

Relationship Between Improvement In Lung Function And Symptoms In Chronic Obstructive Pulmonary Disease With Dupilumab

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Conclusion

The presence of significant causal mediation and significant modest correlations between improvements in lung function and changes in PROs suggests that enhanced lung function contributes meaningfully to PRO improvements, alongside other influencing factors



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Objective

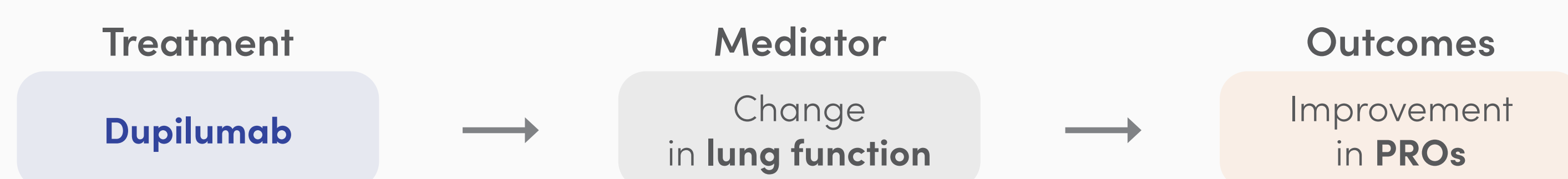
To examine the correlation between lung function improvement and change in PROs in patients with COPD and type 2 inflammation who were treated with dupilumab

Background

- In COPD, correlations between improvements in lung function and changes in PROs have been previously reported¹⁻³
 - Generally, though significant, correlations tend to be modest, reflecting both inter- and intra-patient variability in these outcome measures⁴
- In BOREAS and NOTUS, add-on dupilumab reduced moderate or severe exacerbations and improved lung function and quality of life in patients with COPD and type 2 inflammation⁵⁻⁷
 - Safety was consistent with the known dupilumab safety profile⁵⁻⁷

Methods

- BOREAS (NCT03930732)⁵ and NOTUS (NCT04456673)⁶, phase 3, randomized, double-blind, placebo-controlled trials, enrolled patients (40 to 85 years^a) with COPD, moderate-to-severe airflow limitation, and type 2 inflammation (screening blood eosinophils ≥ 300 cells/ μ L) on LABA/LAMA/ICS
 - Patients received add-on subcutaneous dupilumab 300 mg or matching placebo q2w for 52 weeks
- Endpoints: Pearson correlation coefficient (r) and causal mediation analysis^b, considering pre- or post-bronchodilator FEV₁ as the mediator, and changes in SGRQ or E-RS: COPD total scores^c from baseline to Week 52 were evaluated in patients who received dupilumab. Pearson correlation coefficient was also assessed for SGRQ symptoms and activity, and E-RS: COPD breathlessness and chest symptoms scores



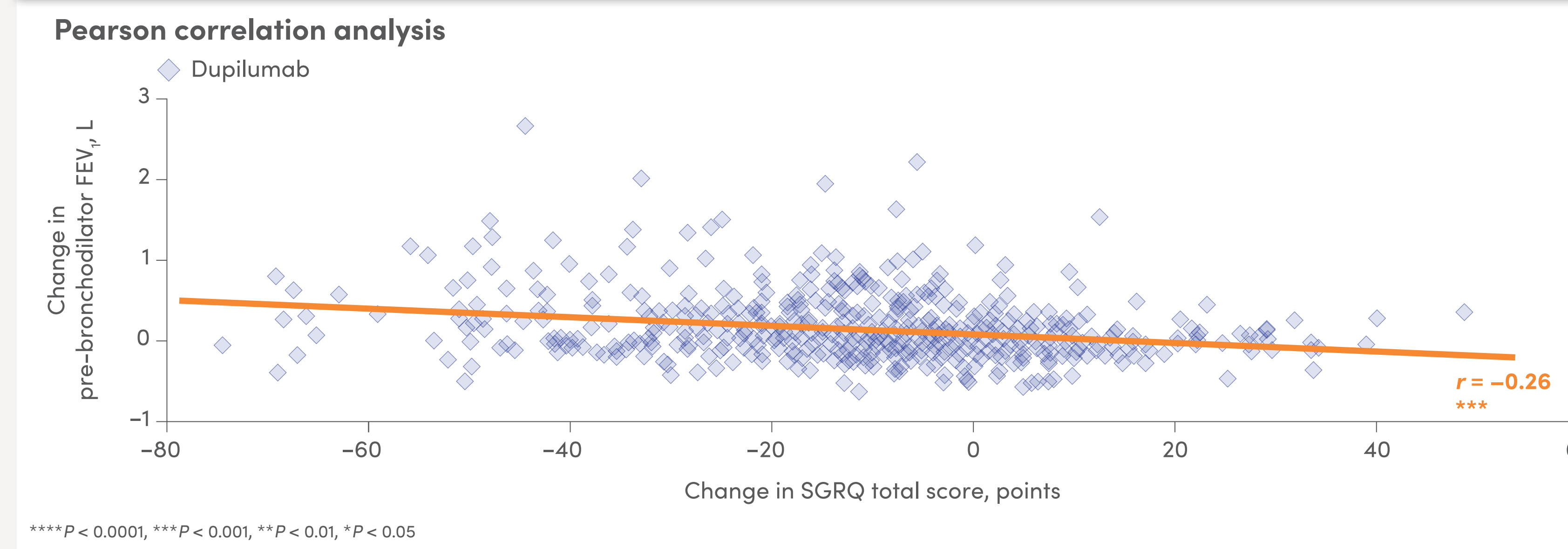
^aAge criteria for BOREAS: 40 to 80 years; for NOTUS: 40 to 85 years.
^bA causal mediation analysis was conducted to determine the extent to which the changes in lung function parameters explained the effect of dupilumab on changes in PROs. This analysis considered dupilumab and placebo as treatment factors, E-RS: COPD and SGRQ total scores as outcomes, and pre- and post-bronchodilator FEV₁ as mediators. The analysis was controlled for age (continuous variable), sex (male vs female), smoking status (current vs former), and the number of moderate or severe COPD exacerbations in the previous year (continuous variable).
^cSGRQ and E-RS: COPD total scores range from 0 to 100 or 0 to 40, respectively, with lower scores indicating better quality of life (SGRQ) or reduced symptom severity (E-RS: COPD).

Results

Increase in lung function significantly mediates improvements in quality of life as measured by SGRQ

Mediator	Total effect of dupilumab on Δ SGRQ, points (95% CI)	P value vs placebo	Percentage Δ SGRQ mediated by lung function improvement with dupilumab (95% CI)	P value vs placebo
Pre-bronchodilator FEV ₁	-3.58 (-5.39, -1.77)	0.0001	23.9% (8.5%, 39.3%)	0.0024
Post-bronchodilator FEV ₁	-3.56 (-5.38, -1.75)	0.0001	23.4% (8.0%, 38.7%)	0.0028

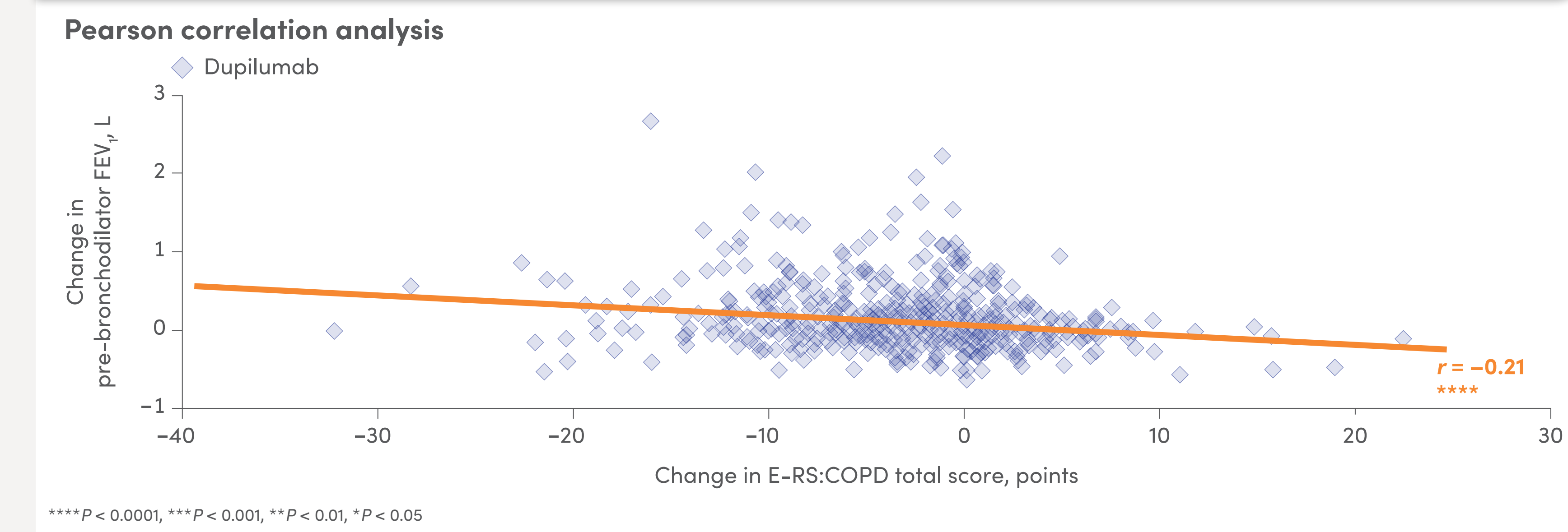
Changes in pre-bronchodilator FEV₁ and SGRQ total score showed a modest yet significant correlation



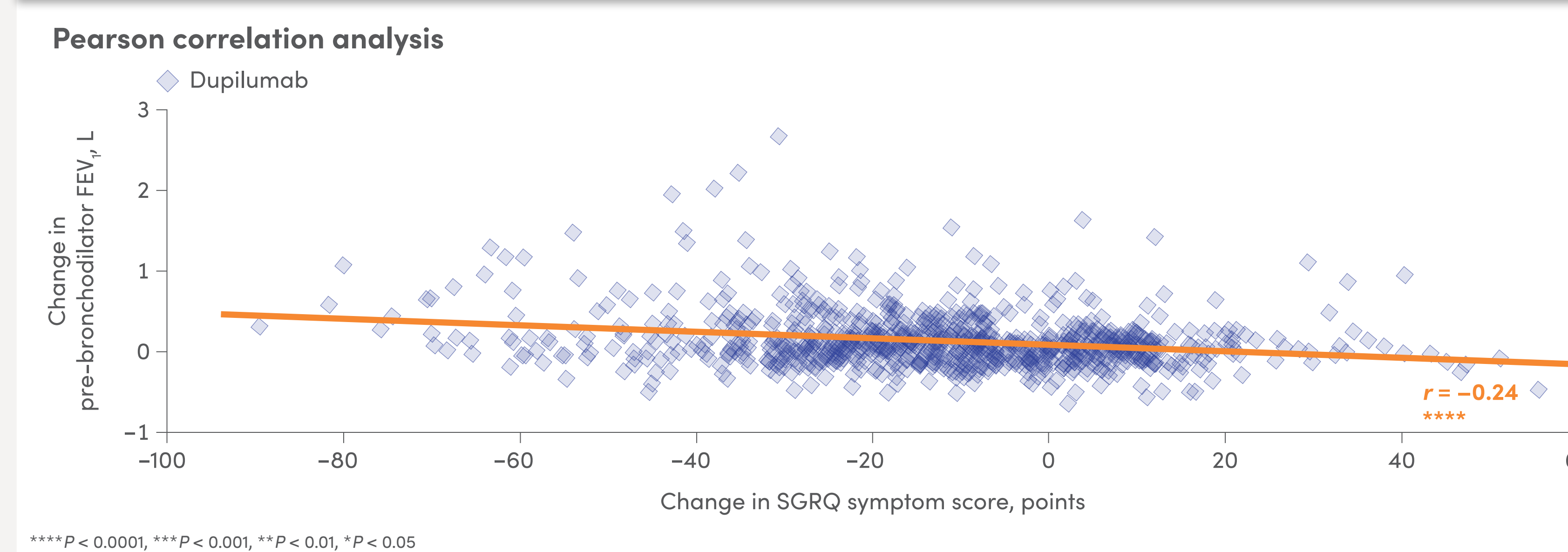
Increase in lung function significantly mediates improvements in quality of life as measured by E-RS: COPD

Mediator	Total effect of dupilumab on Δ E-RS: COPD, points (95% CI)	P value vs placebo	Percentage Δ E-RS: COPD mediated by lung function improvement with dupilumab (95% CI)	P value vs placebo
Pre-bronchodilator FEV ₁	-1.00 (-1.59, -0.40)	0.0010	17.7% (3.4%, 31.9%)	0.0151
Post-bronchodilator FEV ₁	-0.99 (-1.58, -0.39)	0.0012	15.9% (2.5%, 29.3%)	0.0202

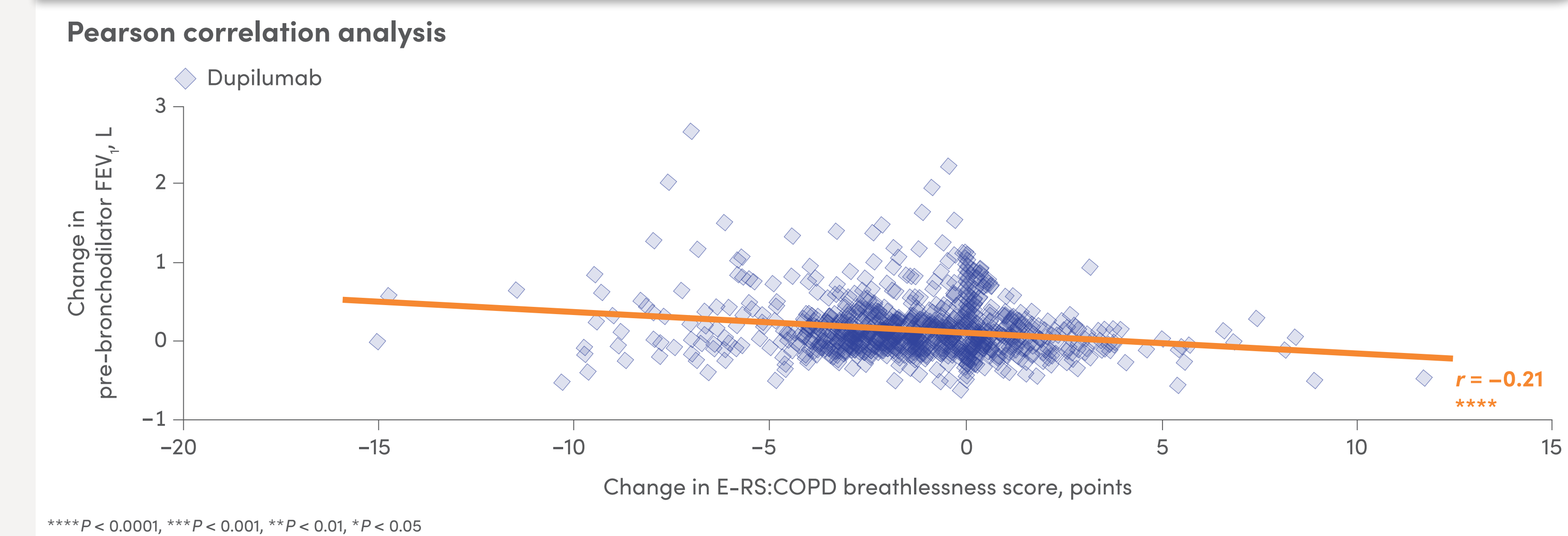
Changes in pre-bronchodilator FEV₁ and E-RS: COPD total score showed a modest yet significant correlation



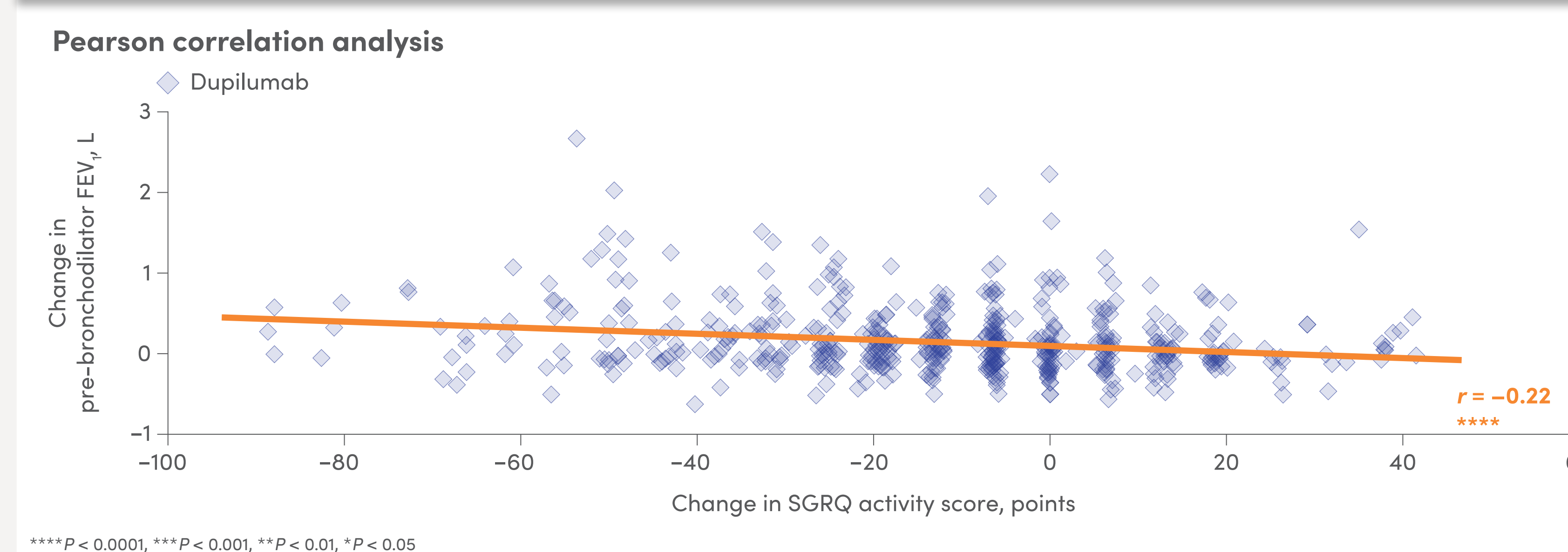
Changes in pre-bronchodilator FEV₁ and SGRQ symptom component score showed a modest yet significant correlation



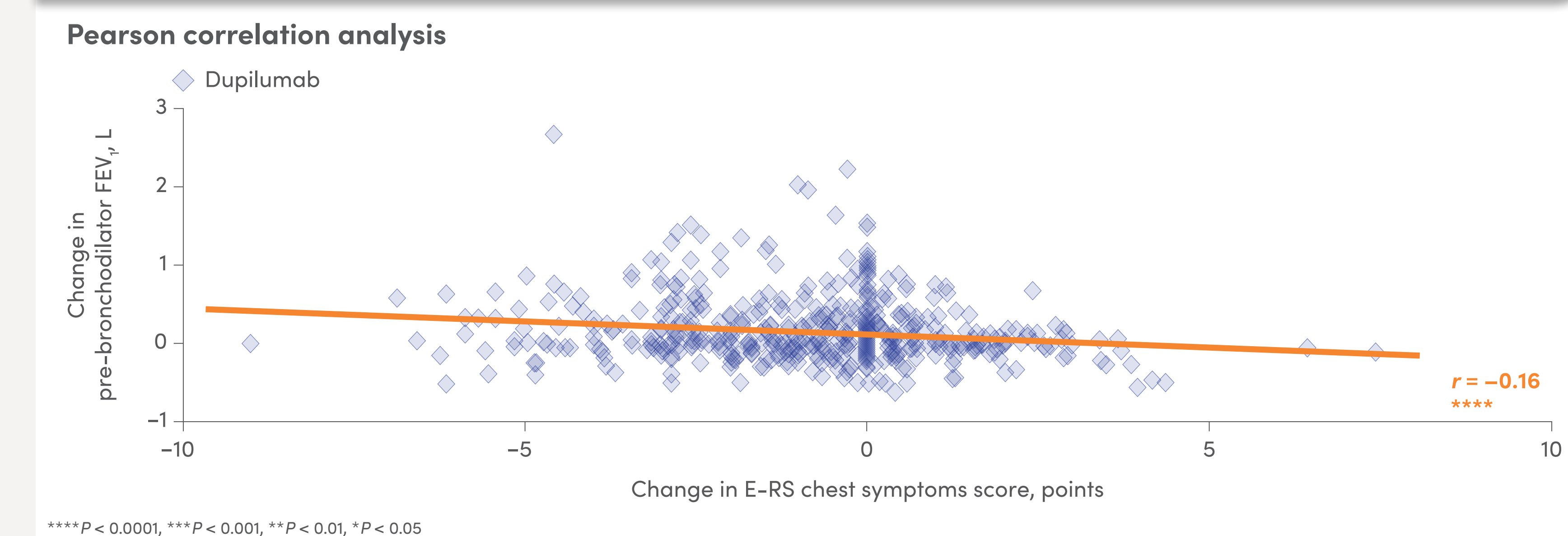
Changes in pre-bronchodilator FEV₁ and E-RS: COPD breathlessness component score showed a modest yet significant correlation



Changes in pre-bronchodilator FEV₁ and SGRQ activity component score showed a modest yet significant correlation



Changes in pre-bronchodilator FEV₁ and E-RS: COPD chest symptoms component score showed a modest yet significant correlation



CI, confidence interval; COPD, chronic obstructive pulmonary disease; E-RS: COPD, Evaluating Respiratory Symptoms in COPD; FEV₁, forced expiratory volume in 1 second; ICS, inhaled corticosteroid(s); LABA, long-acting β 2-agonist(s); LAMA, long-acting muscarinic antagonist(s); PROs, patient-reported outcomes; q2w, every 2 weeks; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire.

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