A Textbook of Pharmacoepidemiology and Pharmacovigilance for Pharmacy Students

Lesson 7:

Drug Utilization Metrics

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Lesson 7. Drug Utilization Metrics

Contents

7.1. Introduction to drug utilization metrics

Drug utilization research provides the methodological foundation to quantify and evaluate how medications are prescribed, dispensed, and used in populations. Standardized metrics are essential for transforming raw prescription data into actionable insights, enabling comparisons across time, regions, and healthcare systems. These metrics serve critical roles in public health policy, formulary management, and clinical practice, helping stakeholders identify overuse, underuse, or misuse of medications and assess the impact of interventions.

The World Health Organization (WHO) defines drug utilization research 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***". This discipline bridges clinical pharmacology and epidemiology, offering tools to monitor trends, evaluating guideline adherence, and optimizing resource allocation.

Standardized metrics address three core questions in drug utilization research:

1. What drugs are being used (e.g., specific agents, therapeutic classes)?
2. How much is being used (e.g., volume, cost)?
3. How appropriately are they being used (e.g., adherence to guidelines, dosing accuracy)?

Metrics such as the **DDD**, **Drug Utilization 90% (DU90%)**, and incidence/prevalence rates provide objective answers to these questions. For instance, the DDD — a WHO-developed metric — allows comparisons of antibiotic consumption between the Netherlands (8.94 DDDs per 1,000 inhabitants daily) and Greece (32.15 DDDs), revealing disparities that inform stewardship programs[1]. Similarly, **DU90%** analyses help hospitals streamline formularies by identifying the drugs accounting for 90% of use, ensuring cost-effective and guideline-aligned prescribing.

[1] Bruyndonckx R, Adriaenssens N, Versporten A, et al. Consumption of antibiotics in the community, European Union/European Economic Area, 1997-2017. *J Antimicrob Chemother*. 2021;76(12 Suppl 2):ii7-ii13. doi:10.1093/jac/dkab172

However, these metrics have limitations. The DDD, while invaluable for cross-country comparisons, does not account for **real-world dosing adjustments** or **off-label use**. **Prescribed Daily Dose (PDD)** calculations address this gap by reflecting actual prescribing patterns but require granular data often limited to specific settings. Despite these challenges, the harmonization of metrics through initiatives like the WHO's Anatomical Therapeutic Chemical (ATC)/DDD system has enabled global surveillance of drug use, from opioids to antidiabetics.

This chapter explores the core metrics used in drug utilization studies, emphasizing their applications, strengths, and limitations. By mastering these tools, pharmacists and researchers can contribute to safer, more effective, and equitable medication use worldwide.

7.2. Defined Daily Dose (DDD)

7.2.1 Definition and WHO methodology

The **defined daily dose (DDD)**, established by the WHO Collaborating Centre for Drug Statistics Methodology (https://atcddd.fhi.no/atc_ddd_index/), is the most used metric for standardizing drug consumption measurements in pharmacoepidemiology. DDD's primary purpose is to enable consistent comparisons of medication use across populations, healthcare systems, and time periods, independent of variations in dosing regimens, formulations, or pricing. The DDD is defined as ***"the assumed average maintenance dose per day for a drug used for its main indication in adults"***, serving as a technical unit rather than a clinical recommendation. This distinction is critical, as the **DDD reflects population-level use, not individual patient dosing**.

The need for the DDD concept.

Which community is using more amoxicillin?

A. 1300 packages of 12 capsules of 250 mg
B. 400 packages of 24 capsules of 500 mg
C. 700 packages of 12 capsules of 500 mg

Prior to the DDD, comparing global drug utilization was hindered by inconsistent dosing practices, diverse formulations, and fragmented prescribing habits. The DDD addresses these challenges by providing **a fixed reference dose** for each drug, standardized to its primary therapeutic indication. For example, the DDD for amoxicillin (1.5 grams) aligns with its use for moderate bacterial infections, while the DDD for omeprazole (20 mg) corresponds to its standard dose for gastroesophageal reflux disease.

DDDs are assigned solely to medicines with designated Anatomical Therapeutic Chemical (ATC) codes and typically correspond to monotherapy dosages. The process of establishing a DDD begins with the selection of the **average adult dose recommended for the drug's main indication**, as outlined by the ATC code. Sources considered include national and international drug guidelines, product characteristics, and patterns of usage in clinical practice. For most substances, the DDD is based on **an adult weighing 70kg**; for drugs intended only for pediatric use, the recommended maintenance dose for children is assigned. DDDs are allocated by the

WHO Collaborating Centre for Drug Statistics Methodology in Oslo, in consultation with a working group of experts. **Only a single DDD is assigned per ATC code and route of administration**, and exceptions are made for certain pharmaceutical forms. The **DDDs are reviewed periodically**[2], and any modifications are carefully considered to ensure continued relevance and international comparability. Products with highly individualized dosing schedules, such as those for rare diseases, may not receive a DDD. The methodology and interpretative guidelines for DDD assignment are regularly updated to reflect advances in clinical practice and pharmacotherapy[3].

J ANTIINFECTIVES FOR SYSTEMIC USE
J01 ANTIBACTERIALS FOR SYSTEMIC USE
J01C BETA-LACTAM ANTIBACTERIALS, PENICILLINS
J01CA Penicillins with extended spectrum

ATC code	Name	DDD	U	Adm.R	Note
J01CA01	ampicillin	2	g	O	
		6	g	P	
		2	g	R	
J01CA02	pivampicillin	1.05	g	O	
J01CA03	carbenicillin	12	g	P	
J01CA04	amoxicillin	1.5	g	O	
		3	g	P	
J01CA05	carindacillin	4	g	O	

[2] DDD alterations list: https://atcddd.fhi.no/atc_ddd_alterations__cumulative/ddd_alterations/
[3] Principles for DDD assignment: https://atcddd.fhi.no/ddd/definition_and_general_considera/

Comparing DDD calculations across amoxicillin presentations

The Defined Daily Dose (DDD) for amoxicillin, as established by the WHO, is 1.5 gram (1,500 mg) for oral formulations. This metric standardizes consumption comparisons across different presentations (e.g., capsules, tablets, suspensions) and package sizes. Below, we compare DDD calculations for common amoxicillin formulations, demonstrating how dosage strength and package size influence the total DDDs per unit.

1. Amoxicillin Capsules
   - Strength: 500 mg/capsule
   - Package size: 24 capsules
   - Total drug per package: 500 mg×24=12,000 mg
   - DDDs per package: 12,000mg/ 1,500mg per DDD = 8 DDDs

2. Amoxicillin Tablets
   - Strength: 875 mg/tablet
   - Package size: 12 tablets
   - Total drug per package: 875mg×12=10,500mg
   - DDDs per package: 10,500mg/1,500mg per DDD = 7 DDDs

3. Amoxicillin Oral Suspension
   - Strength: 250 mg/5 mL
   - Bottle volume: 120 mL (24 doses of 5 mL each)
   - Total drug per bottle: 250mg×24=6,000mg
   - DDDs per bottle: 6,000mg / 1,500mg per DDD = 4 DDDs

4. Dispersible Amoxicillin Tablets
   - Strength: 250 mg/tablet
   - Package size: 12 tablets
   - Total drug per package: 250mg×12=3,000mg
   - DDDs per package: 3,000mg / 1,500mg per DDD = 2 DDDs

7.2.2 DDD per 1,000 Inhabitants per Day

The **DDD per 1,000 inhabitants per day** is the main metric for quantifying outpatient drug exposure at the population level. Developed by the World Health Organization (WHO), this indicator standardizes drug utilization data across regions and time periods, enabling comparisons of therapeutic exposure in ambulatory care settings. Its primary purpose is to **estimate the proportion of a population receiving a specific drug on any given day**, providing insights into prescribing patterns, public health priorities, and the burden of chronic diseases.

The need for the DDDs/1,000 inhabitants/day

Which community is using more amoxicillin?

A. 1 million inhabitants consumed 10,000 DDD of amoxicillin in 3 months.
B. 2 million inhabitants consumed 100,000 DDD of amoxicillin in 1 year.
C. 5 million inhabitants consumed 200,000 DDD of amoxicillin in 1 year.

In ambulatory care, drug use varies widely due to differences in disease prevalence, prescribing habits, and formulary policies. The DDD per 1,000 inhabitants per day addresses these disparities by:

1. **Standardizing doses**: Converting diverse formulations (e.g., tablets, suspensions) into a common unit (DDD).
2. **Controlling for population size**: Expressing consumption relative to 1,000 individuals, facilitating cross-regional comparisons.
3. **Enabling trend analysis**: Tracking changes in drug use over time, such as the impact of guidelines or public health campaigns.

For example, a value of **10 DDDs/1,000 inhabitants/day implies that, on average, 1% of the population (10 out of 1,000) receives the drug daily**. The formula for DDD per 1,000 inhabitants per day is:

$$\text{DDD/TID} = \frac{\text{Total DDDs consumed}}{\text{Population} \times \text{Days}} \times 1{,}000$$

Where:

- Total DDDs consumed = Sum of DDDs for all dispensed/prescribed units.
- Population = Number of inhabitants in the study area.
- Days = Duration of the study period (e.g., 365 for annual data).

Example: Consider a region with a population of 500,000 where 45,000 DDDs of amoxicillin (J01CA04) are consumed over 30 days:

- Total DDDs consumed: 45,000
- Population: 500,000
- Days: 30

Applying the formula:

$$\text{DDD/TID} = \frac{45{,}000}{500{,}000 \times 30} \times 1{,}000 = \frac{45{,}000}{15{,}000{,}000} \times 1{,}000 = 3\,\text{DDDs/1,000 inhabitants/}$$

This result indicates that, on average, 0.3% of the population (3 out of 1,000) received a daily dose of amoxicillin during the 30-day period.

Abbreviating DDD/1000 inhabitants/day

Unfortunately, no standardized abbreviation for the metric DDD/1000 inhabitants/day exists. WHO recommends using the DDD/1000 inhabitants/day form, which may not be feasible in an abstract reporting data for several drugs or several geographic areas.

DHD (H for habitant) or **DID** (I for inhabitant) or **DTD** (T for thousand) or **DUD** (U for users) are also used to abbreviate DDD/1000 inhabitants/day.

Can we aggregate DDD? And, DDD/1000 inhabitants/day?

DDD is a mass metric, and we can aggregate (sum) the DDD consumed in two regions of a country, or during two periods of time. For example, during one year the Northern region consumed 250,000 DDD of amoxicillin and the Southern region consumed 300,000 DDD of amoxicillin, thus we can say that both regions together consumed 550,000 DDD of amoxicillin in that year. This is possible because one DDD of amoxicillin equals 1.5 g of amoxicillin, so 250,000 DDD of amoxicillin are 375,000 g of amoxicillin, 300,000 DDD of amoxicillin are 450,000 g of amoxicillin, and subsequently 550,000 DDD of amoxicillin are 825,000 g of amoxicillin (550,000 * 1.5 = 375,000 + 450,000).

This example could be applicable also to two periods of time, let us say the first and the second semester of the year.

However, we cannot always aggregate (sum) DDD/1000 inhabitants/day. While DDD is a mass metric, DDD/1000 inhabitants/day is a proportion of the population exposed to the drug. Proportions are quotients (See: "Ratios, Proportions, and Rates" in the chapter "Measures of risk and association"). To be able to sum the result of two quotients, denominators should be identical. Thus, we can aggregate two DDD/1000 inhabitants/day when population and days (period of time) are identical. This means that:

We **cannot** aggregate (sum) the DDD/1000 inhabitants/day of two regions (because they have different populations).

We **can** aggregate (sum) the DDD/1000 inhabitants/day of two drugs from a given class consumed in a population during a specific period. We can aggregate 3.5 DDD/1000 inhabitants/day of plain amoxicillin consumed in Northen region during 2025 with 6.5 DDD/1000 inhabitants/day of amoxicillin (formulated together with clavulanic acid) consumed in Northen region during 2025, and we can say that 10 DDD/1000 inhabitants/day of amoxicillin were consumed in Northen region during 2025. These two calculations have the same population and the same period of time.

7.2.3 DDD per 100 (or 1,000) Patient-Days/Bed-Days (Hospital)

The **DDD per 100 bed-days** is a metric to quantify **drug consumption intensity in hospital settings**. Unlike ambulatory care, where drug use is distributed across a stable population, hospital drug utilization is influenced by **patient turnover**, **acuity**, and **length of stay**. This metric normalizes consumption relative to **inpatient bed occupancy**, enabling comparisons between wards, hospitals, or countries while accounting for variations in admission rates and resource utilization.

In hospitals, drug use patterns differ significantly from outpatient settings due to factors such as:

- **Higher therapeutic intensity**: Critically ill patients often require multiple high-dose medications.
- **Variable lengths of stay**: A patient admitted for one day may receive more drugs than a patient staying for a week.

- **Specialized formularies**: Hospitals prioritize IV formulations, high-potency analgesics, or antibiotics not typically used in primary care.

The DDD per 100 bed-days addresses these complexities by estimating the average daily therapeutic exposure per occupied bed. For example, a value of 50 DDDs/100 bed-days implies that, on average, 50% of inpatients received one DDD of the drug daily. This metric is particularly useful for benchmarking antimicrobial stewardship programs or opioid use across surgical wards.

The formula for DDD per 100 bed-days is:

$$\text{DDD/100 bed-days} = \frac{\text{Total DDDs consumed}}{\text{Total bed-days}} \times 100$$

Where:

- Total DDDs consumed: Sum of DDDs for all administered drugs.
- Total bed-days[4]: Average daily bed count × study duration.

Example: A hospital with 200 beds operates at 80% occupancy over 30 days:

1) Total bed-days: 200 beds×0.8 (occupancy)×30 days=4,800 bed-days
2) Total DDDs consumed (e.g., antibiotics): 2,400 DDDs
3) DDD/100 bed-days: (2,400/4,800)×100 = 50 DDDs/100 bed-days

This result indicates that, on average, 50% of inpatients received one DDD of the antibiotic daily.

In hospital settings, **bed-days quantify the total occupancy of beds over a specific time**, providing a standardized denominator for evaluating resource utilization. The calculation reflects the **aggregate number of days all patients occupy hospital beds**.

To calculate Bed-Days in a hospital with n patients, the basic formula is:

$$\text{Bed-days} = \sum_{i=1}^{n} (\text{Discharge date}_i - \text{Admission date}_i)$$

For example, if one patient is hospitalized for 5 days and another for 7 days, the total bed-days are: 5 + 7 = 12

Bed-days and occupancy are closely linked, as bed-days measure the total actual use of hospital beds over a period, while bed occupancy rate quantifies how fully those beds are used. The hospital bed occupancy rate is defined as:

$$\text{Bed Occupancy Rate (\%)} = \frac{\text{Total Bed-Days Used}}{\text{Number of Beds} \times \text{Number of Days in Period}} \times 100$$

[4] Bed-day definition: A bed-day represents a 24-hour period during which a bed is occupied, excluding day cases (patients admitted and discharged the same day).

Comparing DDD/1000 inhabitants/day (DDD/TID) and DDD/100 Bed-Days

Below is a comparison of DDD per 1,000 inhabitants per day (DDD/TID) and DDD per 100 bed-days, highlighting their distinct purposes, calculations, and interpretations.

DDD per 1,000 Inhabitants per Day (DDD/TID) Measures outpatient drug use in a population.

$$\text{DDD/TID} = \frac{\text{Total DDDs consumed}}{\text{Population} \times \text{Days}} \times 1{,}000$$

DDD per 100 Bed-Days Quantifies inpatient drug intensity relative to hospital occupancy.

$$\text{DDD/100 bed-days} = \frac{\text{Total DDDs consumed}}{\text{Total bed-days}} \times 100$$

Aspect	DDD/TID	DDD/100 Bed-Days
Denominator	General population	Hospital bed occupancy
Setting	Outpatient/community	Inpatient/hospital
Focus	Population-wide exposure	Therapeutic intensity per bed-day
Data Source	Pharmacy claims, prescriptions	Hospital administration records
Limitations	Assumes uniform dosing in population	Excludes day cases, varies by acuity

7.3. Prescribed Daily Dose (PDD)

The **prescribed daily dose (PDD)** is **the average daily amount of a drug 'actually' prescribed to patients, as derived from real-world prescription data**. Unlike the defined daily dose (DDD), which is a fixed theoretical unit, the PDD reflects actual dosing practices in clinical settings. It is calculated by analyzing prescriptions or pharmacy records to determine the average dose patients receive over a defined period. The formula for PDD is:

$$PDD = \frac{Amount\ drug\ dispensed}{days}$$

Example: A patient prescribed 20 tablets of amoxicillin 500 mg for a 10-day course receives a total of 10,000 mg. The PDD is:

$$PDD = \frac{10{,}000\ mg}{10\ days} = 1{,}000\ mg/day$$

This contrasts with the DDD for amoxicillin (1,500 mg), highlighting potential **discrepancies between prescribed and standardized doses**.

7.3.1. PDD/DDD Ratio and Its Interpretation

The **PDD/DDD ratio** quantifies the relationship between real-world prescribing and the WHO's theoretical standard. It is calculated as:

$$\text{PDD/DDD ratio} = \frac{\text{PDD}}{\text{DDD}}$$

The interpretation PDD/DDD ratio is:

- PDD/DDD ratio **≈ 1**: Prescribed doses align with WHO standards.
- PDD/DDD ratio **> 1**: Prescribed doses are higher than standard dosing.
- PDD/DDD ratio **< 1**: Prescribed doses are lower than standard dosing.

A case study to depict the use of PDD/DDD ratio could be the use of antihypertensive drugs in Germany. In this study, that analyzed 149,704 patients receiving antihypertensives[5]:

- **ACE inhibitors**: PDD/DDD = 2.17 (indicating double the DDD).
- **Beta-blockers**: PDD/DDD = 0.84 (16% below DDD).
- **ARBs**: PDD/DDD = 1.88 (88% above DDD).

These ratios revealed systemic patterns: switching from beta-blockers (PDD/DDD = 0.79) to ACE inhibitors (PDD/DDD = 2.17) doubled the daily dose, independent of patient factors.

[5] Grimmsmann T, Himmel W. Discrepancies between prescribed and defined daily doses: a matter of patients or drug classes?. Eur J Clin Pharmacol. 2011;67(8):847-854. doi:10.1007/s00228-011-1014-7

The Pitfalls of Fixed DDDs—Lessons from Statin Utilization in Portugal

A study by Abrantes and colleagues (Br J Clin Pharmacol, 2021) explored the impact of discrepancies between the Defined Daily Dose (DDD) and the Prescribed Daily Dose (PDD) on long-term drug utilization research, using statin consumption in Portugal as a case study. Over an 18-year period (2000–2018), the authors analyzed national dispensing data for all statins and compared three different approaches for calculating utilization rates: DDDs based on the WHO value for each year (DDD_YEAR), DDDs based on the final year's value (DDD_LAST), and PDDs derived from actual prescribed doses.

The study found that changes in the WHO-assigned DDDs for several statins in 2009 (e.g., simvastatin, atorvastatin, fluvastatin) led to abrupt and artificial shifts in utilization rates when calculated using the DDD_YEAR approach. For example, simvastatin consumption appeared to drop by 40% in a single year, not due to real changes in prescribing but because the DDD was revised. In contrast, the PDD-based approach and the DDD_LAST method showed more gradual and realistic trends in statin use over time. Importantly, the authors demonstrated that the use of fixed, international DDDs can result in substantial errors—sometimes overestimating or underestimating true drug use by 30% to 80%—especially when national prescribing habits differ from WHO assumptions.

The study also highlighted that for some statins, such as lovastatin and fluvastatin, the average prescribed dose in Portugal was consistently below or above the DDD, respectively, throughout the study period. This mismatch caused systematic bias in estimates of population exposure and could mislead health policy or cost analyses based on DDDs alone.

Abrantes et al. conclude that the DDD system, while invaluable for international benchmarking, should be more flexible and responsive to national prescribing patterns. They recommend that DDDs be updated more frequently and, where robust national data exist, tailored to local practice to improve the accuracy and relevance of drug utilization research.

Reference:
Abrantes C, Tonin FS, Reis-Pardal J, Castel-Branco M, Furtado C, Figueiredo IV, Fernandez-Llimos F. Implications of a defined daily dose fixed database for drug utilization research studies: The case of statins in Portugal. *Br J Clin Pharmacol*. 2021;87(9):3542-3549. doi:10.1111/bcp.14770.

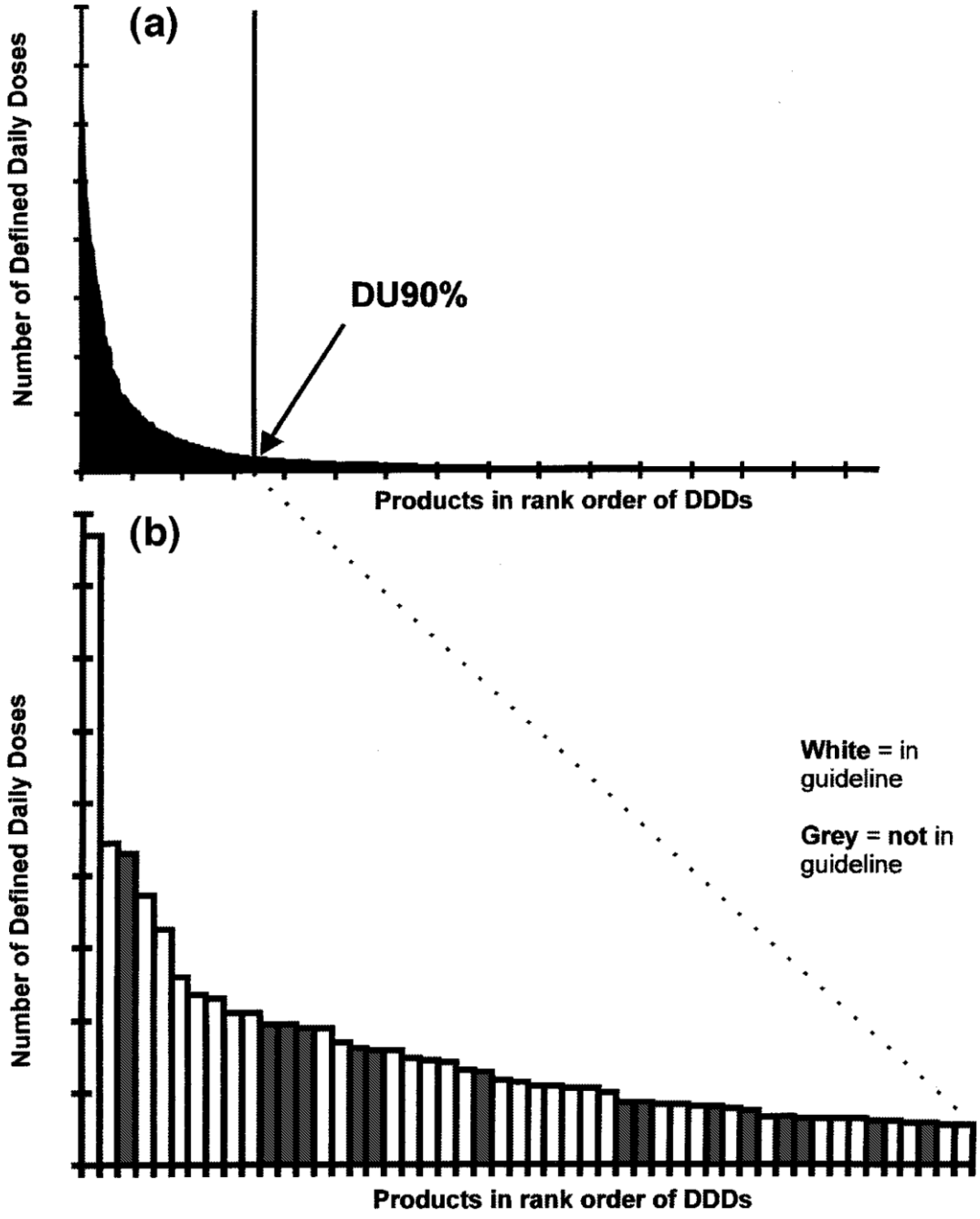
7.4. Drug Utilization 90% (DU90%)

The **Drug Utilization 90% (DU90%)** metric is a simple yet powerful tool for analyzing **prescribing patterns and assessing the quality of drug use in clinical practice**. Originally proposed in Sweden and now recommended by the World Health Organization, **the DU90% method focuses on the core group of medications that make up the vast majority of prescribing volume within a given setting**, such as a general practice, hospital, or region.

The **DU90% is defined as the number of unique drugs (usually identified by their chemical substance or ATC code) that together account for 90% of total drug use**, measured in defined daily doses (DDDs) or number of prescriptions, over a specified period. **To calculate the DU90%**, all drugs prescribed are **ranked in descending order according to their volume** (in DDDs or

prescriptions). The cumulative sum is then calculated **until 90% of the total volume is reached**; **the number of different drugs included in this segment is the DU90% value**.

For example, if a general practice prescribes 120 different medicines over a year, but only 35 of this account for 90% of all DDDs dispensed, the DU90% is 35. The remaining 85 drugs, although available, are prescribed infrequently and make up only 10% of the total volume. The DU90% can be visualized by plotting drugs in rank order of DDDs on the x-axis and the DDDs on the y-axis, highlighting the concentration of prescribing within a limited set of medicines.



Example from: Bergman U, et al. Drug utilization 90%--a simple method for assessing the quality of drug prescribing. Eur J Clin Pharmacol. 1998;54(2):113-118.

The DU90% method has several applications in formulary management and quality assurance. **A lower DU90% value typically indicates more rational and focused prescribing**, as it suggests that prescribers rely on a smaller, well-understood set of medicines, often those recommended by clinical guidelines or local formularies. Conversely, a higher DU90% may reflect less rational prescribing, with frequent use of less familiar or non-recommended drugs, which can increase the risk of errors, adverse effects, and unnecessary costs.

By identifying which drugs constitute the DU90% segment, healthcare organizations can assess adherence to recommended formularies and guidelines. For example, a study in Swedish primary care found that the majority of drugs in the DU90% segment were included in local therapeutic guidelines, and that adherence to these guidelines was associated with higher quality prescribing[6]. Similarly, in the UK and Ireland, DU90% profiles have been used to provide

Evaluating the DU90% Method for Quality Assessment of Prescribing in Primary Care

A study by Wettermark and colleagues (Pharmacoepidemiol Drug Saf. 2003) evaluated the Drug Utilization 90% (DU90%) method as a tool for assessing the quality of prescribing in primary health care centers in Stockholm, Sweden. The DU90% metric identifies the number of unique drugs that together account for 90% of the total prescribing volume, measured in defined daily doses (DDDs), and assesses how well this core group aligns with local guideline recommendations.

In this intervention project, 38 primary health care centers participated, with their prescribing profiles analyzed before and after the introduction of feedback based on DU90% profiles. The results revealed considerable variation in prescribing patterns: while the total number of drugs prescribed at each center ranged from 358 to 674, the number of drugs constituting the DU90% segment ranged from 117 to 194. Importantly, adherence to local drug committee guidelines within the DU90% segment varied between 56% and 74% and improved over the course of the project.

Feedback was provided to prescribers through DU90% profiles, which highlighted both the range of drugs most commonly used and the degree of alignment with evidence-based recommendations. General practitioners rated the method highly, describing the profiles as clear, relevant, and useful for improving the quality of their prescribing. The study also found that providing this feedback, especially when combined with group discussions and economic incentives, led to increased adherence to recommended drugs.

The authors concluded that the DU90% method is an inexpensive, flexible, and practical approach for monitoring and enhancing prescribing quality in primary care. By focusing on the most frequently used medicines and benchmarking them against guidelines, DU90% profiles serve as a catalyst for rational drug use, peer discussion, and continuous quality improvement.

Wettermark B, Pehrsson A, Jinnerot D, Bergman U. Drug utilisation 90% profiles—a useful tool for quality assessment of prescribing in primary health care in Stockholm. *Pharmacoepidemiol Drug Saf*. 2003;12(6):499–510. doi:10.1002/pds.852.

[6] Wettermark B, Pehrsson A, Jinnerot D, Bergman U. Drug utilisation 90% profiles--a useful tool for quality assessment of prescribing in primary health care in Stockholm. Pharmacoepidemiol Drug Saf. 2003;12(6):499-510. doi:10.1002/pds.852

feedback to general practitioners, highlighting opportunities to streamline prescribing and reduce the use of low-value or high-risk medications[7].

The DU90% can also be used for benchmarking between practices, hospitals, or regions, and for tracking changes over time in response to interventions, policy changes, or educational initiatives. Its simplicity and flexibility make it a valuable addition to the pharmacoepidemiologist's toolkit, complementing more detailed drug-specific quality indicators.

7.5. Days of Therapy (DOT)

The **Days of Therapy (DOT)** metric has become a relevant tool in hospital pharmacoepidemiology, particularly for monitoring antimicrobial use and stewardship efforts. **DOT reflects the actual number of days a patient receives a specific drug, regardless of dose or frequency**, and is increasingly regarded as a preferred measure of drug exposure in acute care settings.

A DOT is defined as one day during which a patient receives a single agent, regardless of the number of doses or the strength administered on that day. For example, if a patient receives vancomycin twice daily for five days, this counts as 5 DOTs for vancomycin. If the same patient receives two antibiotics (e.g., vancomycin and ceftriaxone) each day for five days, the total DOT for antibiotics is 10 DOTs (five for each agent). DOT captures the duration of therapy rather than the quantity of drug administered, making it especially useful for benchmarking and stewardship in populations with variable dosing requirements, such as pediatrics or critically ill adults.

7.5.1 DOT per 100 Patient-Days

To enable meaningful comparisons between hospitals or wards of different sizes and **case mixes**, DOT is typically normalized to patient-days (or bed-days), producing the metric DOT per 100 (or 1,000) patient-days. The formula is:

$$\text{DOT/100 patient-days} = \frac{\text{Total DOTs in period}}{\text{Total patient-days in period}} \times 100$$

For example, if a hospital unit administers 600 DOTs of antibiotics during a month in which there are 1,200 patient-days, the DOT/100 patient-days is:

$$\frac{600}{1,200} \times 100 = 50 \text{ DOTs/100 patient-days}$$

This means that, on average, patients received 0.5 DOTs per day, or that half the patients were on at least one antibiotic each day.

7.5.2 Comparison DOT with DDD

While both DOT and defined daily dose (DDD) are used to quantify drug consumption, they have important differences. DDD is based on a fixed, theoretical average maintenance dose for adults,

[7] Chiedozie C, Murphy ME, Fahey T, Moriarty F. How many medications do doctors in primary care use? An observational study of the DU90% indicator in primary care in England. BMJ Open. 2021;11(3):e043049. doi:10.1136/bmjopen-2020-043049

and is independent of actual prescribed or administered doses. In contrast, DOT ignores dose and instead measures each day of exposure to a drug as one unit. Numerous studies have found that DDD and DOT can yield discordant results, especially in populations where dosing deviates from the WHO standards, such as in pediatrics, renal impairment, or critical care.

DOT also enables more accurate assessment of combination therapy, as each agent is counted separately. However, DOT may overestimate exposure in cases of combination therapy and requires detailed administration data, which may not be available in all settings.

Why DOT can be more accurate than DDD in critically ill patients

DOT (Days of Therapy) can be more accurate than **DDD (Defined Daily Dose)** for measuring drug consumption in critically ill patients, mainly because DOT reflects the true exposure of the patient to the drug, regardless of the dose administered, while DDD is based on a theoretical standard dose that often does not match real clinical practice in these settings.

In critically ill patients, the doses of antimicrobials and other medications are often significantly higher (or lower) than the DDDs assigned by the WHO, due to factors such as disease severity, altered pharmacokinetics, renal failure, or the need for combination treatments and frequent adjustments. For example, in an ICU, it is common for patients to receive doses higher than the DDD to achieve adequate therapeutic concentrations. When DDD is used as an indicator, this can lead to an **overestimation of actual consumption** (if the administered dose is higher than the DDD) or an **underestimation** (if it is lower), and it does not reflect how many patients have been treated or for how many days.

DOT, on the other hand, counts each day a patient receives at least one dose of the medication, regardless of the amount given. Thus, if a patient receives meropenem three times a day for five days, 5 DOTs are counted, whereas the DDD calculation could vary greatly depending on the total daily dose and its relation to the WHO DDD for that drug. In this way, DOT **minimizes the impact of the dose used** and allows for comparison of the actual duration of exposure between patients, services, and hospitals.

Studies in ICUs have shown that consumption measured by DDD is often significantly higher than that measured by DOT, precisely because the daily dose administered is usually higher than the WHO DDD, which can lead to errors in interpretation and comparison between centers. For this reason, **guidelines and antimicrobial stewardship programs (ASPs) recommend the use of DOT as the main indicator of consumption in critically ill patients**.

Vallès J, Fernández S, Cortés E, et al. Comparison of the defined daily dose and days of treatment methods for evaluating the consumption of antibiotics and antifungals in the intensive care unit. Med Intensiva (Engl Ed). 2020;44(5):294-300.