Introduction
Quadriiceps muscle dysfunction is an important prognostic comorbidity in COPD. MicroRNAs (miRs) are small non-coding RNAs that regulate gene expression. Skeletal muscle expresses a number of tissue-specific microRNAs including miR-1, which modulates muscle phenotype. MicroRNAs can be secreted from cells and maintained in blood within exosomes. Elevated levels of circulating miR-1 have been demonstrated in a number of human and animal models of muscle disease. We hypothesised that plasma levels of miR-1 would be elevated in COPD patients and would correlate with important physiological parameters.

Methods
103 COPD patients and 25 controls were studied. MiR-1 was quantified in stored plasma samples using q-RT PCR. MiR-16 and miR-122 were quantified as negative controls. Results were normalised to an exogenous spiked-in control.

Results
Characteristics as mean (SD); COPD patients: M: 67, F: 36, age=66.47 (8.4), FEV1 % pred= 45.3 (18.6), 6-minute walk (6MW) = 394 (120). Controls: M: 14, F: 11, age=67 (8.1), FEV1 % pred=111.2 (13.1), 6MW=613 (83). Plasma miR-1 was significantly elevated in COPD patients, p=0.002. There was no difference in miR-16 and miR-122. MiR-1 was negatively associated with FEV1 % predicted (r = -0.3, p<0.001) and with Tlco (r=-0.3, p<0.001), but it was not possible to distinguish between GOLD stages using ANOVA.

Conclusion
Our results show that stable COPD patients have elevated plasma levels of muscle-specific miR-1. The increase in miR-1 may be due to increased muscle degradation or turnover in the COPD patients studied. Our work raises the possibility of using other muscle-specific microRNAs in the future as potential biomarkers of muscle dysfunction in patients with COPD.

REFERENCE
Spoken sessions

ASSOCIATION OF MICROTUBE INSTABILITY WITH DEFECTIVE PHAGOCYTOSIS IN COPD

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Acute exacerbations of COPD are the commonest cause of acute medical admissions in the UK and ≈50% are associated with bacterial infection. Alveolar macrophages (AM) normally clear inhaled bacteria but defective phagocytosis may lead to chronic colonisation and increased exacerbations. Monocyte-derived macrophages (MDM), used to model AM, were obtained from COPD, smoking and healthy subjects. MDM phagocytosis of fluorescently-labelled polystyrene beads, Haemophilus influenzae (HI) or Streptococcus pneumoniae (SP) was measured by in vitro phagocytosis assays at 4 h. Using a total of 214 BAL samples, we investigated HI phagocytosis in relation to COPD, smoking and healthy MDM. Pre-incubation with epothilone B was associated with significantly increased levels of acetylated tubulin in COPD cells. No significant differences were seen in the expression of HDAC6 or Sirt2 in COPD compared to healthy cells. MDM from smoking and COPD subjects show reduced phagocytosis of common respiratory bacterial pathogens. Acetylation of microtubules appears to be reduced in COPD, whereas, increasing tubulin acylation is associated with improvements in phagocytosis, which may allow for targeted development of future therapies to treat colonisation and prevent exacerbations of COPD.

Abstract S52 Table 1 Relative fluorescence values (RFU×10^5) for MDM phagocytosis assays at 4 h

<table>
<thead>
<tr>
<th></th>
<th>HI</th>
<th>SP</th>
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<tbody>
<tr>
<td>Healthy</td>
<td>11.5±0.9 RFU×10^5</td>
<td>8.2±1.4 RFU×10^5</td>
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<tr>
<td>Smoker</td>
<td>4.6±0.6 (p&lt;0.001)</td>
<td>3.7±0.6 (p&lt;0.001)</td>
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<tr>
<td>COPD</td>
<td>8.4±1 (p&lt;0.01)</td>
<td>5.7±0.7 (p&lt;0.05)</td>
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ALARMINS IN BRONCHIOLITIS OBLITERANS SYNDROME AFTER LUNG TRANSPLANTATION

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Introduction Survival after lung transplantation is limited to a median of 5-year due to development of bronchiolitis obliterans syndrome (BOS). BOS is the clinical manifestation of chronic allograft dysfunction, characterised by inflammation and fibrosis of small/medium-sized airways leading to airflow obstruction. Numerous insults to the transplanted lungs have been associated with BOS development. Alarmins are cell derived danger signals released from damaged tissue which activate innate and adaptive immune responses. We hypothesised that the release of alarmins into the airway compartment after lung transplantation may contribute to BOS pathogenesis.

Methods A retrospective longitudinal study of 52 lung transplant recipients from 2005 to present was performed (26 recipients developed BOS; 26 remained free from BOS). All recipients had lung function and bronchoalveolar lavage (BAL) performed at 1, 5, 6 and 12 months post transplant. Further samples were taken if the diagnostic criteria for BOS were fulfilled. A total of 214 BAL samples were analysed by ELISA for the alarmins Interleukin-1α (IL-1α) and High Motility Group-Box1 (HMG-B1). Data were analysed using Mann–Whitney tests.

Results Both BOS and non-BOS recipients with culture positive BAL samples had significantly higher concentrations of IL-1α and COFD MDM by 20% (p<0.05) and SP phagocytosis in smoker MDM by 40%. Levels of acetylated tubulin increased on exposure to bacteria alone in healthy and smoker MDM but not in COPD MDM. Pre-incubation with epothilone B was associated with significantly increased levels of acetylated tubulin in COPD cells. No significant differences were seen in the expression of HDAC6 or Sirt2 in COPD compared to healthy cells. MDM from smoking and COPD subjects show reduced phagocytosis of common respiratory bacterial pathogens. Acetylation of microtubules appears to be reduced in COPD, whereas, increasing tubulin acylation is associated with improvements in phagocytosis, which may allow for targeted development of future therapies to treat colonisation and prevent exacerbations of COPD.

Abstract S53 Figure 1 IL-1α assay on culture negative BAL samples.