Abstract S65 Figure 1. Expression of Ki67 (A), SIRT1 (B), p16 (C) and H2AX (D) in large AECs and small AECs (E, F, G and H, respectively). Results are expressed as mean ± SEM. Statistics: Kruskal-Wallis and Mann-Whitney U test. * p < 0.05, ** p < 0.01, *** p < 0.001.

Results In large AECs, expression of the proliferation marker ki67 and the anti-ageing protein sirtuin 1 (SIRT1) was decreased in COPD as compared to bronchiectasis and controls. There was no difference in expression of the cell-cycle inhibitor p16 and the DNA damage associated foci ?H2AX between the three groups. In small AECs, SIRT1 was decreased in COPD compared to controls and p16 and ?H2AX were increased. Here, ki67 expression did not differ between groups. In bronchiectasis, there was no significant change in senescence marker expression compared to controls, with the exception of decreased SIRT1 in large AECs. Marker expression was not significantly correlated with FEV_1 or smoking history. Preliminary work suggests potential co-localisation of ?H2AX at telomeres with ongoing analysis underway.

Conclusions Differential expression of senescence-associated markers between large and small airways in COPD may reflect the distinct patterns of inflammation and functional impairment occurring in the two airway compartments. There is some evidence suggesting a role for senescence in bronchiectasis, though this is less clear than for COPD. Further markers need to be investigated.

| S66 | TARGETING ANTI-AGEING MOLECULE AMPK RESTORES CORTICOSTEROID SENSITIVITY IN COPD |

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Rationale Chronic obstructive pulmonary disease (COPD) is an irreversible inflammatory lung disease and is currently the fourth greatest burden of disease of worldwide. However a key issue is that patients show a lack of response to corticosteroid treatment. Corticosteroid insensitivity is mainly caused by oxidative stress which directly stimulates inflammatory transcription factors and reduces the activity of co-adaptor proteins essential for the inhibitory actions of corticosteroids. AMP-activated kinase (AMPK) is a serine/threonine protein kinase that regulates cellular energy homeostasis and anti-oxidant defences, and has recently been labelled as an anti-ageing molecule. We hypothesised that activation of AMPK using Quercetin reverses corticosteroid resistance caused by cigarette smoke extract (CSE) in a monocytic cell line.

Methods Human monocytic cell line, U937s, were initially incubated with Quercetin (20μM) for 24 hours and then exposed to CSE for 2 hours. Cells were then treated with dexamethasone (1×10^{-11} to 1×10^{-6}M) for 45 minutes and stimulated with TNF-a (10ng/ml) for 24 hours. Supernatants were collected and CXCL-8 was measured using ELISA. Corticosteroid resistance was calculated as the ability of dexamethasone to inhibit 25% of TNF-a-induced CXCL-8 (IC_{25}). Activation of AMPK by Quercetin was measured using the levels of the phosphorylated AMPK by Western Blot. Nuclear factor erythroid related factor 2 (Nrf-2) levels and glucocorticoid receptor (GR) nuclear translocation were also assessed using Western Blot.

Results CSE induced corticosteroid resistance in U937s (IC_{25} = 30nM vs IC_{25} = 5nM). Interestingly Quercetin restored corticosteroid sensitivity by approximately 3 fold (IC_{25} = 11nM) compared to CSE. Quercetin increased levels of activated AMPK and also up-regulated the expression of Nrf-2. However, Quercetin was unable to restore GR nuclear translocation.

Conclusions Quercetin was found to be a potential novel therapy for restoration of corticosteroid sensitivity in COPD. Although the mechanism of action remains to be elucidated, Nrf-2 and AMPK activations which increase anti-oxidant levels and prevents oxidative damage could be a key the mechanism of action Activation of AMPK could therefore be a potential novel mechanism for the restoration of corticosteroid sensitivity and Quercetin could be used as an add-on treatment to corticosteroids in COPD.

Delivering better, safer care

| S67 | COPD–IN THE NEWS! |

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NICE[1] recommends 'track and trigger' systems for all adult acute hospital admissions and the RCP[2] advocates the use of the National Early Warning Score (NEWS) to promptly highlight high risk patients. In non-selected medical patients a higher admission NEWS correlates with higher mortality, with a stepwise increase as the score increases. Anecdotally patients with COPD have high rates of NEWS alerting. No studies have looked at the validity of the NEWS in COPD patients though the issue was raised in a previous abstract.

We retrospectively interrogated an electronic observation database in our Trust (two acute sites) over a year (February 2012–January 2013). We compared acute medical unit (AMU) admissions aged over 50 years (n = 13,291) with patients admitted with a primary diagnosis of COPD (n = 1119). Despite a similar age profile (median 74 & 77) and inpatient mortality
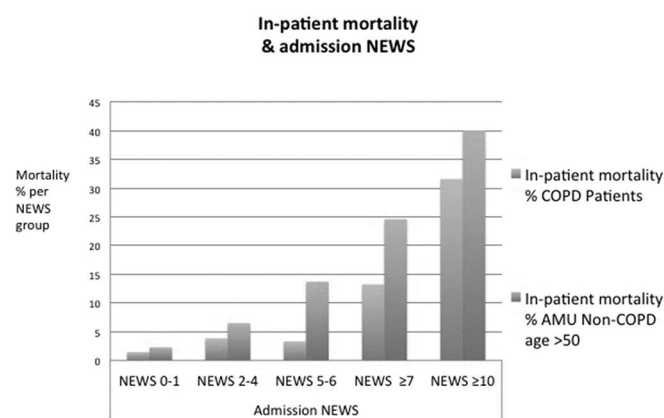
(5.3% & 6.2%), the COPD cohorts admission NEWS was double that of the AMU patients (median 4 vs 2). This difference persisted throughout admission to discharge.

Admission NEWS showed a step-wise increase in mortality amongst the AMU patients. In contrast, the COPD cohort with NEWS of 5 or 6 had *lower* in-patient mortality compared to COPD patients scoring 2–4. NEWS of ≥7 is used to trigger urgent medical attention and 20% of patients with COPD fulfilled this criteria (compared to 6.6% of non-COPD patients). When NEWS score was ≥10, mortality in both groups was high (31.6% in COPD patients, 40% in AMU patients)(graph 1).

In conclusion, we have shown that acute COPD patients have similar mortality to other emergency medical admissions yet persistently higher NEWS. This requires addressing possibly by adjusting the NEWS to take into account lower oxygen saturation targets in selected COPD patients (median 93% compared to 96% in AMU patients) and thus reduce over-alerting of those not necessarily at high risk of death.

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Abstract S67 Figure 1.

S68 | **THE NATIONAL EARLY WARNING SCORE (NEWS) & IATROGENIC HARM - COULD THE NEWS FOR COPD PATIENTS BE IMPROVED?**

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The National Early Warning Score (NEWS) system is in use throughout NHS Acute Trusts. It reliably picks up the small proportion of patients at high risk of death during their admission. However, during Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD), where target saturations are 88–92% in selected patients, a high proportion of patients have NEWS 'alerts' when their oxygen levels are within the target range set by their clinician. This results in referral for urgent review by medical staff and/or an inappropriate increase of inspired oxygen which could exacerbate hypercapnic respiratory failure.

We therefore propose a simple modification to the NEWS system in patients at risk of hypercapnic respiratory failure.

Three points are added for target saturations of 85% or less and two points are added for target saturations of 86–87%. For target saturations of 88–92%, no additional points will be added. This modification would be at the senior clinicians' discretion.

We reviewed the observations of 1119 patients admitted with a primary diagnosis of AECOPD and compared them to 15,953 patients aged over 50 admitted to one of two acute medical units. Admission saturations were reviewed and compared with in-patient mortality.

Use of the current NEWS system resulted in 40% of patients with AECOPD scoring 2–3 points on their saturation alone despite most being in the saturation range recommended by the BTS[1]. In addition, their risk of mortality was significantly lower than patients without COPD in the same saturation range (See table 1). Our proposed modified NEWS system results in an improved ability to identify the patients at higher risk of mortality, thereby resulting in more efficient utilisation of medical resources and the reduction of inappropriate use of oxygen and risk of hypercapnic respiratory failure.

We have shown that the current NEWS system leads to a significant number of patients with AECOPD alerting when they have nationally recommended target oxygen saturations. A simple adjustment of the alerting threshold in this cohort could improve the system. This could also be applicable to other respiratory patients with or at risk of hypercapnic respiratory failure.
1. BTS guideline for emergency oxygen use.

Current NEWS	NEWS 3 (≤91%)	NEWS 2 (92-93%)	NEWS 1 (94-95%)	NEWS 0 (≥96%)
AMU aged ≥50 % (n=)	6.8 (900)	6.6 (879)	16.1 (2133)	70.5 (9347)
AMU ≥50 Mortality %	17%	9.3%	6.2%	4.9%
COPD Patients % (n=)	23.6 (264)	17.1 (191)	21.7 (243)	37.6 (421)
COPD Mortality % (n=)	9.9%	5.2%	3.3%	3.6%

New Adjusted NEWS	≤85% = 3 pts	86-87% = 2 pts	88-92%	93-100%
COPD % (n=)	7.6 (85)	2.8 (31)	20.7 (232)	68.9 (771)
COPD Mortality	15.3% (n=13)	9.7% (n=3)	5.6% (n=13)	3.9% (n=30)

Abstract S68 Figure 1.

S69 | **IMPLEMENTATION OF A COPD DISCHARGE CARE BUNDLE AND HOSPITAL READMISSIONS IN LONDON**

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Background Acute exacerbations of COPD (AECOPD) are a major cause of morbidity, mortality and hospital admissions. Audit data shows significant variation in delivery of evidence-based interventions and readmission rates suggesting that optimising the care process may be beneficial. One approach is the "care bundle" where a series of evidence-based interventions