S112 ESTIMATING PARTICIPATION RATES OF COPD PATIENTS IN PULMONARY REHABILITATION AND SELF-MANAGEMENT PROGRAMMES: THE IMPORTANCE OF DEFINING PARTICIPATION

doi:10.1136/thoraxjnl-2012-202678.117

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Introduction and Objectives Delivery of pulmonary rehabilitation (PR) and self-management (SM) support programmes to patients living with chronic obstructive pulmonary disease (COPD) is emphasised in national guidelines, but these interventions are not always routinely available. One potential explanation for the lack of implementation could be the poor patient participation and retention reported in the literature. We conducted a systematic review to determine a true estimate of participation and dropout rates.

Methods Studies were identified from eight electronic databases including MEDLINE. Controlled clinical trials of structured SM, PR and health education (HE) programmes for COPD were included. Data extraction included *'participant flow'* data using the Consolidated Standards of Reporting Trials (CONSORT) statement and its extension to pragmatic trials. Patient *'participation rates'* (study participation rate (SPR), study dropout rate (SDR) and intervention dropout rate (IDR)) were calculated using prior definitions consistent with CONSORT Random effects logistic regression analysis was conducted to examine effects of four key study characteristics on participation rates.

Results 56 quantitative studies (51 randomised controlled trials, three quasi-experimental and two before-after studies) evaluated PR (n=31), SM (n=21) and HE (n=4). Reports of participant flow were generally incomplete; *'numbers of potential participants identified'* were only available for 16%, and *'numbers assessed for eligibility'* for only 39% of studies. Although *'numbers eligible'* were better reported (77%), we were unable to calculate SPR for 23% of studies.

Overall we found *'participation rates'* for studies (n=43) were higher than previous reports; only 19% of studies had less than 50% SPR and just over one third (34%) had a SPR of 100%; SDR and IDR were less than or equal to 30% for around 93% of studies. There was no evidence of effect of study characteristics on participation rates.

Conclusion Unlike previous reports, we found high participation and low dropout rates in studies of PR or SM support for COPD Previous studies adopted different participation definitions; some reported proportions without stating definitions clearly, obscuring whether proportions referred to the study or the intervention. Clear, uniform definitions of patient participation in studies are needed to better inform the wider implementation of effective interventions.

S113 LONG TERM EXERCISE (LTE) FOR COPD PATIENTS POST-PULMONARY REHABILITATION (PR) PROLONGS THE DURATION OF BENEFITS DERIVED FROM PR

doi:10.1136/thoraxjnl-2012-202678.118

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Introduction PR is associated with functional, emotional and resource benefits for breathless COPD patients which decline over 12–18 months. Patients who complete PR express the desire to continue exercising regularly with other breathless patients but there is currently no evidence for efficacy. This study evaluated regular community-based LTEfor these patients.

Methods Patients completing PR were recruited to once weekly LTE held in accessible venues by 2 exercise instructors (Loughborough trained for exercising patients with chronic respiratory disease). Baseline demographics and disease severity were collected and outcomes: 6 minute walk test (6MWT), Hospital Anxiety & Depression (HAD) score, COPD Assessment Test (CAT), Chronic Respiratory Questionnaire (CRQ) and patient satisfaction measured at baseline, 6 and 12 months. Patients who accepted referral for LTE but never attended or dropped-out were recalled for outcomes at 12 months. Hospital admissions were audited for 12 months after PR-completion.

Results Between June-2010 and January-2012 75 patients mean(SD) age 69.3(9.7)yrs, FEV_1 1.26(0.54)L, MRC 3.16(0.81) 63% female, 19.2% current smokers and 3 on LTOT accepted referral to LTE. 35% (26/75) never attended and 27%(20/75) dropped out after starting; 39% (29/75) continued to exercise for at least 6 months and 25% (19/75) exercised to 1 yr. For patients who exercised for 12 months there was no significant decline in exercise capacity (6MWT), a significant improvement in CAT over 6/12 (p=0.002) maintained to 12/12 (p=0.02) and no increase in anxiety levels, which remained below clinical relevance for the 12 months post PR. In comparison, patients who did not continue LTE had a significant (p=0.001) decline in 6MWT, no change in CAT score and a significant(p=0.04) increase in anxiety to a clinically important range (table 1). Self reported hospital admissions in the year following PR were higher for patients who did not exercise (mean 0.61 (SD 1.47)) compared to those who did, 0.16 (0.50).

Conclusions This pilot demonstrates that community-based LTE with trained instructors is safe and realistic for breathless patients after completing PR and, for the first time, demonstrates significant prolongation of functional and emotional benefits. This offers acheaper, more durable alternative to repeating PR.

Inflammatory cell phenotype and activation in asthma

S114 ADAPTIVE AND INNATE-LIKE T CELL PHENOTYPES IN ASTHMA IN RELATIONSHIP TO COMPARTMENT AND SEVERITY

doi:10.1136/thoraxjnl-2012-202678.119

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Introduction and Objectives Asthma is a heterogeneous disease affecting 150–300 million people. Underlying mechanisms remain unclear. T_H17 cells expressing interleukin-17 are widely hypothesised to play a role, particularly in severe neutrophilic asthma. Mucosal associated invariant T (MAIT) cells are novel innate-like T-cells of unknown function which express CD161 and an invariant TCRα chain (Vα7.2-Jα33) and recognise the highly conserved restriction molecule MR1.

We undertook to analyse IL-17 and key T-cell subsets, namely T_H17, T_H1, T_H2, $T_{REG,}$ and MAIT cells in relation to asthma severity and virus-induced exacerbations.

Methods Cross sectional study: 76 subjects underwent detailed phenotyping, sputum induction, phlebotomy, and bronchoscopy. Samples were analysed by 9-colour flow-cytometry, RT-PCR, multiplex ELISA, microarray, and deep sequencing of the airway microbiome. Longitudinal study: 35 frequently exacerbating asthmatics: followed at 7 time-points during a naturally occurring cold.

Abstract S113 Table 1 Health related quality of life and exercise capacity at baseline (end-PR) 6 months and 12 months of long-term exercise

	Baseline n=74	6/12 Attenders n=23	p	12/12 Attenders n=19	p	12/12 DNA n=27	p DNA v baseline
Median(range) class attendance	—	**15 (6–21)**	—	**27 (12–41)**	—	0 (0–10)	—
CAT score Mean (±SD)	22.92 (6.9)	16.48 (1.56)	0.002	17.32 (1.80)	0.02	21.59 (7.71)	0.34
CRQ Dyspnoea	3.31 (1.36)	3.7 (1.73)	0.22	3.33625 (1.18)	0.96	3.37 (1.58)	0.96
CRQ Fatigue	4.01 (1.48)	4.10 (1.37)	0.82	3.78 (1.61)	0.62	3.59 (1.37)	0.21
CRQ Emotional Function	4.66 (1.44)	4.84 (1.42)	0.79	4.52 (1.81)	0.77	4.46 (1.52)	0.51
CRQ Mastery	4.74 (1.64)	5.28 (1.51)	0.79	4.86 (1.47)	0.77	4.75 (1.78)	0.51
HADS Anxiety	7.45 (4.78)	4.9 (3.45)	0.04 ↓	6.17 (4.51)	0.37	10.32 (6.02)	0.04 ↑
HADS Depression	5.61 (3.91)	4.73 (3.11)	0.41	5.88 (3.19)	0.63	6.93 (4.65)	0.24
6 MWT (metres)	352.7 (108.0)	329.6 (78.1)	0.11	321.3 (78.8)	0.14	283.1 (94.1)	0.001

Improvement in pt condition indicated by: ↓ CAT, HADS; ↑ CRQ, 6MWT

Results Contrary to initial hypotheses T_H17 cell frequencies did not differ between health and any asthmatic phenotype, in any tissue compartment. T_H2 cell frequencies were elevated in asthma in bronchoalveolar-lavage (BAL) (ANOVA p=0.041) and markedly in bronchial biopsies (p=0.048), as expected[1]. BAL T_H1 cell frequencies were also increased in asthma (p=0.01) as described[2], whilst T_{REG} frequencies were lower in severe asthma (p=0.019).

T_H2 cytokines were increased in asthma in sputum (IL-5 p=0.005) and BAL (IL-5 p<0.0001, IL-13 p=0.017), but IL-17 was elevated only in BAL in steroid-naive, mild asthmatics (ANOVA p=0.04) who were older (p=0.039).

Longitudinal follow-up revealed no significant differences in T-cell frequencies during exacerbations, though sputum T_H17 cells tended to increase (NS).

We observed that frequencies of Vα7.2+CD161+ (MAIT) cells in blood are lower in asthma than in health (p=0.013), and correlated with severity in blood (p for linear trend <0.0001), and sputum (p=0.018, Figure 1). This deficiency is specific to MAIT cells, and is not related to age or inhaled steroid therapy.

Conclusions A role for T_H17 cells in asthma, particularly severe neutrophilic disease has been widely hypothesised, but is not supported by these data. High BAL IL-17 levels in older, steroid-naive, mild asthmatics may have a different cellular source. We describe a novel finding of deficient Vα7.2+CD161+ (MAIT) cells in severe asthma.

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S115 NADPH OXIDASE 4 OVER-EXPRESSION MEDIATES EPITHELIAL CILIARY DYSFUNCTION IN NEUTROPHILIC ASTHMA

doi:10.1136/thoraxjnl-2012-202678.120

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Objective Epithelial ciliary dysfunction is a feature of asthma and contributes to persistent symptoms and recurrent exacerbations. We sought to examine whether its cause is due to an altered airway environment or an intrinsic abnormality.

Methods Primary epithelial cells were obtained from 46 subjects with asthma and 28 healthy controls for culture. Air-Liquid-Interface (ALI) cultures fully differentiated from human primary airway epithelial cells were stimulated with asthmatic sputum, with or without the presence of antibiotics. Ciliary function was assessed using video-microscopy. Bacterial 16S load in sputum and ALI culture before and after addition of sputum were assessed by qPCR. Oxidative stress was enumerated by 8-oxo-dG expression in bronchial biopsies using immunohistochemiatry in 27 asthmatics and 9 healthy controls, and in basal epithelial cells following hydrogen peroxide (H_2O_2) stimulation assessed by the DCFDA assay. NADPH oxidase (NOX) subtype 4 mRNA expression was quantified using qPCR. The effect of NOX4 inhibition, using GKT137831, on ciliary dysfunction was evaluated using fresh epithelial strips from 13 asthmatics.

Results In *ex vivo* ciliated epithelial ALI cultures ciliary dysfunction did not persist, but was evident in cells from asthmatics following exposure to sputum. Bacterial load increased in the epithelial cultures following exposure to sputum, but were not different between health and disease suggesting that both exposure to an asthmatic environment and a susceptibility to stress is necessary to induce ciliary dysfunction in asthma. *In vivo* the oxidative stress burden in the bronchial epithelium was heightened and related to airflow obstruction and neutrophilic inflammation. NOX4 mRNA expression was significantly elevated in epithelial cells from neutrophilic asthmatics, and H_2O_2-induced intracellular reactive oxygen species generation was increased compared to health and attenuated by NOX4 inhibition. Critically, in fresh epithelial cells from asthmatics inhibiting NOX4 markedly improved ciliary function and was related to the intensity of neutrophilic inflammation.

Conclusions These data suggest that in asthma NOX4 up-regulation promotes the susceptibility of the bronchial epithelium to develop ciliary dysfunction in the presence of an abnormal microenvironment. NOX4 inhibition attenuates ciliary dysfunction. This implicates NOX4 as a potential therapeutic target for asthma, particularly in those with neutrophilic predominant disease.