Medical Sains : Jurnal Ilmiah Kefarmasian
Vol. 8 No. 3, July – September 2023
https:/ojs.stfmuhammadiyahcirebon.ac.id/index.php/iojs

REVIEW: APPLICATION OF THE ATC/DDD METHOD FOR ANTIBIOTIC EVALUATION IN INDONESIA

Yusna Fadliyyah Apriyanti[1], Saepudin[1*]
[1]*Master of Pharmacy Study Program, Department of Pharmacy, FMIPA, Indonesian Islamic University*
Jl. Kaliurang No. Km. 14.5, Krawitan, Umbulmartani, Kec. Sleman, Sleman Regency, Special Region of Yogyakarta 55584
** Email Corresponding: saepudin@uii.ac.id*

Submitted: 3 August 2023 Revised : 1 September 2023 Accepted: 26 September 2023

ABSTRACT

The global consumption of antibiotics has increased rapidly by 65% in units of daily doses over the last 15 years. Researchers predict that there will be a 200% increase in global antibiotic consumption by 2030, if there is no change in policy implementation. This article aims to provide knowledge regarding the use of the anatomical therapeutic chemical/defined daily doses (ATC/DDD) method to evaluate antibiotics in Indonesia, which is expected to provide additional knowledge for the quantitative evaluation of antibiotics. The literature data sources used were PubMed and Google Scholar online databases, using the Mendeley® tool for manager reference. There were 71 articles that met the criteria and were discussed systematically. Most of the ATC/DDD methods were used to evaluate antibiotics in 90.1% of inpatients and 9.9% of outpatients. In the application of this method, 94.4% of the data collection was carried out retrospectively, with most study designs using a cross-sectional 76%. The selected research period varied from 1 month to 5 years, with 59.1% of the study locations being carried out at the tertiary service level. The ATC/DDD method can also be used in a quasi-experimental design that examines comparisons before and after the intervention. The use of this method as an evaluation of the use of antibiotics in the specified study population resulted in the highest DDD/100 days of ceftriaxone hospitalization in 27 articles. Amoxicillin had the highest DDD/1000 patient-days in of 6/7 articles in the outpatient population. This ATC/DDD method can be used by health practitioners and other researchers to evaluate the use of antibiotics in view of its conformity with disease management guidelines and accuracy with existing disease conditions in hospitals or other health services in Indonesia.

Keywords : Antibiotics, ATC/DDD Method, Antibiotic Quantity, Use Evaluation, Indonesia

INTRODUCTION

Antimicrobial resistance (AMR) is a significant threat to human health. (Antimicrobial Resistance Collaborators, 2022) estimate that 4.95 million fatalities have been caused by AMR in 2019. The consumption of antibiotics in 76 countries from 2000 to 2015, expressed in daily quantities (defined daily dose/DDD), increased by 65 percent over the past 15 years, as shown by the results of an analysis of antibiotic consumption from 2000 to 2015 in those countries. (Klein et al., 2018) estimate that global antibiotic consumption will increase by 200 percent by 2030 if there is no change in policy implementation. The widespread overuse of antibiotics by physicians is a drug option based on its low cost and the prescription of broad-spectrum antibiotics that are ultimately ineffective against the bacteria causing the infection (Dadgostar, 2019). Resistance to antimicrobials necessitates evaluation of drug use, particularly antibiotic formulations (Ismail, 2022).

Periodically, drug use must be evaluated as a form of surveillance to enhance healthcare and drug policies. A survey of six hospitals in Indonesia revealed a high rate of antibiotic use, which deviated from the recommendations (Limato et al., 2021). The public perception that antibiotics are more effective than other medications, pressure on health practitioners to prescribe antibiotics, and lack of community-level education about antibiotic resistance contribute to their excessive use (Marasine et al., 2021). The primary purpose of evaluating drug use is to determine whether a substance is rationally utilized (Menkes RI, 2017). Both quantitative and qualitative evaluations of substance use are possible. Using defined daily doses (DDD), prescribed daily doses (PDD), and days of therapy (DOT), quantitative evaluation of antibiotic use can be performed. PDD and DOT have disadvantages in that they cannot be used to compare hospitals and DOT regardless of the dose and quantity used in their calculations (Sukriya et al., 2022).

Since 1996, the WHO has recommended the Anatomical Therapeutic Chemical (ATC)/Defined Daily Doses (DDD) system to evaluate drug use (WHO, 2022). The Anatomical Therapeutic Chemical (ATC) system is a classification system used for drug taxonomy that groups drugs based on their anatomy in the target organs of therapy, pharmacological or therapeutic properties, and chemical substance content (WHO, 2022). The Defined Daily Dose (DDD) is a measurement of drug use recommended by the World Health Organization (WHO) as standard data that can be compared nationally and internationally. From the defined daily dose unit, antibiotic consumption can be calculated as a daily dose using DDD/100 bed-days for inpatients and DDD/1000 population for outpatients (WHO, 2022). The ATC/DDD classification system is an option for identifying the multiple aspects of antibiotic misuse and overuse.

According to a 2022 assessment of antibiotic use in Indonesia, ceftriaxone has the highest quantitative stability and 30% of antibiotic use is irrational (Diah, 2022). The ATC/DDD method derived from monthly data provides a clear picture of the total consumption of antibiotics and trends in their use to attain antibiotic control goals (Zhu et al., 2021). ATC/DDD methodology has not been previously reviewed in the context of studies assessing antibiotic use in Indonesia. The scope of the quantitative evaluation of antibiotic usage using the ATC/DDD technique is described in this review, which is the first review to do so until November 2022. This systematic review aimed to learn more about how the ATC/DDD technique can be used to track antibiotic consumption in Indonesia. Health professionals and researchers can utilize the findings from this systematic observation as a template for evaluating the efficacy of antibiotics in practice.

RESEARCH METHODS

This study employs a systematic review research methodology to investigate the application of the Anatomical Therapeutic Chemical (ATC)/Defined Daily Dose (DDD) technique in the assessment of antibiotic usage in Indonesia. The present study employed the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) criteria. The prism guide outlines a systematic approach to conducting a search, which encompasses four distinct stages: identification, screening, eligibility assessment, and inclusion. The PRISMA framework serves as a comprehensive tool for researchers, providing guidance on the proper execution of systematic reviews and meta-analyses in adherence to evidence-based principles (Page et al., 2021).

The articles included in this study met the following criteria:1) they focused on antibiotics as the subject of research and evaluated them using the ATC/DDD method, 2) they were written in either Indonesian or English, 3) the research was conducted in Indonesia, 4) the articles were accessible online, and 5) the research was published until November 5, 2022. The initial phase of identification involves performing a search on the PubMed and Google Scholar digital databases, employing specific keywords as search strings. The specified keywords for this study are "ATC", "DDD", "antibiotics", and "Indonesia". To effectively manage and organize references, the Mendeley® tool can be utilized. Once the search process has concluded, the articles undergo a screening procedure to identify and remove any duplicate articles with identical titles. Furthermore, the articles were organized and arranged according to the predetermined inclusion criteria, which involved removing articles that were not available in their entirety for viewing. The third phase involved assessing eligibility, wherein the researcher thoroughly examined all the chosen articles and excluded any that failed to fulfill the predetermined criteria. The concluding phase encompasses the evaluation of the selected articles in terms of their quality and quantity, achieved by the extraction of data from research studies that provide accurate and relevant information. The extraction process was conducted using criteria such as the author's name, year of publication, location, total defined daily dose (DDD) per 100 bed-days, and DDD per 1000 patient-days.

RESULTS AND DISCUSSION

The search results for articles from two online databases, Google Scholar and PubMed, yielded 520 and 10 articles, respectively. After filtering articles based on the inclusion, exclusion, and duplication criteria, 207 relevant articles were obtained. Based on the screening results, 159 articles published between January 2018 and November 2022 were selected. The 159 articles were then thoroughly read to select and eliminate related articles that did not quantitatively evaluate the use of antibiotics using the ATC/DDD method, and 71 articles that met the requirements were obtained. A summary of the search and selection of the articles is shown in **Figure 1**.

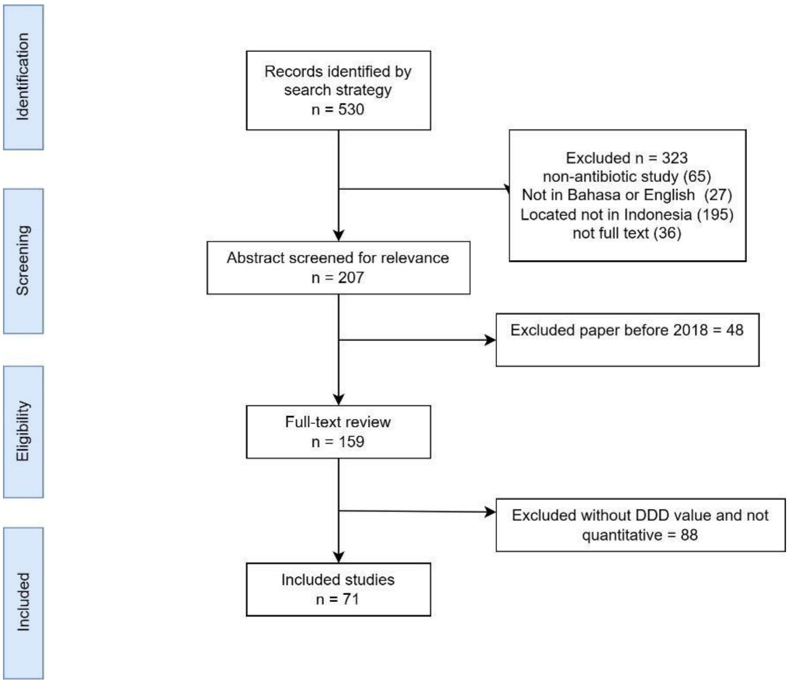

Figure 1. Flowchart for searching and selecting articles used as study material by following the PRISMA method

Based on Table I regarding the research characteristics of the collected articles, the evaluation of the use of antibiotics using the ATC/DDD method was conducted in an observational manner using a descriptive research design, with the data collected retrospectively in 94.4% of the articles, prospectively in 4.2% of the articles, and both retrospectively and prospectively in 1 article (1.4%). Because incomplete medical record writing is a weakness of retrospective data collection, (Herawati et al., 2019) chose to combine the two data collection methods for pediatric patients so that they could be contrasted and discussed. In the selected articles, three types of research design were employed: cross-sectional, 76%; quasi-experimental, 11.2%; and case study, 2.8%. A cross-sectional study design was used to analyze data collected at a particular time point. This is the most popular study design because the researcher can determine the study period and data can be collected both retrospectively and prospectively. A quasi-experimental research design appears to be experimental because of the provided intervention, but data collection can also be determined retrospectively by researchers. When evaluating the use of antibiotics before and after intervention, for example, Guidelines for Antibiotic Use (PPAB) (Karuniawati et al., 2021), Antimicrobial Resistance Control Program (PPRA) (Kartika et al., 2019), and Clinical Pathway (Adiwisastra et al., 2019). (Evano Putra et al., 2021) and (Ilmi et al., 2020) selected pneumonia patients in the lung room at the RSUD dr. Iskak Tulungagung for their case studies on the use of antibiotics during the Covid-19 pandemic at the Diponegoro National Hospital.

Table I. Description of the Use of ATC/DDD Based on Research Characteristics

Article Characteristics	Total (n = 71)	Percentage (%)
Research design		
Retrospective Observational	67	94.4%
Prospective Observational	3	4.2%
Combination Observation	1	1.4%
Study Design		
Cross-sectional	54	76%
Case study	2	2.8%
Quasi-Experimental	8	11.2%
Research Period		
< 6 months	14	19.7%
6 Months – 1 Year	42	59.2%
2 years	6	8.5%
3 years	5	7%
5 years	2	2.8%
Without explanation	2	2.8%
Study Population		
Inpatient :	**64**	**90.1%**
All Patients	5	
ICU	3	
Pediatrics	9	
Mature	2	
Diabetic Ulcer	2	
Covid-19	5	
Internal disease	9	
Surgery	14	
Pneumonia	14	
Sepsis	1	
Outpatient :	**7**	**9.9%**
Gonorrhea Patients	1	
ISPA Non Pneumonia	1	
All Patients	5	

The duration of the investigation period for the selected articles ranged from one month to five years. Six months to one year is the most preferred time frame because it is believed to be adequate for comparing antibiotic use in the two locations. Most researchers (90.1%) chose to evaluate the use of antibiotics in inpatients, while only 9.9% did so in outpatients. DDD/100 bed-days for inpatients and DDD/1000 patient-days for outpatients were used to calculate the DDD value. The inpatient population of the study can be optimally evaluated because of the availability of complete data in the patients' medical records. Among the selected articles for inpatients, the selection of the study population of patients with pneumonia and surgery yielded the maximum number of articles, with 14 each, followed by patients with internal disease, covid-19, diabetic ulcer, and sepsis. The inpatient study population could also be selected based on the pediatric age (1 to 18 years). 9 articles, 2 articles for adults (> 18 years), and 5 articles for all patient categories. In the selected articles for outpatients, the majority of researchers selected all patients (5 articles) so that more data could be acquired. However, there were also researchers who selected specific outpatient conditions, such as gonorrhea (1 article) and non-pneumonia ARI (1 article).

The sampling method for the selected articles was determined using the data source to be accessed. According to Table II, the most popular data source chosen by researchers was patient medical record data, at 95.8%, because medical record data allow some researchers to evaluate the qualitative use of antibiotics. Another source of information is drug use reports, which account for 4.2%; therefore, it can be concluded that there are few studies evaluating the overall use of antibiotics in health services. 53.5 percent of the total population was sampled using the total population was sampled. After determining very specific inclusion and exclusion criteria by selecting a specific time period, fewer than 50 samples were obtained; for instance, in one study (O. N. Putra et al., 2022)Click or tap here to enter text. that evaluated the use of prophylactic antibiotics for surgical debridement in 2018-2020 at Dr. Soetomo, 30 patients met the inclusion criteria. Other researchers (Effendy et al., 2022) calculated the use of antibiotics in Bangil Hospital inpatient diagnosed with pneumonia from October 2021 to February 2022, and prospectively identified 35 patients who met the inclusion criteria. A total of 32.4% of the samples were collected using a technique called purposive sampling, in which the researcher relied on his own discretion to select samples from a population based on predetermined inclusion and exclusion criteria. This method was selected so that time could be used more efficiently; however, it has the potential to misrepresent the selected population (Dahlan, 2010). Prof. dr. Margono Soekarjo Purwokerto obtained a sample of 100 patients using a straightforward random sampling technique (Lestari et al., 2018). To satisfy the predetermined number of samples, up to 5.6% of the respondents opted to collect sequential samples that were encountered for the first time using the consecutive sampling method.

Table II. Description of ATC/DDD Usage Based on Data Sources

Article Characteristics	Total (n = 71)	Percentage (%)
Data source		
Medical records	68	95.8%
Drug Use Report	3	4.2%
Sampling Method		
Total Population Sampling	38	53.5%
Purposive Sampling	23	32.4 %
Simple Random Sampling	6	8.5%
Consecutive Sampling	4	5.6%

Based on the selection of research locations in Table III, 59.1% of the ATC/DDD methods for evaluating the use of antibiotics in Indonesia were conducted at the tertiary service level, specifically in type A and type B hospitals, because a more diverse use of antibiotics would be observed compared to secondary service level hospitals. or principal. The tertiary service level prioritizes subspecialties extensively and transforms them into a referral hospital if the subspecialty cannot be managed at the secondary service level. Several studies were conducted in secondary care institutions (28.2%), while the remaining 9.8% were conducted in primary care facilities. One article (Sholih et al., 2019) evaluated inpatients in primary care. The majority of primary service locations were selected by researchers who evaluated the outpatients. In Java, 71.8% of the population utilized the ATC/DDD method. There were 20 articles that chose research locations outside the island of Java, with 13 articles choosing Sumatra, 4 choosing Bali, and 1 each choosing Sulawesi, Kalimantan, and East Nusa Tenggara. As a result, it was determined that the evaluation of the use of antibiotics using the ATC/DDD method was still very limited outside Java and could be a future option for other researchers.

Table III. Description of the Use of ATC/DDD Based on Research Locations

Article Characteristics	Total (n = 71)	Percentage (%)
Health Care Level		
Primary	7	9.8%
Secondary (Hospital Type C & D)	20	28,2
Tertiary (Hospital Type A & B)	42	59.1%
Without explanation	2	2.9%
Research sites		
Java Island :	**51**	**71.8%**
East Java	31	
Central Java	6	
West Java	7	
In Yogyakarta	6	
DKI Jakarta	1	
Outside of Java Island :	**20**	**28.2%**
Sumatra	13	
Bali	4	
Sulawesi	1	
Borneo	1	
East Nusa Tenggara	1	

The ATC/DDD system can be used to collect drug use statistics from a variety of locations and sources, including sales data, drug prescription and use data, and patient encounter-based data collected through specially designed sampling (WHO, 2022). Typically, these data are only accessible in healthcare settings such as hospitals, clinics, and primary hospitals. This evaluation began with the selection of data sources to be collected, followed by the determination of the population, design of research procedures, acquisition of permits, collection of data, and subsequent analysis. Researchers can retrieve data on antibiotic use from the selection of samples to be studied, such as in patients receiving internal medicine (Hanifah et al., 2022), surgery (Noer et al., 2022), pneumonia (Andarsari et al., 2022), or Covid-19 (Aeny Rizky Kurniasari, 2022). As is the case, data collection can also be conducted using monthly drug use reports (Rahmawati et al., 2019).

The classification of antibiotics was based on the ATC code and the DDD value in grammes, which is a WHO standard and can be accessed at www.whocc.no/atc_ddd_index. Researchers collected data on the use of antibiotics and then classified these antibiotics based on the ATC code and DDD value in grams. For the value to be calculated, researchers also considered the duration of stay during the study period or the number of outpatient visits. The length of stay was determined by multiplying the number of inpatients by the number of hospital stays, whereas the number of Outpatient Visits (KPRJ) was derived from information on patient visits during the study period. The analysis began with the collection of antibiotic names, dosage forms, dosage strengths in grams, and number of antibiotics used during the study period. The total DDD value for antibiotic use was then determined by dividing the total amount of antibiotics collected by the WHO standard DDD. Calculate the DDD/100 bed-days of treatment by multiplying the total DDD value of antibiotic use by 100 and dividing by the number of days of treatment. Meanwhile, DDD/1000 Patient-days were determined by multiplying the total DDD of antibiotic use by 1000 and dividing by the KPRJ value.

DDD is the presumed average daily maintenance dose of a drug for its primary indication in adults. However, this procedure cannot accurately describe its use in pediatric patients who require dose adjustments based on body weight. Because of dose variability, it is not possible to estimate the prevalence of antibiotic use among children using data from general use reports. Daily dose and indication should also be considered when evaluating the use of antibiotics in children (WHO, 2021). It is possible to obtain a low value when performing a quantitative evaluation with DDD, so it can be added to the calculation using DOT and PDD. PDD is the average dose administered based on the total number of prescriptions (Herawati et al., 2019). DOT is the total number of days that each unit of a specific antimicrobial agent is administered to a specific patient (quantifier) divided by the number of patients (denominator). However, Castagnola et al. (2022) demonstrated that the DDD method can be used to measure antibiotic consumption in pediatric patients without the need for PDD evaluation. Nine articles were selected for this review to assess the use of antibiotics in children.

Table IV. The description of the use of ATC/DDD is comparative

No.	Research Population	Health Service Level	Comparative Research	Research period	Number of Patients	Reference
1	Pediatrics	3	Comparing the 2016 antibiotic use data taken retrospectively and the 2017 data prospectively.	1 year and 8 months	1476/21	(Herawati et al., 2019)
2	Child Pneumonia	2	Comparing data on the use of antibiotics for inpatients with pneumonia at hospitals in Yogyakarta and hospitals in Jakarta.	11 months	68/59	(Bidara et al., 2021)
3	All Patients	3	Comparing all data on the use of antibiotics per year in 2013-2017.	5 years	all data per year	(Saepudin et al., 2022)
4	Covid-19	3	Comparing medical record data for 2 groups of Covid-19 patients with Ventilators and Non Ventilators.	6 months	43/85	(Sinuor & Dewi Kurniawati, 2022)
5	Contaminated Clean Surgery	3	Comparing data on prophylaxis and therapy in clean-contaminated surgical patients.	1 year	40 patients	(Nisak et al., 2022)

The DDD value is proportional to the number of antibiotics used; if the value decreases, it can be concluded that the prescription for these antibiotics is becoming more selective; however, the high use of antibiotics does not necessarily indicate that the drug is being used without justification, as antibiotic use varies by hospital (Andarsari et al., 2022). Excessive or insufficient drug use can be determined by comparing the level of drug consumption in one health service unit to that of others. Occasionally, the results of this research cannot be compared to the selectivity of consumption levels in other hospitals because of differences in the period (duration of the study) and research methodologies (Anggraini et al., 2021). However, the ATC/DDD method can still be used to evaluate antibiotic use as input to the Antibiotic Stewardship Team (PGA), which is part of the hospital's Antimicrobial Resistance Control Committee (KPRA), to evaluate drug use beginning with conformity with the formulary, compliance with guidelines for disease management, or accuracy with disease conditions in the hospital (Menkes RI, 2021). Five articles compared the use of antibiotics in two different patient population choices, in one location over an extended period of time, and in two locations. tabulated in Table IV. Table V displays that eight of the sixty-four articles were quasi-experimental studies that evaluated the effect of intervention on antibiotic use. The remaining 51 articles quantitatively evaluated the use of antibiotics by providing DDD values/100 bed days for each study and evaluating the highest DDD values/100 bed days (**Table VI**).

Table V. An overview of the use of ATC/DDD with the provision of interventions

No.	Research Population	Intervention	Research period	Number of Patients	Reference
1	Surgery	Guidelines for the Use of Antibiotics (PPAB)	1 month & 1 month	200/200	(Narulita et al., 2020)
2	Pneumonia	Guidelines for the Use of Antibiotics (PPAB)	3 months & 3 months	48/48	(Karuniawati et al., 2021)
3	All Patients	Antimicrobial Resistance Control Program (PPRA)	3 months & 3 months	212/212	(Ermawati et al., 2021)
4	Pediatrics	Clinical Pathway (CP)	1 year & 1 year	60/61	(Lizikri et al., 2020)
5	Sepsis Patient	Guidelines for the Use of Antibiotics (PPAB)	8 months & 8 months	112/112	(Sumardi et al., 2019)
6	GEA Pediatrics	Clinical Pathways	3 months & 3 months	141/141	(Adiwisastra et al., 2019)
7	Internal disease	Antimicrobial Resistance Control Program (PPRA)	NA	34/34	(Kartika et al., 2019)
8	All Patients	Antimicrobial Resistance Control Program (PPRA)	9 months & 12 months	all data	(Susanto et al., 2019)

Table VI shows that of the 51 articles that quantitatively evaluated the DDD value/100 bed-days, 27 articles had the highest DDD value/100 bed-days of Ceftriaxone, with the smallest value range being 10 DDD/100 bed-days (Anggraini et al., 2020) and the largest value being 76.15 DDD/100 bed-days (S. C. Putri et al., 2019). The maximum DDD value/100 bed-days of ceftriaxone inpatient care was observed in articles on ICU, pediatric, diabetic ulcer, internal medicine, surgery, and pneumonia patient populations. Ceftriaxone is still the drug of choice because it is a broad-spectrum cephalosporin antibiotic with activity against both gram-positive and gram-negative bacteria and because it has an extended half-life, providing patients with cost and convenience benefits (Sukriya et al., 2022). Ceftriaxone is the most effective antibiotic against penicillin-resistant strains of pneumococci; consequently, it is extensively used as a prophylactic treatment for severe infections (Andarsari et al., 2022). Cephalosporins are first-line empiric therapies based on the pattern of antibiotic sensitivity in Jombang Hospital, which demonstrates a fairly high sensitivity of 67.9% against gram-positive bacteria and 52.2% against gram-negative bacteria (Ambami, 2020). However, the use of third-generation cephalosporins is associated with an increased incidence of ESBL-producing bacteria (Kresnawati et al. 2021b).

The antibiotics oral azithromycin and parenteral levofloxacin were found to have the maximum DDD value per 100 bed-days in five articles. DDD/100 bed-days for oral azithromycin, with the lowest value range of 26.26 DDD/100 bed-days (Triamyanti et al., 2022) in Covid-19 patients and the highest value of 68.4 DDD/100 days (Dewi & Dhirisma, 2021) in patients with pneumonia. The maximum DDD/100 bed-days value for oral azithromycin was found in three articles: evaluation of the use of antibiotics in all patients during a pandemic and selection of the pneumonia population. Based on in vitro and in vivo testing, azithromycin and levofloxacin reach high concentrations in the lungs, allowing their use as an empirical treatment for Covid-19 pneumonia (Evano Putra et al., 2021). The evaluation of the precision of antibiotic selection pertains to the initial diagnosis of Covid-19 patients. According to the most recent COVID-19 management guidelines published on July 14, 2021, the treatment of COVID-19 varies, with asymptomatic, mild, and moderate COVID-19 cases not requiring antibiotics. COVID-19 is treated exclusively with antiviral agents. This seeks to prevent an increase in bacterial resistance among COVID-19 patients (Triamyanti et al., 2022).

DDD/100 bed-days for parenteral levofloxacin, with the lowest value range of 15.22 (Yulia et al., 2020) in pneumonia patients and the highest value of 48.80 (Hanifah et al., 2022) in internal medicine patients. There were two articles with the highest DDD/100 bed-days of 29,17 DDD/100 bed-days (Effendy et al., 2022) and 143,18 DDD/100 bed-days (Wikantiananda et al., 2019). Because this respiratory fluoroquinolone class of antibiotics is effective in treating upper and lower respiratory tract infections with high activity against gram-positive bacteria and atypical bacteria that cause pneumonia, levofloxacin is frequently prescribed to patients with pneumonia. Levofloxacin is a broad-spectrum antibiotic that is susceptible to the development of resistance when excessively used (Yulia et al., 2020). According to the results of an FDA-approved in vitro screening study, levofloxacin has a potent inhibitory effect on SARS CoV-2 virus. In addition, the relationship between pharmacokinetic properties, safety profile, anti-inflammatory activity, and affinity for SARS-CoV-2 virus-binding protease indicates that levofloxacin can be used to treat COVID-19 pneumonia (Ikasanti et al., 2022).Click or tap here to enter text.

Table VI. **Summary of Study Based on Inpatients (Expressed in terms of Defined Daily Dose (DDD) per 100 bed-days)**

No	Population	Level	∑ Ab	∑ Px	Total	Ceftriaxone	Meropenem	Cefotaxime	Cefixime	Levofloxacin O	Levofloxacin P	Azithromycin O	Cefoperazon	Amoxicillin	Ampicillim	Another high score	Reference
1	All	2	12	NA	350.86	34,29			14.35	33,44	6,40			40,87		Ofloxacin **49,46**	(Rahmawati et al., 2019)
2	All	2	10	86	135.08	21,13	3.80	2.96		44.01		**48,12**			0.95		(Evano Putra et al., 2021)
3	ICU	2	14	156	72,31	**26,26**	13.50	0.77		8,44		1.30	0.81		3.79		(W. A. Putra et al., 2021)
4	ICU	3	14	57	295.72	30,62	49.88	2.97		**143,2**							(Wikantiananda et al., 2019)
5	ICU	3	12	77	117,81	**76,15**	5,42	7,18	0.30				2,28	0.46			(S. C. Putri et al., 2019)
6	Pediatrics	2	6	93	31.83	**16,37**		8,26	2.77					0.19			(Amnifu et al., 2021)
7	Pediatrics	2	20	402	47,24	**10.30**	0.30	1.70	5,60			2.30		3.90	4,40		(Norcahyanti et al., 2021)
8	Pediatrics	3	13	162	18,17	**15,10**	0.14	1.49	0.69					0.54	0.10		(Rukminingsih, 2021)
9	Pediatrics	3	15	188	37.90	**11.30**	1.78	8,22	2,14			0.36	0.12	0.04	3.76		(Rachmawati et al., 2020)
10	Pediatrics	3	7	30	10.50	1.97	**3.49**				1.14				1.06		(Upa et al., 2020)
11	Pediatrics	3	8	103	50,90	4,5	0.3	5,10							**26,1**		(Muslim, 2018)
12	Mature	3	13	75	66,44	20,18	0.84	8,27		3,24	3.45	1.05	**20,72**	0.21			(Anggraini et al., 2021)

No	Population	Level	∑ Ab	∑ Px	Total	Ceftriaxone	Meropenem	Cefotaxime	Cefixime	Levofloxacin O	Levofloxacin P	Azithromycin O	Cefoperazon	Amoxicillin	Ampicillim	Another high score	Reference
13	Mature	1	4	81	144.52	2.70							45.89	**65.75**			(Sholih *et al.* , 2019)
14	Diabetic Ulcer	3	12	84	138.08	**52,31**	3.96		1.10		0.66		0.66				(Sidabalok and Widayati, 2022)
15	Diabetic Ulcer	2	6	59	52,86	**31.88**	7.06						1.45				(Wahyudi *et al.* , 2018)
16	Covid-19	3	10	32	143,24	0.17	32.35			**71,16**		4.55	3.07	0.11			(Kristanti *et al.* , 2022)
17	Covid-20	3	8	100	97.44	9,82	13.46				25.30	**26,26**	0.16				(Triamyanti *et al.* , 2022)
18	Covid-21	3	5	100	114.79	8.75	0.29		0.57	44,51		**60,67**					(Aeny Rizky Kurniasari, 2022)
19	Covid-22	3	7	94	86.56		0.45			22.70	1.23	**50,42**					(Ikasanti *et al.* , 2022)
20	Internal disease	3	26	522	144.58	10.44	9.70	1.10	11.44	9.53	**48,8**	13.67	0.34				(Hanifah *et al.* , 2022)
21	Internal disease	2	15	164	116,41	**62,31**	0.35	3.99	1.84	11.66		3.94	1.53				(Dirga *et al.* , 2021)
22	Internal disease	2	8	1221	47,45	4,11	0.09	**39,13**							0.09		(Primary, 2019)
23	Internal disease	3	10	482	76.03	**37,56**	0.21	0.60			6.05						(Ridwan *et al.* , 2019)
24	Internal disease	3	14	100	60,94	**36,15**		2.83	2.03	0.37							(Lestari *et al.* , 2018)

No	Population	Level	∑ Ab	∑ Px	Total	Ceftriaxone	Meropenem	Cefotaxime	Cefixime	Levofloxacin O	Levofloxacin P	Azithromycin O	Cefoperazon	Amoxicillin	Ampicillim	Another high score	Reference
25	Internal Medicine (Typhoid)	2	2	32	70.30	**50,10**		20,20									(Khoirin & Arismunandar, 2021)
26	Internal Medicine (Typhoid)	3	4	36	114.79	**83,80**				2.82	**24.65**	3.52					(Sukmawati et al., 2020)
27	Internal Medicine (UTI)	2	3	64	55,65	**33.85**			6,21								(Yuniarti et al., 2021)
28	Surgery	2	10	213	136,20	25.05	0.11	20,14	**67,79**	0.54							(Azyenela et al., 2022)
29	Surgery	3	9	130	53,60	10.78		8,42	1.68	0.28			6,81	0.37		Cefuroxime **17.41**	(Izzati & Goni, 2022)
30	Prophylactic Surgery	3	19	162	48,32	**25.89**	1.00	0.11	0.34			0.19	0.11				(Hidayati et al., 2022)
31	Neurosurgery	3	3	34	75,78	20,16										Cefepime **45.80**	(Noer et al., 2022)
32	Debridement Surgery	2	9	75	69,77	**27,54**		0.54	6,21			0.45		0.54			(Panu et al., 2022)
33	Digestive Surgery	3	10	30	2.68	0.43	0.02								0.01	Cefazolin **0.87**	(O. N. Putra et al., 2022)
34	Surgery	3	5	75	81,21	**64,41**			1.16	2.44							(Sihite et al., 2021)
35	Surgery	3	10	382	72,12	**34.50**	5,21	0.60			6.05						(Rokhani et al., 2021)

No	Population	Level	∑ Ab	∑ Px	Total	Ceftriaxone	Meropenem	Cefotaxime	Cefixime	Levofloxacin O	Levofloxacin P	Azithromycin O	Cefoperazon	Amoxicillin	Ampicillim	Another high score	Reference
36	Surgery	NA	11	164	144,22	**75.02**	20.87	0.08		0.78				0.72			(Muliani et al., 2021)
37	Acute Appendicit is Surgery	2	10	59	52.01	**10.00**			0.20								(Anggraini et al., 2020)
38	Surgery	3	8	463	102.93	**53,92**	3,28	2,32			1.09						(Pratama, 2019)
39	Cesarean and Hernia Surgery	NA	11	79	71,91	**47.90**		1.63	10.69		1.14		0.76				(Nuraliyah et al., 2019)
40	Pneumonia in ICU	3	13	68	73,64	20.45	14,29			2.76	**21.92**		0.41		0.93		(Andarsari et al., 2022)
41	Pneumonia	3	7	35	64,47	18.75	2,31			**29,17**							(Effendy et al., 2022)
42	Pneumonia	3	9	74	71.00	**44.90**	1.20	0.80	0.40	0.80	18.50	1.70					(Sukriya et al., 2022)
43	Pneumonia	3	13	91	78,13	18,24	1.74	0.60	0.80	0.20	3.01	5,34				Moxifloxacin **42.89**	(Zavira et al., 2021)
44	Pneumonia	2	20	251	44.96	**19.54**	0.29	0.13	2.82	1.91	2,11	0.95					(H. A. Putri et al., 2021)
45	Pneumonia	2	15	97	149.70	32,10	5,60	1.40	2.60	0.70	12.60	**68,40**	8.70				(Dewi & Dhirisma, 2021)
46	Pneumonia	3	6	113	77,25	**38,79**		28.88		2.36	3,29						(Kresnawati et al., 2021a)

No	Population	Level	∑ Ab	∑ Px	Total	Ceftriaxone	Meropenem	Cefotaxime	Cefixime	Levofloxacin O	Levofloxacin P	Azithromycin O	Cefoperazon	Amoxicillin	Ampicillim	Another high score	Reference
47	Pneumonia	3	14	153	35,53	9,23	4,34		0.88	0.55	**15,22**						(Yulia et al., 2020)
48	Pneumonia	3	4	37	83.25	**41.78**	2.35				37,56				1.56		(Ambami, 2020)
49	Pneumonia	3	8	130	51,28	8,71	0.06	0.91	0.03		**40,14**						(Ilmi et al., 2020)
50	Pediatric Pneumonia	3	6	41	296.32	3.07		8.89	**141.6**						123.5 1		(Polii et al., 2018)
51	Pneumonia	2	7	44	50.35	**23.86**		2,23		2.79		3.72	5,81				(Prasetyo & Kusumaratni, 2018)

Note:
Level is the level of health services (3 (tertiary) = Hospital Type A and Type B, 2 (secondary) = Hospital Type C and Type D, 1 (primary) = primary clinic or health center), ∑ Ab is the number of types of antibiotics found in 1 article, and ∑ Px is the number of patients studied. No related data were found for NA (unavailable). The DDD value/100 bed-days displayed are the 10 selected antibiotics with the highest DDD/100 bed-days values in each study.

Table VII. Outpatient Study Summary (Expressed in Defined Daily Dose DDD/1000 Patient-days)

No	Population	Health Care Level	∑ Ab	∑ Px	Total	Amoxicillin	Ciprofloxacin	Cefadroxil	Chloramphenicol	Erythromycin	Metronidazole	Cefixime	Reference
1	gonorrhea	3	9	66	54,33	3,20	1.70	0.50				**28.80**	(F. E. Putri et al., 2018)
2	All Patients	1	4	832	38,66	**31,44**	5,14	1.55	0.53				(Ruliansyah et al., 2020)
3	All Patients	1	4	992	1097,31	**997,40**	82.98	5.83	11,10				(Aleksander et al., 2020)
4	All Patients	1	5	1255	63.50	**45,70**	14.70	1.10	1.20	0.80			(Perdaka et al., 2020)
5	All Patients	1	5	462	69.30	**40,40**	18.50	6,40	0.20	3.80			(Andriani et al., 2020)
6	All Patients	1	4	4053	61,10	**38.90**	11,10	5.50		5,60			(Trisia et al., 2020)
7	ISPA Non Pneumonia	1	5	1724	1625,23	**742.58**	741.80	138,17	1.90		1.18		(Sitepu et al., 2020)

Note:
Health Care Level (3 (Tertiary) = Hospital Type A and Type B, 2 (secondary) = Hospital Type C and Type D, 1 (primary) = primary,
∑ Ab is the number of types of antibiotics administered found in 1 article, ∑ Px is the number of patients in the sample. The DDD value shown is the 7 most antibiotics found in the 7 selected articles.

The other antibiotics with the highest DDD/100 bed-days were Meropenem, Ampicillin, Cefotaxime, Cefixime, Cefoperazone, Amoxicillin, Cefazolin, Cefuroxime, Cefepime, Moxifloxacin, and Ofloxacin, each with 1 article. 3.49 DDD/100 bed-days was the highest DDD/100 bed-days for meropenem antibiotics (Upa et al., 2020) based on the profile of antibiotic use in different referral pediatric patients (Muslim, 2018) who received Ampicillin as DDD/100 bed-days the most treatment with a value of 26.1 DDD/100 bed-days. The differences in the cases encountered by the two researchers indicate that the types of antibiotics with high consumption differ between referral patients and ordinary patients (non-referrals), with pediatric patients referred for more severe cases and the use of broad-spectrum antibiotics being more prevalent (Upa et al., 2020). Cefotaxime (Pratama, 2019) had the second-highest DDD value/100 bed-days for the cephalosporin group, at 39.13 DDD/100 bed-days. In contrast to other studies, (Polii et al., 2018) discovered the highest consumption of cefxime antibiotics, 67.79 DDD/100 bed-days, because it complies with the use of the national formulary in hospitals during the implementation of the National Health Insurance (JKN). Cefoperazone (Anggraini et al., 2021) had the maximum DDD value in this study, with a value of 20.72 DDD/100 bed-days, as it was the preferred third-generation cephalosporin at the research site. Cefazolin with a value of 0.87 DDD/100 bed-days in the article (O. N. Putra et al., 2022) evaluating the use of prophylactic antibiotics for surgical debridement in burns, Cefuroxime with a value of 17.41 DDD/100 bed-days (Izzati & Goni, 2022) in surgical patients in Yogyakarta, Indonesia, was the other cephalosporin group that was the highest.

Amoxicillin is the antibiotic with the maximum DDD/100 bed-days in (Sholih et al., 2019), 65.75 DDD/100 bed-days, because he chose to conduct research at the first health service level. Because of its broad spectrum, this beta-lactam drug class is frequently used to treat infections for which the causative bacteria are unknown. As a result, its utilization is quite high. However, it should be emphasized that the irrational use of amoxicillin can cause beta-enzyme-producing bacteria to develop resistance (Sholih et al., 2019). Moxifloxacin and Ofloxacin had the highest DDD/100 bed-days in (Zavira et al., 2021) and (Rahmawati et al., 2019), with DDD values of 42.89 and 49.46 %, respectively. Moxifloxacin, the antibiotic with the highest number of uses, is influenced by several factors, including its bactericidal activity with killing power against bacteria dependent on antibiotic levels and its 99% bioavailability in the body, making it the antibiotic of choice for pneumonia patients and the drug of choice for pneumonia patients.

The DDD/1000 Patient-day values for the DDD units in the designated outpatient population are presented in Table VII. According to most studies, amoxicillin had the highest DDD/1000 patient-days. This was followed by (Sitepu et al., 2020) with a value of 742.8 DDD/1000 Patient-days for the outpatient population with non-pneumonia ARI in primary care for 9 months. Cefixime, with a value of 28.8 DDD/1000 patient-days, had the second-highest DDD/1000 patient-days value in the article that selected the gonorrhea patient population. This is due to the fact that cefixime is the antibiotic of preference for eradicating the Neisseria gonorrhoeae bacteria (F. E. Putri et al., 2018).

DDD must sometimes be reviewed because doses may change over time, for example, as a result of the introduction of a new primary indication or new research necessitating adjustments to DDD. The limitations of this study include the absence of standard DDD data collected by the researchers in each article. In 2019, the WHO standard DDD values for amoxicillin increased from 1 gramme to 1.5 grammes, ampicillin increased from 2 to 6 g, cefepime decreased from 2 to 4 g, and meropenem decreased from 2 to 3 g (WHO, 2022).

CONCLUSION

The ATC/DDD approach is a valuable tool to assess antibiotic use in Indonesia. This method enables the collection of comprehensive information on drug usage from many sources, including sales data, prescription records, and patient encounter-based data, obtained through well-designed sampling techniques. A total of 71 articles that satisfied the established criteria were subjected to rigorous analysis and discussion. The predominant application of the Anatomical Therapeutic Chemical (ATC)/Defined Daily Dose (DDD) methodology involved the assessment of antibiotics, with 90.1% of such evaluations conducted among inpatients and 9.9% among outpatients. The implementation of this method involved retrospective data collection in 94.4% of the cases, with cross-sectional study designs being the most commonly used, accounting for 76% of the total. The duration of the research period ranged from one month to five years, with 59.1% of the study locations being conducted at the tertiary service level. The application of the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Dose (DDD) methodology can also be implemented within a quasi-experimental research design that examines pre- and post-intervention comparisons. The utilization of this approach as an assessment of the efficacy of antibiotics within the designated study group yielded the highest DDD/100 days of ceftriaxone across 27 papers. Amoxicillin was reported to have the highest defined DDD/1000 patient-days in 5 out of 7 articles within the outpatient population. Comparisons between research findings on consumption levels across different hospitals may be limited owing to variations in the study duration and methodologies employed. However, the ATC/DDD method can serve as a valuable tool for healthcare professionals and researchers to assess antibiotic usage in relation to adherence to disease management guidelines and alignment with the prevailing healthcare conditions in Indonesian hospitals and other healthcare facilities.

ACKNOWLEDGE

The researcher would like to thank the supervisor of the scientific writing course at the Islamic University of Indonesia, Dr. apt. Asih Triastuti, M.Pharm. and apt. Suci Hanifah, M.Si, Ph.D who has provided many inputs in the process of writing this article.

REFERENCES

Adiwisastra, N. G., Arozal, W., & Utami, H. (2019). Efektivitas Implementasi Clinical Pathway pada Pasien Anak Gastroenteritis Akut (GEA) dengan Dehidrasi yang Dirawat Inap di Rumah Sakit Permata Bekasi. *Jurnal Medical Profession*, *3*(3).

Aeny Rizky Kurniasari, I. D. K. (2022). Profil Kuantitas Penggunaan Antibiotik pada Pasien Covid-19 Non Ventilator di RSUD dr. R.Koesma Tuban. *Jurnal Darma Agung*, *30*(2), 169–173.

Aleksander, O., Andriani, Y., & Andriani, M. (2020). Pola Penggunaan Antibiotik dengan Metode ATC/DDD dan DU 90% di Puskesmas Paal V Kota Jambi Periode 2017-2019. *Journal of Healthcare Technology and Medicine*, *6*(1), 259–275.

Ambami, S. (2020). *Evaluasi Penggunaan Antibiotik dengan Metode ATC/DDD pada Pasien Pneumonia di RSUD Jombang Periode Januari-Desember 2019*. Universitas Islam Negeri Maulana Malik Ibrahim.

Amnifu, A. G., Lutsina, N. W., & Klau, M. E. (2021). Profil Penggunaan Antibiotik Pada Pasien Pediatri Rawat Inap di RSUD S. K. Lerik. *CHM-K Pharmaceutical Scientific Journal*, *4*(2), 264–269.

Andarsari, M. R., Norachuriya, Z., Nabila, S. M., Aryani, T., & Rosyid, A. N. (2022). Assessment of Antibiotic Use in ICU Patients with Pneumonia Using ATC/DDD as a Quantitative Analysis Method. *Jurnal Farmasi Dan Ilmu Kefarmasian Indonesia*, *9*(2), 138–145. https://www.e-journal.unair.ac.id/JFIKI/article/view/33623

Andriani, Y., Meirista, I., & Aprio, Y. (2020). Evaluasi Penggunaan Antibiotik dengan Metode ATC / DDD dan DU 90 % di Puskesmas Kebun Handil Kota Jambi Periode 2018 dan 2019. *Journal of Healthcare Technology and Medicine*, *6*(2), 700–707.

Anggraini, W., Sugihantoro, H., & Ludfiyah, F. (2021). Evaluasi Kuantitatif Penggunaan Antibiotik di Ruang Perawatan Airlangga dan Peta Kuman RSUD Kanjuruhan Malang Periode Juli-Desember 2018. *Jurnal Farmasi Klinik Indonesia*, *10*(2), 90–99. https://doi.org/10.15416/ijcp.2021.10.2.90

Anggraini, W., Wiraningtias, N. B., Inayatilah, F. R., & Indrawijaya, Y. Y. A. (2020). Evaluasi Penggunaan Antibiotik pada Pasien Pasca Bedah Apendisitis Akut di RSUD Kabupaten Pasuruan Tahun 2018. *Pharmaceutical Journal of Indonesia*, *6*(1), 15–20.

Antimicrobial Resistance Collaborators. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*, *399*(10325), 629–655. https://doi.org/10.1016/s0140-6736(21)02724-0

Azyenela, L., Tobat, S. R., & Selvia, L. (2022). Evaluasi Penggunaan Antibiotik di Instalasi Rawat Inap Bedah RSUD M . Natsir Kota Solok Tahun 2020. *Jurnal Mandala Pharmacon Indonesia*, *8*(1), 1–10.

Bidara, F., Saputri, M., Perwitasari, D. A., Fatah Kumara, I., & Ardhani, M. (2021). Studi Penggunaan Antibiotik Pasien Pneumonia Anak dengan Metode DDD dan DU 90%. *Jurnal Ilmiah Ibnu Sina*, *6*(1), 108–115.

Castagnola, E., Lorenzi, I., Barabino, P., & Pistorio, A. (2022). Antibiotic defined daily dose in pediatrics. A single center study to proof the principle that a specific pediatric definition could be not needed. *Enfermedades Infecciosas y Microbiología Clínica*. https://doi.org/10.1016/j.eimc.2022.08.008

Dadgostar, P. (2019). Antimicrobial Resistance: Implications and Costs. *Infection and Drug Resistance*, *Volume 12*, 3903–3910. https://doi.org/10.2147/IDR.S234610

Dahlan, M. S. (2010). *Besar sampel dan cara pengambilan sampel dalam penelitian kedokteran dan kesehatan*. Salemba Medika 5; 1-2.

Dewi, T. P. ;, & Dhirisma, F. (2021). Penggunaan Antibiotika pada Pasien Dewasa Pneumonia dengan Metode DDD (Defined Daily Dose) di Rawat Inap RSU PKU Muhammadiyah Bantul Periode Tahun 2019. *Jurnal Kefarmasian Akfarindo*, *6*(1), 8–13.

Diah, F. (2022). Rationality of Antibiotics Use With Quantitative and Qualitative Methods at Hospital In Indonesia. *Pharmacology, Medical Reports, Orthopedic, and Illness Details (COMORBID)*, *1*(1), 73–82.

Dirga, D., Khairunnisa, S. M., Akhmad, A. D., Setyawan, I. A., & Pratama, A. (2021). Evaluasi Penggunaan Antibiotik pada Pasien Rawat Inap di Bangsal Penyakit Dalam RSUD. Dr. H. Abdul Moeloek Provinsi Lampung. *Jurnal Kefarmasian Indonesia*, *11*(1), 65–75. https://doi.org/10.22435/jki.v11i1.3570

Effendy, R., Yulia, R., Herawati, F., & Jaelani, A. K. (2022). Analisis Penggunaan Antibiotik dan Peta Kuman pada Pasien Pneumonia di Rawat Inap Rumah Sakit Umum Daerah Bangil. *Jurnal Ilmiah Indonesia*, *7*(7).

Ermawati, Khambri, D., & Almasdy, D. (2021). The Difference of Using Antibiotics Before and After Antimicrobial Resistance Control Program (PPRA) at RSUP Dr. M. Djamil Padang. *Andalas Obstetrics and Gynecology Journal*, *5*(1), 29–42.

Evano Putra, D., Retnoningrum, D., Arkhaesi, N., & Pramudo, S. G. (2021). Pola Pemberian Antibiotik di Era Pandemi Covid-19 (Studi Kasus di Rumah Sakit Nasional Diponegoro). *Medica Hospitalia : Journal of Clinical Medicine*, *8*(2), 194–199. http://medicahospitalia.rskariadi.co.id/medicahospitalia/index.php/mh/article/view/578

Hanifah, S., Melyani, I., & Madalena, L. (2022). Evaluasi Penggunaan Antibiotik dengan Metode ATC/DDD DAN DU90% pada Pasien Rawat Inap Kelompok Staff Medik Penyakit Dalam di Salah Satu Rumah Sakit Swasta di Kota Bandung. *Farmaka*, *20*(1), 21–26.

Herawati, F., Yulia, R., Hak, E., Hartono, A. H., Michiels, T., Woerdenbag, H. J., & Avanti, C. (2019). A Retrospective Surveillance of the Antibiotics Prophylactic Use of Surgical Procedures in Private Hospitals in Indonesia. *Hospital Pharmacy*, *54*(5), 323–329. https://doi.org/10.1177/0018578718792804

Hidayati, A., Candradewi, S. F., & Erhan, S. (2022). Define Daily Dose (Ddd) Penggunaan Antibiotika Pada Profilaksis Pembedahan Di Rsud Cilacap. *Medical Sains : Jurnal Ilmiah Kefarmasian*, *7*(3), 635–644.

Ikasanti, P. A. I., Yulia, R., Hartono, R., Hanum, P. S., & Herawati, F. (2022). Analysis Of The Use Of Antibiotics in Asymptomatic, Mild, and Moderate Covid-19 Patients

Treated In Bhayangkara Hospital. *Jurnal Berkala Epidemiologi*, *10*(2). https://doi.org/10.20473/jbe.v10i22022.179

Ilmi, T., Restyana;, A., Kadir;, M. B. A., & Yuniarto, P. F. (2020). Profile of Antibiotic Use and Germ Map in Pneumonia Patients in Pulmonary Space (Case Study at RSUD dr. Iskak Tulungagung). *Journal of Physics: Conference Series PAPER*. https://doi.org/10.1088/1742-6596/1569/3/032064

Ismail, D. (2022). Cost of antibiotics in medical intensive care. *Journal of Hospital Infection*, *124*, 47–55. https://doi.org/10.1016/j.jhin.2022.03.003

Izzati, U., & Goni, N. A. (2022). Evaluation of Antibiotic Use In Surgical Patients at RSPAU dr . S. Hardjolukito Yogyakarta with ATC / DDD System. *Pancasakti Journal of Public Health Science and Research*, *2*(1), 1–5. https://doi.org/10.47650/pjphsr.v2i1.315

Kartika, N. T. M., Lestari, E. S., Farida, H., & Ciptaningtyas, V. R. (2019). Kualitas dan kuantitas penggunaan antibiotik pada kasus penyakit dalam sebelum dan setelah penyuluhan PPRA Di Rumah Sakit Nasional Diponegoro. *Jurnal Kedokteran Dipenogoro*, *8*(4). https://ejournal3.undip.ac.id/index.php/medico/article/view/25491

Karuniawati, H., Yulianti, T. R. I., Aini, D. K., & Nurwienda, F. I. (2021). Impact of Antimicrobial Stewardship Program on The Use of Antibiotics in Pneumonia Patients at Teaching Hospital in Surakarta. *Int J App Pharm*, *13*(1), 20–23.

Khoirin, & Arismunandar, G. (2021). Evaluasi Penggunaan Antibiotik pada Pasien Demam Tifoid Dengan Metode ATC/DDD di Ruang Rawat Inap RSUD Pratama Lubai Ulu Tahun 2021. *Jurnal Kesehatan Lentera 'Aisyiyah*, *4*(2), 519–528. https://backup.politasumbar.ac.id/index.php/jl/article/view/108

Klein, E. Y., Van Boeckel, T. P., Martinez, E. M., Pant, S., Gandra, S., Levin, S. A., Goossens, H., & Laxminarayan, R. (2018). Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proceedings of the National Academy of Sciences*, *115*(15). https://doi.org/10.1073/pnas.1717295115

Kresnawati, V., Herawati, F., … H. C.-M. (Media, & 2021, undefined. (2021a). Analisis Penggunaan Antibiotik Pada Pasien Pneumonia Komunitas di RSUD Kabupaten Kediri. *Journal.Ubaya.Ac.Id*, *3*(4). https://journal.ubaya.ac.id/index.php/MPI/article/view/4468

Kresnawati, V., Herawati, F., … H. C.-M. (Media, & 2021, U. (2021b). Analisis Penggunaan Antibiotik Pada Pasien Pneumonia Komunitas di RSUD Kabupaten Kediri. *Media Pharmaceutica Indonesiana*, *3*(4). https://journal.ubaya.ac.id/index.php/MPI/article/view/4468

Kristanti, W., Yulia, R., & Herawati, F. (2022). Analysis of Antibiotic Use in COVID-19 Patients at a Hospital in Sidoarjo. *Jurnal Farmasi Dan Ilmu Kefarmasian Indonesia*, *9*(2), 200–208. https://doi.org/10.20473/jfiki.v9i22022.200-208

Lestari, P. D., Utami, E. D., Suryoputri, M. W., Farmasi, J., Kesehatan, F. I., & Soedirman, U. J. (2018). Evaluasi Penggunaan Antibiotik di Bangsal Penyakit Dalam RSUD Prof. Dr. Margono Soekarjo Purwokerto. *Acta Pharmaciae Indonesia*, *6*(1), 20–28. https://doi.org/10.5281/zenodo.3707171

Limato, R., Nelwan, E. J., Mudia, M., de Brabander, J., Guterres, H., Enty, E., Mauleti, I. Y., Mayasari, M., Firmansyah, I., Hizrani, M., & Hamers, R. L. (2021). A multicentre point prevalence survey of patterns and quality of antibiotic prescribing in Indonesian hospitals. *JAC-Antimicrobial Resistance*, *3*(2), dlab047. https://doi.org/10.1093/jacamr/dlab047

Lizikri, A., Arozal, W., & Ramadaniati, H. U. (2020). Effects of Clinical Pathway Implementation in Management of Pediatric Inpatients with Pneumonia : A Cross-Sectional Study in Indonesia. *Int. J. Res. Pharm. Sci.*, *11*(4), 7281–7288.

Marasine, N., Shrestha, S., Sankhi, S., Paudel, N., Gautam, A., & Poudel, A. (2021). Antibiotic utilization, sensitivity, and cost in the medical intensive care unit of a tertiary care teaching hospital in Nepal. *Journals.Sagepub.Com*. https://journals.sagepub.com/doi/abs/10.1177/20503121211043710

Menkes RI. (2017). *Petunjuk Teknis Evaluasi Penggunaan Obat*.

Menkes RI. (2021). *Peraturan Menteri Kesehatan RI Nomor 28 Tahun 2021 tentang Pedoman Penggunaan Antibiotik*.

Muliani, N., Herawati, F., Yulia, R., & Wijono, H. (2021). Quantity and quality profiles of antibiotics pre, on, and postsurgery in a hospital setting. *International Journal of Clinical Pharmacy*, *43*(5), 1302–1310. https://doi.org/10.1007/s11096-021-01251-0

Muslim, Z. (2018). Antibiotic Prescription to Pediatric in Hospital Bengkulu, Indonesia: ATC/DDD Index. *Int J Pharm Pharm Sci*, *10*(5), 31–34. https://doi.org/10.22159/ijpps.2018v10i5.25291

Narulita, L., Bilal, R., Akram, M., & Suharjono. (2020). Analysis of Antibiotics on Patients Surgery, Before and After Used Guidelines for Antibiotics (PPAB). *Jurnal Pharmascience*, *07*(01), 51–61. https://ppjp.ulm.ac.id/journal/index.php/pharmascience/article/view/8074

Nisak, N. A., Yulia, R., Hartono, R., & Herawati, F. (2022). Evaluasi Penggunaan Antibiotik pada Pasien Bedah Bersih Terkontaminasi di Rumah Sakit Bhayangkara Surabaya. *Jurnal Pharmascience*, *9*(1), 1–10. http://repository.ubaya.ac.id/41576/

Noer, S. S., Yulia, R., Herawati, F., & Zamroni, A. (2022). Analisis Penggunaan Antibiotik pada Pasien Bedah Saraf di Ruang ICU RSUD Dr. R Sosodoro Djatikoesoemo Bojonegoro. *Jurnal Ilmiah Indonesia*, *7*(7).

Norcahyanti, I., Rosyidah, M., Jaelani, A. K., & Pratama, A. N. W. (2021). Antibiotic use on paediatric inpatients in a public hospital in Bangil , Indonesia. *Pharmacy Education*, *21*(2), 163–167.

Nuraliyah, N., Ramadhaia, Z. M., & Sofiah, E. (2019). Evaluasi Penggunaan Antibiotik pada Pasien Bedah Caesar dan Hernia di Salah Satu Rumah Sakit di Jawa Barat. *Majalah Farmasetika*, *4*(5), 139–145.

Page, M. J., Mckenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-wilson, E., Mcdonald, S., … Moher, D. (2021). *The PRISMA 2020 statement: an updated guideline for reporting systematic reviews*. 1–11.

Panu, N. I., Pani, S., & Supu, R. D. (2022). Evaluation of The Use of Antibiotics Using The ATC/DDD Method in Post-Surgical Patients at The Inpatient Unit of RSUD dr. Zainal Umar Sadiki. *Journal of Health, Technology and Science*, *2*(3), 63–72.

Perdaka, W., Sagita, D., & Pratama, S. (2020). Studi Penggunaan Antibiotik Berdasarkan ATC / DDD Dan Du 90 % Di Puskesmas X Kota Jambi Periode 2017-2018. *Journal of Healthcare Technology and Medicine*, *6*(1), 26–32.

Polii, E. S., Mambo, C. D., & Posangi, J. (2018). Gambaran Evaluasi Terapi Antibiotik pada Pasien Bronkopneumonia di Instalasi Rawat Inap Anak RSUP Prof. Dr. R. D. Kandou Manado Periode Juli 2017 – Juni 2018. *Jurnal E-Biomedik (EBm)*, *6*(2), 205–209.

Prasetyo, E. Y., & Kusumaratni, D. A. (2018). Pada Pasien Pneumonia Rawat Inap Di Rs Dkt Kota Kediri Dengan Metode Atc-Ddd Tahun 2018. *Jurnal Institut Kesehatan Bhakti Wiyata Kediri*, 7–12.

Pratama, S. (2019). Monitoring penggunaan antibiotik di Bangsal Penyakit Dalam RSUD Kerinci. *Riset Informasi Kesehatan*, *8*(1), 57–62. https://doi.org/10.30644/rik.v7i1.225

Putra, O. N., Saputro, I. D., Vitari, V. D., & Hapsari, A. R. (2022). Evaluasi Penggunaan Antibiotik Profilaksis Untuk Tindakan Surgical Debridement Pada Luka Bakar Anak Menggunakan Metode ATC/DDD. *Jurnal Ilmiah Kefarmasian*, *7*(3), 551–560.

Putra, W. A., Sari, Y. O., Arifin, H., & Sumatra, W. (2021). A Quantitative Study of Antibiotic Use Using ATC / DDD in the ICU (Intensive Care Unit) at Petala Bumi Hospital, Riau Province in 2018-2019. *International Journal of Innovative Science and Research Technology*, *6*(7), 1584–1590.

Putri, F. E., Mahmudah, F., & Kuncoro, H. (2018). Evaluasi Penggunaan Antibiotik pada Pasien Gonore di RSUD AWS Samarinda Berdasarkan ATC/DDD dan DU90%. In *Proceeding of the 7th Mulawarman Pharmaceuticals Conferences*.

Putri, H. A., Akrom, A., & Risdiana, I. (2021). Analisis Penggunaan Antibiotik pada Pasien Community-Acquired Pneumonia (CAP) di RS PKU Muhammadiyah Gamping. *Jurnal Farmasi Sains Dan Praktis*, *7*(1), 25–33.

Putri, S. C., Untari, E. K., & Yuswar, M. A. (2019). Profil Antibiotik pada Pasien Intensive Care Unit (ICU) di Rumah Sakit dr. Soedarso Pontianak Periode Januari-Juni 2019. *Jurnal Mahasiswa Farmasi Fakultas Kedokteran UNTAN*.

Rachmawati, S., Masito, D. K., & Rachmawati, E. (2020). Evaluasi Penggunaan Antibiotik pada Pasien Anak Rawat Inap di RSD dr. Soebandi Jember. *Jurnal Farmasi Galenika*, *6*(2), 212–220. https://repository.unej.ac.id/handle/123456789/91940

Rahmawati, D. P., Herawati, F., & Wardani, S. A. (2019). Evaluasi Penggunaan Obat di Rumah Sakit Marsudi Waluyo, Kabupaten Malang Tahun 2016. *Jurnal Ilmiah Mahasiswa Universitas Surabaya*, *7*(2), 1604–1617.

Ridwan, A., Narulita, L. ;, Widyadi, E. D. ;, & Suharjono. (2019). Analisis Penggunaan Antibiotika pada Pasien Penyakit Dalam di RSUD Dr . H . Slamet Martodirdjo Pamekasan dengan Metode ATC / DDD. *Jurnal Sains Farmasi & Klinis*, *6*(3), 237–242. https://doi.org/10.25077/jsfk.6.3.237-242.2019

Rokhani, R., Ulfa, M., Narulita, L., Akram, M., & Sumarno. (2021). Analisis Penggunaan Antibiotik Pada Pasien Bedah di RSUD dr. Slamet Martodirjo Pamekasan dengan Metode ATC/DDD. *Cendekia Journal of Pharmacy*, *5*(2), 176–184.

Rukminingsih, F. (2021). Analisis Penggunaan Antibiotik Pada Pasien Anak di Ruang Theresia Rumah Sakit St. Elisabeth Semarang dengan Metode ATC/DDD. *Jurnal Riset Kefarmasian Indonesia*, *3*(1).

Ruliansyah, Andriani, Y., & Andriani, M. (2020). Evaluasi Penggunaan Antibiotik dengan Metode ATC/DDD dan DU 90% di Puskesmas Payo Selincah Kota Jambi Periode 2017-2019. *Journal of Healthcare Technology and Medicine*, *6*(2), 2085–4714. https://scholar.archive.org/work/sxymo5qza5fctak3gutwt5dyra/access/wayback/http://www.jurnal.uui.ac.id/index.php/JHTM/article/download/977/469

Saepudin, S., Sendysagita, C., & Yuniarti, E. (2022). Drug Utilization 90% Profile of Antibiotics Use during the Period of 2013 – 2017 at a Private Teaching Hospital in Yogyakarta. *Journal of Pharmaceutical Sciences and Community*, *19*(1), 8–14. https://doi.org/10.24071/jpsc.003061

Sholih, M., Sudarjat, H., & Saula, L. (2019). Gambaran penggunaan antibiotik berdasarkan metode ATC/DDD dan DU 90% di salah satu Puskesmas Karawang. *Health Science Growth (HSG) Journal*, *4*(1), 31–37. https://journal.unsika.ac.id/index.php/HSG/article/view/1950

Sidabalok, R., & Widayati, A. (2022). Evaluasi Penggunaan Antibiotik dengan Metode Defined Daily Dose (DDD) pada pasien Ulkus Diabetikum di Rawat Inap RSUD Sleman. *Jurnal Farmasi Dan Kesehatan Indonesia*, *II*(September), 26–36.

Sihite, E. N., Ramadhan, A. M., & Samsul, E. (2021). Evaluasi Penggunaan Antibiotik Secara Kuantitatif dan Kualitatif Pada Pasien Bedah Digestif di RSUD Abdul Wahab Sjahranie Samarinda. *Proceeding of Mulawarman Pharmaceuticals Conferences*, *14*, 214–221. https://doi.org/10.25026/mpc.v14i1.552

Sinuor, C., & Dewi Kurniawati, I. (2022). Profil Kuantitas Penggunaan Antibiotik pada Pasien Kritis Covid-19 dengan Ventilator dan NonVentilator di ICU RSUD Dr.R. Koesma Tuban. *Jurnal Ilmiah Indonesia*, *7*(10).

Sitepu, R., Cahyono, T. T., & Monica, E. (2020). Evaluasi Penggunaan Antibiotik dengan Metode ATC/DDD dan PDD dengan DU 90% pada Penderita ISPA Non-Pneumonia di Puskesmas Kabupaten Sampang. *Jurnal JKFT*, *5*(1), 16–22.

Sukmawati, D., Jaya, M. K. A., & Swastini, D. A. (2020). Evaluasi Penggunaan Antibiotik pada Pasien Tifoid Rawat Inap di Salah Satu Rumah Sakit Pemerintah Provinsi Bali dengan Metode Gyssens dan ATC/DDD. *Jurnal Farmasi Udayana*, *9*(1), 37–44. https://doi.org/10.24843/JFU.2020.v09.i01.p06

Sukriya, Manggau, Djaharuddin, A., M., & Irawaty. (2022). Evaluasi Penggunaan Terapi Antibiotik Empiris Terhadap Luaran Klinis Pasien Pneumonia Komunitas Rawat Inap.

Majalah Farmasi Dan Farmakologi, *26*(April), 19–25. https://doi.org/10.20956/mff.v26i1.18888

Sumardi, U., Filani, A., Susandi, E., & Parwati, I. (2019). Defined Daily Dose and Cost of Therapy of Empirical Ceftriaxone Pre- and Post-Antimicrobial Stewardship Program Model Implementation in Sepsis Patients in A Tertiary Hospital in Indonesia. *International Journal of Integrated Health Sciences*, *7*(2), 96–101. https://doi.org/10.15850/ijihs.v7n2.1693

Susanto, M., Qanti, P. O., Anggraini, D., & Enda, W. G. (2019). Decline in Antibiotic Use after Implementation of Restriction Program at Eka Hospital, Pekanbaru, Riau. *The 5th International Conference on Public Health*, *February*, 491–497. https://doi.org/10.26911/theicph.2019.04.44

Triamyanti, V. Y., Herawati, F., Yulia, R., & Jaelani, A. K. (2022). Analysis of Drug Use in Non-Ventilator Covid-19 Patients at Bangil Hospital. *Jurnal Farmasi Dan Ilmu Kefarmasian Indonesia*, *9*(2), 168–176. https://doi.org/10.20473/jfiki.v9i22022.168-176

Trisia, F. J., Sagita, D., & Pratama, S. (2020). Evaluasi Penggunaan Antibiotik dengan Metode ATC/DDD dan DU 90% di Dua Puskesmas Kota Jambi periode 2017-2018. *Journal of Healthcare Technology and Medicine*, *6*(2). http://jurnal.uui.ac.id/index.php/JHTM/article/view/678

Upa, N. F. P., Widyati, & Prasetyadi, F. O. H. (2020). Profil Penggunaan Antibiotik Pada Pasien Pediatri Rujukan Berdasarkan Sistem Defined Daily Dose (DDD). *Media Pharmaceutica Indonesiana*, *3*(1), 44–51.

Wahyudi, A. E., Fadraersada, J., & Masruhim, M. A. (2018). Evaluasi Penggunaan Antibiotika Berdasarkan Metode Defined Daily Dose (DDD) pada Pasien Ulkus Diabetikum. *Proceeding of Mulawarman Pharmaceuticals Conferences*, *8*(November), 21–29. https://doi.org/10.25026/mpc.v8i1.298

WHO. (2021). *2021 AWaRe classification*. https://www.who.int/publications/i/item/2021-aware-classification

WHO. (2022). *ATC/DDD Index 2022*. https://www.whocc.no/atc_ddd_index/

Wikantiananda, T., Tjahjadi, A., & Sudjud, R. (2019). *Antibiotic Utilization Pattern in Tertiary Hospital Intensive Care Unit in West Java, Indonesia*. https://www.academia.edu/download/77864966/1436.pdf

Yulia, R., Mariza, J., Respiratory, F. H.-C., & 2020, U. (2020). Bacterial Profile and Antibiotic Use in Pneumonia Patients at Dr. Soetomo General Hospital. *Current Respiratory Medicine Reviews*, *16*, 21–27. https://doi.org/10.2174/1573398X16666200217122825

Yuniarti, E., Rani, A. M., & Handayani, E. W. (2021). Evaluasi Penggunaan Antibiotika pada Infeksi Salurah Kemih dengan Metode ATC / DDD DI RSUD Dr. Sosedirman Kebumen. *Journal Farmasi Klinik Dan Sains*, *01*(01), 7–12.

Zavira, N., Jaelani, A. K., Herawati, F., Yulia, R., & Surabaya, U. (2021). Evaluation on The Use of Antibiotics for Pneumonia Patients Nada. *Jurnal Kesehatan Prima*, *15*(August).

Zhu, Y., Qiao, Y., Dai, R., Hu, X., & Li, X. (2021). Trends and Patterns of Antibiotics Use in China's Urban Tertiary Hospitals, 2016–19. *Frontiers in Pharmacology*, *12*. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8595100/