

Determination of significant change in LCI of zFEV

These thresholds were selected based on reproducibility data from this dataset that were recently published (32). The threshold of a 15% relative change in LCI and an absolute change of 1.3 z-scores in zFEV were considered outside of the inter-visit variability of the tests and were therefore considered to represent a physiological change.

A relative change in LCI was used because the within-subject standard deviation of the change in LCI is proportional to its magnitude, such that the variability is greater at higher values of LCI.

An absolute change of 1.3 z-scores in zFEV was used as it represented the 95% limits of agreement for absolute change seen in health.

Figure S1 – Schematic diagram of visit classification. Baseline visit was defined as the closest asymptomatic visit to the symptomatic event, whereas follow-up was the first visit following the symptomatic visit.

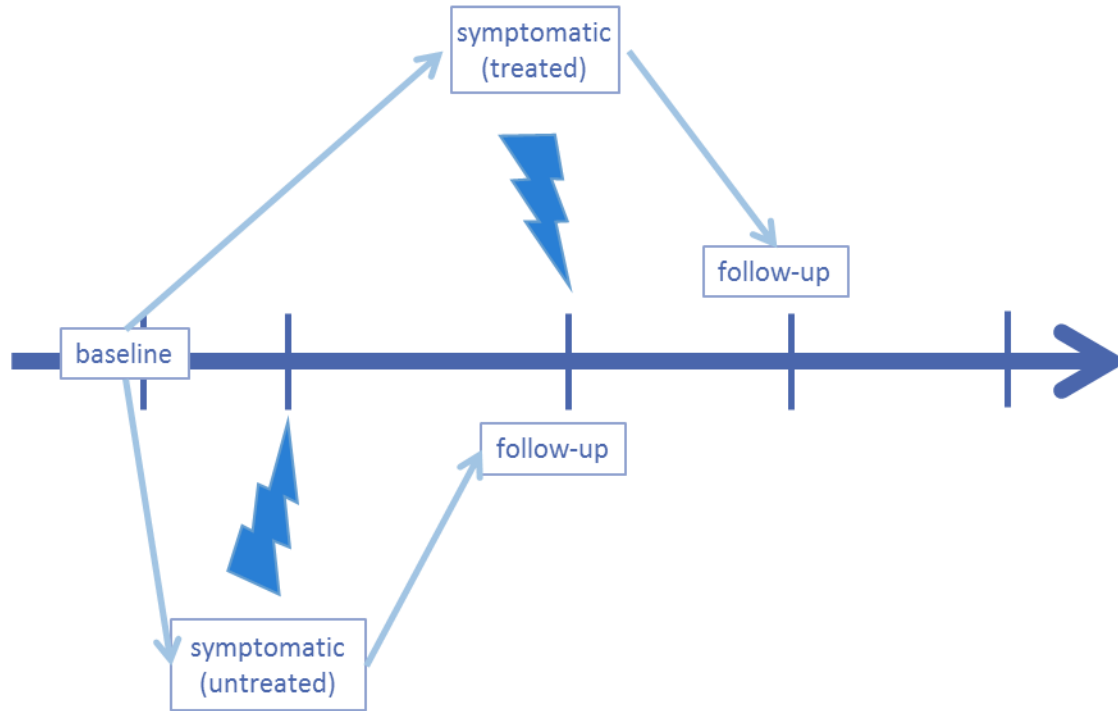


Table S1 – Sensitivity analyses demonstrating the relative change in LCI from baseline to symptoms and the average treatment effect in different subgroups. Data presented as mean(95% confidence interval).

	Treated	Untreated	p
Limited to visits with no preceding unobserved pulmonary exacerbations *			
Relative LCI change from baseline to symptoms (treated n=27, untreated n=28)	25.2 (15.2, 35.1)	11.6 (1.7, 21.4)	0.04
Average treatment effect (relative LCI change)#	-15.4 (-27.3, -3.5)		0.01
Limited to first symptomatic visit for each participant included**			
Relative LCI change from baseline to symptoms (treated n=21, untreated n=15)	32.3 (16.9, 47.7)	6.3 (0.0, 13.1)	0.008
Average treatment effect (relative LCI change)#	-20.7 (-42.2, 0.7)		0.06
Limited to visits where LCI had deteriorated by 15% or more from baseline*			
Relative LCI change from baseline to symptoms (treated n=26, untreated n=10)	43.8 (36.5, 51.1)	26.4 (12.5, 40.3)	0.03
Average treatment effect (relative LCI change)#	-14.3 (-22.1, -6.3)		<0.001
Limited to those exacerbations that were treated with oral antibiotics only			
Relative LCI change from baseline to symptoms (treated n=48, untreated n=45)	23.6 (15.7, 31.6)	10.5 (2.1, 19.0)	0.02
Average treatment effect (relative LCI change)#	-14.5 (-24.0, -5.0)		0.003

* Data presented as estimated mean values as determined by linear regression using generalised estimating equation models to account for multiple measurements in the same participant. p-value shown for Wald chi-square test comparing treated and untreated groups.

** This dataset is limited to a single event per participant, thus p-value shown for t-test comparison of mean values between treated and untreated groups.

Average treatment effect estimated using propensity score matching, displayed as average relative change in LCI (95% confidence interval).

Figure S2. Summary of individual LCI changes between visits.

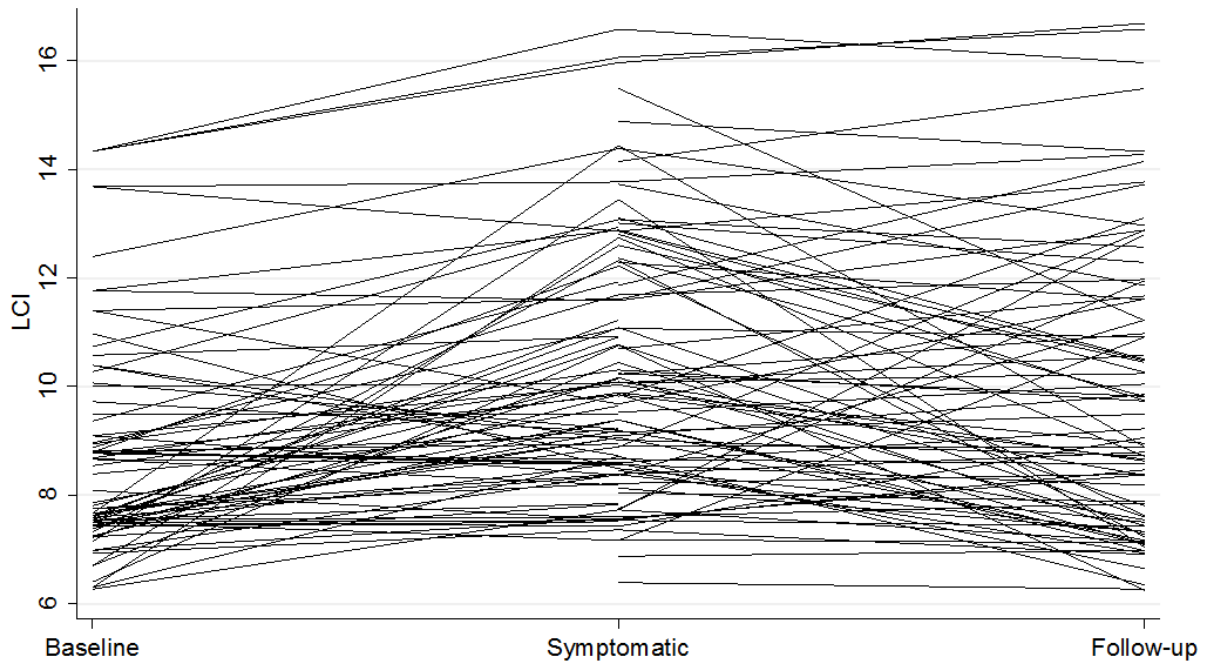


Figure S3 - Relative change in percent-predicted FEV (ppFEV) between study timepoints. Mean relative values of ppFEV at baseline, symptomatic and follow-up visits for treated (solid line) and untreated (dashed line) symptomatic visits. Data points and the 95% confidence interval (vertical bars) are estimated from linear regressions using a generalised estimating equation model to account for multiple measurements in the same participant.

