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Title: Differential dropout may affect exacerbation risk estimates differently in moderate-to-very severe COPD

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Body: BACKGROUND:Differential withdrawal of patients from clinical trials (dropout) complicates interpretation of the effect of intervention on the exacerbation frequency in COPD studies. We examined the impact of differential dropout on exacerbations in moderate-to-very severe COPD (GOLD grades 2–4). METHODS:Patients in 3 pooled COPD studies[1,2,3] were randomised to budesonide/formoterol (B/F 320/9µg bid) or placebo (P) via Turbuhaler®. Exacerbations, dropouts and a composite of the two outcomes were examined over the first 3 months of treatment. RESULTS:1583 COPD patients were studied (24% moderate; 61% severe, 14% very severe). B/F improved time to first exacerbation in moderate and severe but not very severe COPD ($HR_{B/F}/_{P}$: 0.43 [95% CI 0.25–0.72], 0.45 [0.33–0.63] and 0.58 [0.32–1.05]) vs. P.

Time to dropout was improved by B/F vs. P, the differences being larger with increasing COPD severity ($HR_{B/F}/_{P}$: 0.62 [0.34–1.11], 0.56 [0.39–0.81] and 0.38 [0.18–0.80]). A composite measure of time to first exacerbation or dropout showed a significant effect of B/F in all severities. CONCLUSIONS:Differential study dropout (greater with P than B/F) increased as the severity of COPD worsened. This should be considered when interpreting clinical COPD trial data. 1.Calverley et al.ERJ2003;22:912–9 2.Szafranski et al.ERJ2003;21:74–81 3.Welte et al.AJRCCM2009;180:741–50.