

Figure 1. Patient serum IgG titre specific for LPS isolated from B4 determined by ELISA.

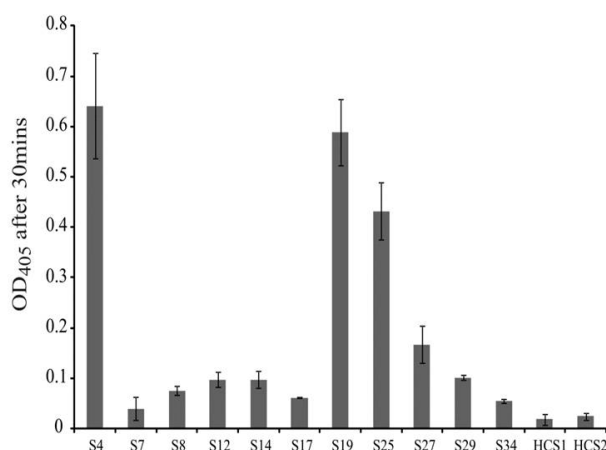


Figure 1: Only the 3 patients who had impaired serum killing (S4, S19 and S25) had high antibody titres to the LPS indicating that the LPS in strains isolated from these patients was responsible for high levels of IgG2 that impairs killing of the PA strain.

Abstract S105 Figure 1

measured by flow cytometry. Using RT-PCR, we observed an increase of PDL1 mRNA after X31 infection suggesting that the expression of this protein is transcriptionally regulated. In addition, we saw an increase in type I interferon expression by MDMs in response to X31 infection, but no expression of IFN $\gamma$ . In contrast we observed a trend towards decreased expression of IL-10 mRNA. In further experiments, infection of alveolar macrophages with X31 also caused significant increases in HLA-DR and PDL1 cell surface expression.

**Conclusions** These data indicate that, in contrast to HIV infection of macrophages<sup>2</sup> influenza-induced expression of PDL1 may not be regulated by IL-10 in human macrophages.

1. Erickson et al (2012) J Clin Invest doi: 10.1172/JCI62860.
2. Rodriguez-Garcia, et al. (2011) J Leukoc Biol 89(4):507–15.

#### S107 EFFECTS OF EXPOSURE TO CIGARETTE SMOKE CONDENSATE ON PNEUMOCOCCAL GENE EXPRESSION IN RELATION TO BIOFILM FORMATION

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Although cigarette smoking is well-recognised as being the strongest independent risk factor for development of invasive pneumococcal disease, little is known about its direct effects on the expression of virulence factors by the pneumococcus. The primary objectives of the current study were to investigate the effects on gene expression in relation to biofilm formation following exposure of the pneumococcus to cigarette smoke condensate (CSC). Strain 172 (serotype 2–3F) of the pneumococcus was exposed to CSC (20–160  $\mu$ g/ml) for 16

hours at 37°C in 6-well tissue culture plates to facilitate adherence and biofilm formation. Following incubation, biofilm associated with the adherent bacteria was stained with 0.1% crystal violet, extracted and assayed spectrophotometrically. In the case of gene expression, the bacteria ( $2 \times 10^8$  colony forming units/ml) were exposed to CSC (160  $\mu$ g/ml) or solvent for 60 min at 37°C, after which RNA was extracted and converted to cDNA by reverse transcriptase-PCR (RT-PCR) and whole genome gene expression profiles determined using the *Streptococcus pneumoniae* TIGR4 DNA Microarray Chip. Six microarrays were performed (in triplicate for the control and CSC-treated systems). Exposure of the pneumococcus to CSC resulted in dose-related augmentation of biofilm formation which attained statistical significance ( $P < 0.05$ ) at concentrations of 80 and 160  $\mu$ g/ml. CSC-mediated augmentation of biofilm formation was associated with selective and significant up-regulation of the genes encoding the two-component 11 system (TCS11), consisting of the genes *hk11* (histidine kinase) and its cognate response regulator, *rr11*, which has been implicated in biofilm formation by *S. mutans*. Relative to the non-exposed control system, the respective levels of up-regulation of each gene were 19.7- and 22.5-fold ( $P < 0.001$  and  $P < 0.0006$ ). Induction of biofilm formation, probably as a stress response resulting in activation of TCS11, may underpin cigarette smoke-mediated colonisation of the respiratory tract by the pneumococcus.

#### Evaluating impact in pulmonary rehabilitation

#### S108 THE EFFECT OF AN INTERDISCIPLINARY REHABILITATION PROGRAMME ON DAILY PHYSICAL ACTIVITY FOR PATIENTS WITH LESS ADVANCED COPD IN A PRIMARY CARE SETTING: A SYSTEMATIC REVIEW

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**Introduction** The natural course of COPD is characterised by progressive airflow limitation and complicated by the development of systemic consequences and co-morbidities. Daily physical inactivity (DPA) is believed to mediate those systemic consequences or co-morbidities. Recent research demonstrates that even in the early stages of COPD, DPA plays a role in developing systemic consequences and co-morbidities. Hence, interventions that enhance or maintain DPA in this population, such as pulmonary rehabilitation (PR), should be considered. Due to the low accessibility and high cost of PR in a specialised care setting, rehabilitation in primary care could be an added value for patients with less advanced COPD-related problems. Despite the widespread belief in the benefits of PR in a primary care setting, it remains unclear if such PR programmes are (cost) effective for patients with less advanced COPD.

**Objective** To evaluate data from clinical trials assessing the effect of PR in primary care for patients with less advanced COPD on DPA, exercise capacity (EC) and quality-of-life (QoL).

**Methods** The electronic databases PEDro, CENTRAL, Pubmed and EMBASE were searched. Only randomised and controlled clinical trials were eligible for inclusion, provided they investigated the effects of interdisciplinary PR in primary care for patients with less advanced COPD (GOLD I-II). Independent data extraction was performed by two authors. Risk of bias was rated using the Cochrane Collaboration 'Risk of bias' tool. Primary outcome is the level of DPA, secondary outcomes are EC and QoL.

**Results** Eight studies were found and methodological quality is displayed in table 1. One study objectively measured DPA by a pedometer and showed a significant improvement in DPA. EC was significantly improved in 7/8 studies. QoL is measured in all 8 studies, 3/8 had a significant improvement and two revealed to have clinical relevant effect on QoL.

**Conclusions** PR in primary care for patients with less advanced COPD improves EC and QoL and could be beneficial in improving DPA. Since recent insights in the systemic burden of COPD and the role of DPA in this matter, future research must focus on the transfer of PR benefits to DPA, including a cost-effective analysis.

#### Abstract S108 Table 1

**Table 1: Cochrane Collaboration 'risk of bias' summary**

	Chavannes et al. 2009	Effing et al. 2010	Hoogendoorn et al. 2010	Monnikhof et al. 2003	Monnikhof et al. 2004	Rea et al. 2004	Van wetering et al. 2010a	Van wetering et al. 2010b
Random sequence generation	-	+	+	+	+	+	+	+
Allocation concealment	-	+	+	+	+	?	+	+
Blinding of participants	?	?	+	-	-	?	+	+
Blinding of personnel	?	?	?	-	-	?	?	?
Blinding of outcome data	?	?	?	?	?	?	?	?
Selective reporting	+	+	+	+	+	+	+	+
Other bias	+	+	?	+	+	+	+	+
Legend: -: high risk of bias / ?: unclear risk / +: low risk of bias								

#### S109 FIVE-REPETITION SIT-TO-STAND TEST: RELIABILITY, VALIDITY AND RESPONSE TO PULMONARY REHABILITATION IN COPD

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**Background** Validated field exercise tests, such as the six minute walk test and incremental/endurance shuttle walks, require space and may be time-consuming as repeat walks are needed due to learning effect. Hence they are rarely used outside the research or pulmonary rehabilitation (PR) setting. The five-repetition Sit to Stand test (STS) is a simple test that is feasible in most settings. It measures the quickest time taken to stand and sit five times from a chair, with arms folded. We hypothesized that the STS would be reliable, correlate with the incremental shuttle walk (ISW), and be responsive to PR.

**Methods** The STS was measured in 80 COPD patients on two occasions 24–48 hours apart. Test-retest reliability was calculated using ICCs. STS and ISW were measured in a convenience sample of 396 COPD patients (Mean (SD) age 69 (10); FEV1%predicted 47 (20); ISW 202 (141)) recruited from hospital outpatient clinics. Spearman rank correlation was used to evaluate the relationship between STS and ISW. The STS was measured before and after an 8-week outpatient PR programme in 168 COPD patients. Paired t-tests were used to compare pre- and post-PR outcomes.

**Results** The STS demonstrated excellent test-retest reliability with an ICC value of 0.99 with no learning effect. A significant correlation was seen between STS and ISW ( $\rho = -0.68$ ;  $p < 0.001$ ). The STS improved significantly following PR (Pre: 20.91 (16.23) versus Post: 17.87 (14.93) seconds; 95% confidence interval -1.5 to -4.6 seconds;  $p < 0.001$ ).

**Conclusions** The STS is reliable, correlates with the incremental shuttle walk, and is responsive to PR in patients with COPD. The STS is a practical functional outcome measure suitable for use in most healthcare settings.

#### S110 PULMONARY REHABILITATION OUTCOMES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) VS MATCHED PATIENTS WITH INTERSTITIAL LUNG DISEASE (ILD)

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**Introduction** Pulmonary rehabilitation is an effective intervention for patients with COPD. There is now also good evidence of benefit for patients with ILD. We have compared the outcome of the same PR programme in patients with COPD and ILD.

**Methods** Patients with various forms of ILD (predominantly IPF or UIP) were matched with the same number of COPD patients for baseline MRC grade and for age. All patients had completed the same 7 week, 14 visit hospital based outpatient PR program.

Outcome Measures and desaturation during exercise were compared between the two groups.

**Results** 51 ILD patients, age range 34–85, mean initial MRC grade 3.5(0.94), 30 male were compared with 51 COPD patients, age range 47–85, mean baseline MRC grade 3.5(0.94), 31 male.

**Discussion** Our PR program produced clinically important improvements in ISWT and all domains of the CRDQ for COPD patients. ILD patients produced a smaller mean change in ISWT although this was not statistically significant between the groups. ILD patients also showed smaller changes in all domains of the CRDQ although again this was not statistically significant between the groups. The improvement in ESWT was similar in both groups. Desaturation during the baseline ISWT was more severe in the ILD group regardless of oxygen usage and despite a marginally higher pre-exercise value. This may account for the lower ISWT value seen in these patients. PR produces measurable improvements in both groups of patients. Interpretation is hampered by a lack of defined MCID values for ILD patients.