

Clinical Burden of Patients with Moderate-to-Severe Chronic Obstructive Pulmonary Disease: A Focused Literature Review

Ernesto Mayen Herrera¹, Richard H. Stanford², Annete Njue³, Matt Lyall³, Weyinmi Nuabor³, Vijay D'Souza³, Hugo Dubucq⁴, Sandeep Moola⁵

¹Sanofi, Cambridge, MA, USA; ²AESARA Inc., Chapel Hill, NC, USA; ³RTI Health Solutions, Manchester, UK; ⁴Sanofi, Barcelona, Spain; ⁵Sanofi, Hyderabad, India



Copies of this poster obtained through Quick Response (QR) Code are for personal use only

BACKGROUND

- Chronic obstructive pulmonary disease (COPD) is the third leading cause of global death with 3.23 million deaths in 2019.¹ The Global Initiative for Chronic Obstructive Lung Disease (GOLD) classified COPD patients into four categories A to D based on risk and symptoms. In 2023, Groups C and D have been merged into Group E.² The groups are:
 - Group A: low risk, fewer symptoms
 - Group B: low risk, more symptoms
 - Group E: high risk
- GOLD guidelines grade COPD severity using post-bronchodilator forced expiratory volume in one second (FEV₁) once FEV₁/FVC < 0.7 is confirmed.²
- However, studies on clinical burden in patients with type 2 inflammation (high eosinophil levels ≥ 300 cells/μL) is scarce.²

OBJECTIVE

- To conduct a focused literature review (FLR) on the clinical burden of patients with moderate-to-severe COPD.

METHODS

Data sources

- Databases such as Embase, MEDLINE, the Cochrane Library and conference abstracts were searched, as well as key websites, including GOLD and the American College of Chest Physicians. The search covered publications from 2012 to 2022.

Study selection and data extraction

- Studies were selected after the two-level screening process, in accordance with predefined inclusion and exclusion criteria. Study selection is further described in Figure 1.
- The FLR identified studies that reported data on clinical burden in patients with COPD in the United States (US), Europe (France, Germany, Italy, Spain and the United Kingdom [UK]), or China.

RESULTS

- After the two-level screening, a total of 143 articles were included in the report. Of which, 37 articles (5 systematic literature reviews [SLRs], meta-analyses, or large registry studies + 17 other literature reviews + 15 other additional articles) were identified with the clinical burden outcome (Figure 1).

Figure 1. Study selection process flow diagram



*5 SLRs, meta-analyses, or large registry studies + 17 other literature reviews from total 143 articles in the report, and additional 15 articles identified based on inflammation status. CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane Central Register of Controlled Trials; SLR, systematic literature review.

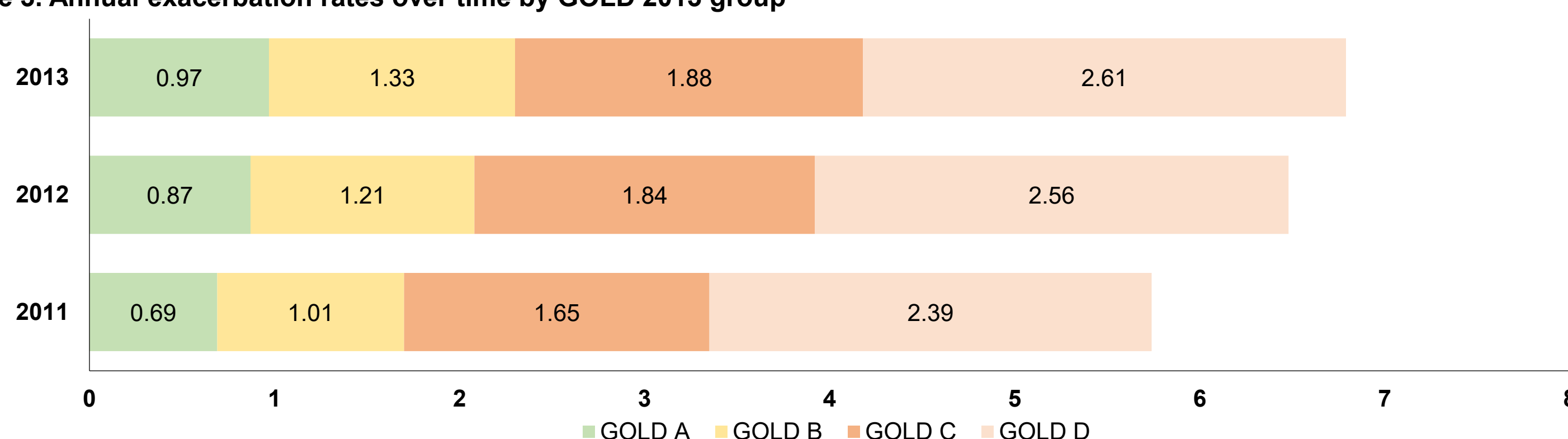
- COPD is associated with substantial burden; more than 80% of patients with COPD experience a range of daily symptoms, including: dyspnoea, cough, sputum production, wheezing, chest tightness, chest congestion, fatigue and pain.^{3,4}
- Patients in GOLD Groups B and D had higher frequency of respiratory symptoms compared with those in Groups A and C.⁵
- A cross-sectional study from Spain reported that patients in GOLD Groups B and D also had worse CAT (COPD Assessment Test) and CASIS (COPD and Asthma Sleep Impact Scale) scores, indicating a greater impact of COPD symptoms on wellbeing and daily life (CAT) and worse sleep quality (CASIS).⁵
- Patients in GOLD Group D experience more exacerbations and have a higher comorbidity burden than patients in GOLD Group A. Data from the UK indicate that GOLD Group D patients experience nearly three times the number of exacerbations compared with those in GOLD Group A.⁶
- Exacerbation rate increased by severity of COPD, ranging from 0.83 exacerbations per person-year in GOLD Group A to 2.51 in GOLD Group D (Figure 2).⁶
- The annual exacerbation rates increased significantly over time from 2011 to 2013 across all GOLD groups (Figure 3).⁶

Figure 2. Exacerbation rates by GOLD 2013 group

| GOLD Group | Exacerbations rate, per person-year (95% CI) | Total person-years at risk | Total no. of exacerbations |
|--------------|----------------------------------------------|----------------------------|----------------------------|
| GOLD A | 0.83 (0.81–0.85) | 31,967.67 | 26,562 |
| GOLD B | 1.17 (1.14–1.19) | 18,437.71 | 21,480 |
| GOLD C | 1.78 (1.74–1.82) | 16,638.72 | 29,666 |
| GOLD D | 2.51 (2.47–2.55) | 23,077.24 | 57,893 |
| All patients | 1.43 (1.42–1.45) | 106,382.69 | 152,403 |

Source: Merinopoulou et al. (2016).⁶
CI, confidence interval; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

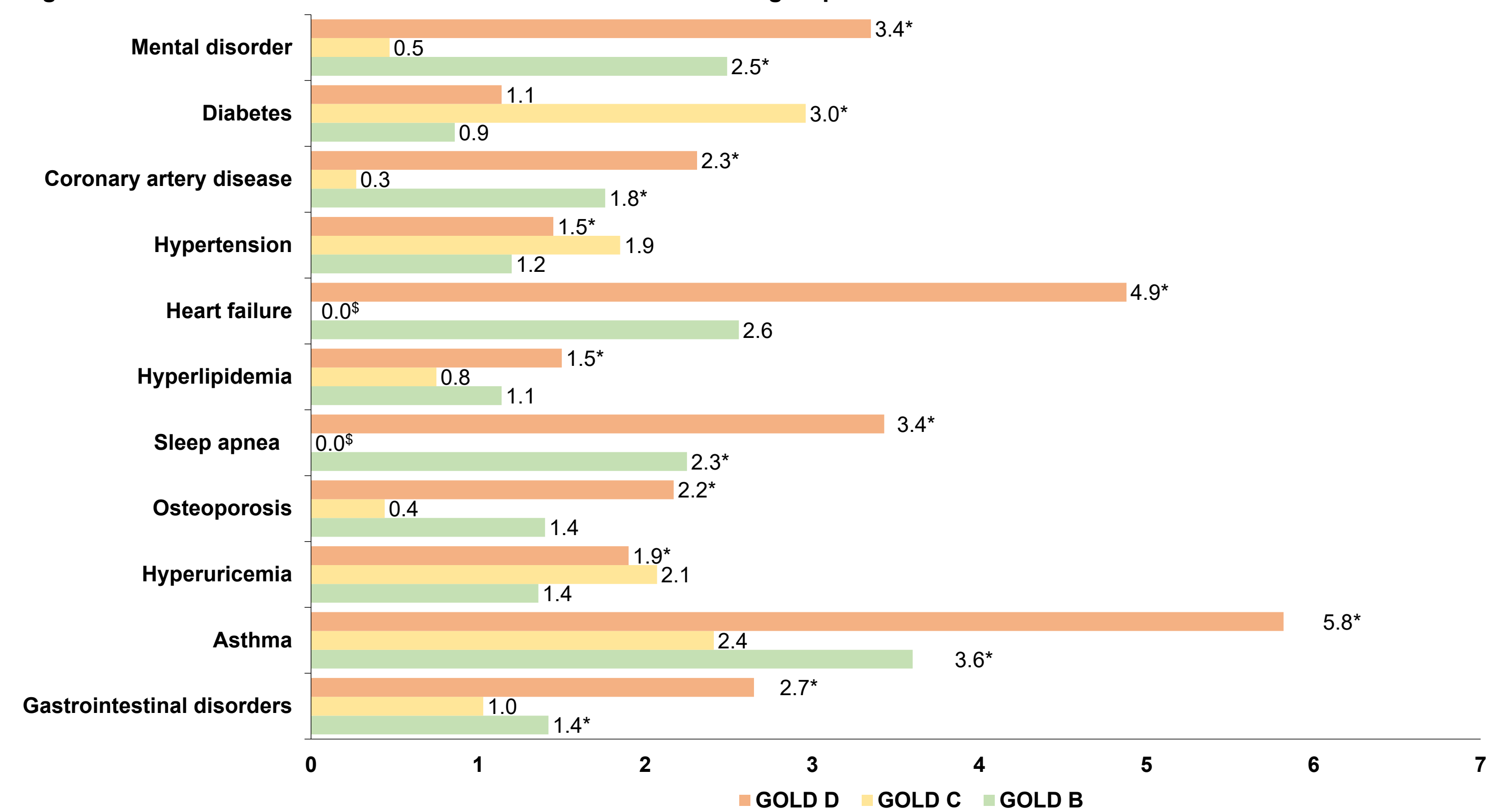
Figure 3. Annual exacerbation rates over time by GOLD 2013 group



Source: Merinopoulou et al. (2016).⁶
GOLD, Global Initiative for Chronic Obstructive Lung Disease.

- COPD-associated comorbidities include asthma, cardiovascular disease, gastrointestinal diseases, skeletal muscle dysfunction, diabetes, and cognitive impairment, and almost all patients with COPD (94%) report at least one comorbidity.^{7,8}
- The German COPD and Systemic Consequences-Comorbidities Network (COSYCONET) cohort study found that the GOLD 2017 groups were associated with a number of comorbidities due to COPD. With GOLD Group A as the reference, GOLD Group D was associated with most of the comorbidities (Figure 4).⁹

Figure 4. Odds ratios for comorbidities in relation to GOLD 2017 groups^a



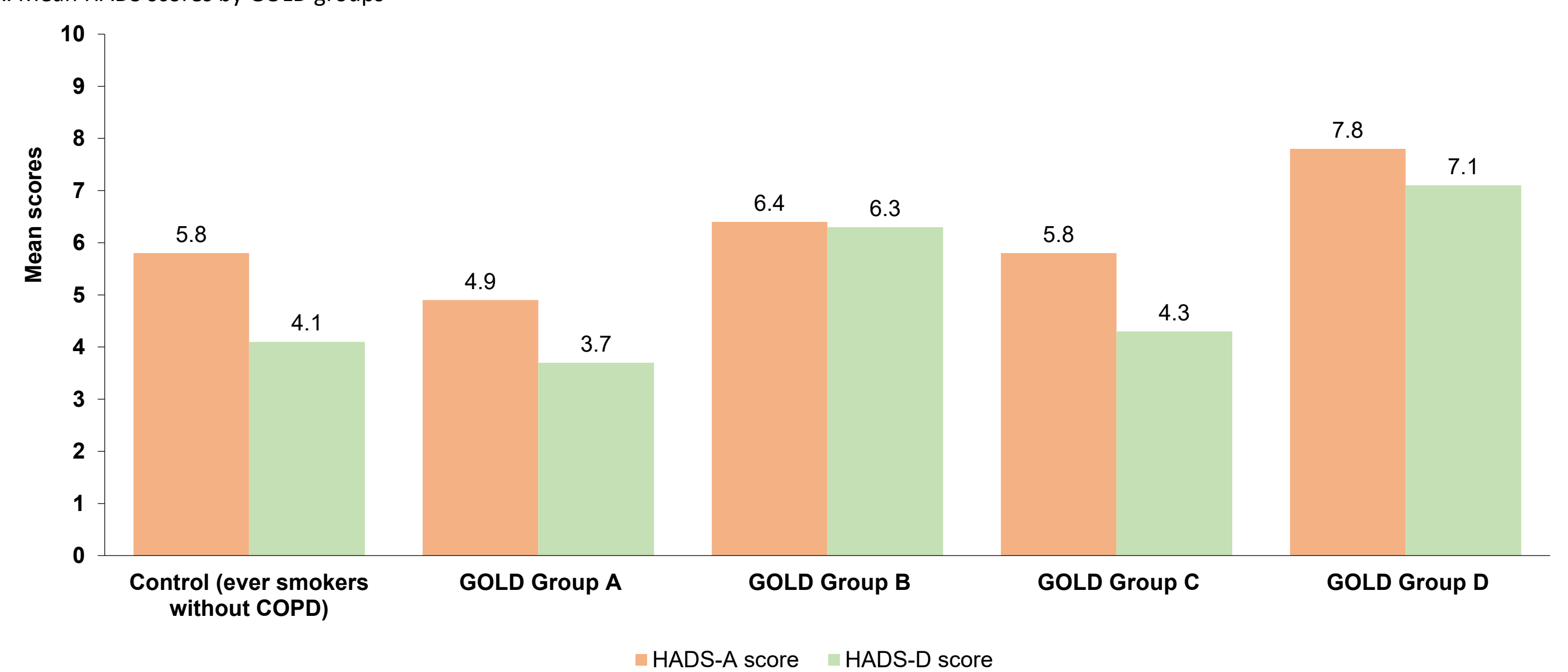
Source: Kahnert et al. (2018).⁹

^aP < 0.05. ^bNot estimated. ^cPatients were classified into GOLD groups on the basis of CAT score. Results presented show binary logistic regression analyses with comorbidities as dependent variables and GOLD Groups B-D as categorical independent variables, with Group A as reference. CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

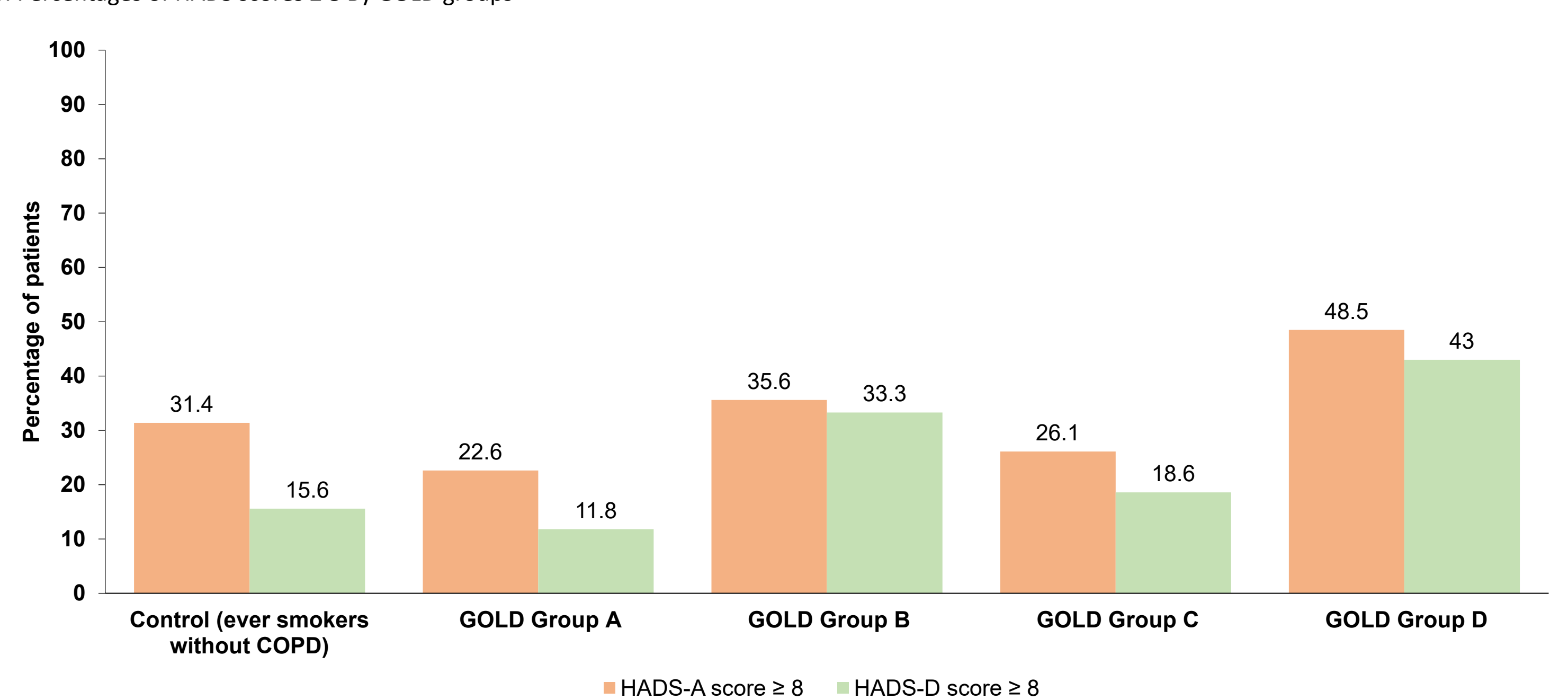
- Anxiety and depression are common and often neglected comorbidities in COPD. They have a significant impact on patients' functional status and ability to cope with their illness.¹⁰
- Anxiety and depression symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS [HADS-A and HADS-D]). Patients in GOLD Groups B and D had higher mean HADS-A and HADS-D scores (higher scores indicate higher levels of anxiety and depression) compared with GOLD Groups A and C (Figure 5).¹⁰
- Patients in GOLD Groups B and D also had a higher proportion of patients with elevated anxiety and depression scores (HADS-A and HADS-D ≥ 8; a score of ≥ 8 indicates clinically significant anxiety or depression) (Figure 5).¹⁰

Figure 5. Mean HADS scores and percentages of HADS scores ≥ 8 By GOLD group

A. Mean HADS scores by GOLD groups



B. Percentages of HADS scores ≥ 8 By GOLD groups



Source: Weiss et al. (2023).¹⁰

Note: All mean scores and percentages of scores ≥ 8 were statistically significant across all groups (HADS-A and HADS-D, P < 0.0001). GOLD, Global Initiative for Chronic Obstructive Lung Disease; HADS-A, Hospital Anxiety and Depression Scale, Anxiety Subscale; HADS-D, Hospital Anxiety and Depression Scale, Depression Subscale.

- A cross-sectional study assessing clinical characteristics of patients with COPD by GOLD classification reported that at least 20% of patients in each GOLD 2018 group had blood eosinophil count (BEC) ≥ 300 cells/μL.¹¹
- The literature review revealed existing evidence^{12–14} about the role of FeNO in COPD; however, its significance and interaction with BEC in guiding COPD management and patient classification remain unclear.
- Detailed, further studies are necessary to better understand how FeNO levels and BEC influence the severity, exacerbation patterns and characterisation of COPD patients.

CONCLUSION

- This literature review elucidates the clinical burden among COPD patients in different GOLD groups, emphasising the need for improved management strategies.

REFERENCES

- World Health Organization. [https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-\(copd\)](https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)). Assessed on 04 October 2023.
- Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 Report. <https://goldcopd.org/2023-gold-report-2/>. Assessed on 04 October 2023.
- Machado A, et al. *Expert Rev Respir Med*. 2021;15(1):131–42.
- Miravittles M, et al. *Respir Med*. 2017;18(1):67.
- Izquierdo JL, et al. *Arch Bronconeumol (Engl Ed)*. 2018;54(11):559–67.
- Merinopoulou E, et al. *Int J COPD*. 2016;11(1):697–709.
- Dursunoglu N, et al. *Tuberk Toraks*. 2016;64(4):289–98.
- Negewo NA, et al. *Respir Investig*. 2015;53(6):249–58.
- Kahnert K, et al. *Respir Med*. 2018;134:79–85.
- Weiss JR, et al. *J Acad Consult Liaison Psychiatry*. 2023;64(1):45–57.
- Jian W, et al. *J Thorac Dis*. 2021;13(10):5701–16.
- Liu X, et al. *COPD*. 2020;17(2):121–7.
- Kobayashi S, et al. *Respir Investig*. 2021;59(3):364–6.
- Rio Ramirez MT, et al. *COPD*. 2018;15(4):369–76.

FUNDING

This study was sponsored by Sanofi and Regeneron Pharmaceuticals, Inc.

CONFLICTS OF INTEREST

RHS is a paid consultant for Sanofi.

AN, ML, WN and VD are full-time employees of RTI Health Solutions, which received research funding from Sanofi to perform this study. RTI Health Solutions is a unit of Research Triangle Institute, an independent, non-profit, research organisation that does work for government.

EMH and HD are employees and stockholders of Sanofi.

SM was an employee of Sanofi during the conduct of this study.

ACKNOWLEDGEMENTS: Medical writing support was provided by Purushottam Shrinat and Avinash Thakur of Sanofi.