

Standardisation of Clinical Assessment, Management and Follow-Up of Acute Hospitalised Exacerbation of COPD: A Europe-Wide Consensus

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Background: Despite hospitalization for exacerbation being a high-risk event for morbidity and mortality, there is little consensus globally regarding the assessment and management of hospitalised exacerbations of COPD. We aimed to establish a consensus list of symptoms, physiological measures, clinical scores, patient questionnaires and investigations to be obtained at time of hospitalised COPD exacerbation and follow-up.

Methods: A modified Delphi online survey with pre-defined consensus of importance, feasibility and frequency of measures at hospitalisation and follow-up of a COPD exacerbation was undertaken.

Findings: A total of 25 COPD experts from 18 countries contributed to all 3 rounds of the survey. Experts agreed that a detailed history and examination were needed. Experts also agreed on which treatments are needed and how soon these should be delivered. Experts recommended that a full blood count, renal function, C-reactive protein and cardiac blood biomarkers (BNP and troponin) should be measured within 4 hours of admission and that the modified Medical Research Council dyspnoea scale (mMRC) and COPD assessment test (CAT) should be performed at time of exacerbation and follow-up. Experts encouraged COPD clinicians to strongly consider discussing palliative care, if indicated, at time of hospitalisation.

Interpretation: This Europe-wide consensus document is the first attempt to standardise the assessment and care of patients hospitalised for COPD exacerbations. This should be regarded as the starting point to build knowledge and evidence on patients hospitalised for COPD exacerbations.

Keywords: COPD, disease exacerbation, hospitalisation, patient care, consensus development, expert opinion

Introduction

Hospitalised exacerbations of chronic obstructive pulmonary disease (COPD) account for a significant proportion of bed pressures and hospital costs throughout the world, including Europe^{1,2} and North America.³ These exacerbations also confer a high risk of in-hospital mortality of approximately 5–8%^{4,5} and carry up to 58% risk of re-admissions within 1 month^{6,7} and up to a 20–25%⁵ risk of mortality in the 12 months following discharge.

Major international COPD guidelines^{8,9} provide clinicians with very little guidance for standardisation of clinical assessment, examination, laboratory and radiological tests and treatment in hospitalised exacerbations of COPD (HECOPD).

There is also no consensus on patient follow-up frequency and the details on what should be measured during the post hospitalisation follow-up phase. For example, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) suggests measuring spirometry in everyone hospitalised for an exacerbation of COPD.⁸ A 2016 European audit⁴ showed that more than half of patients admitted to hospital for an exacerbation of COPD had never had a spirometry recorded. Similarly, the GOLD report⁸ recommends the measurement of an arterial blood gas, yet uptake of this is incomplete.⁴ Even in long-term treatment decisions, such as the use of long-term oral corticosteroids, physician practices do not match the guidelines.¹⁰

Our colleagues in other fields of acute hospital care, such as cardiology and rheumatology, have enviable evidence-based guidelines.^{11,12} These often define what, when, how and the frequency a patient should have assessment of symptoms, tests, outcomes and treatments. This has led to standardisation of treatment protocols and clinical trial endpoints. Without a doubt, this has played a major contributory role in the improvements in patient outcomes in rheumatoid arthritis¹³ and myocardial disease.¹⁴ There are also clear lessons that COPD specialists can take on board from other clinical areas. In 2004,¹⁵ the Outcome Measures in Rheumatology (OMERACT) collaborative set out to achieve an expert consensus statement on different outcome measures and treatment goals in caring for patients with psoriatic arthritis. Like for HECOPD, they set out from a place of limited evidence and aimed to achieve a standardised starting point to then build their evidence base on. Within a few years, the collaborative achieved global expert consensus on outcomes in psoriatic arthritis care,¹⁶ which was then taken up by major international professional bodies.¹⁷

With this context, we have investigated consensus as well as the areas of disagreement in the evaluation of the expert view on demographic, clinical characteristics, comorbidities, investigations and clinical outcomes for patients who are hospitalised for acute exacerbations of COPD as part of the CICERO collaboration.¹⁸

Methods

This study used a modified, 3-round online survey based on the Delphi method¹⁹ to establish a defined list of variables that should be measured at the time of a HECOPD. The survey was conducted via a secure online survey platform (surveymonkey.com). The variables were divided

into symptoms, examination findings, co-morbidities, clinical scores, laboratory tests, point of care test (eg, ECG, spirometry), other tests (eg, radiology, detailed lung function tests), treatments and clinical outcomes of importance. All the items were assessed for use at time of hospitalisation and at the post hospitalisation follow-up phase. Excepting the history-taking sections, the feasibility of undertaking each of these assessments and treatments was also assessed. Ethics or institutional review board approval was not required. This survey was exempt from approval as it was non-invasive, undertaken voluntarily by medical professionals and did not involve any patients.

Expert Selection

To understand current practice in Europe and to derive a consensus list of variables, we set out to invite a diverse panel of COPD experts from as many countries in Europe as possible. Policy Delphi²⁰ methodologists recommend a panel size of between 15–40 experts to achieve an appropriate balance between points of view. Experts were contacted by the European Respiratory Society if they met 2 or more of the following criteria:

1. Board-certified pulmonologists who currently spend at least 20% of their time caring for patients hospitalised for acute exacerbation of COPD
2. Evidence of publication of important COPD research relevant to assessment or management of patients hospitalised for exacerbations of COPD
3. A history of participation in the development of local or national guidelines for the management of COPD

Delphi Process

The modified Delphi process consisted of 3 iterative rounds (subsequently called rounds 1, 2 and 3). Each expert was provided a unique secure link to an online questionnaire platform. The variables were listed in groups, and experts were asked to rate the importance, feasibility and a suggested frequency on a Likert scale. Experts were reminded that the survey sought to obtain their opinion on clinical care for HECOPD. Free text capability for expert comments were sought for each section. Any new item suggested was added to the following round of the electronic survey. Members then returned the completed online surveys anonymously. Experts were asked to return surveys within a 3-week period. Reminder e-mails were sent to encourage completion,

and extensions were given when necessary. This is summarised in Figure 1.

Consensus, dissensus and stability criteria for the Delphi process were pre-determined prior to Delphi process commencement. Consensus^{21,22} was defined as an interquartile range (IQR) of ≤ 1 for a 4- or 5-point Likert scale item. For 3-point Likert scales and for Yes/No items, an IQR of 0 was needed to achieve consensus. A Wilcoxon

signed rank test was performed on paired results of expert's responses to assess stability of responses between rounds. If the responses were not statistically significantly different (p value ≥ 0.05), responses were considered stable. At the completion, any item that reached a score of "important", "important to very important" or "very important" was included in the final consensus list. The corresponding feasibility and frequency were also reported

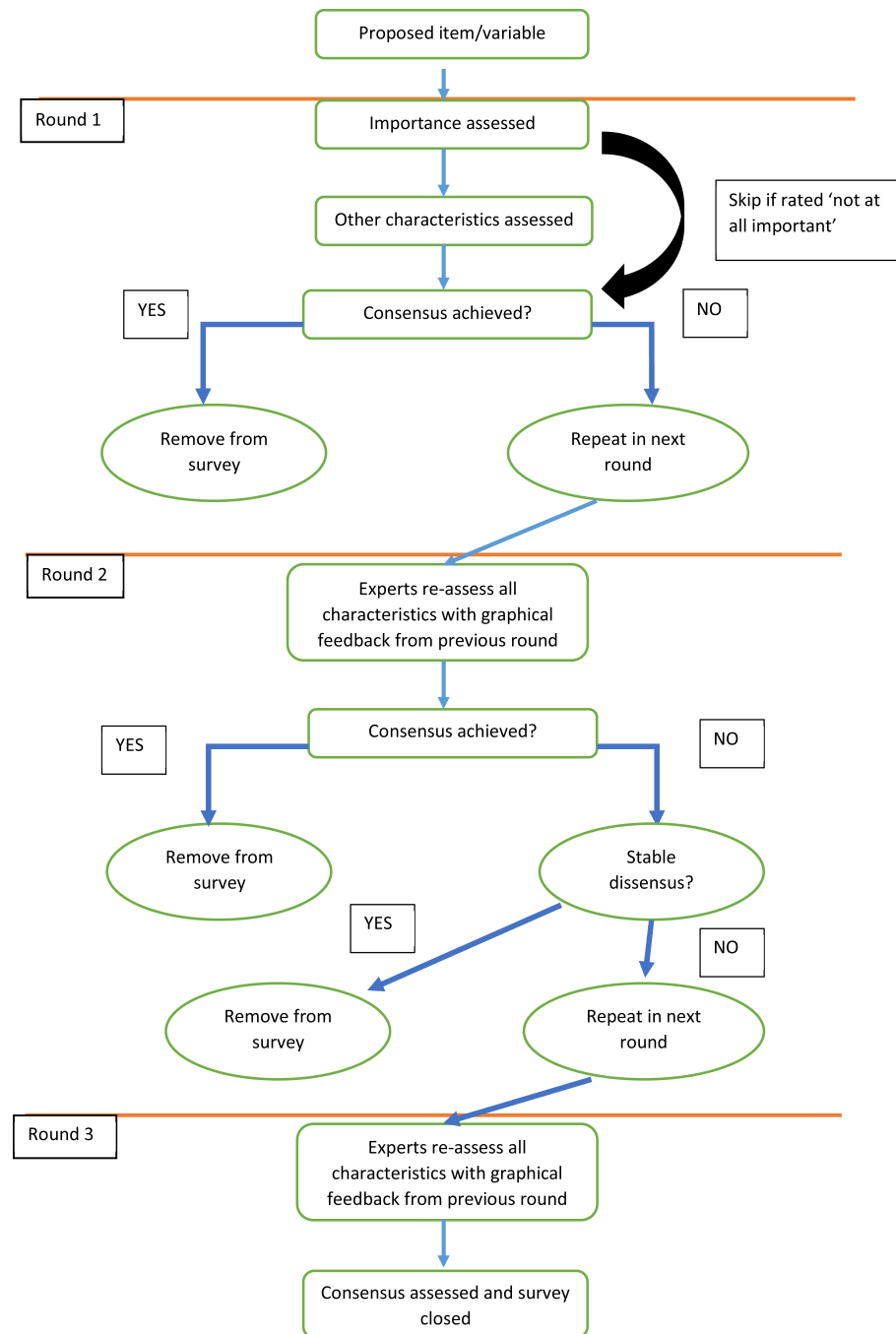


Figure 1 Schematic illustrating the Delphi survey process.

if consensus was achieved. If items were rated “neutral” or “neutral to important”, they were assigned as “to be considered” in any future evaluation. Items where consensus was not achieved are also reported.

Variable Selection

A detailed literature review was undertaken by SR and MB to assess the current evidence basis for symptoms, examination findings, co-morbidities, clinical scores, laboratory tests, point of care test (eg, electrocardiogram, spirometry), other test (radiology, detailed lung function tests), treatments and clinical outcomes of importance for use in hospitalised patients with exacerbation of COPD (search criteria used are available in [supplementary Table 1](#)), prior to design of the Delphi survey. A final decision for survey input was made at a face to face meeting by SR, MB, WJ and AH.

Round 1

As we were aiming to establish experts’ views on many variables and many aspects of the variable (importance, frequency, feasibility etc), a skip logic was programmed to help reduce the survey burden. If an expert marked a variable as “Not at all important” on the importance Likert scale, the item was removed from the survey for that expert for all subsequent lower order items (eg, feasibility). In other words, if experts rated something as not important, then aspects of that item, eg, feasibility and frequency, were deemed irrelevant for the remainder of round 1.

Round 2

All items that achieved consensus in round 1 were removed from round 2. If consensus was only achieved on one aspect of the item, for example the importance of a particular clinical test, but not the feasibility or frequency, the importance section was not re-evaluated in round 2, but the other aspects were re-evaluated. Any variable that was re-evaluated was accompanied by a histogram of the previous round’s expert responses and a median of the responses. Any items suggested by experts in round 1 were also included in round 2. No skip logic was programmed for round 2.

Round 3

Again, variables achieving consensus were removed. For items that did not achieve consensus, stability was assessed. If a variable remained in dissensus and remained stable, the item was removed and marked as

“stable disagreement”. If a variable remained in dissensus but had changed significantly, the item was marked for re-evaluation in round 3. Like round 2, any new suggestions from experts in round 2 were included. Questions were modified for clarity and/or specificity in response to experts’ suggestions. There was no skip logic. Any variable that was re-evaluated was accompanied by a histogram of the previous round’s expert responses and a median of the responses for both rounds.

Results

A total of 25 COPD experts from 19 European countries completed all 3 rounds of the Delphi survey. There were 3 experts from the UK; 2 each from the Netherlands, France, Germany and Italy; and 1 each from Belgium, Spain, Switzerland, Portugal, Croatia, Estonia, Serbia, Latvia, Sweden, Turkey, Slovenia, Finland, Greece and Poland. There were 8 (32%) female experts, and the majority were aged between 41–50 years (56%). All experts worked in the field of COPD in secondary or tertiary/academic institutions. On average, experts spent 22% of their time caring for respiratory inpatients. All but one of the experts were actively involved with research into COPD care. After round 2, no further new items were recommended to gain consensus. The survey was sent and completed prior to the coronavirus disease 2019 (COVID-19) pandemic.

Expert Consensus Opinion During an Acute Hospitalised Exacerbation of COPD

Symptoms

There were 29 symptoms that were assessed for importance, method of symptom data capture (binary vs severity scale) and frequency of symptom capture. After 3 rounds, no consensus was achieved on 3 items (low mood, sneezing and poor sleep). A further 2 symptoms, namely runny eyes and itchiness, were excluded by experts. Of the remaining 24 symptoms, experts recommend that 12 symptoms must be recorded at time of exacerbations and 12 that ought to be considered (see [Table 1](#)). The experts endorse that most symptoms could be recorded in a binary form (ie, present or absent). For the symptoms of cough and sputum purulence respectively, experts could not agree whether this should be reported quantitatively (on a scale of severity) or qualitatively (absent or present) after 3 rounds.

Table 1 Recommended Symptom Data Capture at Time of Hospitalised Exacerbation

Must Be Recorded		
Symptoms	How to Measure	Frequency
Dyspnoea	Severity scale	Daily
Wheeze	Binary	Daily
Increased sputum volume	Binary	Daily
Sputum purulence	No consensus achieved	Daily
Cough	No consensus achieved	Daily
Fever	Binary	Twice a day to daily
Use of rescue medication	Severity scale	Daily
Increased inhaler use	Binary	Daily
Reduced exercise tolerance	Severity scale	Daily to once in admission
Confusion	Binary	Daily
Loss of consciousness	Binary	Daily
Orthopnoea	Binary	Daily to once in admission
Consider Recording		
Chest tightness	Binary	Daily
Chest pain	Binary	Daily
Haemoptysis	Binary	Daily
Cough at night	Binary	Daily
Myalgia	Binary	Daily
Fatigue	Binary	Daily
Drowsiness	Binary	Daily
Poor appetite	Binary	Daily
Palpitations	Binary	Daily
Sore throat	Binary	Daily
Runny nose	Binary	Daily
Headache	Binary	Daily

Co-Morbidities

Respondents recommended that a complete and detailed medical history was necessary at time of exacerbation. Some medical history items, namely, history of atopy, osteoporosis, chronic kidney disease, human immunodeficiency virus (HIV) status and non-lung primary malignancy were rated as being less important for routine recording but should be considered.

Clinical Signs

Consensus was achieved on the importance of recording respiratory clinical signs. However, expert opinion was

that treating physicians need only consider recording some cardiac signs, such as heart murmurs, pulsus paradoxus, jugular venous pressure (JVP), in addition to body weight at time of hospitalised exacerbations (see [Table 2](#)). Experts agreed that menstrual cycle, forearm and quadriceps strength, abdominal distension, abdominal tenderness and pulsatile liver edge did not need to be actively recorded unless relevant to the patient history. The consensus list of clinical signs to elicit at the post hospitalisation follow-up phase are listed in [supplementary Table 2](#).

Clinical Tests

An expert consensus was reached on which tests should be performed at the time of a severe hospitalised exacerbation of COPD (see [Table 3](#)). Experts recommend that a full blood count, renal function, C-reactive protein (CRP), cardiac troponin and BNP are essential tests and should be completed within 4 hours of hospitalisation. Similar to this, the experts recommended that a chest radiograph and ECG should be performed as soon as possible. The optimum timing of when other essential tests should be performed (namely arterial blood gas, sputum cultures and viral swabs) could not be decided. Other routinely available tests were recommended by experts to be investigations to consider, reflecting on occasion the healthcare system available to experts. This included common tests such as lactate dehydrogenase (LDH) and nasopharyngeal swab for non-influenza respiratory viruses. Tests not included in the consensus recommendation are listed in [supplementary Table 3](#). Experts could not agree on the importance of performing any point of care assessment of lung function or inflammation at time of acute exacerbation (including peak flow, spirometry and exhaled nitric oxide). All tests at the post hospitalisation follow-up phase that were recommended for consideration and excluded by expert consensus are listed in [supplementary Table 3](#).

Clinical Scores and Questionnaires

A wide range of related clinical severity scores and questionnaires were assessed for their utility and feasibility (see [supplementary Table 4](#)). Experts felt that only 3 should be done at time of hospitalised exacerbation; these were the modified Medical Research Council (mMRC) dyspnoea scale, the COPD assessment test (CAT) and asking about frequency of exacerbations (frequent exacerbator phenotype) (see [Table 4](#)). The majority of clinical scores/questionnaires were excluded by consensus (see [supplementary](#)

Table 2 Recommended Clinical Signs Data Capture at Time of Hospitalised Exacerbation

Clinical Signs	Inclusion	Frequency
Blood oxygen saturation	Must	At least once every 4 to 12 hours
Supplemental oxygen amount	Must	At least once every 12 hours
Heart rate	Must	At least once every 12 hours
Respiratory rate	Must	At least once every 12 to 24 hours
Use of accessory respiratory muscles	Must	At least once every 12 to 24 hours
Change in mental state	Must	At least once every 12 to 24 hours
Blood pressure	Must	At least once every 12 to 24 hours
Temperature	Must	At least once every 12 to 24 hours
Wheeze on assessment/examination	Must	At least once every 12 to 24 hours
Irregular pulse	Must	At least once every 12 to 24 hours
Silent chest	Must	At least once every 12 to 24 hours
Orthopnoea	Must	At least once every 12 to 24 hours
Crackles	Must	At least once a day
Ronchi	Must	At least once a day
Pursed lip breathing	Must	At least once a day
Ankle oedema	Must	At least once a day
Presence of raised JVP	Must	At least once a day
Colour of sputum	Must	At least once a day
Body mass index	Must	Once during admission
Degree of raised JVP	Consider	Once a day to once during admission
Heart murmurs	Consider	Once a day to once during admission
Hoover's sign	Consider	Once a day to once during admission
Weight	Consider	Once a day to once during admission
Pulsus paradoxus	Consider	Once a day to once during admission

Abbreviation: JVP, jugular venous pressure.

[Table 5](#)), including the SGRQ, APACHE and EXACT-Pro. These recommendations also extended to the post hospitalisation follow-up phase (see [supplementary Table 5](#)).

Pharmacological Treatments (When Indicated)

Expert opinions related to treatments, when clinically indicated, achieved the greatest amount of consensus early in the Delphi, including the treatments that need to be given and when they should be commenced (see [Table 5](#)). When clinically indicated, experts recommended that patients hospitalised with an exacerbation of COPD be treated with systemic corticosteroids and antibiotics, for 5 to 7 days in total, with systemic corticosteroids dosing equivalent to 30–50 mg of prednisolone daily. Experts recommended that nebulised therapy duration should be given for a maximum of 5 days, although there was a greater variation of opinion on duration. Experts strongly recommended that long-term inhaler optimisation should be performed prior to discharge.

Non-Pharmacological Treatments

Experts expected smoking cessation advice to be provided at every hospitalisation, in addition to seeing a respiratory physiotherapist. A referral to pulmonary rehab was considered a routine requirement. Although ideal, seeing a COPD specialist

nurse at every hospitalisation was not deemed feasible. Experts also recommend that it was very important and very feasible to discuss palliative care, goals of care, symptom control and resuscitation status at every hospitalised exacerbation.

Outcomes at the Post Hospitalisation Follow-Up Phase

The consensus opinion among experts was that patients should only be considered stable at 6 weeks (median, IQR 6 to 12 weeks) post hospitalisation for COPD exacerbation. Experts were also able to make recommendations on the list of outcomes that should be used to define “treatment failure”, both in clinical practice and in research (see [Table 6](#)).

Potential Controversies

Experts recommended that an echocardiogram should be part of clinical care for patients with a hospitalised exacerbation of COPD following round 3; however, no consensus was reached as to when this should be performed (ie, in hospital or after discharge) or whether this should be performed routinely or only if clinically indicated. Computed tomography (CT) scans of the thorax and peak flow measurements led to strongly conflicting opinions of experts saying it was

Table 3 Recommended Tests to Perform at Time of Hospitalised Exacerbation of COPD

Tests	Inclusion	Within 4 Hours	Within 8 Hours	Within 12 Hours	Within 24 Hours	Within Admission
Full blood count	Must	✓				
Urea, electrolytes, creatinine	Must	✓				
Troponin	Must	✓				
BNP	Must	✓				
CRP	Must	✓				
Glucose	Must	No consensus achieved on time to first test				
Liver function tests	Must	No consensus achieved on time to first test				
ABG	Must	No consensus achieved on time to first test				
Chest X-ray	Must	As soon as possible during admission				
Electrocardiogram	Must	As soon as possible during admission				
Echocardiogram	Must	No consensus achieved on time to first test				
Sputum MCS	Must	No consensus achieved on time to first test				
Influenza viral throat swab	Must	No consensus achieved on time to first test				
6-minute walk test	Must	No consensus achieved on time to first test				
Lactate dehydrogenase	Consider	No consensus achieved on time to first test				
High-sensitivity CRP	Consider	No consensus achieved on time to first test				
Procalcitonin	Consider	No consensus achieved on time to first test				
Urine dipstick	Consider	No consensus achieved on time to first test				
Viral throat swab	Consider	No consensus achieved on time to first test				
CT scan of thorax	Consider	No consensus achieved on time to first test				
Grip strength	Consider	No consensus achieved on time to first test				
Quadriple strength	Consider	No consensus achieved on time to first test				
Overnight oximetry	Consider	No consensus achieved on time to first test				

Abbreviations: BNP, brain natriuretic peptide; CRP, C-reactive protein; ABG, arterial blood gas; MCS, microscopy, culture and sensitivities; DLCO, diffusing capacity of lung for carbon monoxide; CT, computed tomography.

either “not at all important” or “very important”, and these polarised opinions were not resolved after 3 rounds.

Discussion

We report here the expert consensus recommendations from a detailed Delphi study in standardisation of measurements in

the management of patients with HECOPD. These included symptoms, examination findings, co-morbidities, clinical scores, laboratory tests, point of care tests and treatments.

This is the first proposal of standardised data collection in clinical practice for severe hospitalised exacerbations of COPD (see <https://www.cicero-copd.net/> for hospital

Table 4 Recommended Clinical Scores and Questionnaires to Be Taken at Time of Hospitalised Exacerbation

Clinical Score/Questionnaires	Inclusion	Frequency
mMRC dyspnoea index	Must	At the start and end of admission
COPD assessment test	Must	At the start and end of admission
Frequent exacerbator phenotype	Must	Once during admission
BODEx	Consider	Once during admission
CURB-65	Consider	Once during admission
Glasgow Coma Scale	Consider	Once during admission
GOLD I-IV	Consider	Once during admission
GOLD A-D	Consider	Once during admission
Visual analogue scale for symptoms	Consider	At the start and end of admission
Early warning chart*	Consider	Daily
HADS*	Consider	Once during admission
DECAF*	Consider	Once during admission
Clinical COPD questionnaire*	Consider	No consensus achieved

Notes: *European experts felt that these scores may not be feasible in some centres. References for clinical scores and questionnaires listed in [Supplementary Table 4](#). **Abbreviations:** mMRC, modified Medical Research Council; BODEx, body mass index, degree of airflow obstruction, dyspnoea, exacerbations; CURB-65, confusion, urea, respiratory rate, blood pressure, age >65; GOLD, global initiative for chronic obstructive lung disease; HADS, hospital anxiety and depression scale; DECAF, dyspnoea, eosinopenia, consolidation, acidemia and atrial fibrillation.

Table 5 Recommendations Regarding Treatment Allocation, if Indicated, at the Time of Hospitalised Exacerbation of COPD

Treatment	Within 30 Minutes	Within 60 Minutes	Within 4 Hours	Within 24 Hours
Oxygen	✓			
Nebulised short-acting beta agonists	✓			
Nebulised short-acting muscarinic agents	✓			
Systemic corticosteroids		✓		
Intravenous fluids		✓		
Non-invasive ventilation		✓		
Antibiotics			✓	
Opiates			✓	
Diuretics			✓	
Chest physiotherapy				✓
Assisted mobilisation				✓

Table 6 Recommended Treatment Failure Assessments at 30 Days After Hospitalised Exacerbation of COPD

Treatment Failure Outcome to Assess	Inclusion
Mortality	Must
Intensive care admission requirement	Must
Re-admission	Must
Re-treatment with steroids and/or antibiotics for COPD exacerbation	Must
Health care utilisation (any of hospital presentation, primary care or urgent care visit)	Must
Length of stay	Must
New or worsening co-morbidities following the index exacerbation event (eg, diabetes, osteoporosis)	Must
Increase in short-acting inhaled therapy	Must
Cumulative use of systemic steroids	Must
Change in symptom scores	Consider
Quality of life scores	Consider

exacerbation standardisation tool). This Delphi survey is a robust method to obtain consensus on standardisation of many aspects of hospitalised COPD management and provides a real-life perspective on the components prioritised by COPD physicians. The experts selected represent COPD physicians from across Europe with diverse health systems. We believe our high retention rate of experts throughout the three survey rounds is indicative of the importance of gaining standardisation for hospitalised exacerbation management, in addition to certain features of programming such as skip logics which ultimately reduced participant “click” burden. We found that, overall, there was a great deal of consensus amongst COPD experts. We specifically assessed importance and feasibility separately to establish an ideal set of measures; this assessment of a clinician's opinion on importance and how feasible a measure is has not been made before.⁸ We also pre-defined consensus and stability criteria prior to study commencement to prevent post hoc adjustments to affect

inclusion threshold.²² We found very few occasions where an item (eg, a question in the survey) was found to be rated important and regarded as not feasible simultaneously.

As expected, all experts agreed that a detailed medical history and physical exam were important at time of hospitalisation, as per current recommendations.⁸ However, the inability of experts to agree on how to measure two very common symptoms, such as cough and sputum purulence, clearly exemplifies the need to urgently standardise recording of these symptoms. Our effort will almost certainly aid clinical practice, research practice and consequently patient outcomes. Furthermore, it is recognised that cardiovascular disease is a substantial cause of morbidity and mortality in patients with COPD,²³ however, the expert opinion in our survey predominantly graded respiratory physical signs of higher importance than cardiac signs. This may reflect bias in asking respiratory experts or that simply assessing cardiac

signs alone is insufficient to address cardiovascular risk. Moreover, it is worth noting that our experts recommend that cardiac biomarkers such as BNP, troponin, ECG and echocardiogram are essential tests in the management of a patient hospitalised with an exacerbation, and in the case of BNP, troponin and an ECG these should be performed within 4 hours (or as early as possible) of the admission. This recommendation highlights the importance of assessing cardiovascular risk in patients with COPD, where mortality is high.²³ It is recognised that there is an increased risk of cardiovascular events within 30 days of hospitalisation for an exacerbation of COPD²⁴ and that it is highly likely that clinical or sub-clinical cardiovascular disease may worsen during a severe exacerbation.

The experts' views on blood, radiology and assessments of lung function at the time of hospitalised COPD exacerbation were interesting. Unlike asthma guidelines, current COPD guidelines do not recommend point of care lung function testing during an exacerbation.^{8,9} This was also reflected by our experts not agreeing on any point of care test (including peak flow) and thus not recommending this as an investigation at time of hospitalisation. This could reflect the limitations with spirometry or peak flow as an available tool²⁵ and the lack of evidence to suggest it alters clinical management at the time of an exacerbation. This contrasts with the expert consensus regarding the value of spirometry at time of follow-up, as a diagnostic requirement. It is conceivable, however, that other more sensitive tools assessing airway obstruction, such as impulse oscillometry testing,²⁶ need to be considered at time of hospitalisation or follow-up.

In contrast to this, there was expert consensus and recommendation that full blood count, renal function and CRP should be performed within 4 hours of an admission. The use of the peripheral blood eosinophil count²⁷ and serum C-reactive protein²⁸ during a HECOPD is still being evaluated. Meanwhile, although other tests were considered to be important, there was no consensus as to when these should be performed. We believe that the variability in the severity of HECOPD could impact on timeline decision-making and is thus reflected as dissensus in this survey.

The experts recommended that a chest radiograph should be performed as soon as possible within the admission. This is in line with current recommendations. Chest X-ray is used frequently²⁹⁻³¹ despite evidence showing that it rarely alters³⁰ clinical management. Research on

the value of a CT of the chest during HECOPD is ongoing,³² whilst the relative infeasibility of CT scans likely contributed to strongly polarised views on its importance at time of HECOPD.

Finally, experts agreed that only the mMRC³³ and the CAT³⁴ must be assessed at time of hospitalisation. Despite there being a wide variety of risk tools to assess COPD exacerbation and mortality risk, external validation of these risk tools at the time of a hospital admission is limited³⁵ and is likely to have attributed to expert opinion on which risk tools/scores are required at the time of a hospitalisation of COPD.

Following this expert consensus, we have defined a patient to be stable following a hospitalisation of COPD at 6 weeks, with a range of timepoints from 6 to 12 weeks to define stability, after hospitalisation. We believe it is of great importance that our experts were able to provide opinion on how to define a treatment failure. Our experts recommended that a treatment failure outcome should be measured at 30 days; in addition to currently approved definitions (of death or re-treatment for example), we should also capture outcomes related to cumulative systemic corticosteroid use, use of short-acting inhaler use and new or worsening of concomitant co-morbidities. These additional components seek to address harm of treatment, where the evidence is now increasing.³⁶

There are several limitations to discuss. Firstly, it is important to note that the consensus decisions derived from this survey reflect expert opinion, and there is little evidence supporting the practice of measuring these outcomes at time of hospitalisation for an exacerbation of COPD. However, due to the paucity of evidence or best practice, this is where the Delphi method works best. In particular, this Delphi approach in management of hospitalised COPD exacerbations can serve to act as a springboard to start standardising, building evidence and importantly to improve care. We feel that COPD physicians should not accept the status quo simply because there is no evidence to guide change. Secondly, as expected,¹⁹ an expert-led Delphi process would favour more detail and intervention than that which is potentially plausible in day to day practice. To resolve this, we specifically asked about the feasibility of all items, especially considering local costs, and practice limitations. All the items proposed reached a rating of "feasible to very feasible". We believe that our success at bringing together a broad expert panel from across Europe makes this

document workable in clinical practice across Europe. This has led to recommendations of symptoms, signs, tests and outcomes which are all eminently feasible. A further limitation is that our experts were pre-selected pulmonologists practising in Europe. This may potentially make our results difficult to generalise to low- and middle-income countries; however, we feel this limitation will only apply to the selection of investigations at the time of a hospitalised exacerbation. The exclusion of allied health professionals from the expert panel could also limit the generalisability/acceptability of the proposed standardisation consensus. As part of the CICERO clinical research collaborative, we are now seeking patients' views on our expert consensus through a multi-national, multi-lingual survey, run in collaboration with the European Lung Foundation. This standardisation is also being piloted in a Europe-wide cohort study of 1000 hospitalised COPD exacerbations, another pre-defined goal of the CICERO collaboration. These novel, patient and end-user driven validation attempts are unique in clinical care standardisation. Finally, we limited the survey to three rounds a priori, where further rounds may yield further consensus,¹⁹ although in current practice a minimum of 3 rounds are commonly recommended.²² The statistical approaches used to define consensus and dissensus, and the use of the Wilcoxon signed rank test could have falsely shown stability. However, very few elements failed to achieve stability of either consensus or dissensus after 3 rounds.

In conclusion, we have developed an expert consensus tool through a pre-defined Delphi process, that recommends which measures should be undertaken as part of standardisation of routine clinical care. To improve COPD clinical care, the respiratory field should move beyond the status quo from a position of limited standardisation. Adoption of this expert consensus will provide the first starting point to do this for patients hospitalised for exacerbations of COPD.

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