THE LANCET Respiratory Medicine

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Bhatt SP, Wells JM, Kim V, et al. Radiological correlates and clinical implications of the paradoxical lung function response to β2 agonists: an observational study. *Lancet Respir Med* 2014; published online Sept 10. http://dx.doi.org/10.1016/S2213-2600(14)70185-7.

Supplemental Tables

Table 1: Predictors of Paradoxical Response defined by 10% reduction in FEV_1: Multivariate Logistic regression

Predictor	Unadjusted Odds Ratio	95% CI	Adjusted Odds Ratio	95% CI
Age (per ten years)	0.99	0.98 to 1.0	1.13	0.92 to 1.37
Female gender	0.80	0.63 to 1.02	0.86	0.63 to 1.18
African American Race	2.20 †	1.73 to 2.81	2.26 †	1.67 to 3.05
Current smoking	1.47 **	1.15 to 1.89	1.17	0.85 to 1.61
Packyears	1.01 **	1.0 to 1.01	1.01 *	1.0 to 1.01
Respiratory medications#	1.25	0.96 to 1.62	1.23	0.86 to 1.74
Pre-bronchodilator FEV1	0.90	0.79 to 1.03	1.11	0.88 to 1.41
Emphysema (Perc15 for every 10HU)	0.96 *	0.92 to 1.0	0.99	0.95 to 1.04
Wall Area%	1.10 †	1.06 to 1.14	1.08 †	1.04 to 1.12

*p<0.05. **p,0.01. †p<0.001

FEV_1 = Forced Expiratory Volume in the first second. Perc15 = the density of lung in HU below which 15% of the voxels had the lowest attenuation numbers at full inspiration. Wallarea% = Bronchial wall area at segmental level. #Respiratory medications include one or more of inhaled long acting beta agonists, long acting antimuscarinic agents or a combination of inhaled corticosteroids/long acting beta agonists.

Table 2: Predictors of Paradoxical Response defined by 15% reduction in FEV_1: Multivariate Logistic regression

Predictor	Unadjusted Odds Ratio	95% CI	Adjusted Odds Ratio	95% CI
Age (per ten years)	0.68 **	0.54 to 0.86	0.86	0.63 to 1.18
Female gender	0.75	0.51 to 1.11	0.72	0.44 to 1.17
African American Race	2.90 †	1.97 to 4.26	2.27 **	1.42 to 3.61
Current smoking	1.88 **	1.25 to 2.81	1.18	0.71 to 1.97
Packyears	1.0	0.99 to 1.01	1.0	0.99 to 1.01
Respiratory medications#	1.05	0.68 to 1.61	1.13	0.65 to 1.97
Pre-bronchodilator FEV1	0.94	0.76 to 1.16	1.01	0.70 to 1.44
Emphysema (Perc 15 for every 10HU)	0.93 *	0.88 to 0.99	1.0	0.93 to 1.08
Wall Area%	1.13 †	1.07 to 1.20	1.12 **	1.04 to 1.20

*p<0.05. **p,0.01. †p<0.001

FEV_1 = Forced Expiratory Volume in the first second. Perc15 = the density of lung in HU below which 15% of the voxels had the lowest attenuation numbers at full inspiration. Wallarea% = Bronchial wall area at segmental level. #Respiratory medications include one or more of inhaled long acting beta agonists, long acting antimuscarinic agents or a combination of inhaled corticosteroids/long acting beta agonists.

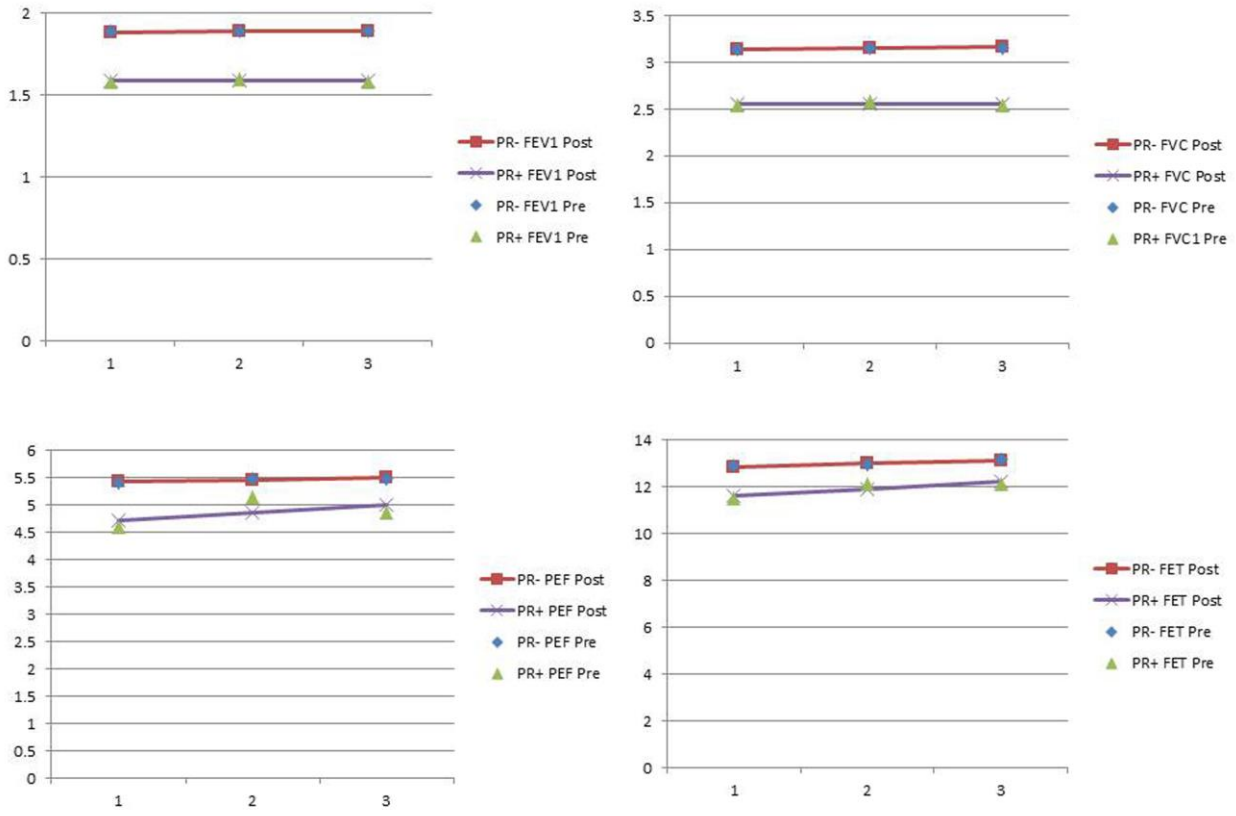
Table 3: Predictors of Paradoxical Response: Multivariate Logistic regression

Variable	Adjusted Odds Ratio	95%CI
Female Gender	0.96	0.76 to 1.22
African American Race	1.87†	1.48 to 2.36
Current Smoking	1.18	0.92 to 1.51
Packyears	1.004	1.0 to 1.008
Respiratory Medications#	1.10	0.83 to 1.44
Pre-bronchodilator FEV_1	0.91	0.76 to 1.09
Emphysema (Perc15 for every 10HU)	0.96*	0.92 to 0.99
Wall-area%	1.04*	1.01 to 1.08
Age		
Quartile 1 (reference)	1.00	
Quartile 2	1.11	0.85 to 1.45
Quartile 3	0.98	0.71 to 1.35
Quartile 4	1.05	0.73 to 1.52

*$p<0.05$. †$p<0.001$

#Respiratory medications include one or more of inhaled long acting beta agonists, long acting antimuscarinic agents or a combination of inhaled corticosteroids/long acting beta agonists. FEV_1 = Forced Expiratory Volume in the first second. Perc15 = the density of lung in HU below which 15% of the voxels had the lowest attenuation numbers at full inspiration. Wallarea% = Bronchial wall area at segmental level.

Supplemental Figure 1:



Regression models evaluated linear trends over repeated efforts. We observed that the estimated linear trends of predicting FEV_1, FVC and PEF are not statistically significant at significance level, α=0.05. Linear Trend of FET showed an upward movement with repeated efforts in the pre bronchodilator group in the PR- group ($p = 0.02$). FEV_1 = Forced expiratory volume in the first second. FVC = Forced vital capacity. PEF = Peak expiratory flow. FET = Forced expiratory time.