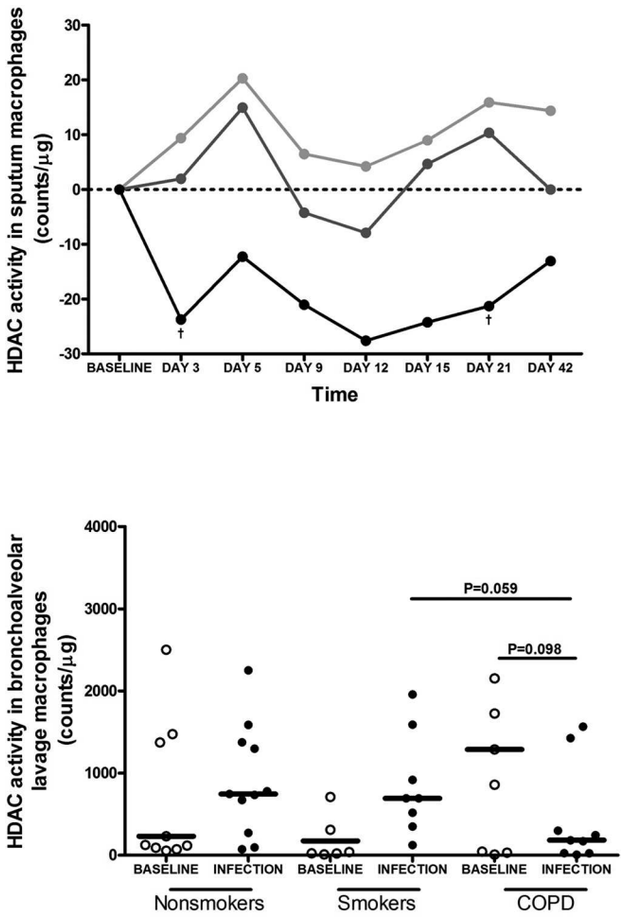

Abstract S112 Figure 1.

was significantly lower in the COPD subjects compared to non-smokers on days 5 and 42 (P < 0.05), and there was a trend towards lower levels of HDAC in BAL macrophages at infection compared to the non-smokers (P = 0.095) and smokers (P = 0.059) (Figure 1).

Lower sputum macrophage HDAC2 activity at baseline was associated with greater sputum virus load (r = -0.82, P = 0.022) and higher sputum levels of neutrophil elastase (r = -0.81, P = 0.022) and TNF- (r = -0.79, P = 0.028).HDAC2 activity in BAL macrophages at infection correlated inversely with peak NL virus load (r = -0.8, P = 0.0096), peak sputum GM-CSF (r = -0.67, P = 0.0499), TNF- (r = -0.72, P = 0.03), neutrophil elastase (r = -0.67, P = 0.0499) and sputum nitrite levels (r = -0.78, P = 0.0125).

Conclusions Following rhinovirus infection HDAC2 activity in airway macrophages is reduced and relates to airway inflammatory markers. Restoring HDAC activity is a potential therapeutic option for COPD exacerbations.

S113 HAEMOPHILUS INFLUENZAE STIMULATION OF ALVEOLAR MACROPHAGES FROM COPD PATIENTS; EFFECTS OF CORTICOSTEROIDS

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Background The lower airways of COPD patients are often chronically colonised by bacteria such as Non-typeable *Haemophilus influenza* (NTHI). Bacteria are a common cause of COPD exacerbations. Corticosteroids are often used to prevent and treat COPD exacerbations.

The aim of this study was to investigate the effect of corticosteroids on the *in vitro* inflammatory response of COPD alveolar macrophages (AM) to NTHI infection. We also investigated the cell signalling pathways activated by NTHI infection.

Methods AM from 12 COPD patients and 9 smoking controls were infected with live NTHI at multiplicity of infection (MOI) of 100:1 (bacteria: AM) for 24 hours. AM were pre-treated with dexamethasone (up to 1 M) for 1 hour. Supernatants were analysed for TNF- , IL-6, IL-8 and IL-10 by ELISA. AM protein was extracted for Western blot analysis of nuclear factor B (NF B), p38 and extracellular regulated mitogen activated protein kinases (p38 and ERK) activation.

Results NTHI stimulated release of TNF- , IL-6, IL-8 and IL-10 (p < 0.05) from both COPD patients and controls.

TNF- , IL-6 and IL-10 production was significantly inhibited by dexamethasone at 1 and 0.1 M (p < 0.05). Inhibition of TNF- and IL-6 release was significantly higher in AM from smokers compared to COPD patients. Dexamethasone had no effect on IL-8 production (see table 1).

NTHI infection activated NF B, p38 and ERK MAPK signalling pathways in AM.

Conclusion NTHI infection stimulated COPD AM to release inflammatory cytokines which are only partially responsive to corticosteroids; importantly, there was no suppression of the neutrophil chemoattractant IL-8. The production of this corticosteroid resistant chemokine is associated with NF- B and MAPK activation; these signalling pathways drive bacteria induced inflammation in COPD airways.

Abstract S113 Table 1. Dexamethasone inhibition of NTHI induced mediator production in alveolar macrophages.

	Percentage inhibition by 1 M dexamethasone	
Cytokine	**COPD**	**Smokers**
TNF-	42.5% ***#	67.3% ***#
IL-6	26% **#	43.2% **#
IL-8	-29%	16.2%
IL-10	44% ***	38.7% **

,* = significant bellow dimethyl sulfoxide (DMSO) control (p< 0.01, 0.001)
= significant difference between COPD and Smokers (p<0.05)

S114 SIMVASTATIN IMPROVES NEUTROPHIL MIGRATORY TARGETING IN COPD: *IN VITRO* STUDIES SUPPORTING STATIN USE AS A POTENTIAL ADJUVANT THERAPY

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Introduction Statin use in COPD is associated with a reduction in all cause mortality, with greatest reductions seen in patients with the highest inflammatory burden. However, the mechanism for these effects is poorly understood, as statin treatment has not been found to lower systemic inflammation and *in vitro* studies of cellular effects use concentrations that exceed the therapeutic range. Neutrophils are key effector cells in COPD, and correlate with disease severity and inflammation. Recent *in vitro* studies