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Title: Higher than expected prevalence of alpha-1-antitrypsin deficiency (AATD) may not necessarily impact on airflow, gas exchange or acute exacerbation rate (AER)

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Body: AATD is estimated to occur in 1-3% of COPD patients and is believed to accelerate disease. To determine its prevalence in a community practice and impact on disease progression, all patients with COPD, >10 pack-year smoking history and a post-bronchodilator FEV1/FVC < 0.70 were offered testing for AATD. Spirometry and diffusing capacity (DLco) were measured respecting ATS criteria, and serum AAT levels were assayed. Of 323 patients, 291 (90%) accepted screening. 44 (15%) had low serum AAT levels (AATD mean 0.76g/L±0.02SE vs. non-AATD 1.57±0.03). Age (74years±1 vs. 72±1), smoking history (43pack-years±3 vs. 48±2), FEV1 (63%of predicted±3 vs. 61±1) and FEV1/FVC (54%±2 vs. 54±1) were similar. 40 AATD and 187 non-AATD patients had DLco measured and were similar (64%of predicted±4 vs. 62±2). Annual AER and prior spirometry was available in 44 AATD and 217 non-AATD and prior DLco in 39 AATD and 167 non-AATD subjects. Annual AER (1.0infections/year±0.1 vs. 1.2±0.1 over 4.1years±0.1) and annual decline of both FEV1 (18ml/year±19 vs. 3±6 over 6.5years±0.3) and DLco (0.60±0.2ml/min/mmHg/year vs. 0.50±0.1 over 6.4years±0.3) were similar. In this population, AATD prevalence was 5 times greater than previously reported, yet no difference in FEV1, and DLco decline, or AER was observed. Whether this lack of difference is due to strict smoking cessation, medication compliance, aggressive management of exacerbations or a predominance of heterozygotes remains to be determined.