Enhancing COPD Outcomes: Early Intervention, Outcome Measures, and the Power of Exacerbation Diaries

Lauren Crooks, MSc & Elias Ketiar, MD, MRCP

Chronic Obstructive Pulmonary Disease (COPD) is a major global health issue, ranking as the 3rd leading cause of death worldwide. It primarily affects older adults and is characterized by symptoms like cough, dyspnea, wheezing, and increased sputum production.[1] Exacerbations, which are sudden and sustained worsens in these symptoms, are a significant concern as they can lead to rapid declines in lung function, increased hospitalizations, and even be life-threatening.

Defining COPD exacerbations: Challenges and the 'Rome proposal' consensus

COPD exacerbations are heterogeneous in nature, caused by bacterial infection, respiratory viruses, environmental pollutants or other underlying health conditions - clinical manifestations of exacerbations may therefore be difficult to define.[2] The search for a robust and universally accepted definition of COPD exacerbations is ongoing, where clinical studies currently implement a variety of definitions and, based on which definition is used, can impact the accuracy of the recorded incidence of exacerbations amongst patients.

In the recent "Rome proposal," a consensus on an updated definition was reached, defining an exacerbation as *"an event characterized by dyspnea and/or cough and sputum that worsen over ≤14 days, which may be accompanied by tachypnea and/or tachycardia and is often associated with increased local and systemic inflammation caused by airway infection, pollution, or other insult to the airways."*[3]

Importance of early detection of COPD exacerbations

Efforts such as the "Rome proposal" aim to continually refine the definition of exacerbations and emphasize the importance of accurate and identification and intervention of exacerbation events, where early and effective detection is crucial for

several reasons:

1. **Preventing severe health deterioration:** Timely treatment can prevent severe exacerbations and complications like respiratory failure.
2. **Reducing hospital admissions:** Early intervention can often be managed at home, reducing hospital stays.
3. **Improving quality of life:** Prompt management reduces the severity and duration of symptoms.
4. **Reducing healthcare costs:** Preventing severe exacerbations can decrease the economic burden of COPD management.

Outcome measures used in the detection of COPD exacerbations

Due to the complexity of COPD, physiological outcome measures alone may not accurately reflect the impact of exacerbations on quality of life, and therefore the effectiveness of the therapeutics being investigated.[4] To provide a comprehensive assessment of COPD exacerbations, clinicians should aim to apply a combination of measures including spirometry, patient-reported outcome measures, and clinical assessments.

- **Lung function:** Decline in lung function is a hallmark of exacerbations and COPD progression. Standardized spirometry measures[5], such as the fixed ratio of forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) are commonly implemented to objectively determine exacerbation severity. In addition, daily monitoring of peak expiratory flow (PEF) can help detect early signs of exacerbations.
- **Daily activity measures:** Reduction in daily activity is an important predictor of COPD outcome and is associated with a higher risk of exacerbation.6 Daily activity can be measured using performance outcomes (PerfOs), such as the 6-Minute Walk Test (6-MWT) or can be quantified daily with accelerometry-based electronic devices, such as actigraphy wristwatches.
- **Dyspnea:** Dyspnea, or breathlessness, is one of the most common indicators of COPD exacerbations. The experience of dyspnea is subjective, making it challenging to assess objectively. As a result, outcome measures evaluating dyspnea rather assess impact on quality of life and daily activity. These outcome measures include the Baseline and Transition Dyspnea Indices (BDI/TDI), Medical Research Council Dyspnea Scale (MRC Dyspnea Scale), as well as the Borg Dyspnea Scale.[7]

- **Health-related quality of life:** Exacerbations are associated with poor health-related quality of life in COPD patients. Patient-reported outcomes (PROs), such as the Exacerbation of Chronic Pulmonary Disease Tool (EXACT) are useful in determining the impact of COPD exacerbations on a patient's perceived health status.[8]
- **Cough monitoring:** Increased cough is commonly seen as a reliable early predictor of COPD exacerbations. Although subjective measures, such as the cough severity visual analog scale (VAS) are valuable tools in assessing the impact of cough on patients, objective measurement via digital health tools can allow for quantification of cough frequency.[9]
- **Exacerbation diaries:** COPD exacerbations are associated with impaired quality of life and are a significant cause of mortality in patients with COPD. Exacerbation diaries can provide detailed patient-reported data on the frequency, duration, severity, and impact of exacerbations, facilitating detection of changes in symptoms and the timely treatment of exacerbation events.[10]

The role of exacerbation diaries in COPD management

Exacerbation diaries are increasingly valuable for monitoring symptoms and assessing disease impact. They allow for accurate tracking of exacerbation duration, frequency, and periods free from exacerbations. In addition, exacerbation diaries can aid determining exacerbation-free time, which may better reflect the burden of exacerbations in patients than exacerbation duration and frequency alone, where longer periods free from exacerbation indicate better disease stability and control.[11]

Exacerbation diaries can also reveal patterns and potential triggers of exacerbation events even if the patient does not explicitly report it[12], leading to earlier recognition of impeding exacerbations and prompt intervention.

Integrating patient exacerbation e-diaries into COPD clinical trials

Although not mandatory, electronic patient diaries, or e-diaries, are being increasingly used to reduce data entry errors associated with traditional paper-based diaries and improve compliance, as well as to support patients in self-management of their disease.[13]

Important considerations when integrating patient e-diaries into COPD clinical trials include:

1. **Ease of use:** It is essential to design the e-diary interface to be user-friendly, with straightforward navigation and clear instructions to accommodate patients of all ages and technological skill levels. This is particularly crucial in COPD, where older patients may have difficulty or anxiety using new technology.
2. **Reminders and alerts:** Integrating automatic reminders and alerts encourages patients to complete their e-diary entries, enhancing compliance and enabling timely identification of exacerbation events.
3. **Training and support:** Proper training on the device is necessary to address uncertainty and unfamiliarity with using new technology, providing sufficient support and guidance for older COPD patients.[14]

At Signant Health, our in-house team of scientists and medical experts understand these challenges. Our extensive experience with e-diary design and implementation allow our scientific team to provide expert guidance in developing best practice solutions, offering tailored recommendations and comprehensive support throughout COPD trials.

Conclusion

COPD exacerbations pose a significant challenge, but a multifaceted approach to detection and management can substantially improve patient outcomes.

As technology advances, the role of electronic diaries in both clinical trials and everyday management becomes increasingly valuable, offering a more comprehensive and patient-centered approach to managing this complex disease.

If you want to learn more about how Signant Health is working to improve patient outcomes in COPD clinical trials, contact our team today.

Authors

Lauren Crooks, MSc has comprehensive cross-functional experience within the life sciences and information technology sectors. At Signant, she combines this experience to provide scientific consultation and support to clients on the implementation of eCOA to optimize patient care and outcomes in clinical trials. She has supported eCOA projects across multiple therapeutic areas, including dermatology and neurology, with a current focus on respiratory diseases.

Elias Ketiar, MD, MRCP, serves as the Clinical Vice President, Science & Medicine, at Signant Health. Dr. Ketiar draws on his wealth of more than 20 years of academic and

clinical experience to advise on clinical trial design, execution, and governance.

He has extensive experience in General Internal Medicine and Cardiology and is a Member of Royal College of Physicians (London), UK. Dr Ketiar has been engaged in academic research and was involved in a pioneering project investigating genetic causes of congenital heart disease, which culminated in a Medical Doctorate with St George's University of London, UK.

References

1. Adeloye, D., Chua, S., Lee, C., Basquill, C., Papana, A., Theodoratou, E., Nair, H., Gasevic, D., Sridhar, D., Campbell, H., Chan, K.Y., Sheikh, A., & Rudan, I. (2015). Global and regional estimates of COPD prevalence: Systematic review and meta-analysis. Journal of Global Health, 5(2), 020415.

2. Sapey, E., & Stockley, R.A. (2006). COPD exacerbations · 2: Aetiology. Thorax, 61(3), 250-258.

3. Celli, B.R., Fabbri, L.M., Aaron, S.D., Agusti, A., Brook, R., Criner, G.J., Franssen, F.M.E., Humbert, M., Hurst, J.R., O'Donnell, D., Pantoni, L., Papi, A., Rodriguez-Roisin, R., Sethi, S., Torres, A., Vogelmeier, C.F., & Wedzicha, J.A. (2021). An updated definition and severity classification of chronic obstructive pulmonary disease exacerbations: The Rome proposal. American Journal of Respiratory and Critical Care Medicine, 204(11), 1251-1258.

4. Jones, P.W., & Agusti, A.G.N. (2006). Outcomes and markers in the assessment of chronic obstructive pulmonary disease. European Respiratory Journal, 27(822-832).

5. Miller, M.R., Hankinson, J., Brusasco, V., Casaburi, R., Coates, A., Crapo, R., Enright, P., van der Grinten, C.P.M., Gustafsson, P., Jensen, R., Johnson, D.C., MacIntyre, N., McKay, R., Navajas, D., Pederson, O.F., Pellegrino, R., Viegi, G., & Wagner, J. (2005). Standardisation of spirometry. European Respiratory Journal, 26(2), 319-338.

6. Shin, K.C. (2018). Physical activity in chronic obstructive pulmonary disease: clinical impact and risk factors. Korean Journal of Internal Medicine, 33(1), 75-77.

7. Rabe, K.F., Hurd, S., Anzueto, A., Barnes, P.J., Buist, S.A., Calverley, P., Fukuchi, Y., Jenkins, C., Rodriguez-Roisin, R., van Weel, C., & Zielinski, J. (2007). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. American Journal of Respiratory and Critical Care Medicine, 176(6), 532-555.

8. Mackay, A.J, Kostikas, K., Murray, L., Martinez, F., Miravitlles, M., Donaldson, G., Banjeri, D., Patalano, F., & Wedzicha, J.A. (2018). Patient-reported Outcomes for the Detection, Quantification, and Evaluation of Chronic Obstructive Pulmonary Disease Exacerbations. American Journal of Respiratory and Critical Care Medicine, 198(6), 730-738.
9. Hall, J.I., Lozano, M., Estrada-Petrocelli, L., Birring, S., & Turner, R. (2020). The present and future of cough counting tools. Journal of Thoracic Disease, 12(9), 5207-5223.
10. Seemungal, T.A., Donaldson, G.C., Paul, E.A., Bestall, J.C., Jeffries, D.J., & Wedzicha, J.A. (1998). Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. American Journal of Respiratory and Critical Care Medicine, 157, 1418-1422.
11. Calverley, P.M.A., Papi, A., Page, C., Rogliani, P., Dal Negro, R.W., Cazzola, M., Cicero, A.F., & Wedzicha, J.A. (2022). The Effect of Maintenance Treatment with Erdosteine on Exacerbation Treatment and Health Status in Patients with COPD: A Post-Hoc Analysis of the RESTORE Dataset. International Journal of Chronic Obstructive Pulmonary Disease 17, 1909-1920.
12. Wedzicha, J.A., & Donaldson, G.C. (2003). Exacerbations of chronic obstructive pulmonary disease. Respiratory Care, 48(12), 1204-1213.
13. McCabe, C., McCann, M., & Brady, A.M. (2017). Computer and mobile technology interventions for self-management in chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews, 5(5), CD011425.
14. Garner, K., & Byrom, B. (2020). Attitudes of older people/seniors to completion of electronic patient-reported outcome measures and use of mobile applications in clinical trials: results of a qualitative research study. Journal of Comparative Effectiveness Research, 9(4), 307-315.

Interested in reading more blogs from The Signal?

SUBSCRIBE

WHO IS SIGNANT HEALTH?

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

Signant Health is the evidence generation company. We are focused on leveraging software, deep therapeutic and scientific knowledge, and operational expertise to consistently capture, aggregate, and reveal quality evidence for clinical studies across traditional, virtual, and hybrid trial models. For more than 25 years, over 600 sponsors and CROs of all sizes – including all Top 20 pharma – have trusted Signant solutions for remote and site-based eCOA, EDC, eConsent, RTSM, supply chain management, and data quality analytics. Learn more at **www.signanthealth.com**.