



Patterns and Determinants of Opioid Analgesic Utilization: A Narrative Review

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ABSTRACT :

Background: Opioid analgesics remain important medicines for the management of moderate-to-severe acute pain, perioperative pain, cancer-related pain, palliative-care needs, and selected chronic pain conditions. However, variation in prescribing, prolonged exposure, potentially inappropriate utilization, and unequal access to analgesic treatment have generated continuing concerns regarding medication safety and quality of pain management. Drug utilization research provides a framework for examining patterns of medicine use, identifying determinants of prescribing, and evaluating the appropriateness and consequences of opioid exposure.

Objective: This narrative review synthesizes evidence concerning patterns and determinants of opioid analgesic utilization across outpatient, emergency, inpatient, postoperative, chronic non-cancer pain, cancer and palliative-care settings. It further examines approaches used to quantify opioid utilization, patient-, prescriber- and system-level determinants, potentially inappropriate utilization, opioid stewardship interventions, the role of clinical pharmacists, and important gaps in current research.

Methods: A narrative literature synthesis was undertaken using peer-reviewed literature indexed in PubMed and literature relevant to drug utilization research, opioid prescribing, opioid consumption, prescribing determinants, hospital utilization and opioid stewardship. Observational studies, systematic reviews, meta-analyses and intervention studies were considered across different populations and healthcare settings. The World Health Organization Anatomical Therapeutic Chemical/Defined Daily Dose methodology was considered as a standardized framework for medicine-utilization measurement.

Results: Opioid utilization varies substantially between countries, regions, populations, clinical indications and healthcare settings. High-income countries have historically demonstrated greater opioid consumption than many low- and middle-income countries, although low consumption may represent either appropriate lower exposure or inadequate access to analgesic medicines. Within healthcare systems, substantial variation has been observed between hospitals, departments and individual prescribers. Patient characteristics, pain diagnosis, previous opioid exposure, comorbidities, socioeconomic factors and geography may influence utilization. Prescriber characteristics, institutional culture, guidelines, workload and electronic prescribing systems are additional determinants. Postoperative and hospital-discharge prescribing represent important points of potential excess exposure because prescribed quantities may exceed actual patient requirements. Common measures of utilization include prescription prevalence, days of supply, Defined Daily Dose, prescribed daily dose and morphine milligram equivalents, each with specific methodological limitations.

Conclusion: Opioid analgesic utilization is determined by a complex interaction of clinical, patient-related, prescriber, institutional, socioeconomic and regulatory factors. Drug utilization research can identify variations in prescribing, potentially inappropriate utilization and possible unmet analgesic needs. Future research should integrate standardized utilization measures with clinical indication, pain outcomes, patient-reported outcomes and safety indicators. Multidisciplinary opioid stewardship, including clinical pharmacist involvement, may improve the balance between adequate pain management and minimization of avoidable opioid-related harm.

Keywords: opioid analgesics; drug utilization research; prescribing pattern; analgesic utilization; pharmacoepidemiology; morphine milligram equivalents; Defined Daily Dose; opioid stewardship; pain management; prescribing determinants.

1. Introduction

Pain is one of the most common reasons for seeking healthcare and occurs across surgical, medical, emergency, oncological and palliative-care settings. Opioid analgesics have an established therapeutic role in moderate-to-severe pain, particularly when other analgesic approaches are insufficient or inappropriate.^{1,2}

At the population level, opioid utilization has demonstrated considerable geographical and temporal variation. A country-level observational study examining prescription opioid consumption in 76 countries between 2009 and 2019 demonstrated substantial differences between income groups and individual countries.³ A separate longitudinal analysis of 66 countries and regions from 2015 to 2019 similarly identified marked regional differences in opioid consumption, with increases in several regions but declining consumption in North America and Oceania.⁴

The interpretation of opioid utilization requires particular caution because high and low consumption can both represent potential problems. High utilization may indicate excessive or prolonged exposure, whereas very low utilization may indicate inadequate access to essential analgesics. Earlier global analyses demonstrated profound disparities between opioid consumption and estimated need for pain treatment, particularly in countries with limited access to controlled analgesic medicines.⁵

Drug utilization research (DUR) provides a systematic approach for examining the prescription, distribution and use of medicines within populations. The WHO Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) methodology was developed to permit standardized measurement and comparison of medicine consumption at international, national and local levels.⁶

The Defined Daily Dose is a technical measurement unit representing the assumed average maintenance dose per day for a medicine used for its main indication in adults.⁶ Importantly, the DDD does not necessarily correspond to the prescribed daily dose or to an appropriate dose for an individual patient because actual therapeutic requirements vary according to patient and disease characteristics.⁷

Opioid utilization therefore requires assessment using multiple complementary measures. Prescription prevalence, treatment duration, quantity supplied, prescribed daily dose, DDD-based measures and morphine milligram equivalent (MME) measures each provide different information regarding exposure.⁷

The purpose of the present narrative review is to synthesize evidence concerning patterns and determinants of opioid analgesic utilization across different populations and healthcare settings, with particular emphasis on drug-utilization methodology, patient and prescriber factors, hospital and outpatient prescribing, clinical appropriateness, safety and opioid stewardship.

2. Narrative Review Methodology

This narrative review was developed using literature relevant to opioid analgesic utilization and drug utilization research. PubMed-indexed studies were prioritized, with emphasis on systematic reviews, meta-analyses, observational studies, hospital-based drug-utilization studies and intervention research. The literature was organized thematically according to: global opioid consumption; outpatient and chronic pain utilization; emergency-department prescribing; inpatient and postoperative utilization; population-level determinants; prescriber and health-system determinants; measurement methodologies; opioid-related adverse outcomes; stewardship interventions; and future research needs.

The review does not constitute a systematic review or meta-analysis. Consequently, pooled quantitative estimates are reported only when they originate from previously published systematic reviews or meta-analyses.

3. Concept and Importance of Drug Utilization Research

Drug utilization research examines the prescription, distribution and use of medicines and the associated medical, social and economic consequences.⁶ The WHO ATC/DDD system provides an internationally standardized framework for classifying medicines and quantifying their utilization.⁶

The ATC classification organizes medicines according to anatomical, therapeutic, pharmacological and chemical characteristics.⁶ The DDD provides a standardized denominator-independent unit that facilitates comparisons of consumption across populations and over time.⁶

The methodology is particularly useful for opioid research because opioid prescribing differs substantially in formulation, strength, route and therapeutic indication. Standardized measures allow researchers to examine broad consumption trends without relying solely on product-specific quantities.⁶

However, utilization statistics should not be interpreted as direct indicators of prescribing appropriateness. WHO specifically notes that DDD is a technical unit and may differ substantially from the actual prescribed daily dose.⁷ Therefore, meaningful opioid DUR requires integration of quantitative consumption measures with clinical information, including indication, age, disease severity, duration of therapy and concomitant treatment.⁷

Opioid DUR can address several questions:

- Which opioid analgesics are most frequently prescribed?
- What proportion of patients receive opioids?

- How does utilization differ between departments?
- What are the usual treatment durations?
- How does utilization vary by age, sex or diagnosis?
- What proportion of prescribing is potentially inappropriate?
- How does actual consumption compare with prescribed quantity?
- What factors explain variation between prescribers or institutions?
- Do stewardship interventions modify utilization without compromising pain management?

These questions demonstrate that DUR extends beyond simply counting prescriptions and can contribute to quality improvement, pharmacoepidemiology and health-policy development.

4. Global Patterns of Opioid Analgesic Utilization

Global opioid utilization demonstrates substantial heterogeneity. Jayawardana et al. evaluated prescription opioid analgesic consumption across 76 countries between 2009 and 2019 and reported a decline in the global consumption rate from 216.3 to 151.5 MME per 1,000 inhabitants per day.³

The same study demonstrated markedly higher median consumption in high-income countries compared with upper-middle-income and low- or lower-middle-income countries.³ Physician density, national income and other socioeconomic characteristics were associated with consumption in some income groups.³

Another longitudinal study using pharmaceutical sales data from 66 countries or regions found that overall opioid analgesic consumption increased between 2015 and 2019, although trends differed substantially by region.⁴ Consumption declined in North America and Oceania but increased in South America, eastern Europe, Asia and western and central Europe.⁴

The apparent contradiction between these studies illustrates an important feature of opioid epidemiology: conclusions depend on the period studied, countries included and utilization measure employed. Therefore, global opioid consumption should not be interpreted as a single uniform trend.

International differences may reflect differences in disease burden, healthcare infrastructure, availability of analgesic medicines, clinical practice, prescribing regulations, socioeconomic conditions and cultural attitudes toward opioids.^{3–5}

Earlier analyses have also demonstrated a mismatch between opioid availability and estimated need for pain management.⁵ Such disparities highlight the importance of distinguishing **excessive utilization** from **insufficient access** when interpreting international opioid statistics.⁵

5. Opioid Utilization in Outpatient and Chronic Non-Cancer Pain

Chronic non-cancer pain is one of the most extensively studied contexts of opioid prescribing. A systematic review and meta-regression involving 42 studies and more than 5 million participants estimated that approximately 30.7% of patients with chronic non-cancer pain were prescribed an opioid.⁸

The review found that strong opioids were prescribed more frequently than weak opioids in the studies providing information by opioid strength.⁸

A separate systematic review involving 60 observational studies and approximately 3.96 million individuals found that 26.8% of people with chronic non-cancer pain reported opioid use.⁹ Weak opioids were more commonly reported than strong opioids, and opioid use was lower in Europe than in North America.⁹

The distinction between **prescription** and **actual use** is important. Prescription-based studies estimate what was supplied or prescribed, whereas utilization studies based on patient reports or medication records may provide information regarding actual consumption.^{8,9}

The prevalence of problematic opioid use among patients receiving opioids for chronic non-cancer pain is also clinically relevant. A 2024 systematic review and meta-analysis of 148 studies involving more than 4.3 million participants reported substantial heterogeneity in estimates of dependence, opioid use disorder and aberrant behavior.¹⁰ The authors emphasized that prevalence estimates were strongly influenced by study setting, design and diagnostic method.¹⁰

Long-term opioid treatment also presents methodological challenges. Earlier systematic reviews identified uncertainty regarding long-term efficacy and reported adverse effects and treatment discontinuation among patients receiving prolonged opioid therapy for chronic non-cancer pain.¹¹ More recent evidence similarly indicates that the certainty of evidence regarding long-term efficacy and safety remains limited.¹²

Therefore, outpatient DUR should distinguish between short-term exposure, recurrent prescribing and long-term therapy rather than treating all opioid prescriptions as equivalent.

6. Opioid Utilization in Emergency Departments

Emergency departments are important settings for opioid DUR because acute pain is common and prescribing decisions frequently occur under time constraints.

A five-hospital study demonstrated substantial physician- and facility-level variation in opioid prescribing for discharged emergency-department patients even after adjustment for patient and situational characteristics.¹³

Another study examining opioid prescribing by emergency physicians found that opioid prescriptions varied substantially between individual providers. During 2009–2018, approximately 14% of emergency-department visits in the study received an opioid prescription, while individual provider prescribing proportions ranged from 1% to 17%.¹⁴

The variation observed between providers suggests that patient clinical characteristics alone do not fully explain opioid prescribing. Qualitative research involving emergency physicians identified three broad groups of determinants: pain characteristics, patient-related considerations and practice-environment factors.¹⁵ Physicians described the influence of clinical presentation, perceived risk, patient characteristics, institutional policies, regulations and guidelines on prescribing decisions.¹⁵

Geographical differences are also important. A multilevel analysis of acute work-related low back pain found substantial between-state variation in early opioid prescribing, with contextual factors explaining much of the geographic variability.¹⁶

A national emergency-department study of acute low back pain reported opioid prescribing in approximately one-third of eligible visits and found that higher pain scores were associated with greater likelihood of opioid prescribing.¹⁷ Geographic differences were also observed.¹⁷

These findings indicate that emergency-department opioid utilization is influenced by a combination of clinical need, provider preferences and contextual factors.

7. Inpatient and Hospital-Based Opioid Utilization

Hospital-based opioid utilization differs from outpatient prescribing because opioids may be administered for acute postoperative pain, trauma, cancer-related pain, palliative care and acute medical conditions.

Hospital DUR studies frequently employ DDD per 100 bed-days, prescribed daily dose, treatment duration and morphine-equivalent measures.⁷

Fang et al. evaluated opioid utilization in a large Chinese teaching hospital using ATC/DDD methodology.¹⁸ Prescribed opioid consumption increased from 3.16 to 3.74 DDD per 100 bed-days between 2012 and 2017.¹⁸ The study also demonstrated differences in treatment duration between cancer and non-cancer patients, emphasizing the influence of clinical indication on utilization.¹⁸

These findings illustrate the importance of combining consumption measures with patient-level variables. A high DDD/100 bed-days value may reflect an institution treating a larger proportion of patients with severe pain, cancer or major surgery rather than inappropriate prescribing.

Similarly, low utilization cannot automatically be considered evidence of optimal prescribing. Low consumption may reflect limited availability, prescribing restrictions, clinician concerns or undertreatment of pain.^{3–5}

Hospital DUR should therefore incorporate:

- Diagnosis
- Department
- Pain indication
- Opioid selection
- Route
- Prescribed dose
- Duration
- Concurrent analgesics
- Patient characteristics
- Relevant clinical outcomes

8. Postoperative and Hospital-Discharge Opioid Utilization

The transition from hospital to community is a particularly important point in opioid utilization research.

A systematic review by Bicket et al. evaluated postoperative opioid prescribing across six studies involving 810 patients.¹⁹ Between 67% and 92% of patients reported unused opioids, and 42% to 71% of obtained opioid tablets were unused across the included studies.¹⁹

These findings demonstrate that prescription quantity is not equivalent to actual consumption.¹⁹ This distinction has major implications for DUR because administrative prescription data may overestimate the amount of medication ultimately taken by patients.

Excess postoperative prescribing may also create an unused medication reservoir. The systematic review reported that many patients did not dispose of unused opioids using recommended methods, indicating an additional medication-safety concern.¹⁹

Consequently, postoperative DUR should ideally examine both **prescribed quantity** and **patient-reported consumption**.

Hospital-discharge prescribing has also become an important target for opioid stewardship. A systematic review of organizational interventions found that patient- or procedure-specific guidelines, prescriber education with feedback and electronic prescribing changes were among interventions associated with reductions in opioid prescribing.²⁰

This evidence supports the use of discharge-specific prescribing criteria rather than relying exclusively on fixed quantities or habitual prescribing patterns.

9. Population and Patient-Related Determinants

9.1 Age

Age is an important determinant of opioid utilization. Multinational population-based research has demonstrated substantial differences in opioid prescribing according to age and sex.²¹

Older adults may have greater exposure because of higher prevalence of painful chronic conditions, cancer and postoperative conditions. At the same time, multimorbidity and polypharmacy can complicate opioid treatment in this population.

A Medicare-based study of more than 2.3 million older adults annually found that the proportion receiving a new opioid prescription increased during part of the study period before subsequently declining.²² Long-term use among new users also declined during the observation period.²²

More recent Medicare data from 2013–2020 similarly showed an overall decline in new prescription opioid use among older adults after 2016, accompanied by reductions in average MME and high-dose prescribing.²³

9.2 Sex

Sex differences in opioid prescribing have been reported in multinational studies, although the magnitude and direction vary between populations.²¹

9.3 Pain diagnosis and severity

The clinical indication remains one of the strongest determinants of opioid utilization. Cancer pain, postoperative pain, trauma and acute severe pain represent different therapeutic contexts from chronic non-cancer pain.

9.4 Previous opioid exposure

Previous opioid exposure may influence subsequent prescribing because clinicians may continue established therapy or because patients may have ongoing analgesic requirements. Distinguishing opioid-naïve from previously exposed patients is therefore important in DUR.

9.5 Comorbidity and polypharmacy

Comorbidities can influence both the decision to prescribe and the potential risk associated with opioid exposure. A systematic review of high-dose opioid prescribing identified depression, emergency-department visits and benzodiazepine co-prescribing among factors associated with high-dose opioid prescribing.²⁴

9.6 Socioeconomic factors

Socioeconomic and insurance-related characteristics may affect access to healthcare, continuity of care and availability of alternative pain-management approaches.

10. Prescriber-Related Determinants

Prescriber behavior is a major contributor to variation in opioid utilization.

Emergency-department studies have consistently demonstrated significant variation between individual clinicians even after adjustment for patient characteristics.^{13, 14}

Qualitative evidence suggests that prescribing decisions are influenced by clinicians' assessment of pain characteristics, perceptions of patient risk, previous clinical experiences, institutional policies, legislation and clinical guidelines.¹⁵

Prescriber-level variation may therefore arise from differences in:

- Clinical experience
- Knowledge of pain-management recommendations
- Perception of opioid-related risk
- Familiarity with alternative analgesic strategies
- Expectations concerning patient satisfaction
- Institutional culture
- Workload
- Previous experience with opioid-related complications

However, variation between prescribers should not automatically be considered inappropriate. Patients differ in diagnosis, severity and therapeutic goals. The more relevant question is whether observed variation remains substantial after appropriate adjustment for clinical factors.

This distinction is important in DUR because the objective should be to identify **unexplained or potentially inappropriate variation**, rather than eliminate clinically justified variation.

11. Geographic, Socioeconomic and Health-System Determinants

Geographic variation in opioid utilization has been demonstrated both between countries and within individual countries.^{3,4,16}

At the international level, differences in opioid consumption are associated with socioeconomic development, healthcare resources, physician availability, cancer burden and geographic factors.^{3,4}

A multilevel study of work-related low back pain demonstrated that contextual state-level factors explained much of the observed geographic variation in early opioid prescribing.¹⁶

Disparities may also occur within healthcare systems. A systematic review and meta-analysis of racial disparities in opioid prescribing in the United States found that Black patients were less likely than White patients to receive opioid analgesia and that Hispanic patients were also less likely than non-Hispanic White patients to receive opioid analgesia.²⁵

These findings should not be interpreted as evidence that differences in opioid prescribing are inherently inappropriate. Rather, they indicate potential differences in access to analgesia that require evaluation alongside pain severity, diagnosis, healthcare access and other contextual variables.

Health-system determinants include:

- Medicine availability
- Prescribing regulations
- Institutional guidelines
- Pain-management services
- Palliative-care availability
- Electronic prescribing systems
- Prescription-monitoring systems
- Reimbursement structures
- Opioid stewardship programs

Thus, opioid utilization is best conceptualized as the outcome of interacting **patient, provider, institutional and societal determinants**.

12. Opioid Utilization in Cancer and Palliative Care

Opioid utilization in cancer and palliative care differs substantially from utilization for many chronic non-cancer pain conditions.

Opioids remain important medicines for moderate-to-severe cancer-related pain. An overview of Cochrane reviews evaluated nine systematic reviews involving more than 13,000 participants and found that opioids were commonly used in the management of moderate-to-severe cancer pain, although the quality of evidence varied considerably between opioid agents and comparisons.²⁶

The review reported that adverse events were common and that treatment withdrawal because of adverse events occurred in a proportion of patients.²⁶

Consequently, opioid utilization in cancer should be evaluated according to the therapeutic objective. A treatment pattern considered excessive in uncomplicated acute pain may be clinically justified in advanced cancer or palliative care.

Hospital-based DUR research has demonstrated differences in opioid treatment duration between cancer and non-cancer populations.¹⁸ In the Chinese teaching-hospital study, cancer patients had longer median treatment duration than non-cancer patients.¹⁸

Therefore, utilization studies should stratify populations according to clinical indication rather than combining all opioid exposure into a single category.

13. Measurement of Opioid Utilization

13.1 Prescription prevalence

Prescription prevalence describes the proportion of a population receiving at least one opioid prescription during a specified period. It is useful for assessing the extent of exposure but provides limited information about dose or duration.

13.2 Incidence or new use

New-user designs identify patients who begin opioid treatment after a defined opioid-free period. This approach is useful for distinguishing treatment initiation from continuation.

13.3 Days of supply

Days of supply provide information about treatment duration and can distinguish short-term exposure from prolonged treatment.

13.4 Defined Daily Dose

The DDD is the assumed average maintenance dose per day for the main adult indication.⁷ It provides a standardized technical measure for comparing drug consumption.⁷

Common hospital DUR indicators include:

- DDD/100 bed-days
- DDD/1,000 inhabitants/day
- DDD/patient
- DDD per treatment period

13.5 Prescribed Daily Dose

The prescribed daily dose reflects the actual daily amount prescribed by clinicians. WHO emphasizes that PDD and DDD may differ considerably and that diagnosis and patient characteristics should be considered when interpreting PDD.⁷

13.6 Morphine Milligram Equivalents

MME-based measures convert different opioid exposures into a common morphine-equivalent metric. They are useful for population-level comparison and risk assessment but should be interpreted as standardized exposure measures rather than exact measures of clinical equivalence.

13.7 Prescription quantity

Prescription quantity is particularly relevant for postoperative and discharge studies. However, quantity prescribed cannot be assumed to represent quantity consumed.¹⁹

Overall methodological consideration

No single utilization measure is sufficient. A comprehensive DUR study should ideally combine **prevalence + dose + duration + quantity + indication + actual consumption + outcomes**.

14. Potentially Inappropriate Opioid Utilization

Potentially inappropriate opioid utilization may include prescribing without an appropriate documented indication, unnecessarily prolonged therapy, excessive quantity, potentially hazardous combinations, therapeutic duplication and inadequate reassessment.

The interpretation of inappropriate utilization must remain clinically contextual. A high opioid dose or prolonged treatment period does not automatically establish inappropriate prescribing because legitimate clinical indications may require individualized treatment.

High-dose prescribing has been associated with several patient and treatment characteristics. Richards et al. found associations between high-dose opioid prescribing and benzodiazepine co-prescribing, depression, emergency-department visits, unemployment and male sex.²⁴

These factors should therefore be considered potential markers for closer review rather than automatic indicators of inappropriate prescribing.

Potentially inappropriate utilization can also be evaluated using process indicators. Consensus work on hospital opioid stewardship has identified indicators such as duplicate PRN opioid indications, opioid exposure among opioid-naïve patients, average daily MME administered and prolonged discharge prescriptions as potentially useful quality measures.²⁷

A major advantage of such indicators is that they can be incorporated into electronic health-record-based quality-improvement programs.

15. Safety Outcomes Associated With Opioid Utilization

The importance of opioid DUR extends beyond prescription volume because opioid exposure can be associated with adverse effects and medication-related harm.

A systematic review of opioid adverse events in chronic non-malignant pain found increased rates of adverse events compared with placebo, with dry mouth, nausea and constipation among commonly reported events.²⁸

An overview of Cochrane reviews involving 14 opioid reviews and more than 18,000 randomized participants found an increased risk of adverse events with opioids compared with placebo.²⁹ Specific adverse events included constipation, dizziness, drowsiness, fatigue, nausea, pruritus and vomiting.²⁹

Adverse effects are also important in cancer pain management. A systematic review examining opioid side-effect management identified constipation, pruritus, nausea and vomiting, sedation, respiratory depression and delirium among clinically relevant adverse effects.³⁰

Therefore, opioid DUR should ideally move beyond measuring utilization and incorporate safety outcomes such as:

- Opioid-related adverse drug events
- Medication errors
- Emergency visits
- Hospitalization
- Prolonged exposure
- Clinically significant interactions
- Patient-reported treatment outcomes

This approach converts conventional consumption-based DUR into **outcome-oriented drug-utilization research**.

16. Opioid Stewardship

Opioid stewardship refers broadly to coordinated interventions intended to promote appropriate opioid prescribing and use while minimizing avoidable harm.

Stewardship interventions can target:

- Prescriber education
- Clinical guidelines
- Audit and feedback
- Electronic prescribing systems
- Clinical decision support
- Patient education
- Medication reconciliation
- Discharge prescribing
- Multidisciplinary review
- Institutional quality indicators

A systematic review of hospital inpatient interventions found that multifaceted interventions were commonly used and that provider education reinforced by written material and feedback was associated with improved concordance with local prescribing guidelines.³¹

A systematic review of organizational interventions at hospital discharge also reported beneficial effects from procedure-specific guidelines, prescriber education with feedback and electronic prescribing changes.²⁰

Another systematic review specifically examining extended-release opioid prescribing found that system-level forcing functions, including prescribing restrictions and prior authorization, reduced extended-release/long-acting opioid prescribing and improved guideline adherence.³²

A broader systematic review of opioid stewardship interventions found low-to-moderate strength evidence that stewardship programs can reduce opioid prescriptions, long-term opioid use and days of supply, while evidence for reducing opioid dosage was somewhat stronger.³³

More recent evidence from an AHRQ rapid review suggests that clinical decision support, electronic-health-record interventions and multicomponent stewardship programs may reduce opioid prescribing or dosage without increasing pain, emergency visits or hospitalizations, although the overall strength of evidence remains low.³⁴

17. Role of Clinical Pharmacists in Opioid Drug Utilization

Clinical pharmacists are well positioned to contribute to opioid-utilization optimization because medication review is central to their professional role.

Pharmacist involvement can include:

- Medication-history assessment
- Prescription review
- Identification of duplicate or potentially inappropriate therapy
- Assessment of treatment duration
- Evaluation of concomitant medicines
- Medication reconciliation
- Patient education
- Monitoring of medication-related problems
- Development of institutional guidelines
- Drug-utilization evaluation
- Participation in opioid stewardship committees

The importance of pharmacists is reflected in multidisciplinary opioid stewardship models and in the development of hospital quality indicators involving pharmacists, physicians, nurses and other stakeholders.²⁷

Clinical pharmacists may be particularly valuable during transitions of care, including hospital admission and discharge, where discrepancies between inpatient and outpatient analgesic therapy can arise.

The pharmacist-led component of DUR can also bridge the gap between quantitative prescription data and clinical interpretation. Instead of simply identifying high opioid consumption, pharmacists can help determine whether the utilization is consistent with diagnosis, treatment goals and relevant clinical guidance.

18. Critical Synthesis of the Evidence

The evidence reviewed demonstrates that opioid utilization is not a single-dimensional phenomenon.

18.1 Utilization is highly heterogeneous

Global studies demonstrate major differences in opioid consumption between countries and regions.^{3, 4} These differences reflect both variation in prescribing and unequal access to analgesic treatment.

18.2 Clinical indication strongly modifies interpretation

Opioid use for cancer and palliative care should not be interpreted using exactly the same criteria as opioid use for uncomplicated acute or chronic non-cancer pain.^{18, 26}

18.3 Prescriber variation is substantial

Emergency-department research demonstrates considerable variation between individual clinicians and institutions.^{13–15} This variation suggests that provider and organizational factors contribute substantially to opioid utilization.

18.4 Patient factors are important but insufficient

Age, sex, diagnosis, pain severity, previous exposure, comorbidity and socioeconomic characteristics influence opioid prescribing.^{21–24} However, these factors do not completely explain the variation observed between clinicians or regions.

18.5 Prescription data do not equal consumption

Postoperative studies demonstrate that a substantial proportion of prescribed opioids may remain unused.¹⁹ Therefore, prescription databases may over-estimate actual patient consumption.

18.6 Measurement methodology influences conclusions

DDD, PDD, MME, prescription prevalence and days of supply describe different aspects of opioid exposure.⁷ Consequently, researchers should avoid relying on a single indicator.

18.7 Stewardship should focus on appropriateness rather than simple reduction

The goal of opioid stewardship should not be indiscriminate reduction in opioid use. Rather, the objective should be to achieve appropriate analgesic treatment while reducing unnecessary exposure and preventable harm.^{33, 34}

19. Research Gaps

Despite extensive research, several important gaps remain.

19.1 Lack of standardized definitions

Studies differ in their definitions of opioid initiation, long-term use, high-dose prescribing, problematic use and inappropriate utilization. This heterogeneity limits direct comparison between studies.

19.2 Overreliance on administrative prescription data

Many studies measure prescriptions or dispensing rather than actual consumption.¹⁹ This is particularly important for postoperative and short-term treatment.

19.3 Limited clinical context

Administrative databases may not contain detailed information regarding pain severity, clinical reasoning, treatment goals or patient preferences.

19.4 Limited evidence from low- and middle-income countries

Global research demonstrates major differences in opioid availability and utilization, but comprehensive patient-level DUR data remain limited in many low- and middle-income countries.^{3–5}

19.5 Insufficient integration of clinical outcomes

Many utilization studies measure prescription frequency or dose without simultaneously measuring pain relief, functional recovery, quality of life or adverse effects.

19.6 Limited multidisciplinary evidence

Although pharmacist- and multidisciplinary stewardship models are increasingly used, additional studies are required to determine which components produce the greatest improvements in prescribing quality.

19.7 Need for longitudinal research

Longitudinal studies are needed to distinguish short-term exposure from recurrent and persistent use and to examine how initial prescribing decisions influence subsequent utilization.

19.8 Need for patient-centered outcomes

Future DUR should incorporate patient-reported pain relief, functional recovery, quality of life and satisfaction alongside traditional utilization indicators.

19.9 Need for better stewardship outcome measures

A 2025 systematic review identified 49 unique opioid-stewardship quality indicators, but only a small proportion were outcome indicators.³⁵ The authors emphasized the need for better collection of patient-level outcome data to enable more holistic evaluation of stewardship programs.³⁵

20. Future Directions

Future opioid-utilization research should move from simple prescription counting toward integrated, patient-centered pharmacoepidemiology.

A comprehensive conceptual model can be represented as:

Patient characteristics → Clinical indication → Prescriber factors → Institutional factors → Prescription characteristics → Actual utilization → Clinical outcomes

Future studies should combine electronic prescribing information with pharmacy-dispensing data and clinical records where possible.

Research should also prioritize:

- Multicenter studies
- Standardized definitions
- Indication-specific utilization measures
- Risk-adjusted comparisons
- Actual consumption data

- Patient-reported outcomes
- Adverse-event monitoring
- Pharmacist-led interventions
- Equity-focused analyses
- Implementation science
- Longitudinal evaluation of opioid stewardship

The development of standardized hospital opioid-stewardship quality indicators provides an important foundation for future research.^{27,35}

Research should also distinguish between **reducing inappropriate opioid exposure** and **reducing appropriate analgesic treatment**. This distinction is particularly important in cancer, palliative care and severe acute pain, where opioids may remain essential components of treatment.²⁶

21. Conclusion

Opioid analgesic utilization demonstrates substantial variation across countries, populations, clinical indications and healthcare settings. Global research indicates major disparities in opioid consumption, while hospital and emergency-department studies demonstrate considerable variation between institutions and individual prescribers.^{3,4,13,14}

Patient characteristics, pain diagnosis, previous opioid exposure, comorbidities, socioeconomic factors and geographic location contribute to utilization patterns. Prescriber preferences, institutional culture, healthcare resources, regulations and prescribing systems provide additional determinants.^{15,16,24}

Drug utilization research provides an important framework for identifying these variations. The WHO ATC/DDD methodology allows standardized comparison of medicine consumption, but DDD should not be interpreted as an individualized therapeutic dose.^{6,7}

A comprehensive assessment of opioid utilization should therefore integrate prescription prevalence, dose, duration, quantity, indication, actual consumption and clinical outcomes.

The evidence also demonstrates that prescribing quantity does not necessarily represent actual opioid consumption, particularly after surgery.¹⁹ Consequently, future research should increasingly combine prescribing data with patient-level consumption and outcome measures.

The ultimate objective of opioid-utilization research should not be indiscriminate reduction of opioid prescribing. Instead, the goal should be **appropriate, evidence-based and patient-centered analgesic utilization**, ensuring access for patients with legitimate clinical needs while reducing avoidable exposure and medication-related harm.

Multidisciplinary opioid stewardship, supported by physicians, clinical pharmacists, nurses and healthcare administrators, provides an important framework for achieving this balance.^{27,33–35}

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