

Research Article

Aging-Related Considerations When Evaluating the Forced Expiratory Volume in 1 Second (FEV1) Over Time

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Abstract

Background: Forced expiratory volume in 1 second (FEV1) over time is commonly expressed in liters and percent predicted (%Pred), or alternatively in L/m³ and Z-scores—which approach is more clinically meaningful has not been evaluated. Because it uniquely accounts for the effect of aging on FEV1 and spirometric performance, we hypothesized that the Z-score approach is more clinically meaningful, based on associations between cardiopulmonary predictors and FEV1 over time.

Methods: Using linear mixed-effects models and data from the Baltimore Longitudinal Study on Aging, including 501 white participants aged 40–95 who had completed at least three longitudinal spirometric assessments, we evaluated the associations between cardiopulmonary predictors (obesity, smoking status, hypertension, chronic bronchitis, diabetes mellitus, and myocardial infarction) and FEV1 over time, in liters, %Pred, L/m³, and Z-scores.

Results: Mean baseline values for FEV1 were 3.240 L, 96.4%Pred, 0.621 L/m³, and –0.239 as a Z-score (40.6th percentile). The annual decline in FEV1 was 0.040 L, 0.234 %Pred, 0.007 L/m³, and 0.008 Z-score units. Baseline age was associated with FEV1 over time in liters and L/m³ ($p < .001$), and included a time interaction for %Pred ($p < .001$), but was not associated with Z-scores ($p = .933$). The associations of cardiopulmonary predictors with FEV1 over time were all significant when using Z-scores ($p < .05$), but varied for other methods of expressing FEV1.

Conclusion: A Z-score approach is more clinically meaningful when evaluating FEV1 over time, as it accounted for the effect of aging and was more frequently associated with multiple cardiopulmonary predictors.

Keywords: Aging—Spirometry—Lung diseases—Cardiovascular diseases—Epidemiology

The evaluation of spirometric function over time is most often based on forced expiratory volume in 1 second (FEV1), because it is associated with health outcomes and, among older persons, is more likely to be successfully completed than the forced vital capacity (1–9). Prior work has shown that a low FEV1 is associated with respiratory symptoms, physical disability, hospitalization, and death (3,5–9).

A decline in FEV1 often results from the onset and progression of cardiopulmonary disease, affecting predominantly middle-aged and older persons (1–3,5–11). Normal aging, however, can also lead to a decline in FEV1, a consequence of increased rigidity of the chest

wall and decreased elastic recoil of the lung (1,2,12,13). In addition, normal aging is associated with increased variability in spirometric performance (12). Hence, before attributing a decline in FEV1 to cardiopulmonary disease, it is imperative to account for normal aging.

The current standard of practice for evaluating spirometric function over time expresses FEV1 in volume units (liters or milliliters) or percent predicted (2). Two alternative approaches express the FEV1 as volume units standardized to height-cubed (L/m³) or as a Z-score (12–16). Which approach is more clinically meaningful in middle-aged and older persons has not yet been evaluated. Given substantial

methodological differences in accounting for aging-related changes in spirometric function (see [Box 1](#)), we postulated that associations between cardiopulmonary predictors and FEV1 over time would also differ based on the FEV1 approach.

Accordingly, using data from the Baltimore Longitudinal Study on Aging (BLSA) ([18](#)), including 501 white participants aged 40–95 who completed at least three longitudinal spirometric assessments, we evaluated and compared the effect of age and cardiopulmonary predictors on FEV1 over time, expressed in liters, L/m³, percent predicted, and as a Z-score. The results of this work may inform the most clinically meaningful method by which the FEV1 should be evaluated over time.

Methods

Study Population

The BLSA is an ongoing American cohort study conducted by the intramural research program of the National Institute on Aging ([18](#)). The BLSA was initiated in 1958 for men and in 1978 for women, with spirometric assessments occurring at varying time intervals between 1962 and 2008. All participants gave written informed consent, as approved by the Institutional Review Board.

For our analytical sample, we included participants who were aged 40 years or older at their first spirometric visit and had at least three longitudinal spirometric assessments, each of which had to achieve two or more acceptable and reproducible spirometric maneuvers (described below). We selected age ≥ 40 because aging-related changes in lung function and the occurrence of cardiopulmonary disease are more prevalent starting at age 40 ([1,12,13,19–22](#)). We selected at least three longitudinal spirometric assessments because the precision of the rate of FEV1 decline improves with increasing frequency of measurement and duration of follow-up ([23](#)). Lastly, we selected only white participants because the proportion of non-whites was too small to support the analyses.

Among the 1,372 white participants in BLSA who were aged 40 years or older, 501 (37%) completed three or more longitudinal spirometric assessments and formed the final analytical sample. The mean number of spirometric assessments per participant was 4.3 (*SD* 1.5), and the mean follow-up across spirometric assessments was 15.9 years (*SD* 8.2 years).

Demographic and Clinical Characteristics

Demographic and clinical characteristics included age, sex, height, and several cardiopulmonary predictors: obesity (body mass index ≥ 30 kg/m²), smoking status, hypertension (systolic blood pressure ≥ 140 or diastolic ≥ 90 mm Hg), diabetes mellitus (fasting glucose ≥ 126 mg/dL, abnormal glucose tolerance test, or use of hypoglycemic drugs) ([24](#)), and self-reported chronic bronchitis and myocardial infarction. Because tobacco exposure in pack-years was not available, we evaluated smoking status as never-smoker (vs ever-smoker), postulating this variable as a protective cardiopulmonary predictor. The selection of these cardiopulmonary predictors was based on their known associations with cardiopulmonary disease ([1,5,10,11,25,26](#)) and their availability at the time of the spirometric visits. The latter allowed us to evaluate the cardiopulmonary predictors as time-varying factors.

Spirometry

The BLSA protocol used three different spirometers ([26,27](#)), including a Collins counter-weighted spirometer during 1962–1976, a Stead-Wells spirometer during 1977–1987, and a Collins DS

water-seal spirometer since 1987. (As discussed in the Statistical Analysis section, the study results did not differ according to the type of spirometer.)

Participants were included in the analytical sample if they achieved at least two acceptable and reproducible maneuvers, defined respectively by contemporary protocols and the two largest FEV1 values matching within 5%, at each spirometric visit ([26,27](#)). The highest FEV1 value was then selected for analysis and expressed in liters, percent predicted (%Pred), L/m³, and Z-scores ([13,28,29](#)). The global lung function initiative equations were used to calculate %Pred and Z-scores ([13](#)). As a basis for interpreting the FEV1 results, a Z-score of -1.645 defined the lower limit of normal (LLN) as the 5th percentile of the distribution ([1,12](#)).

Statistical Analysis

Baseline measurements, including demographic and clinical characteristics, as well as FEV1 in liters, L/m³, %Pred, and Z-scores, were summarized as means and standard deviations, or counts and percentages. Baseline was defined as the first spirometric visit starting at age ≥ 40 .

Next, to inform the regression analysis, the mean structure of the outcomes over time was examined graphically and covariance structures were investigated using variograms. The amount of missing data on predictor variables in the analytical sample was minimal ($<5\%$), so complete case analyses were undertaken. Potential predictors included baseline age, obesity, smoking status, hypertension, diabetes mellitus, chronic bronchitis, and myocardial infarction. Except for baseline age, these predictors were time-varying. Importantly, time-varying parameter estimates, in the absence of interaction or higher-order terms, denote the associations of the trajectories of predictor variables over time with the trajectories of FEV1 over time.

Linear mixed-effects models were estimated to evaluate the associations of predictor variables with the outcome of FEV1 in liters, %Pred, L/m³, and Z-scores, as measured at each spirometric visit across the study period (FEV1 over time). Adjusted models were initially fit using the same variables, including a random intercept and random slope for time to account for the serial correlation of repeated measurements over time. Subject-specific interpretations of random effects in regression model results were not of primary clinical interest and so are not reported. The model fitting process also included an assessment of higher-order terms for baseline age, and for predictor variable-by-time interactions. The inclusion of indicator variables for spirometer type in the model did not affect study results, and they were, therefore, not retained in the model. Model fit was assessed using residual analyses and influence diagnostics.

Predictor variables were interpreted as statistically significant if *p*-values were $<.05$ for two-sided tests, and interaction and higher-order terms are described as statistically significant when *p*-values were $<.01$ for two-sided tests. This lower level of significance was used to account for the multiplicity of time-interactions. SAS version 9.4 software was used for all analyses.

Results

[Table 1](#) provides baseline characteristics of the analytical sample; mean age was 56.4, 28.3% were female, mean height was 172.7 cm, 8.6% were obese, 34.1% were never-smokers, 24.0% had hypertension, 11.6% had chronic bronchitis, 8.4% had diabetes, and 1.2% had a prior myocardial infarction. The mean baseline FEV1 was 3.240 L, 0.621 L/m³, 96.4%Pred, and -0.239 as a Z-score. The latter Z-score value corresponded to the 40.6th percentile, which was well

Box 1. Analytical Approaches to Expressing FEV1 OverTime

FEV1	Advantages	Disadvantages
<i>Current practice</i>		
Liters (or milliliters)	<ul style="list-style-type: none"> • Widely employed (10,11) • Evaluates the actual spirometric measurement. 	<ul style="list-style-type: none"> • Does not include comparisons to a reference population of healthy nonsmokers and, in turn, cannot directly account for aging-related changes in FEV1, including variability in spirometric performance (1,6,7,16)
Percent predicted (%Pred)*	<ul style="list-style-type: none"> • Widely employed (2) • Directly accounts for aging-related decline in FEV1, based on comparisons with a reference population of healthy nonsmokers (2) 	<ul style="list-style-type: none"> • Does not account for aging-related increased variability in spirometric performance. Hence, the %Pred value that corresponds to the LLN varies across the lifespan (1,6,7,16) • The reference equations that estimate aging-related changes in FEV1 are not derived from longitudinal data, but are instead based on cross-sectional data collected across multiple age groups
<i>Alternative approach</i>		
Liter/meter ³	<ul style="list-style-type: none"> • Evaluates a simple adjustment of the actual spirometric measurement • Accounts for differences in the size of individuals (14,15) 	<ul style="list-style-type: none"> • Does not include comparisons to a reference population of healthy nonsmokers and, in turn, cannot directly account for aging-related changes in FEV1, including variability in spirometric performance (1,6,7,16)
Z-score [†]	<ul style="list-style-type: none"> • Accounts for the aging-related decline in FEV1 and increased variability in spirometric performance, based on comparisons with a reference population of asymptomatic lifelong nonsmokers (12,13) • Strong clinical precedence, as in pediatric growth charts and bone density testing (osteoporosis) (12,17) 	<ul style="list-style-type: none"> • The reference equations that estimate aging-related changes in FEV1 are not derived from longitudinal data, but are instead based on cross-sectional data collected across multiple age groups

Notes: FEV1, forced expiratory volume in 1 second; LLN, lower limit of normal (5th percentile); %Pred, percent predicted.

* (Measured/Predicted) × 100, wherein the predicted FEV1 is calculated from reference equations that include variables for age, sex, height, and ethnicity (13).

[†]Calculated by the Lambda Mu Sigma (LMS) method, using reference equations from the global lung function initiative (GLI) (12,13). The LMS method calculates FEV1 Z-scores by incorporating: the median (Mu), representing how spirometric measures change based on predictor variables (age, sex, height, and ethnicity); the coefficient-of-variation (Sigma), representing the spread of reference values (ie, between subject variability in spirometric performance); and the skewness (Lambda), representing departure from normality (12). A Z-score of -1.645 defines the LLN as the 5th percentile of distribution (12,13).

above the LLN (Z-score of -1.645). As compared with the analytical sample, excluded participants were likely to be older (mean age of 64.6 vs 56.4, $p < .001$) and female (35.8% vs 28.3%, $p = .005$), and had a shorter height (170.7 vs 172.7 cm, $p < .001$) and higher prevalence of hypertension (33.2% vs 24.0%, $p < .001$), diabetes (12.2% vs 8.4%, $p = .030$), and myocardial infarction (5.6% vs 1.2%, $p < .001$). No statistically significant differences were found between the two groups for body mass index, obesity, smoking status, or chronic bronchitis.

Table 2 provides longitudinal associations of characteristics, including time-varying cardiopulmonary predictors, with FEV1 in liters over time. FEV1 declined by 0.040L (40 mL) per year ($p < .001$). For each additional year of baseline age (beyond the mean baseline age), FEV1 declined significantly ($p < .001$) by 0.044L (44 mL) across the study period. Among other potential predictors, when compared to their respective absence, only obesity and myocardial infarction were significantly associated with a lower FEV1 in liters over time ($p < .05$), whereas smoking status, hypertension, chronic bronchitis, and diabetes mellitus were not. Interactions with time were not statistically significant; data not shown.

Table 2 also provides longitudinal associations of characteristics, including time-varying cardiopulmonary predictors, with

FEV1 as %Pred over time. FEV1 %Pred declined by 0.234 per year ($p < .001$) for those of average age at baseline. A significant interaction of baseline age with time of follow-up was observed ($p < .001$), yielding an additional decline in FEV1 %Pred of 0.011 per year of follow-up, for each year that a participant was older than the mean baseline age of the study sample. Among other potential predictor variables, when compared to their respective absence, only obesity, smoking status, diabetes mellitus, and myocardial infarction were significantly associated with a lower FEV1 %Pred over time ($p < .05$), whereas hypertension and chronic bronchitis were not.

Table 3 provides longitudinal associations of characteristics, including time-varying cardiopulmonary predictors, with FEV1 in L/m³ over time. FEV1 declined by 0.007L/m³ (7 mL/m³) per year ($p < .001$). For each additional year of baseline age (beyond mean baseline age), FEV1 declined significantly ($p < .001$) by 0.006L/m³ (6 mL/m³) across the study period. Among other potential predictors, when compared to their respective absence, only obesity, chronic bronchitis, diabetes mellitus, and myocardial infarction were significantly associated with a lower FEV1 in L/m³ over time ($p < .05$), whereas smoking status and hypertension were not. Interactions with time were not statistically significant; data not shown.

Table 1. Baseline Characteristics—Baltimore Longitudinal Study on Aging

Characteristic	Analytical Sample	Excluded Participants ⁵	<i>p</i> Value [¶]
	N = 501	N = 871	
	Mean ± SD or No. (%)		
Age (years)	56.4 ± 11.4	64.6 ± 13.9	<.001
Females	142 (28.3%)	312 (35.8%)	.005
Height (cm)	172.7 ± 9.2	170.7 ± 9.4	<.001
BMI (kg/m ²)	25.3 ± 3.4	25.6 ± 4.0	.237
Obesity (BMI ≥30 kg/m ²)	43 (8.6%)	103 (11.8%)	.061
Never-smoker	171 (34.1%)	334 (38.3%)	.119
Hypertension*	120 (24.0%)	289 (33.2%)	<.001
Chronic bronchitis	58 (11.6%)	101 (11.6%)	.992
Diabetes mellitus [†]	42 (8.4%)	106 (12.2%)	.030
Myocardial infarction	6 (1.2%)	49 (5.6%)	<.001
FEV1 Liters	3.240 ± 0.846	Not applicable	
FEV1/Height ³ (L/m ³)	0.621 ± 0.199		
FEV1 %Pred	96.4 ± 14.8		
FEV1 Z-score [‡]	-0.239 ± 1.012		

Notes: BMI = body mass index; FEV1 = forced expiratory volume in 1 second; %Pred = percent predicted ([measured/predicted] × 100).

*Systolic blood pressure ≥140 or diastolic ≥90 mm Hg.

[†]Based on fasting hyperglycemia, abnormal glucose tolerance test, or use of hypoglycemic drugs (see text).

[‡]A Z-score of -0.239 corresponds to the 40.6th percentile, which is well above the lower limit of normal (defined by a Z-score of -1.645 as the 5th percentile of distribution in a reference population of asymptomatic lifelong nonsmokers).

⁵Were age-eligible but did not complete at least three longitudinal spirometric assessments, each of which had to achieve two or more acceptable and reproducible spirometric maneuvers (see text).

[¶]Comparisons between the analytical and excluded sample were conducted using chi-square tests for categorical variables and *t* tests for continuous variables.

Table 2. Longitudinal Associations of Characteristics, Including Time-Varying Cardiopulmonary Predictors, With the Outcome of FEV1 Over Time, Expressed in Liters and %Pred (current practice)—Baltimore Longitudinal Study on Aging (N = 501)

Characteristics	FEV1 Liters Over Time			FEV1 %Pred Over Time		
	Regression Coefficient	95% CI	<i>p</i> Value	Regression Coefficient	95% CI	<i>p</i> Value
Intercept	3.270	3.196, 3.344	<.001	95.966	94.344, 97.588	<.001
Time of follow-up (years)	-0.040	-0.042, -0.039	<.001	-0.234	-0.297, -0.171	<.001
Baseline age (years)*	-0.044	-0.049, -0.038	<.001	0.001	-0.113, 0.116	.983
Baseline age × time interaction	Not applicable			-0.011	-0.169, -0.005	0.011
Obesity	-0.092	-0.135, -0.490	<.001	-2.917	-4.269, -1.566	<.001
Never-smoker	-0.040	-0.154, 0.073	.483	3.433	0.767, 6.098	.012
Hypertension [†]	-0.019	-0.040, 0.003	.095	-0.532	-1.221, 0.156	.129
Chronic bronchitis	-0.022	-0.087, 0.043	.504	-1.844	-3.829, 0.141	.069
Diabetes mellitus [‡]	-0.045	-0.093, 0.003	.067	-1.895	-3.424, -0.367	.015
Myocardial infarction	-0.083	-0.161, -0.006	.036	-2.854	-5.375, -0.333	.027

Notes: BMI = body mass index; CI = confidence interval; FEV1 = forced expiratory volume in 1-second; %Pred = percent predicted ([measured/predicted] × 100).

*Centered at baseline mean.

[†]Systolic blood pressure ≥140 or diastolic ≥90 mm Hg.

[‡]Based on fasting hyperglycemia, abnormal glucose tolerance test, or use of hypoglycemic drugs (see text).

Table 3 also provides longitudinal associations of characteristics, including time-varying cardiopulmonary predictors, with FEV1 as Z-scores over time. FEV1 Z-score declined by 0.008 per year ($p < .001$). Baseline age was not significantly associated with FEV1 Z-scores over time ($p = .933$). All other potential predictors, when compared to their respective absence, were significantly associated with a lower FEV1 Z-score over time ($p < .05$), including obesity, smoking status, hypertension, chronic bronchitis, diabetes mellitus, and myocardial infarction. Interactions with time were not statistically significant; data not shown.

Higher-order terms for baseline age were not statistically significant and, hence, were not retained in the multivariable models in either Table 2 or Table 3.

Discussion

Using data from the BLSA, we found that associations of baseline age and cardiopulmonary predictors with FEV1 over time varied considerably according to the method for reporting FEV1. In particular, baseline age was associated with FEV1 over time in liters and L/m³, and included a time interaction for %Pred, but was otherwise not associated with Z-scores. In addition, the associations of cardiopulmonary predictors with FEV1 over time were all significant when using Z-scores, but varied for other methods of expressing FEV1.

As discussed earlier, the FEV1 declines progressively in middle-aged and older persons due to normal aging and the onset and progression of

Table 3. Longitudinal Associations of Characteristics, Including Time-Varying Cardiopulmonary Predictors, With the Outcome of FEV1 Over Time, Expressed in L/m³ and Z-score (alternative approach)—Baltimore Longitudinal Study on Aging (N = 501)

Characteristics	FEV1/Height ³ (L/m ³) Over Time			FEV1 Z-score Over Time		
	Regression Coefficient	95% CI	p Value	Regression Coefficient	95% CI	p Value
Intercept	0.621	0.610, 0.632	<.001	-0.276	-0.385, -0.168	.529
Time of follow-up (years)	-0.007	-0.007, -0.006	<.001	-0.008	-0.114, -0.004	<.001
Baseline age (years)*	-0.006	-0.007, -0.005	<.001	-0.0003	-0.008, 0.007	.933
Obesity	-0.019	-0.027, -0.011	<.001	-0.201	-0.286, -0.117	<.001
Never-smoker	0.011	-0.006, 0.029	.196	0.230	0.056, 0.404	0.01
Hypertension [†]	-0.004	-0.008, 0.000	.076	-0.044	-0.088, -0.001	.046
Chronic bronchitis	-0.013	-0.025, -0.001	.031	-0.158	-0.281, -0.034	.012
Diabetes mellitus [‡]	-0.010	-0.019, -0.001	.027	-0.108	-0.202, -0.014	.025
Myocardial infarction	-0.017	-0.032, -0.003	.021	-0.201	-0.355, -0.047	.011

Notes: BMI = body mass index; CI = confidence interval; FEV1 = forced expiratory volume in 1 second.

*Centered at baseline mean.

[†]Systolic blood pressure ≥140 or diastolic ≥90 mm Hg.

[‡]Based on fasting hyperglycemia, abnormal glucose tolerance test, or use of hypoglycemic drugs (see text).

cardiopulmonary disease (1,10–13). Hence, before attributing a decline in FEV1 to cardiopulmonary predictors, it is imperative to account for normal aging (1). The results of the current study suggest that the Z-score approach may be more clinically meaningful than standard approaches when evaluating the FEV1 over time, as it accounted for the effect of baseline age and better reflected the adverse effects of multiple cardiopulmonary predictors. As described in the Box 1, global lung function initiative-calculated Z-scores rigorously account for aging-related declines in spirometric function and increased variability in spirometric performance, based on comparisons with reference populations of asymptomatic lifelong nonsmokers (12,13).

Conversely, when expressed in liters, L/m³, and %Pred, the effect of baseline age on FEV1 over time was statistically significant and, in turn, may have attenuated the associations of cardiopulmonary predictors with FEV1 over time. As described in the Box 1, FEV1 in liters or L/m³ does not account for aging-related changes in lung function (1,12,13), whereas FEV1 %Pred assumes incorrectly that spirometric variability does not differ across the adult lifespan (12,16,30). In the current study, the significant time interaction for baseline age on FEV1 when expressed as %Pred provides further evidence of the potential limitations of the %Pred assumption. To illustrate the effect of age on %Pred over time, prior work has shown that, in a reference population of healthy nonsmokers, a white male of average height has an FEV1 at the LLN that corresponds to 74%Pred at age 30 but only 63%Pred by age 70 (30).

The Z-score approach additionally provides substantial advantages when comparing spirometric data across cohorts that differ in age, and when establishing normal versus abnormal results. In the current study, for example, the mean values for baseline FEV1 were 3.240L, 0.621 L/m³, and 96.4%Pred, but these values cannot be easily compared across cohorts that differ in age (eg, BLSA vs. Cardiovascular Health Study) (5,11,18). In particular, as discussed in Box 1, the threshold values for liters, L/m³, and %Pred that correspond to the LLN differ by age (12,13,16,30). In contrast, the BLSA mean value for baseline FEV1 Z-score of -0.239 (40.6th percentile) will be comparable across cohorts differing in age, because Z-scores account for aging-related changes in lung function and spirometric performance, based on reference populations of asymptomatic lifelong nonsmokers (12,13). Moreover, the normalcy of FEV1 results is defined relative to a threshold Z-score of -1.645 (5th percentile), establishing

an LLN that remains the same across all ages (12,13,16,30). These advantages of the Z-score approach have important implications for public health research, as it allows comparisons of the FEV1 over time across multiple cohorts of differing age.

The current study has several strengths, including a large data set of 501 participants who were aged 40–95 years and had completed a mean of 4.3 longitudinal spirometric assessments over a mean follow-up of 15.9 years. We acknowledge, however, several potential limitations. First, we required at least three longitudinal spirometric assessments, restricting our analysis to a spirometric sample that was younger and healthier. As a result, trajectories of FEV1 over time may have been attenuated by the younger age and healthier status of the analytical sample. Nonetheless, the size of the longitudinal spirometric sample and duration of follow-up remained substantial, and provided a unique opportunity to evaluate FEV1 over time. Second, the global lung function initiative reference equations used to calculate FEV1 %Pred and Z-scores were based on serial cross-sectional data (13), although we partially addressed this limitation by using models that included random intercepts and random slopes to account for serial correlation of repeated measurements over time. Third, different types of spirometers were used in BLSA, yet inclusion of a variable for spirometer type in regression models did not alter study results. Fourth, the association between smoking status and FEV1 over time could not be fully evaluated, because exposure in pack-years was not available. Fifth, our results were obtained from a sample that was restricted to whites, thus racial/ethnic differences were not evaluated. Lastly, clinically meaningful was based on associations of available cardiopulmonary predictors with FEV1 over time. Future work should evaluate additional predictors in even larger cohorts, including the effect of FEV1 over time on cardiopulmonary and non-cardiopulmonary morbidity and mortality.

In conclusion, using data from the BLSA, we found that the effect of cardiopulmonary predictors on FEV1 over time varied by the method for reporting FEV1, including liters, L/m³, %Pred, and Z-scores. In particular, only the Z-score approach yielded significant associations between all of the available cardiopulmonary predictors and the outcome of FEV1 over time. In addition, only the Z-score approach accounted for the effect of age on FEV1 over time. These results suggest that the Z-score approach is more clinically meaningful when evaluating FEV1 over time.

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