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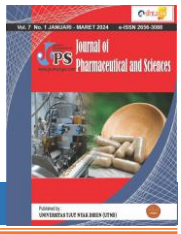

# Drug-Related Problems in Chronic Obstructive Pulmonary Disease: Literature Review

# Drug-Related Problems Pada Penyakit Paru Obstruksi Kronis: Literatur Review

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## Abstract

Chronic Obstructive Pulmonary Disease (COPD) is one of the leading causes of global morbidity and mortality, with a continuously increasing health burden. The complexity of long-term therapy in COPD increases the risk of Drug-Related Problems (DRPs), which can affect patient clinical outcomes. This literature review was conducted descriptively by searching articles in the PubMed, Scopus, Google Scholar, and ScienceDirect databases using keywords related to DRPs and COPD. The selection was made on publications from the last 10 years (2015–2025) relevant to the topic and available in full text. Based on studies by Li et al., (2019) and Apikoglu-Rabus et al., (2016), the classification of DRPs according to PCNE V9.0 mainly included aspects of medication safety (54.2%), inappropriate drug selection (up to 8.7%), excessive dosage (19.9%), excessive duration of therapy (17.7%), and errors in the drug use process (up to 63.3%). Patient factors such as non-compliance (25%) and incorrect inhalation techniques were the main contributors to the occurrence of DRPs. Inappropriate use of medications, drug-herb interactions, and lack of therapy monitoring were also consistently found. The findings suggest that DRPs significantly worsen symptom control and increase the risk of exacerbations. Pharmacists are critical in identifying, preventing, and managing DRPs through patient education, therapy review, and ongoing therapy monitoring. DRPs in COPD patients are a serious challenge that requires a multidisciplinary approach. Ongoing education, monitoring of therapy rationality, and collaboration between healthcare professionals are needed to improve patient safety and the effectiveness of COPD treatment.

***Keywords*: COPD, Drug-related problems, Inhalation therapy, Patient compliance, PCNE**

## Abstrak

Penyakit Paru Obstruktif Kronis (PPOK) merupakan salah satu penyebab utama morbiditas dan mortalitas global, dengan beban kesehatan yang terus meningkat. Kompleksitas terapi jangka panjang pada PPOK meningkatkan risiko terjadinya Masalah Terkait Obat (MTO), yang dapat mempengaruhi luaran klinis pasien. Tinjauan literatur ini dilakukan secara deskriptif dengan mencari artikel di database PubMed, Scopus, Google Scholar, dan ScienceDirect menggunakan kata kunci yang terkait dengan MTO dan PPOK. Pemilihan dilakukan pada publikasi dari 10 tahun terakhir (2015–2025) yang relevan dengan topik dan tersedia dalam teks lengkap. Berdasarkan studi dato Li et al., (2019) dan Apikoglu-Rabus et al., (2016), klasifikasi MTO menurut PCNE V9.0 sebagian besar mencakup aspek keamanan obat (54,2%), pemilihan obat yang tidak tepat (hingga 8,7%), dosis berlebihan (19,9%), durasi terapi berlebihan (17,7%), dan kesalahan dalam proses penggunaan obat (hingga 63,3%). Faktor pasien seperti ketidakpatuhan (25%) dan teknik inhalasi yang salah merupakan kontributor utama terjadinya MTO. Penggunaan obat yang tidak tepat, interaksi obat-herbal, dan kurangnya pemantauan terapi juga secara konsisten ditemukan. Temuan menunjukkan bahwa MTO secara signifikan memperburuk kontrol gejala dan meningkatkan risiko eksaserbasi. Peran apoteker sangat penting dalam mengidentifikasi, mencegah, dan mengelola MTO melalui edukasi pasien, tinjauan terapi, dan

pemantauan terapi berkelanjutan. MTO pada pasien PPOK merupakan tantangan serius yang memerlukan pendekatan multidisiplin. Edukasi berkelanjutan, pemantauan rasionalitas terapi, dan kolaborasi antar tenaga kesehatan diperlukan untuk meningkatkan keselamatan pasien dan efektivitas pengobatan PPOK.

***Kata Kunci: PPOK, DRP, Terapi inhalasi, Kepatuhan pasien , PCNE.***



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## Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a significant health problem in Indonesia, with a prevalence that continues to increase along with risk factors such as smoking habits, air pollution, and exposure to smoke from biomass fuel combustion.[1,2]. According to data from the Ministry of Health, the prevalence of COPD in Indonesia reaches 5.6%, equivalent to about 4.8 million sufferers, with the highest prevalence found in Lampung Province at 1.4%[3,4]. COPD is one of the leading causes of morbidity and mortality worldwide, with a health and economic burden that continues to increase every year. COPD is characterized by progressive and not fully reversible airflow obstruction, and often experiences periods of deterioration known as acute exacerbations [5,6]. COPD management generally requires long-term therapy with various pharmacological regimens, such as bronchodilators, inhaled corticosteroids, antibiotics, mucolytics, and other supportive treatments. The complexity of this therapy increases the risk of drug-related problems (DRPs). Several studies have shown a relationship between DRPs and increased rehospitalization rates and mortality in COPD patients.

DRPs (Drug-Related Problems) encompass various aspects, ranging from errors in drug selection, inappropriate doses, drug interactions, patient non-adherence, to adverse drug reactions. The presence of DRPs in COPD management can worsen disease control, increase exacerbation frequency, and worsen patient clinical prognosis.[7–9]One of the internationally widely used DRP classification systems is the Pharmaceutical Care Network Europe (PCNE). It has undergone several revisions, with the latest version providing a more systematic structure in identifying, grouping, and managing DRPs based on problem domains, causes, and required interventions.[10–12]. However, the available data is still scattered and has not been systematically reviewed in the context of COPD exacerbations. Additionally, variability in definitions, classifications, and approaches to DRP identification, including using different classification systems such as PCNE, poses a challenge in comprehensively concluding their impact on patient clinical outcomes.

Therefore, this literature review aims to present a comprehensive analysis of the incidence of Drug-Related Problems in COPD patients. This review will evaluate the types of DRPs that most frequently occur in COPD patients. Through a deeper understanding of DRP incidence, it is hoped that healthcare professionals can play an active role in identifying, preventing, and addressing DRP incidence in COPD patients to improve overall patient clinical outcomes.

## Methods

This literature review was compiled using a descriptive approach to explore and analyze various scientific publications discussing the incidence of Drug-Related Problems (DRPs) in Chronic Obstructive Pulmonary Disease (COPD) patients. Data searches were conducted through several trusted online databases

such as Google Scholar, PubMed, Scopus, and ScienceDirect, using the keywords: "Drug Related Problem" OR "DRP" AND "Chronic Obstructive Pulmonary Disease" OR "COPD" AND "Exacerbation". Articles included in this review were selected based on the following criteria: published between 2015 and 2025, written in Indonesian or English, available in full-text version, and are primary or secondary studies that specifically discuss the relationship between COPD and DRPs. The exclusion criteria included: articles irrelevant to the topic of COPD or DRPs, non-scientific publications such as editorials or conference abstracts, duplicate articles, and articles that do not have adequate methodological quality or do not present DRP outcomes clearly. The selection process was carried out in stages, starting with identifying 117 articles. After screening for duplication and selecting based on titles and abstracts, 28 articles were identified as eligible for full-text review. After rigorous application of inclusion and exclusion criteria, two articles were identified as suitable for further analysis in this study.

## Result and Discussion

**Table 1.** Results of literature search on DRP events in COPD patients.

| No | Author (year) | DRP Classification | DRP incident (%) | Drugs causing DRP |
|---|---|---|---|---|
| **1.** | Li et al., (2019) | 1. Treatment safety | 54.2 | 1. Antibiotics |
| | | 2. Drug selection | | 2. Corticosteroids |
| | | a. Drug not according to formulary/guidelines | 0.3 | 3. Proton pump inhibitors |
| | | | 6.2 | |
| | | b. Drug according to guidelines, but contraindicated | 5.0 | |
| | | c. No indication for the drug | 8.7 | |
| | | d. Inappropriate drug combination (drug-drug, drug-herbal, drug-supplement) | 4.2 | |
| | | e. Duplication of therapeutic group or active ingredient | 3.0 | |
| | | 3. Drug form | | |
| | | 4. Dose selection | 19.9 | |
| | | a. Dose too high | 1.6 | |
| | | b. Dose regimen too frequent | 17.7 | |
| | | c. Treatment duration | | |
| | | 5. Dispensing | 2.0 | |
| | | a. Incorrect drug, strength preparation, or dose regimen (OTC drug) | | |
| | | 6. Drug use process | 4.5 | |
| | | a. Incorrect administration time or dose interval | 1.6 | |
| | | 7. Patient-related | 13.5 | |
| | | a. Incorrect administration time or interval | | |
| | | b. Patient uses the drug incorrectly | 12.1 | |
| | | 8. Other causes | | |
| | | a. Absence or inadequacy of outcome monitoring | | |
| **2.** | Apikoglu-Rabus et al., (2016) | 1. Drug selection | 1.6 | Not mentioned |
| | | 2. Dose selection | | |
| | | a. Dose too low | 0.8 | |
| | | b. Requires dose adjustment | 1.6 | |
| | | 3. Drug use process | 63.3 | |
| | | a. Incorrect administration time | 0.8 | |
| | | b. Drug underused | 15.6 | |
| | | c. Drug overused | 1.6 | |



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| | |
|---|---|
| d. Drug not administered | 21.1 |
| e. Patient cannot use the drug | 24.2 |
| 4. Patient | |
| Patient forgets to take medication | 25.0 |
| 5. Other causes | 7.8 |

DRP classification continues to evolve, but one widely used classification system is from the Pharmaceutical Care Network Europe (PCNE). According to PCNE V9.0 classification, DRPs are grouped into several main domains based on problem type and cause. Based on problem type, they are divided into three primary domains and seven sub-domains. Based on causes, DRPs are divided into nine primary domains and 41 sub-domains. Therefore, a good understanding and knowledge are required.

Classification aims to provide DRP information when providing pharmaceutical care and interventions, for research and data exchange related to DRPs. DRP classification must have clear definitions, validation publications, and a hierarchical structure, and be used in practice. PCNE meets these requirements because it has been used internationally and fulfills a hierarchical structure (separating problems, causes, and interventions). Table 1 shows the literature search results. 2 articles identify DRP incidence in COPD patients.

**Treatment safety (Adverse Drug Reaction)**

Based on the literature, treatment safety is the highest drug-related problem (DRP) classification in COPD patients, at 54.2% [14]Primary COPD therapy uses bronchodilators (antimuscarinics, beta2 agonists, methylxanthines), corticosteroids, and antibiotics during exacerbations.[15–17]. Significant side effects include tachycardia and arrhythmia due to beta2 agonists, dry mouth and urinary disorders from antimuscarinics, and risks of osteoporosis and hyperglycemia due to long-term oral corticosteroids. The combination of beta2 agonists and inhaled corticosteroids can also cause tremor and tachycardia, which decreases quality of life and increases exacerbations.[18,19].

**Drug selection**

DRP incidence in the drug selection category in COPD patients was found in two articles. Li et al. (2019) divided this category into several sub-domains, with the highest percentage being inappropriate drug combinations at 8.7%, most commonly combinations of proton pump inhibitors (PPIs) with other drugs and herbal medicines (38 cases), particularly with clopidogrel, which can reduce the cardioprotective effect of that drug.[14]. Other research found inappropriate drug combinations at 19.0%, including the use of traditional medicines with interaction risks at 8.3%[20]. DRP incidence due to contraindicated drugs was reported at 6.2%, although without specific drug details. This data shows that drug selection, whether due to combinations, contraindications, or use without indication, occurs in COPD patients with a direct impact on therapy effectiveness and safety. COPD patients often use many drugs to manage various aspects of their disease, so it is essential to ensure no overlap or dangerous interactions occur. Medical personnel monitoring and therapy adjustment are critical to prevent complications and provide optimal treatment.

**Dose selection**

Appropriate dose selection in COPD patients is essential because dosing errors directly impact symptom control, exacerbation risk, and side effects. A study by Li et al., (2019) Showed that excessively high doses occurred in 19.9% of patients, becoming the most common DRP. Additionally, excessively frequent dose regimens (1.6%) and overly long therapy duration (17.7%) contributed to therapy inappropriateness. This inappropriateness increases the risk of systemic effects such as hypertension and hyperglycemia. [14,21]. The Apikoglu-Rabus et al., (2016) The study reported that 1.6% of patients required dose adjustment and 0.8% received doses too low, showing a need for individual therapy dose evaluation. Doses that are too low, such as in inhaled corticosteroid use, can cause poor symptom control and worsen exacerbations, while doses that are too high risk causing systemic side effects such as increased blood pressure or hyperglycemia, which can increase complications during exacerbations. [7,21].

**Treatment Duration**

Inappropriate treatment duration, whether too long or too short, is one of the leading causes of drug-related problems (DRPs) in COPD patients. According to a study by Li et al. (2019), DRPs due to excessively long therapy duration reached 17.7%: excessive therapy duration, particularly antibiotics, risks increasing


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resistance. Long-term PPI use can also cause infections, hip fractures, and vitamin B12 deficiency.[14]. Thus, inappropriate treatment duration becomes an essential factor that can affect COPD therapy success. Intensive monitoring and patient education are necessary to prevent errors in therapy duration.

**Drug use process**

Studies from two articles reported that DRP prevalence due to drug use process errors varies, ranging from 4.5% [14] to 63.3% [7]Both articles mentioned incorrect administration times or intervals, and 24.2% of patients were unable to use drugs. A study on COPD patients supports this finding, that 47.9% of patients made errors in drug administration schedules.[20]. Other research reported that 20.83% of patients experienced drug administration timing errors. [22]. As many as 1.6% of patients used drugs excessively. This is supported by Adisa et al. (2024) research, which reported 47.9% of patients doubling doses if they forgot to take medication. Other DRP incidence in COPD patients is drug underuse at 15.6%. As many as 43.7% of patients stopped medication when symptoms improved without medical guidance, which can increase exacerbation risk and decrease disease control.[20].

This low drug use effectiveness worsens symptom control, increases exacerbation risk, decreases quality of life, and adds burden to the healthcare system. These errors are mainly due to a lack of patient education and adequate therapy monitoring by healthcare professionals. Therefore, educational interventions and regular monitoring must improve therapy success and reduce DRP incidence.

**Patient-Related Factors**

Patient factors become a dominant cause in drug-related problems (DRPs) incidence in COPD patients, mainly due to non-adherence and incorrect drug use techniques. Based on data from Apikoglu-Rabus et al. (2016), 25% of patients forgot to take medication. Meanwhile, Li et al. (2019) noted that 13.5% of patients misused drugs and 1.6% had incorrect administration timing, evidence that patient use aspects are critical in COPD therapy effectiveness.[7,14]. Incorrect inhaler technique use was also significantly found in the Rodrigues et al. (2021) study, where 79% of patients misused inhalers. Only 22.8% of intervention and 21.6% of control patients used pMDI properly. [20]Non-adherence, especially to inhaled corticosteroid use, has been proven to be closely related to increased exacerbations.[21]. Incorrect inhalation technique reduces drug effectiveness and triggers symptom worsening. Therefore, patient education, correct inhalation technique training, and good communication between patients and healthcare professionals become essential strategies to suppress DRPs and improve therapy outcomes.

**Others**

The "others" category in Drug-Related Problems (DRPs) incidence in COPD patients includes factors not specifically classified but still have a clinical impact. Li et al. (2019) reported that 12.1% of DRPs were caused by inadequate therapy outcome monitoring, such as a lack of blood glucose monitoring after high-dose glucocorticoid administration in COPD patients with diabetes, which can cause hyperglycemia.[14]. Apikoglu-Rabus et al. (2016) also noted that 7.8% of similar cases were not explained in detail but still showed an essential contribution from this category.[7]. Overall, this category reflects weak therapy monitoring, lack of education, and minimal patient involvement, potentially worsening disease control and increasing exacerbation risk.

**Pharmacist Role in Managing DRPs in COPD Patients**

Drug-Related Problems (DRPs) in COPD patients include errors in drug selection, dose, therapy duration, drug use techniques, and patient adherence, all of which require special attention from pharmacists. Based on data from Li et al., (2019), the most dominant errors are in treatment safety aspects (54.2%) and excessively high doses (19.9%), as well as unduly long therapy duration (17.7%)[14]. Pharmacists are essential in conducting therapy rationality assessments to prevent these errors. Additionally, inappropriate drug combinations, including interactions with herbal medicines (8.7%), as Li et al., (2019) dan Adisa et al., (2024), shows the need for medication review by pharmacists to prevent adverse effects[14,20].

Problems with medication adherence and proper inhaler technique use can also affect poor disease control. Adherence barriers in COPD patients include lack of knowledge (30.7%) and practical barriers (36.5%) [20]. This emphasizes the importance of pharmacists' education on the inhalation technique as part of clinical pharmacy services. Technology development to help patients improve adherence and continuous education has become essential in preventing related DRP incidence.



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Additionally, weak therapy monitoring, as reported by Li et al., (2019) (12,1%) contributes to DRPs that risk increasing drug side effects[14]. Here, the pharmacist's role in pharmacovigilance becomes crucial. Overall, data from various studies show that proactive pharmacist involvement in DRP management through therapy review, education, monitoring, and interprofessional collaboration contributes significantly to reducing exacerbation risk, improving adherence, and optimizing disease control in COPD patients.

**Limitations of the Study**

The diversity of study designs among the analyzed literature provides valuable insights into Drug-Related Problems (DRPs) in patients with Chronic Obstructive Pulmonary Disease (COPD). However, heterogeneity in research methods, population characteristics, and the classification systems used to identify DRPs, such as differences in the application of the PCNE classification version (e.g., PCNE V9.0 vs. other versions), poses significant limitations. These variations hinder the ability to conduct a robust and consistent quantitative synthesis. Additionally, differences in how DRPs are defined and reported reduce comparability across studies and may limit the generalizability of the findings. Despite these challenges, the descriptive review still highlights key patterns and emphasizes the critical need for standardized methodologies in future DRP-related research in COPD populations.

## Conclusions

Drug-related problems (DRPs) in COPD patients remain a significant challenge in pharmaceutical practice. Based on PCNE V9.0 classification, DRPs encompass various domains, including drug selection, dose, therapy duration, and the patient drug use process. Literature shows that incorrect drug use, inappropriate doses, and lack of patient understanding are dominant factors causing DRPs. The high incidence of incorrect drug use and low adherence shows the need for continuous education, therapy monitoring, and interprofessional collaboration in pharmaceutical care practice to improve patient safety and COPD therapy effectiveness.

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No

## Authors' Contributions

Muhammad Zaini Fahmi analyzed and interpreted the data and drafted the manuscript. Hidayah Karuniawati and Wan Ismahanisa Ismail wrote the final draft.

## Conflict of Interest

The authors declare no conflicts of interest related to this study.

## Ethical Consideration

No

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