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Title: Impact of a single chronic obstructive pulmonary disease (COPD) exacerbation on lung function decline: Analysis of UPLIFT®

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Body: Background: Frequent COPD exacerbations are linked to rapid decline in lung function. Little is known about the impact of a single exacerbation on rate of decline. Aims and objectives: To examine the effect of a single COPD exacerbation on rate of decline in lung function, using data from a 4-y, randomized, double-blind, placebo-controlled trial of tiotropium in moderate-to-very severe COPD (UPLIFT®). Methods: Retrospective analysis of annual rate of decline in pre- and postbronchodilator (BD) forced expiratory volume in 1s (FEV₁) and forced vital capacity (FVC), before and after first COPD exacerbation (increase in/new onset of >1 respiratory symptom lasting \geq 3 days and treated with antibiotic/systemic corticosteroids). Eligible patients (pts) had \geq 3 pulmonary function tests (PFTs) before (\geq 24 days after treatment start) and \geq 3 months after the exacerbation (no further exacerbations permitted for next 3 PFT measurements). Rate of decline was calculated by linear regression and P-values by Wilcoxon signed-rank test. Results: 462 pts were eligible (mean age 64 y, 78% male, mean baseline FEV₁ 1.19 L and FEV₁/FVC 0.44). Mean annual rate of decline in pre- and post-BD FEV₁ and pre-BD FVC significantly increased (Table).

	Mean Rate of Decline n		
	First exacerbation		
	Before	After	P-value
Pre-BD FEV ₁	-27.5 (-101.1, 49.5)	-48.7 (-134.1, 22.2)	0.0006
Post-BD FEV ₁	-27.8 (-97.0, 41.7)	-59.0 (-132.7, 15.7)	0.0002
Pre-BD FVC	-54.9 (-202.5, 99.8)	-61.1 (-230.3, 94.2)	0.0403

Post-BD FVC	-58.6 (-187.3, 92.4)	-65.5 (-216.6, 61.2)	0.0775
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Conclusion: A single exacerbation can lead to a significantly larger rate of decline in lung function in COPD pts 1-2 years post exacerbation.