

# BMJ Open Antibiotic prescribing practice using WHO Access, Watch and Reserve classification and its determinants among outpatient prescriptions dispensed to elderly population in six community chain pharmacies in Asmara, Eritrea: a cross-sectional study

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**To cite:** Abdu N, Idrisnur S, Tewelde T, *et al.* Antibiotic prescribing practice using WHO Access, Watch and Reserve classification and its determinants among outpatient prescriptions dispensed to elderly population in six community chain pharmacies in Asmara, Eritrea: a cross-sectional study. *BMJ Open* 2024;**14**:e085743. doi:10.1136/bmjopen-2024-085743

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<https://doi.org/10.1136/bmjopen-2024-085743>).

Received 28 February 2024  
Accepted 21 May 2024



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## ABSTRACT

**Objective** To assess antibiotic prescribing practice and its determinants among outpatient prescriptions dispensed to the elderly population.

**Design** A prescription-based, cross-sectional study.

**Setting** Six community chain pharmacies in Asmara, Eritrea.

**Participants** All outpatient prescriptions dispensed to the elderly population (aged 65 and above) in the six community chain pharmacies in Asmara, Eritrea.

**Data collection and analysis** Data were collected retrospectively, between 16 June 2023 and 16 July 2023.

Antibiotic prescribing practice was assessed using the 2023 World Health Organization (WHO) Access, Watch and Reserve (AWaRe) classification system. Descriptive statistics and logistic regression were performed using IBM SPSS (V.26.0). P values less than 0.05 were considered as significant.

**Results** Of the 2680 outpatient prescriptions dispensed to elderly population, 35.8% (95% CI: 34.0, 37.6) contained at least one antibiotic. Moreover, a total of 1061 antibiotics were prescribed to the elderly population. The most commonly prescribed antibiotics were ciprofloxacin (n=322, 30.3%) and amoxicillin/clavulanic acid (n=145, 13.7%). The Access category accounted for the majority of antibiotics (53.7%) with 32.1% from the Watch category. Prescriber qualification (Adjusted Odds Ratio (AOR)= 0.60, 95% CI: 0.44, 0.81) and polypharmacy (AOR= 2.32, 95% CI: 1.26, 4.27) were significant determinants of antibiotic prescribing in the elderly population. Besides, sex (AOR=0.74, 95% CI: 0.56, 0.98), prescriber qualification (AOR=0.49, 95% CI: 0.30 to 0.81) and level of health facility (AOR 0.52, 95% CI 0.34 to 0.81) were significant determinants of a Watch antibiotic prescription.

**Conclusion** Antibiotics were prescribed to a considerable number of the elderly population, with more than half of them falling into the Access category. Further efforts by policy-makers are needed to promote the use of Access antibiotics while reducing the use of Watch antibiotics to mitigate risks associated with antimicrobial resistance.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The study used the latest version of the Access, Watch and Reserve classification system (2023), engaged rigorous data quality control and management protocols.
- ⇒ Due to the cross-sectional nature of the study, the cause-and-effect relationship was not established.
- ⇒ Indication for antibiotic use and detailed demographic and clinical characteristics of the elderly outpatients cannot be obtained from the prescriptions.

## INTRODUCTION

The use of antibiotics has revolutionised the practice of medicine by prolonging life expectancy and decreasing the incidence of morbidity and mortality due to infectious diseases. However, excessive and inappropriate use of antibiotics may lead to antimicrobial resistance (AMR).<sup>1</sup> AMR is a term used to indicate antibiotics' loss of effectiveness to treat infections. AMR arises due to an evolutionary process in microbials that can be further accelerated by misuse of antibiotics and poor infection control practices.<sup>1</sup> AMR is a major public health concern worldwide, leading the WHO and the US Centers for Disease Control and Prevention to declare it as an urgent issue that requires global efforts.<sup>2-4</sup> A review conducted by Murray *et al* estimated that AMR causes approximately 4.95 million deaths, with 1.27 million of those deaths attributable to resistant strains of bacteria.<sup>5</sup> Low-income and middle-income countries bear the highest burden of AMR.<sup>5</sup> Several studies have projected that the number of AMR-related deaths will increase

to 10 million by 2050, with 4.2 million of those deaths occurring in sub-Saharan Africa.<sup>6,7</sup>

The global increase in the elderly population contributes to the rise in antibiotic consumption.<sup>8,9</sup> Numerous studies have reported antibiotic use among the elderly population ranging from 4.9% to 48.5%.<sup>10–16</sup> Furthermore, a quarter of antibiotic prescriptions in the elderly population are inappropriate.<sup>11</sup> As the elderly population is susceptible to multiple comorbidities and weakened immunity, they are at higher risk of acquiring infections.<sup>9</sup> Challenges in the diagnosis and management of the elderly population include undetectable or blunt fever, pharmacokinetic alterations and the existence of polypharmacy.<sup>9,17,18</sup> Additionally, the habit of sharing antibiotics for perceived similar conditions in the elderly population contributes to AMR.<sup>19</sup>

To address these concerns, the WHO has developed the Access, Watch and Reserve (AWaRe) classification, which aims to guide antibiotic prescription and preserve the effectiveness of last-resort antibiotics.<sup>20</sup> This classification tool categorises antibiotics into three groups: AWaRe. The Access group includes antibiotics with a narrow spectrum of activity and low resistance potential.<sup>20</sup> The Watch group consists of antibiotic classes with broader-spectrum antibiotics intended for severe and resistant infections compared with Access antibiotics.<sup>20</sup> The Reserve group includes antibiotics that should be used as last-resort options.<sup>20</sup>

Despite the Ministry of Health of Eritrea has developed a national strategic action plan and implementing a complete restriction on antibiotic dispensing without a prescription, inappropriate use of antibiotics in Eritrea remains a concern.<sup>21–23</sup> No previous study has been conducted on antibiotic outpatient prescriptions for the elderly population in Eritrea. Therefore, the aim of this study was to assess antibiotic outpatient prescription and its determinants among the elderly population. The results of this study are expected to provide baseline information for a broader study on antibiotic use that can contribute to ensure the safe use of antibiotics in the elderly population.

## METHODS

### Study design and setting

A cross-sectional study was conducted in six community chain pharmacies in Asmara (the capital city of Eritrea). These pharmacies are government-owned and represent 50% of all community chain pharmacies in Eritrea. Moreover, the community chain pharmacies receive and fill prescriptions ordered from several health facilities including national referral hospitals. Data were collected retrospectively, between 16 June 2023 and 16 July 2023, for 1 month.

### Target population

The study population included all outpatient prescriptions dispensed to the elderly population (aged 65 and

above) in the study areas during the data collection period.

### Patient and public involvement

Patients were not involved during the design, review and analysis of data.

### Data collection tool and variable measurement

A tool was developed to collect the necessary data, reflecting the WHO antibiotic use by the AWaRe classification.<sup>20,24,25</sup> The data collection tool consisted of two sections. Section A included sociodemographic characteristics of patients, prescriber qualification, level of health facility and polypharmacy. In this context, outpatient prescriptions for the elderly population containing five or more medicines were considered polypharmacy.<sup>26</sup> Section B was used to assess antibiotic prescribing practice based on the 2023 WHO AWaRe classification system. The percentage of encounters with antibiotics prescribed was calculated by dividing the number of encounters with antibiotics by the total number of encounters surveyed, multiplied by 100.<sup>25</sup> Moreover, an Anatomic Therapeutic Chemical (ATC) classification was assigned to the prescribed antibiotics. The study used the WHO's previously defined definition of 'antibiotic' to avoid confusion.<sup>25</sup> A prescriber in the Eritrean healthcare system consists of specialists, medical doctors, dentists, nurse practitioners, dental technicians and other lower health cadres. Besides, nurse practitioners include degree nurses, registered nurses (diploma level) and associate nurses (certificate level).

### Variables

The dependent variables were the prescription of an antibiotic and the prescription of a watch antibiotic. The independent variables included age, sex, prescriber qualification, polypharmacy and level of health facility.

### Quality assurance

A validated and pretested data collection tool was used for the study. A group of professionals in the fields of medicine, pharmacy, public health and epidemiology assessed the tool to ensure face and content validity. The tool was then subjected to a pretest, which involved 40 outpatient prescriptions dispensed to the elderly population, from a randomly selected community chain pharmacy. The findings from the pretest were excluded from the main survey analysis. Based on expert comments and the pretest results, the data collection tool was modified and used for the main study. Well-trained pharmacy professionals were included as data collectors and received training on the study objectives and protocols, data collection approaches, familiarity with the ATC codes and the WHO AWaRe classification system and pretest demonstration. The study methods followed WHO protocols and involved well-trained data collectors, ensuring data reliability.

## Statistical analysis

The collected data were double entered and cleaned and analysed using Census and Survey Processing system (V.7.3)<sup>27</sup> and Statistical Package for Social Sciences (V.26.0),<sup>28</sup> respectively. Descriptive analysis of the demographic variables, level of health facility, prescriber qualification and polypharmacy were computed using frequency (percentage), mean (SD) and median (IQR). Associates of antibiotic prescription and 'watch' antibiotic prescription were assessed primarily using bivariate logistic regression. Furthermore, factors that were significant at bivariate were retained for multivariable logistic regression and adjusted ORs (AORs) were computed to assess the determinants. Tables were used to present the results. The OR with 95% CI was reported in all logistic regression analyses. A  $p < 0.05$  was considered significant in all analysis.

## RESULTS

### Sociodemographic characteristics of study population and particulars of prescribers

A total of 2680 outpatient prescriptions for the elderly population were analysed. Of these, 57% were females and 43% were males, with ages ranging from 65 to 118 years (Md=73, IQR=11). The majority of the prescriptions were issued from tertiary-level health facilities (72.7%) while primary and secondary levels accounted for 8.4% and 18.9%, respectively. Most of the outpatient prescriptions for the elderly population were ordered by general practitioners (n=1251, 46.7%), followed by nurse practitioners (n=1115, 41.6%), specialists (n=242, 9.0%) and general practitioner interns (n=72, 2.7%). Specialisation of the specialists comprised of internal medicine (52%), paediatrics (31%), and gynaecology and obstetrics (19%). Moreover, only 1.6% of all participants were prone to polypharmacy.

### Antibiotic prescribing practice

The prevalence of antibiotic prescription was 35.8% (95% CI 34.0% to 37.6%). A total of 1061 antibiotics were prescribed from the 2680 outpatient prescriptions filled for the elderly population. The average number of antibiotics per prescription was 0.40 (SD=0.57). The majority of the antibiotic prescriptions (n=959) contained a single antibiotic (89.9%) with 11.1% of them with multiple antibiotics (table 1).

Out of the total 1061 antibiotics prescribed, the most commonly prescribed antibiotics were ciprofloxacin (n=322, 30.3%), amoxicillin/clavulanic acid (n=145, 13.7%) and amoxicillin (n=118, 11.1%).

When assessing antibiotic prescriptions by prescriber qualification and level of health facility, 40.1% of all general practitioners (n=502/1251) and 28.7% of all nurse practitioners (n=320/1115) prescribed antibiotics. Furthermore, 38.3% of outpatient prescriptions

**Table 1** Description of outpatient antibiotic prescription for the elderly population (n=959)

Total number of antibiotics per prescription (M=0.40, SD=0.57)	Frequency	Percentage
One	862	89.9
Two	93	9.7
Three and above	4	0.4
M, mean.		

from tertiary-level health facilities contained antibiotics (n=747/1948) (table 2).

### AWaRe classification of antibiotics

More than half of the prescribed antibiotics (n=1061) were from the Access category (53.7%), 32.1% were from the Watch category, and none were from the Reserve category. Moreover, 14.1% of the antibiotics were ungrouped in these three AWaRe classification categories (online supplemental file 1). The most commonly prescribed antibiotics from the Access category were amoxicillin/clavulanic acid (25.4%, n=145/570) and amoxicillin (20.7%, n=118/570). Ciprofloxacin (94.4%, n=322/341) was the most prescribed antibiotic within the Watch category (table 3).

### Factors associated with antibiotic prescription among elderly outpatients

Binary logistic regression analysis showed that prescriber qualification ( $p < 0.001$ ), polypharmacy ( $p = 0.002$ ) and level of health facility ( $p < 0.001$ ) were found to have a significant association with antibiotic prescribing in elderly outpatients (table 4).

Multivariable logistic regression indicated that nurse practitioner prescribers were 40% less likely to prescribe an antibiotic than a medical specialist prescriber (AOR 0.60, 95% CI 0.44 to 0.81). Moreover, elderly outpatients exposed to polypharmacy were two times more likely to have an antibiotic prescription than their counterparts (AOR 2.32, 95% CI 1.26 to 4.27) (table 4).

Moreover, binary logistic regression analysis showed that sex ( $p = 0.022$ ), prescriber qualification ( $p < 0.001$ ) and level of health facility ( $p < 0.001$ ) were found to have a significant association with prescription of a Watch category antibiotic in elderly outpatients (table 5).

Multivariable logistic regression indicated that males were 26% less likely to be prescribed a Watch category antibiotic than females (AOR 0.74, 95% CI 0.56 to 0.98). Furthermore, being a nurse practitioner prescriber was 51% less likely to prescribe a Watch antibiotic than a medical specialist (AOR 0.49, 95% CI 0.30 to 0.81). Prescriptions from a secondary-level health facility were 48% less likely to have a Watch antibiotic than prescriptions from a



**Table 2** Distribution of antibiotic prescription vis-à-vis prescriber qualification and level of health facility

Variable	Category	Antibiotic prescription		Total number
		Yes n (%)	No n (%)	
Prescriber qualification	Specialist	103 (42.6)	139 (57.4)	242
	GP	502 (40.1)	749 (59.9)	1251
	Nurse practitioner	320 (28.7)	795 (71.3)	1115
	GP intern	34 (47.2)	38 (52.8)	72
Level of health facility	Primary	62 (27.6)	163 (72.4)	225
	Secondary	150 (29.6)	357 (70.4)	507
	Tertiary	747 (38.3)	1201 (61.7)	1948

GP, general practitioner.

tertiary-level health facility (AOR 0.52, 95% CI 0.34 to 0.81) (table 5).

## DISCUSSION

In this study, at least one antibiotic was prescribed to almost one-third of elderly outpatients (35.8%). This finding is higher than studies conducted in Spain (4.9%),<sup>16</sup> Bangladesh (25.3%)<sup>29</sup> and India (25.2%).<sup>13</sup> Moreover, it is higher than the recommended WHO optimal value (20%–26.8%).<sup>25 30</sup> However, it is lower than studies conducted in Ethiopia (58.1%),<sup>30</sup> Italy (39.1%),<sup>14</sup> Nepal (48.46%),<sup>15</sup> Sierra Leone (94.9%)<sup>31</sup> and United Arab Emirates (43.8%).<sup>32</sup> The variation in results could be due to differences in study design, study setting and study population. Caution should be exercised when comparing results between the current study and studies conducted in Bangladesh, Ethiopia, Sierra Leone and the United Arab Emirates due to differences in the study population. The main reasons for the considerable antibiotic prescription in this study might be due to the increased risk of infections in the elderly population, lack of comprehensive laboratory setup in developing countries

resulting in empiric therapy and authorisation of lower health cadres to prescribe antibiotics.

The most commonly prescribed antibiotic was ciprofloxacin. The increased risks associated with *Clostridium difficile* infection, central nervous system adverse effects and QT interval prolongation as a result of fluoroquinolones place the elderly population at a greater risk of morbidity and mortality.<sup>33 34</sup> Due to an age-related decline in renal function, dosage adjustment of fluoroquinolones,<sup>35</sup> where possible, investigation of liver and renal function tests before therapy initiation, and close monitoring during treatment should be considered to mitigate the risks associated with these medications.

In this study, more than half of the prescribed antibiotics (53.7%) were from the Access category, whereas about one-third of them (32.1%) were from the Watch category. Moreover, no single antibiotic was from the Reserve category. This finding is not comparable to studies conducted in Italy,<sup>14</sup> India<sup>13</sup> and Bangladesh<sup>29</sup> where they reported that antibiotics in the Watch group were more frequently used than those in the Access group. Besides, it is slightly lower than the WHO recommended value for Access

**Table 3** AWARe classification of antibiotics

AWARe classification	Antibiotics	ATC code	Frequency	Percentage
Access (n=570)	Amoxicillin/clavulanic acid	J01CR02	145	25.4
	Amoxicillin	J01CA04	118	20.7
	Metronidazole	J01XD01	79	13.9
	Doxycycline	J01AA02	71	12.5
	Tinidazole	J01XD02	60	10.5
Watch (n=341)	Ciprofloxacin	J01MA02	322	94.4
	Clarithromycin	J01FA09	13	3.8
	Erythromycin	J01FA01	5	1.5
	Ceftriaxone	J01DD04	1	0.3

ATC, Anatomic Therapeutic Chemical classification; AWARe, Access, Watch and Reserve.

**Table 4** Factors associated with antibiotic prescribing in elderly outpatients at bivariate and multivariable levels in Asmara, Eritrea, 2023

Variable	Category	Bivariate analysis		Multivariable analysis	
		COR (95% CI)	P value	AOR (95% CI)	P value
Age	–	1.01 (0.99 to 1.02)	0.129	–	–
Sex	Male	1.05 (0.90 to 1.23)	0.546	–	–
	Female	<i>Ref.</i>	–	–	–
Prescriber qualification	Specialist	<i>Ref.</i>	–	<i>Ref.</i>	–
	GP	0.90 (0.68 to 1.20)	0.904	0.91 (0.69 to 1.21)	0.515
	Nurse practitioner	0.54 (0.41 to 0.72)	<0.001	0.60 (0.44 to 0.81)	0.001
	GP intern	1.21 (0.71 to 2.05)	0.484	1.22 (0.72 to 2.07)	0.457
Polypharmacy	Yes	2.64 (1.44 to 4.83)	0.002	2.32 (1.26 to 4.27)	0.007
	No	<i>Ref.</i>	–	<i>Ref.</i>	–
Level of health facility	Primary	0.61 (0.45 to 0.83)	0.002	0.83 (0.60 to 1.16)	0.270
	Secondary	0.68 (0.55 to 0.84)	<0.001	0.83 (0.66 to 1.04)	0.098
	Tertiary	<i>Ref.</i>	–	<i>Ref.</i>	–

AOR, adjusted OR; COR, crude OR; GP, general practitioner; Ref, reference.

antibiotics (60%).<sup>20</sup> Though the finding is encouraging, further efforts are needed to recommend the use of Access antibiotics while reducing the use of Watch antibiotics. Besides, Access antibiotics have a low potential for resistance which can be used as a first-line and second-line treatments.<sup>20</sup>

Prescriber qualification and polypharmacy were significant determinants of antibiotic prescribing in elderly outpatients. This finding is comparable with a finding from Italy.<sup>14</sup> A nurse practitioner was less likely to prescribe an antibiotic than a medical specialist. Specialists are more knowledgeable in infectious diseases than nurse practitioners, which

could contribute to the increased number of antibiotic prescriptions by the specialists. However, this finding does not have any relationship with the appropriateness of the prescribed antibiotics. Further research is required to address such an issue. Prescriptions containing five or more medicines were more likely to have an antibiotic prescribed. The elderly population with multiple comorbidities requires multiple medications for their management, increasing the risk of acquiring an infection. Healthcare professionals should consider the health status of the elderly population and review the patient's medication list before initiating antimicrobial

**Table 5** Factors associated with prescription of a watch category antibiotic in elderly outpatients at bivariate and multivariate levels in Asmara, Eritrea, 2023

Variable	Category	Bivariate analysis		Multivariable analysis	
		COR (95% CI)	P value	AOR (95% CI)	P value
Age	–	1.00 (0.99 to 1.03)	0.555	–	–
Sex	Male	1.37 (1.05 to 1.80)	0.022	0.74 (0.56 to 0.98)	0.034
	Female	<i>Ref.</i>	–	<i>Ref.</i>	–
Prescriber qualification	Specialist	<i>Ref.</i>	–	<i>Ref.</i>	–
	GP	0.93 (0.60 to 1.42)	0.926	0.99 (0.64 to 1.52)	0.959
	Nurse practitioner	0.39 (0.24 to 0.62)	<0.001	0.49 (0.30 to 0.81)	0.005
	GP intern	1.70 (0.78 to 3.71)	0.184	1.65 (0.76 to 3.62)	0.209
Polypharmacy	Yes	1.04 (0.46 to 2.36)	0.928	–	–
	No	<i>Ref.</i>	–	–	–
Level of health facility	Primary	0.40 (0.22 to 0.76)	0.005	0.66 (0.34 to 1.29)	0.219
	Secondary	0.40 (0.26 to 0.61)	<0.001	0.52 (0.34 to 0.81)	0.004
	Tertiary	<i>Ref.</i>	–	<i>Ref.</i>	–

AOR, adjusted OR; COR, crude OR; GP, general practitioner; Ref, reference.

therapy to reduce the risk of potential drug–drug interactions and adverse effects.

Sex, prescriber qualification and level of health facility were significant determinants of Watch antibiotic prescription. Females were more likely to receive an antibiotic prescription than males, possibly due to an increased occurrence of urinary tract infections in females with ciprofloxacin being the most prescribed Watch antibiotic. Prescribers should first select antibiotics from the Access category instead of prescribing a Watch antibiotic as a first-line treatment. Prescriptions from tertiary health facilities were more likely to have Watch antibiotics than those from secondary health facilities. Nurse practitioners were less likely to prescribe a Watch antibiotic than medical specialists. With an increase in the level of health facility from secondary to tertiary, the number of authorised medicines to prescribe also increased. Taking these facts into consideration, there may be a high chance of prescribing a Watch antibiotic in tertiary health facility by the specialists.

The elderly population faces multiple comorbidities and is at high risk of infection due to age-related physiological alterations.<sup>36</sup> Moreover, irrational prescribing of antibiotics is common in this population, leading to a greater risk of adverse health outcomes.<sup>16</sup> The significance of this survey and its results is of specific attention to countries with comparable socioeconomic status as Eritrea. To improve antibiotic prescribing in the elderly population, sensitisation programmes targeting healthcare professionals, implementation of antibiotic stewardship programmes, adherence to national and international standard treatment protocols, introduction of guidelines on the safety of prescribing in the elderly population and formulation of electronic medical records are highly recommended.

This is the first study in Eritrea to assess antibiotic prescribing practice and its determinants in elderly outpatients. The study used the latest version of AWaRe classification system (2023) and engaged rigorous data quality control and management protocols. Due to the cross-sectional nature of the study, cause-and-effect relationship was not established. Furthermore, indication for antibiotic use, detailed demographic and clinical characteristics of the elderly population, and work experience of prescribers cannot be obtained from the outpatient prescriptions. Finally, the results from this study were not representative of the country. Therefore, further broader research is endorsed to obtain a comprehensive picture of antibiotic use in the elderly population.

## CONCLUSION

Antibiotics were prescribed to a considerable number of elderly ambulatory patients. More than half of the prescribed antibiotics fell into the Access category,

which is encouraging. Moreover, prescriber qualification and polypharmacy were significant factors in antibiotic prescribing for elderly population. Sex, prescriber qualification and level of health facility were also significant factors in the prescription of Watch antibiotics.

To further improve antibiotic prescribing in elderly outpatients, incorporation of the WHO AWaRe classification in the national action plan for AMR, educational programmes targeting healthcare professionals, implementation of antibiotic stewardship programmes, strengthening hospital medicine and therapeutic committees and formulation of guidelines on safety of antibiotic prescribing is highly recommended.

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**Acknowledgements** The authors sincerely acknowledge the data collectors and heads of the community chain pharmacies for their cooperation and contribution during the data collection process.

**Contributors** NA is the guarantor of the study. Conceptualisation, NA; Methodology, NA, SI, TT and EHT; Validation, NA, SI, TT and EHT; Formal analysis, NA, SI and EHT; Investigation, NA, SI and TT; Resources, NA, SI and TT; Data curation, NA and SI; Writing—original draft preparation, NA and SI; Writing—review and editing, NA, SI, TT and EHT; Visualisation, NA, SI and EHT; Supervision, NA; Project administration, NA and SI. All authors have read and agreed to the published version of the manuscript.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** Ethical clearance was obtained from the Ministry of Health Research Ethics and Protocol Review Committee (Reference number: 16/02/2022). Besides, consent to conduct the study was obtained from the heads of the community chain pharmacies. Information obtained from the prescriptions was kept confidential and used only for the study. Patients' and prescribers' details were deidentified, and only aggregated information was reported. This study conforms to the principles outlined in the Declaration of Helsinki.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** All data relevant to the study are included in the article or uploaded as online supplemental information.

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### Antibiotics uncategorized in the WHO Access, Watch, and Reserve classification (n=150)

Name of antibiotic	Frequency	Percent
Chloramphenicol eye drop	61	40.7
Mebendazole	17	11.3
Neomycin/Bacitracin Ointment	15	10.0
Chloramphenicol eye ointment	9	6.0
Clotrimazole cream	8	5.3
Griseofulvin	6	4.0
Miconazole cream	6	4.0
Clotrimazole	5	3.3
Tetracycline eye ointment	5	3.3
Ciprofloxacin eye drop	3	2.0
Fluconazole	3	2.0
Silver cream	3	2.0
Benzoic acid/Salicylic acid	2	1.3
Dexamethasone/Chloramphenicol eye drop	2	1.3
Gentamicin eye drop	2	1.3
Chloramphenicol ear drop	1	.7
Clotrimazole ear drop	1	.7
Clotrimazole vaginal suppository	1	.7
Total	150	100.0



### Antibiotics uncategorized in the WHO Access, Watch, and Reserve classification (n=150)

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