home for use in the event of an exacerbation. Whilst this approach is established with a strong evidence base in asthma, evidence suggestive that this is effective in reducing hospital admissions and readmissions in COPD is inconsistent.[1]

**Aims and Objectives** This study aims to assess the impact of implementing a unified self management strategy, consisting of self management plan, education and rescue medications, in reducing hospital inpatient readmissions at 30 and 90 days.

**Methods** The study was carried out over six months, across three acute hospitals, between November 2010 and April 2011. All patients admitted with a primary diagnosis of COPD exacerbation were included and given the following unless there were any contra-indications for providing this:

A unified written self management plan

Rescue medication of a 7 day course of prednisolone and 5 day course of antibiotic

Education on self management and how to use their rescue medication

To assess the impact of the self management strategy, data was collected for both patients who did and did not receive this intervention. For the purpose of accuracy, 10% of data was cross-checked by an independent person.

**Results** During the 6 month audit period, 457 patients with acute hospital admission for COPD exacerbation were recruited, with 68%, 54.6% and 24.5% (mean 40.1%) of patients at each of the 3 sites receiving a self management plan and rescue medication. Main reasons for not receiving included patients not speaking English, couldn't understand self management advice or refused to self manage.

**Conclusions** Self management and rescue medication is associated with a reduction in 30 and 90 day readmission rates by 12.5% and 4.3% respectively. A high proportion of patients did not receive these for practical reasons which need addressing for future evaluations.

**References**

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## P248 BARRIERS TO UPTAKE OF OXYGEN THERAPY IN MALAWI: A QUALITATIVE STUDY

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**Introduction and Objectives** Oxygen is a scarce resource in many developing countries and there are current efforts to increase its availability. Clinicians in Malawi often report refusal of oxygen by patients. This qualitative study explores attitudes to oxygen therapy in Malawi.

**Method** Focus group discussions involving 86 participants were held in rural and urban communities in Malawi until no new ideas were found. Framework analysis of transcripts of the audio recordings was carried out by at least two researchers to identify recurring themes.

**Results** We found that participants' knowledge of oxygen was limited, although many recognised that oxygen is used for respiratory diseases in adults and children. Knowledge of oxygen arose from personal experience, observation in hospital and discussion in local communities. Participants were keen to receive further education about oxygen therapy.

Attitudes to oxygen varied. Some participants recognised that it could benefit those with respiratory and other diseases, and had positive experiences of using it. Others expressed fear or anxiety about using oxygen and cited this as a reason for refusing it. Many of the participants had witnessed a patient's death following the use of oxygen: *"they are afraid that the patient is going to die ... because they had previously seen another patient dying after being placed on the machine"*. Some had heard in their local communities that oxygen was used prior to the death of a patient: *"even at the funeral ceremony people are told that the deceased went to the hospital and there he was put on oxygen and he died there, so this message terrifies people"*.

Participants found the appearance and noise from oxygen concentrators alarming: *"that device is fearsome just by looking at it. When you think of someone inserting this device in the nose or mouth, you may think they want to finish off the life of your child"*.

**Conclusion** This study impacts on efforts to increase the use of oxygen in Malawi and other developing countries. We have shown a need for education at a community level and for guidance for health workers seeking to increase the uptake of oxygen.

# Mechanisms of chronic lung disease

## P249 COULD AN INTRONIC SNP IN THE ALPHA-1-ANTITRYPSIN GENE CONFER PROTECTION TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE?

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Chronic obstructive pulmonary disease (COPD) results from complex interactions between both environmental and genetic factors. This is evidenced by the considerable variation found in the risk of developing COPD despite the established dose-response relationship from the biggest known risk factor, tobacco smoking. Thus, genetic susceptibility remains poorly understood given the best-characterised genetic determinant of COPD, severe alpha-1-antitrypsin (AAT) deficiency, only affects1–2% of all COPD patients.

A genome-wide association study implicated an intronic single nucleotide polymorphism (SNP) rs3748312 within AAT gene as the strongest locus associated with lung function (a heritable surrogate predictor of COPD). Thus, this was investigated as part of a larger research project aimed at identifying rare sequence variants of the AAT gene that may be associated with COPD.

A sample of 230 COPD patients of European descent either predicted to carry one of six haplotypes conferring COPD risk, or who presented with severe early-onset COPD were genotyped for SNP rs3748312 within the AAT gene utilising TaqMan® assay with >5% of samples sequenced for concordance. The data was compared against control data of 60 patients of European ancestry from dbSNP.

In examining the allelic distribution ($p$=0.049, OR 0.57 95% CI: 0.323–1.003) borderline significance was noted, however no significant difference between cases and controls was found in the genotype distribution ($p$=0.096OR 0.583, 95% CI 0.308–1.106).

This preliminary study suggests the SNP merits further work in a more adequately powered investigation with adjustment for covariates such as age, smoking history and lung function given the borderline nature of the findings indicative of a protective effect for developing COPD with the minorallele (A). It is feasible that associated functional SNPs in linkage disequilibrium reflect the true association.

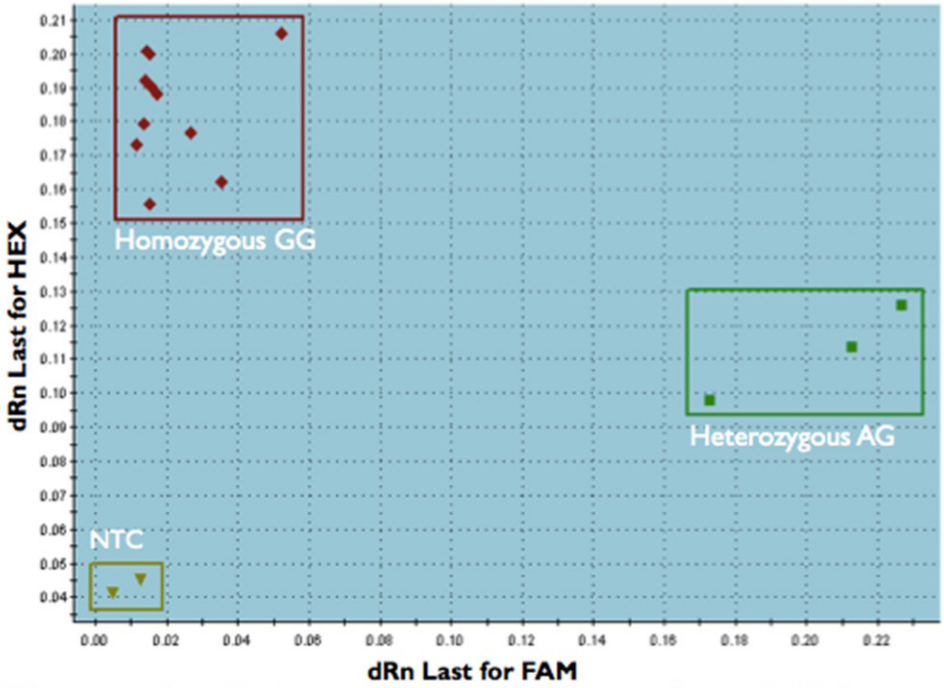


FIGURE 1: A sample TaqMan® assay of 16 samples (including 2 negative controls, NTC). Fluorescence of the different allele-specific fluorophores used (HEX and FAM) allows differentiation between genotypes GG, GA, AA.

Abstract P249 Figure 1 A sample TaqMan® assay of 16 samples (including 2 negative controls, NTC). Fluorescence of the different allele-specific fluorophores used (HEX and FAM) allows differentiation between genotypes GG, GA, AA.

## P250 ASSOCIATION BETWEEN PGRN AND AIRWAY INFLAMMATION IN COPD

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**Background** Progranulin (PGRN) is an anti-inflammatory protein, which is converted into pro-inflammatory granulin peptides (GRNs) by neutrophil elastase (NE) and proteinase-3 (PR3) (1). Neutrophilic inflammation is implicated in the pathophysiology of COPD, therefore the influence of PGRN on mechanisms of neutrophilic inflammation may be of great relevance to understanding and treating inflammation in the disease.

**Methods** Sputum and serum samples were obtained from COPD patients with chronic bronchitis at exacerbation and in the subsequent clinically stable state. Sputum samples were graded by purulence and cultured for quantitative microbiology. PGRN was measured in sputum sol phase together with leukotriene B4 (LTB4), interleukin 8 (IL-8), myeloperoxidase (MPO), tumour necrosis factor α (TNFα), NE and PR3. PGRN and C-reactive protein (CRP) were measured in the serum.

**Results** PGRN was lower in purulent sputum (median=38.91 ng/ml (IQR=1.55–89.71 ng/ml)) than mucoid (median=79.78 ng/ml (IQR=51.57–111.24 ng/ml)) (p=0.024, n=69). In purulent sputum PGRN correlated negatively with bacterial load and markers of inflammation (Table 1). Serum PGRN did not correlate with CRP, but was higher in stable COPD patients (median=65.71 ng/ml (IQR=0–86.46 ng/ml)) than healthy controls (median=38.55 ng/ml (IQR=36.11–44.82 ng/ml)) (p=<0.001, n=20), and increased further during purulent exacerbations (median=75.43 ng/ml (IQR=64.83–85.28 ng/ml)) (p=0.010, n=25).

**Conclusion** The concentration of PGRN in the lung is associated with the increased inflammation seen with bacterial infection and exacerbation as assessed by markers of inflammation. The conversion of PGRN to GRNs may provide a mechanism by which neutrophil proteases regulate inflammation in COPD. Elevated circulating PGRN may reflect systemic inflammation associated with COPD.

1. Kessenbrock K, et al. J Clin Invest. 2008 Jul; 118(7):2438–47.

Abstract P250 Table 1 Correlations and their significance between PGRN and markers of inflammation measured in sputum sol phase

| | Correlations | n |
|---|---|---|
| IL-8 (nM) | r=–0.512, p=<0.001 | 44 |
| MPO (units/ml) | r=–0.543, p=<0.001 | 36 |
| LTB4 (nM) | r=–0.438, p=0.003 | 44 |
| TNF (pM) | r=–0.647, p=0.032 | 11 |
| NE (nM) | r=–0.614, p=0.002 | 22 |
| PR3 (nM) | r=–0.737, p=<0.001 | 22 |
| Bacterial load (CFU/ml) | r=–0.418, p=0.005 | 44 |

## P251 THE ROLE OF REACTIVE OXIDATIVE SPECIES WITHIN CIGARETTE SMOKE EXTRACT ON APOPTOSIS AND INFLAMMATION IN PRIMARY NASAL EPITHELIAL CELLS

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**Introduction** The responses of the bronchial epithelium to cigarette smoke (CS) are well characterized, but effects on the nasal epithelium, also important in respiratory disease, are not as well defined. The mechanism of cell death due to cigarette smoke extract (CSE) exposure is controversial. As there is convincing evidence that cigarette smoke decreases levels of protective antioxidants, we hypothesised that reactive oxidative species contained within CSE contribute to its immunomodulatory and cytotoxic properties.

**Methods** Nasal brushings were obtained from 16 healthy volunteers from the medial aspect of the inferior turbinate as previously