
PHARMACOEPIDEMOLOGY LITERATURE REVIEW OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): ANALYSIS OF RISK FACTORS, COMORBIDITIES, AND THERAPEUTIC PATTERNS

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ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is a progressive chronic disease associated with high global morbidity and mortality. A pharmacoepidemiological approach is essential to understand risk determinants, comorbidities, patterns, and the rational use of medications in patient populations. A literature review was conducted on 11 observational studies comprising cohort, case-control, and cross-sectional designs. The included studies evaluated COPD risk factors, comorbidities, therapeutic effectiveness, and medication use patterns. COPD is influenced by multifactorial determinants including occupational exposure, smoking behavior, and metabolic conditions such as hyperlipidemia. Comorbidities including depression, malnutrition, and cardiovascular diseases contribute to increased exacerbation rates and mortality. Triple inhalation therapy (ICS/LAMA/LABA) reduced mortality compared with dual therapy. However, inappropriate antibiotic dosing and Drug-Related Problems (DRPs) were still identified. COPD is a complex chronic disease requiring a multidimensional approach through risk factor control, comorbidity management, and optimization of evidence-based pharmacotherapy within the framework of public health pharmacy.

Keywords: COPD, pharmacoepidemiology, risk factors, comorbidities, inhalation therapy, public health

Received: April 2026,

Accepted: May 2026,

Published: June 2026

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive inflammatory chronic respiratory progressive disorder characterized by persistent airflow limitation that is not fully reversible (WHO, 2023). COPD is currently ranked among the top three leading causes of death globally, accounting for approximately 3.2 million deaths annually. With signs of chronic respiratory symptoms (exacerbation), disorders of airways (bronchitis), and/or alveoli (emphysema), which is developed through complex interactions between a person's genetic factors and environmental exposures, which eventually lead to damage in the lungs (Cho, et al., 2022).

COPD represents one of the leading causes of mortality and disability worldwide, with projections to increase in the coming

decades due to continued exposure to COPD risk factors and population aging, imposing significant social and economic burdens (GOLD, 2024). Beyond mortality, COPD significantly contributes to disability-adjusted life years (DALYs), recurrent hospitalizations, reduced productivity, and impaired quality of life (Vlachaki, et al., 2025). Acute exacerbations are the primary drivers of hospitalization and healthcare expenditure, accelerating lung function decline and increasing mortality risk. Indirect costs related to productivity loss and disability further amplify this burden. Although cigarette smoking remains the primary risk factor, COPD is increasingly recognized as a multifactorial and systemic disease. Occupational exposure to environmental pollutants, metabolic disorders, and genetic predisposition all contribute to disease

development (Lukito, 2025). Moreover, COPD is strongly associated with cardiovascular disease, depression, anxiety, and metabolic syndrome, suggesting shared inflammatory pathways (Borghi-Silva, et al., 2025).

Pharmacoepidemiology, defined as the study of the use and effects of drugs in large populations, provides a framework for evaluating medication utilization, effectiveness, safety, and real-world prescribing patterns (Strom, 2012). Given the increasing clinical and economic burden of COPD, a pharmacoepidemiological review is urgently needed to assess therapeutic efficiency and rational medication use. Pharmacotherapy plays a central role in COPD management, including long-acting bronchodilators (LABA, LAMA), inhaled corticosteroids (ICS), systemic corticosteroids, and antibiotics during exacerbations (GOLD, 2024). Long-term medications in COPD present challenges related to treatment effectiveness, safety, and rational drug use. Pharmacoepidemiology also plays a critical role in the analysis of risk factors, comorbidities, and therapeutic patterns. Therefore, this literature review aims to integrate findings related to COPD determinants and their implications for public health pharmacy practice.

MATERIALS AND METHODS

a. Materials

The materials used in this study consisted of scientific articles related to Chronic Obstructive Pulmonary Disease (COPD) obtained from electronic journal databases such as Google Scholar, PubMed, Elsevier, as well as relevant national and international journals. The included articles were published between 2016 and 2025 and were available in full-text format. The instruments used in this study included a computer connected to the internet for literature searching and word

processing software for data management and analysis.

b. Method

This study employed a systematic literature review method to identify and analyze research related to COPD. The literature search process was conducted using keywords such as “COPD,” “PPOK,” “risk factor,” “therapy,” “comorbidities,” and “clinical outcomes.” The retrieved articles were screened based on inclusion criteria, namely studies evaluating COPD risk factors, comorbidities and prognostic factors, as well as patterns of medication use and therapeutic outcomes in COPD patients. This review included 11 observational studies consisting of 6 cross-sectional studies, 3 cohort studies, and 2 case-control studies. Data extracted from each selected article included the authors, year of publication, country, study design, sample characteristics, research variables, and main findings. The extracted data were then analyzed narratively to identify major themes and relationships among the study findings.

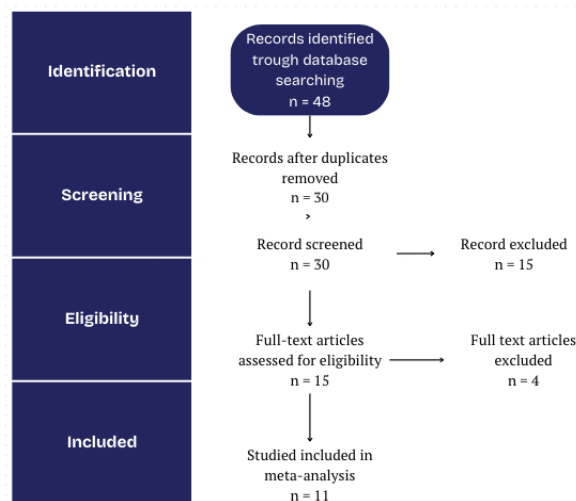


Figure 1. PRISMA flowchart showing study selection process.

RESULT

Author(s)	Country	Study Design	Sample	Variable Studied	Result
Rachmaw an & Hajma (2024)	Indonesia	Cross-sectional	n=46, patients with acute exacerbati on of COPD in the inpatient unit of Surakarta General Hospital	Types of antibiotics used for therapy and evaluation of antibiotic appropriateness	Ampicillin sulbactam (54.35%), levofloxacin (50%), ciprofloxacin (17.39%), azithromycin (17.39%), meropenem (15.22%), ceftriaxone (6.52%), gentamicin (4.35%), piperacillin tazobactam (2.17%), ceftazidime (2.17%), and doxycycline (2.17%). The evaluation of antibiotic use in patients with acute exacerbation of COPD showed that 91.30% were appropriate for the indication, 96.44% were appropriate for the patient, 76.60% were appropriate for the drug, and 32.90% were appropriate for the dose.
Wang et al. (2025)	United States of America	Cohort	n=220, COPD patients over 40 years of age	Depression and anxiety on clinical outcomes	A total of 18 patients (8%) met the MINI criteria for depression and 17 (8%) for anxiety. Depression was associated with more severe dyspnea ($p = 0.045$), a higher COPD disease burden ($p < 0.001$), poorer sleep quality ($p = 0.001$), and worse health-related quality of life ($p < 0.001$).
Kraïm-Leleu et al. (2016)	France	Case-control	n=1519, patients with COPD stage 1	Frequency of exposure across occupational variations and the potential risk of COPD	Foundry workers were the only group shown to have an increased risk of COPD in this study ($p < 0.0001$). Physical activity was found to be protective, while living in urban areas was identified as a risk factor. The primary metals used included cast iron, aluminum, and alloys. Molds and cores were mostly made from sand and synthetic resins. The most common activities were machine maintenance

Author(s)	Country	Study Design	Sample	Variable Studied	Result
					(65.2%), molding (49.6%), finishing (41.1%), and casting (41.0%). Nearly all workers (95.1%) cleaned floors and machinery using brushes or compressed air.
Fazmi et al. (2023)	Indonesia	Cross-sectional	n=90, outpatient and inpatient COPD patients at RSUA	Smoking exposure and consumption on the quality of life of COPD patients	The study results showed that patients with chronic obstructive pulmonary disease (COPD) had significantly poorer quality of life if they smoked ($p = 0.023$). COPD patients who engaged in smoking behavior had a threefold higher risk compared to non-smoking COPD patients, as indicated by a Prevalence Ratio (PR) of 2.67.
Koarai et al. (2021)	Japan	Cohort	n=220, stable COPD patient	Clinical symptoms of depression and anxiety, severity of shortness of breath, sleep quality, and annual frequency of exacerbations	Patients with comorbid mental conditions (depression) experience a significantly higher symptom burden. The CAT score shows a value of 27.1 (very severe) compared to only 17.4 in patients without depression. This demonstrates that emotional factors greatly influence the control of COPD.
Husnah (2020)	Indonesia	Cross-sectional	n= 60, COPD patients receiving treatment at the	Measurement of COPD severity using spirometry, malnutrition risk using	Among 60 COPD patients, 75% were found to be malnourished, and the most common COPD severity was moderate (47.7%). Analysis using the Spearman test showed $p = 0.001$ with $r = -0.665$, indicating a significant relationship with a

Author(s)	Country	Study Design	Sample	Variable Studied	Result
			pulmonary polyclinic at Meuraxa Regional Hospital	MNA, and the relationship between COPD and malnutrition	moderate strength between COPD severity and malnutrition.
Fajrin et al. (2022)	Indonesia	Cross-sectional	n = 105, patients with acute exacerbation of COPD at a regional hospital in Jember	Bronchodilator and corticosteroid therapy patterns, oxygen saturation levels, and additional breath sounds	Combination therapy significantly ($p < 0.05$) improved clinical parameters. Corticosteroids played an important role in increasing oxygen saturation during acute exacerbations.
Li et al. (2025)	China	Cohort	n=13, COPD patients with moderate to severe degrees	Types of Triple inhalation therapy and clinical outcomes in COPD patients (mortality, exacerbations, cardiovascular events)	Triple inhalation therapy (ICS/LAMA/LABA) in patients with moderate to severe chronic obstructive pulmonary disease (COPD) is more effective than dual therapy. It has been shown to reduce all-cause mortality by 24% compared to LAMA/LABA therapy. In addition, this therapy also reduces the risk of moderate to severe COPD exacerbations (RR = 0.93; $p = 0.0003$). From a cardiovascular safety perspective, triple therapy decreases the incidence of

Author(s)	Country	Study Design	Sample	Variable Studied	Result
					cardiovascular adverse events by 25% (RR = 0.75) and reduces major cardiovascular events by approximately 38% (RR = 0.62) compared to dual therapy.
Lin et al. (2025)	Taiwan	Cohort	n=38,928, COPD patients in Taiwan	The variables analyzed included the GOLD 2023 ABE classification, demographic characteristics, Charlson Comorbidity Index (CCI) scores, treatment utilization, spirometry results, mortality, and COPD exacerbations	The GOLD E group exhibited the highest risk of mortality and COPD exacerbations compared to groups A and B. The patient distribution was as follows: group A (30.2%), group B (46.4%), and group E (23.5%). Comorbidities such as acute myocardial infarction, congestive heart failure, and lung disease were associated with an increased risk of mortality and exacerbations in COPD patients
Yang et al. (2022)	Taiwan	Case-control	n=108,950, Patients aged ≥20 years registered	Hyperlipidemia as a risk factor and the incidence of COPD	Patients with hyperlipidemia have a higher risk of developing chronic obstructive pulmonary disease (COPD) compared to those without hyperlipidemia. The incidence of COPD in the hyperlipidemia group was 36.14 per 1,000 person-years, whereas in the non-hyperlipidemia group it was 22.29 per 1,000 person-years.

Author(s)	Country	Study Design	Sample	Variable Studied	Result
			red in the Taiwan ese nation al health databa se, consist ing of patient s with hyperli pidiemi a and a contro l group withou t hyperli pidiemi a.		Analysis showed that patients with hyperlipidemia had a 1.48-fold higher risk of developing COPD ($p < 0.001$). Additionally, factors such as older age, female sex, hypertension, congestive heart failure, and nephropathy were also associated with an increased risk of COPD.
Febriyanti et al. (2025)	Indonesia	Cross-sectional	n=90, COPD patients hospitalized at R.T. Notopuro	The pattern of glucocorticoid use in COPD patients includes the type of drug,	A total of 75% of patients received glucocorticoid monotherapy, while 25% received combination therapy. The most commonly used glucocorticoid was systemic methylprednisolone (98.9%), administered both by injection and orally,

Author(s)	Country	Study Design	Sample	Variable Studied	Result
			Regional Hospital, Sidoarjo, from January 2023 to December 2024.	dose, route of administration, frequency, duration of therapy, as well as recognition of Drug Associated Problems (DRPs) such as drug interactions.	whereas inhaled therapies included budesonide (20.8%) and fluticasone (4.2%). The most frequent dosing regimen was three times daily, with a therapy duration of less than five days. Drug-related problems (DRPs) identified included major drug interactions (methylprednisolone + levofloxacin), moderate interactions (methylprednisolone + vitamin D), and minor interactions (methylprednisolone + salbutamol).

Table 1. Summary of Reviewed Studies through Systematic Literature Review

DISCUSSION

The reviewed studies indicate that COPD has multifactorial and multidimensional risk determinants. Occupational exposure, particularly in metal smelting industries, significantly increases the risk of COPD. Activities involving exposure to metal dust and airborne particles contribute to chronic airway inflammation. This is supported by a case-control study in France which showed that foundry workers had a significantly increased risk of COPD ($p < 0.0001$) (Kraïm-Leleu, et al., 2016). Workers exposed to iron casting, aluminum alloys, dust, and industrial particulates had elevated risk, highlighting the importance of occupational health interventions. This indicates that COPD prevention strategies must extend beyond smoking cessation programs to include workplace safety regulations and environmental protection policies. Smoking behavior was shown to significantly worsen quality of life among COPD patients, with nearly a threefold higher risk compared to non-smokers (PR 2.67). This

finding aligns with Fazmi et al. (2023), who found that smoking was significantly linked to poorer quality of life in COPD patients ($p = 0.023$) and increased their risk compared with non-smoking COPD patients. Smoking remains the primary determinant of COPD in public health contexts. Additionally, hyperlipidemia was identified as a risk factor, increasing COPD risk by 1.48 times. A population based case-control study in Taiwan found that the incidence of COPD in the hyperlipidemia group was 36.14 per 1,000 person-years compared to 22.29 per 1,000 person-years in the non-hyperlipidemia group, with a 1.48-fold increased risk ($p < 0.001$) (Yang, et al., 2022). This finding supports the hypothesis that systemic inflammation and metabolic dysregulation contribute to COPD pathogenesis, suggesting that preventive approaches should not be limited solely to inhalational exposures.

Comorbidities significantly influence COPD progression and outcomes. Mental disorders such as depression and anxiety increase symptom burden, worsen sleep quality, and reduce overall quality of life. Wang et al. (2025) found that depression was linked to more severe dyspnea ($p = 0.045$), a

greater COPD disease burden ($p < 0.001$), poorer sleep quality ($p = 0.001$), and lower health related quality of life ($p < 0.001$). Clinically, patients with depression demonstrate higher symptom assessment scores, indicating poorer disease control. Koarai et al. (2021) reported that COPD patients with comorbid depression had substantially higher CAT scores (27.1) than those without depression (17.4), showing that emotional factors strongly affect COPD symptom control. Malnutrition was significantly associated with COPD severity ($p=0.001$), reinforcing the concept that COPD is a systemic condition affecting nutritional status. Husnah (2020) found that 75% of COPD patients were malnourished. Spearman correlation analysis also revealed a significant association between COPD severity and nutritional status ($p = 0.001$, $r = -0.665$). According to the GOLD 2023 classification, high-risk groups (GOLD E) exhibit the highest mortality and exacerbation rates. Lin et al. (2025) found that patients in the GOLD E group faced the highest risk of mortality and COPD exacerbations compared with groups A and B. The patient distribution was: group A 30.2%, group B 46.4%, and group E 23.5%. Cardiovascular comorbidities, including heart failure and myocardial infarction, further increase mortality risk. Lin et al. (2025) also found that acute myocardial infarction and congestive heart failure were linked to higher risks of mortality and COPD exacerbations. Pharmacoepidemiological Interpretation: Comorbidities may influence medication adherence, therapeutic response, and adverse event risk. Therefore, COPD management should adopt an integrated and comprehensive approach.

Evaluation of therapeutic patterns indicates that combination inhalation therapy provides superior outcomes compared to dual therapy. Triple inhalation therapy (LABA/LAMA as bronchodilator and ICS as antiinflammatory) reduced mortality by 24% and lowered exacerbation risk. Li et al. (2025) found that triple therapy lowered all-cause mortality by 24% versus LAMA/LABA therapy ($RR = 0.76$; $p = 0.03$) and also

decreased the risk of moderate-to-severe COPD exacerbations ($RR = 0.93$; $p = 0.0003$). During acute exacerbations, bronchodilators and corticosteroids significantly improved clinical parameters. Fajrin et al. (2022) found that combination therapy produced significant improvements in clinical parameters ($p < 0.05$). They also reported that corticosteroids were important for raising oxygen saturation during acute exacerbations. Antibiotics are widely used in COPD exacerbations, despite evidence that viral infections and non-infectious inflammatory triggers often predominate. In a study of hospitalized COPD patients, up to 43% showed no detectable bacterial infection during exacerbations, suggesting potential antibiotic overuse (Sievi, et al., 2025). Indiscriminate antibiotic prescribing contributes to antimicrobial resistance, a major global health threat. This underscores the need for evidence-based antibiotic stewardship guided by clinical, microbiological, and pharmacological data. However, inappropriate antibiotic dosing was reported (only 32.90% appropriate dosing). Rachmawan and Hajma (2024) found that antibiotic use for acute exacerbations of COPD was largely appropriate for indication (91.30%) and patient suitability (96.44%), and reasonably appropriate for drug selection (76.60%). However, only 32.90% of prescriptions had an appropriate dosage. Drug-Related Problems (DRPs), including major and moderate drug interactions, were identified. Febriyanti et al. (2025) found that systemic methylprednisolone was the most frequently used glucocorticoid (98.9%). Among inhaled treatments, budesonide was used by 20.8% of patients and fluticasone by 4.2%. The study also reported drug-related problems: a major interaction between methylprednisolone and levofloxacin, a moderate interaction between methylprednisolone and vitamin D, and a minor interaction between methylprednisolone and salbutamol (Febriyanti et al., 2025). These findings suggest a gap between evidence-based guidelines and actual clinical practice.

CONCLUSION

Chronic Obstructive Pulmonary Disease (COPD) remains a major public health challenge characterized by complex, multifactorial etiologies and substantial systemic consequences. This pharmacoepidemiological review highlights that COPD is influenced by smoking, environmental exposure, and metabolic and inflammatory factors, while frequently coexisting with cardiovascular and psychological comorbidities that worsen prognosis and increase healthcare costs. Evidence supports the use of long-acting bronchodilators and triple therapy in reducing exacerbations and mortality among selected patients. However, variability in real-world prescribing patterns, including potential overuse of antibiotics during non-bacterial exacerbations, underscores the importance of rational pharmacotherapy and antimicrobial stewardship. Strengthening pharmacoepidemiological surveillance can bridge the gap between clinical guidelines and practice, ensuring safer, cost-effective, and patient-centered treatment strategies. Optimizing medication use and integrating pharmacist-led interventions are essential steps toward reducing the long-term clinical and economic burden of COPD.

REFERENCES

- Borghi-Silva, A., Camargo, P. F., Caruso, F. C. R., da Luz Goulart, C., Trimer, R., Darlan Santos-Araújo, A., Dourado, I. M., & da Silva, A. L. G. (2025). Current perspectives on the rehabilitation of COPD patients with comorbidities. *Expert review of respiratory medicine*, 19(1), 11–28. <https://doi.org/10.1080/17476348.2025.2452441>
- Cho MH, Hobbs BD, Silverman EK. Genetics of chronic obstructive pulmonary disease: understanding the pathobiology and heterogeneity of a complex disorder. *Lancet Respir Med*. 2022;10(5):485–496. doi:10.1016/S2213-2600(21)00510-5
- Fajrin, K. A., Artanti, K. D., & Setiawan, H. W. (2023). Hubungan perilaku merokok terhadap kualitas hidup pasien penyakit paru obstruktif kronis (PPOK). *AVERROUS: Jurnal Kedokteran dan Kesehatan Malikussaleh*, 9(1), 1–12. <https://jurnal.unimal.ac.id/averrous/article/view/10051>
- Fazmi, T. I. K., Artanti, K. D., & Setiawan, H. W. (2023). Hubungan perilaku merokok terhadap kualitas hidup pasien penyakit paru obstruktif kronis (PPOK). *AVERROUS: Jurnal Kedokteran dan Kesehatan Malikussaleh*, 9(1), 1–12. <https://doi.org/10.29103/averrous.v9i1.11036>
- Global Initiative for Chronic Obstructive Lung Disease [Internet]. United States: Global Initiative for Chronic Obstructive Lung Disease; 2024 [cited 2024 June 25]. Available from: <https://goldcopd.org/2024-gold-report/>.
- Husnah. (2020). Hubungan derajat PPOK dengan risiko malnutrisi menggunakan MNA pada pasien di Poli Paru RSUD Meuraxa. *Jurnal Kedokteran Syiah Kuala*, 20(2), 85–89. <https://jurnal.usk.ac.id/JKS/article/view/18295>
- Koarai, A., Sugiura, H., Yamada, M., Ichikawa, T., Fujino, N., Kanda, S., ... Ichinose, M. (2021). Impact of mental comorbidities on clinical symptoms and exacerbation frequency in patients with stable COPD. *Respiratory Research*, 22(1), 1–10. <https://doi.org/10.1186/s12931-021-01777-x>
- Kraïm-Leleu, M., Lesage, F. X., Dridi, I., Ladhari, N., Gharbi, R., & Deschamps, F. (2016). Occupational exposure and risk of COPD in smelting workers: A case-control study. *PLOS ONE*, 11(6), e0158719. <https://doi.org/10.1371/journal.pone.0158719>
- Li, Y., Li, J., Yang, H., & Zhang, Y. (2025). Effect of triple therapy on mortality and cardiovascular risk in patients with moderate to severe COPD: A meta-analysis of

randomized controlled trials. *BMC Pulmonary Medicine*, 25(1), 345. <https://doi.org/10.1186/s12890-025-03823-6>

Lin, R. T., et al. (2025). Characteristics and clinical outcomes of COPD patients according to GOLD 2023 ABE classification in Taiwan. [PubMed]. <https://pubmed.ncbi.nlm.nih.gov/40406989/>

Lukito, J. I. (2025). Diagnosis dan farmakoterapi penyakit paru obstruktif kronis. *CDK-345*, 52(10), 656–662. <https://cdkjournal.com/index.php/cdk/article/view/1682/1165>

Purbosari, I., Sandhori, F. J., & Febriyanti, A. N. A. (2026). Studi penggunaan glukokortikoid pada pasien penyakit paru obstruktif kronik di RSUD RT Notopuro Sidoarjo. *Jurnal Sains dan Kesehatan*, 6(3), 96–107. <https://doi.org/10.30872/jsk.v6i3.828>

Rachmawan, A. D., & Hajma, N. (2024). Evaluasi ketepatan penggunaan antibiotik pada pasien PPOK eksaserbasi akut di instalasi rawat inap rumah sakit umum Surakarta. *Jurnal Sains dan Kesehatan*, 6(1), 45–52. <https://jsk.ff.unmul.ac.id/index.php/JSK/article/view/828>

Sievi, N. A., Schmidt, F., Fricke, K., et al. (2025). Acute COPD exacerbation despite triple inhaled therapy: A molecular insight – TripleEx study. *Respiratory Research*, 26, 273. [https://doi.org/10.1186/s12931-025-03352-](https://doi.org/10.1186/s12931-025-03352-0)

Strom, B.L. (2012). Basic Principles of Clinical Epidemiology Relevant to Pharmacoepidemiologic Studies. In *Pharmacoepidemiology* (eds B.L. Strom, S.E. Kimmel and S. Hennessy). <https://doi.org/10.1002/9781119959946.ch3>

Vlachaki, I., Donhauser, S., Wise, R. A., Chen, Y., Madoni, A., Scaffidi Argentina, U., Mir, J. N., & Quint, J. K. (2025). A systematic literature review of the humanistic, economic,

sociodemographic, and environmental burden associated with severe COPD. *International Journal of Chronic Obstructive Pulmonary Disease*, 20, 2493–2523. <https://doi.org/10.2147/COPD.S510623>

Wang, J., et al. (2025). Depression and anxiety in COPD patients: Impact on clinical outcomes and health-related quality of life. *Journal of the COPD Foundation*, 12(1). <https://journal.copdfoundation.org>

WHO. Chronic obstructive pulmonary disease (COPD) [Internet]. Geneva: WHO; 2023 [cited 2024 June 25]. Available from: [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))

Yang, T. H., Chien, C. W., Tsai, S. T., Lin, M. S., & Chou, P. (2022). Hyperlipidemia as a risk factor for the development of chronic obstructive pulmonary disease: A population-based case-control study in Taiwan. *International Journal of Environmental Research and Public Health*, 19(19), 12331. <https://doi.org/10.3390/ijerph191912331>