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Title: The respiratory microbiome in chronic obstructive pulmonary disease (COPD) exacerbations: Relationships with clinical characteristics

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Body: Background: There has been recent interest in the significance of the respiratory microbiome in COPD. Methods: Within an observational COPD study, spontaneous and/or induced sputum samples were obtained from 30 COPD patients at four time points: stable state, exacerbation onset, 2 and 6 weeks post exacerbation. 454 high-throughput pyrosequencing was performed on samples from each of these visits to examine changes to the global microbiome. Results: Firmicutes and Proteobacteria were the major phylum groups in most of the samples. Streptococcus, Haemophilus and Moraxella were the most frequently occurring operational taxonomic units at genus level. Cluster analysis revealed 3 groups that could be defined by the Proteobacteria:Firmicutes(P:F) ratio; 1)high firmicutes, 2)mixed proteo-firmicutes and 3)high proteobacteria. Comparing clinical characteristics of these patients, there were no significant differences between groups with regards to GOLD stage, gender, smoking history, BMI, number of exacerbations in the previous 12 months and post bronchodilator FEV1. In the high proteobacteria group the sputum neutrophil count was increased and there was a non-significant trend towards better quality of life as measured by the SGRQ and CRQ. Dynamic changes in the microbiome were observed between stable, exacerbation and recovery visits, although these changes did not reach statistical significance. Conclusions: The COPD microbiome can be defined using molecular techniques, but more research is required to further determine its clinical importance in COPD exacerbations.