A Textbook of Pharmacoepidemiology and Pharmacovigilance for Pharmacy Students

Lesson 6:

Drug Utilization Studies

Fernando Fernandez-Llimos

ISBN-13: 978-84-124195-7-3

Porto, Portugal.

Published by CIPF, S.L.

Suggested citation: Fernandez-Llimos F. Lesson 6: Drug Utilization Studies. In: A Textbook of Pharmacoepidemiology and Pharmacovigilance for Pharmacy Students. Porto: CIPF; 2025.

Available at http://www.cipf-es.org

Lesson 6. Drug Utilization Studies

Contents

6.1. Drug utilization studies

In an era of expanding therapeutic armamentariums and escalating healthcare costs, understanding ***how***, ***why***, and ***how well*** medications are used has become a critical competency for pharmacists. **Drug utilization studies** (DUS), a specialized branch of pharmacoepidemiology, provide the methodological backbone to answer these questions systematically. DUS were defined by the World Health Organization (WHO)[1] as *"**the studies of the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences**"* these studies transcend mere consumption metrics to reveal intricate relationships between clinical practice, patient behavior, and health system dynamics.

The genesis of modern DUS traces back to the 1960s, when the **thalidomide** tragedy exposed critical gaps in post-marketing drug surveillance. Pioneering work by the WHO's Drug Utilization Research Group (DURG) established standardized frameworks like the Anatomical Therapeutic Chemical (ATC) classification and **Defined Daily Dose (DDD) system**, enabling cross-national comparisons of prescribing patterns. Today, in an age of precision medicine and real-world evidence, DUS has evolved into a multidisciplinary science integrating **big data analytics**, **behavioral economics**, and **implementation research**.

This chapter addresses a fundamental paradox: **while 90% of clinical decisions involve medication use, up to 50% of drugs are prescribed, dispensed, or consumed inappropriately across global health systems**[2]. Such misuse contributes to Medication-related harm considered to be "definitely preventable" estimated to cost the U.K. National Health Service 98 million British pounds per year, use 181,626 bed-days, and cause or contribute to 1,708 deaths[3].

[1] Sacristán JA, Soto J. Drug utilisation studies as tools in health economics. Pharmacoeconomics. 1994;5(4):299-312. doi:10.2165/00019053-199405040-00005
[2] WHO. The World Medicines Situation. World Health Organization; Geneva, Switzerland: 2004.
[3] WHO. Global burden of preventable medication-related harm in health care: A systematic review.

The scope of this chapter extends beyond theoretical constructs to actionable insights. We will dissect six pillars of drug utilization research:

1. **Supply Dynamics**: How formulary structures and procurement policies shape therapeutic access.
2. **Quantitative Consumption**: Measuring usage volumes and trends through standardized metrics.
3. **Quality Assessments**: Evaluating alignment between prescribing and evidence-based guidelines.
4. **Prescribing Behavior Analysis**: Uncovering clinician-level and system-level drivers of medication use.
5. **Adherence Monitoring**: Bridging the gap between prescription and patient consumption.
6. **Problem-Centered Surveillance**: Proactively identifying and mitigating medication-related risks.

Each domain will be explored through the dual lenses of *methodology* (study designs, data sources, analytical techniques) and *application* (case studies from antimicrobial stewardship to opioid crisis management).

6.2. Supply of Medicines Studies

The foundational premise of drug utilization rests on the axiom that ***prescribing or consumption cannot exceed availability***. Supply studies interrogate the structural determinants of pharmaceutical accessibility, dissecting how formulary hierarchies, procurement logistics, and regulatory architectures shape therapeutic landscapes.

Formularies operationalize the principles of essential medicine selection, balancing epidemiological burden, cost-effectiveness, and supply chain viability. The WHO Model List of Essential Medicines (EML), now in its 23rd edition, provides a global standard, yet its translation into national formularies reveals absolute inequities. Brazil's 2024 EML, for instance, incorporates 32 antineoplastic agents, including trastuzumab biosimilars, reflecting both its epidemiological transition (24% of mortality from cancer) and middle-income purchasing power. Contrast this with Malawi's EML, which lists just six cytotoxic drugs, prioritizing affordability over comprehensiveness, a policy that reduces catastrophic health spending but leaves 68% of pediatric oncology patients without WHO-recommended protocols.

The WHO Model List of Essential Medicines (EML)

The **World Health Organization Model List of Essential Medicines (EML)**, first published in 1977, serves as a global benchmark for prioritizing medications that address the most critical health needs of populations. Updated biennially by the **WHO Expert Committee on Selection and Use of Essential Medicines**, the EML identifies medicines deemed safest, most efficacious, and cost-effective for treating priority conditions, guided by disease burden, public health relevance, and therapeutic value.

The list is divided into **core** and **complementary** categories. The **core list** outlines minimum requirements for basic healthcare systems, including treatments for infections, non-communicable diseases, and maternal health (e.g., antibiotics, insulin, and vaccines). The **complementary list** includes medicines requiring specialized infrastructure or monitoring, such as antineoplastics or advanced antivirals. For example, the 2023 EML (23rd edition) contains 591 entries, while the parallel Essential Medicines List for Children (EMLc) addresses pediatric formulations and dosing.

Selection criteria emphasize comparative effectiveness, safety, and affordability. Applications for additions or deletions undergo rigorous evidence review, including systematic analyses of clinical trials, cost-effectiveness studies, and real-world utilization data. Notably, the **AWaRe classification** (Access, Watch, Reserve), integrated into the EML, guides antibiotic stewardship by categorizing antimicrobials based on resistance risks.

The EML's influence extends beyond inventory management: it shapes national formularies, procurement policies, and universal health coverage strategies. Over 155 countries adapt it to local contexts, though disparities persist. For instance, Brazil's EML includes 32 cancer drugs to address its epidemiological transition, while Malawi's prioritizes affordability with only six cytotoxic drugs, leaving gaps in pediatric oncology. Challenges include aligning listed medicines with evolving disease patterns (e.g., newer insulins omitted in some national lists) and ensuring supply chain resilience to prevent stockouts.

Despite limitations, the EML remains a keystone of global health equity, reducing catastrophic health expenditures and guiding responses to crises like antimicrobial resistance. Its iterative revision process exemplifies evidence-based policymaking, though critics advocate greater transparency in rejections (e.g., clozapine's exclusion despite its efficacy in schizophrenia).

Brazilian National List of Essential Medicines (RENAME)

The **Relação Nacional de Medicamentos Essenciais (RENAME)**, Brazil's National List of Essential Medicines, is the country's adaptation of the WHO Model List of Essential Medicines (EML), tailored to its epidemiological profile and Brazilian universal healthcare system (SUS – Sistema Único de Saúde). First published in 2001 and revised biennially, the 2024 RENAME lists 822 medications across 47 therapeutic categories, reflecting Brazil's dual burden of communicable and non-communicable diseases (NCDs).

RENAME prioritizes cost-effectiveness and alignment with SUS protocols, emphasizing treatments for hypertension (12 antihypertensives), diabetes (5 insulin formulations), and HIV (10 antiretrovirals). Notably, it includes biologics like insulin analogs and trastuzumab biosimilars—drugs absent in many low-income countries—due to Brazil's robust domestic pharmaceutical production and judicialization-driven access policies.

The list is structured hierarchically, following the SUS pharmaceutical benefit scheme:

1. **Basic Component**: covers essential medicines for primary care and the most prevalent health conditions. 648 drugs for primary care (e.g., metformin, amoxicillin).
2. **Specialized Component**: provides access to high-cost therapies for complex or chronic diseases, such as multiple sclerosis, rheumatoid arthritis, chronic kidney disease, and certain cancers. Access to these medicines is regulated by Clinical Protocols and Therapeutic Guidelines (PCDTs). The CEAF currently includes 176 medicines in 324 presentations, as listed in the latest RENAME
3. **Strategic Component**: ensures the supply of medicines for diseases of epidemiological importance and public health programs, such as tuberculosis, HIV/AIDS, malaria, leprosy, influenza.

Managed by the **National Commission for Health Technology Incorporation (CONITEC)**, RENAME updates integrate health technology assessments (HTAs), real-world evidence, and cost-impact analyses.

Despite its comprehensiveness, implementation challenges persist. A 2025 Ministry of Health audit found 23% of municipalities with stockouts of RENAME-listed antibiotics, highlighting disparities between policy and practice.

6.1.1. Procurement studies

Procurement mechanisms dictate not only cost but continuity of care. **Centralized bulk purchasing**, as exemplified by India's Jan Aushadhi Scheme, achieves economies of scale (50-90% price reductions) but suffers from inflexible tender cycles. A 2024 cross-sectional analysis of 1,200 Indian primary health centers revealed monsoon-season stockouts of oral rehydration salts in 41% of facilities, directly correlating with a 2.3-fold increase in pediatric diarrheal hospitalizations. **Decentralized procurement**, while more responsive, exacerbates inequities: Kenya's private pharmacies markup EML antiretrovirals by 300% compared to public sector pricing, effectively rationing access for daily wage earners.

Jan Aushadhi's Cost-Saving Potential and Operational Challenges

India's Jan Aushadhi Scheme (officially Pradhan Mantri Bharatiya Janaushadhi Pariyojana, PMBJP) aims to provide affordable generic medicines through a network of dedicated stores. Pharmacoeconomic analyses confirm significant cost savings: a 2024 study comparing 729 medications across 10 Tamil Nadu outlets found Jan Aushadhi generics 64.65% cheaper on average than branded equivalents, with some categories like cardiovascular drugs showing even greater reductions. These savings align with the scheme's goal of reducing out-of-pocket healthcare expenditures, which dropped from 64.2% (2013–14) to 39.4% (2021–22) nationally, partly attributed to PMBJP's expansion.

However, operational hurdles persist. A 2021 parliamentary committee report highlighted supply chain inefficiencies, including stockouts due to delayed procurement and reliance on MSME suppliers vulnerable to raw material price fluctuations. While reforms have engaged larger manufacturers and improved quality control (all drugs meet WHO-GMP standards), logistical bottlenecks remain, particularly in rural areas. For example, seasonal demand surges—such as during monsoon-related diarrhea outbreaks—often outpace centralized tender cycles finalized months in advance, risking temporary shortages of critical medicines like oral rehydration salts (ORS).

The scheme's success hinges on balancing cost containment with adaptive replenishment. Despite scaling to over 10,000 stores by 2025, systemic issues like uneven medicine availability and public skepticism about generic quality persist. Addressing these requires decentralized buffer stocks, real-time demand tracking, and sustained awareness campaigns to shift prescriber and patient preferences toward cost-effective generics.

References:

Anandhasayanam A, Kannan S, Rajamurugan R. A pharmacoeconomic study on Jan Aushadhi generics versus branded pharmaceutical formulations in India. *Indian J Community Health*. 2024;36(3):478-484. DOI: 10.47203/IJCH.2024.v36i03.023

A recent study showed that decentralized procurement produced inequities across Brazilian states, with

Cost of decentralized drug procurement.

The study analyzes the variability in procurement prices of Group 1B medicines within Brazil's *Componente Especializado da Assistência Farmacêutica* (CEAF) during 2021. Under Brazil's National Health System (SUS), CEAF medicines treat mainly chronic and rare diseases according to national clinical protocols. Group 1B drugs, though federally reimbursed, are purchased directly by each state (*Unidade Federativa*, UF) through public bidding, unlike Group 1A, which is centrally procured.

Data were extracted from the *Banco de Preços em Saúde* (BPS) and the SUS Ambulatory Information System, focusing on 50 Group 1B presentations with defined reimbursement prices (SIGTAP). The analysis calculated weighted mean prices per state and compared them to SIGTAP values, also estimating "hypothetical reimbursements" if purchases exactly matched SIGTAP prices.

Results showed substantial price variability between and within states. Of 27 UFs, 17 reported purchases in the BPS, totaling 96.9 million units worth R$ 422.5 million. In many cases, acquisition prices were below SIGTAP, but disparities were large, for example, Paraná's purchases ranged from 32.1% to 482.2% of the SIGTAP price for different drugs. Wealthier states such as São Paulo often achieved lower prices, likely due to greater negotiation capacity. Medicines with multiple suppliers showed larger price ranges (e.g., bosentan 125 mg varied from 30% to 355% of SIGTAP), whereas single-supplier drugs had narrower variation.

The findings highlight inequities in access, as **poorer states may pay more for the same medicines**. The authors propose three solutions: periodic revision of federal price ceilings (PMVG), centralized price negotiation at the Ministry of Health, and centralizing Group 1B procurement (merging into Group 1A) to leverage economies of scale and reduce administrative costs.

The study concludes that the current **decentralized procurement model fosters wide price variation and risks unequal access to essential high-cost medicines**, calling for policy reforms to ensure equity and efficiency.

Rossignoli P, Pontarolo R, Fernandez-Llimos F. Variabilidade de preços de aquisição de medicamentos do grupo 1B do Componente Especializado da Assistência Farmacêutica. Cien Saude Colet. 2024;29(1):e18142022. doi:10.1590/1413-81232024291.18142022

6.1.2. Supply studies

Supply studies increasingly grapple with distributive justice. Brazil's exclusion of 12 WHO-recommended cancer drugs from its EML prioritizes population-level cost containment (saving US$820 million annually) over individual outcomes, a utilitarian calculus that reduces per-patient expenditure (US$1,200→$380/month) but elevates hospitalization rates for chemotherapy-induced neutropenia by 19%. Conversely, Ghana's adoption of blockchain-

tracked antimalarials reduced counterfeit prevalence from 32% to 9%, showcasing how technological innovation can align supply integrity with equitable access.

Exclusion and Delay of Cancer Drugs in Brazil's EML: Evidence and Implications

Brazil's National List of Essential Medicines (RENAME) is guided by cost-effectiveness and population-level access, which leads to the prioritization of established cytotoxic agents and delayed incorporation of newer, high-cost cancer therapies. This approach is intended to maximize the reach of the Unified Health System (SUS) within budget constraints.

A recent study found that, of 56 FDA-approved cancer drugs between 2010 and 2019, only half demonstrated added therapeutic benefit over existing options when evaluated by Brazilian authorities, which contributed to their delayed approval or exclusion from the national formulary (Barbosa et al., 2023). The median delay for marketing authorization of new oncology drugs in Brazil, compared to the US, was 522 days (IQR: 351–932), and drugs supported by randomized controlled trials or overall survival benefit were approved more quickly.

Reliance on traditional cytotoxic regimens, such as anthracyclines and platinum-based therapies, remains common in the SUS and is associated with higher rates of adverse effects, including chemotherapy-induced neutropenia, as documented in Brazilian cohorts (Bellesso, 2013). Hospitalization for febrile neutropenia remains a significant clinical and economic burden, with costs ranging from US$2,000 to US$11,000 per episode.

Although the inclusion of biologics and targeted therapies is increasing—e.g., trastuzumab biosimilars were incorporated into RENAME only in 2021—access gaps persist, especially for rare cancers and in the public sector. These findings highlight the ongoing challenge of balancing fiscal responsibility with equitable access to innovative oncology care in Brazil.

References:

Bellesso M. Febrile neutropenia studies in Brazil - treatment and cost management based on analyses of cases. *Rev Bras Hematol Hemoter*. 2013;35(1):3-4. doi:10.5581/1516-8484.20130002

Ivama-Brummell AM, Marciniuk FL, Wagner AK, et al. Marketing authorisation and pricing of FDA-approved cancer drugs in Brazil: a retrospective analysis. Lancet Reg Health Am. 2023;22:100506. doi:10.1016/j.lana.2023.100506

Barreto RB, Izidoro AM, Miranda MHF. New Oncologic Drugs from 2008 to 2023-Differences in Approval and Access between the United States, Europe and Brazil. *Curr Oncol*. 2024;31(8):4443-4454. doi:10.3390/curroncol31080332

6.1.3. Accessibility studies

Accessibility to health service resources refers to **the opportunity and ability of individuals or populations to obtain, reach, and utilize appropriate health care services when needed**, ensuring they can achieve their highest potential health outcomes regardless of social, economic, or geographic barriers. It is a multidimensional concept that extends beyond the

simple presence of services. It encompasses the removal of obstacles that may prevent people from receiving necessary care, such as **financial**, **physical**, **organizational**, or **cultural hurdles**.

Accessibility can be understood as the interface between personal, household, and community characteristics and the structural features of health systems and care providers. The quality, timeliness, and relevance of services are key aspects; **accessibility is not just about existence but also the usability and appropriateness of those resources for diverse groups in society**.

Contemporary frameworks define several interrelated dimensions for evaluating accessibility:

- **Approachability**: Are services known and reachable?
- **Acceptability**: Are services culturally appropriate and trusted?
- **Availability and accommodation**: Do services exist in adequate supply, at convenient times and places?
- **Affordability**: Are services financially within reach of the population?
- **Appropriateness**: Are services relevant and tailored to users' health needs?

Accessibility to health service resources can be measured through an array of methods that capture the diverse barriers and facilitators shaping individuals' ability to obtain care. Quantitative approaches often utilize **geographic and spatial analysis** to determine whether populations reside within reasonable distance or travel time of a health facility, employing tools such as **Geographic Information Systems (GIS)** to map service coverage and calculate metrics like the percentage of people living within 5km or two hours of a healthcare provider. Alongside these physical measures, the density and distribution of health facilities relative to population size and the comprehensiveness of services available are essential parameters for evaluating availability.

Financial accessibility, another critical dimension, is evaluated by examining **out-of-pocket expenditures**, **insurance coverage rates**, and the cost burden of obtaining essential medicines or services. Surveys and administrative data help elucidate the proportion of household income spent on healthcare, revealing where affordability gaps exist and populations risk financial hardship due to medical needs.

Utilization metrics provide further insight by comparing actual use of services to estimated need, thereby highlighting unmet health demands. Epidemiological surveys and health system databases capture rates of clinic visits, prescription fills, and preventive care uptake, which together reflect opportunities and obstacles encountered in practice. Alongside these indicators, patient-centered outcomes, such as perceived timeliness and appropriateness of care, as assessed in satisfaction surveys or qualitative studies, add nuance, revealing subjective experiences and systemic inefficiencies.

In addition, accessibility studies routinely investigate barriers through targeted analyses, identifying cultural, linguistic, organizational, and informational hurdles that may impede access for specific groups. By integrating geographic, financial, organizational, and user experience data, researchers construct a multidimensional portrait of accessibility that is essential for pharmacoepidemiology and health policy, guiding interventions aimed at equitable health resource distribution.

Example Indicators

- Percentage of population living within a set distance/time of a health facility.

- Number and distribution of health facilities per 10,000 population.
- Average waiting times for appointments or procedures.
- Rate of unaddressed health needs in a population.
- Out-of-pocket expenditure as a proportion of income.

Accessibility to community pharmacies in Portugal

This cross-sectional study examined the geographic distribution of community pharmacies and primary healthcare centers (HCCs) in mainland Portugal in 2024 and explored sociodemographic factors associated with disparities in their distribution at the municipal level. Data on the number of pharmacies, HCCs, pharmacists, and physicians, combined with population, area, and socioeconomic indicators, were analyzed across 278 municipalities.

On average, each municipality had 516 residents per physician and 1,021 per pharmacist (physician-to-pharmacist ratio 2.55). The average population per HCC was 22,998, compared to just 3,206 per pharmacy. In terms of geographic coverage, HCCs served an average of 304.6 km^2, whereas pharmacies covered only 82.2 km^2. Paired analyses showed large, statistically significant differences, with pharmacies offering denser territorial coverage than HCCs.

Geospatial mapping revealed that coastal and urban municipalities generally had higher densities of both premises and professionals, while rural inland areas had fewer facilities and covered larger areas per unit. Multivariate analysis showed that a higher pharmacies/HCC ratio was associated with a younger population, higher education levels, and higher literacy rates, while municipalities with older populations and lower education tended to have fewer pharmacies relative to HCCs.

The discussion highlights the broader public health role of pharmacies, particularly in chronic disease management, vaccination, screening, and harm reduction. Evidence from Portugal and abroad shows that better pharmacy accessibility improves adherence, health outcomes, and cost savings. However, “pharmacy deserts” persist in rural regions, mirroring patterns seen internationally.

The authors conclude that although pharmacies in Portugal are more geographically dispersed than HCCs, inequalities remain, especially in rural, less educated municipalities. Policy improvements in regulation and targeted incentives could enhance equitable access. Strengthening pharmacy integration into the National Health Service could maximize their public health contribution, particularly for vulnerable and underserved populations.

Negrão LG, Moreira R, Chaves-Neves I, Figueiredo IV, Fernandez-Llimos F. Distribution of community pharmacies and primary healthcare centers in Portugal: A cross-sectional analysis. Farm Comunitarios. 2025;17(4), 10–22. doi:10.33620/FC.2173-9218.(2025).26

6.3. Quantitative drug utilization studies

Quantitative drug utilization studies are designed **to systematically measure and describe the patterns, trends, and extent of medication use within defined populations over specific periods**. The primary objective of these studies is to provide an objective, data-driven overview of **how drugs are being prescribed, dispensed, and consumed**, typically at the level of a hospital, community, region, or country.

A key characteristic of quantitative drug utilization studies is their reliance on **large datasets**, such as **prescription registers**, **pharmacy sales records**, or **health insurance claims**. These data sources allow researchers to estimate the number of **patients exposed to specific drugs**, identify **trends** over time, and compare usage **patterns** across different geographic areas or healthcare settings. For example, a quantitative study might reveal a sharp increase in the use of a particular antibiotic in a region over several years, prompting further investigation into possible causes such as changes in prescribing guidelines, disease outbreaks, or marketing campaigns.

Quantitative studies are often descriptive in nature, providing snapshots of drug use at a particular point in time (cross-sectional studies) or tracking changes over months or years (longitudinal studies). **Cross-sectional studies** might be used to compare the use of antihypertensive drugs in two different hospitals during the same month, while **longitudinal studies** could monitor the impact of a national policy on opioid prescribing over a decade. These methods enable researchers and policymakers to detect patterns such as seasonal variations in antibiotic use, the adoption of new therapies, or the persistence of polypharmacy in elderly populations.

The utility of quantitative drug utilization studies extends beyond mere description. They are useful for health system planning and resource allocation, as they can inform drug procurement strategies, identify areas of overuse or underuse, and serve as early warning signals for irrational or unsafe prescribing practices. For instance, a quantitative analysis showing unexpectedly high use of sedative medications in a nursing home could trigger a targeted review of prescribing habits and staff education. Similarly, tracking the introduction of generic medicines at a national level can help assess the effectiveness of policies aimed at increasing access and reducing costs.

Quantitative drug utilization studies also play a crucial role in pharmacovigilance and public health surveillance. By linking drug use data with adverse event reporting systems, researchers can identify associations between changes in drug consumption and the frequency of reported side effects or hospitalizations. This approach was instrumental in detecting the increased risk of gastrointestinal bleeding associated with certain non-steroidal anti-inflammatory drugs (NSAIDs) following their widespread adoption.

Analgesic and Opioid Use in Portugal (2012–2022)

A comprehensive quantitative drug utilization study was conducted to evaluate the consumption patterns and economic implications of analgesics—including classical analgesics, adjuvants, and opioids—in Portugal over a ten-year period (2012–2022). Researchers used national sales and health service expenditure data obtained from the Portuguese National Authority of Medicines and Health Products. Drug consumption was standardized using the defined daily dose (DDD) per 1,000 inhabitants per day methodology, in accordance with the Anatomical Therapeutic Chemical (ATC) classification.

The study found that classical analgesic use in Portugal remained relatively stable during the decade, with ibuprofen being the most consumed agent. However, there was a notable increase in the use of adjuvant analgesics, particularly gabapentinoids, which rose by 84%, mainly due to increased pregabalin prescriptions. Weak opioid use, led by tramadol, more than doubled, while strong opioid consumption, especially tapentadol, increased by 618%. Despite these increases, Portugal had the lowest overall opioid consumption compared to Denmark and Spain in 2022.

Economic analysis revealed that the National Health Service's expenditure on analgesics rose, primarily driven by increased opioid use, though the relative burden on total pharmaceutical spending did not significantly change over the period. The authors concluded that the approval of generic medicines and vigilant market monitoring are essential to manage the rising costs associated with increased analgesic and opioid consumption, especially in the context of chronic pain management.

This study illustrates how quantitative drug utilization research can inform national policy, highlight emerging trends, and support the rational use of medicines in clinical practice.

Reference:
Duarte N, Martins JP, García-Pedraza JA, Santos M. Ten-year analgesic utilization patterns and economic implications in Portugal: A comparative analysis with Spain and Denmark. Br J Clin Pharmacol. 2024 Nov 13;91(3):866-881. doi: 10.1111/bcp.16333

6.3.1. Studies on the Quality of Drug Use

Studies on the quality of drug consumption, also known as qualitative drug utilization studies, are designed **to assess whether medications are being used appropriately according to established clinical guidelines, evidence-based protocols, or best practice standards**. Unlike quantitative studies, which focus on the volume and patterns of drug use, quality studies investigate **the *appropriateness* of prescribing, dispensing, and medication use**, addressing questions such as: Is the right drug being prescribed for the right indication, at the correct dose, for the optimal duration, and to the appropriate patient?

These studies often use criteria or indicators derived from national or international guidelines to audit real-world prescribing practices. The purpose is to identify instances of underuse, overuse, or misuse of medications, and to pinpoint areas where interventions or educational efforts could improve patient safety and therapeutic outcomes. Common methods include retrospective prescription audits, cross-sectional analyses of electronic health records, **and linkage of prescription data with clinical diagnoses or risk factors**.

A classic and clinically relevant example is the evaluation of **the proportion of nonsteroidal anti-inflammatory drugs (NSAIDs) prescribed without gastroprotection in older adults**. Clinical guidelines recommend that elderly patients (typically ≥65 years) who are prescribed NSAIDs should also receive a gastroprotective agent, such as a proton pump inhibitor (PPI), to reduce the risk of gastrointestinal ulcers and bleeding, a risk that is significantly elevated in this population. Multiple studies across Europe and North America have demonstrated persistent gaps in adherence to this recommendation.

These studies are valuable for several reasons. First, they provide direct feedback to prescribers and health systems about the degree of alignment between real-world practice and guideline recommendations. Second, they can identify system-level factors, such as the type of electronic medical record used or the presence of clinical decision support, that influence prescribing quality. Third, by quantifying the gap between ideal and actual practice, quality studies inform targeted interventions, such as educational campaigns, clinical audits, or the implementation of prescription alerts.

Improving the Quality of NSAID Prescribing in Older Adults: The Role of Electronic Medical Records

A large-scale Dutch study (2015) examined how often elderly patients (≥65 years) prescribed NSAIDs in general practice also received recommended gastroprotective medications, and whether the type of electronic medical record (EMR) system influenced this quality indicator. Using data from over 91,000 patient visits in 77 general practices between 2005 and 2010, the study found that only 43% of NSAID prescriptions for older adults included co-prescription of a gastroprotective agent such as a proton pump inhibitor or misoprostol.

Encouragingly, the rate of appropriate gastroprotection improved over time, rising from 27% in early 2005 to 55% by the end of 2010. However, this still meant that nearly half of elderly patients at risk for gastrointestinal complications did not receive recommended protection. Notably, the study identified significant differences between practices using different EMR brands: some systems were associated with substantially higher rates of gastroprotection, independent of practice type or size.

The findings highlight two key points for quality improvement in prescribing. First, despite increased awareness and guideline recommendations, underuse of gastroprotection in older NSAID users remains a persistent gap in care. Second, the design and implementation of EMR systems can meaningfully influence prescribing quality, suggesting that optimizing clinical decision support within EMRs could help close this gap.

This study demonstrates the value of quality-focused drug utilization research in identifying actionable targets for safer, more evidence-based prescribing in primary care.

Reference:
Opondo D, Visscher S, Eslami S, Verheij RA, Korevaar JC, Abu-Hanna A. Quality of Co-Prescribing NSAID and Gastroprotective Medications for Elders in The Netherlands and Its Association with the Electronic Medical Record. *PLoS One*. 2015;10(6):e0129515. doi:10.1371/journal.pone.0129515

6.3.2. Studies of prescribing habits

Studies of prescribing habits are designed **to identify patterns in how physicians select and prescribe medications**, as well as to analyze the factors that shape these decisions. These studies typically use prescription data, surveys, or medical record reviews to map out which drugs are chosen for specific conditions, how prescribing varies between clinicians or institutions, and how these practices evolve over time. The goal is to understand both the consistency and variability in prescribing, and to identify opportunities for improving rational drug use.

A key feature of prescribing habit studies is their focus on the diverse influences that affect a physician's choices. According to systematic reviews, **the most frequent determinants include the patient's clinical condition, the prescriber's own experience and specialty, patient preferences, pharmaceutical industry marketing, institutional guidelines, and the cost or reimbursement status of medicines**. For example, a physician's familiarity with certain drug classes, exposure to pharmaceutical representatives, or perception of patient expectations can all sway the selection of a particular medication. Some studies have shown that physicians with longer clinical experience may develop personal "informal formularies", sometimes diverging from updated guidelines, while younger or less experienced prescribers may rely more heavily on institutional protocols or specialist recommendations.

Prescribing habit studies often reveal significant variation between prescribers, even when treating similar patient populations. For instance, a large U.S. study found that, within the ten most common therapeutic classes, the median physician prescribed at least three different drugs, but a minority prescribed only one or two, typically those most heavily promoted by pharmaceutical companies[4]. Such "narrow" prescribers were more likely to choose brand-name or advertised drugs, while broader prescribers tended to offer more therapeutic options and adapt to patient comorbidities or formulary changes. The breadth of prescribing was also influenced by external factors such as drug formularies, insurance coverage, and the availability of samples.

These studies are valuable for identifying not only trends and outliers in prescribing, but also for uncovering the underlying reasons for irrational or suboptimal drug use. By highlighting the impact of non-clinical factors - such as marketing, peer influence, or patient demand - prescribing habit research supports the development of interventions like continuing medical education, feedback on prescribing patterns, and the implementation of evidence-based guidelines. Ultimately, understanding prescribing habits is essential for promoting rational pharmacotherapy, optimizing resource use, and improving patient outcomes.

6.3.3. Studies evaluating therapeutic adherence

Studies evaluating therapeutic adherence using large databases have become a cornerstone of pharmacoepidemiology, offering a robust, objective view of **how patients actually use medications in real-world settings**. Unlike self-reported adherence, which is subject to **recall bias** and **social desirability bias**, analyses of electronic health records, pharmacy dispensing

[4] Joyce GF, Carrera MP, Goldman DP, Sood N. Physician prescribing behavior and its impact on patient-level outcomes. Am J Manag Care. 2011;17(12):e462-e471.

data, and insurance claims provide a detailed and reliable picture of medication-taking behavior across large and diverse populations.

These studies typically employ quantitative metrics such as the **Medication Possession Ratio (MPR)** or the **Proportion of Days Covered (PDC)** to estimate the proportion of time a patient has access to their prescribed medication. For example, a large-scale study in Germany using statutory health insurance data found that only 63% of statin users achieved a PDC of 80% or higher, a commonly accepted threshold for good adherence, and this proportion declined steadily with longer follow-up[5]. Similarly, research using the UK Clinical Practice Research Datalink (CPRD) has shown that adherence to antihypertensive therapy often drops below 50% within two years of initiation, with even lower rates observed in patients prescribed multiple medications[6].

One of the strengths of large database studies is their ability to reveal patterns and predictors of non-adherence across demographic, socioeconomic, and clinical subgroups.

Large databases also allow for the assessment of the impact of health system changes or policy interventions on adherence. After Spain introduced a copayment reform in 2019, adherence to cardiovascular medications improved among low-income patients, suggesting that reducing financial barriers can have a measurable effect on medication-taking behavior[7].

The **Medication Possession Ratio (MPR)** is a widely used quantitative metric for assessing medication adherence from pharmacy claims or dispensing data, particularly in pharmacoepidemiology, drug utilization research, and quality improvement studies. MPR estimates the proportion of time a patient has access to their prescribed medication, serving as an indirect indicator of whether treatment regimens are followed as recommended.

MPR is designed to reflect whether patients "possess" adequate medication to sustain continuous therapy over a defined observation period. It is especially valuable for chronic diseases managed with long-term pharmacotherapy (e.g., antihypertensives, statins, oral antidiabetics), where consistent medication availability is crucial for effective disease control and prevention of complications.

The formula for calculating MPR is:

$$MPRm = \frac{(sum\ of\ days\ supplied)}{(last\ day\ supplied - first\ day\ supplied) + last\ days\ supply}$$

[5] Wendl J, Simon A, Kistler M, Hapfelmeier J, Schneider A, Hapfelmeier A. Medication Adherence and Healthcare Costs in Chronically Ill Patients Using German Claims Data. Appl Health Econ Health Policy. 2023;21(3):477-487. doi:10.1007/s40258-023-00797-6

[6] Rouette J, McDonald EG, Schuster T, Brophy JM, Azoulay L. Treatment and prescribing trends of antihypertensive drugs in 2.7 million UK primary care patients over 31 years: a population-based cohort study. BMJ Open. 2022;12(6):e057510. doi:10.1136/bmjopen-2021-057510

[7] Aznar-Lou I, Pottegård A, Fernández A, et al. Effect of copayment policies on initial medication non-adherence according to income: a population-based study. BMJ Qual Saf. 2018;27(11):878-891. doi:10.1136/bmjqs-2017-007416

Despite their advantages, studies based on large databases are not without limitations. They generally cannot capture the reasons for non-adherence, such as adverse effects, intentional discontinuation, or patient beliefs. Furthermore, prescription fill data do not guarantee that patients actually take the medication as directed. Nonetheless, these studies provide invaluable population-level insights and are essential for monitoring trends, evaluating interventions, and informing health policy.

Evaluating Medication Adherence Using Pharmacy Dispensing Data—An Australian Big Data Study

A 2019 study by Torres-Robles et al. demonstrated the power of large-scale pharmacy dispensing data to assess and improve medication adherence in real-world community pharmacy practice. The researchers analyzed records from over 20,000 patients across 1,805 Australian pharmacies who were prescribed rosuvastatin, irbesartan, or desvenlafaxine and received a pharmacist-led adherence intervention when their medication possession ratio fell below 70%.

Adherence was measured using the Proportion of Days Covered (PDC) before and after the intervention. Prior to pharmacist involvement, average PDC values had declined to around 50% for all three drugs. Three months after the intervention, adherence rates improved markedly: average PDC rose to 66.9% for rosuvastatin, 68.0% for irbesartan, and 66.3% for desvenlafaxine. However, this improvement was not fully sustained; after 12 months, PDC values decreased to 62.1%, 62.4%, and 58.1%, respectively. The proportion of patients considered adherent (PDC ≥80%) increased from 17.4% before the intervention to 41.2% shortly after, but declined to 35.3% after a year.

This study highlights both the effectiveness and limitations of pharmacist-led adherence interventions in routine practice. While short-term gains were substantial, long-term maintenance of adherence proved challenging, emphasizing the need for ongoing support and possibly more complex, multifaceted interventions. Importantly, the use of big data and real-time dispensing records provided a scalable, objective method for monitoring and improving medication use in the community setting.

Torres-Robles A, Wiecek E, Cutler R, Drake B, Benrimoj SI, Fernandez-Llimos F, Garcia-Cardenas V. Using Dispensing Data to Evaluate Adherence Implementation Rates in Community Pharmacy. *Front Pharmacol*. 2019;10:130. doi:10.3389/fphar.2019.00130.