ISSN 2985-5667 (Online) | 2985-6353 (Print) | Vol. 4, No. 3, August (2026), pp. 198-206

Published by: IARN Institute

International Journal on Health and Medical Sciences

Journal homepage: https://journals.iarn.or.id/index.php/HealMed/index

Association between drug interactions and disease severity in patients with chronic obstructive pulmonary disease at dr. M. Djamil General Hospital, Padang

Orchidea Fairuza[1], Puspa Pameswari[2], Zulkarni R[3]

[1,2,3]Department of Pharmacy, Faculty of Pharmacy, Universitas Perintis Indonesia, Padang, Sumatera Barat, Indonesia

Article Info

Article history:

Received Jul 23, 2026
Revised Aug 13, 2026
Accepted Aug 30, 2026

Keywords:

Chronic Obstructive Pulmonary Disease;
Disease Severity;
Drug Interactions;
Hospitalized Patients;
Pharmaceutical Care.

ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disease that frequently requires multiple medications due to disease complexity and comorbidities, increasing the risk of potential drug–drug interactions (DDIs). Previous studies have described potential DDIs and their risk factors in patients with COPD; however, evidence regarding their association with disease severity remains limited, particularly among hospitalized patients in Indonesia. Objective: This study aimed to determine the association between potential DDIs and disease severity among hospitalized patients with COPD at Dr. M. Djamil General Hospital, Padang. Methods: A quantitative observational study with a cross-sectional design was conducted prospectively among hospitalized patients with COPD from February to April 2026. Total sampling was applied, resulting in 25 eligible patients. Potential DDIs were identified using the Lexicomp® Drug Interactions database and classified according to severity and mechanism. Descriptive statistics were used to summarize patient characteristics and potential DDIs, while Fisher's Exact test was performed to analyze the association between potential DDIs and disease severity at a significance level of $p < 0.05$. Results: Most patients were male (76.0%), aged ≥60 years (56.0%), and received ≥10 medications (76.0%). Most were classified as GOLD II (72.0%). Potential DDIs were identified in 24 patients (96.0%), comprising 185 interaction events. Moderate interactions predominated (74.05%), followed by major (17.84%) and minor (8.11%) interactions. Pharmacodynamic interactions accounted for 93.51%, while pharmacokinetic interactions accounted for 6.49%. Potential DDIs occurred in all patients with GOLD II and GOLD III disease but not in the single GOLD I patient. Fisher's Exact test showed a significant association between potential DDIs and disease severity ($p = 0.040$). Conclusion: Potential DDIs were highly prevalent and predominantly moderate and pharmacodynamic. Their association with COPD severity highlights the need for routine medication review and closer monitoring, particularly in patients with moderate and severe COPD.

Corresponding Author:

Orchidea Fairuza,
Departement of Pharmacy,
Universitas Perintis Indonesia,
Jl. Adinegoro, Simpang Kalumpang, Lubuk Buaya, Padang, Sumatera Barat, 25173, Indonesia
Email: orchideafairuza@gmail.com

1. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive chronic respiratory disease characterized by persistent airflow limitation caused by chronic airway inflammation following long-term exposure to harmful particles or gases, particularly cigarette smoke and air pollution. COPD has become one of the leading causes of morbidity and mortality worldwide and continues to impose a substantial burden on healthcare systems because of its chronic nature, frequent exacerbations, and declining pulmonary function. According to the World Health Organization (WHO), COPD ranked as the fourth leading cause of death worldwide in 2024, accounting for approximately 3.5 million deaths or nearly 5% of all global deaths. The majority of COPD-related deaths occur in low- and middle-income countries, where tobacco smoking, household biomass exposure, occupational hazards, and environmental pollution remain highly prevalent (World Health Organization, 2023). Likewise, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) reported that the global burden of COPD continues to increase due to population aging, persistent smoking habits, and prolonged exposure to environmental pollutants, emphasizing the need for early diagnosis and comprehensive disease management (Global Initiative for Chronic Obstructive Lung Disease [GOLD], 2024).

In Indonesia, COPD remains an important public health concern because of its increasing prevalence and clinical burden. Data from the 2018 National Basic Health Research (Riskesdas) demonstrated that chronic respiratory diseases continue to contribute substantially to morbidity among the Indonesian population (Badan Penelitian dan Pengembangan Kesehatan, 2018). In West Sumatra Province, COPD ranked 23rd among 34 provinces, with a prevalence of 3.1%, representing approximately 164,000 affected individuals (Sari et al., 2023). Furthermore, medical record data from Dr. M. Djamil General Hospital, Padang, documented 28 hospitalized patients with COPD during July–August 2022, indicating that COPD remains an important regional health problem requiring continuous clinical attention (Mahardika, 2023). The Indonesian Society of Respirology also recognizes cigarette smoking, biomass fuel exposure, occupational hazards, and air pollution as the principal risk factors contributing to COPD development and progression (Perhimpunan Dokter Paru Indonesia, 2021; Antariksa et al., 2023). These findings are further supported by the Indonesian Ministry of Health, which reported that worsening air pollution has contributed to the increasing incidence of respiratory diseases throughout Indonesia (Kementerian Kesehatan Republik Indonesia, 2023).

COPD is commonly accompanied by multiple chronic comorbidities, including cardiovascular disease, diabetes mellitus, hypertension, chronic infections, and metabolic disorders, requiring long-term pharmacological management involving multiple medications. Consequently, patients with COPD are particularly vulnerable to polypharmacy and potential drug–drug interactions (DDIs). Hanlon et al. (2018) reported that more than half of patients with COPD received five or more medications daily, while the prevalence of polypharmacy increased to 62.4% among patients aged 65 years or older. Similarly, Alwafi et al. (2024) demonstrated that polypharmacy and multiple comorbidities are highly prevalent among hospitalized patients with COPD. The increasing complexity of pharmacotherapy substantially elevates the likelihood of DDIs, which may reduce therapeutic effectiveness, increase adverse drug reactions, prolong hospitalization, and compromise patient safety.

Drug–drug interactions occur when one medication alters the pharmacological effect of another through pharmacokinetic or pharmacodynamic mechanisms (Baxter, 2010; Tatro, 2011). In patients with COPD, interactions frequently involve bronchodilators, corticosteroids, antibiotics, diuretics, cardiovascular agents, and medications prescribed for accompanying comorbidities. As disease severity progresses, patients generally require more intensive pharmacotherapy and a greater number of medications, thereby increasing the probability of clinically significant DDIs. If these interactions are not identified appropriately, they may contribute to treatment failure, respiratory deterioration, prolonged hospitalization, and additional medication-related complications (Stojadinovic et al., 2020).

Previous studies have consistently demonstrated the occurrence of polypharmacy and potential DDIs among patients with COPD. Muriyanto et al. (2022) reported that polypharmacy significantly increased the risk of drug interactions capable of reducing therapeutic effectiveness and increasing the likelihood of adverse clinical outcomes. Likewise, Panduwiguna et al. (2023) emphasized that pharmacotherapy evaluation is essential to optimize COPD treatment and minimize medication-related problems. Stojadinovic et al. (2020) further identified medication burden as one of the major predictors of potential DDIs in hospitalized patients with COPD. Although these studies have described the prevalence, patterns, and risk factors of potential drug interactions, evidence evaluating the association between potential DDIs and disease severity remains limited, particularly among hospitalized patients in Indonesia. Moreover, no published study has specifically investigated this association at Dr. M. Djamil General Hospital, Padang.

Despite the existing evidence on polypharmacy and potential DDIs in patients with COPD, an important evidence gap remains in Indonesia regarding whether the occurrence of potential DDIs differs according to COPD disease severity and what characteristics these interactions present in hospitalized patients. Existing Indonesian studies have primarily focused on medication use, polypharmacy, or the occurrence of potential drug interactions, without specifically examining their relationship with COPD severity. In addition, limited evidence is available regarding the distribution of potential DDIs according to their clinical severity and pharmacological mechanism in hospitalized Indonesian patients with COPD. Addressing this gap is important because patients with more severe COPD may require more complex pharmacotherapy and therefore may be at greater risk of medication-related problems.

This study may also contribute to the optimization of clinical pharmacy services by providing evidence to support systematic medication review and early identification of potential DDIs in hospitalized patients with COPD. Information on the frequency, severity, and mechanisms of potential DDIs can help pharmacists identify patients who require closer monitoring and prioritize medication review, particularly among patients with moderate and severe COPD. These findings may strengthen collaboration between pharmacists and physicians in evaluating medication regimens, preventing clinically relevant drug interactions, improving medication safety, and optimizing pharmaceutical care for patients with COPD.

Therefore, this study was conducted to determine the association between potential drug–drug interactions and disease severity among hospitalized patients with chronic obstructive pulmonary disease at Dr. M. Djamil General Hospital, Padang. The findings are expected to provide scientific evidence supporting the early identification and prevention of potential drug interactions in clinical practice, thereby assisting physicians and pharmacists in optimizing pharmacotherapy, improving medication safety, minimizing drug-related problems, and ultimately enhancing clinical outcomes among patients with COPD.

2. RESEARCH METHOD

This study employed an analytic observational design with a cross-sectional approach to determine the association between potential drug–drug interactions and disease severity among hospitalized patients with chronic obstructive pulmonary disease (COPD) at Dr. M. Djamil General Hospital, Padang, Indonesia. The study was conducted from February to April 2026 using retrospective secondary data obtained from patients' medical records.

The study population comprised all hospitalized patients diagnosed with COPD during the study period. Samples were selected using the total sampling technique, resulting in 25 patients who met the inclusion criteria. The use of total sampling was based on the limited number of hospitalized COPD patients who met the eligibility criteria during the study period. Therefore, all eligible patients were included in the study rather than selecting a subset of the population. The final sample of 25 patients represented the entire accessible population that fulfilled the inclusion criteria during the study period. Eligible participants were hospitalized patients diagnosed with COPD who received

pharmacological treatment and had complete medical records, including demographic characteristics, prescribed medications, dosage, route of administration, and disease severity. Patients with incomplete medical records were excluded from the study.

The collected data included patients' demographic characteristics, prescribed medications, disease severity based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification, and potential drug–drug interactions. Potential drug interactions were identified using the Lexicomp® Drug Interactions database and classified according to their clinical significance (Baxter, 2010; Tatro, 2011). COPD severity was determined according to the GOLD classification documented in the patients' clinical records. The classification of airflow limitation was based on post-bronchodilator forced expiratory volume in one second (FEV_1) as a percentage of the predicted value, with GOLD I representing mild airflow limitation (FEV_1 ≥80%), GOLD II representing moderate airflow limitation (FEV_1 50–79%), GOLD III representing severe airflow limitation (FEV_1 30–49%), and GOLD IV representing very severe airflow limitation (FEV_1 <30%). The GOLD classification was used to categorize disease severity based on the documented clinical assessment of each patient.

Descriptive statistics were used to summarize patient characteristics and the occurrence of potential drug–drug interactions as frequencies and percentages. The association between potential drug–drug interactions and disease severity was analyzed using Fisher's Exact test because the assumptions for the Chi-square test were not fulfilled. Statistical significance was established at $p < 0.05$. Data analysis was performed using SPSS software (Sugiyono, 2019; Notoatmodjo, 2010).

3. RESULTS AND DISCUSSIONS

A total of 25 hospitalized patients diagnosed with chronic obstructive pulmonary disease (COPD) who met the inclusion criteria were included in this study. The findings are presented according to the study objectives, including patient characteristics, the profile of potential drug–drug interactions, the most frequently identified interacting drug pairs, and the association between potential drug–drug interactions and disease severity.

Patient Characteristics

Table 1. Characteristics of hospitalized patients with chronic obstructive pulmonary disease (n = 25)

Characteristics	Frequency (n)	Percentage (%)
Sex		
Male	19	76.0
Female	6	24.0
Age (years)		
<60	11	44.0
≥60	14	56.0
Number of medications		
<5 medications	1	4.0
5–9 medications	5	20.0
≥10 medications	19	76.0
Disease severity		
GOLD I	1	4.0
GOLD II	18	72.0
GOLD III	6	24.0

Source: Authors' analysis based on patients' medical records, 2026

Most hospitalized patients with COPD were male (76.0%) and aged ≥60 years (56.0%). Polypharmacy was common, with 19 patients (76.0%) receiving ten or more medications during hospitalization. Based on disease severity, most patients were categorized as GOLD II (72.0%), followed by GOLD III (24.0%), while only one patient (4.0%) had mild COPD (GOLD I).

The predominance of male patients in this study is consistent with the epidemiological characteristics of COPD, in which cigarette smoking remains the leading risk factor. According to the Indonesian Society of Respirology, smoking is the principal contributor to COPD incidence in

Indonesia (Perhimpunan Dokter Paru Indonesia, 2021). Similar findings were reported by Hanlon et al. (2018) and Alwafi et al. (2024), who observed that COPD predominantly affects older men with multiple comorbidities. The high proportion of patients aged ≥60 years also reflects the progressive nature of COPD, which develops following long-term exposure to tobacco smoke and environmental pollutants (GOLD, 2024). Furthermore, the high prevalence of polypharmacy observed in this study is expected because hospitalized patients frequently require bronchodilators, corticosteroids, antibiotics, and medications for accompanying comorbidities, thereby increasing medication burden and the potential for drug-related problems (Hanlon et al., 2018; Alwafi et al., 2024).

Profile of Potential Drug–Drug Interactions

Table 2. Profile of potential drug–drug interactions

Variable	Category	n	%
Occurrence of potential DDIs	Yes	24	96.0
	No	1	4.0
Severity	Minor	15	8.11
	Moderate	137	74.05
	Major	33	17.84
Mechanism	Pharmacodynamic	173	93.51
	Pharmacokinetic	12	6.49
Number of DDIs per patient	None	1	4.0
	1–10	18	72.0
	11–20	5	20.0
	≥21	1	4.0

Source: Authors' analysis based on patients' medical records, 2026

Potential drug–drug interactions were identified in 24 of the 25 patients (96.0%). A total of 185 potential interaction events were detected during hospitalization. Moderate interactions predominated (74.05%), followed by major (17.84%) and minor interactions (8.11%). Based on the interaction mechanism, pharmacodynamic interactions accounted for 173 events (93.51%), whereas pharmacokinetic interactions accounted for only 12 events (6.49%). Most patients experienced between one and ten potential interaction events (72.0%), while one patient experienced more than 21 interaction events.

The high proportion of patients with potential DDIs (96.0%) may be related to the substantial medication burden observed in this study, as 76.0% of patients received ten or more medications during hospitalization. Hospitalized patients with COPD may receive multiple drugs concurrently to manage respiratory symptoms, acute exacerbations, and comorbid conditions. The simultaneous use of several therapeutic classes increases the number of possible drug combinations and consequently increases the likelihood of potential DDIs. In addition, the older age of most patients (56.0% aged ≥60 years) and the presence of complex pharmacotherapy may further contribute to the risk of medication-related problems. These findings are consistent with previous studies identifying polypharmacy and medication burden as important factors associated with potential DDIs in patients with COPD.

The high prevalence of potential drug–drug interactions observed in this study reflects the complexity of pharmacotherapy among hospitalized patients with COPD. Patients commonly receive multiple medications simultaneously to manage respiratory symptoms, acute exacerbations, and accompanying comorbidities. Consequently, increasing medication burden substantially elevates the likelihood of clinically significant drug interactions. Similar findings were reported by Muriyanto et al. (2022), who found that polypharmacy was strongly associated with the occurrence of potential drug interactions in patients with COPD. Stojadinovic et al. (2020) also identified medication burden as one of the principal predictors of potential DDIs among hospitalized patients with COPD.

Moderate interactions represented nearly three-quarters of all identified interactions (74.05%). Although moderate interactions do not necessarily require discontinuation of therapy,

their high frequency indicates that medication regimens should not be considered low risk and may require clinical monitoring, dose adjustment, or modification of therapy depending on the interacting drug combination. In clinical pharmacy practice, these interactions can be used to prioritize medication review and monitoring, particularly when patients receive multiple medications or have additional risk factors for adverse drug events. Therefore, the predominance of moderate interactions in this study emphasizes the need for routine monitoring of treatment response and potential adverse effects during hospitalization rather than relying solely on identification of major interactions.

Interacting Drug Pairs

Table 3. Most frequently identified drug–drug interaction pairs

Drug Combination	Frequency	Percentage (%)
Corticosteroids + Antibiotics	16	8.65
Bronchodilators + Methylxanthines	8	4.32
Corticosteroids + Antihypertensives	8	4.32
Bronchodilators + Prokinetics	7	3.78
Antibiotics + Antihypertensives	7	3.78
NSAIDs + Diuretics	6	3.24
Diuretics + Antihypertensives	6	3.24

Source: Authors' analysis based on patients' medical records using the Lexicomp® Drug Interactions database, 2026

The most frequently identified interaction involved corticosteroids combined with antibiotics (8.65%), followed by bronchodilators combined with methylxanthines and corticosteroids combined with antihypertensive agents (4.32% each). These combinations were frequently prescribed because they represent common pharmacotherapeutic regimens for hospitalized patients with COPD.

The interaction patterns identified in this study indicate that combinations involving corticosteroids, antibiotics, bronchodilators, methylxanthines, antihypertensive agents, diuretics, and NSAIDs were among the most frequently encountered interacting drug classes. These combinations reflect the multidrug treatment commonly required to manage COPD and its associated conditions. In particular, corticosteroid–antibiotic combinations were the most frequently identified interaction, accounting for 8.65% of all interaction events, while bronchodilator–methylxanthine and corticosteroid–antihypertensive combinations each accounted for 4.32%. Therefore, these drug classes may warrant particular attention during medication review, especially when several of them are prescribed concurrently.

Corticosteroids and antibiotics are routinely administered during acute exacerbations to reduce airway inflammation and manage bacterial infections, thereby increasing the probability of potential interactions. Likewise, bronchodilator–methylxanthine combinations remain common despite the narrow therapeutic index of methylxanthines, requiring close clinical monitoring (GOLD, 2024; Baxter, 2010). These findings emphasize the importance of comprehensive medication review by physicians and clinical pharmacists to identify clinically significant interactions and optimize pharmacotherapy.

Association Between Potential Drug–Drug Interactions and Disease Severity

Table 4. Association between potential drug–drug interactions and disease severity

Disease Severity	Potential DDIs n (%)	No Potential DDIs n (%)	Total	*p*-value
GOLD I	0 (0.0)	1 (100.0)	1	
GOLD II	18 (100.0)	0 (0.0)	18	0.040
GOLD III	6 (100.0)	0 (0.0)	6	

Source: Authors' analysis based on patients' medical records, 2026 Fisher's Exact test.

Potential drug–drug interactions occurred in all patients with moderate and severe COPD, whereas the only patient with mild disease did not experience any potential interaction. Statistical

analysis using Fisher's Exact test demonstrated a significant association between potential drug–drug interactions and disease severity (p = 0.040).

This finding suggests that increasing COPD severity is associated with greater pharmacotherapeutic complexity and a higher likelihood of potential drug interactions. Patients with moderate and severe COPD generally require more intensive treatment, including combinations of bronchodilators, corticosteroids, antibiotics, and medications for accompanying chronic diseases, resulting in increased medication burden. Similar findings were reported by Stojadinovic et al. (2020), who identified medication burden as one of the principal determinants of potential DDIs among patients with COPD. Hanlon et al. (2018) also demonstrated that multimorbidity and polypharmacy substantially increase the risk of medication-related problems in patients with COPD. Likewise, Alwafi et al. (2024) reported that patients with multiple comorbidities were significantly more likely to experience polypharmacy and potential DDIs.

The significant association observed in the present study highlights the importance of routine medication review, particularly among patients with moderate and severe COPD. Early identification of potential DDIs may assist healthcare professionals in optimizing pharmacotherapy, preventing adverse drug events, and improving medication safety during hospitalization.

4. CONCLUSION

Potential drug–drug interactions were highly prevalent among hospitalized patients with chronic obstructive pulmonary disease (COPD) at Dr. M. Djamil General Hospital, Padang, with interactions identified in 96.0% of patients. Most potential interactions were classified as moderate in severity and occurred through pharmacodynamic mechanisms. Statistical analysis demonstrated a significant association between potential drug–drug interactions and disease severity (p = 0.040), indicating that patients with more severe COPD were more likely to experience potential drug interactions because of increasingly complex pharmacotherapy.

These findings highlight the importance of incorporating routine medication review and systematic screening for potential drug–drug interactions into clinical pharmacy services for hospitalized patients with COPD. Medication review should pay particular attention to patients receiving multiple medications and those with moderate or severe COPD, with appropriate monitoring of potential adverse effects and therapeutic response. Collaboration between pharmacists and physicians can support the identification and management of potential interactions, thereby improving medication safety and optimizing pharmacotherapy.

Future research should involve larger and multicenter populations to strengthen the evidence regarding the relationship between potential drug–drug interactions and COPD disease severity. Prospective studies with longer follow-up are also needed to evaluate whether identified potential interactions are associated with clinically relevant outcomes, such as adverse drug events, treatment response, exacerbations, and length of hospitalization. Further studies should also examine specific interacting drug combinations and potential confounding factors, including polypharmacy, comorbidities, age, and COPD treatment intensity.

These findings emphasize the importance of routine medication review and early identification of potential drug–drug interactions as part of pharmaceutical care for hospitalized patients with COPD. Collaboration among physicians, pharmacists, and other healthcare professionals is essential to optimize pharmacotherapy, minimize drug-related problems, and improve patient safety and therapeutic outcomes..

ACKNOWLEDGEMENTS

The authors would like to express their sincere gratitude to the Faculty of Pharmacy, Universitas Perintis Indonesia, for providing academic support throughout this study. The authors also gratefully acknowledge Dr. M. Djamil General Hospital, Padang, for granting permission to conduct this

research and facilitating access to the medical record data used in this study. Appreciation is extended to all healthcare professionals who assisted in the research process.

REFERENCES

Alwafi, H., Naser, A. Y., Ashoor, D. S., et al. (2024). Prevalence and predictors of polypharmacy and comorbidities among patients with chronic obstructive pulmonary disease: A cross-sectional retrospective study in a tertiary hospital in Saudi Arabia. *BMC Pulmonary Medicine, 24*, 453. https://doi.org/10.1186/s12890-024-03274-5

Antariksa, B., Bakhtiar, A., Wiyono, W. H., Djajalaksana, S., Yunus, F., Amin, M., et al. (2023). *Perhimpunan Dokter Paru Indonesia*.

Badan Penelitian dan Pengembangan Kesehatan. (2018). *Laporan nasional Riset Kesehatan Dasar (Riskesdas) 2018*. Kementerian Kesehatan Republik Indonesia.

Baxter, K. (2010). *Stockley's drug interactions* (9th ed.). Pharmaceutical Press.

Broaddus, V. C., Mason, R. J., Ernst, J. D., King, T. E., Lazarus, S. C., Murray, J. F., & Nadel, J. A. (Eds.). (2016). *Murray & Nadel's textbook of respiratory medicine* (6th ed.). Elsevier.

Fitriani, N. D., Zatihulwani, E. Z., Wibowo, S. A., Wasilah, N. H., Rahmawati, E. Y., Fathia, N. N. A., Sari, G. M., et al. (2023). *Asuhan keperawatan gangguan sistem pernapasan*. PT Nuansa Fajar Cemerlang.

Global Initiative for Chronic Obstructive Lung Disease. (2024). *Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease*. https://goldcopd.org

Global Initiative for Chronic Obstructive Lung Disease. (2025). *Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease*. https://goldcopd.org/digital-gold-report/

Hanlon, P., Nicholl, B. I., Jani, B. D., McQueenie, R., Lee, D., Gallacher, K. I., & Mair, F. S. (2018). Examining patterns of multimorbidity, polypharmacy and risk of adverse drug reactions in chronic obstructive pulmonary disease: A cross-sectional UK Biobank study. *BMJ Open, 8*(1), e018404. https://doi.org/10.1136/bmjopen-2017-018404

Irawan, E., Lengga, V. M., Faqih, M. U., Ryandini, T. P., Cahyono, S. W. T., Lusiani, E., Putro, D. U. H., Maharina, F. D., Suprapti, F., Sihombing, F., Wilandika, A., Herawati, A. T., Yunita, M., Saputro, D. N. H., Deri, M., Septiawan, T., & Husnul, N. I. H. (2025). *Buku ajar keperawatan medikal bedah I*.

Kementerian Kesehatan Republik Indonesia. (2023, April 4). *Polusi udara sebabkan angka penyakit respirasi tinggi*. https://kemkes.go.id/id/polusi-udara-sebabkan-angka-penyakit-respirasi-tinggi

Kurniasih, E., & Daris, H. S. (2017). *Buku ajar gangguan sistem pernapasan*. Samudra Biru.

Mahardika, A. N. (2023). *Asuhan keperawatan pada pasien PPOK: Pola nafas tidak efektif dengan intervensi relaksasi nafas dalam* [Diploma thesis, Universitas Kusuma Husada Surakarta].

Madania, M., & Sawitri, N. E. (2022). Seorang laki-laki 64 tahun dengan penyakit paru obstruktif kronik (PPOK). In *Proceeding Book Call for Papers Fakultas Kedokteran Universitas Muhammadiyah Surakarta* (pp. 314–329).

Muriyanto, M., Rosmiati, M., & Setyaningsih, Z. I. (2022). Analisis polifarmasi dan interaksi obat PPOK pada pasien BPJS rawat jalan di Rumah Sakit Karya Medika I periode Juli–September 2020. *Cerdika: Jurnal Ilmiah Indonesia, 2*(2), 158–174. https://doi.org/10.36418/cerdika.v2i2.332

Notoatmodjo, S. (2010). *Metodologi penelitian kesehatan*. Rineka Cipta.

Panduwiguna, I., Baniu, A. S., Renaldi, F. S., Hasan, A. F., & Tasmin, T. (2023). Evaluasi pengobatan penyakit paru obstruktif kronik di instalasi rawat jalan Rumah Sakit Umum XYZ Jakarta Barat. *Jurnal Farmasi Kryonaut, 2*(1), 1–7. https://doi.org/10.59969/jfk.v2i1.20

Perhimpunan Dokter Paru Indonesia. (2021). *Pedoman diagnosis dan penatalaksanaan penyakit paru obstruktif kronik (PPOK)*.

Sari, D. K., Sabri, R., & Afriyanti, E. (2023). Pengaruh edukasi gaya hidup multikomponen terhadap manajemen diri pada pasien penyakit paru obstruktif kronik (PPOK) stabil. *Jurnal Keperawatan, 13*(4).

Stojadinovic, D., Zivkovic Zaric, R., Jankovic, S., Lazic, Z., Cekerevac, I., & Susa, R. (2020). Risk factors for potential drug–drug interactions in patients with chronic obstructive pulmonary disease. *Irish Journal of Medical Science, 189*(3), 1123–1125. https://doi.org/10.1007/s11845-019-02155-9

Suardi, H. N., Suryawati, S., & Mulia, V. D. (2021). Interaksi obat potensial pada pasien usia lanjut. *Jurnal Kedokteran Syiah Kuala, 21*(1). https://doi.org/10.24815/jks.v21i1.21272

Sugiyono. (2019). *Metode penelitian kuantitatif, kualitatif, dan R&D*. Alfabeta.

Tatro, D. S. (2011). *Drug interaction facts*. Wolters Kluwer Health.

Varmaghani, M., Dehghani, M., Heidari, E., Sharifi, F., Moghaddam, S. S., & Farzadfar, F. (2019). Global prevalence of chronic obstructive pulmonary disease: Systematic review and meta-analysis. *Eastern*

Mediterranean Health Journal, 25(1), 47–57. https://doi.org/10.26719/emhj.18.014
World Health Organization. (2023). *Chronic obstructive pulmonary disease (COPD).* https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)