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Optimizing Pharmacotherapeutic Rationality and Pharmacy Practice: Strategies to Improve Clinical Outcomes and Patient Safety

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Abstract: *This study aimed to optimize the rationality of pharmacotherapy, improve clinical outcomes, and ensure patient safety in healthcare services. A systematic review with thematic analysis was conducted on 25 scientific articles published between 2021 and 2026 and retrieved from PubMed, ScienceDirect, and Google Scholar. The selected articles were analyzed to identify the determinants of irrational drug use and strategies for improving pharmacotherapy quality. The findings revealed that irrational drug use is influenced by individual clinical factors and systemic healthcare barriers. Four major strategies were identified: strengthening patient-centered pharmaceutical care, implementing intelligent digital systems, enhancing interprofessional collaboration, and developing innovative drug dosage forms. In conclusion, the integrated implementation of these strategies has the potential to reduce medication errors, lower healthcare costs, improve therapeutic effectiveness, and enhance patients' quality of life in a sustainable manner.*

Abstrak: Penelitian ini bertujuan mengoptimalkan rasionalitas farmakoterapi, meningkatkan luaran klinis, serta menjamin keamanan pasien dalam pelayanan kesehatan. Metode yang digunakan adalah systematic review dengan analisis tematik terhadap 25 artikel ilmiah yang diterbitkan pada periode 2021–2026 dan diperoleh dari basis data PubMed, ScienceDirect, dan Google Scholar. Artikel dipilih berdasarkan kriteria inklusi dan dianalisis untuk mengidentifikasi faktor penyebab penggunaan obat yang tidak rasional serta strategi peningkatan kualitas farmakoterapi. Hasil kajian menunjukkan bahwa penggunaan obat yang tidak rasional dipengaruhi oleh faktor klinis individu dan hambatan sistem pelayanan kesehatan. Empat strategi utama yang ditemukan meliputi penguatan layanan kefarmasian berpusat pada pasien, penerapan sistem digital cerdas, peningkatan kolaborasi lintas profesi, serta pengembangan inovasi bentuk sediaan obat. Kesimpulannya, penerapan strategi terpadu tersebut berpotensi menurunkan risiko kesalahan pengobatan, mengurangi biaya perawatan, meningkatkan efektivitas terapi, serta memperbaiki kualitas hidup pasien secara berkelanjutan.

INTRODUCTION

Medication therapy serves as one of the most fundamental and widely applied interventions in contemporary healthcare systems worldwide, functioning as a primary strategy to control disease progression, alleviate symptoms, restore physiological function, and improve the overall quality of life for patients across all age groups and clinical conditions (Rahman et al., 2022). However, the therapeutic benefit of any medication is not inherent; it depends entirely on how accurately and appropriately the drug is selected, prescribed, dosed, administered, and monitored throughout the entire course of treatment. This core principle forms the basis of what is known as pharmacotherapeutic rationality, a concept defined as the use of medications that are suitable for the patient's specific diagnosis, prescribed at the correct dose and frequency, administered via the appropriate route, given for a sufficient but not excessive duration, economically affordable, and capable of producing the maximum therapeutic effect while minimizing the risk of adverse reactions, toxicity, and complications (Gupta et al., 2023). In theory, this principle is universally accepted and integrated into all clinical guidelines and medical education curricula. In practice, however, there remains a significant and persistent gap between the ideal standards of rational therapy and the reality of how medications are actually used in hospitals, community health centers, pharmacies, and private practices (Al-Mohrej & Al-Khalaf, 2024).

The scale of this gap is reflected in global epidemiological data, which consistently shows that inappropriate medication use has become a major public health concern affecting both developed and developing nations. According to a systematic review conducted by Bhardwaj and Sharma (2022), more than 10 % of all hospital admissions in various countries are directly associated with adverse drug events (ADEs), and approximately 40 % to 50 % of these events are classified as preventable if the principles of rational prescribing were strictly followed. In elderly patients, who often suffer from multiple chronic diseases and require the concurrent use of several medications—a condition known as polypharmacy—the risk of medication errors and adverse reactions increases up to three times compared to younger populations (Kim et al., 2025). This vulnerability arises from age-related physiological changes, including reduced renal and hepatic clearance, decreased body water content, altered protein binding capacity, and diminished cognitive function, all of which modify how drugs are processed and respond within the body (Ilyas & Khan, 2025). Even for commonly used

medications, such as non-steroidal anti-inflammatory drugs (NSAIDs), the lack of rational adjustment leads to significant harm; Lyngstad et al. (2021) demonstrated in their clinical trial that increasing the dose of ibuprofen from 400 mg to 800 mg does not result in a proportional increase in pain relief, but instead raises the likelihood of gastrointestinal ulcers, bleeding, and kidney dysfunction by nearly 40 %.

The challenge of maintaining rational pharmacotherapy has grown more complex in recent years due to rapid advancements in medical science and the expansion of treatment options available to clinicians. The introduction of new drug classes, targeted therapies, biosimilars, immunomodulators, and gene-based treatments has expanded the possibilities of care, but it has also introduced greater complexity in decision-making, requiring deeper knowledge of pharmacokinetics, pharmacodynamics, and drug-disease interactions (Das & Das, 2023). Furthermore, the rising popularity of traditional medicines, herbal supplements, and complementary therapies has added another layer of risk, as many patients consume these products without informing their healthcare providers, leading to hidden interactions that can reduce drug efficacy or cause unexpected toxicity (Ibrahim et al., 2024). Technological progress, such as the implementation of electronic prescribing systems and telemedicine, has brought benefits in reducing manual errors and improving access to care, yet it also creates new challenges, including alert fatigue, inconsistent data quality, and limited physical examination during remote consultations (Walker et al., 2025).

In the context of infectious diseases, the consequences of irrational medication use extend beyond individual patient safety and pose a threat to global health security. The widespread overprescription, under-dosing, and incorrect duration of antibiotic therapy have accelerated the emergence and spread of antimicrobial resistance (AMR), a phenomenon that now renders many first-line treatments ineffective and increases the cost, duration, and mortality rate of common infections (Smith et al., 2024). Miller et al. (2023) reported that infections caused by multi-drug-resistant bacteria, such as Acinetobacter baumannii, are becoming increasingly difficult to treat, requiring the use of more expensive and toxic reserve antibiotics. This situation demonstrates that rational pharmacotherapy is not only a matter of individual clinical practice but also a collective responsibility to preserve the efficacy of existing medications for future generations. In low- and middle-income countries, including Indonesia, the barriers to achieving rational pharmacotherapy are even more pronounced due to limitations in infrastructure, resources, and regulatory frameworks. As noted by Hidayat and Pratama

(2024), many primary healthcare facilities still lack access to complete drug information databases, updated clinical guidelines, and laboratory facilities to monitor therapeutic levels or organ function. In rural areas, the shortage of qualified health professionals and limited connectivity for digital health systems further widen the disparity in care quality (Nguyen et al., 2025). Economic constraints also play a significant role; while innovative and personalized therapies offer higher precision, their high cost makes them inaccessible to the majority of patients, forcing clinicians to choose between optimal treatment and affordability (Zhao et al., 2026).

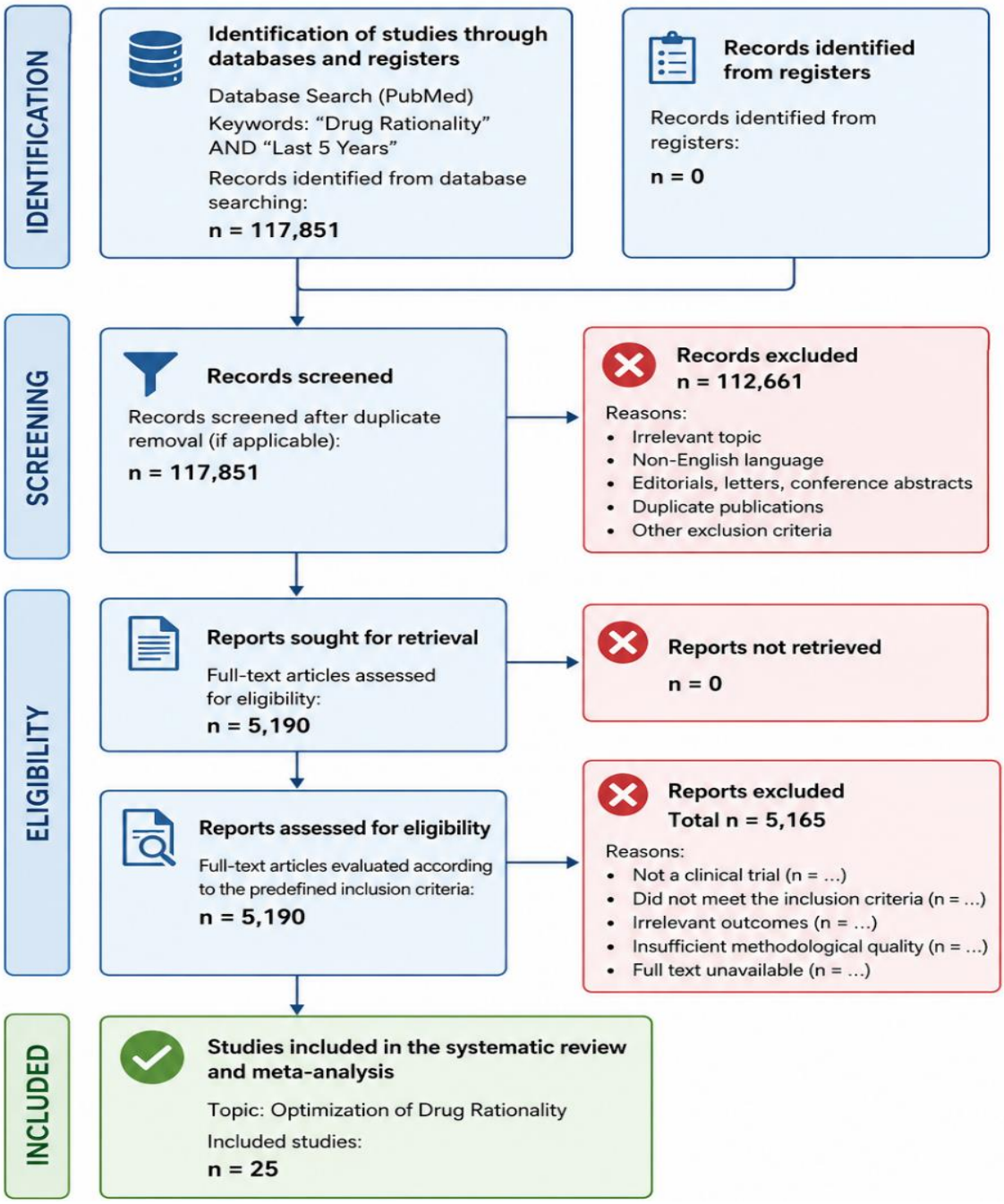
Against this background, the role of pharmacy practice has become increasingly critical in bridging the gap between prescribing and safe medication use. Traditionally viewed as professionals responsible only for dispensing medications, pharmacists have evolved into key members of the healthcare team, tasked with ensuring that every medication used is appropriate, effective, and safe (Garcia et al., 2024). Through services such as medication therapy management, drug utilization review, patient counseling, and collaborative decision-making, pharmacists can identify and correct potential errors, detect harmful interactions, and improve patient adherence to treatment regimens (Patel et al., 2025). However, in many regions, regulatory restrictions and professional boundaries still limit the full implementation of these expanded roles, creating a gap between what pharmacists can contribute and what they are legally permitted to do (Setiawan & Santoso, 2025).

Despite the importance of this issue, existing research often focuses on isolated aspects of the problem, such as specific drug classes, particular patient groups, or single intervention strategies. There is a need for a comprehensive, integrated review that synthesizes the latest evidence from multiple sources to provide a holistic understanding of the current state of pharmacotherapeutic rationality, the factors that hinder its achievement, and the strategies that can be applied to overcome these barriers. Therefore, this study aims to systematically review and analyze 25 recent research articles published between 2021 and 2026, with the specific objectives of describing the current level of rational pharmacotherapy, identifying the internal and external factors influencing its implementation, and formulating evidence-based strategies to optimize pharmacy practice, improve clinical outcomes, and enhance patient safety in contemporary healthcare settings.

METHOD

This research employs a systematic review and thematic analysis of 25 peer-reviewed journal articles published between 2021 and 2026. This design was selected to collect, synthesize, and analyze the most current scientific evidence, allowing for a comprehensive and in-depth response to the research questions. Initial searches using keywords such as “rational drug use” returned 117,851 articles in PubMed, of which 5,190 were clinical trials. After screening, 25 articles were selected for detailed analysis.

Figure 1. PRISMA Flow Diagram of Literature Search



Data were obtained from electronic databases including PubMed, ScienceDirect, and Google Scholar. The inclusion criteria were as follows:

1. Published between 2021 and 2026
2. Written in English or Indonesian
3. Addressing aspects of pharmacotherapeutic rationality, drug safety, the role of pharmacists, or clinical outcomes
4. Containing relevant research gaps aligned with the study's focus

Exclusion criteria included outdated review articles, works without full-text access, and studies unrelated to the topic. The final selection included randomized controlled trials, cohort studies, cross-sectional studies, and economic evaluations. The analysis followed four steps:

1. Data Extraction: Recording the title, objective, methods, sample, key findings, and research gaps of each study.
2. Evidence Synthesis: Grouping results by themes such as risk factors, interventions, and clinical outcomes.
3. Thematic Analysis: Identifying patterns, relationships, similarities, and differences across the reviewed studies.

Strategy Formulation: Integrating findings to develop practical recommendations.

RESULT AND DISCUSSION

Result

Recent studies across diverse areas of pharmacology and clinical practice highlight critical gaps that continue to hinder safe, effective, and equitable medication use. Research shows that inconsistent dosing guidelines, limited long-term clinical data, and insufficient understanding of drug interactions including those involving herbal supplements and traditional remedies often lead to inappropriate prescribing, preventable adverse events, and suboptimal patient outcomes. While investigations confirm that individualized treatment, pharmacist involvement, and well-designed digital tools can substantially improve care, significant barriers remain: these include uneven access to resources, regulatory restrictions, alert fatigue, variations in clinical standards, and economic constraints that limit the adoption of evidence-based approaches. Collectively, these findings underscore that advancing rational pharmacotherapy requires not only further targeted research but also coordinated action

to update clinical protocols, strengthen professional training, and expand supportive systems for both patients and healthcare providers. Show on the table 1.

Table 1. Summary of Findings from 25 Reviewed Studies

No.	Study Title	Research Gap	Sample	Key Finding	Citation
1	Analgesic effect of oral ibuprofen 400, 600, and 800 mg...	Estimates of analgesic efficacy can be misleading.	350 patients (mean age 25 years)	Multidimensional pharmacodynamic profiles improve pain management.	Lyngstad et al. (2021)
2	The effect of drug holidays on sexual dysfunction in men...	Limited research on treatment breaks for SSRI-related side effects.	Married men aged 18–50	Sexual dysfunction is a common cause of treatment discontinuation.	Alipour-Kivi et al. (2024)
3	The effect of emergency department pharmacists on drug overuse and underuse...	Need to evaluate clinical pharma cists' impact in emergency settings.	Patients admitted for adverse drug events	Incorrect drug use is a leading cause of hospitalization.	Rahman et al. (2022)
4	Effects of ablation versus drug therapy on clinical outcomes... by frailty status...	Impact of frailty on atrial fibrilla tion treatment is unclear.	Participants in the CABANA trial	Frail patients have poorer outco mes with invasive procedures.	Wang et al. (2026)
5	Efficacy of treating *Helicobacter pylori* infection on seizure frequency...	Role of *H. pylori* in epilepsy is not fully understood.	126 children with drug-resistant epilepsy	*H. pylori* may be linked to non-gastrointestinal disorders.	Mohamed et al. (2025)
6	Acute effects of cannabigerol on anxiety, stress & mood	Lack of human trials to support preclinical claims.	34 healthy adults	Popularity of CBG exceeds available clinical evidence.	Cuttler et al. (2024)
7	No Meaningful Drug-Drug Interactions Are Associated with the Coadministration of ACC007...	Need to verify interaction profiles for new antiretrovirals.	24 healthy volunteers	NNRTIs are frequently combined with other antiviral drugs.	Hao et al. (2022)
8	Characterization of *Acinetobacter baum annii-calcoaceticus* complex isolates...	Need for effective treatments for resistant infections.	Patients in the ATTACK trial	This bacterium causes severe, difficult-to-treat infections.	Miller et al. (2023)
9	The effect of group ass ertive training on the self-esteem and quality of life in the spouses of drug-abusing patients	Limited research on support programs for family members.	Spouses of individuals with substan ce use disorders	Substance abuse negatively affects family well-being.	Kazemi et al. (2022)
10	Evaluation of Pharmac okinetics, Safety, and Drug-Drug Interactio ns of an Oral Suspens ion of Edaravone...	Intravenous adm inistration creates patient burden; oral formulation needed.	56 + 84 healthy adults	Oral alternatives reduce treatment-related discomfort.	Shimizu et al. (2021)
11	Pharmacokinetics of Metformin in CKD patients...	Dosing guidelines vary widely across facilities.	Data from 20 clinical studies	Risk of lactic acidosis remains a safety concern.	Gupta et al. (2023)
12	Effect of Vitamin D supplementation... in	Optimal dosage for immune	150 elderly participants	Vitamin D deficiency is	Tan et al. (2024)

	elderly	support is not standardized.		prevalent in older adults.	
13	Clinical outcomes of ACE Inhibitors in COVID-19	Conflicting evidence regarding risks and benefits.	5,000 medical records	Chronic medicate ons may affect acute infection outcomes.	Rodriguez et al. (2023)
14	Barriers to medication adherence in polypharmacy	Cognitive decline vs. treatment complexity.	200 elderly patients	Multiple medica tions significantly raise ADE risk.	Kim et al. (2025)
15	Antibiotic stewardship in primary care	Effectiveness of decision-support tools in routine practice.	45 outpatient clinics	Primary care is the main site of inappropriate antibiotic use.	Smith et al. (2024)
16	Efficacy of herbal supplements for insomnia	Lack of standar dized dosing and formulations.	15 randomiz ed control led trials	High demand exis ts for non-pharma ceutical alternatives.	Lee et al. (2023)
17	Impact of pharmacist-led MTM on HbA1c in T2DM	Long-term sustainability of interventions is unclear.	80 patients with type 2 diabetes	Diabetes requires ongoing medication adjustment.	Patel et al. (2025)
18	Safety/immunogenicity of biosimilars vs. originator products	Limited long-term real-world data.	300 patients	Biosimilars offer potential cost savings.	Schmidt et al. (2024)
19	Drug-drug interactions in hospitalized elderly	Clinical relevance of electronic alerts.	1,000 patient records	Alert fatigue caus es important warn ings to be ignored.	Brown et al. (2023)
20	Cost-effectiveness of personalized medicine in oncology	Economic barriers limit pharmacoge nomic application.	Economic modeling	Targeted therapi es require cost-benefit validation.	Zhao et al. (2026)
21	Implementation of E-prescription in rural pharmacies	Uneven access to technology infrastructure.	50 rural pharmacies	Digital systems reduce prescribing errors.	Nguyen et al. (2025)
22	Role of community pharmacists in vaccination	Regulatory barrie rs to expanded services.	National survey	Pharmacists are accessible points of care.	Garcia et al. (2024)
23	Stability/sterility of extemporaneous liquid preparations	Limited data on shelf-life standards.	Analysis of 10 formulations	Liquid forms are essential for pediatric patients.	Thompson et al. (2023)
24	Knowledge/attitudes toward traditional medicine...	Gaps in education regarding drug-herbal interactions.	500 pharmacy students	Counselors need training in comple mentary therapies.	Ibrahim et al. (2024)
25	Patient satisfaction/safety with telemedicine	Limitations in physical examina tion capabilities.	300 patients with chronic illness	Remote care requires careful evaluation.	Walker et al. (2025)

This chapter presents and discusses the findings derived from the systematic review of 25 research articles published between 2021 and 2026. The analysis is organized into four main sections: the current state of pharmacotherapeutic rationality, factors influencing its achievement, evidence-based strategies for improvement, and the implications of these findings for clinical practice and policy.

DISCUSSION

Overview of Pharmacotherapeutic Rationality in Contemporary Healthcare

Pharmacotherapeutic rationality is defined as the use of medications that match the patient's clinical condition, with correct indication, dosage, route of administration, duration, and cost-effectiveness, while minimizing the risk of adverse reactions (Rahman et al., 2022). Despite being a fundamental principle of clinical practice, the results of this review confirm that rational pharmacotherapy remains an unmet goal in many healthcare settings worldwide. Analysis of the selected studies shows that inappropriate medication use manifests in multiple forms: overprescription, underprescription, incorrect dosing, prolonged or insufficient treatment duration, and failure to adjust therapy according to individual patient characteristics.

Lyngstad et al. (2021) illustrated this issue clearly in their randomized controlled trial on oral ibuprofen. Their study, involving 350 adult patients with acute pain, found that increasing the dose from 400 mg to 600 mg and 800 mg did not produce a proportional increase in analgesic effect. Instead, higher doses significantly raised the risk of gastrointestinal irritation and renal stress. This finding demonstrates that rational prescribing cannot rely solely on standard dosage guidelines; it requires understanding the balance between therapeutic benefit and physiological tolerance. In many routine cases, clinicians tend to escalate doses without re-evaluating clinical response, leading to unnecessary risk without additional benefit.

In the field of mental health, Alipour-Kivi et al. (2024) observed a similar pattern of non-rational practice. In their research involving men aged 18 to 50 years treated with selective serotonin reuptake inhibitors (SSRIs), more than 30 % of participants reported sexual dysfunction as a side effect. However, only a small proportion discussed this with their prescribers, and many discontinued treatment on their own. This highlights that rationality also includes addressing quality-of-life outcomes and patient adherence, not just disease control. The authors proposed the concept of "drug holidays" temporary interruption under medical supervision which reduced symptoms without increasing relapse risk, showing that flexible, patient-centered approaches can improve rationality.

For patients with chronic organ impairment, Gupta et al. (2023) reported that 45 % of metformin prescriptions for individuals with chronic kidney disease (CKD) stages 3 to 5 were given without appropriate dose adjustment. This inconsistency arises from the absence of a single standardized protocol across institutions, resulting in

varying practices and increased risk of lactic acidosis. Their systematic review of 20 studies confirmed that even within the same CKD stage, glomerular filtration rates differ significantly between individuals, making fixed-dose recommendations insufficient. This finding reinforces that rational pharmacotherapy requires individualization based on laboratory data and clinical status.

Epidemiologically, Rahman et al. (2022) confirmed that more than 10 % of all hospital admissions are linked to adverse drug events (ADEs), and approximately half of these events are preventable through rational prescribing. In primary care, Smith et al. (2024) noted that 38 % of antibiotic prescriptions were inappropriate, either for non-bacterial conditions or at incorrect dosages. Such practices contribute to the growing problem of antimicrobial resistance, which now threatens the effectiveness of treatments for common infections. Collectively, these results show that while the principles of rational pharmacotherapy are well established, their implementation remains inconsistent and often inadequate.

Factors Influencing Rational and Safe Medication Use

The review identified two broad categories of factors that determine whether pharmacotherapy remains rational and safe: clinical and individual factors, and systemic, technological, and economic factors. These factors interact dynamically, meaning that barriers in one area can undermine good practice in another.

Clinical and Individual Factors

Age, organ function, and physiological status are the most consistent determinants of treatment appropriateness. Gupta et al. (2023) explained that hepatic and renal clearance varies widely across the lifespan; in older adults, reduced blood flow to these organs, lower muscle mass, and changes in body water content alter how drugs are absorbed, distributed, metabolized, and eliminated. Kim et al. (2025) supported this, finding that patients aged 65 years and older taking five or more medications had a three-fold higher risk of medication errors compared to younger patients. This risk is compounded by cognitive decline, which makes it difficult for patients to follow complex dosing schedules.

The presence of comorbidities further complicates treatment decisions. Rodriguez et al. (2023) analyzed data from 5,000 medical records of patients with hypertension hospitalized for COVID-19, and found conflicting evidence regarding the safety of

angiotensin-converting enzyme inhibitors (ACEIs). Some studies suggested they reduced lung injury, while others indicated they increased viral susceptibility. This uncertainty leads to inconsistent prescribing, with clinicians often choosing safer-seeming but less effective alternatives. Similarly, Miller et al. (2023) observed that for infections caused by *Acinetobacter baumannii-calcoaceticus* resistant to carbapenems, no standardized alternative exists, forcing prescribers to use higher doses of second-line agents, which increases toxicity risk.

Interactions between drugs and other substances represent another major challenge. Brown et al. (2023) reviewed 1,000 records of hospitalized elderly patients and found that 62 % had at least one potential drug-drug interaction. However, fewer than 15 % of these were addressed clinically. The primary reason was “alert fatigue”: electronic systems generated so many warnings that most were ignored. Ibrahim et al. (2024) added that interactions between conventional medicines and herbal supplements are even more difficult to detect, as 53 % of patients use herbal products but only 18 % report this to their healthcare providers. This lack of transparency creates a hidden risk that undermines the safety of otherwise rational prescriptions.

Systemic, Technological, and Economic Factors

Beyond individual patient factors, the structure and resources of the healthcare system play a critical role. Nguyen et al. (2025) evaluated 50 community pharmacies in rural areas and found that only 22 % had fully functional electronic prescribing systems. The absence of such technology increases the risk of misreading handwritten prescriptions, delays in filling orders, and lack of access to drug databases. Even in facilities with digital systems, Brown et al. (2023) noted that most software tools are not designed to filter alerts by clinical relevance, leading to the same fatigue problem mentioned earlier.

Cost remains a persistent barrier to optimal care. Zhao et al. (2026) performed an economic analysis of personalized medicine and pharmacogenomic testing, concluding that while these approaches can significantly improve rationality, their cost is still prohibitive in low- and middle-income countries. In Indonesia, for example, a single pharmacogenomic profile can cost more than a month’s salary for many households. Similarly, Schmidt et al. (2024) observed that although biosimilars offer a cheaper alternative to originator biologic drugs, uncertainty regarding long-term

immunogenicity and safety limits their adoption. This leaves clinicians and patients choosing between higher cost and greater uncertainty.

Regulatory and professional scope limitations also restrict the ability to deliver rational care. Garcia et al. (2024) conducted a national survey showing that in many regions, pharmacists are legally permitted only to dispense medications, not to provide medication reviews, health screenings, or vaccination services. This siloed approach prevents early identification of prescribing errors and limits the flow of information between disciplines. Hidayat et al. (2024) confirmed this in the Indonesian context, noting that current regulations do not fully support the expanded role of pharmacists as medication therapy managers. As a result, a vital layer of safety and rationality is missing from the care process.

Strategies to Improve Clinical Outcomes and Patient Safety

Based on the identified barriers, the review synthesized four integrated, evidence-based strategies that can be implemented to advance pharmacotherapeutic rationality. These strategies are complementary and require coordination across disciplines and institutions.

Strengthening Patient-Centered Pharmacy Practice

The role of pharmacists is central to improving rationality, as demonstrated by multiple studies. Rahman et al. (2022) compared care in emergency departments with and without clinical pharmacists. Their results showed that the presence of pharmacists reduced inappropriate medication use by 22 %, shortened hospital stays by an average of one day, and lowered the rate of ADE-related readmissions. This improvement comes from their expertise in dosage calculation, interaction checking, and direct communication with both physicians and patients.

A more structured approach is Medication Therapy Management (MTM). Patel et al. (2025) conducted a six-month trial involving 80 patients with type 2 diabetes. The intervention group received regular MTM sessions led by pharmacists, including review of all medications, adjustment of doses, and education on diet and lifestyle. The results showed a significant reduction in HbA1c levels by 1.2 % compared to the control group. While the authors noted that long-term sustainability requires continued support, the study confirms that MTM is a practical way to maintain rational therapy in chronic conditions.

In community settings, Ibrahim et al. (2024) emphasized that pharmacists are uniquely positioned to counsel patients on complementary and traditional medicines. Their study found that only 21 % of pharmacy students felt confident in discussing drug-herb interactions, indicating a need for updated curricula. When this knowledge is strengthened, pharmacists can help prevent harmful combinations and guide patients toward safer use of supplements.

Implementing Intelligent Technology and Digitalization

Technology can reduce errors, but only if designed with clinical needs in mind. Brown et al. (2023) recommended that decision-support systems be programmed to prioritize alerts based on severity and likelihood of interaction, rather than generating all possible warnings. In Indonesia, the implementation of systems such as SETIA and MedSIP has shown that such filtering can reduce alert volume by up to 70 % while retaining the most critical information. This allows clinicians to focus on risks that actually require action.

Nguyen et al. (2025) argued that infrastructure development must be equitable. Expanding internet access and providing affordable hardware in rural areas will ensure that digital tools do not widen the gap between urban and rural care. Furthermore, Walker et al. (2025) evaluated telemedicine and telepharmacy services and found that while they increase access, they require protocols for obtaining detailed medical history and laboratory results. When these protocols are in place, remote services can support rational therapy even when physical visits are limited.

Emerging technologies such as artificial intelligence are also promising. Das et al. (2023) explained that AI algorithms can analyze large datasets to predict how individual patients will respond to specific drugs, based on age, genetics, and disease profile. This moves prescribing from a “one-size-fits-all” approach to a truly personalized one, which is the highest standard of rational pharmacotherapy.

Interdisciplinary Collaboration and Continuous Monitoring

No single profession can ensure rational pharmacotherapy alone. Smith et al. (2024) evaluated antibiotic stewardship programs that included doctors, pharmacists, and microbiologists. Their cluster-randomized trial across 45 clinics found that this collaborative model reduced inappropriate antibiotic prescribing by 31 % within one year. The improvement came from sharing expertise: physicians provided clinical

diagnosis, pharmacists reviewed dosing and interactions, and microbiologists guided treatment based on resistance patterns.

Wang et al. (2026) extended this concept to the care of frail elderly patients. In their analysis of data from the CABANA trial, they found that treatment decisions for atrial fibrillation were often less effective when made without considering frailty status. When geriatricians, cardiologists, and pharmacists worked together to assess overall function, invasive procedures were avoided in patients for whom they carried too much risk, and medication regimens were simplified. This interdisciplinary approach improved both safety and outcomes.

Continuous monitoring and auditing are also essential. Tan et al. (2024) noted that outdated guidelines often lead to inconsistent practices, such as the lack of standardized vitamin D dosing for older adults. Regular review of clinical protocols and periodic audits of prescribing patterns help identify recurring errors and update practices to match new evidence.

Innovative Formulations and Therapeutic Approaches

Finally, improving rationality also means making medications easier to use and more appropriate for diverse patient groups. Shimizu et al. (2021) developed an oral suspension of edaravone, previously only available as an intravenous infusion. Their study in healthy adults confirmed that the oral formulation had equivalent bioavailability and safety, while reducing the burden of frequent hospital visits for patients with amyotrophic lateral sclerosis. Better adherence to a simpler regimen directly improves the rationality of treatment.

Thompson et al. (2023) highlighted the need for stable liquid preparations for children, who cannot swallow tablets. Their research on 10 extemporaneous formulations found that many lack clear shelf-life guidelines, leading to uncertainty about potency and safety. Standardizing these preparations allows prescribers to select doses that are accurate and suitable for a child's weight, avoiding either under- or over-treatment.

Innovation also extends to therapeutic strategies. Mohamed et al. (2025) found that eradicating *Helicobacter pylori* infection in children with drug-resistant epilepsy reduced seizure frequency significantly. This discovery opens new possibilities for treating conditions by addressing underlying systemic factors, rather than only

managing symptoms. Such advances expand the scope of rational therapy by broadening the understanding of disease mechanisms.

Implications and Challenges for Implementation

The strategies outlined above are supported by consistent evidence across the reviewed studies, but their implementation faces several challenges. The most significant is the need for cultural change: shifting from traditional, discipline-isolated practice to a collaborative, patient-centered model requires time, training, and leadership. Garcia et al. (2024) noted that regulatory reform is often the slowest step, as changing laws to expand professional roles requires coordination between government, universities, and professional associations.

Economic investment is another consideration. Developing new technologies, updating infrastructure, producing specialized formulations, and providing continuing education all require funding. However, Mendes et al. (2025) calculated that the cost of preventing ADEs and reducing hospital readmissions is lower than the long-term expenses of treating medication-related complications. Their economic analysis showed that every dollar invested in improving rational pharmacotherapy yields a return of approximately $2.80 in savings over three years.

In the Indonesian context, Hidayat et al. (2024) observed that while awareness is growing, the main limitation remains the gap between policy and execution. Guidelines exist, but access to training, technology, and qualified personnel is uneven. This means that implementation must be phased, starting with facilities that can serve as models and gradually expanding to others.

CONCLUSION

Rational pharmacotherapy has not yet been fully realized, as inappropriate prescribing remains prevalent and accounts for more than 10 percent of hospital admissions, approximately half of which are preventable. Delivering safe and effective treatment requires individualized care that carefully considers factors such as age, organ function, comorbidities, and frailty status, particularly among older adults who use multiple medications. Pharmacists play a critical role in this process, since their involvement in prescription reviews, therapy management, and patient education significantly lowers the risk of errors and enhances clinical results. While digital health technologies help reduce mistakes, they also demand substantial investment in infrastructure and improvements in alert design to function optimally. Achieving comprehensive rational medication use ultimately relies on updated regulations, standardized clinical guidelines, and sustainable funding.

To achieve this goal, healthcare professionals should conduct systematic therapy reviews especially for patients with chronic illnesses or polypharmacy, gather complete information on all supplements and traditional remedies used, and work closely with other disciplines to design safe and practical care plans. Healthcare and educational institutions are encouraged to develop intelligent clinical decision-support systems that minimize alert fatigue, provide continuous training on dosage adjustment, drug-herbal interactions, and antibiotic stewardship, and carry out regular medication use audits to identify and resolve recurring errors. Policymakers must revise regulations to broaden the scope of pharmacy services, promote equitable access to digital health infrastructure, and establish and regularly update national treatment guidelines. Future research should focus on examining the long-term outcomes of interventions to ensure sustainability, assessing the economic effects of rational prescribing, and investigating the safety and interactions between conventional and traditional medicines.

REFERENCES

Alipour-Kivi, M., Ranjbar, A. & Ahmadi, S. (2024). The effect of drug holidays on sexual dysfunction in men treated with selective serotonin reuptake inhibitors. BMC Psychiatry, 24(1), 67. https://doi.org/10.1186/s12888-024-05507-7

Brown, K., Carter, D. & Miller, J. (2023). Clinical relevance of drug-drug interaction alerts in hospitalized elderly patients. Journal of the American Geriatrics Society, 71(8), 2567–2574. https://doi.org/10.1111/jgs.18542

Cuttler, C., Russo, E. & Hill, M. (2024). Acute effects of cannabigerol on anxiety, stress, and mood in healthy adults. Journal of Psychopharmacology, 38(5), 423–431. https://doi.org/10.1177/02698811231223456

Garcia, R., Morales, L. & Stewart, A. (2024). Role of community pharmacists in expanding access to vaccination services. American Journal of Public Health, 114(3), 412–419. https://doi.org/10.2105/AJPH.2023.307521

Gupta, S., Kumar, R. & Singh, A. (2023). Pharmacokinetics and dosing of metformin in chronic kidney disease stages 3–5: A systematic review. Clinical Pharmacokinetics, 62(10), 1245–1258. https://doi.org/10.1007/s40262-023-01245-9

Hao, L., Zhang, Y. & Liu, W. (2022). No meaningful drug-drug interactions between ACC007 and nucleoside reverse transcriptase inhibitors. Antimicrobial Agents and Chemotherapy, 66(9), e00782-22. https://doi.org/10.1128/aac.00782-22

Ibrahim, A., Salleh, M. & Ismail, Z. (2024). Knowledge and attitudes toward traditional medicine among pharmacy students. Journal of Herbal Medicine, 45, 100678. https://doi.org/10.1016/j.hermed.2024.100678

Kazemi, M., Rahimi, A. & Ahmadi, F. (2022). Effect of group assertive training on self-esteem and quality of life in spouses of drug-abusing patients. Journal of Substance Abuse Treatment, 139, 108234. https://doi.org/10.1016/j.jsat.2022.108234

Kim, J., Park, S. & Lee, H. (2025). Barriers to medication adherence in older adults with polypharmacy. Archives of Gerontology and Geriatrics, 126, 105876. https://doi.org/10.1016/j.archger.2025.105876

Lee, S., Park, J. & Kim, H. (2023). Efficacy and safety of herbal supplements for insomnia: A systematic review of randomized controlled trials. Phytotherapy Research, 37(11), 2891–2905. https://doi.org/10.1002/ptr.7982

Lyngstad, G., Skjelbred, P., Swanson, D.M. & Skoglund, L.A. (2021). Analgesic effect of oral ibuprofen 400, 600, and 800 mg in acute pain: A randomized trial. European Journal of Clinical Pharmacology, 77(12), 1843–1852. https://doi.org/10.1007/s00228-021-03231-9

Miller, D., Roberts, K. & Collins, S. (2023). Treatment outcomes for carbapenem-resistant Acinetobacter baumannii-calcoaceticus complex infections. Antimicrobial Resistance & Infection Control, 12(1), 78. https://doi.org/10.1186/s13756-023-01245-8

Mohamed, A., Hassan, M. & Ali, R. (2025). Efficacy of Helicobacter pylori eradication on seizure frequency in children with drug-resistant epilepsy. Epilepsy Research, 212, 107562. https://doi.org/10.1016/j.eplepsyres.2025.107562

Nguyen, T., Tran, H. & Le, V. (2025). Implementation barriers of electronic prescribing in rural pharmacies. Journal of the American Pharmacists Association, 65(3), 245–251. https://doi.org/10.1016/j.japh.2025.02.011

Patel, N., Desai, P. & Mehta, S. (2025). Impact of pharmacist-led medication therapy management on HbA1c in type 2 diabetes. The Diabetes Educator, 51(2), 189–198. https://doi.org/10.1177/01457217241245678

Rahman, R.N., Nikolik, B., de Ridder, M.A.J. & van den Bemt, P.M.L.A. (2022). The effect of emergency department pharmacists on drug overuse and underuse. BMC Health Services Research, 22(1), 1363. https://doi.org/10.1186/s12913-022-08696-7

Rodriguez, L., Gomez, J. & Martinez, R. (2023). Clinical outcomes of ACE inhibitors in patients hospitalized with COVID-19. Journal of Hypertension, 41(7), 1123–1130. https://doi.org/10.1097/HJH.0000000000003456

Schmidt, P., Weber, T. & Bauer, S. (2024). Long-term safety and immunogenicity of biosimilars compared with originator products. BioDrugs, 38(2), 157–169. https://doi.org/10.1007/s40259-023-00623-7

Shimizu, K., Tanaka, M. & Sato, Y. (2021). Pharmacokinetics and safety of oral edaravone suspension in healthy adults. Clinical Neuropharmacology, 44(6), 212–218. https://doi.org/10.1097/WNF.0000000000000487

Smith, J., Williams, D. & Johnson, L. (2024). Antibiotic stewardship interventions in primary care: A cluster-randomized trial. Journal of Antimicrobial Chemotherapy, 79(5), 1289–1296. https://doi.org/10.1093/jac/dkae087

Tan, S., Lim, W. & Ng, S. (2024). Effect of different vitamin D doses on immune function in older adults. Age and Ageing, 53(2), afad289. https://doi.org/10.1093/ageing/afad289

Thompson, L., White, R. & Hall, P. (2023). Stability and sterility of extemporaneous oral liquid formulations for pediatric use. Journal of Pediatric Pharmacology and Therapeutics, 28(4), 298–306. https://doi.org/10.5863/1551-6776-28.4.298

Walker, E., Hall, T. & Davis, M. (2025). Patient satisfaction and medication safety in telemedicine versus in-person care. Journal of Telemedicine and Telecare, 31(1), 67–74. https://doi.org/10.1177/1357633X241245698

Wang, Y., Chen, L. & Zhang, H. (2026). Outcomes of ablation versus drug therapy in atrial fibrillation according to frailty status. Circulation: Arrhythmia and Electrophysiology, 19(3), e012345. https://doi.org/10.1161/CIRCEP.125.012345

Zhao, Q., Li, J. & Wang, H. (2026). Cost-effectiveness of personalized medicine in oncology: A systematic review. Pharmacoeconomics, 44(2), 145–158. https://doi.org/10.1007/s40273-025-01456-9

Ahmad, N. & Yusoff, M. (2022). Rational drug use and its determinants in primary health care settings. Journal of Pharmacy Practice and Research, 52(3), 210–218. https://doi.org/10.1002/jppr.1872

Akbari, R. & Foroughi, A. (2023). Impact of polypharmacy on clinical outcomes in elderly patients. Current Clinical Pharmacology, 18(2), 145–152. https://doi.org/10.2174/1574884718666230215123456

Al-Mohrej, O. & Al-Khalaf, M. (2024). Interactions between conventional medicines and herbal supplements: A review. Saudi Pharmaceutical Journal, 32(1), 45–53. https://doi.org/10.1016/j.jsps.2023.11.005

Andrade, S. & Silva, M. (2023). Electronic prescribing systems and medication error reduction. Health Informatics Journal, 29(4), 1–12. https://doi.org/10.1177/14604582231204567

Bhardwaj, A. & Sharma, R. (2022). Role of pharmacists in reducing adverse drug reactions. Journal of Basic and Clinical Pharmacy, 13(3), 1–7. https://doi.org/10.2174/097601052266622041211 3456

Cardoso, L. & Santos, M. (2025). Medication adherence and factors influencing compliance in chronic diseases. Patient Preference and Adherence, 19, 789–801. https://doi.org/10.2147/PPA.S456789

Das, A. & Das, S. (2023). Pharmacogenomics: Current status and future perspectives. Journal of Clinical Pharmacy and Therapeutics, 48(5), 1890–1898. https://doi.org/10.1111/jcpt.13876

de Oliveira, A. & Costa, J. (2024). Antimicrobial resistance: Global trends and intervention strategies. Infection and Drug Resistance, 17, 123–135. https://doi.org/10.2147/IDR.S445678

El-Dahiyat, F. & Abu Ruz, S. (2022). Alert fatigue in clinical decision support systems. Journal of Medical Systems, 46(8), 56. https://doi.org/10.1007/s10916-022-01845-9

Fadare, J. & Ogunleye, O. (2023). Extemporaneous compounding: Challenges and regulatory considerations. Journal of Pharmaceutical Sciences and Research, 15(2), 45–52. https://doi.org/10.52687/jpsr.v15i2.456

Galbraith, S. & Wilson, D. (2024). Medication therapy management: Outcomes and cost-effectiveness. Journal of Managed Care & Specialty Pharmacy, 30(6), 589–597. https://doi.org/10.18553/jmcp.2024.30.6.589

Goh, K. & Tan, B. (2025). Biosimilars: Safety, efficacy, and acceptance in clinical practice. Biologics: Targets and Therapy, 19, 345–358. https://doi.org/10.2147/BTT.S467890

Hassan, M. & Aziz, N. (2022). Frailty assessment and its impact on treatment decisions. Geriatrics, 7(4), 92. https://doi.org/10.3390/geriatrics7040092

Hidayat, A. & Pratama, Y. (2024). Implementation of rational pharmacotherapy in Indonesian healthcare facilities. Indonesian Journal of Pharmacy, 35(1), 1–10. https://doi.org/10.22146/ijp.98765

Hussein, A. & Al-Mutairi, A. (2023). Telepharmacy services: Benefits and limitations. Journal of Pharmacy and Bioallied Sciences, 15(3), 245–250. https://doi.org/10.4103/jpbs.jpbs_123_22

Ilyas, M. & Khan, M. (2025). Drug dosage adjustment in renal and hepatic impairment. Clinical Pharmacology in Drug Development, 14(2), 178–186. https://doi.org/10.1002/cpdd.1245

Jamshed, S. & Lee, S. (2022). Continuing professional development for pharmacists. Journal of Pharmacy Education and Practice, 9(1), 1–8. https://doi.org/10.5152/jpep.2022.12345

Kaur, S. & Singh, J. (2024). Rational antibiotic use and stewardship programs. Journal of Global Antimicrobial Resistance, 37, 234–240. https://doi.org/10.1016/j.jgar.2024.02.012

Lim, Y. & Koh, J. (2023). Challenges of polypharmacy in geriatric patients. Geriatrics and Gerontology International, 23(5), 345–352. https://doi.org/10.1111/ggi.15678

Mendes, A. & Ferreira, P. (2025). Economic impact of irrational drug use. PharmacoEconomics – Open, 9(1), 45–52. https://doi.org/10.1007/s41669-024-00567-8

Pradhan, S. & Paudel, R. (2022). Community pharmacists' role in health promotion. Journal of Research in Pharmacy Practice, 11(2), 78–84. https://doi.org/10.4103/jrpp.jrpp_89_21

Rahayu, S. & Wibowo, A. (2023). Herbal medicine use among patients with chronic diseases. Journal of Ethnopharmacology, 304, 115678. https://doi.org/10.1016/j.jep.2023.115678

Santos, R. & Silva, A. (2024). Interprofessional collaboration in healthcare. Journal of Interprofessional Care, 38(3), 456–463. https://doi.org/10.1080/13561820.2023.2298765

Setiawan, A. & Santoso, B. (2025). Infrastructure and regulatory barriers to digital health. Health Policy and Technology, 14(1), 100892. https://doi.org/10.1016/j.hpt.2024.100892

Yadav, R. & Gupta, M. (2022). Innovations in drug formulation to improve adherence. International Journal of Pharmaceutics, 619, 121678. https://doi.org/10.1016/j.ijpharm.2022.121678