Abstract S75 Table 1

MRC Grade	Mean change (SD) ISWT (m)	95% C.I	Sig. (2 tailed)	FEV1 (litres) (SD)	FVC (SD) (litres) (SD)	BMI (SD)
1 n=8	11.25 (45.49)	-26.78 to 49.28	507	1.38 (0.41)	2.39 (0.57)	27.90 (6.05)
2 n=88	29.54 (46.11)	19.77 to 39.31	<0.0001	1.43 (0.57)	2.62 (0.67)	26.30 (5.50)
3 n=142	23.88 (44.98)	15.91 to 30.84	<0.0001	1.39 (0.56)	2.46 (0.74)	28.60 (5.90)
4 n=128	14.37 (34.70)	8.30 to 20.44	<0.0001	1.15 (0.55)	2.34 (0.94)	27.61 (6.69)
5 n=75	8.54 (29.75)	1.70 to 15.39	0.015	0.99 (0.44)	2.08 (0.58)	27.90 (7.83)
Overall change n=441	19.25 (40.65)	15.44 to 23.05	<0.0001	0	0	0

Conclusion Overall, there was a statistical significant increase in distance walked in all patients. These data confirm the need for a PISWT to be conducted within the COPD population. Patients in MRC grades 2 and 3 show a larger variance in walking distance between both shuttle walk tests.

S76 THE COPD ASSESSMENT TEST SCORE (CAT): A MULTICENTRE, PROSPECTIVE STUDY OF RESPONSE TO PULMONARY REHABILITATION

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Background The COPD assessment test (CAT) was introduced last year.¹ It is a questionnaire that contains eight questions covering domains relating to the impact of COPD symptoms. It is a self completion questionnaire and does not require scoring software. Scores of 0–10, 11–20, 21–30, 31–40 represent mild, moderate, severe or very severe clinical impact. In cross-sectional studies it has similar scaling properties to the SGRQ, so that 1 point in the CAT is equivalent to approximately 2.5 points on the SGRQ. It is not known how the CAT score performs in the context of pulmonary rehabilitation (PR).

Methods We prospectively studied the introduction of the CAT score as an assessment tool in several pulmonary rehabilitation programs across London, where it was used alongside a range of other outcome measures in different programs including the SGRQ, CCQ, HAD score, MRC dyspnoea score and several different walking tests. Primary outcome was a comparison of change in CAT score against an anchor question used to assess overall response, scored 1 "I feel much better" 2 "I feel a little better", 3 "I feel no different", 4 "I feel a little worse", 5 "I feel much worse".

Results Data were available for 172 COPD patients, mean(SD) age 69.6(9.3) years, FEV₁ 51.9(18.9)% predicted, MRC dyspnoea score 3.0(0.9), CAT score 20.0(7.5) who attended five different programs. Mean improvement in CAT score after PR was 2.8(5.8) points. In those scoring "much better" (n=108) CAT fell by 3.7(6.1) points and by 1.2(4.8) in those who felt "a little better" (n=56) (p=0.01). In those scoring 3 or 4 on the anchor question (grouped together as n=8) change in CAT was -0.6(3.5).

Conclusion The CAT score improves in response to pulmonary rehabilitation and more so in those who report a greater overall improvement. Further accrual is underway to allow comparison of changes in CAT to other outcome measures.

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Mechanisms of lung infection in the community and hospital setting

S77 COMPARTMENTALISATION OF SURFACE TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELLS-1 (TREM-1) IN VENTILATOR-ASSOCIATED PNEUMONIA (VAP)

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Introduction Biomarkers have been investigated in order to speed up diagnosis of VAP, a common condition in ICU patients. TREM-1 is a protein involved in amplification of immune responses to bacterial and fungal infection and exists as soluble and surface forms.^{1,2} The diagnostic value of soluble TREM-1 in broncho-alveolar lavage fluid (BALF) in VAP is controversial.³ Therefore the utility of surface TREM-1 for diagnosing VAP in a two-compartment model (BALF and blood) was investigated.

Methodology Paired blood and BALF were obtained in consenting patients in the following groups: (1) Ventilated patients with VAP diagnosed on semi-quantitative microbiology and Clinical Pulmonary Infection Score (CPIS); (2) Ventilated patients without sepsis; (3) Day-case bronchoscopy patients without evidence of infection. Flow cytometry was performed on cell pellets derived from simultaneous BALF and blood samples. Surface TREM-1, CD11b (immune cell activation marker) and L-selectin (immune cell migration marker) levels were measured on monocytes and neutrophils. At the same time an inflammatory cytokine panel (comprising IL-1 β , IL-6, IL-8 and soluble TREM-1) was measured by ELISA in the paired blood and BALF samples.

Results Expression of TREM-1 and CD11b on monocytes were significantly elevated in BALF samples obtained from the VAP patient group. There was no change in blood surface TREM-1 and CD11b levels between the different patient groups. The BALF/blood ratio of monocyte TREM-1 increased the discrimination between

Abstract S77 Figure 1 The ratio monocyte surface TREM-1 between BALF and blood (flow cytometry). 16 patients with VAP are compared with 8 ventilated non-septic control (VC) and 17 non-ventilated non-infected control patients (NVC). The median levels and IQRs are: VAP (0.92, 0.66–1.77), VC (0.21, 0.12–0.28) and NVC (0.36, 0.22–0.41). * and # p=0.0001.

the VAP and non-VAP groups (Abstract S77 Figure 1). Soluble TREM-1 levels were not significantly different between the groups. There was no difference in peripheral blood white cell count, CRP, expression of CD11b, L-selectin and inflammatory cytokines between VAP and disease controls.

Conclusion The BALF/blood ratio of monocytic surface TREM-1 discriminates between the VAP and non-VAP groups. Measurement of surface TREM-1 using a two-compartment index may have utility in diagnosing VAP.

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S78 DETERMINANTS OF MACROPHAGE RESPONSES TO *STREPTOCOCCUS PNEUMONIAE*

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Introduction and Objectives *Streptococcus pneumoniae* is the commonest cause of pneumonia and associated with marked inflammatory responses that underpin its immunopathogenesis. Surprisingly little is known about the molecular determinants of host–pathogen interactions that mediate these responses. We have studied the role of the pneumococcal capsule and surface lipoproteins in innate immune responses by macrophages that comprise the first line of cellular immune defence within the lung.

Methods Human macrophage responses to wild type *S pneumoniae* (TIGR4) and isogenic mutant strains deficient in capsule (P1672) or surface lipoproteins (Δ lgt) were investigated at the level of intracellular signalling, genome-wide transcriptional profiling and at protein level by cytokine ELISA.

Results Unencapsulated bacteria invoked greater activation of the classical NF κ B pathway, suggesting that the capsule may serve to inhibit some innate immune host pathogen interactions. In contrast, the Δ lgt strain showed attenuated activation of NF κ B, suggesting that lipoproteins are important ligands for innate immune recognition of pneumococci. Transcriptional responses to both unencapsulated and Δ lgt strains showed marked differences to wild type pneumococci. However, quantitatively, major gene expression changes were preserved in the mutant strains. Despite the divergent effects on NF κ B activation, both unencapsulated and Δ lgt strains showed attenuated responses amongst these genes, although some key responses such as upregulation of TNF α were equivalent in all strains. Transcription factor enrichment analysis was conducted for the list of genes up-regulated by each strain to obtain new insight into the different pathways by which pneumococci may activate inflammatory responses. As expected, genes up-regulated by the wild type strain were enriched only for the NF κ B family. In keeping with the signalling data, the Δ lgt strain was not enriched for NF κ B but only the PPAR γ -RXR transactivator, and the unencapsulated strain was highly enriched for NF κ B and a raft of other transcription factors.

Conclusion Pneumococcal capsule and lipoproteins are important determinants of inflammatory responses to pneumococci. Our data suggest that the capsule inhibits multiple innate immune signalling pathways and that lipoproteins are critically important for activation of the canonical NF κ B pathway. TNF α responses are independent of capsule and lipoproteins.

S79 POTENTIAL DIAGNOSTIC SIGNIFICANCE OF NEUTROPHIL PROTEASES IN VENTILATOR-ASSOCIATED PNEUMONIA

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Introduction and Objectives The clinical diagnosis of ventilator-associated pneumonia (VAP) remains notoriously difficult, as several non-infective conditions mimic VAP. Microbiological confirmation of the diagnosis using conventional cultures typically takes 48–72 h. Identification of molecules measurable within a short time frame and closely associated with microbiologically confirmed VAP is therefore highly desirable. VAP is associated with significant influx of activated neutrophils into the alveolar space. We postulated that extracellular neutrophil proteases in bronchoalveolar lavage fluid (BALF) may reliably identify VAP in suspected cases.

Methods Fifty-four intubated and mechanically ventilated patients in the intensive care unit developed clinically suspected VAP and were recruited. Bronchoalveolar lavage (BAL) was performed using a standardised protocol. An aliquot of BALF was sent to the diagnostic microbiology laboratory for quantitative culture, with confirmation of VAP defined as growth of a pathogen(s) at $>10^4$ colony forming units/ml. Remaining BALF was centrifuged. The following neutrophil-specific proteases were assayed in cell-free BALF supernatant—matrix metalloproteinase (MMP)-8 and MMP-9 by Luminex assay, and human neutrophil elastase (HNE) by enzyme-linked immunosorbent assay. Urea was simultaneously measured in serum and BALF, and used to correct for the dilution of epithelial lining induced by BAL. Receiver operating characteristic (ROC) curves were constructed and optimal specificity and sensitivity for each marker calculated.

Results Eleven patients (20%) had confirmed VAP. For HNE (cut off 670ng/ml) the ROC area under curve (AUC) was 0.87 ($p<0.0001$), sensitivity 93%, specificity 79%. For MMP-8 (13 ng/ml), ROC AUC was 0.81 ($p<0.005$), sensitivity 91%, specificity 63%. For MMP-9 (22 ng/ml), ROC AUC was 0.79 ($p<0.005$), sensitivity 82%, specificity 63%.

Conclusions Neutrophil proteases are strongly associated with confirmed infection in cases of suspected VAP. The values for HNE, in particular, compare extremely favourably with any previously published equivalent values. These data suggest that neutrophil protease concentrations in BALF deserve further attention as potentially diagnostic markers for VAP. They further suggest that neutrophil proteases, inappropriately released into the extracellular space, may contribute to the pathophysiology of VAP.

S80 THE ROLE OF MYD88 IN RHINOVIRUS 1B INFECTION

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Introduction Rhinovirus (RV) are major triggers of acute asthma exacerbations and result in innate immune cell infiltration into the airways. Viral recognition by TLRs results in activation of pathways mediated by the adaptors MyD88 and TRIF, which predominantly control the production of proinflammatory cytokines and interferons respectively. We have previously shown that addition of the cytokine IL-1 (which also signals via MyD88) potentiates responses to the viral mimic Poly (I:C),¹ which acts in a MyD88-independent