these measures was assessed using the intra-class correlation coefficient (Ri) and is expressed below as Ri (95%CI).

Results 145 subjects were recruited; 101 were male with a mean (SD) FEV1 (L) and FEV1/FVC ratio (%) of 1.34 L (0.57) and 53% (14.6) respectively.

Spirometry values showed excellent repeatability; FEV1 [0.93 (0.84 to 0.92) and 0.89 (0.83 to 0.92)] and FVC [0.80 (0.73 to 0.86) and 0.81 (0.72 to 0.87)] after 3 and 6 months respectively.

Sputum biomarkers of inflammation showed moderate repeatability at 3 and 6 months respectively; sputum neutrophils (%) [0.59 (0.43 to 0.71) and 0.50 (0.33 to 0.64)] and eosinophils (%) [0.62 (0.48 to 0.73) and 0.32 (0.13 to 0.49)].

The blood biomarkers peripheral blood white cell count (WCC), neutrophil and eosinophil counts demonstrated good repeatability after 3 and 6 month intervals respectively; WCC [0.68 (0.56 to 0.77) and 0.73 (0.62 to 0.81)], neutrophil count [0.66 (0.54 to 0.76) and 0.71 (0.59 to 0.79)] and eosinophil count [0.66 (0.54 to 0.76) and 0.73 (0.63 t o0.81)]. CRP showed fair repeatability [0.34 (0.16 to 0.5) and 0.30 (0.11 to 0.47) at both time intervals.

Discussions Sputum differential cell counts (%) and peripheral blood differential cell counts are repeatable after 3 and 6 month intervals. These findings may have clinical implications when targeting therapies to sub-groups of COPD patients.

P211 TIME-COURSE OF RHINOVIRUS AND BACTERIAL INFECTION DURING COPD EXACERBATION RECOVERY

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Introduction Airway bacteria and viruses are aetiological triggers of COPD exacerbations. Changes in prevalence of rhinovirus and typical airway bacteria together have not been examined during COPD exacerbation recovery. We compared the prevalence of the clinically relevant microorganisms (CRMs) human rhinovirus and typical pathogenic bacteria (*H. influenzae*, *M. catarrhalis* and *S. pneumoniae*) at five time points during COPD exacerbation recovery.

Methods London COPD cohort patients recorded any new or increased respiratory symptoms on daily diary cards and contacted the clinical team when symptoms worsened. Exacerbations were defined using our usual symptomatic criteria; an increase in respiratory symptoms for two consecutive days, with at least one symptom being major (dyspnoea, sputum purulence or volume) and the other a major or minor symptom (wheeze, cold, sore throat, cough). Reverse-transcription quantitative PCR was used to detect rhinovirus and real-time quantitative PCR was utilised to identify typical bacteria in sputum samples collected at exacerbation presentation (median 2 days after symptom onset), and at days 3, 7, 14 and 35 post-presentation.

Results Nineteen patients with moderate to severe COPD (mean age 68.8 years (SD±8.1); FEV_1 48.4% predicted (±19.2%); current smoker 37%; FEV_1/FVC 0.46 (SD±0.14); FEV_1 1.2L (SD±0.4); male gender 74%) provided 89 of 110 potential sputum samples at 5 time points during 22 exacerbations.

Rhinovirus prevalence progressively fell from 71.4% at exacerbation presentation to 0% at day 35 with significant decreases in prevalence between presentation and days 7, 14 and 35 (all $p<0.002$) (Figure 1). No exacerbation was negative for rhinovirus detection at presentation but positive at later time points. For typical bacteria, 64.7% of samples taken at presentation were positive. This proportion fell at days 3 and 7 but these falls were non-significant ($p=0.08$ and $p=0.09$, respectively) – all events were treated with antibiotics. Seven of the 22 exacerbations (31.8%) were positive for both CRMs at presentation.

Conclusion The prevalence of CRMs varies during recovery from a COPD exacerbation. Rhinovirus prevalence steadily decreases over 2 weeks whilst bacterial prevalence is more variable, presumably due to the background effects of lower airway bacterial colonisation. This emphasises the importance of rhinovirus as a major exacerbation trigger.

P212 ASSESSING THE REPEATABILITY OF BACTERIAL DETECTION IN STABLE COPD USING SEVERAL METHODS

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Background Stable COPD patients are colonised if potentially pathogenic organisms are identified on sputum culture. Associations between colonisation and clinical features such as exacerbation

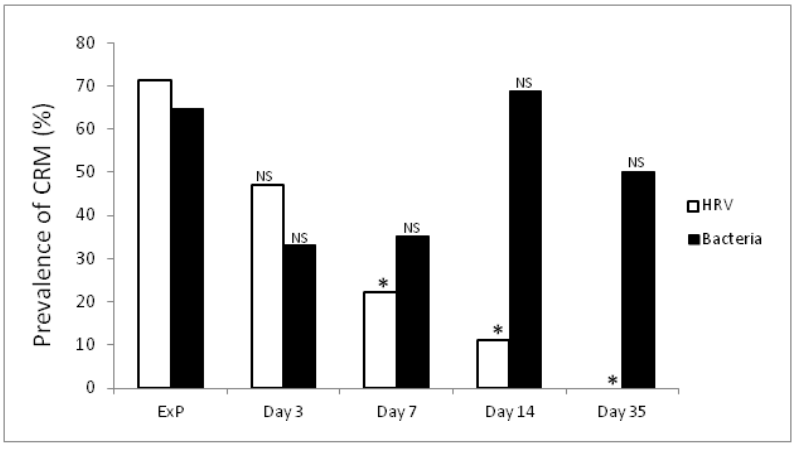

Figure 1. Changes in the prevalence of human rhinovirus (HRV) and typical bacteria at exacerbation and during recovery.

NS: No significant difference found between exacerbation presentation and each time point.

*: Significant decrease in prevalence between exacerbation presentation and each time point (all p<0.002).

Abstract P211 Figure 1

frequency and airway inflammation have been suggested. There is however limited data describing the reproducibility of sputum microbiology results in clinically stable COPD patients.

Aims Examine repeatability of sputum microbiology in subjects with stable COPD over time.

Methods Subjects with COPD were enrolled into an observational study and seen at baseline and at stable visits after 3 and 6 months. Sputum was obtained and samples were divided and analysed over time using standard culture, semi-quantitative bacterial count (colony forming units, CFU), PCR for potentially pathogenic organisms [*(Haemophilus influenzae* (HI), *Streptococcus pneumoniae* (SP), *Staphylococcus aureus* (SA), *Moraxella catarrhalis* (MC)] and quantitative bacterial 16S analysis.

Results 63 subjects provided paired sputum samples; 52 were male with a mean (SD) FEV1 (L) and FEV1/FVC ratio (%) of 1.48(0.54) and 53% (12.8) respectively. 40% were current smokers with an exacerbation frequency of 3 in the preceding year.

Results for standard culture were divided into two groups (culture positive or negative). Results are expressed as Kappa values (95% CI). There was moderate agreement after 3 months, Kappa = 0.48 (0.24 to 0.71); and after 6 months, Kappa = 0.50 (0.25 to 0.76). Individual PCR revealed fair agreement after both time intervals. After 3 months, HI=0.17(–0.08 to 0.43), SA=0.27(–0.03 to 0.56), SP=0.30(0.06 to 0.53), MC=0.19(–0.04 to 0.43). After 6 months, HI=0.09(–0.18 to 0.35), SA=0.10(–0.22 to 0.43), SP=0.37(0.13 to 0.62) and MC= –0.14(–0.4 to 0.11).

Quantitative bacterial analysis demonstrated no differences (mean difference; 95% CI) at 3 or 6 months in bacterial load measured by CFU (–0.18; –0.41 to 0.04, p=0.11 and –0.06; –0.32 to 0.2, p=0.65 respectively) or 16S (–0.03; –0.28 to 0.33, p=0.86 and –0.1; –0.42 to 0.22, p=0.54 respectively).

Discussions These results demonstrate that sputum microbiological assessment in stable COPD is complex. Further longitudinal assessments of sputum microbiology and associations with clinical features are needed.

P213 THE PREVALENCE AND IMPACT OF GASTRO-OESOPHAGEAL REFLUX SYMPTOMS IN STABLE COPD PATIENTS

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Introduction Gastro-oesophageal reflux disease (GORD) has been associated with increased COPD exacerbation frequency (Terada et al, Thorax 2008) and was independently associated with the frequent exacerbator phenotype in the ECLIPSE study (Hurst et al, NEJM 2010). We aimed to quantify the prevalence and impact of GORD in stable COPD in terms of airflow limitation, dyspnoea, health status and exacerbation frequency in a well-characterised cohort.

Methods Stable outpatients from the London COPD cohort completed the Frequency Scale for the Symptoms of Gastro-oesophageal reflux (FSSG), Hull Airway Reflux Questionnaire (HARQ), MRC dyspnoea score, and St George's Respiratory Questionnaire (SGRQ) during clinic visits. Spirometry was performed in accordance with ATS/ERS guidance. Comorbidities including GOR and all medications were recorded by clinical research staff. Exacerbations were defined using our usual symptomatic criteria from daily diary cards (Seemungal et al, AJRCCM 1998).

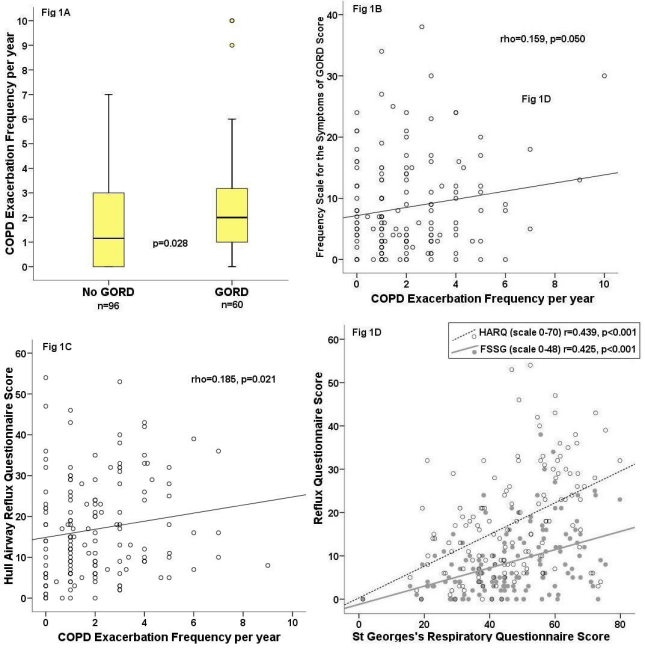
Results 156 stable COPD patients had a mean±SD age of 72.2±9.7 years, 63% male, 29% current smokers, median (IQR) 46 (25,59) pack years, mean±SD FEV1 1.34±0.57L and 54.4±20.2%predicted, BMI 26.5±5.7kg/m^2.

60 (38%) patients had a diagnosis of GORD, of whom 45 (75%) were taking regular acid suppression therapy (42 proton pump inhibitors, 3 H_2 antagonists).

COPD patients with GORD had a higher exacerbation frequency than those without (median (IQR) 2.0 (1.0,3.4) vs 1.2 (0.0, 3.0) per year, p=0.028). In those with GORD, the use of acid suppression therapy did not impact exacerbation frequency (median (IQR) 2.0 (1.0,4.0) (n=45) vs 2.0 (1.0, 3.0) (n=15) per year, p=0.431).

FSSG and HARQ scores were both related to COPD exacerbation frequency (rho=0.159, p=0.050 and rho=0.185, p=0.021 respectively) and more strongly to SGRQ (r=0.425, p<0.001 and r=0.439, p<0.001 respectively). They were not related to MRC dyspnoea score (rho=0.079, p=0.367 and rho=0.126, p=0.148 respectively) or FEV1% predicted (r=–0.063, p=0.452 and r=–0.067, p=0.416 respectively).

Conclusions GORD is common in COPD and is associated with higher exacerbation frequency, although acid suppression therapy does not appear to affect this. Higher GORD symptom scores relate to worse health status and higher exacerbation frequency but not to airflow limitation or dyspnoea. Understanding the mechanisms may lead to novel effective interventions in COPD.



Abstract P213 Figure 1

P214 GASTRO-OESOPHAGEAL REFLUX SYMPTOMS DURING COPD EXACERBATIONS

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Introduction Gastro-oesophageal reflux disease (GORD) has been associated with increased COPD exacerbation frequency (Terada et al, Thorax 2008) and was independently associated with the frequent exacerbator phenotype in the ECLIPSE study (Hurst et al, NEJM 2010). We aimed to quantify any changes in GORD symptoms during COPD exacerbations.

Methods Outpatients from the London COPD cohort completed the Frequency Scale for the Symptoms of Gastro-oesophageal reflux (FSSG) and Hull Airway Reflux Questionnaire (HARQ) during stable-state clinic visits and at exacerbation, within a week of symptom-onset, and prior to systemic therapy. FSSG and HARQ scores range from 0–48 and 0–70 respectively, with significant reflux thought to be associated with scores of ≥8 and ≥13 respectively.