Using Simulated Patients to Understand Non-Prescription Antibiotic Dispensing in Indonesia: A Systematic Review

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Abstract

Background: Dispensing antibiotics without a prescription at community pharmacies is a significant contributor to the ongoing global public health issue of antibiotic resistance. Objectives: To estimate the proportion of antibiotics that are dispensed without a prescription in community pharmacies in various Indonesian cities. Methods: A literature review was conducted via PubMed, Science Direct, Google Scholar, Garuda, and Neliti for articles published between January 2007 and December 2022 combined with Boolean operators. The literature search keywords were (simulated patients OR mystery shopper OR sample patients OR dummy patients) AND ("antibiotics without prescription OR non-prescription antibiotics OR self-medication of antibiotics). The keywords are also used in Indonesian language (Bahasa), including “simulasi pasien” OR “sampel pasien” AND “antibiotik tanpa resep” OR “swamedikasi antibiotik”. Results: Seven studies from various cities have complied with the inclusion criteria and were considered when reviewing 199 articles. The findings of our studies were consistent with the extensive use of non-prescription antibiotics throughout the review. A simulation patient study design was used in all seven studies in this review. Amoxicillin recorded the highest percentage of dispensing without a prescription, while other drugs often purchased include chloramphenicol, ciprofloxacin, and cefadroxil. Among the studies reviewed, one study utilized the pre-test and post-test methods, while the others did not. Conclusion: The lack of prescriptions for antibiotics dispensing has often occurred in community pharmacies throughout Indonesia. The community pharmacist’s role is needed as the final gate of pharmaceutical services in providing rational treatment and controlling the dispense of antibiotics without a prescription.

Keywords: antibiotics, mystery shopper, self-medication, simulated patients

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INTRODUCTION

The effects of antibiotic resistance on morbidity, mortality, and healthcare expenditure illustrate that it is one of the world's most pressing public health issues. Low- and middle-income countries (LMICs) are particularly at risk due to the increasing use of antibiotics in their populations (Klein et al., 2018). Community pharmacies and drug stores, which are part of the private drug retail sector, are often the first point of care for minor illnesses in many LMICs because they are close by, trustworthy, easily accessible, and provide essential medicines, such as antibiotics, often without a prescription (Miller and Goodman, 2016; Suy et al., 2019). Antibiotics are readily accessible in urban areas, and people can obtain them from pharmacies and drugstores without the need for prescriptions, even though this practice is against national regulations. This stems from the term "antibiotic therapy" where it's believed that antibiotics could cure many common illnesses such as diarrhea, flu, and many others (Wulandari et al., 2021).

The World Health Organization (WHO) has warned that LMICs misuse between 20% and 50% of antibiotics. According to previous studies, more than two-thirds of the antibiotic sales in the pharmaceutical industry in LMICs are attributed to self-medication (Torres et al., 2019). Indonesia and the rest of Southeast Asia are at the epicenter of a global crisis regarding the emergence and spread of antimicrobial resistance (AMR) due to their large populations, rapid but unequal economic development, weak health systems with widely varying access to quality healthcare, high rates of infectious diseases, and lax enforcement of antibiotic policies (Limato et al., 2022).

There are 3,042 hospitals in Indonesia in 2021, 10,292 primary care clinics, 30,199 pharmacies, and an estimated 9,752 retail pharmacy stores in the community providing OTC medications. In Indonesia, community pharmacies may stand as independent institutions, be part of a larger chain, be connected to a clinic, or be part of both. Antibiotics require prescriptions and may only be supplied by a registered pharmacist. Pharmacies are not allowed to sell antibiotics without prescriptions. In addition, a licensed pharmacist or pharmacy technician must always be present in retail drug stores to monitor the medication distribution. Despite these regulations, research has shown that antibiotics can be purchased through community pharmacies without a prescription or with only a few initial assessments (Hadi et al., 2010; Limato et al., 2022; Puspitasari et al., 2011).

Extrapolating data from various nations may prove difficult as factors leading to antibiotic misbehavior may vary spatially, owing to human behavior, health literacy, economy, and legislation. Several initiatives have been implemented by governments and nonprofit organizations worldwide to decrease the improper distribution of antibiotics (Langford et al., 2021). Controlling antimicrobial resistance (AMR) in public hospitals, including monitoring antibiotic prescriptions, is one of the measures implemented by the Indonesian government to reduce inappropriate antibiotic use. Additionally, it is crucial to monitor policies to ensure that they have the desired effect (Godman et al., 2021).

The simulated patient technique has been used to increase the conformity of policy applications with real-world societal conditions (Soltani et al., 2020). This procedure is widely used to evaluate several aspects of pharmaceutical practice. Simulated patients are used to assess the quality of service, discover how customers react to cognitive benefits, and determine if pharmacy employees adopt training programs in an era when these services are increasingly being established alongside traditional dispensing and sales (Björnsdottrir et al., 2020). This is comparable to self-report methods that allow participants to provide socially desirable responses (Green and Norris, 2015).

Several studies have described the use of simulated patients to understand the dispensing of non-prescription antibiotics in Indonesia. There is a scarcity of systematic reviews on this topic. To address this gap, this study proposes the use of a systematic review to provide a complementary perspective to conclusions from non-prescribed antibiotics.

METHODS

Search strategy

Guidelines for reporting systematic reviews and meta-analyses (PRISMA) 2020 were followed for this systematic review (Page et al., 2021). Articles were sourced from three international databases (PubMed, ScienceDirect, and Google Scholar). In addition, two Indonesian databases (Garuda [Garba Rujukan Digital] and Neliti) were used to find the original articles. The use of Boolean operators (AND/OR) in the literature search yielded the following combinations of terms

- "simulated patients" OR "mystery shopper" OR "sample patients" OR "dummy patients"
- "antibiotics without prescription" OR "non-prescription antibiotics"
Selection criteria

This study evaluated whether each included article was appropriate to the selected criteria for the main research question, "How is non-prescribed use of antibiotics in Indonesia?". The study implemented the following inclusion criteria: i) research published over the last 15 years (2007-2022); ii) research studies that presented findings from primary research; iii) full-text articles that were published in the five databases mentioned above; iv) research locations in the article were carried out in Indonesia; and v) focus on using simulated patients to illustrate the dispensing of antibiotics without a prescription. The decision to focus the literature search more narrowly on several regions in Indonesia to concentrate the search more specifically on one country. Moreover, each nation may have different policies; hence, drawing comparisons between regions in several countries will bias the findings of the review. The authors crosscheck each target database search and then confirm one another to reduce bias in selecting articles in one area.

Screening and eligibility assessment

In this study, steps were taken under the established criteria. After identifying all articles that met the criteria, duplicates were removed. Subsequently, the abstracts and keywords relevant to the study were chosen. Article eligibility was determined using inclusion criteria. Afterwards, it is not only the abstracts and keywords that are read, but also all parts of the article (Patton, 2014). A content analysis of the most relevant data was performed to provide a more in-depth view of the review process and address research questions on dispensing antibiotics without prescriptions in Indonesia (Table 1).

Data extraction

The studies included 199 research articles from five databases. After removing 15 duplicate articles, 184 were screened based on their relevance to the titles and abstracts. Finally, 159 articles were excluded. Consequently, only the 25 remaining full-text articles were assessed for eligibility. Therefore, of the remaining 25 studies, 18 were excluded because they did not meet the inclusion criteria, and seven studies were included in the final systematic review. This process is illustrated in the PRISMA flowchart in Figure 1.

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**Figure 1.** PRISMA diagram outlining the screening and selection process in literature search

![PRISMA diagram](image-url)
<table>
<thead>
<tr>
<th>Authors (years)</th>
<th>Study purpose</th>
<th>Study design and location</th>
<th>Number of pharmacies involved</th>
<th>Number of pharmacies dispensed without prescription (%)</th>
<th>Symptoms of antibiotics dispensed without a prescription</th>
</tr>
</thead>
</table>
| Hadi et al., 2010 | To assess the potential connection between resistance and substandard antibiotics sold in the area | Simulated patients visited pharmacies in Surabaya to request specific antibiotics product | 104 | 79 (76%) | • Amoxicillin (n = 15)  
• Chloramphenicol (n = 18)  
• Ciprofloxacin (n = 14)  
• Cotrimoxazole (n = 14)  
• Tetracycline 250 mg (n = 15)  
• Tetracycline 500 mg (n = 2) |
| Puspitasari et al., 2011 | To assess antibiotic sales without prescription and provision of drug information services | Simulated patients visited pharmacies in Surabaya by the three scenarios for each pharmacy | 88 | 80 (91%) | • Ciprofloxacin (n = 80, 91%)  
• Tetracycline (n = 80, 91%)  
• Amoxicillin (n = 74, 84%) |
| Brata et al., 2019 | To ascertain the appropriate advice given in response to the antibiotic self-medication | Simulated patients test was conducted at community pharmacies in an eastern Indonesian provincial capital | 80 | 36 (45%) | Any antibiotics for diarrhoea |
| Saibi et al., 2020 | To assess the sale of antibiotics without a prescription and drug information services | Simulated patients collected data randomly in pharmacies located in South Tangerang | 100 | 49 (49%) | Cefadroxil for diarrhea |
| Simamora et al., 2020 | To assess antibiotic sales without a prescription | Simulated patients visited pharmacies in the district of Plaju, Kertapati, Jakabaring, and Sungai Musi (South Sumatera) | 17 | 17 (100%) | Random types of antibiotics  
• Amoxicillin (n = 9)  
• Cefadroxil (n = 2)  
• Chloramphenicol (n = 1)  
• Ciprofloxacin (n = 2)  
• Cotrimoxazole (n = 3)  
• Erythromycin (n = 3) |
| Listyorini et al., 2021 | To investigate the actions taken by pharmacists | Simulated patients visited pharmacies in 3 districts located in Tangerang | 55 | 49 (89%) | Random types of antibiotics by showing the old empty strip |
on requests for antibiotics without prescription and drug information services

| Wulandari et al., 2021 | To determine the magnitude of inappropriate dispensing of antibiotics by drug outlets in urban and rural settings | Simulated patients portrayed three different clinical case types to bought antibiotics without a prescription from pharmacies and drug outlets located in Bekasi (an urban area in West Java Province) and Tabalong district (a rural area in South Kalimantan Province) | 362 | 275 (76%) | The clinical cases included diarrhea, tuberculosis, and upper respiratory tract infection.

- Amoxicillin (n = 152)
- Trimethoprim (n = 45)
- Fradiomycin/Gramicidin (n = 39)
- Cefadroxil (n = 35)
- Ciprofloxacin (n = 17)
- Cefixime (n = 15)
- Nifuroxazide (n = 10)
- Ampicillin (n = 5)
- Others (n = 29)

RESULTS AND DISCUSSION

A total of 199 studies were identified by searching various databases, including PubMed, ScienceDirect, Google Scholar, Garuda, and Neliti. Among these, seven were included in the in-depth content analysis (Table. I). This in-depth review helped enhance the accuracy and reliability of the findings, providing valuable insights into the trends and patterns of non-prescribing antibiotic usage in Indonesia through simulated patients.

Study characteristics

All seven studies included in the review on dispensing antibiotics without a prescription from Indonesian community pharmacies used a simulated patient study design. Two studies were reported from Surabaya (Hadi et al., 2010; Puspitasari et al., 2011), one study from Tangerang (Listyorini et al., 2021), South Tangerang (Saibi et al., 2020), and eastern Indonesian provincial capital (Brata et al., 2019). Moreover, one study was conducted in four districts in Palembang (Simamora et al., 2020), and one study was conducted in urban and rural areas, namely Bekasi City and Tabalong District (Wulandari et al., 2021). The purpose of these studies was to investigate the actions taken by community pharmacists on requests for antibiotics without prescriptions. In addition, several studies have sought to assess pharmacists’ provision of drug information services for dispensing antibiotics without a prescription (Listyorini et al., 2021; Puspitasari et al., 2011; Saibi et al., 2020).

The sample size in each study differed based on the number of pharmacies in the study area. Most samples were obtained from research conducted in two cities (Bekasi and Tabalong) with 362 pharmacies, whereas the least sample was obtained from a study in Palembang, with only 17 pharmacies involved. In six studies, ethical approval from the relevant institutions was documented (Brata et al., 2019; Hadi et al., 2010; Listyorini et al., 2021; Puspitasari et al., 2011; Saibi et al., 2020; Wulandari et al., 2021), while one did not include a letter of ethical approval (Simamora et al., 2020). One study applied interaction with audio recordings to minimize bias in the study (Wulandari et al., 2021), and the remaining studies utilized a data sheet (check-list) to record information such as the purchase date, name and address of the pharmacies, the antibiotic’s name (and whether it was obtained with or without a prescription), the antibiotic’s storage conditions, the packaging type, information correctness during antibiotic dispensing, and price.

Types of Simulated patients scenarios

Multiple types of antibiotic requests, including those based on symptoms and specific products, were employed in these analyses. The simulated patients were well prepared to present their cases to pharmacists...
before their in-person visits. Five studies relied solely on direct requests using a product name (Hadi et al., 2010; Listyorini et al., 2021; Puspitasari et al., 2011; Saibi et al., 2020; Simamora et al., 2020), one study used an old empty package of antibiotics to be purchased (Listyorini et al., 2021), and one study reported that family members entrusted the antibiotics purchased (Saibi et al., 2020). Two other studies involved symptom-based requests, specifically employing instances of diarrhea scenarios (Brata et al., 2019), and diverse medical cases, including tuberculosis, diarrhea, and upper respiratory tract infection (Wulandari et al., 2021).

Six studies reported training for simulated patients before data collection, while one did not mention training for simulated patients (Simamora et al., 2020). Most studies have reported that each pharmacy was visited once by simulated patients. However, there are also studies in which pharmacies were visited more than once. For instance, to lessen the likelihood that the same staff member would attend to all three simulated patients, they spread their visits to the pharmacy for one–three days at different times of the day. They presented them with three clinical scenarios (diarrhea, tuberculosis, and upper respiratory tract infections) (Wulandari et al., 2021). Another study was designed with three scenarios for each pharmacy that were visited by three simulated patients during business hours for each of the three scenarios (ciprofloxacin, tetracycline, and amoxicillin) at different times (Puspitasari et al., 2011).

**Significant findings: inappropriate dispensing practices**

Table I displays the names and percentages of antibiotics prescribed in response to patient requests. Amoxicillin had the highest dispensing rates without prescription across all seven studies (Hadi et al., 2010; Simamora et al., 2020; Wulandari et al., 2021). Chloramphenicol, ciprofloxacin, and cefadroxil were also purchased without a prescription. Another study found that amoxicillin, the active ingredient in most over-the-counter antibiotics (86.9%), was analyzed in 61 studies (Batista et al., 2020).

Our research supports the hypothesis that non-prescription antibiotics are widely used in Indonesia. Research conducted in the districts of Plaju, Kertapati, Jakabaring, and Sungai Musi (South Sumatra Province) indicates that among the 17 pharmacies visited, each dispensed antibiotics without requiring a prescription (Simamora et al., 2020). Two studies conducted in Surabaya within a year reported similar results, with 79 and 80 pharmacies dispensing antibiotics without prescriptions, respectively (Hadi et al., 2010; Puspitasari et al., 2011). Another study performed at pharmacies in the provincial capital of eastern Indonesia found that 36 of 80 pharmacies surveyed provided antibiotics without a prescription (Brata et al., 2019). Moreover, research in Tangerang showed that as many as 89% of pharmacy staff dispensed antibiotics without a prescription to simulated patients. However, simulated patients did not identify in more detail whether the staff were pharmacy technicians or others (Listyorini et al., 2021). Interestingly, one of the simulated patients received an antibiotic that was not properly labelled and was packaged in a plastic bag (Wulandari et al., 2021).

Diarrhea and respiratory issues, including tuberculosis, flu, cold, and upper respiratory tract infection, were the most prevalent reasons why antibiotics were administered without a prescription. Similarly, another study found that sore throat, fever, and respiratory disorders, including cold/flu and cough, were the most common conditions in which people used antibiotics without a doctor's prescription (Alhomoud et al., 2017).

Among the seven studies reviewed, one study used pre- and post-test methods. After observing the pre-test with the simulated patients, the pharmacist was educated. The impact of this education can be seen when conducting post-test observations: some pharmacies no longer sell antibiotics without a prescription (Simamora et al., 2020). This approach is more suitable for future research if similar research is conducted. Although it requires a longer time, it could yield a more positive impact in regulating the dispensing of antibiotics without a doctor's prescription.

There are several reasons that may contribute to the dispensing of antibiotics without prescriptions. The most probable cause is the lax approach to law enforcement (Zawahir et al., 2019). Additionally, insufficient or inefficient supervision by the Food and Drug Authority in Indonesia (BPOM) conducts inspections of pharmacies to guarantee proper pharmacy practices. Another factor is that non-licensed pharmacy personnel lack knowledge of antibiotic dispensing regulations. These field studies showed that, despite existing regulations, pharmacies in several regions of Indonesia still dispense antibiotics without a prescription. These antibiotics are available in all community pharmacies and are easy to purchase. A common concern among community pharmacists is that refusing a customer's demand for antibiotics could...
adversely affect their pharmacy business. They also think that if they do not give antibiotics, the customer will seek them elsewhere (Wulandari et al., 2021). This is among the reasons why pharmacists ultimately dispensed antibiotics without prescription. Many prior studies have analyzed this issue. Most of those who used antibiotics for self-treatment lived in Asia (51 of 89 articles) (Batista et al., 2020). Another review found that poor national medicine regulations, shortage of qualified pharmacists, commercial pressure on pharmacy staff, consumer demand, inappropriate prescribing practices, and lack of awareness of antimicrobial resistance all play a role in the sale of antimicrobials that do not require a prescription (Sakeena et al., 2018). A review of 59 articles from LMICs showed that 83.3% dispense antibiotics without a prescription (Batista et al., 2020). Another study found that antibiotics dispensed without prescription had a reasonably high proportion in South America (almost 78%) (Auta et al., 2019).

Research impacts
This systematic review revealed that the number of dispenses of antibiotics without a prescription in Indonesia remains high, particularly in regions with low levels of supervision from related government authorities. Hopefully, this review will lead the government to take stricter actions to ensure that antibiotics are not dispensed without prescription throughout Indonesia. In line with this, studies in China show that the government has striven to curtail non-prescription antibiotic dispensing (NPAD) in the past decades through stricter policies (Wang et al., 2020). Moreover, this research would also impact community pharmacists, who are required to inform the public about the risk of antibiotic resistance. There is an urgent need for community pharmacists and health workers to enhance public awareness of microbial resistance resulting from antibiotic misuse of antibiotics (Halboup et al., 2020).

This research is the initial step to provide a glimpse into some actual conditions that exist in Indonesia with regard to unprescribed antibiotics. To become a concern for policymakers in the formulation of effective policies, research needs to be more extensive and cover a wide range of areas in Indonesia. Other systematic reviews conducted in one country did not use the patient simulation method. For example, a review in Saudi Arabia, which was only concerned with the prevalence of antibiotic misuse in several cities, revealed a considerably high prevalence among the Saudi population (Alnemri et al., 2016). Alternatively, a review conducted in China aimed to estimate the prevalence of the general population's irrational use of antibiotics, including incorrect antibiotic recognition, inappropriate usage, and ignorance of potential adverse outcomes (Duan et al., 2021).

Strengths, limitations, and recommendations
This is the first systematic study to illustrate the availability of antibiotics in Indonesian community pharmacies without a doctor prescription. Owing to variations in scenario types, pharmacy counts, and environmental conditions, a unified statistical analysis was not possible. Therefore, this evaluation can only provide a descriptive analysis of the dispensing of antibiotics for self-medication in different locations. We suggest that researchers conduct studies on a broader scale in Indonesia. Thus, it can describe the conditions of the community and serve as a reference for policymakers to determine the next steps.

CONCLUSION
Based on a literature review, this study concludes that antibiotics are available without a prescription in community pharmacies in many Indonesian cities. No one can do more than community pharmacists to provide appropriate therapy and regulate over-the-counter dispensing of antibiotics. Furthermore, the government's active role in strengthening regulations and supervisory measures and driving the obligation for pharmacists to guarantee the safety of drug services according to their authority and carry out audits to ensure that these services are urgently needed to overcome this.

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CONFLICT OF INTEREST
The authors declared no conflict of interest.

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