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STUDY PROTOCOL

Derivation and Definitions of Clinical Study Variables for Multiple Long Term Conditions in Patients with Chronic Obstructive Pulmonary Disease: Protocol for a Modified Delphi Methods and Consensus Study on Behalf of the International Cardiovascular and Respiratory Alliance

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Background: Standardized variables and their definitions are essential for robust delivery and reporting of clinical studies and quality improvement in chronic obstructive pulmonary disease (COPD). This protocol describes the rationale and methodology for the derivation and definition of clinical study variables for patients with multimorbidity or at high risk of multimorbidity in COPD.

Methods and Analysis: We will follow a four-step process. This will include the formation of an Executive Committee, a Steering Committee and an International Consensus Group. We will conduct a systematic review of the literature from which potential clinical

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study variables will be extracted and their definitions proposed. Using a modified Delphi process, the Steering Committee will select candidate clinical study variables and as necessary refine their definitions. All three groups will then vote and give feedback on the candidate clinical study variables in a modified Delphi process (with rounds until consensus is achieved) to reach a final suite of internationally agreed hierarchically classified clinical study variables.

Ethics and Dissemination: It is anticipated that the results will be published in a peer-reviewed journal and presented in a variety of forums. Ethical approval was not required for this study.

Keywords: COPD, data standards, registry, quality improvement, randomized clinical trial, outcomes, multimorbidity

Introduction

Standardised variables and their associated definitions are essential for robust and valid evaluation of investigational medical products, health service interventions, clinical care and outcomes in randomised clinical trials, observational studies and quality improvement initiatives for chronic obstructive pulmonary disease (COPD).[1,2] Yet, adoption of historically proposed data variables is poor,[3] and it is estimated that only a small number of COPD studies refer to or implement these variables in research and clinical practice.[4] There is a growing need for harmonized, real-world compatible data variable sets that allow for increased standardization across different research settings and study designs and was identified by the Towards Optimum Reporting of Pulmonary Effectiveness Databases and Outcomes (TORPEDO) initiative.[1,5]

Several initiatives have proposed clinical variables for COPD. The TORPEDO initiative aimed to define common datasets for COPD studies.[5] Although TORPEDO provides a list of variables and consensus on study contexts for their use, the variables are not defined. The COllaboratioN on Quality improvement initiative for achieving Excellence in STandards of COPD care (CONQUEST) is a COPD registry and integrated quality improvement programme that focuses specifically on patients with modifiable high-risk COPD (patients at a higher, but modifiable, risk of future exacerbations and cardiac events).[6] However, CONQUEST does not specify which variables may be used in specific contexts, rather it prompts healthcare practitioners to consider key aspects of optimal care.[6] The European Respiratory Society (ERS) produced a core outcome set for COPD exacerbation trials but does not define them nor suggest specific clinical or research contexts.[1] Additionally, all of the aforementioned initiatives lack a structured hierarchy for their variables and there is no internationally agreed consensus for definitions of COPD data variables.

Multimorbidity is defined as the presence of multiple co-existing conditions in an individual.[7] Multimorbidity is likely to increase as medical care improves, and is adding complexity to patient management and placing increasing strain on healthcare settings with finite resources.[7] COPD is highly associated with multimorbidity, especially cardiovascular disease (CVD).[8,9] More patients with COPD die of CVD than respiratory failure in mild-moderate COPD.[10] CVD and associated risk factors in COPD are often underrecognized, and it stands to reason that CV risk management is not optimally managed.[11] COPD and atherosclerotic cardiovascular disease share numerous pathological mechanisms and risk factors, including chronic inflammation and smoking.[12] This also places COPD close to the cardiovascular-kidney-metabolic health axis, as it is well established that CVD is also associated with renal and metabolic disease.[13] Therefore patients with COPD are at high risk of multimorbidity and require a tailored suite of variables to correspond to the increasingly complex healthcare needs.

The International Cardiovascular and Respiratory Alliance (ICRA, https://www.icra-global.com) is a multidisciplinary group of healthcare professionals, researchers and patients formed in 2025 to advance the care of individuals with cardiovascular and respiratory diseases. The Alliance spans over 45 countries and grew from the Global Working Group on Cardiopulmonary Risk in COPD.[9] To date, it has provided definitions for cardiopulmonary events and cardiopulmonary risk, a consensus paper about the identification and management of cardiopulmonary risk and described the knowledge and evidence gaps in cardiopulmonary risk in patients with COPD.[9,10,12]

This protocol paper sets forth the approach that will be taken to develop and define an internationally agreed suite of clinical study variables and accompanying definitions that may be selected for use in clinical care and research that concerns patients with multimorbidity or at high risk of multimorbidity in COPD.

Methods

We will follow the methodology proposed by the Enhancing the QUAlity and Transparency Of health Research (EQUATOR) Network and the ACcurate COnsensus Reporting Document (ACCORD) statement.[14,15] We will conduct a modified Delphi process to create COPD Data Standards for multimorbidity and agree upon an international standard for COPD clinical study variables and their definitions. Surveys will include a consent statement, and consent will be assumed by participation in the survey. Formal informed consent will not be sought. The surveys will be pseudonymized to collect response rates by certain participant categories eg cardiologist, respiratory physician, patient, nurse. The overview of the process is displayed in Figure 1.

Step 1: Formation of Committees

Executive Committee

CPG, DBP, MB and TJ will form the Executive Committee and lead the development of the COPD multimorbidity clinical study variables. The Executive Committee will review the data extracted from the literature search and will subsequently refine this to remove duplicates and unnecessary or inadequate items from the data extraction. There will be online and email correspondence to determine relevant categories of variables, and an initial list will be generated by TJ. The Executive Committee (excluding TJ) will review the resultant list to ensure relevance and, as necessary, refine the list of variables to ensure external generalizability and research and clinical relevance. The Executive Committee will also be able to suggest extra clinical study variables that may not have been identified during the initial search for inclusion.

Steering Committee

The Steering Committee (SC) will consist of 21 experts in respiratory medicine, primary care and cardiology. Members of the SC will be identified by the Executive Committee and formally invited to participate. The SC will be international and conduct the first round of the modified Delphi process.

Following the creation of an initial list of proposed data variables, these will be provided to the SC. The SC will then vote "yes" or "no" as to whether a variable should be included or not. This will be done by an anonymous online survey.[16] If a variable meets the specified thresholds, it will be included in the final list to be sent to the International

Figure 1 Study flow diagram to create multimorbidity standards for COPD.

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Consensus Group. There will be an opportunity to provide written comments, discuss at online meetings, with feedback consolidated and fed back to the SC for ratification. The SC will have the ability to propose and deselect candidate clinical study variables.

International Consensus Group

The International Consensus Group (ICG) will be formed by chain invitation and selected from members of ICRA. Chain invitation denotes the extension of the survey outside of ICRA to potentially interested clinical staff or patients, who must volunteer to participate. To ensure that the clinical study variables are aligned with COPD, we will ensure representation from primary care, allied health care professionals, patients and other medical specialties. We will aim for at least 60–80 voting members because this is the minimum sample size that has been shown to determine consensus in a multidisciplinary group for the modified Delphi process.[17]

Step 2: Literature Review and Formulation of an Initial List of Candidate Clinical Study Variables

A systematic review of the literature will be conducted to create a list of candidate clinical study variables. The search strategy will be adapted from previously utilized and published search strategies in other consensus documents, alongside collaboration from research librarians and the Executive Committee. The systematic review will be reported in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 guidelines.[18] We will search MEDLINE and Embase for relevant studies from inception to the most recent practical date. Studies will be included if they are an observational study (retrospective or prospective) or a randomized clinical trial in adult patients with COPD in any clinical setting and any language. We will exclude editorials, research letters, conference proceedings and comments. Systematic reviews will be excluded; however, their references will be searched in subsequent citation searches. All included papers will have forward and backward citations searched and relevant grey literature will also be searched.

From the identified studies, TJ will extract names of variables used. Collectively, this will produce an exhaustive initial list of candidate clinical study variables. Searches, screening and extraction will be conducted by TJ. This will then be corroborated with pre-existing databases to ensure no discrepancies. If the number of results is too large, we will conduct data extraction based on an iterative saturation approach, which has been shown to yield high degree of completeness in an efficient manner.[19]

Clinical study variables are defined as a potential data field that is to be collected. The candidate list of variables will be carefully chosen based ensure that variables may be collected readily. The main intention is to focus on variables that capture the patient's symptoms and clinical manifestations, investigations, treatment and outcomes in both the clinical and research setting.[2]

Step 3: Developing Executive Committee Consensus on Candidate List of Clinical Study Variables

During online meetings and by Email correspondence, the Executive Committee will review the list of candidate clinical study variables extracted from the systematic review. This list is likely to include duplicate variables or variables with ambiguous definitions that need refinement. Through extensive correspondence, CPG, MB and DP from the Executive Committee will vote to "include" or "do not include" the clinical study variables in the candidate list. This will ensure that a unique and manageable list of candidate clinical study variables is presented to the Steering Committee. Excluded variables will require two-thirds majority to be excluded and will remain on an "excluded list" to be sent to the Steering Committee for ratification and, if necessary, re-inclusion in the candidate list of clinical study variables.

Step 4: Developing Steering Committee Consensus on Candidate List of Clinical Study Variables and Their Definitions

The Steering Committee will be asked to complete an anonymous online survey with "include" or "do not include" for each candidate clinical study variable. Members of the Steering Committee will also be asked to propose new clinical

study variables they feel are missing. Responses will be collated and discussed with the Executive Committee, and if necessary, undergo a subsequent voting round with the revised list of candidate clinical study variables by the Steering Committee. The Steering Committee will review the variables excluded by the Executive Committee to ensure agreement, and if the Steering Committee disagree (quantified as >25%) with any of the exclusions, the variables will be re-added and voted on in a subsequent Delphi round. This is to ensure that the clinical study variables are representative of COPD globally and to allow additional candidate clinical study variables to be added should they not have been captured and/or extracted from the literature previously.

Following the creation of the initial list of proposed data variables, TJ will provide suggested definitions for each variable. The Steering Committee will then be divided into groups to ratify or amend the suggested definitions. These will then be fed back to the full Steering Committee and ratified before variables and their definitions are circulated to the International Consensus Group for the second round of the modified Delphi process. During the definitions stage, the Steering Committee will also provide proposed settings (general community care, specialist ambulatory care, inpatient care, all) for included variables, which will also be ratified during the second round of the modified Delphi process. This provides hierarchical classification to ensure that minimum datasets are collected in each specific context eg clinical specialist, research specialist, primary care.

Once the Steering Committee has agreed upon the final list of candidate clinical study variables and their definitions, the International Consensus Group will be invited to participate in the final stage of clinical study variables selection. Here, they will first be asked to "include" or "do not include" for each variable, "agree" or "disagree" for the definition and "agree" or "disagree" for the proposed settings. Consensus will be achieved using the above-mentioned thresholds, with strong agreement being defined as 90%. There will also be the opportunity to raise questions about the proposed variable name or definition, and further clarification can be given. If during the second round of Delphi there are significant concerns raised about variables, this will then be taken to the Executive Committee for a decision, before seeking ratification with the Steering Committee.

The Executive Committee will set the definition of consensus to be used during the modified Delphi process. This will initially be 60% agreement for the SC, due to smaller numbers of participating respondents and to allow greater variance in opinions, with a minimum response rate of 75%. For the wider modified Delphi process involving the ICG, consensus will be achieved at 75% (with strong agreement at 90%) with a minimum of 60 respondents.[17]

When including patient perspective in the consensus, we will be directed by their preferred level of involvement. We will invite them to review the final set of variables and ask for suggestions to be discussed. If they wish to participate in the modified Delphi process, their votes will also be included and reported separately to assess whether the proposed variables are aligned with the patient perspective.

Step 5: Developing Consensus of the Final List of Clinical Study Variables

The list of clinical study variables will be reviewed by the Executive Committee, whereby changes could be implemented if required, and with further voting by the Groups. Any potentially revised list of clinical study variables will then be reviewed by the Executive Committee and when consensus is achieved, they will be reported in line with the ACCORD statement.[15]

During the consensus building process, we will consider potential conflicts of interest for those completing the modified Delphi process in accordance with the ACCORD statement.[15] This will be managed in part by extending the survey to a large number of individuals in a range of contexts to ensure global validity. Additionally, all participants will be weighted equally. Variables that are at equipoise for inclusion will be re-discussed amongst the Executive Committee and if necessary, the Steering Committee.

Discussion

With this protocol paper, we set out the methodology that we will follow to create an internationally agreed suite of clinical study variables for multimorbidity and those at high risk of multimorbidity in COPD. We will employ the modified Delphi method to ensure international consensus. We anticipate the resultant suite of clinical study variables for multimorbidity and those at high risk of multimorbidity in COPD will inform the design of future studies as well as

quality improvement initiatives for patients with COPD. This is work that will close a scientific gap identified for cardiopulmonary risk in COPD and the management of multimorbidity in COPD.[8,10,12]

CONQUEST identified essential domains to ensure quality improvement in the care of patients with modifiable high-risk COPD.[6] TORPEDO and the COPD exacerbation outcome sets demonstrated feasibility of creating suggested study variables for respiratory diseases, with suggestions for specific variables in certain contexts.[1,5] This current work will build on these prior data sets to ensure international generalizability and identify the list of variables for common clinical contexts for these patients and will encompass the higher rates of multimorbidity and its impact on COPD management.

Because of the variability in outcome reporting, creating a suite of standardized variables, with associated definitions, will enhance replicable and comparable event reporting in studies. This is important because there is a wide variation in COPD morbidity, mortality and its management, which can significantly affect morbidity and prognosis.[20] When compounded with differences in outcome reporting, the translation of findings to practice, and generalizability across international contexts is undermined. With the implementation of our proposed variables, we can embed collaboration and standardization across all contexts to improve care and research quality for patients with COPD. Crucially, this will enable more direct comparison of results and potential linkage of several registries and databases to facilitate even more impactful results. This could translate to more robust conclusions being drawn when studies are conducted with improved generalizability – and thus impact future guideline recommendations and their strength and completeness.

This protocol, and the modified Delphi process, has strengths. Firstly, we will seek international expertise to ensure that the suite of variables produced has external validity and is relevant across all contexts healthcare providers encountering a patient with COPD. Secondly, our sample size is based on prior research to ensure replicability and consistency in the consensus reached.[17] We will undertake a systematic review of the literature to generate our initial list of variables; this will ensure that the initial list is broad, measurable and grounded in scientific literature. We believe that the proposed methodology is transparent and demonstrates a structured approach to derivation and definition of a suite of clinical study variables.

We acknowledge the potential limitations of our approach. The selection of variables by the Executive Committee may be prone to biases, subjectivities and conflicts of interest. We have tried to address these by ensuring a systematic search of the literature is used to determine the initial list of potential clinical study variables and have ensured options for participating members to suggest variables that may have been omitted. Additionally, in borderline cases for inclusion, Executive Committee decisions to proceed from the Steering Committee round will be clearly highlighted to those participating in the International Consensus Group stage. We will also ensure that each voting participant will be weighted equally, intending to reduce the risks of biases by individual voting members.

The proposed suite is also susceptible to becoming outdated and may require iterative improvements or refinements to ensure its ongoing relevance to patients with COPD; it is possible that the inaugural list of variables could serve as a living document and have updates – which could be performed by updated Delphi consensus exercises after the proposed variables have been implemented and will help ensure they are contemporaneous. Additionally, the consensus could produce a large body of study variables.We aim to mitigate this by also proposing the clinical or academic setting in which the variable is expected to be – and so clinicians can select the most appropriate variables to collect for the specific context. In this protocol, we set out our method for the derivation and definitions of clinical study variables for patients with prevalent multimorbidity or at high risk of multimorbidity in COPD. Such a suite of internationally agreed, context classified clinical study variables could be used for quality improvement initiatives and research including COPD registries and prospective studies. We anticipate that the adoption of standardized variables for patients with multimorbidity or at high risk of multimorbidity in COPD will improve clinical event reporting and make clinical studies more robust and applicable to patients with COPD.

Abbreviations

COPD, Chronic Obstructive Pulmonary Disease; CONQUEST, COllaboratioN on Quality improvement initiative for achieving Excellence in STandards of COPD care ; CVD, Cardiovascular Disease; TORPEDO, Towards Optimum Reporting of Pulmonary Effectiveness Databases and Outcomes.

Ethical Considerations

Ethical approval was not required for this study.

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Author Contributions

The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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References

1. Mathioudakis AG, Abroug F, Agusti A, et al. ERS statement: a core outcome set for clinical trials evaluating the management of COPD exacerbations. *Eur Respir J*. 2022;59(5):2102006. doi:10.1183/13993003.02006-2021
2. Batra G, Aktaa S, Wallentin L, et al. Methodology for the development of international clinical data standards for common cardiovascular conditions: european Unified Registries for Heart Care Evaluation and Randomised Trials (EuroHeart). *Eur Heart J Qual Care Clin Outcomes*. 2023;9(2):161–168. doi:10.1093/ehjqcco/qcab052
3. Alkraiji A, Jackson T, Murray I. Barriers to the widespread adoption of health data standards: an exploratory qualitative study in tertiary healthcare organizations in Saudi Arabia. *J Med Syst*. 2013;37(2):9895. doi:10.1007/s10916-012-9895-2
4. Ramakrishnan S, Janssens W, Burgel PR, et al. Standardisation of Clinical Assessment, Management and Follow-Up of Acute Hospitalised Exacerbation of COPD: a Europe-Wide Consensus. *Int J Chron Obstruct Pulmon Dis*. 2021;16:321–332. doi:10.2147/COPD.S287705
5. van Boven JF, Lucas SJ, Parker G, et al. Towards Optimum Reporting of Pulmonary Effectiveness Databases and Outcomes (TORPEDO): identifying a core dataset for asthma and COPD studies. *medRxiv*. 2021;2021:1.
6. Pullen R, Miravitlles M, Sharma A, et al. CONQUEST Quality Standards: for the Collaboration on Quality Improvement Initiative for Achieving Excellence in Standards of COPD Care. *Int J Chron Obstruct Pulmon Dis*. 2021;16:2301–2322. doi:10.2147/COPD.S313498
7. Skou ST, Mair FS, Fortin M, et al. Multimorbidity. *Nat Rev Dis Primers*. 2022;8(1):48. doi:10.1038/s41572-022-00376-4
8. Fabbri LM, Celli BR, Agusti A, et al. COPD and multimorbidity: recognising and addressing a syndemic occurrence. *Lancet Respir Med*. 2023;11 (11):1020–1034. doi:10.1016/S2213-2600(23)00261-8
9. Gale CP, Berg DD, Bhutani M. The Global Working Group on Cardiopulmonary Risk in chronic obstructive pulmonary disease. *Eur Heart J*. 2024;45(44):4676–4678. doi:10.1093/eurheartj/ehae628
10. Gale CP, Hurst JR, Hawkins NM, et al. Identification and management of cardiopulmonary risk in patients with COPD: a multidisciplinary consensus and modified Delphi study. *Eur J Prev Cardiol*. 2025;32(15):1445–1460. doi:10.1093/eurjpc/zwaf119
11. Amegadzie JE, Gao Z, Quint JK, et al. QRISK3 underestimates the risk of cardiovascular events in patients with COPD. *Thorax*. 2024;79 (8):718–724. doi:10.1136/thorax-2023-220615
12. Hurst JR, Gale CP, Hurst JR, Global Working Group on Cardiopulmonary R. MACE in COPD: addressing cardiopulmonary risk. *Lancet Respir Med*. 2024;12(5):345–348. doi:10.1016/S2213-2600(24)00038-9
13. Ndumele CE, Rangaswami J, Chow SL, et al. Cardiovascular-Kidney-Metabolic Health: a Presidential Advisory From the American Heart Association. *Circulation*. 2023;148(20):1606–1635. doi:10.1161/CIR.0000000000001184
14. Moher D, Schulz KF, Simera I, Altman DG. Guidance for developers of health research reporting guidelines. *PLoS Med*. 2010;7(2):e1000217. doi:10.1371/journal.pmed.1000217
15. Gattrell WT, Logullo P, van Zuuren EJ, et al. ACCORD (ACcurate COnsensus Reporting Document): a reporting guideline for consensus methods in biomedicine developed via a modified Delphi. *PLoS Med*. 2024;21(1):e1004326. doi:10.1371/journal.pmed.1004326
16. Diamond IR, Grant RC, Feldman BM, et al. Defining consensus: a systematic review recommends methodologic criteria for reporting of Delphi studies. *J Clin Epidemiol*. 2014;67(4):401–409. doi:10.1016/j.jclinepi.2013.12.002
17. Manyara AM, Purvis A, Ciani O, Collins GS, Taylor RS. Sample size in multistakeholder Delphi surveys: at what minimum sample size do replicability of results stabilize? *J Clin Epidemiol*. 2024;174:111485. doi:10.1016/j.jclinepi.2024.111485
18. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372: n71. doi:10.1136/bmj.n71
19. Veen KM, Joseph A, Sossi F, et al. Standardized approach to extract candidate outcomes from literature for a standard outcome set: a case- and simulation study. *BMC Med Res Methodol*. 2023;23(1):261. doi:10.1186/s12874-023-02052-x
20. Stolz D, Mkorombindo T, Schumann DM, et al. Towards the elimination of chronic obstructive pulmonary disease: a Lancet Commission. *Lancet*. 2022;400(10356):921–972. doi:10.1016/S0140-6736(22)01273-9