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Original Article

ANTIBIOTICS IN INDONESIA: ACCESS, WATCH, AND RESERVE CLASSIFICATION

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ABSTRACT

Objective: The objective of this study is to compare antibiotics listed in the National Essential Medicines List (NEML) and national formulary in Indonesia by determining the proportion of antibiotics in the three groups, Access, Watch, and Reserve (AWaRe), along with median data, range values, and time trends from 2013 to 2021.

Methods: We obtained the compilation of antibiotics from the NEML and national formulary in Indonesia, covering the period from 2013 to 2021. These antibiotics were evaluated according to the 2021 WHO AWaRe classification database. This analysis involved determining the proportion of antibiotics in the AwaRe groups within each healthcare facility. Median data and range values for these antibiotics were also calculated. Trends in the proportion of AWaRe antibiotics were analyzed and visualized using a line chart.

Results: The Indonesian NEML includes 20 antibiotics, categorized into two tiers of healthcare settings. Of these antibiotics, 13 were access, seven were watch, and there was neither a reserve nor a not recommended antibiotic. The Indonesian national formulary includes 42 antibiotics, categorized into three tiers of healthcare settings. Of these antibiotics, 19 were access, 22 were watch, one was not recommended, and there was no reserve antibiotic. The proportion of antibiotics during the pre-and post-establishment of the WHO AWaRe in 2017 showed significant changes in the Indonesian national formulary but not in the NEML.

Conclusion: In recent years, the proportions of antibiotics in the Indonesian NEML and national formulary have varied according to the WHO AWaRe classification.

Keywords: Antibiotics, AWaRe, National essential medicines list, National formulary, Indonesia

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INTRODUCTION

Antimicrobial resistance (AMR) is still a major threat to public health around the world [1]. AMR contributes to increased healthcare expenses, prolonged treatment durations, and higher mortality rates [1, 2]. A recent study estimates that approximately 4.95 million deaths were associated with AMR in 2019, with 1.27 million of these deaths being directly attributed to AMR [1]. One critical factor driving AMR is the misuse of antibiotics in healthcare, including overuse, underuse, and improper administration [3, 4]. While appropriate antibiotic use can effectively prevent and treat bacterial infections, suboptimal utilization of antibiotics can lead to antibiotic resistance, a condition characterized by an alteration in the bacterial response to administered antibiotics [2, 5].

In 2015, the World Health Organization (WHO) established a global action plan (GAP) mandating member nations to develop national strategy plans for AMR encompassing monitoring and reporting, antibiotic stewardship, and infection prevention. The antibiotic stewardship (AMS) program is an intervention within the GAP framework that employs a systematic approach to ensure judicious antimicrobial use, which helps control AMR and minimize improper utilization of antimicrobials [6, 7].

As part of an initiative to manage antibiotics at the local, national, and global levels, in 2017, the WHO proposed a classification of antibiotics into three (3) groups: Access, Watch, and Reserve (AWaRe). This classification takes into account the effect of antibiotics and antibiotic classes on antimicrobial resistance. Additionally, the AWaRe classification has undergone multiple modifications since its development. As of 2021, it encompassed 258 antibiotics distributed across the three groups [8]. The access group comprises primary and secondary antibiotics recommended as initial treatment for common infections and are also included in the Essential Medicines List to enhance accessibility and appropriate usage [8]. The watch group includes antibiotics with higher resistance potential and prioritizing them for stewardship and monitoring programs. However, specific antibiotics within this group are also recommended as either the primary or secondary choice for empirical therapy in particular infections and are listed in the WHO Model list of essential medicines [8]. The reserve group comprises antibiotics considered as last-resort options, necessitating stringent control and prioritization in both national and international stewardship programs to preserve their efficacy [8].

National drug lists, such as the National Essential Medicines List (NEML) or national formulary, play a crucial role in prioritizing available and affordable medicines based on the treatment of diseases in that country [9–11]. Indonesia established its first NEML in 1980, refining the process in line with the WHO Good Governance on Medicines program since 2008, with regular revisions every two years starting from 2011 [12]. Additionally, Indonesia developed a national formulary in 2013, serving as a comprehensive list of medicines used in health insurance schemes in Indonesia [13].

According to the previous study [9] comparing 44 essential antibiotics listed in the NEML sourced from Global Essential Medicines (GEM) with the 2019 WHO Model List, Indonesia has included 16 essential antibiotics in the NEML. These consist of 12 access, four watch, and no reserve antibiotic. Indonesia's antibiotic coverage score for 31 WHO priority infections was 70, slightly lower than the 2019 WHO Model List coverage score of 80 [9].

To our knowledge, no study has been conducted to analyze the antibiotics included in the Indonesian national formulary, despite the widespread use of the formulary by participants of the National Health Insurance (Jaminan Kesehatan Nasional/JKN), covering approximately 92 percent of Indonesia's population as of June 30, 2023 [14, 15]. This study aims to compare antibiotics listed in the Indonesian NEML and national formulary with the WHO AWaRe classification and analyze the development of both classifications from 2013 to 2021.

MATERIALS AND METHODS

Materials

In this study, we utilized data from the Legal Documentation and Information Network, accessed from the official website of the Indonesia Ministry of Health, using the search terms "daftar obat esensial nasional" for the Indonesian NEML and "formularium nasional" for the Indonesian national formulary [16]. The data is provided in the format of legal products, and we collected it covering the period from 2013 to 2021. Additionally, we referred to the "pedoman penggunaan antibiotik" for the Indonesian Guidelines for Antibiotic Use. ATC codes were obtained from the official website of the WHO Collaborating Center for Drug Statistics Methodology [17]. For analysis, we utilized the 2021 WHO AWaRe classification database [18].

The compilation of antibiotics from the Indonesian NEML and national formulary spanning from 2013 to 2021 was obtained. We also used the antibiotics list in the 2021 Indonesian Guidelines for Antibiotic Use as the framework for the AWaRe classification in Indonesia. The comprehensive list of antibiotics used is presented in table 1 (NEML) and table 2 (national formulary). The 2021 WHO AWaRe classification database was employed for analysis, encompassing both essential antibiotics listed in the WHO Model List and those not listed. Within this dataset, antibiotics were categorized into access, watch, reserve, and a group classified as not recommended, which comprises antibiotics not recommended for clinical use due to insufficient evidence supporting their efficacy [18].

Methods

We evaluated the inclusion of antibiotics in the AWaRe database in the Indonesian NEML and national formulary, categorizing them according to their AWaRe classification. Antibiotics for systemic use only were included in this study; no topical, anti-parasitic, or anti-TB formulations were included. This analysis involved determining the proportion of antibiotics in the AWaRe groups within each healthcare facility. Median data and range values for these antibiotics were also calculated. Furthermore, we assessed the appropriateness of antibiotics in the NEML using the 2021 WHO Model List of Essential Medicines. Antibiotics present in the AWaRe database but not listed in the Indonesian NEML or national formulary were excluded from the analysis. Trends in the proportion of AWaRe antibiotics were analyzed and visualized using a line chart. Data analysis was conducted using Microsoft Excel and IBM SPSS Statistics 25.

RESULTS

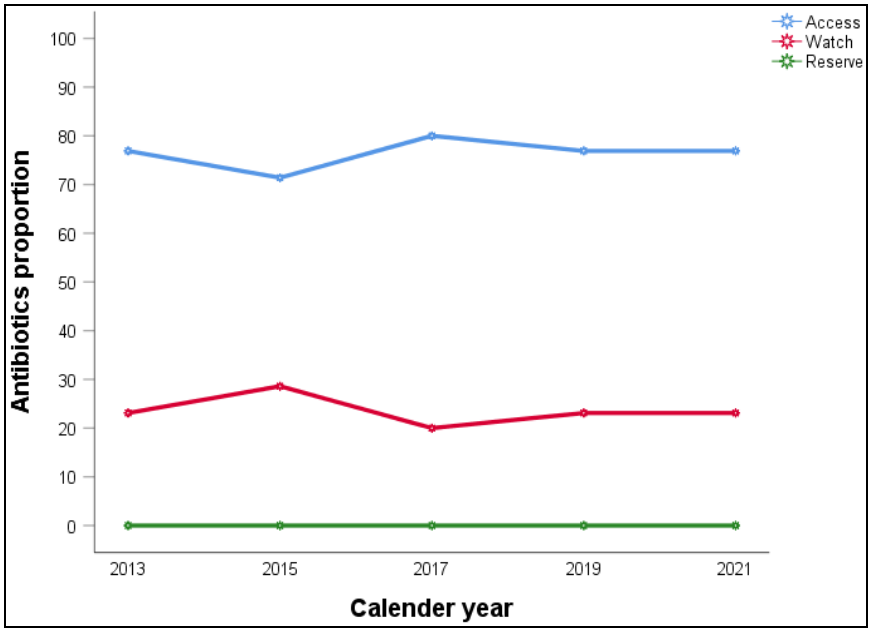
The medicines listed in the Indonesian NEML are categorized into two tiers of healthcare settings: primary healthcare and hospitals. Table 1 presents all antibiotics listed in the 2013-2021 NEML. The list of antibiotics available in primary healthcare and hospital settings comprises the access and watch groups, with no antibiotic from the reserve or not recommended groups. Several antibiotics listed in the NEML are not included in the 2019 WHO Model List. Three antibiotics in primary care settings, including erythromycin, streptomycin_IV, and tetracycline, are not included in the WHO Model List. Five antibiotics are not included in the WHO Model List in hospital settings: erythromycin, oxytetracycline, streptomycin IV, and tetracycline.

Table 1: Recategorization of antibiotics in the Indonesian NEML (2013–2021) based on the 2021 WHO AWaRe classification

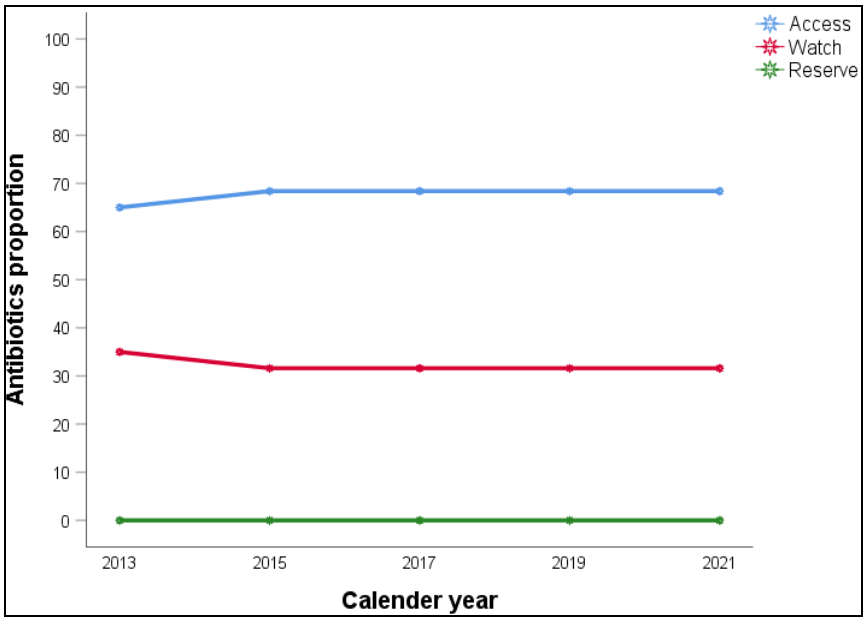
Antibiotic	ATC code	Primary care	Hospital	2021 WHO EML/EMLc
Access group				
Amoxicillin	J01CA04	√	√	Yes
Ampicillin	J01CA01	√	√	Yes
Benzathine-benzylpenicillin	J01CE08	√	√	Yes
Cefadroxil	J01DB05	-	√	No
Cefazolin	J01DB04	-	√	Yes
Chloramphenicol	J01BA01	√	√	Yes
Doxycycline	J01AA02	√	√	Yes
Gentamicin	J01GB03	-	√	Yes
Metronidazole_IV	J01XD01	√	√	Yes
Phenoxymethylpenicillin	J01CE02	√	√	Yes
Procaine-benzylpenicillin	J01CE09	√	√	Yes
Sulfamethoxazole/trimethoprim	J01EE01	√	√	Yes
Tetracycline	J01AA07	√	√	No
Watch group				
Cefixime	J01DD08	-	√	Yes
Ceftriaxone	J01DD04	-	√	Yes
Ciprofloxacin	J01MA02	√	√	Yes
Erythromycin	J01FA01	√	√	No
Oxytetracycline	J01AA06	-	√	No
Streptomycin_IV	J01GA01	√	√	No
Vancomycin_IV	J01XA01	√	√	Yes
Reserve group				
-				
Not-recommended group				
-				

NEML-National Essential Medicines List, AWaRe-Access, Watch and Reserve

The median number of all antibiotics listed in primary care was 13 (range 10-14). The median number of access antibiotics was 10 (8-10), and watch was three (2-4). Meanwhile, the median number of all antibiotics listed in hospital settings was 19 (19-20), access antibiotic was 13 (13-13), and watch was six (6-7). Fig. 1 presents the time trends in the proportion of antibiotics in the NEML from 2015 to 2021. The proportion of access and watch antibiotics in primary healthcare and hospitals showed variations over five years. Still, there was no statistically significant difference in the years preceding and following the establishment of the WHO AWaRe classification in 2017. There was an increase in the average proportion of access antibiotics in primary care and hospital settings before and after 2017 (76.10% to 76.90%, p=0.821 and 67.27% to 68.4%, p=0.414). There was a decrease in the average proportion of watch antibiotics in primary care and hospital settings before and after 2017 (23.90% to 23.10%, p=0.781 and 32.73% to 31.60%, p=0.414).



(a)

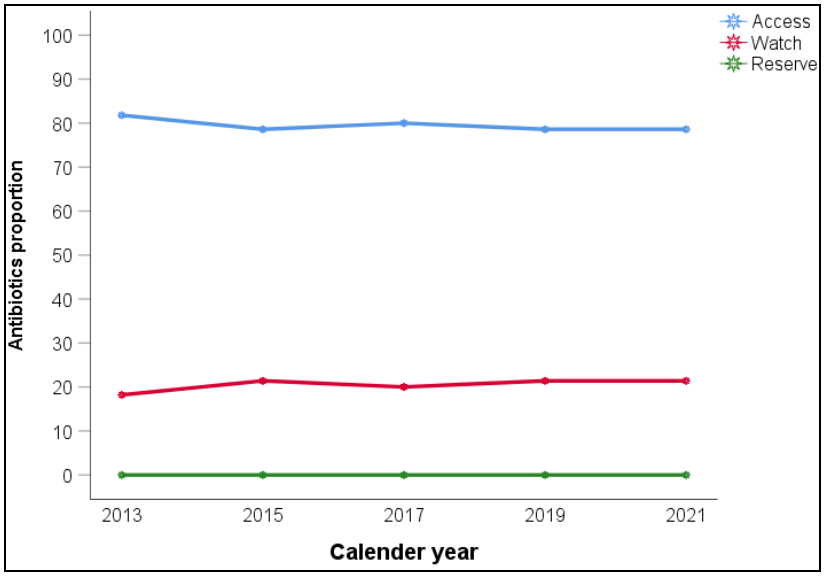


(b)

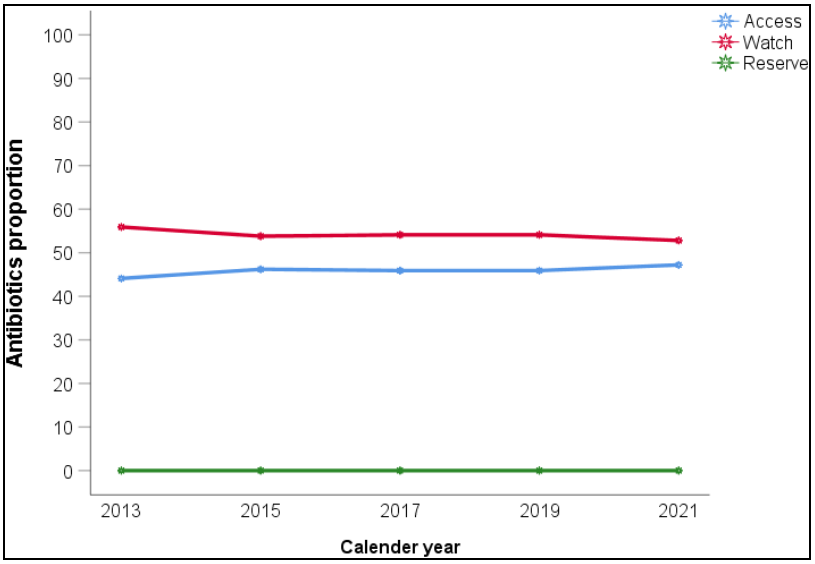
Fig. 1: Proportion of antibiotics in the Indonesian NEML based on the 2021 WHO AWaRe classification (a) primary care (b) hospital

The medicines listed in the national formulary are categorized into three tiers of healthcare settings: primary, secondary, and tertiary healthcare. In 2013–2021, the national formulary included a list of antibiotics classified into the access, watch, and not recommended groups, and there was no reserve group (table 2). The median number of all antibiotics listed in primary care was 14 (11-15), access antibiotic was 11 (9-12), and watch was three (2-3). The median number of all antibiotics listed in secondary care was 37 (34-39), access antibiotic was 17 (15-18), and watch was 20 (19-21). The median number of all antibiotics listed in tertiary care was 41 (35-42), access antibiotic was 18 (15-19), and watch was 21 (19-22). There were two fixed-dose combinations of antibiotics (FDC) that are only available in tertiary care, such as a combination of amoxicillin and clavulanic acid (since 2019) and a combination of cefoperazone and sulbactam (since 2017). Meanwhile, a combination of cefoperazone and sulbactam is classified as a not-recommended antibiotic in the WHO AWaRe.

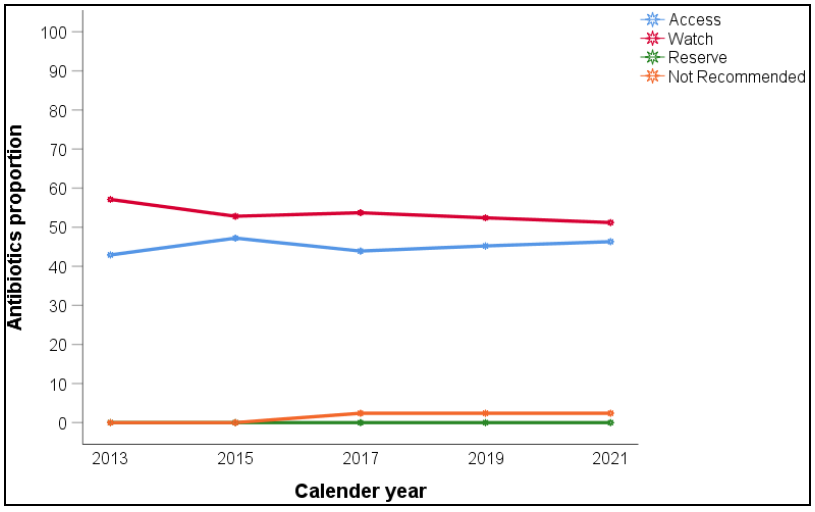
The time trends in the proportion of antibiotics in the national formulary from 2015 to 2021 are presented in fig. 2. The proportion of access and watch antibiotics in primary, secondary, and tertiary care showed statistically significant changes in the years preceding and following the establishment of the WHO AWaRe classification in 2017. The average proportion of access antibiotics decreased in primary care (from 80.13% to 78.6%, p=0.24) but increased in secondary and tertiary care (from 45.40% to 46.55%, p=0.323 and from 44.67% to 45.75%, p=0.506). The average proportion of watch antibiotics increased in primary care (from 19.87% to 21.40%, p=0.24) but decreased in secondary and tertiary care (from 54.60% to 53.45%, p=0.323 and 54.53% to 51.80%, p=0.164).



(a)



(b)



(c)

Fig. 2: Proportion of antibiotics in the Indonesian national formulary based on the 2021 WHO AWaRe classification (a) primary care (b) secondary care (c) tertiary care

Table 2: Recategorization of antibiotics in the Indonesian national formulary (2013–2021) based on the 2021 WHO AWaRe classification

Antibiotic	ATC code	Primary	Secondary	Tertiary
Access group				
Amikacin	J01GB06	-	√	√
Amoxicillin	J01CA04	√	√	√
Amoxicillin/clavulanic-acid	J01CR02	-	-	√/-
Ampicillin	J01CA01	√	√	√
Ampicillin/sulbactam	J01CR01	-	√/-	√/-
Benzathine-benzylpenicillin	J01CE08	√	√	√
Cefadroxil	J01DB05	√/-	√	√
Cefalexin	J01DB01	-	√	√
Cefazolin	J01DB04	-	√	√
Chloramphenicol	J01BA01	√	√	√
Clindamycin	J01FF01	√/-	√	√
Doxycycline	J01AA02	√	√	√
Gentamicin	J01GB03	-	√	√
Metronidazole IV	J01XD01	√/-	√	√
Phenoxymethylpenicillin	J01CE02	√	√	√
Procaine-benzylpenicillin	J01CE09	√/-	√/-	√/-
Sulfadiazine	J01EC02	-	√/-	√/-
Sulfamethoxazole/trimethoprim	J01EE01	√	√	√
Tetracycline	J01AA07	√	√	√
Watch group				
Azithromycin	J01FA10	-	√	√
Cefepime	J01DE01	-	√	√
Cefixime	J01DD08	-	√	√
Cefoperazone	J01DD12	-	√	√
Cefotaxime	J01DD01	-	√	√
Cefpirome	J01DE02	-	√/-	√/-
Cefpodoxime-proxetil	J01DD13	-	√	√
Ceftazidime	J01DD02	-	√	√
Ceftriaxone	J01DD04	-	√	√
Cefuroxime	J01DC02	-	√	√
Ciprofloxacin	J01MA02	√	√	√
Clarithromycin	J01FA09	-	√	√
Erythromycin	J01FA01	√	√	√
Kanamycin_IV	J01GB04	-	√/-	√/-
Levofloxacin	J01MA12	-	√	√
Meropenem	J01DH02	-	√	√
Moxifloxacin	J01MA14	-	√/-	√/-
Ofloxacin	J01MA01	-	√	√
Oxytetracycline	J01AA06	-	√/-	√/-
Spiramycin	J01FA02	-	√	√
Streptomycin_IV	J01GA01	√/-	√	√
Vancomycin_IV	J01XA01	-	√/-	√/-
Reserve group				
-				
Not-recommended group				
cefoperazone/sulbactam	J01DD62	-	-	√/-

AWaRe-Access, Watch and Reserve

DISCUSSION

The composition of antibiotics within the list of medicines in Indonesia, including the NEML and national formulary, has evolved in accordance with the WHO AWaRe classification over the past five years (2013-2021). These changes result from periodic reviews conducted by the Indonesian government to ensure alignment with the latest technological and scientific developments [19, 20]. The inclusion of antibiotic medicines list in the NEML and national formulary holds significant importance as it could substantially impact on their accessibility and utilization [21]. Moreover, it aligns with WHO recommendations aimed at combating antibiotic resistance, where a country's essential medicines list can influence antibiotic prescribing practices [22]. The national action plan for AMR in Southeast Asia, involving Indonesia and nine other ASEAN (Association of Southeast Asian Nations) countries, emphasizes optimizing antibiotic use, including through the adoption of essential medicine lists or other national drug policies [23]. WHO recommended integrating of the AWaRe antibiotic classification into local policies to curb antibiotic resistance and enhance the safety and effectiveness of antibiotic use [24]. A study examining essential medicine lists in 138 countries, including Indonesia, suggests potential revisions to the antibiotic inclusions in NEMLs to better adhere to international guidelines aimed at reducing antibiotic resistance [9].

The proportion of antibiotics in the national formulary changed significantly during the pre-and post-establishment of the WHO AWaRe classification in 2017, unlike the NEML. The disparity may arise because the NEML comprises medicines deemed crucial for widespread availability and affordability across Indonesia in an equitable manner [19, 25]. Conversely, the national formulary serves as a prescribing reference for Indonesia's national health insurance program, covering 92 percent of the population [13, 14]. There are additional notes prescribing restrictions for specific medicines based on the Expert Committee recommendations [20].

In primary care, both the Indonesian NEML and national formulary contain more significant proportion of access groups compared to other antibiotic groups. The tendency mirrors findings from 66 other countries, where access antibiotics feature prominently on national medicines lists [9]. This alignment with WHO recommendations is commendable, as access antibiotics are

recommended for widespread availability due to their efficacy against commonly encountered pathogens and lower resistance potential compared to other antibiotics [8, 26]. According to WHO, nine of the ten most common diseases in primary care can be managed successfully without antibiotics or with access antibiotics [27]. In line with this, a study conducted on the prescription of antibiotics in primary care across 15 low-and middle-income countries (LMICs) reveals that in 12 of these countries, access antibiotics accounts more than 60% of the total antibiotic prescriptions [28]. The consumption of access antibiotics in Indonesia has reached 69%, with the highest levels of consumption found in primary healthcare settings for amoxicillin and cefadroxil [5]. By prioritizing access to antibiotics as essential medicines, especially in primary healthcare settings, Indonesia aims to meet the WHO target of having access to antibiotics account for 60% of national antibiotic consumption by 2023 [22, 27].

There was a difference in the proportion of watch antibiotics listed in the NEML and the national formulary. In the NEML, the proportion of watch antibiotics is no more significant than access antibiotics in both primary care and hospitals. Compared to access antibiotics, the proportion of watch antibiotics in the national formulary is lower in primary care but higher in secondary and tertiary care. A previous study in 138 countries found that 72 countries, including India, Mexico, Portugal, Tunisia, and Vietnam, included more watch antibiotics than access antibiotics on their essential medicines list [9]. According to data collected from several hospitals in Indonesia, watch antibiotic consumption accounted for 67.4% of total antibiotics [29]. The antibiotics commonly prescribed in hospitals are ciprofloxacin for outpatients and ceftriaxone and levofloxacin for inpatients [5]. The same issue occurs in other countries where watch antibiotics are more often administered than access antibiotics, such as the United Kingdom, Bangladesh, Mexico, China, Pakistan, and India [28, 30–32]. Antibiotic stewardship programs closely monitor the watch antibiotic group, which has the potential to cause higher resistance than access antibiotics [8]. The Guidelines for Antibiotic Use in Indonesia have set limits on their use, specifically that they can be administered in advanced healthcare settings with specified indications or when access antibiotics are no longer effective [26]. Therefore, the implementation of antimicrobial stewardship mainly focuses on hospitals and engages multiple relevant stakeholders [33].

Reserve antibiotics are not listed in the Indonesian NEML or national formulary; however, they are included in the Guidelines for Antibiotic Use in Indonesia. Similarly, the same observation was conducted in 56 countries where reserve antibiotics were not included in their essential medicines lists [9]. Reserve antibiotics are antibiotics that must be reserved for the treatment of infections that are confirmed or suspected to be caused by multidrug-resistant (MDR) organisms [8]. Although reserve antibiotics are not included in the Indonesian NEML or national formulary, a study conducted in 2019 revealed that Indonesian hospitals were still prescribing reserve antibiotics, including fosfomycin, tigecycline, colistin, and linezolid, which accounted for 2.4% of the total antibiotics [29]. Based on WHO surveillance reports from 2017-2020, it is known that several countries have experienced a widespread increase in MDR bacterial infections [34]. The presence of reserve antibiotics in a country's health system is a must, with the primary problem being ensuring their proper use. Hence, before the introduction of reserve antibiotics, it is imperative to establish regulations governing their use, develop the necessary infrastructure for policy implementation, and establish robust monitoring mechanisms [22]. The current regulation in Indonesia regarding the use of reserve antibiotics requires authorization from the Antibiotic Stewardship Program (ASP) team, which is managed under the authority of the Antimicrobial Resistance Control Committee (ARCC) at the hospital [26]. Strict regulation of reserve antibiotic consumption is a critical measure for managing their prescription practices in Indonesia.

There is one antibiotic in the national formulary classified as not recommended by the WHO, which is a combination of cefoperazone and sulbactam. Eastern European and Central Asian countries such as the Republic of Moldova, Russia, and Uzbekistan include this combination antibiotic in their list of essential medicines [22]. This combination comprises one antibiotic from the watch group (cefoperazone) and one from the access group (sulbactam) [24]. It is classified within the not recommended antibiotic group, along with other FDC antibiotics, including broad-spectrum antibiotics, lacking scientific support and not recommended by international guidelines [22]. Previous studies typically recommend this combination antibiotic for surgical inpatients in hospitals [5]. According to the findings from an Indonesian study on antibiotic sensitivity patterns, the combination of cefoperazone and sulbactam is an antibiotic with high sensitivity for diabetic foot infections and infections in open fractures [35, 36]. In the Indonesian national formulary, this antibiotic is only used as a third-line antibiotic for severe infections that cannot be treated with a single antibiotic, requiring approval from the pharmacy and therapeutics committee (P and T committee), ARCC, or hospital management [13]. Meanwhile, this antibiotic has been classified as a watch antibiotic in Indonesia's Guidelines for Antibiotic Use [26]. This discrepancy in the grouping of combination antibiotics serves as an evaluative note for the national formulary committee in preparing the drug list in Indonesia, prompting further investigation into the usage pattern of these combination antibiotics due to their potential to contribute to increased MDR bacterial infections. While variations in antibiotic use exist across different countries, adherence to current global guidelines is crucial, particularly in avoiding the utilization of antibiotics classified as not recommended.

The list of antibiotics in the Indonesian NEML, particularly the 2021 NEML, does not entirely align with the 2021 WHO Model List. The antibiotics in the WHO Model List are specific and based on solid evidence, deemed necessary for first-and second-choice empirical treatment of the most common or severe bacterial diseases [22]. The five antibiotics in the Indonesian NEML that are not on the WHO Model List are categorized as access antibiotics (cefadroxil, tetracycline) and watch antibiotics (erythromycin, oxytetracycline, streptomycin IV). These non-WHO Model Lists are divided into two categories. The first includes antibiotics that have never been recommended in the WHO Model List, such as cefadroxil and oxytetracycline [37]. The second part of the list comprises antibiotics that have been removed from the WHO Model List but are still included in the Indonesian NEML. For instance, erythromycin was discontinued in 2017 following a thorough evaluation by the WHO Expert Committee; tetracycline was discontinued in 1995 due to the superior pharmacokinetic profile of doxycycline; and streptomycin IV is no longer indicated as the initial treatment for tuberculosis (TB), although it is still included in the EML and EMLc Supplemental List for secondary use in cases of MDR-TB [37]. According to Indonesia's Guidelines for Antibiotic Use, these five antibiotics are classified as access antibiotics [26]. Along with Indonesia, Eastern European and Central Asian nations, including Albania, Belarus, Kazakhstan, the Republic of Moldova, Turkey, and Uzbekistan, also include these antibiotics in their list of essential medicines [22]. Although the WHO Model List serves as a reference, each country considers its factors when determining which antibiotics are essential for their population. However, it is expected that the medicines list in Indonesia will consistently get updates in alignment with the most recent international guidelines to prevent the prescription of antibiotics that are no longer recommended.

According to study findings on global antibiotic consumption and use from 2000 to 2018, there was a decrease in antibiotic consumption in Indonesia from a median of 63% to 25% [38]. A previous study suggests that a country's drug formulary plays a crucial role in drug prescribing control [9, 22]. A country's drug list or formulary is subject to constant change due to the discovery of new drugs and the publication of new evidence. This dynamic process can lead to the inclusion, modification, or elimination of drugs from the formulary. As a result, the formulary must be evaluated regularly to add new drugs, eliminate outdated ones, and rationalize its contents, given recent advances in science. Improved dissemination of formulary changes and repeated education for all health workers in healthcare facilities are necessary. This effort should include public education on minimizing antibiotic consumption. Moreover, disseminating the rationale behind specific changes can enhance prescribers' understanding and mitigate prescribing practices based on habit [22].

To the best of our knowledge, this is the first study to utilize the WHO AWaRe classification to evaluate the list of antibiotics in the NEML and the national formulary in Indonesia. The strength of our study lies in providing data on antibiotics in the NEML and national formulary from their inception in 2013 to the most recent data in 2021, utilizing the WHO AWaRe database. This study will be beneficial as evaluation material for the Indonesian government and relevant to other countries that have, or plan to have, robust universal health coverage, including NEML, as we evaluate trends in changes in the proportion of antibiotics within a country's drug formulary.

The limitation of this study is that we only present an overview of trends in changes in the proportion of antibiotics in the Indonesian NEML and national formulary from 2013 to 2021, assuming that antibiotics listed in the NEML and national formulary are prescribed more commonly than those not listed. Further research is necessary to determine the trend of changes in the proportion of antibiotics prescribed according to the NEML and national formulary, as well as those outside them, using the WHO AWaRe classification. That will provide a more robust basis for evaluating and updating the NEML and national formulary in the future.

CONCLUSION

In recent years, the Indonesian NEML and national formulary have shown different proportions of antibiotics based on the WHO AWaRe classification. There is evidence of a significant trend in changes in the proportion of antibiotics in the national formulary but not in the NEML. This study provides valuable evaluation material for policymakers and researchers by presenting a comprehensive list of antibiotics in the NEML and the national formulary from their establishment year until the current year, using the WHO AwaRe classification. Additionally, this study highlights discrepancies in the classification of several antibiotics in Indonesia according to the 2021 WHO AWaRe classification. The use of antibiotics not recommended by the WHO should be based on robust and current evidence before being included in the NEML and the national formulary. It is recommended that the Indonesian government review the NEML and the national formulary regularly and adapt them to the most recent international guidelines. Furthermore, they should investigate the issues discovered in this study because coordinated efforts by each country based on international guidelines can be used to control AMR.

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Nil

AUTHORS CONTRIBUTIONS

DSAA conceptualized and designed the study, analyzed and interpreted the data, and wrote the manuscript. PO and IGAT conceptualized the study reviewed and edited the manuscript. All authors read and approved the final version of the manuscript.

CONFLICT OF INTERESTS

Declared none

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