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Title: Cigarette smoke retention and bronchodilation in patients with COPD: A controlled randomized trial

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Body: Many COPD patients use bronchodilators while continuing cigarette smoking. We hypothesized that these agents interact with cigarette smoking and hence affect the risk to develop smoking-related (cardiovascular) disease. In this study we explored if bronchodilation increases pulmonary retention of cigarette smoke and smoking-related biomarkers in patients with COPD. **Methods.** We performed a double-blinded, placebo-controlled, randomized crossover trial. COPD patients smoked cigarettes during undilated conditions at one session and maximal bronchodilated conditions at the other session. Cigarette smoke was measured by pulmonary proportional retention of tar and nicotine. Secondary outcomes included smoke inhalation patterns, and the biomarkers C-reactive protein and fibrinogen. We excluded measurements with possible contamination in a secondary analysis. **Results.** In 35 patients analyzed, bronchodilation did not significantly increase tar retention (-4.5%, p=0.20), or nicotine retention (-2.6%, p=0.11).

Bronchodilation did not significantly affect our secondary outcomes. Secondary analysis revealed potentially less retention due to bronchodilation: tar retention -3.8% (p=0.13), and nicotine retention -3.4% (p=0.01). **Conclusions.** Our results do not support the hypothesis that bronchodilation increases cigarette tar and nicotine retention in COPD patients. Instead, we observed a possibility for less retention.