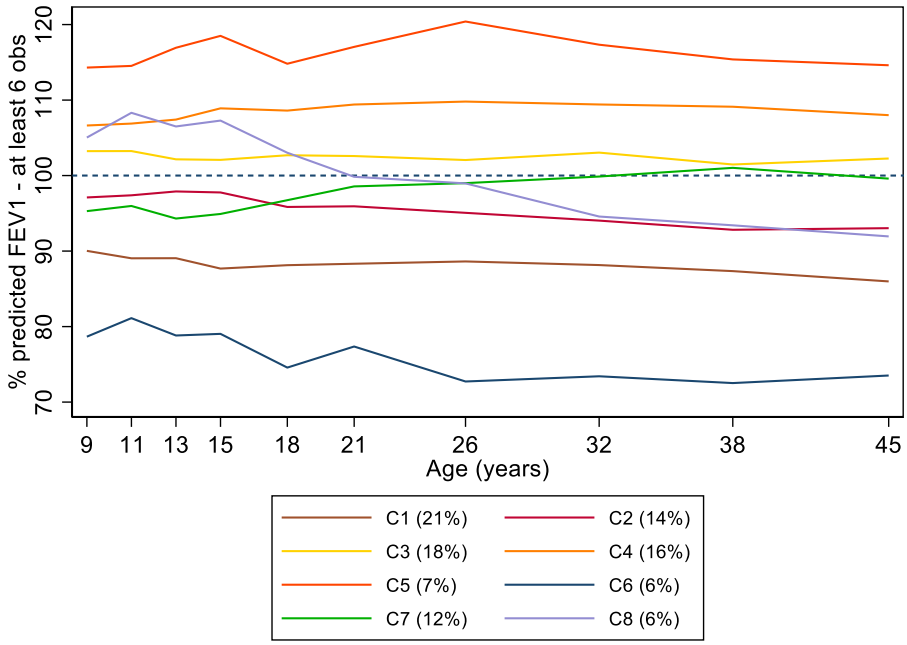
6-class model



7-class model



8-class model



9-class model

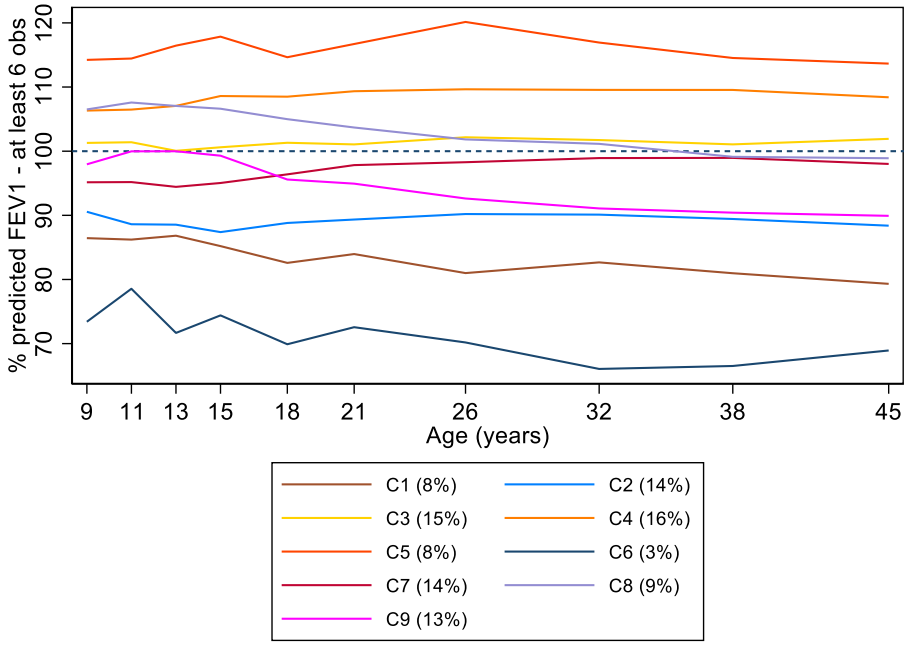
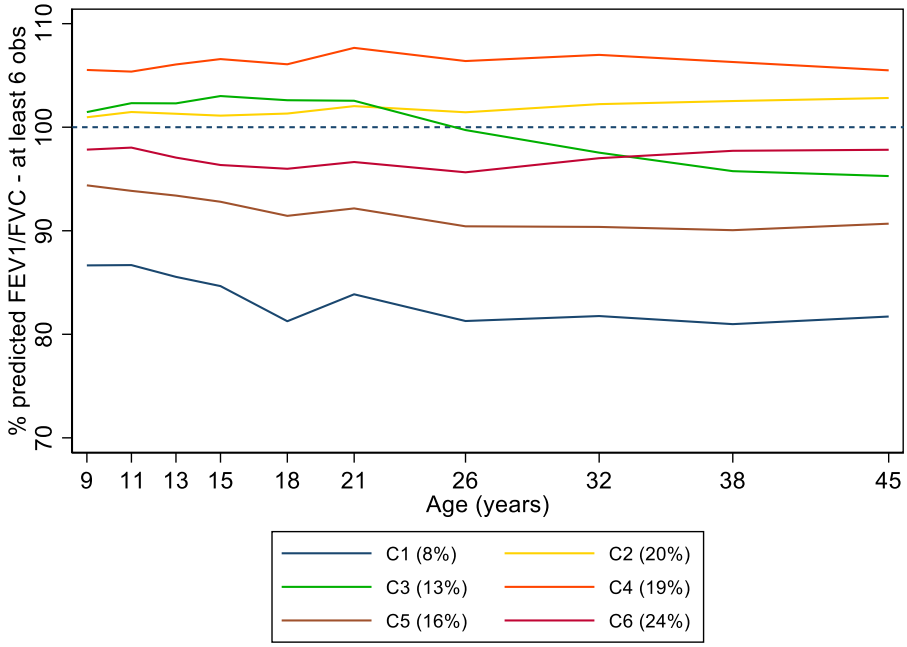
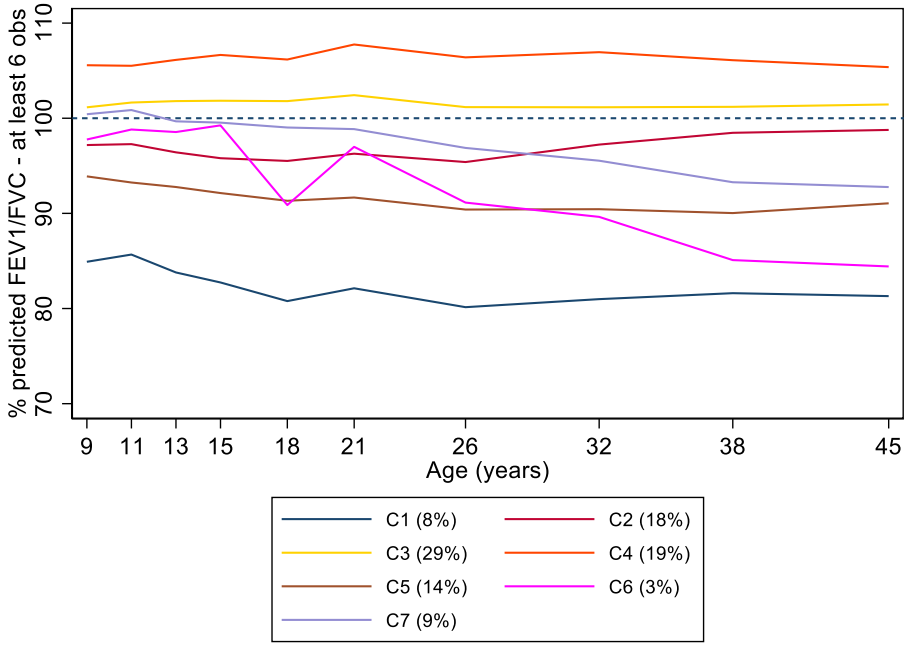


Figure S4 – Distinct trajectories of FEV_1/FVC from age 9 to 45 years, for models with fewer classes

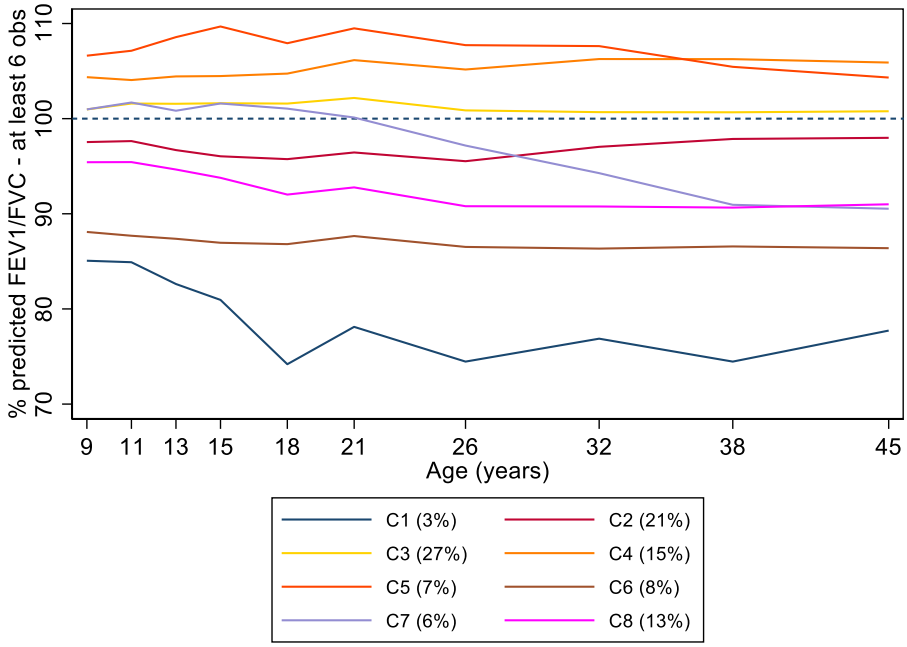
6-class model



7-class model



8-class model



9-class model

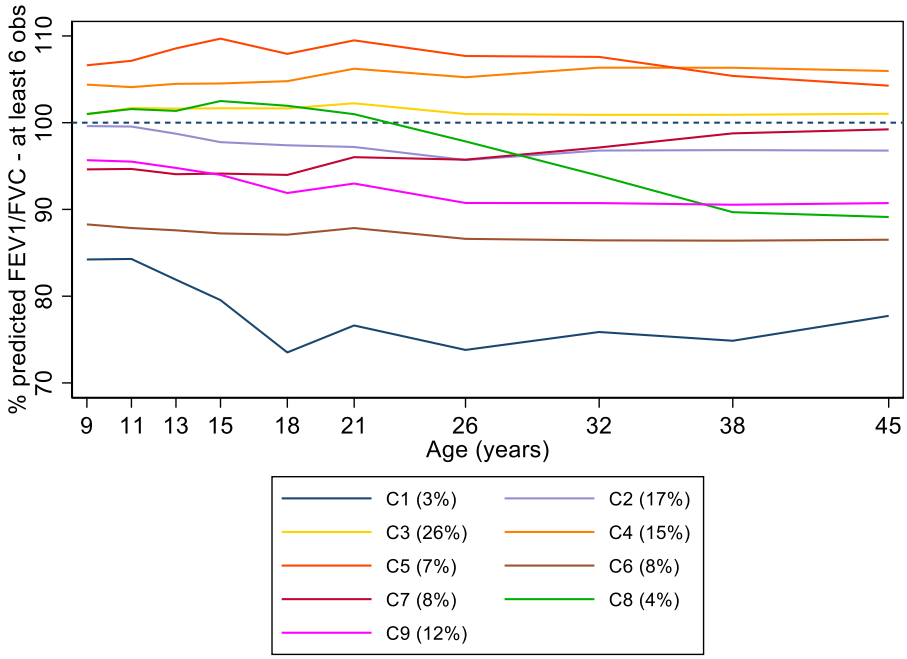
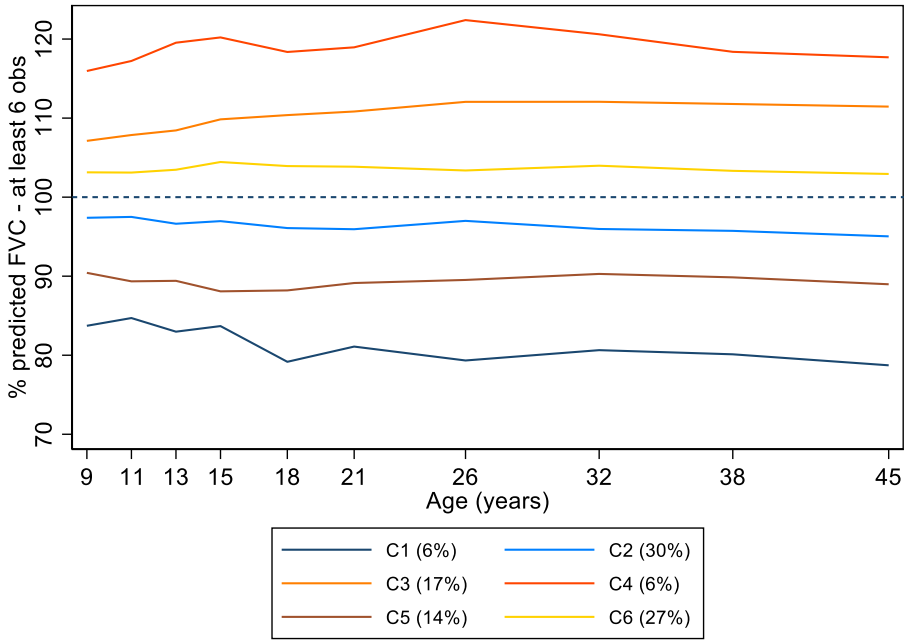
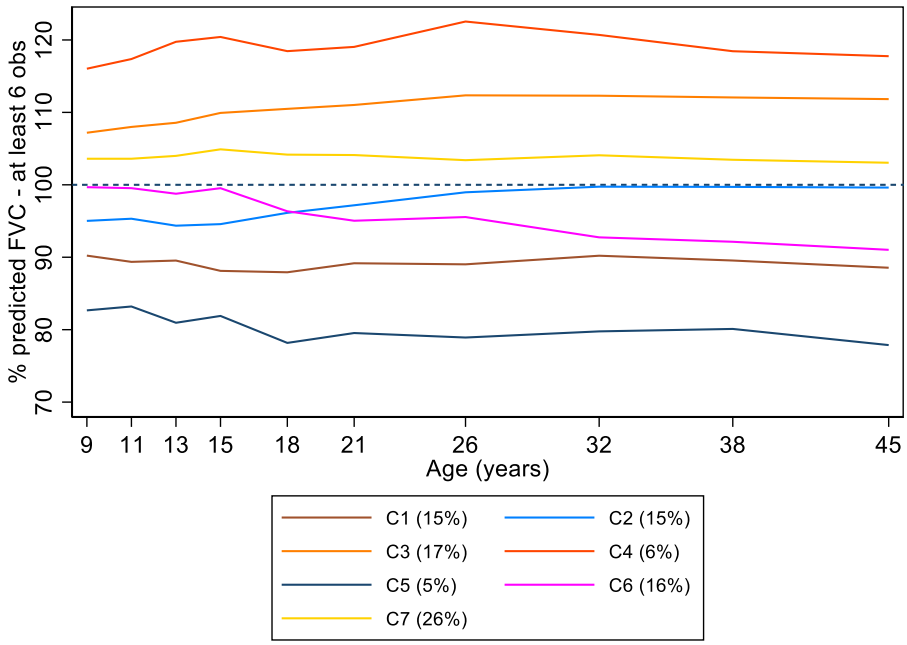


Figure S5 – Distinct trajectories of FVC from age 9 to 45 years, for models with fewer classes

6-class model



7-class model



8-class model

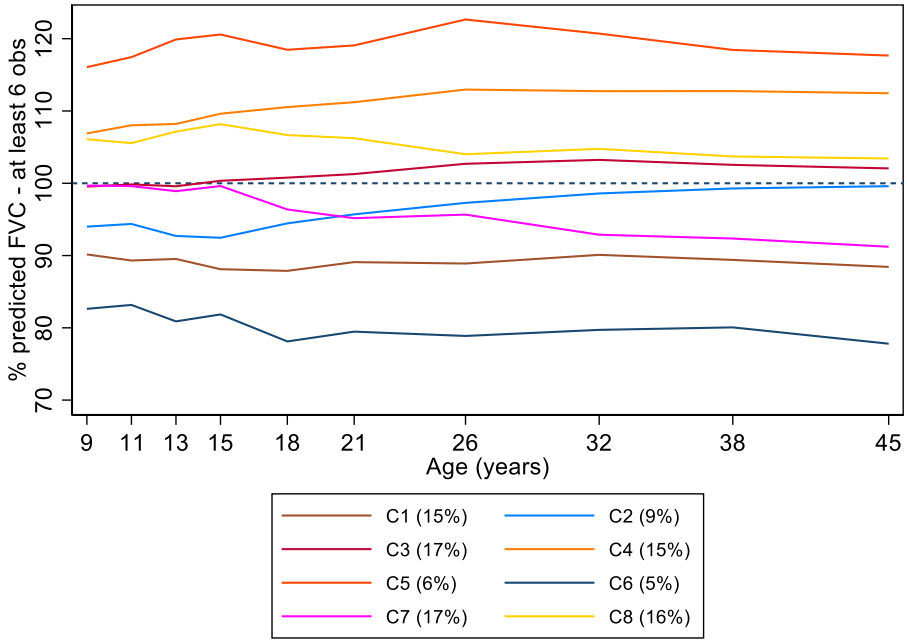


Figure S6. Heatmap showing overlap between trajectories of FEV_1 (rows) and FEV_1/FVC (columns) with darker shades for higher counts. Numbers indicate number of participants.

FEV_1/FVC trajectories

FEV_1 trajectories	Persistently high	Always well above average	Always above average	Above average but with decline	Average	Decline during adulthood	Always below average	Accelerated decline	Always well below average	Persistently low
Persistently high	8	15	13	8	9	4	1	3	2	0
Always well above average	11	25	39	12	19	11	8	1	3	0
Always above average	6	26	19	9	35	11	6	1	4	0
Catch-up	3	15	16	9	10	2	8	1	7	0
Accelerated decline	7	8	9	17	11	16	4	6	3	1
Average	6	21	19	16	28	16	18	4	9	1
Always below average	6	10	21	7	19	7	11	3	14	3
Accelerated decline II	2	1	2	9	17	6	9	14	9	4
Always well below average	1	7	4	5	13	1	6	8	15	3
Persistently low	0	0	0	1	1	0	1	5	7	13

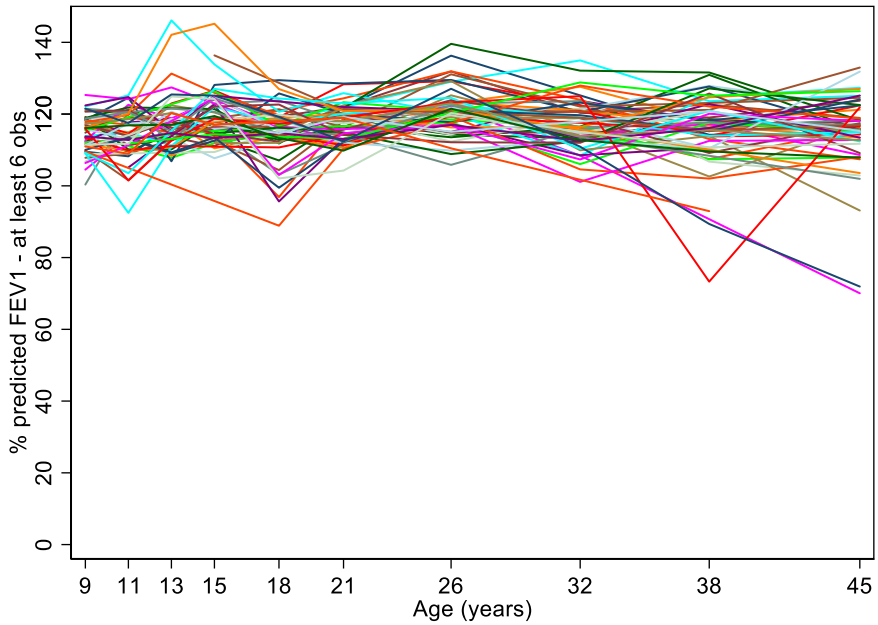
Figure S7. Heatmap showing overlap between trajectories of FVC (rows) and FEV_1/FVC (columns) with darker shades for higher counts. Numbers indicate number of participants.

FEV_1/FVC trajectories

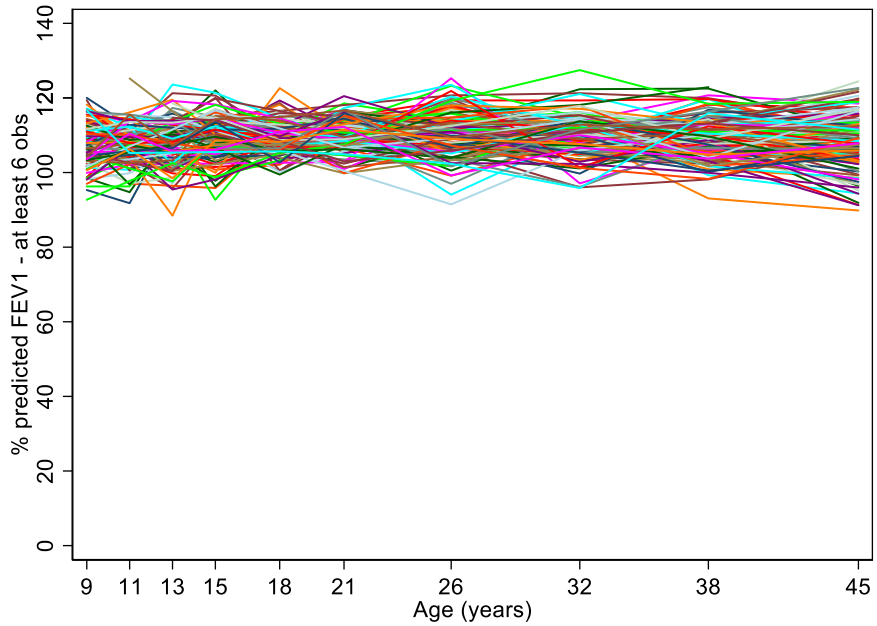
FVC trajectories	Persistently high	Always well above average	Always above average	Above average but with decline	Average	Decline during adulthood	Always below average	Accelerated decline	Always well below average	Persistently low
Persistently high	1	1	3	1	7	3	6	2	7	1
Always well above average	3	10	15	8	25	12	10	4	16	6
Catch-up	4	6	14	6	7	9	7	6	6	0
Always above average	4	17	24	9	29	9	18	3	11	5
Average	6	16	21	16	30	19	7	4	10	0
Catch-up II	4	18	18	20	16	8	10	11	9	0
Accelerated decline	11	24	19	9	20	7	6	7	3	9
Always well below average	11	27	24	18	23	7	6	5	8	0
Persistently low	6	9	4	6	5	0	2	4	3	4

Figure S8 – Individual FEV_1 trajectories (one line per participant) from age 9 to 45 years within each identified FEV_1 trajectory in the main analysis

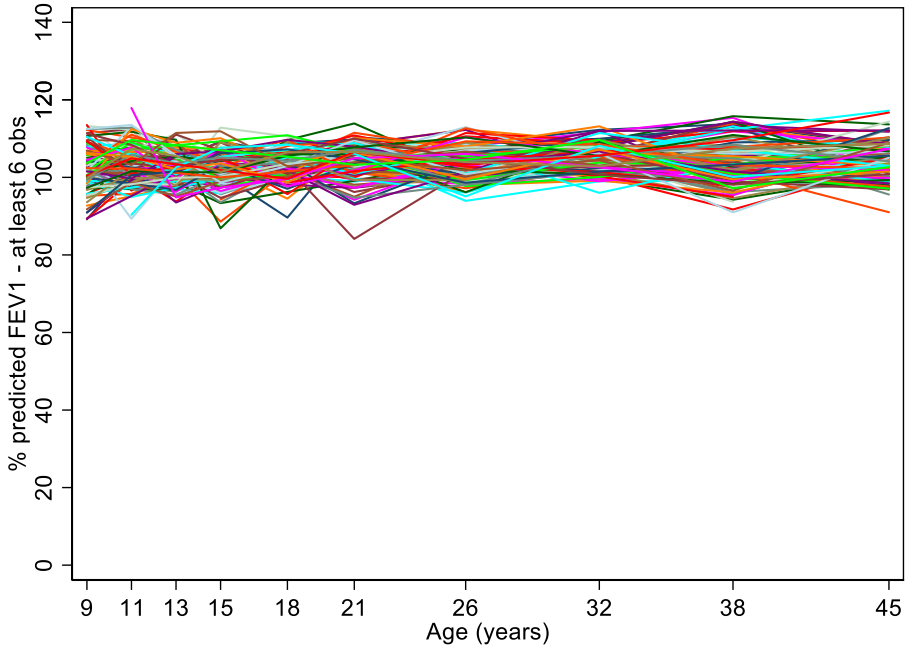
Persistently high (n=63)



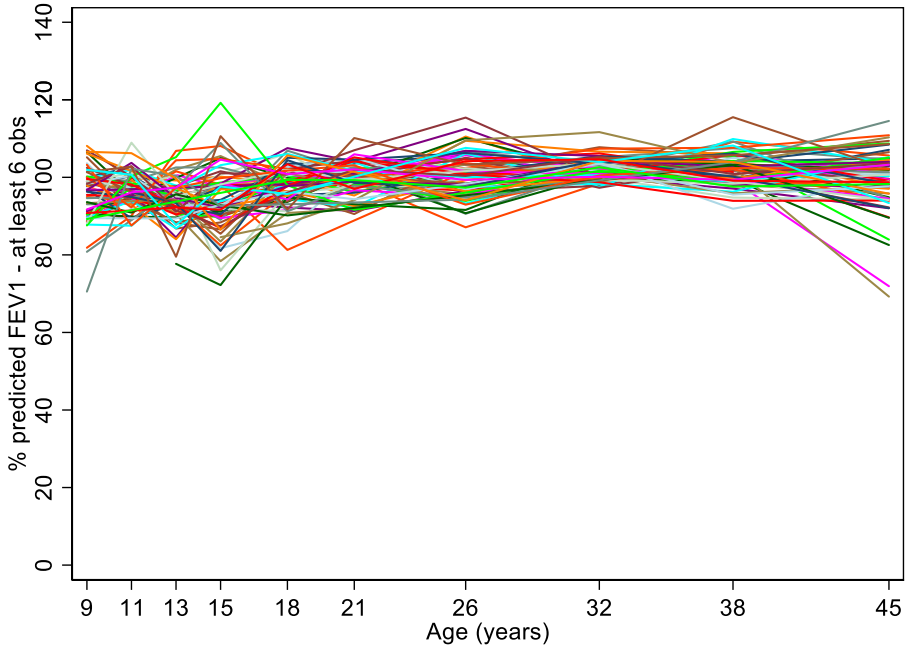
Always well above average (n=129)



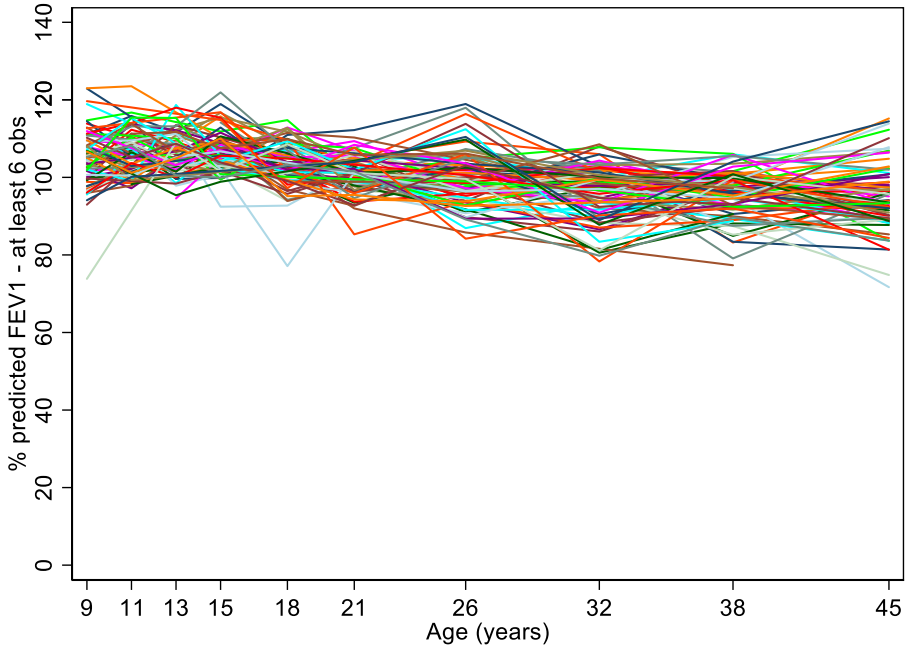
Always above average (n=117)



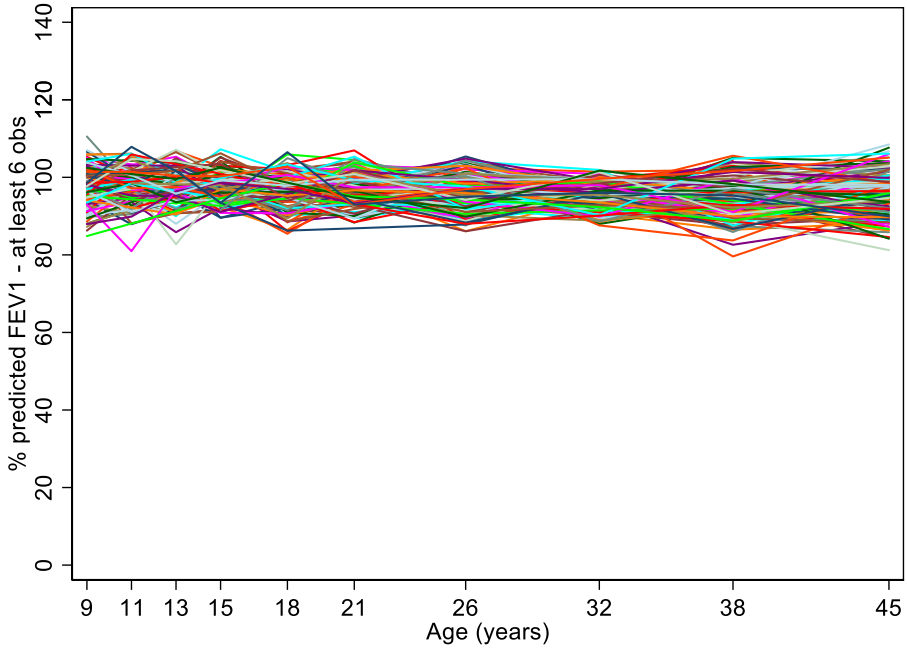
Catch-up (n=71)



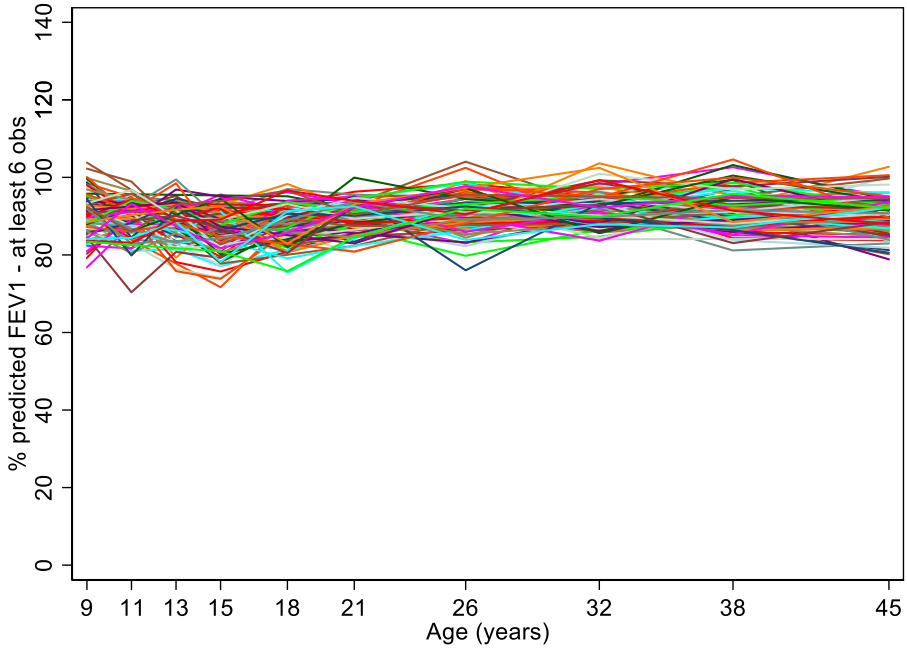
Accelerated decline (n=82)



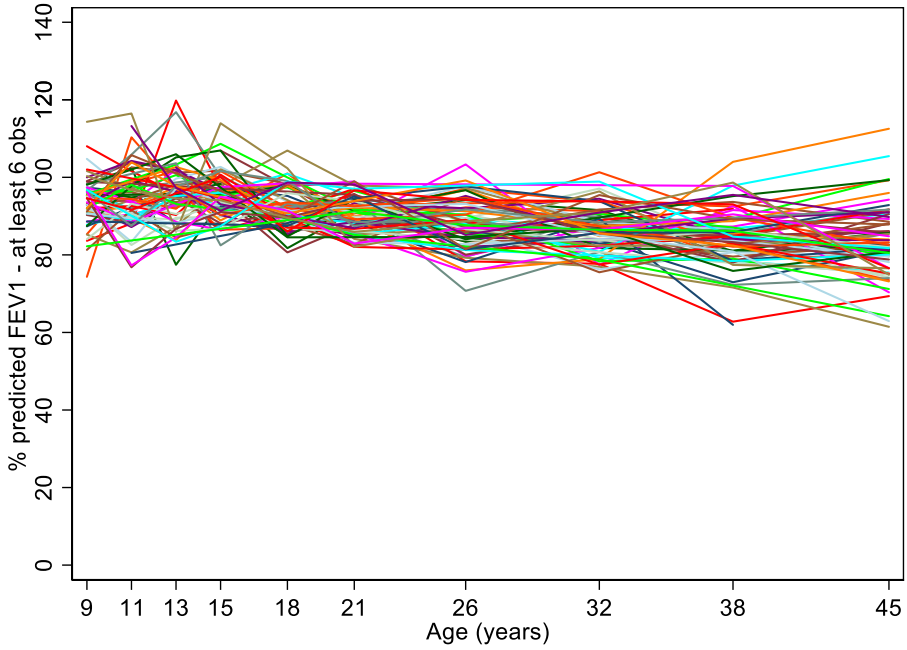
Average (n=138)



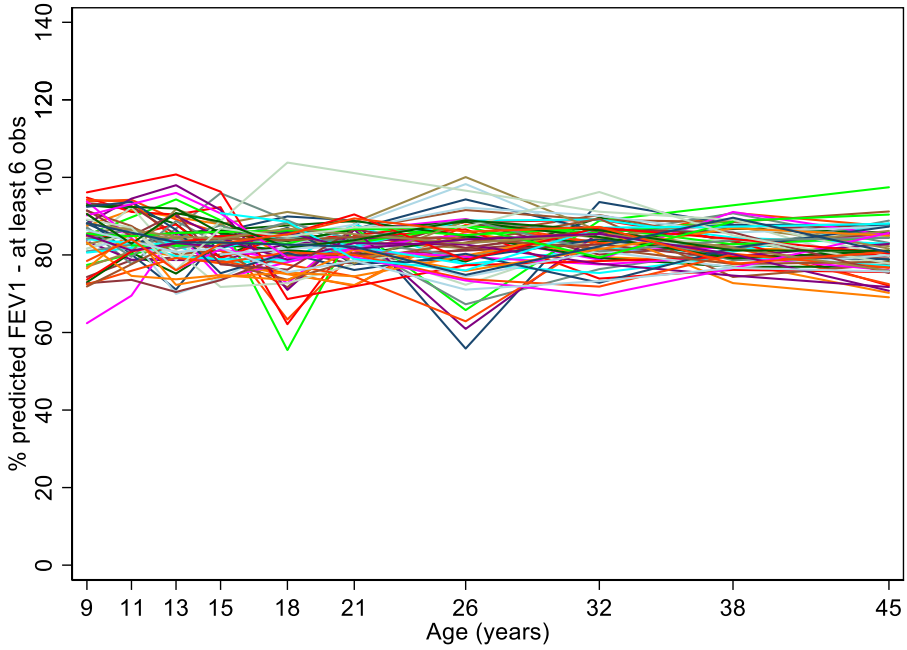
Always below average (n=101)



Accelerated decline II (n=73)



Always well below average (n=63)



Persistently low (n=28)

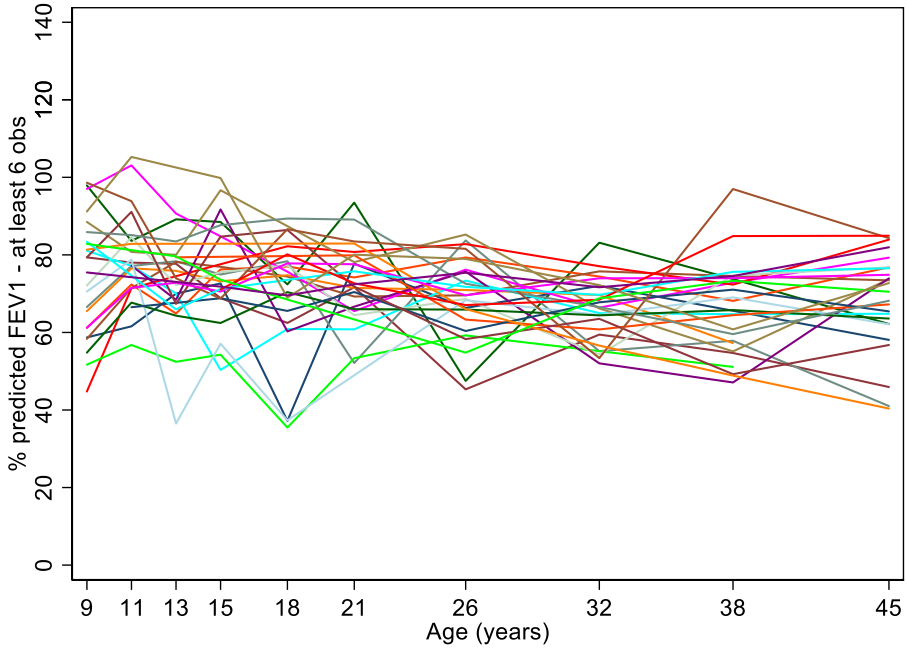
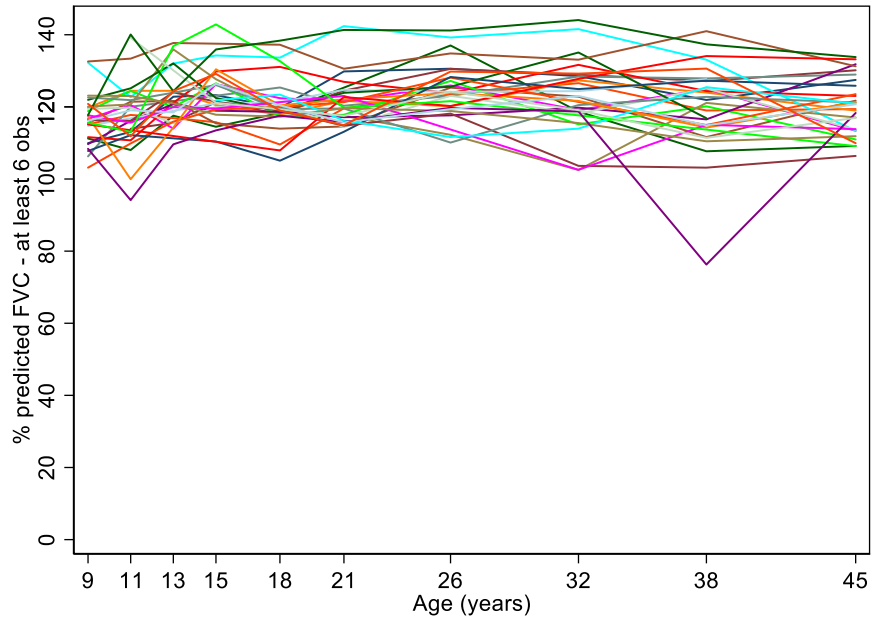
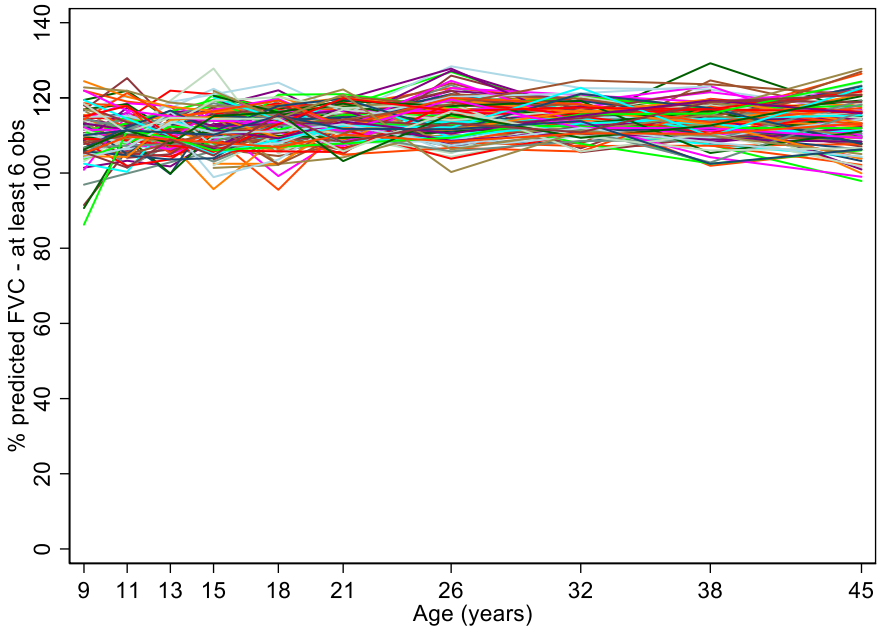


Figure S9– Individual FVC trajectories (one line per participant) from age 9 to 45 years within each identified FVC trajectory in the main analysis

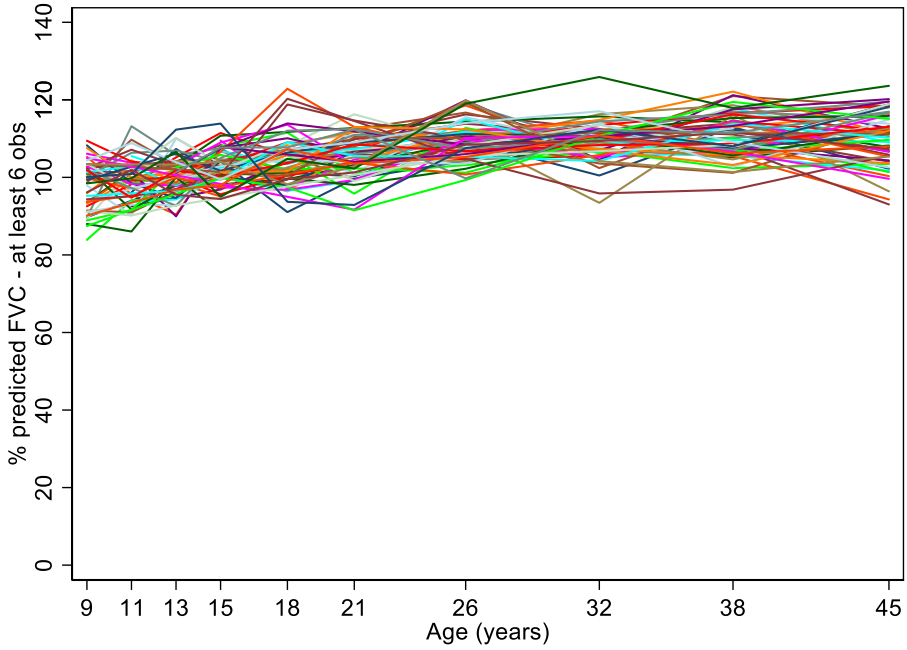
Persistently high (n=32)



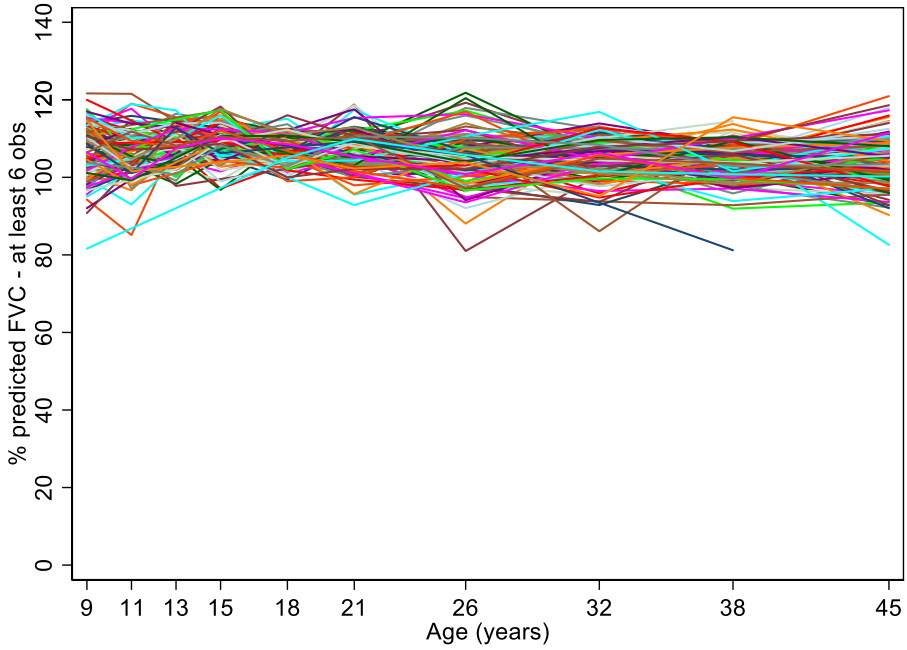
Always well above average (n=109)



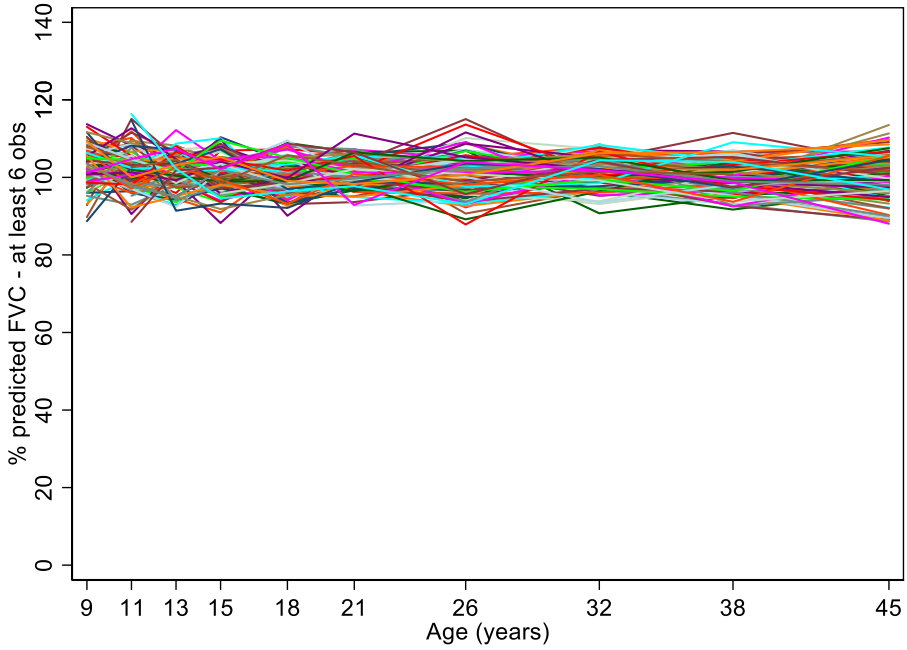
Catch-up (n=65)



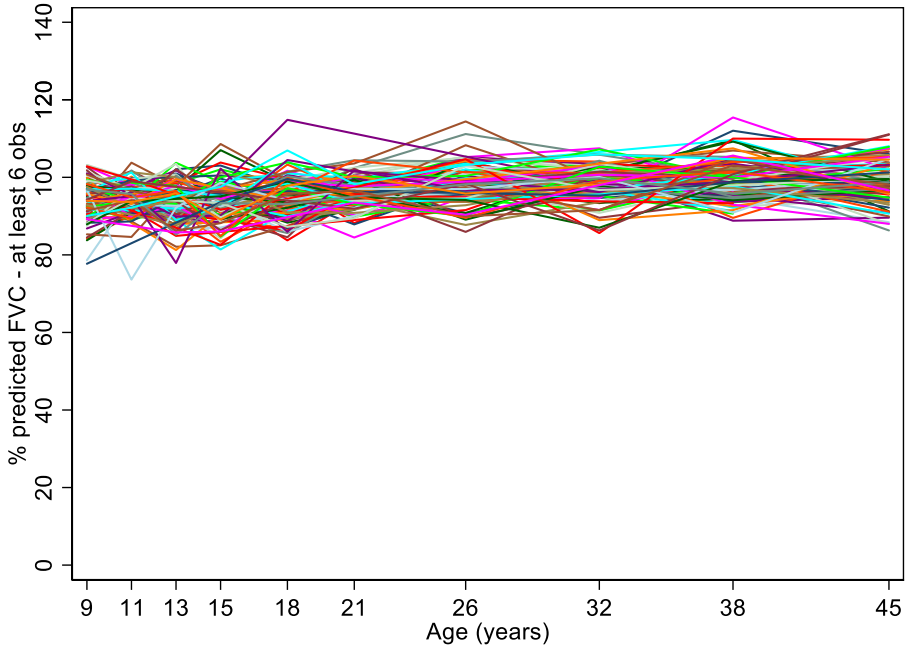
Always above average (n=129)



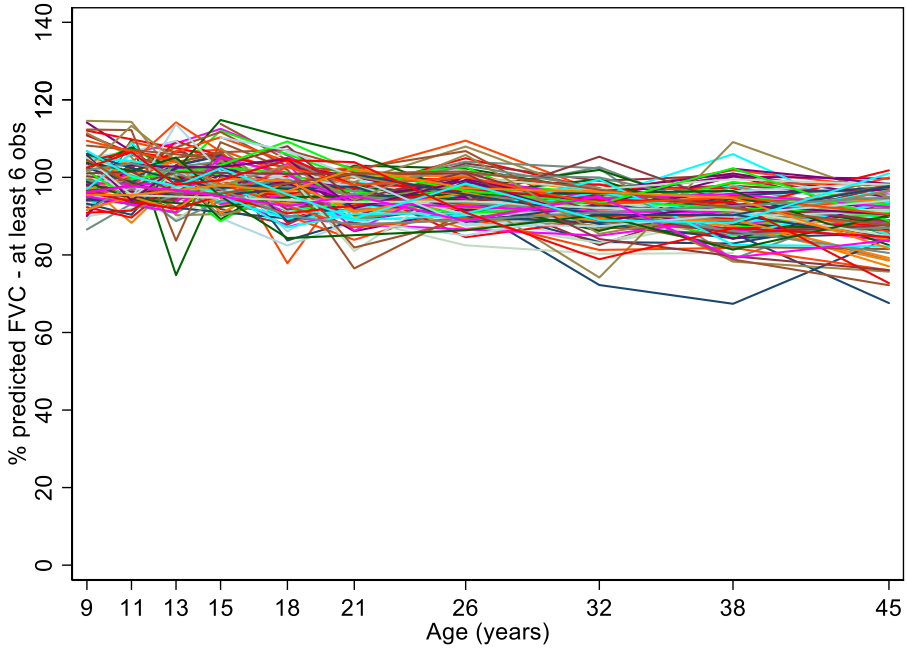
Average (n=129)



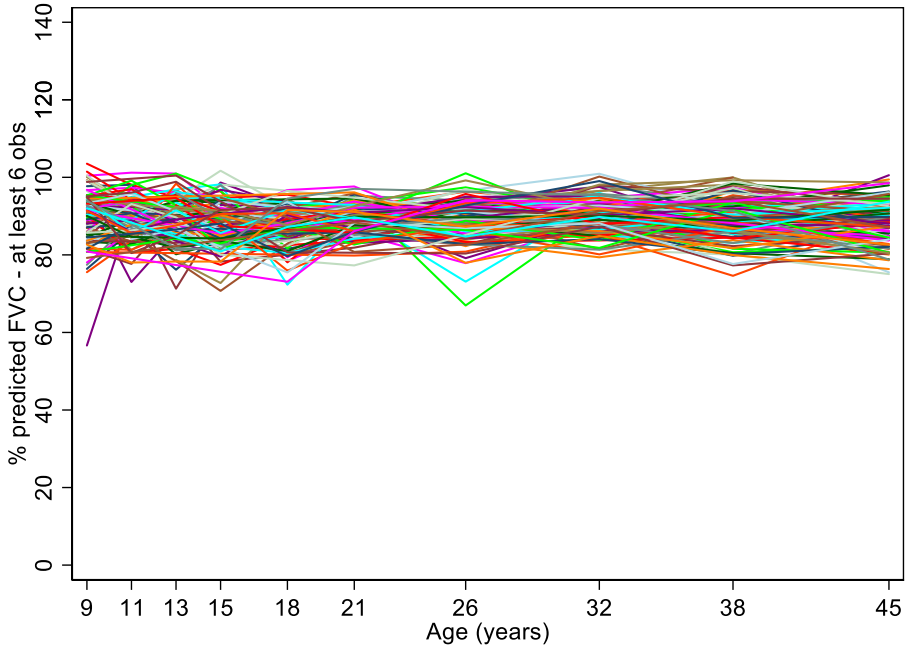
Catch-up II (n=114)



Accelerated decline (n=115)



Always well below average (n=129)



Persistently low (n=43)

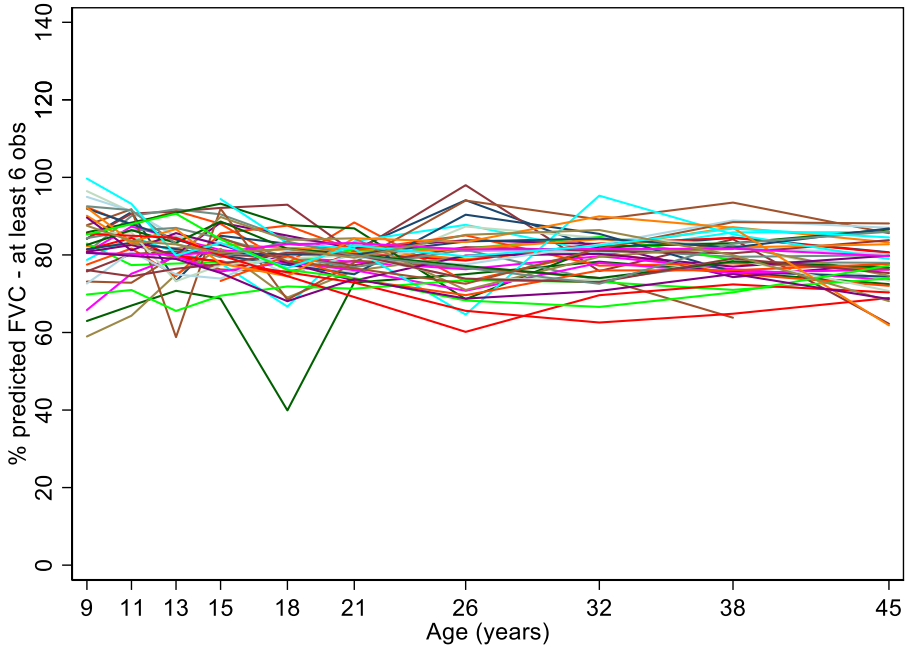
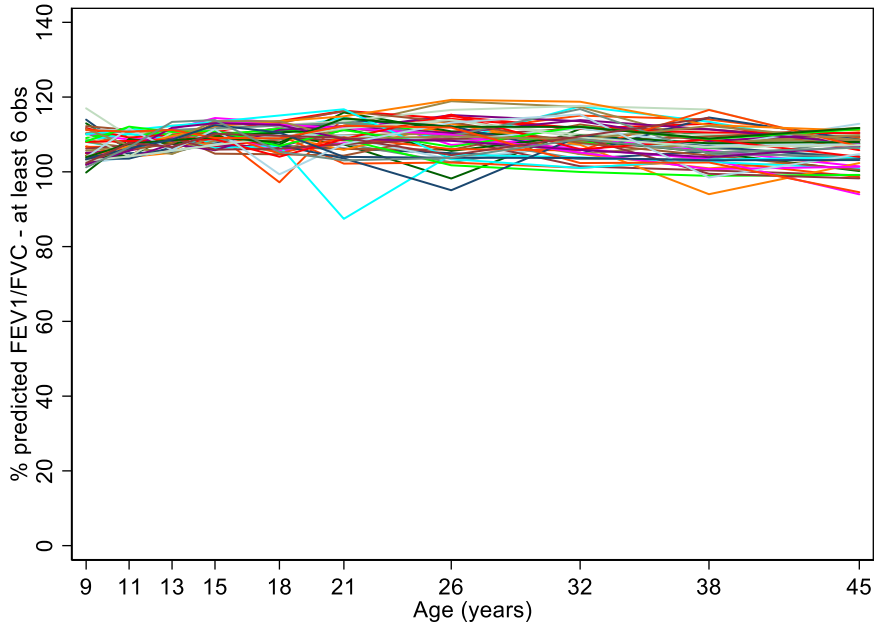
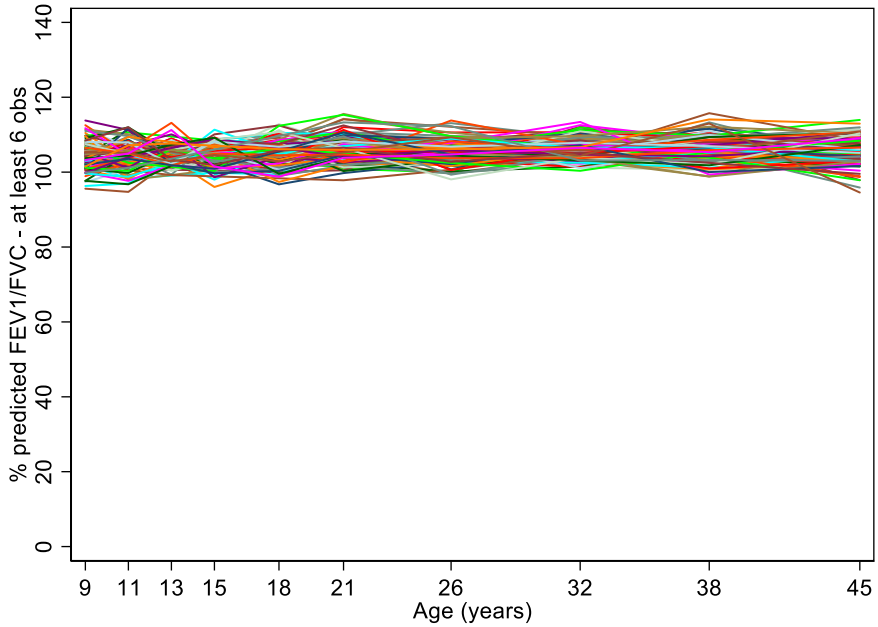


Figure S10 – Individual FEV_1/FVC trajectories (one line per participant) from age 9 to 45 years within each identified FEV_1/FVC trajectory in the main analysis

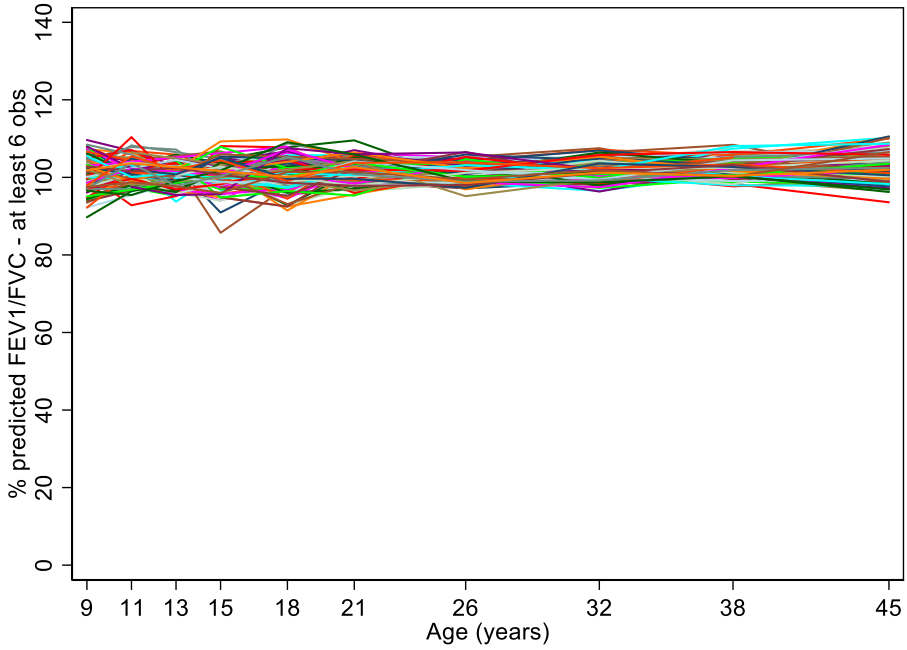
Persistently high (n=50)



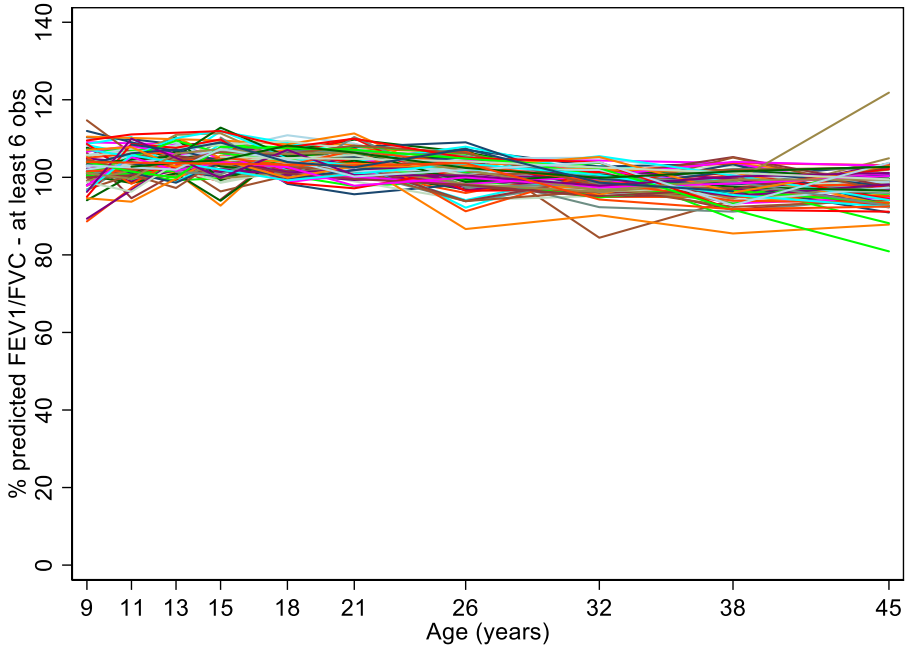
Always well above average (n=128)



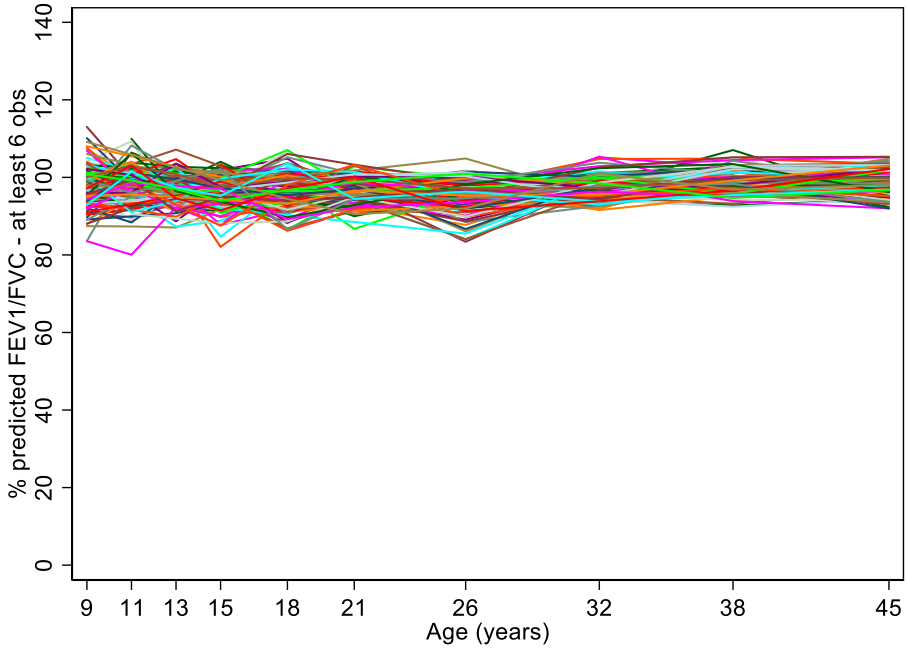
Always above average (n=142)



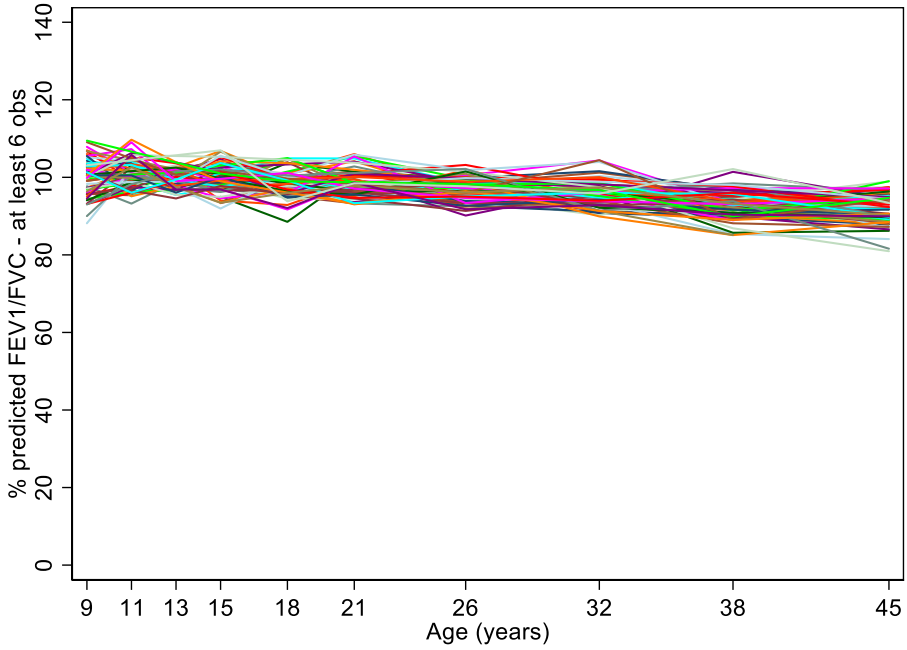
Above average but with decline (n=93)



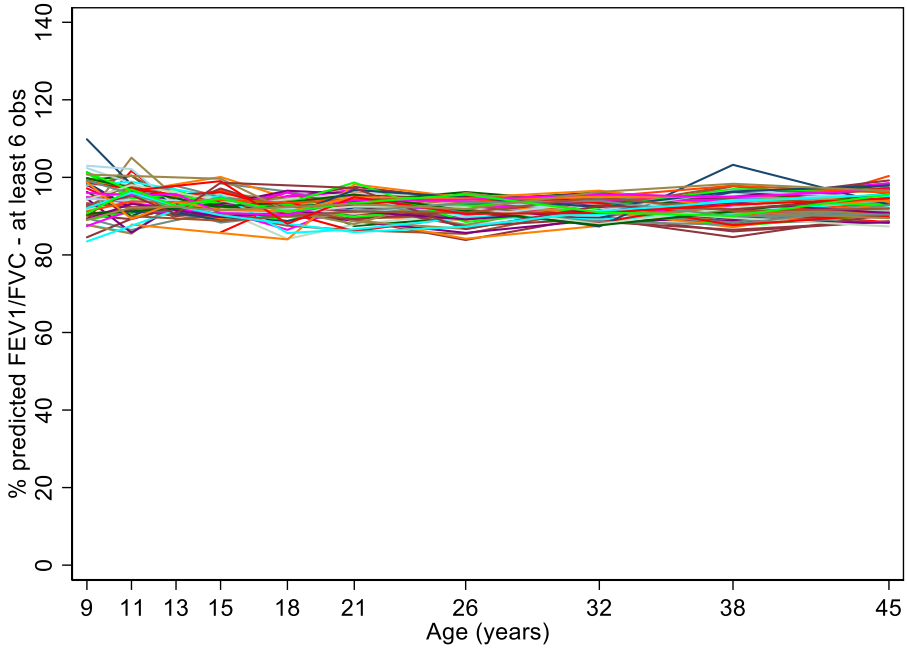
Average (n=162)



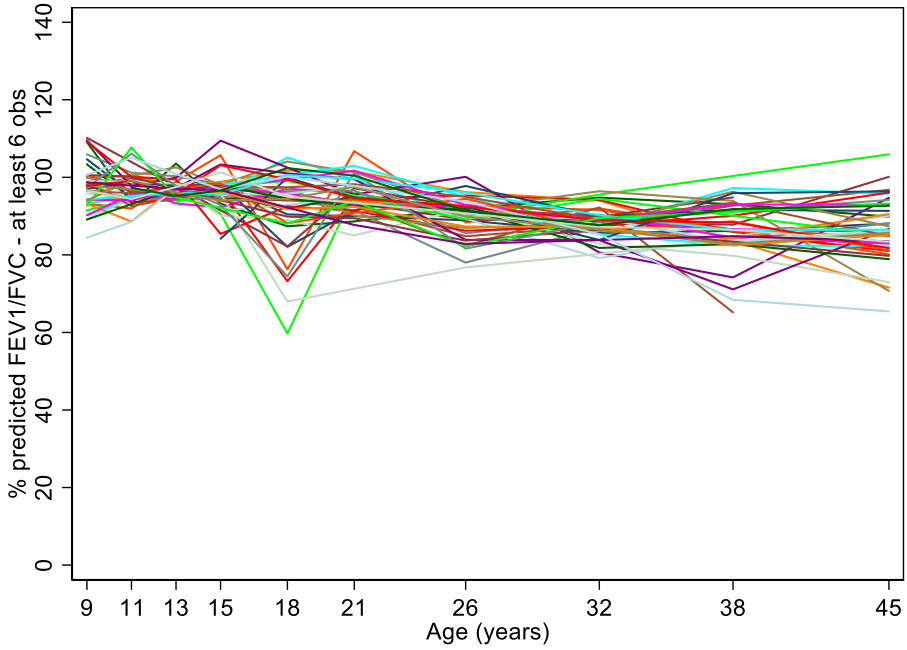
Decline during adulthood (n=74)



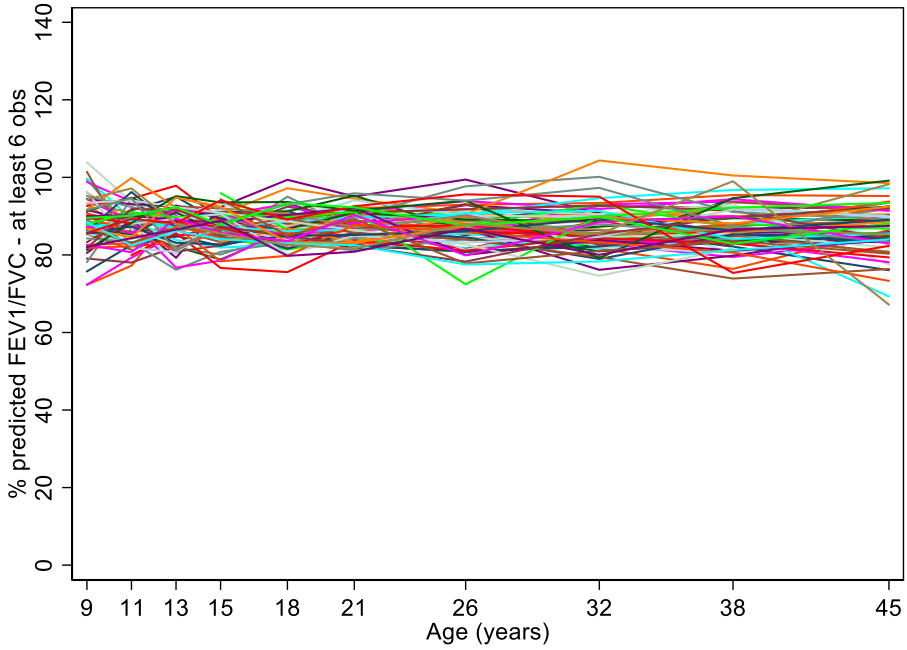
Always below average (n=72)



Accelerated decline (n=46)



Always well below average (n=73)



Persistently low (n=25)