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REVIEW

Chronic Obstructive Pulmonary Disease and the Management of Cardiopulmonary Risk in the UK: A Systematic Literature Review and Modified Delphi Study

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Abstract: Chronic obstructive pulmonary disease (COPD) is linked to increased mortality and morbidity, especially in patients with coexisting cardiovascular disease. These patients face heightened cardiopulmonary risk, which escalates further after acute exacerbations of COPD. While there is some guidance on the management of acute exacerbations of COPD, there is a lack of specific strategies for addressing cardiopulmonary risk in COPD. This program of work aimed to establish UK consensus statements and a clinical pathway for managing cardiopulmonary risk in patients with COPD, synthesizing evidence and expert input through a modified Delphi approach. A multidisciplinary Taskforce conducted a systematic review, focusing on the UK and addressing questions relating to the healthcare burden of acute exacerbations of COPD (AECOPDs), the link between AECOPDs and cardiopulmonary events, the management of cardiopulmonary risk in patients with COPD, and the guidelines and interventions implemented to optimize COPD management. The evidence identified was summarized and used to synthesize preliminary consensus statements reflecting the current situation and recommendations for action. Following iterative voting rounds, consensus was reached on 18 statements. Further to this, a clinical pathway framework to support the recognition and management of cardiopulmonary risk in patients with COPD using the consensus statements was formulated. AECOPDs were identified as a substantial healthcare burden in the UK, contributing to high mortality, frequent healthcare interactions, and elevated costs. These exacerbations were associated with cardiopulmonary events such as myocardial infarction and stroke. Most UK guidelines have focused on the respiratory management of COPD exacerbations, but lack strategies to specifically address cardiopulmonary risk, highlighting the need for integration of care. This consensus program has identified gaps in management, as well as a need to optimize care and reduce the cost of COPD management through the development of new UK policies and clinical guidance.

Keywords: COPD, cardiovascular disease, United Kingdom, interdisciplinary health teams

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Introduction

Chronic obstructive pulmonary disease (COPD) is the fifth-leading cause of premature death in the UK, with over 21,000 COPD-related deaths annually.^{1–3} It is the second-largest cause of emergency hospitalization in the UK, with one in eight admissions attributed to COPD.⁴ Compared with the general population, patients with COPD have nearly twice as many chronic comorbidities, which are key contributors to morbidity and mortality in this population.^{5,6} More specifically, patients with COPD face a 2- to 4-fold increased risk of mortality related to cardiovascular disease (CVD) compared with those without COPD, and CVD is a leading cause of hospitalization among patients with COPD, accounting for nearly half of hospital admissions in this population.⁵

Cardiopulmonary risk is defined as the risk of serious respiratory and/or cardiovascular events in patients with COPD.^{7–9} These include, but are not limited to, COPD exacerbations, myocardial infarction (MI), stroke, heart failure (HF) decompensation, arrhythmia, and death due to any of these events.^{7–10} Notably, there is a strong physiological link between acute exacerbations of COPD (AECOPDs) and cardiovascular events, with several shared risk factors.^{9,11} Though not fully understood, potential mechanisms include systemic inflammation, hyperinflation, and hypoxemia.^{9,11} Consequently, patients experiencing AECOPDs have elevated cardiopulmonary risk, resulting in increased risk of mortality and cardiovascular events.¹² The risk of cardiovascular events (ie, acute coronary syndrome, arrhythmia, HF, and cerebral ischemia) increases sharply after AECOPDs, particularly in the first week, and remains elevated for up to 12 months.¹³ Furthermore, the risk of death increases with the occurrence and severity of exacerbations, with one or more severe AECOPDs at baseline (defined as the first year post COPD diagnosis) associated with an 80% increased risk of death across a decade of follow-up.¹⁴ It has been reported that patients with mild to moderate airflow obstruction (Global Initiative for Chronic Obstructive Lung Disease [GOLD] stages I and II COPD) were more likely to die from cardiovascular causes than respiratory causes.¹⁴

The National Institute for Health and Care Excellence (NICE) defines AECOPDs as a sustained worsening of the patient's symptoms from their usual stable state beyond normal day-to-day variations that is acute in onset. These events are associated with worsening breathlessness, cough, increased sputum production, and change in sputum color, and are classified by NICE as mild, moderate, or severe, depending on the need for treatment and hospital admission.¹⁵ NICE and GOLD (2025 Report) provide guidance for the management of AECOPDs;^{15,16} however, established management guidelines to specifically address cardiopulmonary risk in COPD are absent.^{9,11,17,18} NHS England targets improvements in preventable respiratory-related mortality and admissions, although cardiopulmonary risk recommendations are not currently included.¹⁹

We aimed to evaluate existing information on cardiopulmonary risk and events through a literature review, and to develop consensus statements that address cardiopulmonary risk in patients with COPD. We employed a systematic literature review (SLR) to provide rigor, and to ensure transparency and reproducibility. A modified Delphi approach was used to efficiently generate and revise statements reflecting the perspectives of a multidisciplinary group and to assess whether there was consensus among the group.

In the absence of established approaches to address cardiopulmonary risk in people with COPD, the objectives for the consensus program were: to provide expert UK consensus statements and accompanying actions relating to its clinical relevance, importance, and management; and to develop a clinical pathway framework for its identification and management.

Methods

The consensus program included a review to synthesize published evidence regarding cardiopulmonary risk in patients with COPD in the UK. A modified Delphi approach was adopted to produce consensus statements based on scientific evidence and expert clinical experiences and opinion, with the aim of addressing cardiopulmonary risk in COPD.

Taskforce Members and Program Initiation

In November 2023, a multidisciplinary Taskforce of 11 respiratory and cardiology specialist healthcare professionals (HCPs) convened to identify fundamental clinical questions on the management of cardiopulmonary risk in patients with

COPD in the UK. The Taskforce comprised of specialists from primary and secondary care, including clinicians, pharmacists, and nurses. Taskforce members were selected for their academic and clinical interest in the relationship between AECOPDs and cardiopulmonary risk and/or events. The Taskforce met to define the scope and focus of the SLR and consensus program, including the key objectives, themes, and research questions, and to agree the specific methodologies to be employed.

Literature Review Methodology

An initial scoping search was conducted in November 2023 to identify relevant publications, keywords, and Medical Subject Headings (MeSH). Following this, a search of PubMed was undertaken in January 2024 to identify articles published between January 2013 and January 2024, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.²⁰ Research questions (Supplementary Table 1) and search strings (Supplementary Table 2) were developed using the Patient, Intervention, Comparator, and Outcome (PICO) framework to address the following research questions: What is the healthcare burden of AECOPDs in the UK?; What is the link between AECOPDs and cardiopulmonary events?; How is cardiopulmonary risk currently managed in patients with COPD in the UK?; What guidelines and interventions have been implemented to optimize management of COPD in the UK?

Titles, abstracts, and, where eligibility was uncertain based on review of the abstract, full-text articles were screened against the predefined inclusion and exclusion criteria (<u>Supplementary Table 3</u>). As part of the abstract screening, duplications were detected by a third-party application (Rayyan.ai) and checked and removed by an analyst. The following information was extracted from the included studies: reference details; patient population; geography; study design, intervention/exposure; outcomes (ie, healthcare burden in the UK, link between AECOPDs and cardiopulmonary risk, cardiopulmonary risk management in the UK, and guidelines and interventions for COPD management optimization in the UK); and study limitations.

Consensus Program Design "Assessing Consensus"

The next phase was conducted between April 2024 and December 2024, during which a modified Delphi approach was employed to develop consensus statements relating to the four SLR research questions.²¹ This involved expert review of the information identified by the SLR, followed by the drafting of consensus statements, which were developed based on the evidence reviewed and the clinical experience of the Taskforce. The consensus statements were then subject to three rounds of review, voting, and refinement, until consensus was achieved on all key points or a lack of consensus on a topic was recognized (Supplementary Figure 1).

Round I Voting

After preliminary statements were drafted, consensus was sought and measured by asking the Taskforce to vote via an online survey (Microsoft Forms). This was conducted between May 3, 2024 and May 16, 2024. All statements were listed, and respondents were asked whether they "agreed", "disagreed", or "partially agreed, but with further amends" with the statements. Selection of "partially agreed, but with further amends" would prompt the voting member to provide comment on how the statement could be improved. The threshold for consensus was 75% of respondents voting that they "agreed" with the statements. Following voting, the results of the survey were collated and presented to the Taskforce at a virtual meeting, which allowed for discussion and confirmation of initial revisions to the statements, where required. The statements were then amended in preparation for the second round of voting.

Round 2 Voting

The second round of voting, conducted between May 29, 2024 and June 10, 2024, included two independent voting processes, in which respondents voted on their level of agreement on the amended statements. Respondents were also given the opportunity to suggest edits to the statements. Consensus was again measured among the Taskforce using a survey (Microsoft Forms). Once the Taskforce members had completed voting and consensus was measured, the statements were updated. Following these revisions, external groups were invited to participate in a round of validation

voting. Those invited to vote included UK HCPs who were invited by the Taskforce, selected members of regional and national COPD working groups, and National Respiratory Leadership Forum (NRLF) meeting delegates. The revised statements were presented via a survey and respondents were invited to vote on their level of agreement or disagreement with the statements using a 1–9 Likert scale. The ratings were: 1–3, disagree; 4–6, neither agree nor disagree; and 7–9, agree. The threshold for consensus was set at 75% of respondents giving a rating of 7–9 for a statement.

Round 3 Voting

The third round of voting also included two independent voting processes, in which respondents voted on their level of agreement with the amended statements. Again, consensus was measured using a survey (Microsoft Forms). Those invited to vote included the Taskforce, HCPs from regional and national working groups, and delegates from the NRLF, including representation from primary and secondary care (conducted between October 29, 2024 and December 18, 2024). Similarly to Round 2, respondents were invited to vote on the statements via a survey using a 1–9 Likert scale. There were 77 respondents and the threshold for consensus was set at 75% of respondents giving a rating of 7–9 for a statement.

Clinical Pathway Framework Methodology

To complement the consensus statements and support their implementation in clinical practice, a Taskforce workshop was conducted in November 2024 to formulate a clinical pathway framework to support the recognition and management of cardiopulmonary risk in patients with COPD using the consensus statements. Key factors, clinical characteristics, observations, and assessments as part of risk identification, as well as actions that could be taken to manage cardiopulmonary risk in patients with COPD, were outlined. These were categorized as either "essential" or "desirable" and developed into a Cardiopulmonary Risk Matrix (Figure 1).



Figure I Cardiopulmonary Risk Matrix.

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; BMI, body mass index; BP, blood pressure; CAT, COPD Assessment Test; CHA₂DS₂-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke, vascular disease, age 65–74 years, sex category (stroke risk score); CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CP, cardiopulmonary; CRP, C-reactive protein; ECG, electrocardiogram; FBC, full blood count; HbA1c, hemoglobin A1c; LFT, liver function test; mMRC, modified Medical Research Council dyspnea scale; NT pro-BNP, N-terminal pro b-type natriuretic peptide; QRISK, cardiovascular risk score; TFT, thyroid function test; U&E, urea and electrolytes.

Results

Literature Review

The initial publication search yielded 1649 potentially relevant publications, including 398 relevant to research question 1 and 766, 403, and 82 to clinical questions 2, 3, and 4, respectively. The removal of duplicates and publications that did not meet the inclusion criteria left 57 unique publications relevant for question 1; 124 for clinical question 2; 13 for clinical question 3; and two for clinical question 4. PRISMA diagrams detailing the full screening process can be found in <u>Supplementary Figures 2–5</u>.

Clinical Question I. Burden of Acute Exacerbations of COPD: What is the Healthcare Burden of Acute Exacerbations of COPD in the UK?

Fifty-seven publications met the inclusion criteria for examining the healthcare burden of AECOPDs in the UK.^{12,18,22–74} Most of the studies reported were observational (68%), with randomized controlled trials, interventional studies, prognostic tool design, online surveys, case studies, meta-analyses and SLRs, and model analyses also being included. Most studies examined primary care data (54%) and used the Clinical Practice Research Datalink (CPRD) database, while some linked those data with those available in the Hospital Episode Statistics (HES) and Office for National Statistics (ONS) databases to obtain secondary care and sociodemographic data.

Incidence rates of AECOPDs were reported across several studies, with variation in rates observed. One observational study analyzed data from 340,515 primary and secondary care COPD-patient records, finding that 46.8% of patients had at least one moderate exacerbation during a 15-year follow-up period.⁷² Another primary care observational study analyzed 8282 records and retrospectively reported that 45.4% of patients experienced at least one AECOPD during the 12 months prior to study enrollment.⁶⁰ A primary care study (N=315,184) reported the rate of exacerbations experienced in the follow-up period between 19.3 and 66.6 events/100 person-years.⁷¹

Of 21 publications that investigated mortality, seven found that patients experiencing AECOPDs were at increased risk of mortality compared with patients with stable COPD, with mortality risk being most highly elevated for those experiencing frequent AECOPDs.^{12,25,29,43,70,72,75} Study populations, duration, and how mortality was measured varied across the included studies. A large primary care study including data from 67,516 patients over 14 years demonstrated all-cause mortality, during a mean follow-up period of 4 years, of 28.3% in patients experiencing any AECOPD compared with 22.3% in those not experiencing an AECOPD.⁴³ Another cohort study analyzing 10 years of data reported the effect of AECOPDs in 99,574 patients. In comparison with patients who did not experience an AECOPD during the first year of the study period, those with two or more moderate AECOPD events during the first year were associated with an increased risk of mortality (hazard ratio [HR]: 1.10; 95% confidence interval [CI] 1.03, 1.18).¹²

Six publications provided data for quality of life measurements, indicating that COPD negatively impacts quality of life.^{18,22,29,30,45,66} An online survey found that 27.1% of patients reported unemployment due to their COPD and 17.6% reported fear of exacerbations hindering their ability to get up in the morning.¹⁸

Healthcare burden was identified in 31 publications, and though hospital length of stay varied, likely due to varying study populations and comorbidities considered, patients experiencing AECOPDs had frequent contacts with healthcare providers leading to increased costs.^{18,23,24,28–30,32,33,35–37,39,42,46–48,50,53,56,59,61,62,66,68,69,73–76} A multicenter, retrospective observational study assessing 3 years of primary care data from 511 patients with COPD found that those patients experiencing frequent AECOPDs (\geq 3 exacerbations per year) had a median (interquartile range) of 6.67 (5.33–8.67) primary care contacts per year and 1.0 (0.33–2.67) secondary care contacts per year; 21% were hospitalized for COPD each year.⁶⁶ In contrast, patients experiencing no AECOPD had a median of 1.33 (0.67–2.00) primary care contacts per year and no secondary care contacts; 1% were hospitalized for COPD each year.⁶⁶ Additionally, a large (N=58,589) cohort analysis of UK hospitalizations over 12 months found that the costs of managing exacerbations increased with their frequency, with the majority of COPD-related costs attributable to primary care interactions.⁵⁶ The annual cost of managing patients experiencing two or more exacerbations categorized in stage 4 of GOLD airflow obstruction was £871.16, excluding medications, based on 2010–2011 National Health Service (NHS) reference costs.⁵⁶

Clinical Question 2. What is the Link Between Acute Exacerbations of COPD and Cardiopulmonary Events? A total of 124 publications were included in the final review.^{5,29,33,43,52,63,71–73,77–190} A large proportion (59%) occurred in, or utilized data from, secondary care. Most studies (84%) were observational but relevant case studies, database analyses, systematic reviews, and randomized controlled trials were also identified. The publications covered 35 countries in total, with most reporting studies conducted in the USA, China, the UK, and Europe. Overall, patients experiencing AECOPDs were found to be at high risk of major adverse cardiovascular events (MACE), including MI, stroke, and cardiovascular-related mortality.^{124,139,153}

A meta-analysis of observational studies found an increased risk of MACE in the 1–3 months after an AECOPD compared with no occurrence of AECOPD, reporting a relative risk (RR) of 2.43 (95% CI: 1.40, 4.20) for acute MI and an RR of 1.68 (95% CI: 1.19, 2.38) for stroke.¹³⁹ One publication analyzing the records of 25,764 patients from a UK COPD database, found no association between the frequency of exacerbations and stroke risk (odds ratio [OR] 0.95: 95% CI: 0.89, 1.01).¹⁸³

A large (N=67,516) open-cohort study compared cause-specific mortality rates for up to 14 years and adjusted for a number of risk factors, including sex, socioeconomic status, smoking status, body mass index, GOLD stage, and comorbidities.⁴³ The study found respiratory-related deaths were more frequent in patients experiencing AECOPDs (40.3%) compared with non-exacerbators (29.2%).⁴³ Conversely, CVD-related deaths were slightly more common in non-exacerbators (26.2%) compared with those experiencing AECOPDs (22.9%), possibly because of under-recognition (and consequent under-treatment) of comorbidities in non-exacerbators due to fewer healthcare contacts and hospitalizations where CVD diagnoses could be made.⁴³ Furthermore, a large health registry study including data for 340,515 patients found that those with a history of frequent and severe exacerbations at baseline were more likely to experience higher rates of future exacerbations.⁷² The study identified a correlation between baseline severity and future severity of exacerbations, as well as between baseline frequency and future frequency of exacerbations.⁷²

Clinical Question 3. How is Cardiopulmonary Risk Currently Managed in Patients with COPD in the UK?

Thirteen of the publications included in the review examined the management of cardiopulmonary risk in the UK.^{33,51,114,183,191–200} Most of the publications were observational studies (69%), with the remainder including interventional and prognostic tool design studies. The majority (70%) were large scale, utilizing databases across England or the UK, while four were smaller, single-center studies. There was heterogeneity in study populations, with notable variation in COPD definitions, population age, and comorbidities considered. Ten publications reported concurrent cardiopulmonary events in patients with COPD, but none evaluated the effectiveness or importance of managing the risk of such events.^{33,183,191–194,196–198}

Many studies examined cardiovascular risk in patients with COPD but none evaluated the impact of cardiovascular treatment on COPD outcomes or cardiopulmonary risk management. For example, two studies derived and assessed prognostic tools to evaluate the mortality risk in patients with COPD and AECOPD.^{32,193} Although each of these scores evaluated the risk of cardiovascular comorbidities in patients with COPD, neither discussed the concept or management of cardiopulmonary risk.^{32,193}

Clinical Question 4. What Policy Changes are in Place to Optimize Management of COPD in the UK?

Two relevant guidelines detailing the optimal management of patients experiencing AECOPDs in the UK were identified.²⁰¹ The British Thoracic Society (BTS) 2020 guidelines evaluated evidence supporting the use of long-term, low-dose macrolide therapy for adult respiratory diseases and for reducing rates of AECOPDs. One "good practice point" suggested the optimization of pharmacological and non-pharmacological interventions prior to considering long-term treatment with macrolides, such as smoking cessation, optimized inhaler technique, optimized self-management care plans, airway clearance techniques, and attendance at pulmonary rehabilitation courses. These recommendations were not specifically to address cardiopulmonary risk reduction, which was not discussed in the guideline.²⁰¹ The NICE 2019 guidance offered recommendations for the management of AECOPDs through systemic corticosteroids and bronchodilators, alongside supportive measures like oxygen therapy and non-invasive ventilation, where required.

Cardiopulmonary risk management was not mentioned; however, additional cardiac investigations (eg, electrocardiogram and serum natriuretic peptides) were recommended if CVD or pulmonary hypertension was suspected. An echocardiogram was also recommended if these conditions are suspected, as well as if clinical signs of cardiac or respiratory distress are present (eg, tachycardia, oedema, cyanosis, or features of cor pulmonale).¹⁵ The GOLD Report for 2025 includes recommendations based on CVD risk in patients experiencing AECOPDs but was not included in the SLR because it is not UK specific and was published after this SLR.¹⁶

Consensus Program

Consensus Statements

A preliminary set of statements was drafted and subjected to voting and revision. Following refinement, and consolidation to avoid redundancy, a total of 18 statements were included in the final round of voting and all reached the consensus threshold (Table 1). The statements are divided into four categories: burden of AECOPDs within the UK; the link between AECOPDs and cardiopulmonary events; the management of cardiopulmonary risk in the UK; and guidelines for the management of cardiopulmonary risk. Nine statements reflect the current situation, and nine statements are recommended actions that offer potential benefits.

In the third round of voting, each statement met the requirement for consensus (>75% respondents giving a rating of 7–9 for a statement). There was 100% consensus among the Taskforce members for all statements (Table 1).

Consensus Statements	Score (Mean)	Consensus (ie, Votes Between 7–9) (%)	
Healthcare burden of AECOPDs in the UK			
Approximately half of patients with known COPD experience AECOPDs in the UK. AECOPDs are associated with increased cardiopulmonary risk, further AECOPDs, and mortality.	8.4	95%	
Action: Proactive detection of risk factors and intervention is required to prevent AECOPDs and reduce the risk of cardiopulmonary events.	8.4	95%	
Patients who experience AECOPDs have higher healthcare resource utilization than patients who do not experience AECOPDs, including high hospitalization and readmission rates.	8.7	99%	
Multiple factors contribute to the direct and indirect costs of managing AECOPDs including, but not limited to, COPD disease severity, long-term conditions, AECOPD frequency, general health, medications use, and healthcare resource utilization.	8.6	100%	
Action: Optimizing COPD management through preventing AECOPDs may help address the overall cost of managing COPD.	8.4	96%	
The link between AECOPDs and cardiopulmonary events			
Patients experiencing AECOPDs are at increased risk of cardiopulmonary events, including MI, stroke, HF, arrhythmia, and respiratory or cardiovascular death.	8.5	98%	
Action: Preventing AECOPDs is important for improving cardiopulmonary outcomes, and helping prevent premature mortality.	8.4	95%	
The relationship between cardiopulmonary events and AECOPDs may be bidirectional, with cardiac events such as HF and MI potentially increasing the risk of future AECOPDs, hospitalization, and readmission, and vice versa.	7.8	86%	
Action: Improving management of cardiovascular disease in patients with COPD is likely to improve clinical outcomes.	8.4	96%	
An AECOPD may initiate functional decline in patients with COPD.	8.6	98%	
Action: Preventing AECOPDs is important in limiting functional decline.	8.6	97%	

Table I Consensus Statements

(Continued)

Table I (Continued).

Consensus Statements	Score (Mean)	Consensus (ie, Votes Between 7–9) (%)	
Cardiopulmonary risk management in the UK			
Cardiopulmonary risk is under-recognized and sub-optimally managed in patients with COPD.	8.4	97%	
In patients with concomitant COPD and cardiovascular disease, current management strategies are typically not integrated between specialties and/or between primary and secondary care.	8.4	100%	
Action: An integrated clinical approach for patients with concomitant COPD and cardiovascular disease could provide personalized treatment to improve outcomes.	8.3	95%	
Guidelines and interventions for management in the UK			
Incorporation of patient-centered cardiopulmonary risk management into routine care in patients with COPD is currently limited in the UK.	8.0	95%	
Action: Addressing cardiopulmonary risk has the potential to improve care and outcomes in patients with COPD.	8.4	95%	
Action: Decision-support tools and protocols may help estimate cardiopulmonary risk in patients with COPD, supporting optimal management.	8.2	92%	
Action: Policy, research, and clinical approaches should be designed to reduce cardiopulmonary events in patients with COPD.	8.4	94%	

Abbreviations: AECOPD, acute exacerbation of COPD; COPD, chronic obstructive pulmonary disease; HF, heart failure; MI, myocardial infarction.

Cardiopulmonary Risk Matrix

A Cardiopulmonary Risk Matrix was developed (Figure 1) to provide a clinical pathway framework for those involved in the care of patients with COPD, outlining key assessments and subsequent actions.

Discussion

We conducted an SLR of relevant studies, developed consensus statements using a modified Delphi approach, and established recommended or key actions along with a Cardiopulmonary Risk Matrix. This report identified a significant healthcare burden of AECOPDs within the UK.^{12,18,25,29,36,43–45,54,56,66,72,197} Patients experiencing AECOPDs had higher risk of mortality and MACE, reduced quality of life, and more contacts with HCPs, compared with those who did not exacerbate.^{18,22,29,30,33,43,45,66,70,72,75} Despite these associations, and an increase in management costs with AECOPDfrequency, current UK guidelines lack specificity regarding addressing cardiopulmonary risk.^{33,36,66,183,191-} ^{194,196–198} Only two relevant guidelines discussed AECOPD treatment, with the management of cardiovascular risk only covered in NICE guidelines.^{15,201} In these, cardiac investigations were recommended if there was clinical suspicion of CVD in patients with COPD, but details about when and how best to investigate for CVD were lacking.^{15,201} The increased risk of cardiovascular events following AECOPDs and consequent increased long-term risk for both respiratory and cardiovascular-related mortality has been highlighted by the recent international GOLD 2025 Report.¹⁶ Both NICE and GOLD emphasize the importance of early recognition and provide guidance for the optimized management of AECOPDs.^{15,16} From a CVD perspective, the latest QRISK4 score (QR4) includes COPD as a risk factor, and has shown that COPD is associated with MACE independent of CVD risk factors.²⁰² QR4 can, in turn, be used to evaluate cardiovascular risk in patients experiencing AECOPDs, as outlined in the Cardiopulmonary Risk Matrix (Figure 1). Our matrix was developed to provide HCPs with a framework for incorporating cardiopulmonary risk assessments and management into routine clinical practice.

AECOPDs are key drivers of cardiopulmonary events, though the relationship may be bidirectional, with cardiovascular events also increasing the risk of future AECOPDs.^{124,139,153} Correct identification of AECOPDs and cardiovascular risk is therefore important for cardiopulmonary management, but few studies provided suggestions for the identification of cardiopulmonary risk.^{9,17} A recent review by Jones, et al, suggested substantial under-reporting of AECOPDs by patients to HCPs, hindering the management and prevention of future AECOPDs.²⁰³ In the SLR reported here, several studies discussed the potentially under-recognized burden of AECOPDs, particularly in those patients managing their COPD at home, as well as undiagnosed comorbidities.^{66,182} Further supporting this trend, the COPD cohort of the COSYCONET study found that a large proportion of patients with suspicious echocardiography findings did not have a diagnosis or treatment for CVD.²⁰⁴ COPD and CVD were often treated independently, highlighting the gap in integrated care approaches.¹⁹⁷

Direct and indirect costs of managing AECOPDs and subsequent cardiovascular events could be reduced by treatment optimization, which has been shown to reduce the number of AECOPDs and associated admissions and length of stay.^{26,62} In addition to financial costs, impacts of AECOPDs include reduced quality of life, declining mental health, carer burden, increased breathlessness, and functional decline. These factors contribute to increased risk of falls, and place a strain on carers and healthcare systems.^{205,206} Of note, there are few NHS commissioning frameworks or financial incentives specifically targeting cardiopulmonary risk, with the current focus being on early diagnosis of COPD, pulmonary rehabilitation, and efficiencies.^{207,208} Inclusion of integrated cardiopulmonary strategies could help to align funding with service needs.^{207,208}

The gap in managing cardiopulmonary risk in patients experiencing AECOPDs suggests there is an opportunity to optimize care and reduce the cost of COPD management through the development of new UK policies and clinical guidance.

Clinical Implications

There is a need for multidisciplinary integrated care models including all HCPs involved in managing patients with COPD to identify and manage cardiopulmonary risk, and the Cardiopulmonary Risk Matrix/assessment tool proposed in this review could be a step towards achieving this. The Cardiopulmonary Risk Matrix could be referred to around the time of an AECOPD and/or as part of regular patient follow-up to identify and optimize cardiopulmonary risk in patients with COPD. Further education and training on cardiopulmonary risk identification and management is required to ensure it is prioritized by care systems. Additionally, COPD hospital care bundles should provide guidance on CVD assessment of both atherosclerotic CVD and HF.

Policy Implications

More funding for the development of cardiopulmonary research and guidelines is required in order to allow collection of data for large-scale registries of patients in primary and secondary care, with COPD and comorbid CVD, which in turn could inform future policies. Contract enablers should also be put in place at a national level, such as a framework of cardiopulmonary health outcome indicators for use in managing patients experiencing AECOPDs, which is something this review has highlighted is lacking in current practice.

Strengths and Limitations

The SLR was carried out according to PRISMA guidance to ensure transparency and reproducibility. Evidence was summarized and gaps in the literature were identified to help guide future research. The consensus statements were developed by the Taskforce, and consensus was gained from the group as well as externally validated by a wider group of UK HCPs. This validation process not only strengthens the consensus statements but also ensures they are practical, relevant, and applicable across diverse clinical settings, supporting their adoption in real-world practice. Unintentional bias in selection of Taskforce members cannot be ruled out; however, any potential impacts will have been mitigated by involving the wider group.

A limitation of this review was the heterogeneity of studies included, with a variety of study types, and patient populations included, making interpretation of the whole body of evidence challenging. Additionally, as many included publications reported retrospective cohort studies, database analyses, SLRs, observational studies, or cases reports, there may be variation in the classification of AECOPD severity. Few of the included interventional studies were randomized controlled trials. Another limitation is the complexity of cardiopulmonary risk in this patient population, including the bidirectional nature of MACE and AECOPDs, which makes interplay difficult to synthesize from the current evidence. Generally, consensus statements reflecting the current situation are based primarily on evidence identified through the

SLR and on clinical experience, whereas those recommending action rely, to a greater extent, on opinion and interpretation of available information.

Conclusion

Patients with COPD are at risk of cardiopulmonary events and associated mortality and morbidity. While cardiopulmonary risk is widely reported in the UK, there has been limited guidance on management of that risk in terms of respiratory and cardiac care, especially for those experiencing AECOPDs. This consensus program highlights an opportunity and establishes a foundation for future interdisciplinary research and guide-lines to address these critical needs.

Abbreviations

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; BMI, body mass index; BP, blood pressure; BTS, British Thoracic Society; CAT, COPD assessment test; CI, confidence interval; CHA₂DS₂-VASc, congestive heart failure, hypertension, age \geq 75 years, diabetes mellitus, stroke, vascular disease, age 65–74 years, sex category (stroke risk score); CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CP, cardiopulmonary; CPRD, Clinical Practice Research Datalink; CRP, C-reactive protein; CVD, cardiovascular disease; ECG, electrocardiogram; FBC, full blood count; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HbA1c, hemoglobin A1c; HCP, healthcare professional; HES, Hospital Episode Statistics; HF, heart failure; HR, hazard ratio; LFT, liver function test; MeSH, Medical Subject Headings; MI, myocardial infarction; mMRC, modified Medical Research Council dyspnea scale; NT pro-BNP, N-terminal pro b-type natriuretic peptide; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; NRLF, National Respiratory Leadership Forum; ONS, Office for National Statistics; OR, odds ratio; PICO, Patient, Intervention, Comparator, and Outcome; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; QRISK, cardiovascular risk score; RR, relative risk; SLR, systematic literature review; TFT, thyroid function test; U&E, urea and electrolytes; UK, United Kingdom.

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