

Research Protocol

Title: Characterization of Outcomes in Patients with Chronic Obstructive Pulmonary Disease (COPD) visiting the Emergency Department

Research Question:

Among adults ≥ 40 years presenting to the emergency department with acute exacerbation of COPD, how do acute management patterns and care pathways differ between Johns Hopkins Hospital and Albert Einstein Hospital (Brazil), and how are these patterns associated with

- (1) admission from the index ED visit and
- (2) 30-day hospital readmission after adjusting for patient characteristics (including age and comorbidity burden)?

1. List of abbreviations

AECOPD: Acute Exacerbations of Chronic Obstructive Pulmonary Disease

COPD: Chronic Obstructive Pulmonary Disease

ED: Emergency Department

2. Abstract

Background: COPD remains one of the most common pulmonary conditions in adults that can lead to hospitalization and numerous high-cost, even invasive interventions such as mechanical ventilation.

Purpose: To characterize treatment patterns among COPD patients visiting ED. The outcome of interest includes the need for hospitalization, ED oxygen requirements, in-hospital prescribing patterns (e.g. the need for bronchodilators, systemic steroids), discharge medication prescribing patterns, and the risk for 30-day admission.

Design: Retrospective observational study design.

Subjects: Adults (≥ 40 years) with COPD (or history of COPD for acute dyspnea, increased sputum/ purulence, increased cough, requiring bronchodilator therapy, requiring systemic corticosteroids). The exclusion criteria are cardiopulmonary history, prior surgeries (pulmonary lobectomy, solid organ transplant), history of systemic immunosuppression, and reason for ED visit not COPD exacerbation.

Methods: The treatment and outcome patterns, including need for hospitalization, ED oxygen requirements, in-hospital prescribing patterns, 30-day readmission will be

characterized using descriptive statistics. The patterns will be compared between Johns Hopkins Hospital and Alber Einstein Hospital in Brazil.

Conclusions: Characterizing COPD patient treatment patterns in different institutions is a crucial first step to understand the landscape of the treatment of the disease. The information gathered in this study will serve as evidence for further study in effective intervention.

3. Amendments and Updates

N/A

4. Milestones

Date	Milestone
12/8/2025	Cohort definition and sample size estimation
12/19/2025	Research protocol draft 1

5. Rationale and Background

Chronic obstructive pulmonary disease (COPD) is a highly prevalent chronic respiratory disease worldwide and a major contributor to global morbidity and mortality.[1,2] COPD is characterized by persistent respiratory symptoms and chronic airflow limitation.[3] It also imposes substantial health-system burden through frequent acute-care utilization and hospital-based treatment.[2,4,5] Despite advances in chronic management, acute exacerbations of COPD (AECOPD) commonly prompt emergency department (ED) evaluation and often lead to hospitalization.[4,5] These exacerbations are pivotal events in the disease course and can require high-cost and invasive interventions, including non-invasive ventilation and endotracheal intubation with invasive mechanical ventilation in severe cases.[5–7]

Current clinical guidance (e.g., GOLD) recommends AECOPD management centered on short-acting bronchodilators, systemic corticosteroids, and appropriately titrated oxygen therapy.[3] Randomized trials support systemic corticosteroids for hospitalized AECOPD and inform duration strategies (e.g., shorter courses in selected patients).[8,9] Oxygen strategy matters: controlled/titrated oxygen has been associated with improved outcomes compared with high-flow oxygen in prehospital care, and inpatient oxygen saturation patterns have been linked to mortality differences during AECOPD admissions.[10,11] However, despite these standards, real-world treatment patterns and prescribing practices vary across hospitals and healthcare systems, including adherence to guideline-recommended care during exacerbation admissions and ED management decisions.[12,13] Variation is also observed in escalation practices (e.g., use of non-invasive vs invasive ventilation) across hospitals.[6,14] Discharge prescribing and acute pharmacotherapy appropriateness may influence downstream utilization and readmission risk, and early readmissions after AECOPD hospitalization remain common.[15,16]

Understanding the landscape of AECOPD treatment, such as acute medication use, oxygen requirements, escalation of respiratory support, and discharge management, can identify disparities and opportunities for quality improvement.[12,14,15] Multi-institution comparisons have been used to highlight variation in care processes and outcomes and can serve as a foundation for designing effective interventions and future predictive or population-level analyses.[12,14,15]

6. Study Objectives

- Primary Hypotheses
 - Among adults aged 40 years or older with a documented condition occurrence of COPD, increasing patient age is associated with a higher likelihood of emergency department utilization resulting in hospital admission and increased risk of 30-day readmission.
 - The temporal clinical pathways for patients with COPD exacerbations, including escalation of respiratory support, ICU transfer, and discharge conditions, differ from a major academic hospital in the United States and a private non-profit multi-specialty hospital in Brazil.
- Secondary Hypotheses
 - Patterns of acute management and discharge prescribing vary across patient subgroups.
 - Institutional site is associated with differences in short term outcomes after adjustment for patient characteristics.
- Primary Objectives
 - To characterize the demographic and clinical features of adults presenting to the emergency department with COPD exacerbation.
 - To describe temporal care pathways following ED presentation for COPD exacerbation, including escalation of respiratory support, ICU transfer, discharge disposition, and 30-day readmission.
 - To compare care pathways and outcomes between a major academic hospital in the United States and a private non-profit multi-specialty hospital in Brazil.
- Secondary Objectives
 - To explore associations between patient characteristics and escalation of care or adverse short-term (<30d) outcomes.
 - To assess the consistency of COPD phenotype definitions within a standardized data model framework.
 - To generate hypotheses for future predictive and population level analyses.

7. Research methods

- Study Design
 - Retrospective observational cohort study.
- Data Source(s)

- Electronic health record data from two health systems, harmonized within a common data model.
- Study population
 - *Inclusion Criteria:* Adults aged 40 years or older presenting to the emergency department with a diagnosis of COPD or history of COPD and symptoms consistent with acute exacerbation, including dyspnea, increased cough, or sputum production, or requiring bronchodilator therapy or systemic corticosteroids.
 - *Exclusion Criteria:* Patients with cardiopulmonary history (pulmonary embolism, non-COPD chronic pulmonary conditions MDF immunosuppressant), prior surgeries (pulmonary lobectomy, solid organ transplant), patients on systemic immunosuppression, patients with active malignancy, or patients coming to ED not for COPDs.
- Exposures
 - Primary exposure is patient age at the time of cohort entry defined by COPD condition occurrence and institutional site.
- Outcomes
 - Primary outcome is hospital escalation of care or discharge from the index emergency department visit.
 - Secondary outcomes include escalation of respiratory support, time-to-discharge, time-to-ICU transfer, discharge disposition (discharged to home vs rehab), discharge medications, and 30-day hospital readmission.
- Covariates
 - Demographic variables (age, gender), baseline comorbidity burden (using Charlson and Elixhauser scores), and markers of disease severity (SpO₂ [baseline and on presentation], blood gas measurements [baseline and on presentation], and performance on pulmonary function tests at presentation) will be included as covariates.

8. Data Analysis Plan

TODO

9. Study Diagnostics

TODO

10. Strengths and Limitations of the Research Methods

TODO

11. Protection of Human Subjects

TODO

12. Management and Reporting of Adverse Events and Adverse Reactions

TODO

13. Plans for Disseminating and Communicating Study Results

TODO

14. Appendix: Negative controls

TODO

15. References

1. Adeloye D, Song P, Zhu Y, Campbell H, Sheikh A, Rudan I; NIHR RESPIRE Global Respiratory Health Unit. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. *Lancet Respir Med.* 2022 May;10(5):447-458. doi: 10.1016/S2213-2600(21)00511-7. Epub 2022 Mar 10. PMID: 35279265; PMCID: PMC9050565.
2. GBD Chronic Respiratory Disease Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Respir Med.* 2020 Jun;8(6):585-596. doi: 10.1016/S2213-2600(20)30105-3. PMID: 32526187; PMCID: PMC7284317.
3. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, Bourbeau J, Han MK, Martínez FJ, Montes de Oca M, Mortimer K, Papi A, Pavord I, Roche N, Salvi S, Sin DD, Singh D, Stockley R, López Varela MV, Wedzicha JA, Vogelmeier CF. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. *Eur Respir J.* 2023 Apr 1;61(4):2300239. doi: 10.1183/13993003.00239-2023. PMID: 36858443; PMCID: PMC10066569.
4. Liew CQ, Hsu SH, Ko CH, Chou EH, Herrala J, Lu TC, Wang CH, Huang CH, Tsai CL. Acute exacerbation of chronic obstructive pulmonary disease in United States emergency departments, 2010-2018. *BMC Pulm Med.* 2023 Jun 20;23(1):217. doi: 10.1186/s12890-023-02518-0. PMID: 37340379; PMCID: PMC10283236.
5. Perera PN, Armstrong EP, Sherrill DL, Skrepnek GH. Acute exacerbations of COPD in the United States: inpatient burden and predictors of costs and mortality. *COPD.* 2012 Apr;9(2):131-41. doi: 10.3109/15412555.2011.650239. Epub 2012 Mar 12. PMID: 22409371.
6. Lindenauer PK, Stefan MS, Shieh MS, Pekow PS, Rothberg MB, Hill NS. Outcomes associated with invasive and noninvasive ventilation among patients hospitalized with exacerbations of chronic obstructive pulmonary disease. *JAMA Intern Med.* 2014

- Dec;174(12):1982-93. doi: 10.1001/jamainternmed.2014.5430. PMID: 25347545; PMCID: PMC4501470.
7. Stefan MS, Shieh MS, Pekow PS, Hill N, Rothberg MB, Lindenauer PK. Trends in mechanical ventilation among patients hospitalized with acute exacerbations of COPD in the United States, 2001 to 2011. *Chest*. 2015 Apr;147(4):959-968. doi: 10.1378/chest.14-1216. PMID: 25375230; PMCID: PMC4388126.
 8. Niewoehner DE, Erbland ML, Deupree RH, Collins D, Gross NJ, Light RW, Anderson P, Morgan NA. Effect of systemic glucocorticoids on exacerbations of chronic obstructive pulmonary disease. Department of Veterans Affairs Cooperative Study Group. *N Engl J Med*. 1999 Jun 24;340(25):1941-7. doi: 10.1056/NEJM199906243402502. PMID: 10379017.
 9. Leuppi JD, Schuetz P, Bingisser R, Bodmer M, Briel M, Drescher T, Duerring U, Henzen C, Leibbrandt Y, Maier S, Miedinger D, Müller B, Scherr A, Schindler C, Stoeckli R, Viatte S, von Garnier C, Tamm M, Rutishauser J. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. *JAMA*. 2013 Jun 5;309(21):2223-31. doi: 10.1001/jama.2013.5023. PMID: 23695200.
 10. Austin MA, Wills KE, Blizzard L, Walters EH, Wood-Baker R. Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomised controlled trial. *BMJ*. 2010 Oct 18;341:c5462. doi: 10.1136/bmj.c5462. PMID: 20959284; PMCID: PMC2957540.
 11. Echevarria C, Steer J, Wason J, Bourke S. Oxygen therapy and inpatient mortality in COPD exacerbation. *Emerg Med J*. 2021 Mar;38(3):170-177. doi: 10.1136/emermed-2019-209257. Epub 2020 Nov 26. PMID: 33243839.
 12. Roberts CM, Lopez-Campos JL, Pozo-Rodriguez F, Hartl S; European COPD Audit team. European hospital adherence to GOLD recommendations for chronic obstructive pulmonary disease (COPD) exacerbation admissions. *Thorax*. 2013 Dec;68(12):1169-71. doi: 10.1136/thoraxjnl-2013-203465. Epub 2013 Jun 1. PMID: 23729193.
 13. Freund O, Melloul A, Fried S, Kleinhendler E, Unterman A, Gershman E, Elis A, Bar-Shai A. Management of acute exacerbations of COPD in the emergency department and its associations with clinical variables. *Intern Emerg Med*. 2024 Nov;19(8):2241-2248. doi: 10.1007/s11739-024-03592-w. Epub 2024 Apr 11. PMID: 38602629; PMCID: PMC11582298.
 14. Lindenauer PK, Stefan MS, Shieh MS, Pekow PS, Rothberg MB, Hill NS. Hospital patterns of mechanical ventilation for patients with exacerbations of COPD. *Ann Am Thorac Soc*. 2015 Mar;12(3):402-9. doi: 10.1513/AnnalsATS.201407-293OC. PMID: 25654431; PMCID: PMC4418316.
 15. Jacobs DM, Noyes K, Zhao J, Gibson W, Murphy TF, Sethi S, Ochs-Balcom HM. Early Hospital Readmissions after an Acute Exacerbation of Chronic Obstructive Pulmonary Disease in the Nationwide Readmissions Database. *Ann Am Thorac Soc*. 2018 Jul;15(7):837-845. doi: 10.1513/AnnalsATS.201712-913OC. PMID: 29611719; PMCID: PMC6207114.
 16. Tran M, Xiang P, Rascati KL, Stock EM, Godley PJ, Coleman A, Bogart MR, Stanford RH. Predictors of Appropriate Pharmacotherapy Management of COPD Exacerbations and Impact on 6-Month Readmission. *J Manag Care Spec Pharm*. 2016 Oct;22(10):1186-93. doi: 10.18553/jmcp.2016.22.10.1186. PMID: 27668567; PMCID: PMC10397871.

