Abstract S99 Figure 1 (a) Translational fibre-based FLIM system, with optical imaging fibre (1.42mm outer diameter) delivered via the working channel of a bronchoscope. Fluorescence lifetime images of (b) non-cancerous and (c) cancerous human lung tissue using fibre-based FLIM. (d) Corresponding haematoxylin and eosin stained sections of non-cancerous and cancerous (adenocarcinoma) lung tissue

application of a novel fibre-based FLIM system, which utilises 488nm excitation to enable fluorescence intensity and lifetime imaging, to detect changes in freshly resected lung cancer and adjacent healthy tissue. The mechanisms responsible for alterations in lung cancer fluorescence lifetime are not understood. We investigate the contributions of cancer cells and tumour stroma to fluorescence lifetime signatures using fixed unstained lung cancer and benchtop FLIM.

Methods Paired cancer and non-cancerous lung tissues were obtained from resection patients (n=21). A 488nm fibre-based FLIM platform was used to perform high-resolution fluorescence intensity and lifetime imaging (figure 1). Co-registered fixed unstained lung cancer sections were evaluated using benchtop FLIM and image analysis software.

Results Fluorescence lifetime is significantly reduced in fresh *ex vivo* lung cancer, compared with non-cancerous tissue (mean±SD, 2.15 ± 0.26 ns vs. 1.79 ± 0.40 ns, $p < 0.0001$). Fibre-based FLIM distinguishes lung cancer, from adjacent tissue, with 81.0% sensitivity and 71.4% specificity. Lifetime-based signatures are retained after fixation, as evidenced by benchtop FLIM of fixed unstained lung cancer, which demonstrates no difference in fluorescence lifetimes compared with fresh cancer ($p = 0.55$). By applying this technique on fixed tissues, we demonstrate that cancer cells have significantly longer lifetimes, compared with tumour stroma ($p = 0.027$). Cancer subtype also influences lifetime signatures (mean±SD, adenocarcinoma 1.55 ± 0.38 ns vs. squamous cell carcinoma 2.57 ± 0.47 ns, $p = 0.0005$). Mean fluorescence lifetimes of fixed unstained lung cancer positively correlate with the proportion of cancer cells within tissue section area ($r = 0.80$; $p = 0.033$).

Conclusions Our novel fibre-based FLIM system discriminates lung cancer from adjacent healthy tissue *ex vivo* with good performance characteristics. This minimally invasive technique, which is deliverable via endoscopic platforms, may permit advanced *in situ* diagnostic capabilities in lung cancer. FLIM of fixed unstained tissue enables cellular resolution lifetime characterisation, and highlights the role of cancer cells in

determining the overall fluorescence lifetime signature in lung cancer.

Please refer to page A190 for declarations of interest related to this abstract.

Ease that wheeze: managing risk in COPD

S100

RISK OF CARDIOVASCULAR MORBIDITY AND MORTALITY IN PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE VERSUS THOSE WITHOUT COPD: A STRUCTURED REVIEW OF THE EVIDENCE

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Introduction and Objectives Comorbid chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD) frequently occur together and are associated with worse outcomes for patients. This study provides a synthesis of recent evidence from observational studies determining the excess risk of CVD morbidity and mortality in patients with COPD, and the impact of COPD severity on risk.

Methods A structured review of the literature was conducted, using predefined search strategies, to search Medline and Embase (August 2020) for systematic reviews and meta-analyses (last 10 years) or observational studies (last 5 years) that reported risk of CVD (heart failure, hypertension, dysrhythmia, acute myocardial infarction [AMI], hypercholesterolaemia and stroke), diabetes and CV mortality in patients with COPD compared to those without. Risks are presented as reported in identified studies. Meta-analysis results are presented where available, otherwise an individual study range is reported.

Results A diagnosis of COPD was significantly associated with a two- to three-fold increased risk of CV mortality compared to people without COPD. Additionally, in patients with COPD there was a significantly increased incident risk of up to almost four-fold for hypertension (rate ratio [RR]: 0.95; 95% confidence interval 0.91–0.99 to 3.57; 3.41–3.74), up to six-fold for heart failure (RR: 1.46; 1.38–1.53 to 5.94; 5.50–6.42), up to five-fold for dysrhythmia (RR: 1.19; 0.98–1.43 to 4.74; 4.27–5.26), and up to two-fold for AMI (RR: 1.18; 0.81–1.71 to 1.89; 1.71–2.09). An increased risk was also observed for stroke (hazard ratio: 1.30; 1.18–1.43) and diabetes (risk ratio: 1.25; 1.16–1.34). No data on incident risk were identified for hypercholesterolaemia. A significantly increased risk in CV mortality compared to patients without COPD was demonstrated across all severity categories of mild, moderate and severe COPD; the risk increased further with increasing severity of COPD.

Conclusions There is substantive evidence for an association between COPD and the incidence of specific cardio- and cerebrovascular acute events or diseases. To minimise the risk of poor outcomes, it is important to ensure that patients with comorbid COPD and CVD are diagnosed early and optimally managed at all levels of health-care settings.

Please refer to page A190 for declarations of interest related to this abstract.

S101 METHODS FOR ASSESSING THE SUCCESS OR FAILURE OF COPD EXACERBATION TREATMENTS IN THERAPEUTIC CLINICAL TRIALS: A META-EPIDEMIOLOGICAL SYSTEMATIC REVIEW

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Introduction The overall outcome of a COPD exacerbation (treatment success or failure) is a critical outcome for clinical trials evaluating the management of COPD exacerbations. However, trials use heterogeneous definitions and instruments to evaluate this outcome, limiting the comparability of trial results. Here, we describe how often different measurement instruments are used to evaluate the overall outcome of COPD exacerbations, aiming to promote consistency.

Methods MEDLINE and the Cochrane Airways Trial Register were systemically searched. COPD exacerbation trials (2006–2020) reporting on treatment success or failure were included. Risk of bias was assessed. The definitions and measurement instruments used to assess treatment success/failure were collected and described narratively.

Results 56/176 (31.8%) of COPD exacerbation trials assessed the overall outcome of the exacerbation (treatment success or failure). 9/56 (16.1%) of studies had a low risk of methodological bias. Two categories of outcomes evaluating treatment success or failure were identified. Twenty-four RCTs used composite endpoints consisting of several undesirable outcomes to define treatment failure. The most frequently used components were death (59%), hospital admission (52%),

Abstract S101 Table 1 Frequently used definitions of various COPD exacerbations states

Cure or Resolution	Number of Studies (n = 56)
Complete resolution of all signs and symptoms of the exacerbation.	10
Sufficient improvement of the signs and symptoms such that no additional systemic treatments were prescribed.	5
Improvement	
Improved signs and symptoms, without any new signs or symptoms.	8
Improved symptoms as evaluated by clinical scores.	6
Treatment failure	
Lack of resolution of signs and symptoms, requiring additional treatment, or death.	7
Persistence or worsening of signs and symptoms, or death.	7
Lack of resolution of signs and symptoms, or need for further treatment.	4

treatment intensification (52%) or mechanical ventilation (37%). By comparison, thirty-three RCTs used qualitative descriptions of the status of the exacerbation (such as cure, improvement or failure), which were based on the patients' symptoms and signs (table 1). The overall outcome was evaluated at different timepoints, between 2 hours and 1 year from presentation.

Conclusions There is significant heterogeneity in the instruments used to evaluate treatment success or failure in COPD exacerbation trials. Standardization could promote comparability.

S102 THE UNDER RECOGNISED ROLE OF MODERATE EOSINOPHILIA ON EXACERBATION FREQUENCY IN COPD PATIENTS: A SINGLE CENTRE STUDY

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Introduction and Objectives High eosinophil levels in patients with COPD are a well established risk factor for frequent exacerbations. Our study aimed to determine whether more moderate eosinophil levels are also a significant driver of frequent exacerbations.

Methods We retrospectively identified 213 patients who presented with a severe exacerbation of COPD to our unit from 01 January 2018 to 31 December 2018. Patients were divided into three groups: high eosinophilia (peak eosinophil level ≥ 0.5); moderate eosinophilia (peak eosinophil level 0.3–0.4) and low eosinophilia (peak eosinophil level ≤ 0.2).

The exacerbation frequency and trajectory of patients was followed up for 18 months. Standard univariate statistical analysis was undertaken to determine the impact high, moderate, and low eosinophilia had on exacerbation frequency.

Results For patients who were initially infrequent exacerbators, moderate eosinophilia was associated with a shift towards increased exacerbation frequency ($p < 0.05$). High eosinophilia however was not associated with increased exacerbation frequency ($p = 0.897$).