severe asthma. We wished to investigate the effects on CANO of the addition of coarse or fine particle inhaled corticosteroids to standard therapy in severe asthma.

**Methods** Severe asthmatics taking ≥1600 μg/day budesonide or equivalent performed a randomised open-label crossover study. Subjects with FEV₁ < 50%, gas trapping and elevated CANO (≥ 2 ppb) entered a 6 week dose-ramp run-in of Fluticasone/Salmeterol (FFSM) 250/50 μg twice daily for 3 weeks, then 500/50 μg twice daily for 3 weeks. Patients then received additional HFA-BDP 200 μg twice daily or FP 250 μg twice daily for 3 wks in a cross-over. Participants then received prednisolone (PRED) 25 mg/day for 1 week. Nitric oxide, lung function, mannitol challenge, systemic inflammatory markers and urinary cortisol were measured.

**Results** 15 patients completed perprotocol: mean (SD) age, 51 (12) yr; FEV₁, 58 (13)% predicted; residual volume, 193 (100)% predicted; mannitol PD10 177 (2.3) μg. There was no significant difference between FFSM and any add-on therapy for CANO. FFSM/BDP and FFSM/PRED suppressed JawNO and FENO compared to FFSM alone. There was no significant difference between treatments for pulmonary function or bronchial challenge. ECP, e-selectin and ICAM-1 were significantly suppressed by FFSM/PRED compared to FFSM and FP but not FFSM/BDP. Plasma cortisol was significantly suppressed by FFSM/PRED only.

**Conclusion** In severe asthma, alveolar nitric oxide is insensitive to changes in dose and delivery of inhaled corticosteroids and is not suppressed by systemic corticosteroids. Additional inhaled HFA-BDP caused reductions in FENO and JawNO without adrenal suppression. Oral prednisolone reduced FENO and JawNO with suppression of systemic inflammatory markers and urinary cortisol.

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**Abstract S10 Table 1** Patient characteristics

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>n = 146</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) †</td>
<td>40.6 ± 15.1</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>100/46</td>
</tr>
<tr>
<td>Inhaled corticosteroid (BDP equivalent μg)*</td>
<td>1600 (800–2000)</td>
</tr>
<tr>
<td>Long acting β-agonist, n (%)</td>
<td>142 (97)</td>
</tr>
<tr>
<td>Theophylline, n (%)</td>
<td>75 (51)</td>
</tr>
<tr>
<td>Maintenance oral steroids, n (%)</td>
<td>47 (32)</td>
</tr>
<tr>
<td>FEV₁, (L) % predicted†</td>
<td>79 ± 24</td>
</tr>
<tr>
<td>FEV₁/FVC ratio % †</td>
<td>69 ± 13</td>
</tr>
<tr>
<td>FENO (ppb)*</td>
<td>46 (21–89)</td>
</tr>
<tr>
<td>ICT prescription refill ratio (%)*</td>
<td>89 (49–103)</td>
</tr>
</tbody>
</table>

*Median (IQR). † Mean ± SD.

**Conclusion** While there is a weak relationship between a single point-in-time FeNO measurement and non-adherence to ICT in difficult asthma, this cannot be used as an alternative to our previously described FeNO suppression test.

**REFERENCES**

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**Introduction** BTS/SIGN asthma management guidelines recommend a stepwise approach to the use of anti-inflammatory therapy, including the addition of inhaled combination therapy (ICT) at Step 3. In NI, ICT accounts for 47% (£23 million) of the entire respiratory drug spend suggesting excessive utilisation of ICT.

**Methods** Using data from a large representative sample of GP practices in NI, we looked at subjects who had a new prescription of ICT (Symbicort, Seretide, Fostair). Data were collected from the Information and Registration Unit of the Business Services Organisation in the December 2010 inclusive for subjects aged 5 to 35. We examined treatment prior to ICT, SABA, oral steroid and antibiotic use and, prescription filling in the preceding 6 and 12 months.

**Results** 42 665 subjects received 2 or more prescriptions for any respiratory drug (BNF categories 3.1, 3.2, 3.3) and of these 12 929 received ICT with 3953 new ICT prescriptions. 2642 (67%) of these had no ICS in study year or 6 month lead in period. A further analysis of a 12-month lead in period showed 39 315 subjects with 2 or more respiratory prescriptions and out of these 11 962 received ICT with 2609 new ICT prescriptions. 1595 (52%) had no ICS in the study year or 12-month lead in. A sub-group analysis (n = 600) showed that 51% of first prescriptions for ICT are made in Jan–April but in the previous 6 months only 23% are issued a SABA, 5% receive OCS and 31% receive an antibiotic.

**Conclusion** ICT is initiated in the majority of young asthmatic subjects without prior inhaled steroid therapy. Most prescriptions are initiated in the January–April period and do not appear to be driven by severe asthma exacerbation (oral steroid prescription) or worsening asthma control (SABA use). Significant reductions in ICT, with associated cost savings, would occur if the BTS/SIGN prescribing guidelines were followed in primary care. We are currently trying to identify the drivers and potential economic impact of poor adherence to national prescribing guidelines and...
examine ICT prescribing in other UK regions to identify if this is a more widespread problem.

**S12 UNScheduled HEALTHCARE resource utilisation and health-related quality of life before and after Omalizumab initiation in UK clinical practice: The APEX study**

doi:10.1136/thoraxjnl-2011-201054b.12

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**Objectives** The efficacy and safety of omalizumab for the treatment of severe persistent allergic asthma have been demonstrated in randomised controlled clinical trials. However, there are limited "real world" data on its effects on healthcare resource utilisation or health-related quality of life (QoL) in UK clinical practice.

**Methods** A 10 centre retrospective observational study (APEX) compared 12 months pre- vs 12 months post-omalizumab initiation in patients aged ≥12 years with severe persistent allergic asthma. All patients received ≥1 dose of omalizumab. Patients who had received omalizumab in a clinical trial were excluded. Hospital records were reviewed to obtain data on hospital resource use and routinely used QoL measures for example, Asthma Quality of Life Questionnaire (AQLQ) at baseline (pre-omalizumab), 16 weeks and up to 12 months following omalizumab initiation.

**Results** Mean in-patient hospital admissions fell by 61% from 1.30 to 0.51 (p<0.001) and mean in-patient bed days fell by 70% from 9.10 to 2.74 (p<0.001) per patient. In the subgroup of patients hospitalised for asthma in the 12 months pre-omalizumab (n=81), mean in-patient hospital admissions fell by 70% from 2.19 to 0.65 (p<0.001) and mean in-patient bed days fell by 74% from 14.86 to 3.85 (p<0.001) per patient. Similarly, mean Accident and Emergency department attendances fell by 70% from 1.52 per patient in the 12 months pre-omalizumab to 0.46 in the 12 months post-omalizumab (p<0.001). Other resource use, such as outpatient attendances (excluding visits made solely for omalizumab administration), nurse appointments and telephone consultations remained unchanged following omalizumab initiation. QoL data were not available for all patients at every time point. However, where data were available, mean AQLQ scores increased from 3.09 at baseline to 5.22 at 12 months (n=29).

**Conclusions** Treatment with omalizumab is associated with a clinically and statistically significant reduction in unplanned hospital resource utilisation and improvements in patients' QoL.

**S14 HISTONE DEACETYLASE ACTIVITY IS REDUCED IN COPD SUBJECTS DURING RHIvovirus INDUCED EXACERBATIONS**

doi:10.1136/thoraxjnl-2011-201054b.14

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**Introduction** Histone deacetylase (HDAC) enzymes have a role in suppressing inflammatory gene transcription. There is evidence for reduced HDAC activity in COPD which correlates with the severity of airflow obstruction. Increased inflammation found during exacerbations of COPD may result from a reduction in HDAC activity but this has not been studied in virus induced exacerbations. We sought to investigate HDAC activity following rhinovirus infection in an experimental model of COPD exacerbations.

**Methods** Experimental rhinovirus challenge was performed in GOLD stage II COPD subjects and non-obstructed control smokers and non-smokers. Rhinovirus infection was confirmed with quantitative PCR performed on nasal lavage and sputum samples collected at baseline and days 3, 5, 9, 12, 15, 21 and 42 post virus inoculation. Sputum macrophages were isolated by adhesion and HDAC2 isoenzyme immunoprecipitated, prior to performing a HDAC activity assay.

**Results** 11 non-smokers (NS), 10 smokers (Smk) and 9 COPD subjects were recruited. The mean (SEM) % predicted baseline FEV1 was 22.39 (12.45 to 40.25); Smk 22.91 (18.28 to 28.71) and COPD 48.98 (26.04 to 92.13) (p=0.095). Following rhinovirus infection, in NS HDAC activity but this has not been studied in virus induced exacerbations. HDAC activity increased, in Smk it remained largely unchanged and there was a fall from baseline levels in COPD subjects at all time points, 6.9% (4/58) of patients were positive for HRV at baseline only, 26.3% (15/57) at exacerbation only and 8.5% (4/45) at both time points (p=0.006).

**Conclusions** HDAC load is significantly greater at COPD exacerbation than when detected in the stable state. This emphasises the importance of HRV as a key trigger of COPD exacerbations. HRV can be detected in the stable state; however the loads are very low suggesting asymptomatic carriage rather than chronic infection.

**Unravelling airway infection in COPD**

**S13 DIFFERENTIATED HUMAN RHINOVIRUS LOADS IN STABLE COPD AND AT EXACERBATION**

doi:10.1136/thoraxjnl-2011-201054b.13


**Introduction** Human rhinoviruses (HRV) are the main aetiological agents of virus-associated COPD exacerbations (Seemungal et al, 2001). However the importance of the level of viral load as a trigger for naturally occurring exacerbations is not fully understood. We aimed to assess and quantify HRV prevalence and load in stable and exacerbating patients from the London COPD cohort.

**Methods** A real-time qPCR protocol was utilised to detect HRV presence and quantify load in sputum samples taken at baseline (n=58) and at COPD exacerbation onset (n=57). COPD patients were defined as stable if exacerbation-free for at least 42 days since the previous exacerbation and more than 14 days before the next. Exacerbations were defined using our usual symptom criteria; an increase in respiratory symptoms for two consecutive days, with at least one symptom being a major symptom; dyspnoea, sputum purulence or volume and the other a major or minor symptom; wheeze, cold sore throat, and cough (Anthonisen criteria). A χ² test was used to compare HRV prevalence of the two disease phases, and an independent-samples t test was used to compare the differences in viral load.

**Results** Sixty-four patients provided 115 sputum samples: mean age 70.9 years (SD±8.1); FEV1 45.8% predicted (±20.0%); current smoker 31.5%. There is a significantly higher prevalence of HRV at exacerbation onset, 31.6% (18/57) compared to baseline 15.5% (9/58) (p=0.042). Similarly, the mean viral load was significantly greater at exacerbation onset 1.70 (±1.67) log10 pfu/ml than baseline 0.50 (±0.69) log10 pfu/ml (p=0.025), exhibiting a 25-fold increase in viral load from baseline to exacerbation. 6.9% (4/58) of patients were positive for HRV at baseline only, 26.3% (15/57) at exacerbation only and 8.5% (4/45) at both time points (p=0.006).

**Conclusions** HRV load is significantly greater at COPD exacerbation than when detected in the stable state. This emphasises the importance of HRV as a key trigger of COPD exacerbations. HRV can be detected in the stable state; however the loads are very low suggesting asymptomatic carriage rather than chronic infection.