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Title: The prevalence of clinically relevant micro-organisms in stable and exacerbated COPD using PCR techniques

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Body: Airway bacteria and viruses are aetiological triggers of COPD exacerbations. We investigated the prevalence of clinically relevant micro-organisms (CRMs: human rhinovirus (HRV), H. influenzae, M. catarrhalis and S. pneumoniae) in stable and exacerbated COPD using sensitive PCR techniques. Reverse-transcription PCR and real-time PCR detected HRV and bacteria respectively, in sputum samples collected at baseline (n=57) and at exacerbation onset (n=70) using our usual symptomatic definition (Seemungal et al, 1998 AJRCCM). Exacerbation samples were taken prior to antibiotic and/or steroid therapy. Fifty-four COPD patients provided 127 sputum samples: mean(SD) age 71(±8) years; FEV1 43.7%(±20.0%) predicted; current smoker 26%; male gender 63%. Airway CRMs were more prevalent at exacerbation than in the stable state (75% vs 42%, $p<0.001$). The prevalence of co-infection with HRV and bacteria at exacerbation (29%) was similar to the prevalence of HRV (26%) or bacteria (21%) alone (figure 1A). Co-infection was proportionally reduced in stable COPD than at exacerbation (7% vs 29%, $p=0.002$) (figure 1B). Co-infection in sputum is higher at COPD exacerbation compared to the stable state and 75% of exacerbations are associated with common CRMs. Further work is required to investigate the impact of co-infection on CRM load and the clinical utility of PCR techniques in managing COPD exacerbations.