GUIDELINES TO IMPROVE ANTIBIOTIC PRESCRIBING PRACTICE AT PRIMARY HEALTHCARE FACILITIES IN ETHIOPIA

by

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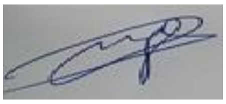
DECLARATION

I declare that **GUIDELINES TO IMPROVE ANTIBIOTIC PRESCRIBING PRACTICE AT PRIMARY HEALTHCARE FACILITIES IN ETHIOPIA** is my own work and that all sources that I have used or quoted have been indicated and acknowledged by means of complete references.

I further declare that this work has not been submitted before for any other degree at UNISA or any other institution.



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Fikru Worku Altaye **Date**

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ABSTRACT

Background

Antibiotics are the most frequently used medicines in healthcare facilities. Since their discovery, antibiotics have played a pivotal role in combating infectious diseases and maintaining health, especially in developing countries where such diseases still remain as a big challenge. In recent years, the benefits derived from antibiotic use are facing great challenges due to the emergence of resistance where many bacteria have become resistant to the most commonly used first-line antibiotics. The major driver of antimicrobial resistance is known to be the huge increase in antibiotic prescribing at primary healthcare facilities, especially in low- and middle-income countries.

Despite the fact that majority of the antibiotics are prescribed at primary healthcare facilities, studies focusing on the prescribing of antibiotics at this level of facilities is very limited. Studies conducted on the prevalence of antibiotic resistance in Ethiopia have shown that the majority of bacteria that cause infections have developed a considerable degree of resistance to commonly used first-line antibiotics. The available evidences show that antibiotics are prescribed at a far higher rate than the optimal value recommended by the World Health Organization, exposing the available antibiotics to the risk of resistance. The specific types of antibiotic prescribing problems, the underlying factors for the antibiotic prescribing problems and the interventions that should be implemented to improve the antibiotics prescribing practice are not yet explored in the country, especially at primary healthcare facilities.

Purpose

The purpose of this study was to describe the rate and patterns of antibiotic prescribing, identify the antibiotic prescribing problems, explore the factors that affect the decisions to prescribe antibiotics, and identify interventions that should be implemented with a view to developing evidence-based and theory-informed intervention guidelines to improve antibiotic prescribing at primary healthcare facilities in Addis Ababa, Ethiopia.

Methods

Guided by the PRECEDE-PROCEED Model, the study was conducted using an Explanatory Sequential Mixed Method Approach. In the first phase of the study (quantitative), data was collected from 2000 prescriptions and patient medical charts sampled from ten randomly selected public health centres situated in five of the sub-cities in Addis Ababa City Administration. The second phase of the study (qualitative) was undertaken through in-depth interview of 20 prescribers from five of the health centres, as well as with 22 key informants from the five health centres, five sub-city health offices and the Health Bureau. The quantitative data was analysed using SPSS version 28 to generate descriptive data on the rate and patterns of antibiotic prescribing and identify factors associated with the rate of antibiotic prescribing. The qualitative data was analysed by applying Thematic Content Analysis using ATLAS.ti 9 to explore the factors influencing the antibiotics prescribing decision of prescribing and identify interventions that can be implemented to improve antibiotics prescribing. Findings of the quantitative and qualitative findings were then integrated using the selected theoretical model as a guide and intervention guidelines to improve antibiotic prescribing were developed.

Results

The average number of medicines per prescription was 1.87 ranging from 1.71 to 2.11 among the health centres. The percentage of prescriptions containing one or more antibiotic (rate of antibiotics prescribing) was 52.5%, with wide variation among the health centres included in the study (41.5% to 61.5%). The rate of antibiotic prescribing was shown to have a statistically significant association with the patient’s age, the qualification of prescriber and the season of prescribing.

Amoxicillin, ciprofloxacin, cloxacillin, doxycycline and cotrimoxazole accounted for nearly 80% of the antibiotics prescribed, with amoxicillin (41.2%), ciprofloxacin (14.1%) and cloxacillin (9.6) being the top three most commonly prescribed. About 56% of the prescribed antibiotics belong to the Penicillins category and majority (92.7%) of the antibiotics were prescribed for oral administration. Nearly 77% of the prescribed antibiotics belong to the “Access” Category and the remaining 23% to the “Watch” Category of the World Health Organization’s Access, Watch and Reserve Categorization of antibiotics.

Unspecified upper respiratory tract infection (21.7%), urinary tract infections (13.1%) and topical infections (9.7%) were the most common diagnoses for prescribing the antibiotics. All kinds of upper respiratory tract infections accounted for 33.8% of the antibiotics prescribed. About 37.3% of the cases for prescribing of antibiotics were respiratory tract infections, the majority (90.7%) being upper respiratory tract infections. Of those prescribed for respiratory tract cases, 59.7% were found appropriate and the rest 40.3% inappropriate. The types of inappropriate antibiotic therapy were unnecessary antibiotic use (53%), high dose (16%), need for additional antibiotic (14%), not choosing the right antibiotic (11%), and low dose (6%).

Cost wise, antibiotics accounted for 36.2% of the total cost of medicines prescribed, with the majority of that being for amoxicillin (39.8%), cloxacillin (15.7%) and ciprofloxacin (10.3%). Five of them (amoxicillin, cloxacillin, ciprofloxacin, amoxicillin/clavulanic acid and cotrimoxazole) accounted for about 81% of the total cost of antibiotics prescribed. Antibiotics prescribed for all kinds of upper respiratory tract cases contributed for over one-third (35.3%) of the total cost of antibiotics prescribed.

There were various types of problems with the prescribing and use of antibiotics at the health centres, including the repeated use of antibiotics for the same diagnosis, use of antibiotics for minor problems, using high level antibiotics, discontinuing medication, and self-medication with antibiotics. The decision of healthcare providers to prescribe antibiotics is influenced by various predisposing, enabling and reinforcing factors. The factors are related with prescribers, patients and the health system, including gaps in the knowledge of health professionals on the use of antibiotics and resistance, low awareness of patients and the public on antimicrobial resistance, shortage of antibiotics and laboratory reagents, lack of updated information on the national and local antibiotic resistance pattern, patient pressure, patient load, excessive antibiotic prescribing at private health facilities, and the dispensing of antibiotics without prescription at private pharmacies.

Series of interventions were suggested by the study participants to improve antibiotic prescribing in the study setting. The suggested interventions include, applying the same clinical protocol for public and private sector health facilities, managing minor cases appropriately, having monitoring and evaluation system, increasing public awareness, providing proper counselling, providing training for healthcare providers, updating knowledge, providing health education to the public, conducting research and disseminating the findings, properly implementing the primary healthcare clinical guidelines, controlling the private sector, improving supply, providing follow-up and support, assigning focal person for Antimicrobial Resistance, strengthening Drug and Therapeutics Committee, and avoiding dispensing of antibiotic without prescription.

Based on the suggested interventions, intervention guidelines were developed in the areas of effective implementation of the Primary Healthcare Clinical Guidelines, capacitating healthcare providers on antibiotics and antibiotic resistance, increasing the awareness of patients and the public on antibiotics and Antimicrobial Resistance, institutionalizing antibiotic use and resistance into the healthcare system, improving availability of antibiotics and laboratory reagents, establishing and strengthening platforms for health professionals to discuss antibiotic use and resistance, strengthening Drug and Therapeutics Committee and Drug Information Service at health Centers, undertaking research on antibiotic use and resistance and disseminating the findings, improving antibiotic prescribing and dispensing in the private sector, and strengthening the planning, monitoring and evaluation system.

Conclusion

The prevalence (rate) of antibiotic prescribing was high that far exceeds the recommended rate for primary healthcare facilities. The majority of antibiotics were prescribed for upper respiratory tract infections which are known to be mostly viral origin. Most of the antibiotics prescribed belong to the Access group of the World Health Organization’s Access, Watch and Reserve Classification. Antibiotics accounted for over one-third of the cost of medicines prescribed. There are various types of antibiotics prescribing and use problems at health centers and the prescribing decision of healthcare providers is influenced by several predisposing, enabling or reinforcing factors that are related with the healthcare providers, patients and the community and the healthcare system. Ten categories of intervention guidelines that can be used to improve the prescribing of antibiotics at the health centres were developed based on the interventions suggested by the study participants and other findings of the study. The guidelines are related with capacitating prescribers, increasing awareness of patients and the community, controlling and supporting the private sector, and institutionalizing the issue of antibiotics and antibiotic resistance in the health system.

Further studies are required to appropriately understand impact of the new clinical guideline on the prevalence (rate) and patterns of antibiotic prescribing up on full implementation and prescribers' adherence to the new Primary Healthcare Clinical guidelines in managing commonly encountered cases (upper respiratory tract infections) at primary healthcare facilities using findings of this study as a baseline. Research should also be undertaken to evaluate effectiveness of the intervention guidelines developed following PRECEED component (implementation, and monitoring and evaluation phases) of the PRECEDE-PROCEED Model that guided this study. Integrated with existing initiatives, the piloting and implementation of the prioritized guidelines requires the active involvement of all stakeholders under the leadership of Ministry of Health and the Health Bureau. The anticipated challenges identified in this study need to be addressed to facilitate implementation of the interventions.

Key words

Addis Ababa, Antibiotics prescribing, AWaRe Categorization, Ethiopia, factors, , intervention guidelines, medicine use problems, PRECEDE-PROCEED, primary healthcare, resistance.

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DEDICATION

I dedicate this PhD work to my late father Mr. Worku Altaye who laid the groundwork for who I am today. He had high hopes for me. Although I am not able to celebrate my success with my beloved father, I am very happy that I have realized what he wished me to be by achieving the highest academic qualification with the help of the Almighty God and the support of family members.

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ACRONYMS AND ABBREVIATIONS

ABR	Antibiotic Resistance
AMR	Antimicrobial Resistance
AMS	Antimicrobial Stewardship
AWaRe	Access, Watch, Reserve
CBHI	Community-Based Health Insurance
CFHC	Chefe Health Center
CI	Confidence Interval
DACA	Drug Administration and Control Authority
DTC	Drug and Therapeutics Committee
DIS	Drug Information Service
EC	Ethiopian Calendar
EFDA	Ethiopian Food and Drug Authority
EFMHACA	Ethiopian Food, Medicine and Healthcare Administration and Control Authority
EFY	Ethiopian Fiscal Year
ETB	Ethiopian Birr (currency)
ENHC	Entoto Health Center
EPHI	Ethiopian Public Health Institute
EPSA	Ethiopian Pharmaceuticals Supply Agency
EPSS	Ethiopian Pharmaceuticals Supply Service
GC	Gregorian Calendar
GLASS	Global Antimicrobial Resistance Surveillance System
HC	Health Center
HO	Health Officer
KMHC	Kuas Meda Health Center
LDHC	Lideta Health Center
LMICs	Low and Middle Income Countries
M&E	Monitoring and Evaluation
MOH	Ministry of Health
MLHC	Millennium Health Center
MS	Medical Service
NU	Nurse

OPD	Outpatient Department
OTC	Over-The-Counter
PHCG	Primary Healthcare Clinical Guidelines
PS	Pharmacy Service
RHB	Regional Health Bureau
SMHC	Shiromeda Health Center
SPSS	Statistical Package for Social Sciences
STG	Standard Treatment Guidelines
TBHC	Tibeb Bekechene Health Center
URTI	Upper Respiratory Tract Infection
UTI	Urinary Tract Infection
WD9HC	Woreda 9 Health Center
WD12HC	Woreda 12 Health Center
WHO	World Health Organization
YKHC	Yeka Health Center

CHAPTER 1: ORIENTATION OF THE STUDY

1.1 INTRODUCTION

Antimicrobials are a group of medicines that include antibiotics (antibacterials), antiparasitics, antivirals and antifungals. Antibiotics are those antimicrobials that are used to prevent and treat infections caused by bacteria (Turnidge et al. 2016: 2). Since their discovery, antibiotics have played a pivotal role in combating infectious diseases and maintaining health especially in those developing countries where such diseases remain a big challenge (Yimenu, Emam, Elemineh & Atalay 2019: 1). Over the years, the role of antibiotics in human medicine has expanded from treating serious infections to the prevention of infections in surgical patients, and protecting cancer patients and people with compromised immune systems (Hellen et al. 2015: 8).

In recent years, the benefits derived from antibiotic use are facing major challenges due to the emergence of drug resistance whereby many bacteria have now become resistant to the most commonly used first-line antibiotics (Yimenu et al. 2019: 1). Antimicrobial resistance (AMR) is the resistance of a microorganism (bacteria, parasites, virus, fungi) to an antimicrobial that was originally effective for treatment of infections caused by it, whereas, antibiotic resistance (ABR) refers specifically to the resistance of pathogenic bacteria to antibiotics (Nathwani 2018: 13). Despite these differences, the term 'Antimicrobial Resistance" is commonly used in the literature to mainly describe antibiotics resistance. The focus of this study is on the use of antibiotics in human medicine and the terms 'Antimicrobial resistance' and 'Antibiotic resistance' will be used interchangeably.

Resistance to antibiotics has become a worldwide challenge to public health leading to treatment failure, increased morbidity, mortality and escalating costs of care (Teixeira Rodrigues et al. 2016: 2). Patients infected with resistant organisms have an increased risk of poor clinical outcomes, including death, and consume more healthcare resources. Currently, 700,000 people die each year globally from drug-resistant infections, and if there is no effective international action, a scenario analysis has indicated that by the year 2050 this will increase to 10 million deaths annually, with a cumulative cost to the global economic output predicted to be USD 100 trillion

(Gasson, Blockman & Willems 2018: 304)**.** According to Chem, Anong and Akoachere (2018: 2), ABR has become a serious concern as the rate of resistance to antibiotics is growing and outpacing the rate at which new classes of antibiotics are discovered and synthesised.

According to Wei et al (2017: e1258), the major cause of antimicrobial resistance is known to be the huge increase in antibiotic prescribing, especially in low- and middle-income countries (LMICs). Primary care is responsible for the majority (about 80%) of the antibiotics used worldwide, with an estimated 20–50% of this use being inappropriate (Low et al. 2018: 1). A systematic review of studies conducted at primary healthcare facilities in different countries (Costelloe, Metcalfe, Lovering, Mant & Hay 2010: 1–11) showed that there is strong evidence of association between the prescribing of antibiotics and the emergence of resistance in bacteria (Tarrant et al. 2019: 1356). Though a global concern, inappropriate use of antibiotics and the resulting consequences of antibiotic resistance are greater in low- and middle-income settings (Kpokiri, Taylor & Smith 2020: 1).

Despite the pressing need for conservative antibiotic use, overuse of antibiotics across human and animal healthcare and agriculture is increasing (Tarrant et al. 2019: 1356). Subsequently, this irrational and excessive use of antibiotics has contributed significantly to the development of antibiotic resistance (Gasson et al. 2018: 304)**.** According to the World Health Organization (WHO) (2016), the world urgently needs to change the way it prescribes and uses antibiotics. WHO has stressed on the need to preserve the efficacy of existing antibiotics through the implementation of measures aimed at minimising the development and spread of resistance (2014: 1). This requires an understanding of the social and behavioural drivers of antibiotic overuse to inform the design and implementation of interventions that can optimise practices (Tarrant et al. 2019: 1357). Without such behavioural change, antibiotic resistance will continue to remain a major threat, even if new medicines are developed.

Evidences show that the greatest proportion of antibiotics for human use are prescribed in primary healthcare facilities. This highlights the need to focus research and action at this level of healthcare (Lum, Page, Whitty, Doust & Graves 2018: 74–84). Because prescribers play a crucial role in the medicine use process, identifying the major problems in antibiotic prescribing at health care facilities, especially in primary health care settings where most patients receive medical care, is an important first step in developing effective interventions aimed at improving antibiotic use (Teixeira Rodrigues et al. 2016: 2; Wang, Wang, Wang, Zheng & Xiao 2014: 1914). Since every dose of antibiotic prescribed and used increases the likelihood of AMR, it is important to ensure that antibiotics are used appropriately. Despite the widespread over prescription of antibiotics and the high rate of antibiotic resistance, studies that focus on identifying the underlying causes and designing evidence-based interventions to improve antibiotics prescribing at primary healthcare facilities are very limited from low-income countries and almost none from Ethiopia.

According to the 2007 – 2037 Population Projection Report of the Central Statistical Agency, Ethiopia had a total population of about 104.5 million in 2021 (CSA 2013: 47). Ethiopia is the second most populous country of Africa, ranking 12th in the world. Ethiopia is a low-income country with a gross domestic product (GDP) per capita of $772 in 2018. In 2019, 58% of disability adjusted life years (DALYs) were due to maternal and neonatal conditions, communicable diseases, and malnutrition (Ministry of Health 2021: 20). Administratively, Ethiopia has ten regional states and two city administrations. Each of the ten regions are divided into zones and each zone into lower administrative units called woredas or districts. Each woreda is subdivided into the lowest administrative unit, called kebele. The two city administrations (Addis Ababa and Dire Dawa) are also divided into sub-city administrations and woredas.

The health system structure has three tiers, consisting of primary health care (primary care hospitals, health centres and health posts), secondary health care (general hospitals) and tertiary health care (comprehensive–specialised and subspecialised hospitals). According to the 2013 EFY (2020/2021) Ethiopian Health and Health-Related Indicators report of Ministry of Health, MOH (MOH 2020: 39–40), there are 367 hospitals, 3,777 health centres, and 17,699 health posts under the public sector. In addition to these, 52 private hospitals, 6,500 other private health facilities and 6,000 medicine retail outlets are known to be available in the country (Ministry of Health & Ministry of Agriulture 2019: 3).

The primary health care unit consists of health posts, health centres, and primary hospitals. One health centre is attached to five satellite health posts to provide services to a total of about 25,000 people. Health centres provide both preventive and curative services, and also serve as referral centres and practical training sites for health extension workers. Primary hospitals offer inpatient and ambulatory services to about 100,000 people, and also provide emergency surgery (including caesarean sections and blood transfusions). General hospitals are categorised under the second tier of health care. These hospitals provide similar services to those of primary hospitals, and serve on average 1 million people. They are referral centres for primary hospitals and training centres for health officers, nurses, and emergency surgeons. The third tier in the Ethiopian health care system, tertiary health care, consists of a specialised hospital that covers a population of approximately 5 million. It also serves as a referral centre for general hospitals (Ministry of Health 2021: 94).

This study was conducted in selected public primary healthcare facilities found in Addis Ababa City which is the capital city of the country. The study was designed to determine the antibiotic prescribing rate and pattern in public primary healthcare facilities, and explore and describe the associated factors and interventions with the view to developing evidence-based and theory-informed guidelines that can be used to improve the prescribing of antibiotics using the PRECEDE-PROCEED Model as a theoretical framework.

1.2 BACKGROUND TO THE RESEARCH PROBLEM

Since the middle of the nineteenth century, humans have achieved unprecedented advances in their war with pathogens. This has mainly been due to three developments; improved public health systems to promote measures such as hygiene, better sanitation, cleaner water and disease surveillance and control, the development of vaccines to control the spread of viruses, and the use of antibiotics to combat bacterial pathogens. These advances underpinned an enormous reduction in the incidence of infectious diseases during the twentieth century, raising hope for a complete victory over infectious diseases. However, over the years, the overuse and misuse of antimicrobials have caused the emergence of AMR and its spread (World Bank 2016: 6).

Antibiotics are life-saving medicines with rapidly declining effects worldwide due to increased antibiotic resistance (Hoa, Lan, Phuc, Chuc & Lundborg 2017: 1). Without effective antimicrobials, diverse medical procedures such as surgery, the care of premature infants, cancer chemotherapy, care of the critically ill, invasive diagnostic and treatment procedures, and transplantation medicine will be severely hampered with a corresponding increase in morbidity and mortality from secondary bacterial infections (Ayukekbong, Ntemgwa & Atabe 2017: 6). The shocking news is that the number of infections due to antibiotic-resistant bacteria is growing and outpacing the rate at which new classes of antibiotics are discovered and synthesised (Chem et al. 2018: 2). As a result, the prospect of the world entering a 'post-antibiotic era' where common infections can no longer be cured is a real possibility (Jasovský, Littmann, Zorzet & Cars 2016: 159).

Antibiotics are unique because they are the only pharmaceutical agents that have transmissible loss of efficacy over time. Because of the inevitable occurrence and transmission of antibiotic-resistant bacteria from patient to patient, every patient's use of antibiotics affects the future ability of every other patient to use those same antibiotics. Thus, antibiotics are a shared community property that health professionals, patients and the public should work together to protect from misuse (Spellberg, Srinivasan & Chambers 2016: 1229).

The major driver of antibiotic resistance has been the huge increase in antibiotic prescribing, especially in LMICs (Wei et al. 2017: e1258). Inappropriate prescribing is known all over the world to be a major problem of healthcare delivery especially in developing countries which is reported as having negative impact on the health and economy of individuals and society leading to wastage of resources and widespread health hazards (Adisa, Fakeye & Aindero 2015: 1319). Globally, antibiotic use has increased by 65% between 2000 and 2015 with the majority of the increase being in LMICs (Wilkinson, Ebata & Macgregor 2019: 1).

According to WHO's global antibiotic consumption report published in 2018, the overall consumption of antibiotics ranged from 4.4 to 64.4 Defined Daily Doses (DDD) per 1000 inhabitants per day (WHO 2018: 5). DDD is one of the two main metrics used to describe the volume of antimicrobials consumed at national level. DDD is the assumed average maintenance dose per day for a medicine used for its main indication in adults. It is a well-established international system used as the basis for the calculation of medicines consumption estimates (WHO 2021a: 155).

It was indicated in the WHO global report 2018 (WHO 2018: 5) that in most countries amoxicillin and amoxicillin/clavulanic acid which belong to Access category of the WHO AWaRe categorization of antibiotics were the most frequently consumed antibiotics. In 49 countries, the Access category of antibiotics represented more than 50% of antibiotic consumption. The report showed great variation in the level of consumption of antibiotics in the Watch category, which accounted for less than 20% of total antibiotic consumption in some countries, but more than 50% in others. Reserve group antibiotics, which should only be used for specific indications such as infections with multidrug-resistant bacteria, accounted for less than 2% of total antibiotic consumption in most high-income countries and were not reported by most low- and middle-income countries.

A model-based estimation of global antibiotic usage for lower respiratory tract infections based on studies conducted from 2000 to 2018 revealed that in 2018, antibiotic usage was highest across the central Europe, Eastern Europe, and central Asia regions with median national antibiotic usage of 72%. The lowest levels of antibiotic usage were estimated for sub-Saharan Africa with a median national usage of 42%. Antibiotic use was considerably higher in North Africa and Middle East with median of 61%. In Southeast Asia, antibiotic usage was very diverse with a median usage of 51%.

Studies conducted in Ethiopia have indicated high prevalence of antibiotic resistance where most bacterial pathogens have become resistant to commonly used antibiotics. A meta-analysis of studies conducted from 2007-2017 to assess the prevalence of *E. coli* resistance in Ethiopia (Tuem et al. 2018a: 5) indicated an overall resistance rate of 45.4% with levels of resistance ranging from 62.6% in Addis Ababa to 27.5% in Tigray Region. A review of blood culture results from the Regional Laboratory of Addis Ababa City Administration in 2015 and 2016 (Terfa Kitila et al. 2018: 2–3) revealed that both gram-positive and gram-negative isolates have developed high resistance to commonly used antibiotics.

Various medicine use studies have been conducted in different parts of Ethiopia. Most of these studies are general prescribing studies conducted mainly in hospitals with few conducted at primary healthcare level. To the knowledge of the researcher, there are few published studies that specifically assessed the rate and pattern of antibiotics prescribing at primary healthcare facilities in the country. The findings of the limited studies that have been conducted in the country indicated a higher rate of antibiotic prescribing than that recommended by the WHO which places the available antibiotics at risk for resistance. Studies focusing on exploring the factors that affect the prescribing of antibiotics and designing appropriate interventions to improve the prescribing practice at primary healthcare facilities are lacking in Ethiopia.

1.3 STATEMENT OF THE RESEARCH PROBLEM

In the last decades, medicines have had an unprecedented positive effect on health which resulted in reduced morbidity and mortality and consequently to an improved quality of life (Muhie 2019: 1). Rational use of medicines is one of the essential elements in achieving and maintaining quality health care (Akl, El Mahalli, Elkahky & Salem 2014: 55). Irrational use of medicines has been primarily observed in the healthcare systems of LMICs where pharmaceutical expenditure accounts for up to 70% of their total healthcare expenditure (Sisay, Mengistu, Molla, Amare & Gabriel 2017). This has resulted in many undesired consequences, including the emergence and spread of AMR which is threatening the world’s ability to successfully treat a growing number of infectious diseases (Muhie 2019: 1).

It is well known that any use of antimicrobials whatever appropriate and justified, contributes to the development of resistance with widespread unnecessary and excessive use making the situation worse (Ayukekbong et al. 2017: 6). Koji, Gebretekle and Tekle (2019: 2) reported that despite the advances, infectious illnesses still account for 25% of deaths worldwide and 45% of mortality in low-income countries. Limiting antibiotic resistance is a question of sustainable development since the current generations' overuse of antibiotics jeopardises their ability to treat bacterial infections. The presence of untreatable illnesses is likely to compromise efforts to eradicate poverty, maintain food security, ensure access to water and sanitation, implement sustainable economic growth as well as promote sustainable consumption and production (Robertson, Jagers & Rönnerstrand 2018: 1).

The problem of AMR is intensified by the fact that most of the world's pharmaceutical companies consider research for new antibiotics as being of "low profit". Consequently, they prefer to invest in the development of medicines for chronic diseases such as diabetes and hypertension as well as those used to improve lifestyle (Ayukekbong et al. 2017: 6). Hence, the pressing need to preserve efficacy of the existing antibiotics through implementation of appropriate interventions.

Studies conducted on the rate of antibiotic resistance in Ethiopia have shown that most of the bacteria that cause infections have developed a considerable degree of resistance to commonly used first-line antibiotics. Almost all of the available studies conducted on the rate of antibiotic prescribing, most of which were conducted at hospitals, reported a far higher rate of antibiotics prescribing than that recommended by WHO. The few studies conducted at primary healthcare facilities in the country showed that the antibiotics prescribing rate ranges from 41.3% (Bantie 2014: 1187) to 82.5% (Bilal, Osman & Mulugeta 2016). The study conducted at primary healthcare facilities in Addis Ababa City in 2017 (Worku & Tewahido 2018: 4) showed an antibiotics prescribing rate (56.0%) that lays somewhere in the middle of these extreme values with wide variations among the primary healthcare facilities included in the study (46.7% to 67.3%).

Though their effectiveness have not been systematically evaluated, there have been initiatives implemented to improve the prescribing and use of medicines, including antibiotics, in the country. These include facility level interventions like introduction of standard treatment guidelines, establishing Drug and Therapeutics Committee (DTC) and Drug Information Service (DIS), providing health education to patients, developing facility-specific medicines list, and introducing good prescribing and good dispensing practice manuals focusing on the public health sector. At national level, AMR has been part of the Health Sector's Transformation Plan and there has been AMR Prevention and Containment Strategy since 2011. There has also been effort to increase public awareness on antibiotics use and resistance through the media. Despite these efforts, the available evidences indicated still high rate of antibiotic prescribing which exposes the existing antibiotics to the risk of resistance. The antibiotic prescribing and use situation in the country, especially at primary healthcare facilities, deserves further investigation with the ultimate goal of designing and implementing appropriate interventions.

To the knowledge of the researcher, there are no published studies conducted at primary healthcare facilities aimed at exploring the factors influencing antibiotic prescribing and designing interventions to improve the antibiotic prescribing in the country in general and in Addis Ababa in particular. This study was conducted to contribute to the knowledge gap in this area.

1.4 PURPOSE OF THE STUDY

The purpose of this study was to describe the rate and patterns of antibiotic prescribing, identify the antibiotic prescribing problems, explore and describe the factors that affect the decisions to prescribe antibiotics, and identify interventions that should be implemented with a view to developing evidence-based and theory-informed intervention guidelines to improve antibiotic prescribing at primary healthcare facilities in Addis Ababa, Ethiopia.

1.5 RESEARCH OBJECTIVES

Objectives of the study were the following:

Phase I: Quantitative

- To determine the prevalence (rate) of antibiotics prescribing at primary healthcare facilities;
- To describe the antibiotics prescribing patterns at primary healthcare facilities;
- To assess appropriateness of the antibiotics prescribed to manage common cases at primary healthcare facilities;

Phase II: Qualitative

- To explore and describe the factors that influence the prescribing of antibiotics at primary healthcare facilities;
- To identify interventions that should be implemented to improve antibiotic prescribing at primary healthcare facilities;

Phase III: Guideline Development

- To develop intervention guidelines that can be used to improve antibiotic prescribing at primary healthcare facilities.

1.6 RESEARCH QUESTIONS

This study was designed to answer the following research questions:

Phase I: Quantitative

- How prevalent is the prescribing of antibiotics at primary healthcare facilities?
- What does the pattern of antibiotics prescribing look like at primary healthcare facilities?
- How appropriate is the prescribing of antibiotics for selected cases at primary healthcare facilities?

Phase II: Qualitative

- What are the factors that influence the prescribing of antibiotics at primary healthcare facilities?
- What interventions should be implemented to improve antibiotic prescribing at primary healthcare facilities?

Phase III: Guideline Development

- What interventions should be developed to improve antibiotics prescribing at primary healthcare facilities?

1.7 SIGNIFICANCE OF THE STUDY

Despite the fact that the misuse and overuse of antibiotics is more prevalent in these countries, little is known about antibiotic prescribing practices in developing countries (Liu, Liu, Wang & Zhang 2019a: 2). According to Sulis et al (2020: 3)**,** most studies investigating the magnitude and determinants of antibiotic use have focused on high income countries, and those from LMICs have been carried out predominantly in hospital settings, leaving a number of unanswered questions about current practices at the primary healthcare level where the bulk of antibiotic use takes place.

Evidences show that the majority of antibiotics used in humans are prescribed in primary care settings worldwide. However, antibiotic use in primary care settings has been poorly evaluated in LMICs (Zhao et al. 2022: 2). The World Health Organization - WHO (2015a: 10) has reported the lack of data on antibiotic use in human beings at the point of care from lower-income countries. The need to undertake further study to fully understand the prescribing practices and identify the associated factors thereby develop appropriate interventions was recommended in a study conducted in the same setting in the City in 2017 (Worku & Tewahido 2018: 8).

The current study was aimed at developing evidence-based and theory-informed intervention guidelines to improve antibiotics prescribing at primary healthcare facilities. This was backed by assessing the existing prescribing practices, and identifying the underlying factors influencing antibiotic prescribing and the interventions suggested by study participants to improve antibiotic prescribing. Studies that focused on antibiotics prescribing practices, especially at primary healthcare facilities, are very limited in Ethiopia. Furthermore, studies that focus on exploring the underlying factors that contribute to the existing prescribing practices and developing contextualised interventions to improve the antibiotic prescribing practices are very limited in developing countries and almost none existent in Ethiopia. As to the knowledge of the researcher, this is the first study that explored and described the factors influencing antibiotic prescribing and designed interventions to improve the practice at primary healthcare facilities in Ethiopia in general and in Addis Ababa in particular.

This study has contributed to filling the gap in the existing body of knowledge related to the rate and patterns of antibiotic prescribing at primary healthcare facilities in a low-income country. This study has also contributed to the existing body of knowledge on factors that influence the prescribing of antibiotics and intervention guideline that can be implemented to improve the prescribing of antibiotics at primary healthcare facilities from a low-income setting. Findings of this study can serve as baseline data to evaluate the effectiveness of the interventions developed in this study and other interventions that will be developed and implemented to improve the prescribing of antibiotics at primary healthcare facilities in the study setting and beyond. Findings of this study will pave the way for further studies that focus on implementing the proposed interventions and evaluating their effectiveness for wider application to improve the antibiotic prescribing practices thereby reduce antibiotic resistance.

This study was further influenced by the global and national AMR strategies 2015-2020 (EFMHACA 2015: 17–20; WHO 2015b: 10). Objective 4 of these strategies, "*optimize the use of antimicrobial medicines in human and animal health",* focuses on addressing the major driving force for the emergence of antibiotic resistance - inappropriate use of antibiotics. The interventions developed in this study can also be used in the development of a national antimicrobial stewardship guidelines for primary healthcare facilities which is not currently available. AMR stewardship encompasses strategies to ensure appropriate antimicrobial prescribing, including better targeting of treatment and reduced rates of prescription for self-limiting and non-bacterial infections. Current evidence suggests stewardship interventions in primary care can be effective in reducing antibiotic prescription and consumption rates (Lucas et al. 2017: 2).

This study was conducted at primary health care facilities where the majority of the population in the country receive medical care. Rationalizing antibiotics prescribing in these settings can contribute a lot to the overall national effort in the prevention and containment of antimicrobial resistance. The set of interventions included in the guidelines developed will be used as a reference material to improve the antibiotics prescribing practices by the practitioners themselves, healthcare administrators and policymakers. This will contribute its part to improving the antibiotics prescribing practices thereby improving the quality of health service at primary healthcare facilities. Though this study was conducted in primary healthcare facilities found in Addis Ababa, the interventions developed could be tested and implemented in primary healthcare facilities throughout the country. Findings of this study can be used as baseline data to monitor the effects of interventions on the prescribing of antibiotics, especially implementation of the Primary Healthcare Clinical Guidelines (PHCG) which is not yet applied at full scale.

Though the quantitative data was taken from prescriptions and medical charts of patients served in the selected health facilities in 2019 and 2020, the in-depth interviews conducted with prescribers who were part of the practices during those years to further explore the antibiotic prescribing practices were conducted in 2021 which shed fresh light on the quantitative findings to pave the way for development of intervention guidelines to improve antibiotic prescribing.

1.8 DEFINITIONS OF KEY TERMS

The following definitions of key terms are used throughout the thesis.

Antimicrobials

Antimicrobials are agents that destroy or inhibit the growth of microorganisms, especially pathogenic microorganisms (EFMHACA 2018: III).

Antimicrobial resistance

Antimicrobial resistance is the ability of microorganisms (bacteria, parasites, viruses and fungi) to grow and spread in the presence of antimicrobial medicines that are normally active against them (Founou, Founou & Essack 2017: 2).

Antibiotics

Antibiotics are a type of antimicrobial medicine used in the treatment and prevention of bacterial infections (EFMHACA 2018: III).

Antibiotics prescribing rate

Antibiotics prescribing rate is the percentage of prescriptions or patient encounters with one or more antibiotics. It shows the prevalence of antibiotic prescribing.

Antibiotics prescribing pattern

Antibiotics prescribing pattern is the types, categories and costs of the antibiotics prescribed, the routes of administration, and the diagnosis for which the antibiotics were prescribed.

Antibiotic resistance

Antibiotic resistance is the ability of bacteria to resist the effects of an antibiotic to which they were once sensitive (EFMHACA 2018: III).

Antimicrobial stewardship programme

Antimicrobial stewardship program is an organizational or system-wide health-care strategy to promote appropriate use of antimicrobials through the implementation of evidence-based interventions (WHO 2019a: X).

Multi-drug resistance

Multi-drug resistance is resistance of a microorganism to at least one or more agents in three or more antibiotics categories (Alemayehu, Ali, Mitiku & Hailemariam 2019: 3).

Appropriate prescribing of antibiotics

An antibiotic prescription is considered to be proper (correct decision) if it contains the standard treatment regimen and duration that was indicated for the patient's clinical infection or prophylaxis (Wang et al. 2014: 1915–1916).

Inappropriate prescribing of antibiotics

Antibiotic use is considered inappropriate when the clinical condition of the patient justified use of antibiotics for treatment or prophylaxis but the treatment regimen or its duration was incorrect and/or the clinical condition of the patient did not justify the use of antibiotics for either treatment or prophylaxis (Wang et al. 2014: 1916).

Predisposing factors

Predisposing factors are antecedents to behavioural change that provide impetus for individuals to adopt a behaviour (Williams & Mummery 2015: 6).

Enabling factors

Enabling factors are antecedents to behaviour and environmental change and include any characteristic of an environment, resource or skill of an individual which supports action (Williams & Mummery 2015: 7).

Reinforcing factors

Reinforcing factors follow behaviour and reward or punish behaviour, and thereby provide incentive for continuation of the behaviour (Williams & Mummery 2015: 7).

Guidelines

Guidelines are information intended to advise people on how something should be done.

Interventions

Intervention is the act of interfering with the outcome or course especially of a condition or process (as to prevent harm or improve functioning). *(https://www.merriam-webster.com/dictionary/intervention) Accessed on: October 29, 2022.*

1.9 THEORETICAL UNDERPINNING OF THE STUDY

Lundborg and Tamhankar (2014: 125) suggested that considering theories or models of behaviour change is helpful in designing and implementing projects or programmes for behavioural change for professionals or consumers with respect to antibiotics. Studies indicate that interventions informed by evidence and theory have the best chance of altering health related behaviours (Lucas et al. 2017: 7). The knowledge and experience the researcher has in the area of promoting the rational use of medicines in general and that of antibiotics in particular, has contributed its part in putting the study into a proper context. The researcher strongly believes that antibiotics should be used rationally through the implementation of contextualised interventions. The researcher also believes in that using social behavioural theories that actively involve study participants in problem identification and designing of the interventions can significantly improve the effectiveness of those interventions which are aimed at improving the prescribing of antibiotics thereby reducing the emergence of antibiotics resistance.

Given its documented effectiveness in various health promotion programs, the researcher used the PRECEDE-PROCEED Model of Health Promotion as a theoretical framework to guide this study to achieve the research objectives and answer the research questions. PRECEDE stands for Predisposing, Reinforcing and Enabling Constructs in Educational/Environmental, Diagnosis and Evaluation. The PRECEDE part of the model has four assessment and planning stages to guide in identifying the health problem to address, examining its underlying environmental and behavioural causes, and planning an intervention. PROCEED, on the other hand, stands for Policy, Regulatory and Organizational Constructs in Educational and Environmental Development. PROCEED includes four implementation and evaluation phases (Porter 2015: 1–12).

PRECEDE-PROCEED is one of the most frequently used models in health education and health promotion (Abd, Mohamed & Khaton 2017: 15). Evidence suggests that strategies that consider the highest ranked predisposing, enabling, and reinforcing factors that affect behaviour are the most likely to be successful (Phillips, Rolley & Davidson 2012: 3). Numerous studies have demonstrated the positive impact the PRECEDE-PROCEED model has had on the effectiveness of health promotion interventions aimed at behavioural change. Some of these studies include behavioural change in oral health hygiene for vulnerable groups (Catherine J. Binkley and Knowlton W. Johnson 2014: 1–18), prevention and management of diabetes mellitus (Ebadifard Azar, Solhi, Nejhaddadgar & Amani 2017: 5024–5030), preventive behaviour for the prevention of drug abuse and addiction among adolescents (Abd et al. 2017: 14–27), and reducing the prescribing of antibiotics for respiratory tract infection in childhood in primary health care facilities (Lucas et al. 2017: 1–10).

The PRECEDE-PROCEED Model was originally developed in the 1970s by Green and colleagues. The most recent (2005) version of the model by Green and Kreuter has eight phases in planning, implementing, and evaluating health promotion programs. The PRECEDE portion of the model (Phases 1-4) includes social, epidemiological, behavioural, environmental, educational, administrative, and policy assessments. The PROCEED portion of the model (Phases 5-8) includes implementation, process evaluation, impact evaluation, and outcome evaluation. The first portion of the model focuses on program planning and the second portion focuses on program implementation and evaluation (Abd et al. 2017: 15). Figure 1.1 depicts the theoretical framework adapted from the model and used in this study.

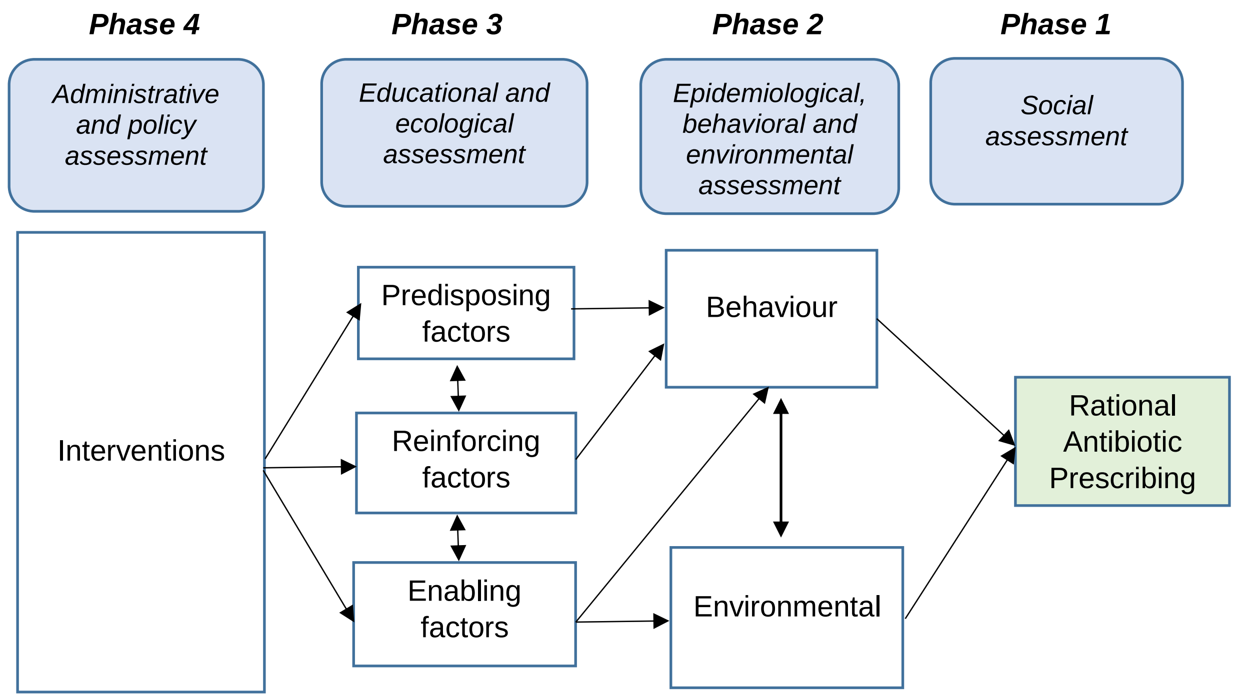


Figure 1.1 Theoretical framework to improve antibiotic prescribing at primary healthcare facilities, adapted from Porter (2015: 3)

The PRECEDE part of the model encompasses 4 phases:

Phase 1, the social assessment and situation analysis, identifies and assesses potential areas for health action.

Phase 2, the epidemiological assessment, identifies and prioritises health issues and sets change objectives (Porter 2015: 5).

Phase 3, the educational and ecological assessment, urges examination of the broader causal factors behind the social and health issues prioritised in the earlier stages. The authors group the Phase 3 causal factors into three categories: predisposing, reinforcing and enabling (Porter 2015: 5). *Predisposing factors* are knowledge and attitudes, which promote or inhibit a specific behaviour, such as knowledge about resistance. *Enabling factors* are individual or organizational factors that facilitate an action, e.g. the availability of easily applicable treatment algorithms for various infectious diseases. *Reinforcing factors* are rewards or punishments that follow a particular behaviour (Lundborg & Tamhankar 2014: 128).

In ***Phase 4***, an action plan is developed to meet the objectives set in the first three phases by selecting interventions that are most likely to be successful in achieving each objective and that are within the capacity of the team.

PROCEED includes Phases 5–8 where Phase 5 is implementation and Phases 6–8 encompass the process, impact and outcome evaluations (Porter 2015: 6).

As the focus of this study is on the development of intervention guidelines to improve the prescribing of antibiotics after assessing the existing practices and exploring the underlying factors through a participatory process, it goes well with the first four phases (PRECEDE part) of the model. This component of the model involves assessing the social problem and identifying the factors that affect the behaviour which inform the development of interventions.

The health problem in the current study that the researcher aimed to address was irrational prescribing of antibiotics at primary health care facilities and the desired outcome of the study for which the intervention guidelines were developed was rational prescribing of antibiotics. The first 4 phases of the selected model allows for assessing the existing prescribing practices, exploring the underlying factors and designing appropriate intervention to address the problem to achieve the desired outcome of rational antibiotic prescribing.

1.10 RESEARCH METHODOLOGY

Guided by the PRECEDE-PROCEED Model of Health Programme Planning and Evaluation, this study was conducted in 10 primary healthcare facilities found in Addis Ababa City Administration. The study was conducted in two phases using Sequential Explanatory Mixed Method Approach. Phase I was a quantitative study aimed at determining the rate, pattern and appropriateness of antibiotic prescribing which was undertaken by reviewing prescriptions and patient medical charts in the selected health facilities. In-depth interviews of prescribers and key informants were applied in the second, qualitative phase of the study. This was followed by development of intervention guidelines to improve the prescribing of antibiotics based on the findings of the quantitative and qualitative studies. Details of the research methods is presented under Chapter 3.

1.11 SCOPE OF THE STUDY

This study was conducted in selected primary healthcare facilities in Addis Ababa, Ethiopia, focusing on the prevalence (rate) and patterns of antibiotic prescribing, factors influencing the prescribing of antibiotics and interventions to improve the prescribing of antibiotics with the ultimate goal of developing evidence-based and theory-informed intervention guidelines to improve the prescribing of antibiotics in the selected setting. Although, the study was conducted in selected healthcare facilities in the city, the findings could be applicable to all primary healthcare facilities found in the city and other parts of the country. The guidelines could also be a useful resource material for the development of Guidelines to establish an Antimicrobial Stewardship Program at Primary Healthcare Facilities in the country.

1.12 STRUCTURE OF THE THESIS

The thesis is structured into the following chapters:

- Chapter 1: Orientation to the study
- Chapter 2: Literature review
- Chapter 3: Research design and method
- Chapter 4: Presentation and discussion of the results
- Chapter 5: Guidelines to improve antibiotics prescribing at primary healthcare facilities
- Chapter 6: Conclusions, recommendations, contribution to knowledge and limitations

1.13 CONCLUSION

This chapter presented a general overview of the study. The chapter covered the introduction, background of the research problem, problem statement, purpose and objectives of the study, the research questions, significance of the study, definitions of key terms used in the study, the theoretic framework selected for the study, brief research methodology, scope of the study, and structure of the thesis. The next chapter (Chapter 2) presents the literature review related to the research topic.

CHAPTER 2: LITERATURE REVIEW

2.1 INTRODUCTION

An overview of the study was covered in Chapter 1. This chapter presents the literature review related to the research topic. No matter the discipline, the foundation of all academic research efforts is building on and connecting it to existing body of knowledge (Snyder 2019: 333). This is achieved through literature review which constitutes an objective, in-depth summary and critical analysis of the pertinent research and non-research literature on the subject under study. Its objective is to update the reader on the state of the field's literature and lay the groundwork for other objectives, such as establishing the case for further research in the area. A good literature review collects data from several sources on a particular issue through a clear search and selection strategy (Abdullah Ramdhani , Muhammad Ali Ramdhani 2014: 48).

Among the literature review methods, scoping review was used in this study. Scoping reviews are an ideal tool to determine the scope or coverage of a body of literature on a given topic and give clear indication of the volume of literature and studies available as well as an overview of its focus. Scoping review is useful to identify the types of available evidence in a given field and to identify and analyse knowledge gaps in a specific area (Munn & , Micah D. J. Peters, Cindy Stern, Catalin Tufanaru 2018: 2).

The aim of the literature review was to place the study within the existing body of knowledge and provide the context for the study by understanding what is already known about the research topic and the gaps in the area. In the literature search, the researcher has consulted different literature sources including internet search engines, online libraries, databases, and websites of local and international institutions. Research articles published during the past 10 years (2012 – 2022) as well as guidelines, strategies and books were collected, reviewed, and the necessary information extracted. The researcher has made effort to make majority of the research articles to be those published during the past 5 years (2017 onwards). Some articles and international reports older than 10 years were considered due to importance of the information they contain. The focus was on those studies conducted at primary healthcare facilities in a developing setting. Studies conducted in Ethiopia and those specifically conducted in Addis Ababa at this level of care were exhausted as much as possible.

During the literature search, the researcher used key words like rational use of antibiotics, antibiotic prescribing, antibiotic resistance, AWaRe category, primary healthcare facilities, factors influencing antibiotics prescribing, and interventions to improve antibiotic prescribing. Depending on their content, the literatures were organized in different folders. Then, each of the literatures were read thoroughly and the required information extracted and used to build the literature review under the different sub-sections of this chapter which are the major areas to be addressed in relation to antibiotics and resistance; the burden of antibiotic resistance, determinants of AMR, impact of AMR, antibiotics prescribing and its determinants, and strategies to promote the rational prescribing of antibiotics, including the prevalence of antibiotic prescribing and the resistance situation in Ethiopia.

2.2 THE BURDEN OF ANTIBIOTIC RESISTANCE

Koji, et al (2019: 2) reported that despite enormous advances, infectious illnesses account for 25% of deaths worldwide and 45% of mortality in low-income countries. In recent years, the benefits derived from the use of antibiotics are facing a great challenge due to the emergence of antibiotic resistance. The magnitude of the threat of antibiotic resistance has been reported to be comparable to that of climate change (Mason et al. 2018: 2). In his Nobel Prize winning speech in 1945, Alexander Fleming, who discovered penicillin in 1928, predicted that the world would one day be facing antibiotic resistance (WHO 2014: 1). As predicted, bacteria and other pathogens have always continued to evolve so that they can resist the new antibiotics that are used to combat them (Reta, Bitew Kifilie & Mengist 2019: 1).

Antibiotic resistance is a natural phenomenon that occurs when microorganisms are exposed to antibiotics. Under the selective pressure of antibiotics, susceptible bacteria are killed or inhibited, while bacteria that are naturally resistant or that have acquired antibiotic-resistant traits have a greater chance of surviving and multiplying (Prestinaci, Pezzotti & Pantosti 2015: 310). Antibiotic resistance develops when bacteria adapt and grow in the presence of antibiotics. This occurs via a range of mechanisms, such as a modified antimicrobial target, enzymatic hydrolysis/degradation, efflux and inhibition of permeability (Founou et al. 2017: 2). Because many antibiotics belong to the same class of medicines, resistance to one specific antibiotic agent can lead to resistance to the entire related class. Resistance that develops in one organism or location can spread rapidly and unpredictably between different bacteria, and can affect antibiotic treatment of a wide range of infectious diseases (WHO 2015c: 2).

AMR, unlike other health issues, is a problem in every country irrespective of its level of income and development as resistant pathogens do not respect borders (O'Neill 2014: 3). Drug-resistant bacteria can circulate in populations of human beings and animals through food, water and the environment, and transmission is influenced by trade, travel and both human and animal migration (WHO 2015d: 2).

The global burden associated with drug-resistant infections assessed across 88 pathogen–drug combinations in 2019 (Murray et al. 2022: 638–641) was estimated to be 4.95 million deaths, of which 1.27 million deaths were directly attributable to drug resistance. Resistance to fluoroquinolones and β-lactam antibiotics (i.e., carbapenems, cephalosporins, and penicillins), which are the antibiotics often considered first-line for empirical therapy of severe infections, accounted for more than 70% of the deaths attributable to AMR across pathogens.

As per the request from member countries, the WHO developed a global priority pathogens list (global PPL) of antibiotic-resistant bacteria to help in prioritizing the research and development (R&D) of new and effective antibiotic treatments. The major objective of the global PPL is to guide the prioritization of incentives and funding, help align R&D priorities with public health needs and support global coordination in the fight against antibiotic resistant bacteria. The WHO PPL targets policy initiatives to incentivise basic science and advanced R&D by both public funding agencies and the private sector investing in new antibiotics. The experts clustered the pathogens according to the type of resistance into three priority tiers: *critical, high and medium* (WHO 2017).

Priority 1: CRITICAL

- *Acinetobacter baumannii*; carbapenem-resistant
- *Pseudomonas aeruginosa*; carbapenem-resistant
- *Enterobacteriaceae*; carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

- *Enterococcus faecium*; vancomycin-resistant
- *Staphylococcus aureus*; methicillin-resistant, vancomycin intermediate and resistant
- *Helicobacter pylori*; clarithromycin-resistant
- *Campylobacter*; fluoroquinolone-resistant
- *Salmonella* spp.; fluoroquinolone-resistant
- *Neisseria gonorrhoeae*; 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

- *Streptococcus pneumoniae*; penicillin-non-susceptible
- *Haemophilus influenza*; ampicillin-resistant
- *Shigella* spp.; fluoroquinolone-resistant

Wangai et al. (2019: 4) reported that there are various levels of drug resistance. Drug resistant is defined as non-susceptibility to at least one antimicrobial agent. Multi-drug resistant (MDR) is non-susceptibility to at least one agent in three or more antimicrobial categories. Extensively drug resistant (XDR) is defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e. bacterial isolates remain susceptible to only one or two categories). Possible pandrug-resistant (PDR) is defined as non-susceptibility to all agents in all antimicrobial categories tested. A total of 98% of the microbes were drug resistant, 88% multidrug resistant, 26% extensively-drug resistant, and 8% possible pandrug-resistant.

According to the systematic review of studies conducted in Africa from 2013-2016 (Tadesse et al. 2017: 3–4), overall resistance of gram negative pathogens to commonly used antibiotics such as amoxicillin (72.9%) and Trimethoprim-sulphamethoxazole (75.0%) was high. Low to moderate resistance was reported for gentamicin (22.1%), ciprofloxacin (16.7%) and ceftriaxone (17.2%). Resistance of *Escherichia coli* to amoxicillin, trimethoprim and gentamicin was 88.1%, 80.7% and 29.8%, respectively. Resistance of *Neisseria gonorrhoeae* for quinolones was 37.5% and carbapenem resistance was common in *Acinetobacter* species and *Pseudomonas aeruginosa.*

A review of studies conducted on antimicrobial resistance in East Africa (Boum et al. 2016: 2–4) from 2013 to 2016 reported high rates of AMR to commonly used antibiotics, including 50-100% resistance to ampicillin and cotrimoxazole, emerging resistance to gentamicin (20-47%) and relatively high levels of resistance to ceftriaxone (46-69%) among gram-negative bacteria. Much of the resistance was reported in *Klebsiella* species and *E. coli.* Among gram-positive infections, extensive resistance was reported to ampicillin (100%), gentamicin and ceftriaxone (50-100%).

Studies conducted in Ethiopia indicated high prevalence of antibiotic resistance where most pathogens are becoming resistant to commonly used antibiotics. A meta-Analysis of studies conducted from 2007-2017 to assess the prevalence of *E. coli* resistance in Ethiopia (Tuem et al. 2018b: 5) indicated an overall resistance rate of 45.4% with level of resistance ranging from 62.6% in Addis Ababa to 27.5% in Tigray Region. The highest resistance was reported for ampicillin (83.8%) followed by amoxicillin (75.8%).

According to the systematic review of studies conducted from 1999 to 2018 on the prevalence of *Shigella* species and its drug resistance pattern in Ethiopia, *Shigella* species were highly resistant to amoxicillin, erythromycin and ampicillin with pooled resistance rates of 86.5%, 83.2% and 83.1%, respectively. On the other hand, relatively low level of resistance was reported for ciprofloxacin (8.9%), ceftriaxone (9.3%), norfloxacin (8.2%) and gentamycin (17.3%) (Hussen, Mulatu & Yohannes Kassa 2019: 22).

The resistance pattern in the City Administration selected for this study (Addis Ababa) is also alarming. As indicated above, the highest level of overall *E. coli* resistance (62.6%) was reported from the City Administration in the meta-analysis of studies conducted from 2007-2017 in the country (Tuem et al. 2018b: 5). A review of blood culture results from the Regional Laboratory of Addis Ababa City Administration in 2015 and 2016 (Terfa Kitila et al. 2018: 2–3) revealed that gram-positive isolates showed high resistance to commonly used antibiotics; Penicillins (83.5%), Trimethoprim-sulphamethoxazole (83.5%), Erythromycin (77.3%), Doxycycline (76.5%), Tetracycline (76.5%), and gentamycin (75.0%). Highly resistant gram-negative isolates were seen in Ampicillin (88.5%), Amoxicillin-clavulanic acid (80%), Trimethoprim-sulphamethoxazole (80%), and ceftriaxone (77.1%).

In the antimicrobial susceptibility test conducted in Addis Ababa among children with diarrhoea (Gebresilasie, Tullu & Yeshanew 2018: 4–5), *E. coli* showed high resistance to ampicillin and amoxicillin-clavulanic acid (83.6%) followed by trimethoprim-sulphamethoxazole (62.3%). Multiple resistances were observed in 72.1% of the isolates, whereas more than 90% of the strains were sensitive to ciprofloxacin and ceftriaxone.

According to the structured review of literatures on AMR conducted from 2016 - 2020 in Ethiopia (Fujita et al. 2022: 122–123), most bacteria isolated were gram-negative organisms (80%), most frequently *E. coli*, *Klebsiella* spp., *Proteus* spp., and *Salmonella* spp. Among the bacteria that were tested, 20% were carbapenem-resistant. When carbapenem susceptibility was assessed, resistance was observed in *Serratia* spp. (60%), *Enterobacter* spp. (53%), *Proteus* spp. (43%), *Citrobacter* spp. (38%), *Klebsiella* spp. (18%), and *E. coli* (13%). *E. coli* had high pooled prevalence of resistance to ciprofloxacin (77%), sulfamethoxazole/trimethoprim (54%), ceftriaxone (46), and ceftazidime (29%). Compared with *E. coli*, *Klebsiella* spp. had higher rates of resistance to sulfamethoxazole/trimethoprim (74%), ceftriaxone (66%), and ceftazidime (52%) but lower rates of resistance to ciprofloxacin (35%). Pooled estimates of *Salmonella* spp. resistance to ciprofloxacin and ceftriaxone were 25% and 17%, respectively.

2.3 THE IMPACTS OF ANTIBIOTIC RESISTANCE

Several fields of modern medicine depend on the availability of effective antibiotics. Chemotherapy for cancer treatment, organ transplantation, hip replacement surgery, intensive care for pre-term new-borns and many other interventions could not be performed without effective antibiotics for the prevention and treatment of infections (Prestinaci et al. 2015: 310). Infections caused by resistant bacterial strains lead to up to two-fold higher rates of adverse outcomes compared with similar infections caused by susceptible strains. According to Friedman, Temkin and Carmeli (2016: 417), these adverse outcomes may be clinical (death or treatment failure) or economic (costs of care, length of stay).

Despite being a global issue, there is a disparate distribution of AMR among countries, with greater impact on the developing countries. This higher burden on developing countries could attribute to limited access to new antibiotics, increased financial burden, and the inability to pay for second-line antibiotics, which may be more expensive, hence causing worse treatment outcomes (Iwu-Jaja et al. 2021: 3–4). In resource-limited areas, insufficient diagnostic infrastructure and laboratory capacity, inconsistent AMR surveillance, and inadequately resourced infection prevention and control contribute to empiric antibiotic use on the basis of syndromic approaches rather than microbiological data. This has led to high rates of antibiotic consumption in LMICs, which creates high selection pressure for resistant organisms (Fujita et al. 2022: 120–121).

Currently, 700,000 people die each year globally from drug-resistant infections (Gasson et al. 2018: 304). It is estimated that by 2050, 10 million deaths will be attributed to AMR annually and a cumulative amount of USD 100 trillion of the world's economic outputs will be lost due to AMR if substantive efforts are not made to contain this threat (Founou et al. 2017: 2). By 2050, Africa is expected to loss 4,150,000 lives due to AMR annually, the second highest among the continents, next to Asia (4,370,000) (Dadgostar 2019: 3906).

According to WHO, Food and Agriculture Organization of the United Nations (FAO) and World Organisation for Animal Health (WOAH) (2019: 3), AMR exists everywhere and can impact anyone of any age, in any country in the world. These organizations further emphasised that the impacts of unchecked AMR are wide-ranging and extremely costly, not only financially but also in terms of global health, food security, environmental well-being and socioeconomic development posing a major threat to the delivery of the 2030 Agenda for Sustainable Development. If AMR is left unchecked, by 2050, the world will be producing between 2% and 3.5% less than it otherwise would (O'Neill 2014: 6–7).

The effects of AMR extend beyond health into poverty as increased antimicrobial resistance will force people into poverty. Despite the shift in the global burden of disease to non-communicable diseases, infectious diseases disproportionately affect those living in poverty. Health systems in the developing world rely on the availability of cheap antibiotics and are not equipped to cope with an increasing burden of resistant infections (Frost, Laxminarayan, McKenna, Chai & Joshi 2018a: 15). The World Bank estimated that AMR could push 28 million people into extreme poverty by 2050 (Frost, Laxminarayan, McKenna, Chai & Joshi 2018b: 7).

2.4 DETERMINANTS OF ANTIBIOTIC RESISTANCE

There are four sectors that contribute to the development and spread of antibiotic resistance. These are human medicine (community and healthcare settings), food production and agriculture, and the environmental sectors. The respective factors that contribute to the development and spread of antibiotic resistance are antibiotic use in the community, antibiotic use in healthcare settings, antibiotic use in food producing animals and in agriculture, and the presence of resistant bacteria in the environment. As presented in Figure 2.1 below, misuse of antibiotics in human beings, animals and agriculture is responsible for the presence of resistant bacteria in the environment (Prestinaci et al. 2015: 310–311).

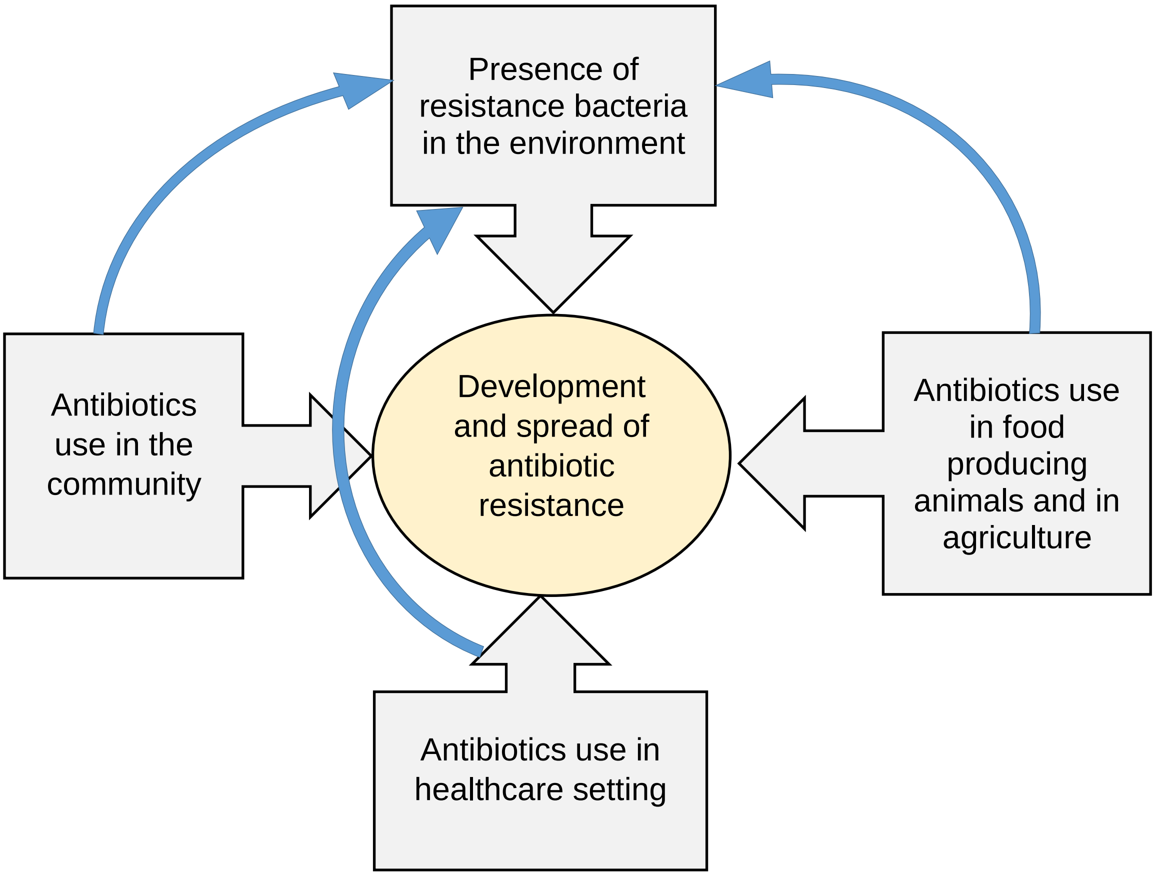


Figure 2.1 Factors involved in the development and spread of antibiotic resistance, adapted from Prestinaci et al (2015: 311)

According to the African Union Framework for Antimicrobial Resistance Control 2020–2025 (Africa Union 2018: 5), many factors contribute to the emergence, persistence, and transmission of AMR. Although AMR strains arise naturally due to genetic changes in microorganisms, their emergence is accelerated by inappropriate use of antimicrobial agents in humans, animals, and the environment, including self-treatment of illness by lay persons, non-indicated administration by healthcare providers, and the addition of antibiotics to animal feed to "promote growth" and prevent illness among animals reared for food consumption. AMR emergence may be further amplified by substandard and/or counterfeit antibiotics, which impair treatment of existing infections and may help select for AMR strains. Transmission of AMR is accelerated by inadequate infection prevention and control (IPC) in healthcare facilities, by contamination of the food supply with resistant bacteria, by impaired access to potable water, and by limitations in public health prevention programmes, including immunization, sanitation, and sexual health.

The problem of AMR is aggravated by the fact that most of the world's pharmaceutical companies consider research for new antimicrobials as being of "low profit" and some speculate that resistance will eventually develop for new antimicrobials anyway. Consequently, they prefer to invest in the development of drugs for chronic diseases (diabetes, hypertension) as well as those used to improve lifestyle. The long-term solution should, therefore, focus on methods to prevent the emergence of resistance or the spread of resistant organisms from one person to another (Ayukekbong et al. 2017: 4).

Several factors are known to play a role in the development and spread of AMR, with inappropriate use of antibiotics being one of its most important drivers (Sulis et al. 2020: 3)**.** As the inappropriate use of antibiotics can arise from a complex interaction between a number of factors (Awad & Aboud 2015: 2), both healthcare professionals and patients are responsible for antibiotic resistance (Mason et al. 2018: 2). Health care providers play an essential role in the treatment and prevention of diseases, but this may be jeopardised if their practices are not evidence-based. Patient non-compliance is also a major contributor to the development of AMR. These practices result in the exposure of surviving microbes to sub-therapeutic concentrations of the antibiotic and consequently, increases the chances of developing resistance (Ayukekbong et al. 2017: 6).

2.5 ANTIBIOTICS PRESCRIBING

According to WHO, more than half of all medicines are inappropriately prescribed, dispensed or sold with such practices deemed to be more prevalent in healthcare settings in the developing world (Ofori-Asenso, Brhlikova & Pollock 2016: 1). Injudicious prescribing and use of antibiotics are considered as principal drivers of increasing resistance (Kpokiri et al. 2020: 1). Furthermore, Summoro et al. (2015: 4551) indicated that the quality of prescribing is a major determinant of how patients use medicines. Taxifulati et al. (2021: 3) reported that excessive and improper use of antibiotics was more common in primary care settings than in secondary and tertiary hospitals although the types of antibiotics prescribed were similar.

Inappropriate use of antibiotics includes, but is not limited to, treatment of conditions for which antibiotics are not clinically warranted, suboptimal dosage regimens, premature cessation of antibiotic treatment, lack of or poor quality consultation with healthcare providers, purchasing antibiotics without prescription and sharing antibiotics with others (Cuevas, Batura, Wulandari, Khan & Wiseman 2021: 755).

Since the late 80s, the WHO together with the International Network for Rational Use of Drugs (INRUD), has been advocating for proper documentation of medicines use and have developed core drug use indicators in the three related areas of prescribing practices, patient care and facility specific factors. The drug use indicators are regarded as objective measures that can be extended to describe patterns of medicines usage in any health facility, country or an entire region. The core drug use indicators include five prescribing indicators which are meant to detail particular prescribing characteristics related to poly-pharmacy, antibiotic use, injection use, generic prescribing and adherence to the essential medicines list (EML). Even though an international standard of the prescribing indicators has not been empirically determined, the WHO has recommended reference values for each of the indicators as presented in Table 2.1 (Ofori-Asenso et al. 2016: 2).

Table 2.1 The WHO prescribing indicators and recommended reference values, adapted from Ofori-Asenso et al. (2016: 2).

WHO prescribing indicator	Reference value
Average number of medicines per encounter	<2
Percentage of medicines prescribed by generic name	100 %
Percentage of encounters with an antibiotic prescribed	<30 %
Percentage of encounters with an injection prescribed	<20 %
Percentage of medicines prescribed from an essential medicines list or formulary	100 %

As presented in the table above, the percentage of encounters with an antibiotic prescribed is one of the core prescribing indicators that is used to objectively measure the patterns of antibiotics prescribing. This indicator has been widely used to determine the prevalence and appropriateness of antibiotics prescribing at facility, region or country level. The WHO recommends that the percentage of encounters with one or more antibiotics prescribed to be less than 30% for general outpatients in primary healthcare facilities, with higher percentages indicating a higher risk of antibiotic resistance. Contrary to this recommendation, most of the medicine use studies conducted at primary healthcare facilities in Ethiopia and other countries reported far higher rate of antibiotics prescribing than the one recommended by WHO as summarised below.

Various medicine use studies have been conducted in different parts of Ethiopia. Most of these studies are general prescribing studies (not antibiotic specific) conducted in hospitals with only a few conducted at primary healthcare level. To the best knowledge of the researcher, there is no published study that specifically assesses the rate and pattern of antibiotics prescribing at primary healthcare facilities in the country in general and in Addis Ababa in particular except the one conducted in Addis Ababa in 2017 (Worku & Tewahido 2018).

Very high rates of antibiotics prescribing was reported from studies conducted in health centres located in Somali Regional State, Eastern Ethiopia (Bilal et al. 2016), a comprehensive specialised university hospital in Northwest Ethiopia (Yimenu et al. 2019: 4) and hospitals in Southern Ethiopia (Summoro et al. 2015: 4555) that reported a value of 82.5%, 69.6% and 66.5%, respectively. Studies conducted in referral hospitals in Eastern Ethiopia (Sisay et al. 2017: 3), primary healthcare facilities in Addis Ababa (Worku & Tewahido 2018: 4), and hospitals in Western Ethiopia (Lenjisa & Fereja 2014: 30) reported slightly lower but still high rates of antibiotics prescribing of 57.9%, 56.0% and 54.7%, respectively.

Three national pharmaceutical sector assessments have been conducted in Ethiopia during the last 20 years, in 2002, 2009 and 2016. According to the 2002 assessment (FMOH and WHO 2003: 23–24), the percentage of antibiotic prescribed per encounter was 58%. Disaggregation by region showed that the average percentage of the antibiotic prescribing rate varied among the six regions in which the study was conducted between 44.2% (Benishangul-Gumuz) to 87.7% (Addis Ababa). By level of health facility, the average percentage of antibiotic prescribing rate was 55.4%, 62.3% and 57.3% for hospitals, health centres and health stations, respectively.

The 2010 national assessment (FMOH and WHO 2010: 32) revealed a similar percentage of antibiotics prescribing rate (60%) indicating the persistence of high level of antibiotic use in the country. The national pharmaceutical sector assessment conducted in 2016 (EFMHACA and WHO 2017: 31) reported an antibiotics prescribing rate of 30% which is far below the value reported by previous national assessments and studies conducted in healthcare facilities in different parts of the country. As to the researcher, this finding does not look realistic since it is not supported by findings from similar studies conducted in different parts of the country as summarized below.

Studies conducted at primary healthcare facilities in the country showed an antibiotics prescribing rate ranging from 41.3% (Bantie 2014: 1187) to 82.5% (Bilal et al. 2016). The study conducted by the researcher at primary healthcare facilities in Addis Ababa City (Worku & Tewahido 2018: 4) reported an antibiotics prescribing rate (56.0%) that lies somewhere in the middle of these extreme values with a wide variation (46.7% to 67.3%) among the primary healthcare facilities surveyed.

The antibiotics prescribing practices at primary healthcare facilities in Ethiopia is comparable with the practices in other developing countries in the similar settings, including a study conducted from 1995-2015 at primary healthcare facilities in the WHO African Region, 46.8% (Ofori-Asenso et al. 2016: 7), Ghana, 59.9% (Ahiabu, Tersbøl, Biritwum, Bygbjerg & Magnussen 2016: 5), Nigeria, 55% (Adisa et al. 2015: 1323), and in six African countries (Ghana, Nigeria, Tanzania, Zimbabwe, Gambia, and Ethiopia), 51.5% (Richard Ofori-Asenso and Akosua Adom Agyeman 2015: 178).

A systematic review of studies published from 2010 to 2019 (Sulis et al. 2020: 9) that assessed antibiotic prescribing at primary healthcare facilities across several countries reported a percentage of prescriptions with one or more antibiotics prescribed at 52% with wide variation among the studies ranging from 19.6% to 90.8%. A study conducted at primary healthcare facilities in China demonstrated that physicians over-prescribed antibiotics with 40% of prescriptions containing an antibiotic and 10% containing two and more antibiotics (Liu et al. 2019a: 5).

Few of the aforementioned studies have assessed the antibiotics prescribing pattern in addition to the rate of antibiotics prescribing. These include identifying the common class and type of antibiotics prescribed, the diagnosis for which the antibiotics were prescribed, the route of administration of the prescribed antibiotics, AWaRe category and cost of the prescribed antibiotics.

In the study conducted at primary healthcare facilities in Addis Ababa, penicillins (51.9%) were the most commonly prescribed category of antibiotics followed by fluoroquinolones (18.3%) and sulphonamides (11.2%), with these three antibiotic categories accounting for over 80% of the antibiotics prescribed (Worku & Tewahido 2018: 4). Similarly, penicillins were the most commonly prescribed (38.2%) category of antibiotics in a study conducted at outpatients of a University hospital in North-western Ethiopia (Yimenu et al. 2019: 4).

In terms of specific antibiotics, amoxicillin (including amoxicillin-clavulanic acid) was the most frequently prescribed antibiotics (47.5%) with about 50% of the amoxicillin prescribed for upper respiratory tract infection (URTI) in the study conducted at primary healthcare facilities in Addis Ababa (Worku & Tewahido 2018: 5). Amoxicillin was the most frequently prescribed antibiotic in many other studies conducted in Ethiopia with the rate of prescribing ranging from 16.4% to 44.4% (Yimenu et al. 2019; Sisay et al. 2017; Bilal et al. 2016; Bantie 2014; Desalegn 2013). Other commonly prescribed antibiotics include ciprofloxacin, cotrimoxazole (Yimenu et al. 2019: 4; Worku & Tewahido 2018: 4; Sisay et al. 2017: 3; Bilal et al. 2016: 4) and metronidazole (Yimenu et al. 2019).

Studies also showed that antibiotics are among the most frequently prescribed medicines in injection form. According to the study conducted to assess prescription pattern of injectable medicines at outpatient level in Adama Hospital Medical College, Central Ethiopia (Kefal Gelaw, Feyissa & Tegegne 2015: 311), ceftriaxone (10.4%), metronidazole (8.2%), gentamicin (7.6%), ampicillin (6.8%), cloxacillin (5.6%) and benzanthin penicillin (4%) were among the top ten frequently prescribed medicines in injection form. In a medicine use study conducted at primary healthcare facilities in

Eastern Ethiopia (Bilal et al. 2016), procaine penicillin fortified (24.0%) and gentamicin (18.0%) were the second and third injectable medicines prescribed. According to a study conducted in a referral hospital in Southern Ethiopia (Desalegn 2013: 4–5), the top five medicines prescribed in injection form were ampicillin (21.4%), cloxacillin (13.4%), crystalline penicillin (12.4%), ceftriaxone (9.8%), and gentamicin (9.8%).

With respect to diagnosis, the most common diagnosis were URTIs (24.5%) followed by urinary tract infections - UTI (11.3%) in the study conducted at primary healthcare facilities in Addis Ababa (Worku & Tewahido 2018: 5), with only 10 disease conditions accounting for 86.4% of the cases for which antibiotics were prescribed. With regard to cost, antibiotics accounted for 46.0% of the cost of medicines prescribed. The highest percentage of the cost of antibiotics (22.7%) was for URTIs followed by topical infections (11.3%) and tonsillitis (8.6%). Only five types of diagnosis took about 59% of the cost of antibiotics. Prescribed as a single medicine, amoxicillin, amoxicillin + clavulanic acid, cotrimoxazole, ciprofloxacin, and cloxacillin constituted 43.5%, 10.3%, 7.4%, 6.9%, and 6.6% of the cost of antibiotics prescribed, respectively, and these five antibiotics consumed 65.4% of the cost of antibiotics prescribed.

Studies from other countries reported similar findings on antibiotics prescribing patterns. According to a study conducted in Cameroon (Chem et al. 2018: 10), the most commonly prescribed group of antibiotics were penicillins, accounting for 45.8% of the antibiotics prescribed. A similar finding was reported from Malaysia (Ab Rahman, Teng & Sivasampu 2016: 3) where penicillins were the most commonly (30.7%) prescribed group of antibiotics with cephalosporins and macrolides being the 2nd (23.6%) and 3rd(16.0%) most frequently prescribed antibiotic groups. According to the study conducted by Taxifulati et al (2021: 3) on patterns of antibiotic prescribing at primary healthcare facilities in China using a three years prescribing data (2015 – 2018), the most commonly prescribed antibiotics were second-generation cephalosporins, fluoroquinolones, and macrolides, accounting for 89.3% of all antibiotic prescriptions.

Amoxicillin was the most commonly prescribed antibiotic, accounting for 25.4%, 73.5%, and 29.3% of medicines prescribed in studies conducted at primary healthcare facilities in Nigeria (Adisa et al. 2015: 1324), Indonesia (Andrajati, Tilaqza & Supardi

2017: 45) and Cameroon (Chem et al. 2018: 8), respectively. The most commonly prescribed antibiotics were amoxicillin (71.7%) and Ampicillin/Cloxacillin (70.1%) while the least was meropenem (4.1%) in a study conducted at primary healthcare facilities in Nigeria (Manga et al. 2021: 2). In a study conducted to investigate antibiotic prescribing trends over a five-year (2015 – 2020) span of national claims data (Gillies et al. 2022) indicated that the most common antibiotics were cefalexin (21%), amoxicillin (20%), amoxicillin with clavulanic acid (18%), doxycycline (9%), and roxithromycin (5%). Cotrimoxazole was the second commonly prescribed antibiotic in studies conducted in Indonesia (Andrajati et al. 2017: 45) and Cameroon (Chem et al. 2018: 8) accounting for 17.4% and 19.1% of the antibiotics prescribed, respectively.

In a study conducted at primary healthcare facilities in China (Taxifulati et al. 2021: 3), acute bronchitis was the most prevalent diagnosis (17.6%) for antibiotic prescribing followed by unspecified acute respiratory tract infection (14.4%), acute tonsillitis (9.9%), and UTI (6.4%). The most prevalent conditions for irrational antibiotic prescribing were acute pharyngitis (16.9%) and paradentitis (16.6%).

2.6 DETERMINANTS OF ANTIBIOTIC PRESCRIBING

While the major driver of antibiotic resistance is known to be the huge increase in antibiotic prescribing, especially in LMICs (Wei et al. 2017: 1258), various other factors have been found to also influence antibiotic prescribing. These include patient characteristics such as low-socioeconomic status, age of patient, the presence of co-morbidity, perceived demand and expectation from patients, educational qualification and experience of prescribers, source of updating knowledge, practice setting, diagnostic uncertainty, influence from medical representatives, and inadequate knowledge (Chem et al. 2018: 3).

A study conducted in China (Liu et al. 2019a: 6) to identify the potential intrinsic and external determinants of antibiotic prescribing in primary care revealed that external factors like patient pressure, time pressure and financial incentives were significantly associated with physicians' antibiotics use rather than internal factors such as physicians' knowledge. In another study by Liu et al. in China (2019b: 10) to measure the knowledge and attitudes of primary care physicians towards antibiotic prescribing, physicians were found to have limited knowledge about antibiotic prescriptions. Poor knowledge, unawareness of antibiotic resistance, and limited motivation to change contributed to physicians' high antibiotics prescriptions. In a study carried out in Cameroon (Chem et al. 2018: 3), drug availability, socioeconomic status of the patient and prescribers' in-service training were identified as major factors influencing prescribing decisions.

A study conducted at primary healthcare facilities in Singapore (Lee et al. 2017: 5) reported that medical knowledge, clinical competency, good clinical practice, availability of diagnostics, and the desire to improve clinical practice were significantly associated with low prescribing of antibiotics. According to a study conducted in Australia (Biezen et al. 2019: 5), decision-making about antibiotic prescribing is dependent on the general practitioner's clinical experience, their knowledge and perception of individual patient expectations, trust and acceptance of guidelines, and social influences from peers. In a study conducted at primary healthcare facilities in South Africa to assess antibiotic prescribing and adherence to guidelines (Gasson et al. 2018: 304), the factors for antibiotic overprescribing were lack of awareness (87.0%), lack of penalty (79.4%), desire to help patients (76.5%), pressure from sales representatives (61.0%) and patient pressure (58.3%).

A study conducted in Nigeria (Kpokiri et al. 2020: 4) indicated that prescribers have an awareness of, and concern about, suboptimal prescribing of antibiotics. The factors identified include lack of system support in local settings, especially inadequate laboratory services; excessive workload in the clinics; costs of drugs, especially in the light of patient socioeconomic status and prevalence of out-of-pocket payments; specific demands from patients; unavailability of products; and shortcomings in training and knowledge; reliance on long-term prescribing habits; and impact of pharmaceutical companies.

A complex range of factors determine the inappropriate use of antibiotics in LMICs. The supply-side factors include lack of knowledge among prescribers or habitual prescribing that is not in line with best practice, inadequate medical education, training and supervision, pharmaceutical promotion, inadequate interaction times between health workers and patients, inaccurate perceptions of patient needs and demands, and limited availability of diagnostic support tools. There are also demand-side factors which include high expectations or beliefs of how effective antibiotic treatment could be, poor availability of information and lack of knowledge about the appropriate use of drugs for different conditions, the ability to easily access medicines over the counter without a prescription, and a strong culture or norm of self-prescribing medicines (Cuevas et al. 2021).

The high level of antibiotic consumption in LMICs is related with multiple factors, including the high burden of infectious diseases, lack of regulations (or weak enforcement) to prevent over-the-counter sale of antibiotics, inadequate training of healthcare professionals, and the limited availability of essential diagnostics, which favours empirical use of antibiotics (Sulis et al. 2020: 3). Any strategy that aims to curb the spread of ABR must tackle these multi-dimensional supply- and demand-side factors in clinical and community settings (Cuevas et al. 2021).

The researcher is not able to get published articles on factors influencing antibiotic prescribing in Ethiopia. This is one area that the study contributes to the existing body of knowledge regarding the factors influencing the prescribing of antibiotics at primary healthcare facilities in a developing setting.

2.7 STRATEGIES TO PROMOTE THE RATIONAL PRESCRIBING OF ANTIBIOTICS

Rational use of antibiotics is one of the measures required to minimise the development and spread of resistance to antibiotics (Mason et al. 2018: 2). The WHO, in its practical toolkit on Antimicrobial Stewardship Programmes in Healthcare Facilities in Low and Middle Income Countries, indicated that antibiotics must be prescribed rationally and that last-resort antibiotics be reserved for those patients who truly need them (WHO 2019a: 2). Interventions to improve antibiotic use are intended to achieve a variety of outcomes, including delaying the development of resistance, decreasing the use of antibiotic in situations for which antibiotics are not effective, increasing the use of a recommended antibiotic when one is indicated, reducing adverse drug events, and decreasing healthcare costs (McDonagh et al. 2018: 3338).

The World Health Assembly's endorsement of the Global Action Plan on Antimicrobial Resistance in May 2015, and the Political Declaration of the High-Level Meeting of the General Assembly on AMR in September 2017, both recognise AMR as a global threat to public health. These policy initiatives acknowledge overuse and misuse of antimicrobials as the main driver for development of resistance, as well as the need to optimise the use of antimicrobials. The Global Action Plan on AMR sets out five strategic objectives as a blueprint for countries in developing national action plans on AMR (WHO 2019a: 1):

Objective 1: Improve awareness and understanding of AMR through effective communication, education and training,

Objective 2: Strengthen the knowledge and evidence base through surveillance and research,

Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures,

Objective 4: Optimise the use of antimicrobial medicines in human and animal health, and

Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions.

In Ethiopia, antimicrobial resistance advocacy and containment efforts began back in 2006. The first antimicrobial resistance stakeholders meeting was conducted in March 2006, followed by the establishment of the National Antimicrobial Resistance Advisory Committee under the leadership of the Drug Administration and Control Authority of Ethiopia, now the Ethiopian Food and Drug Authority (EFDA). The major initiative was capacity-building activities targeting the Drug and Therapeutic Committee as an entry point to support the antimicrobial resistance containment effort (Ministry of Health & Ministry of Agriulture 2019: 6).

A baseline survey on antimicrobial use, resistance and containment was conducted in 2008 which showed a high level of resistance to commonly used first-line antibiotics

(DACA 2009). The first strategic framework for AMR prevention and containment was developed in 2011 (DACA 2009) to address the gaps identified with the baseline survey. The second AMR strategy was issued in 2015, covering the period 2015–2020 (EFMHACA 2015).

In July 2017, the Ethiopian AMR Surveillance System was launched by the Ethiopian Public Health Institute (EPHI) under the MOH with support from EFMHACA and international partners (Ethiopian Public Health Institute 2019: 5). As a result of implementation of the Surveillance System since 2018, substantial progress has been made in building workforce capacity; integrating and coordinating laboratory networks and communication, laboratory data management; provision of laboratory commodities; and promoting EPHI’s Laboratory-Based AMR Surveillance Plan to relevant actors and international collaborators (Ethiopian Public Health Institute 2019: 10).

The One Health Approach to AMR, which uses an interdisciplinary approach for surveillance and implementation of programs, policies, and research, is increasingly recognised as a vital component to national and global AMR strategies (Fujita et al. 2022: 121). In line with the WHO’s Global Action Plan on Antimicrobial Resistance and the country’s Growth and Transformation Plan for the health, agriculture and environment sectors, the third national strategic plan on prevention and containment of AMR was developed in 2019. This third AMR prevention and containment strategic plan that embraces the One Health Approach has the following 5 strategic objectives (Ministry of Health & Ministry of Agriulture 2019: 5):

a) Improve awareness and understanding of antimicrobial resistance through effective behaviour change communication, education and training.
b) Strengthen the knowledge and evidence on antimicrobial use and resistance through surveillance and research.
c) Enhance infection prevention and control through effective environmental health, infection prevention and bio-risk measures in human, animal and plant health.
d) Optimise the use of antimicrobials in human, animal and plant health care.

e) Strengthen and establish partnerships, alliances, governance and resource mobilization at all levels.

Since 2019, the governance of AMR prevention and containment has transitioned from EFDA to the MOH. The current antimicrobial resistance governance mechanism is comprised of a high-level National Inter-ministerial Committee, the National Antimicrobial Resistance Advisory Committee, a national antimicrobial resistance focal point (AMR secretariat) and six multisector technical working groups (on awareness and education, research and surveillance, infection prevention and control and hygiene, antimicrobial stewardship, regulations and pharmacovigilance, and partnership and resource mobilization) to address the strategic objectives of the national action plan. National-level governance is responsible for formulating policies and regulations and providing technical guidance and assistance to regional-level antimicrobial resistance coordinating platforms. Regional AMR governance oversees and assists implementation of the AMR prevention and containment strategy at all levels (Ministry of Health & Ministry of Agriulture 2019: 8).

The MOH has established an AMR Prevention and Containment Team under the Pharmaceutical and Medical Equipment Directorate to coordinate the AMR prevention and control activities at national level. Regional Health Bureaus are assigning AMR focal persons to coordinate regional AMR activities in collaboration with the MOH AMR Team.

Ethiopia, through its Food and Drug Authority (EFDA), has also issued a Rational Medicine Use Control Directive in the local language (Amharic) in 2019. One of the goals of this directive is to prevent the development and spread of AMR by promoting the rational use of antimicrobials (EFDA 2019). The comprehensive medicine use control directive covers contents of prescriptions, electronic prescribing, use and disposal of prescription papers, prescribing and dispensing of medicines, counselling during prescribing and dispensing, preventing the circulation of counterfeit medicines, medicine advertisement and distribution, and control of procurement and distribution of medicines.

Optimizing the use of antimicrobials is one of the priority actions under the 4th strategic objective. To support effective implementation of this strategic objective in LMICs, the WHO has developed and issued a practical toolkit in its antimicrobial stewardship program in 2019, "*Antimicrobial stewardship programmes in health-care facilities in LMICs - A practical toolkit* (WHO 2019a)*.* Antimicrobial stewardship (AMS) is defined as ensuring that every provider selects the right antibiotic, for the right indication (right diagnosis), the right patient, at the right time, with the right dose and route, causing the least harm to the patient and future patients (BSAC 2018: 42–43). AMS programmes optimise the use of antimicrobials, improve patient outcomes, reduce AMR and healthcare-associated infections, and save healthcare costs amongst others (WHO 2019a: 1).

For effective implementation of AMS Program, the following core elements are important (EFMHACA 2018: 5–6):

- *Leadership Commitment*: Dedicating necessary human, financial and information technology resources,
- *Accountability*: Head of clinical or appropriately appointed clinician and other health professionals responsible for program outcomes,
- *Appropriate Expertise*: Appointing a single pharmacist or microbiologist or infection prevention expert, leader responsible for working to improve antibiotic use,
- *Action*: Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. "antibiotic time out" after 48-72 hours),
- *Tracking*: Monitoring antimicrobial rational use and resistance patterns,
- *Reporting*: Regular reporting of information on antimicrobial use and resistance to health professional and other relevant staff as well as appropriate regional and federal organizations, and
- *Education*: Educating clinicians, other healthcare professionals, hospital communities, patients and societies at large about resistance and optimal use of antimicrobial.

Box 1 provides a brief step-by-step guides on setting up, implementing and monitoring health-care facility AMS programmes (WHO 2019a: 4).

Box 1

Key steps to establishing a health-care facility AMS programme

1. Undertake a facility AMS situational/SWOT analysis of:
   1.1. Health-care facility core elements – identify what is in place and the implementation level required;
   1.2. Available data on antimicrobial consumption (AMC) and/or use, prescription audits and AMR surveillance data; and
   1.3. Existing AMS competencies at the facility.
2. Establish a sustainable AMS governance structure based on existing structures
3. Prioritise the health-care facility core elements based on the situational analysis:
4. Identify AMS interventions starting with the low-hanging fruit:
5. Develop a health-care facility AMS action plan that specifies the human and financial resources required.
6. Implement AMS interventions.
7. Monitor and evaluate AMS interventions.
8. Offer basic and continued educational resources and training on optimised antibiotic prescribing.

Several interventions targeted at improving antibiotic prescribing among primary care and hospital care professionals have been implemented around the world (Teixeira Rodrigues et al. 2016: 6). However, interventional studies that focus on improving the prescribing of antibiotics are not as common as the descriptive studies on antibiotics prescribing and use. Published studies on promoting the rational use of antibiotics are rare from LMICs and almost non-existent in Ethiopia.

Most studies showed that reduction in antibiotic prescribing was achieved through interventions focused on clinician education programs such as interactive seminars, mailing campaigns, small group education focusing on evidence-based medicine and communication skills, educational outreach visit, guidelines and leaflets, and a combination of these educational strategies (Lee, Lee, Kang, Jeong & Lee 2015: 3).

Behaviour change interventions, mainly in high-income countries, have shown that educational guidelines and printed educational materials for providers have positive but modest improvements on prescribing behaviour. According to a systematic review by Wei et al. (2017: e1259) on antibiotic use for URTIs in children, strategies targeting both providers and caregivers are more effective than those targeting providers alone.

A systematic review of interventional studies (McDonagh et al. 2018: 3343–3345) showed that educational interventions, procalcitonin testing, and electronic decision support were the only interventions with evidence of improved prescribing without adverse consequences. Three education-based interventions were found to have a benefit with evidence of not increasing adverse consequences. A clinic-based educational intervention for parents of paediatric patients had the largest reduction in overall antibiotic prescribing among the education interventions (21.3%) without increasing the number of return visits. Procalcitonin was the only point-of-care test with evidence of any benefit and was restricted to adults. In a study conducted by Borek et al. (2021: 1), use of procalcitonin testing in the emergency department or in an outpatient setting reduced overall prescribing. Considerable evidence supports various interventions to safely reduce antibiotic prescribing for RTIs. Among them are delayed (back-up, deferred) antibiotic prescriptions and point-of-care C-Reactive Protein testing.

Analysis of prescribing practices and interviews with prescribers highlighted priorities for AMS, which include increased awareness and education about antibiotic resistance, development and provision of policies and guidelines on antibiotic use, monitoring and surveillance of antibiotic use, improved laboratory and diagnostic services and ensuring availability and quality of products (Kpokiri et al. 2020: 204).

The healthcare providers' prescribing behaviour is an important area to promote the rational use of antibiotics. Studies have shown that many countries have been successful in reducing prescribing of antimicrobials in secondary and tertiary hospitals in the past decades. However, irrational use of antibiotics in primary healthcare where the large majority of people are prescribed antibiotics is still problematic. It is estimated that about 80% of antimicrobials are consumed in primary healthcare around the world. Therefore, effective interventions to improve healthcare providers' prescribing behaviours in primary healthcare would greatly improve the rational use of antibiotics (Yao et al. 2020: 2).

A review of interventional studies (Yao et al. 2020: 10) found that educational, audit and feedback, policy change interventions and information system reminders could promote the rational use of antibiotics in primary healthcare settings. Educational interventions in combination with other strategies including financial incentives or providing rapid C-reactive protein tests could achieve significant reductions in antibiotics prescribing. The policy change interventions were more common in LMICs, and it was found that these interventions have good impact on decreasing the antibiotics prescribing rate.

Studies showed that multiplex interventions that combine different strategies to influence behaviour tend to have a higher success rate than interventions based on single strategies. A commonality amongst other reviews is that many of the interventions which worked well were combinations of restrictive and enabling strategies, i.e., educational techniques combined with forms of monitoring (Wilkinson et al. 2019: 11).

In Ethiopia, there is widespread antibiotic overprescribing and many bacterial pathogens have already developed resistance to commonly used first-line antibiotics. Despite these alarming findings, there are no published studies on identifying the factors for the overprescribing of antibiotics, and on designing, implementing and evaluating interventions to improve the prescribing practices. The available outpatient level antibiotic prescribing studies focus only on describing the existing antibiotic prescribing practices in terms of the rate and patterns of antibiotics prescribing and do not address the design and implementation of interventions to promote the prescribing of antibiotics. Though studies are not conducted in this area, various interventions have been implemented to promote the rational use of medicines in general and antibiotics in particular. These include training of prescribers, establishing DTCs in health facilities, development of standard treatment guidelines (STGs), providing health education to patients, and the provision of drug information services. AMR and the use of antibiotics are part and parcel of each of these interventions. So far, effectiveness of these interventions has not been systematically evaluated.

To promote the optimal use of antibiotics and assist antibiotic stewardship efforts, WHO introduced the Access, Watch, Reserve (AWaRe) classification of antibiotics in 2017. This classification underlines that, where appropriate, narrow-spectrum antibiotics included in the Access group should be preferred over broad-spectrum antibiotics from Watch and Reserve groups in order to limit the selection and spread of antibiotic resistance. Accordingly, WHO recommends that Access-group antibiotics should constitute at least 60% of overall antibiotic use (Sulis et al. 2020: 14).

The 2019 WHO AWaRe Classification Database was developed on the recommendation of the WHO Expert Committee on Selection and Use of Essential Medicines. It includes details of 180 antibiotics classified as Access, Watch or Reserve and is intended to be used by countries as an interactive tool to better support antibiotic monitoring and optimal use. The Access group includes antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups. The Access group includes 48 antibiotics, 19 of which are included individually on the WHO Model List of Essential Medicines as first- or second -choice empiric treatment options for specified infectious syndromes (WHO 2019b).

The Watch group antibiotics includes antibiotics that have a higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials for Human Medicine and/or antibiotics that are at relatively high risk of selection of bacterial resistance. Antibiotics in the Watch group should be prioritised as key targets of stewardship programs and monitoring. The Watch group includes 110 antibiotics, 11 of which are included individually on the WHO Model List of Essential Medicines as first- or second -choice empiric treatment options for specified infectious syndromes. The Reserve group includes antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multi-drug-resistant organisms. Antibiotics in the Reserve group should be treated as “last resort” options, which should be accessible, but their use should be tailored to highly specific patients and settings, when all alternatives have failed or are not suitable. These medicines could be protected and prioritised as key targets of national and international stewardship programs involving monitoring and utilization reporting, to preserve their effectiveness. Twenty-two antibiotics have been classified as the Reserve group. Seven Reserve group antibiotics are listed individually on the WHO Model List of Essential Medicines (WHO 2019b).

Measuring antibiotic consumption through quantifying the use of antibiotics in each of the AWaRe categories, allows some inference about the overall quality of antibiotic use in a given country. Countries should first compare national/regional antibiotic use using absolute consumption data, and then relative use according to the AWaRe categories (WHO 2019b). A study conducted at primary healthcare facilities in China (Zhao et al. 2022: 6) reported that Access antibiotics accounted for 45.0% and the Watch category accounted for 54.9%, while Reserve antibiotics were prescribed in only 0.001% of the prescriptions.

2.8 CONCLUSION

This chapter has provided the literature review in the areas of antibiotics resistance and use with a focus on antibiotics prescribing at primary healthcare facilities using both published and grey literatures. The topics covered in this chapter include the burden of antibiotic resistance, determinants of antibiotic resistance, the impacts of AMR, antibiotics prescribing, determinants of antibiotics prescribing, and strategies to promote the rational prescribing of antibiotics. Under each topic, the global and national situations were discussed including the existing knowledge gap in focus areas of the study. The literature review revealed that antibiotic prescribing and use data from primary healthcare facilities in developing setting is very limited and there is paucity of information on factors influencing antibiotics prescribing and interventions that can be applied to improve the prescribing practice at this level of care in developing settings, including Ethiopia. The Research Design and Method applied in the study are presented in the next chapter (Chapter 3).

CHAPTER 3: RESEARCH DESIGN AND METHOD

3.1 INTRODUCTION

Chapter 2 discussed the literature review in relation to the study topic. This Chapter discusses the research design and methods used to achieve the objectives of the study and answer the research questions. It gives a detailed account of the research design, study setting, study population, sample size determination and sampling procedures, data collection, methods employed to ensure validity, reliability and trustworthiness of the collected data, data management, ethical considerations that the researcher applied in undertaking the study, data integration, and development of the intervention guidelines.

This study was conducted in three phases; quantitative phase, qualitative phase, and guideline development phase. The guideline development phase is presented at the end. For the quantitative and qualitative phases of the study, the research design, ethical considerations, and point of integration are presented together, whereas, the remaining research method components are described for each study phase separately with the quantitative phase followed by the qualitative phase. Under each of the methodological descriptions, those parts that apply to both phases of the study are covered under the quantitative phase that is presented first and hence are not repeated under the qualitative part. Findings of the quantitative and qualitative findings were integrated and used to develop the intervention guidelines in Phase III.

3.2 RESEARCH DESIGN

Research designs are plans and the procedures for research that span the decisions from broad assumptions to detailed methods of data collection and analysis. There are three types of research designs quantitative, qualitative, and mixed methods (Creswell 2014: 22). Quantitative research is an approach for testing objective theories by examining the relationship among variables. These variables, in turn, can be measured so that numbered data can be analysed using statistical procedures. Qualitative research, on the other hand, is an approach for exploring and understanding the meaning individuals or groups ascribe to a social or human problem (Creswell 2014: 32).

Mixed methods research is a type of research in which a researcher combines elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the broad purposes of breadth and depth of understanding and corroboration. Mixed methods are well suited to answering research questions that examine a phenomenon that is both qualitative and quantitative in nature (Curry & Nunez-Smith 2017a: 2,4).

In this study, a mixed method approach that combined both qualitative and quantitative data collection and analysis was used. Achieving the objectives of the study required collection and integration of both quantitative and qualitative data. The descriptive part that aimed at determining the rate and patterns of antibiotics prescribing was achieved through a quantitative method (cross-sectional study) whereas identifying the antibiotic prescribing problems and exploring the factors that affect the antibiotic prescribing decision of prescribers, and identifying potential interventions to address the problems was achieved using a qualitative method (in-depth interview). The qualitative data complements and explains the quantitative data. The model selected for this study (PRECEDE-PROCEED) encourages the use of multiple methods to describe and explore public health issues so as to design appropriate interventions.

According to Curry and Nunez-Smith (2017a: 5), a core premise in mixed methods is that using complementary methods in pursuit of a question yields greater insight than would either method alone or both independently. Creswell (2014: 48) indicated that a mixed methods design is useful when the quantitative or qualitative approach, each by itself, is inadequate to best understand a research problem and the strengths of both quantitative and qualitative research (and its data) can provide the best understanding. Quantitative methods can identify the presence of antibiotic use problems and their magnitude, but not necessarily why the problems are occurring. The qualitative methods provide ways to understand why the problems are occurring which is necessary when designing appropriate interventions.

An explanatory sequential mixed method design was selected for this study. The explanatory sequential mixed method approach is a design in mixed methods that appeals to individuals with a strong quantitative background or from fields relatively new to qualitative approaches. It involves two phases in which the researcher collects quantitative data in the first phase, analyses the results, and then uses the results to plan (or build on to) the second, qualitative phase. The quantitative results typically inform the types of participants to be purposefully selected for the qualitative phase and the types of questions that will be asked of the participants (Schoonenboom & Johnson 2017: 117; Creswell 2014: 43).

The overall intent of this design is to have the qualitative data help explain in more detail the initial quantitative results. The data collection is carried out in two distinct phases with rigorous quantitative sampling in the first phase and with purposeful sampling in the second, qualitative phase, as presented in Figure 3.1 (Creswell 2014: 48).

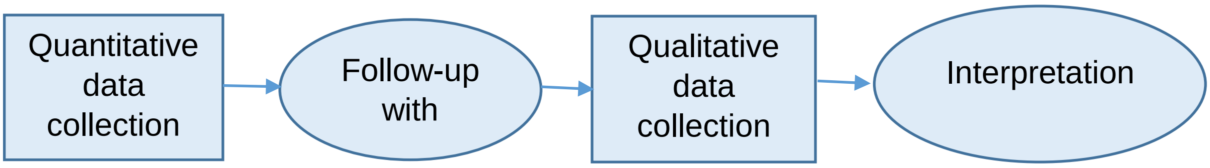


Figure 3.1 Explanatory sequential Mixed Method, adapted from Creswell (2014: 45).

3.3 RESEARCH METHODS: PHASE I (QUANTITATIVE)

Research methods are the forms of data collection, analysis, and interpretation that researchers use for their studies (Creswell 2014: 45). Guided by the selected theoretical model, this study was conducted in three phases using the mixed method approach as indicated in Figure 3.1 above. The first phase was a facility-based survey of antibiotic prescribing across the selected study sites to establish the rate and patterns of antibiotics prescribing, and evaluate appropriateness of the antibiotics prescribed for commonly encountered infectious cases. Details of the study setting, study population, sample size determination and sampling techniques, the data collection tools and procedures used in the study are presented below.

3.3.1 Study Setting

The study was conducted in Addis Ababa City (Figure 3.2), the capital city of Ethiopia. Addis Ababa is located at the centre of the country with total land area of 527 square kilometres. Administratively, the City is divided into 10 Sub-cities and 121 Woredas/Districts and is estimated to have a total population of 3,434,000 (1,625,000 males and 1,809,000 females) according to the population projection for 2017 of the 2007 National Population and Housing Census (Central Statistical Agency 2013). The City has three administrative levels; City Administration, Sub-Cities, and Districts/Woredas. A Woreda or District is the lowest administrative unit in the City. Health is part of each of these administrative levels; there is a City Administration Health Bureau, a Sub-City Health Office in each of the 10 Sub-Cities, and a District/Woreda Health Office in each of the 121 Districts/Woredas found in the City.

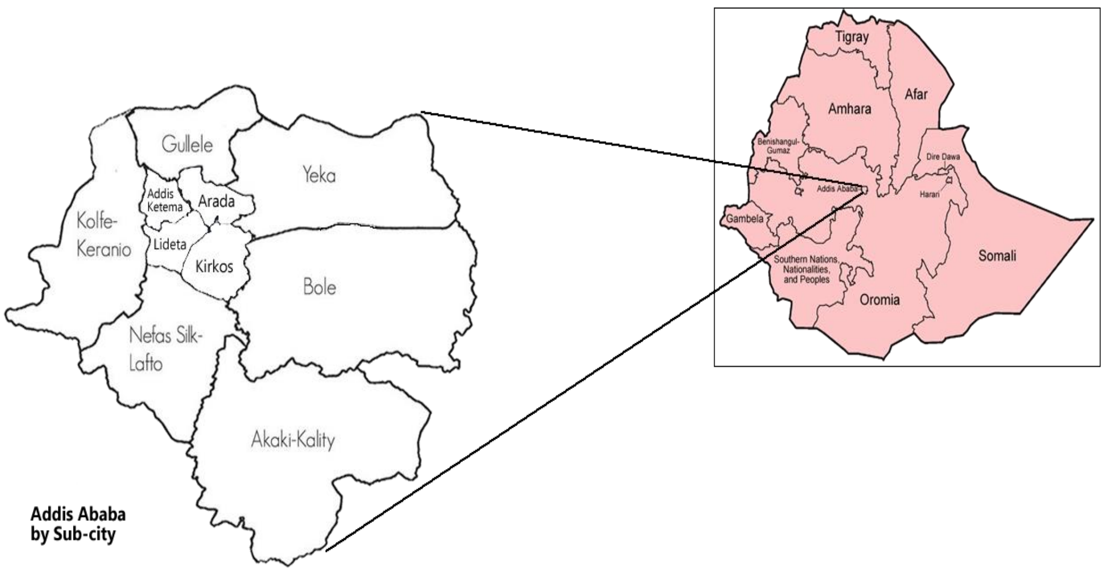


Figure 3.2 Map of Addis Ababa City Administration.

(available at: http://www.addisababa.gov.et/es/web/guest/city-map)

There are a total of 13 public hospitals and 98 public health centres in the City. In the public sector, health centres are the health facilities that provide primary healthcare in the City. There are also private, faith-based, and non-governmental hospitals, clinics, government-owned community pharmacies, and private community pharmacies and drug stores in the City. There is a Health Regulatory body, Addis Ababa Food, Medicine and Healthcare Administration and Control Authority (A.A. FMHACA) that reports directly to the City Administration Council. The quantitative study was conducted in 10 health centres selected from 5 of the sub-cities found in the City.

3.3.2 Sampling method

Sampling is the process through which researchers look at a smaller sample of possible participants in order to draw conclusions about the population as a whole. Theoretically, a good sampling technique should produce a sample that is trustworthy and devoid of bias (each member of the population has an equal probability of being chosen). It is argued that a sample is representative of the full population of interest if it is trustworthy, impartial, and free from bias. A representative sample allows the researcher to investigate the sample while drawing accurate conclusions about the larger population since it correctly reflects the characteristics of the population being studied. A poor sample could lead to meaningless findings based on research that is fundamentally flawed (Fritz & Morgan 2012: 2).

3.3.2.1 Study population

A population consists of all the items or individuals about which a researcher wants to draw a conclusion (Levine, Stephan, Krehbiel & Berenson 2008: 5). Identifying the population of interest is an important first step in designing the sampling method. This entire population is often referred to as the theoretical or target population since it includes all of the participants of theoretical interest to the researcher. These are the individuals about which the researcher is interested in making generalizations (Fritz & Morgan 2012: 2).

The study population for the quantitative phase of the study was prescriptions and medical records of patients who received medical attention in the selected healthcare facilities from September 1, 2019 to August 31, 2020. The following inclusion and exclusion criteria were used for this phase of the study.

Inclusion criteria:

- Prescriptions that were prescribed and dispensed in the selected health centres from September 1, 2019 – August 31, 2020, and
- Medical records of those patients included in the sample for whom one or more antibiotics were prescribed for respiratory tract infections.

Exclusion criteria:

- Prescriptions that were not prescribed during the period September 1, 2019 – August 31, 2020,
- Prescriptions that were not prescribed in the healthcare facility,
- Prescriptions that contained only medical supplies, and
- Patient medical records that did not contain antibiotics prescribed for respiratory tract infections

3.3.2.2 Sample Size Determination

A sample is the portion of a population selected for analysis. Rather than selecting every item in the population, statistical sampling procedures focus on collecting a small representative group of the larger population. The results of the sample are then used to estimate the characteristics of the entire population. There are three main reasons for selecting a sample (Levine et al. 2008: 252):

- Selecting a sample is less time-consuming than selecting every item in the population,
- Selecting a sample is less costly than selecting every item in the population, and
- An analysis of a sample is less cumbersome and more practical than an analysis of the entire population.

According to Acheson (2012: 2), sample size refers to the number of subjects included in a study. Sample size determination is a critical aspect of a study. Running a study with a sample that is too small results in numerous risks including not accurately reflecting the population the sample was drawn from, failing to find a real effect because of inadequate statistical power, and finding apparent effects that cannot be replicated in subsequent experiments. Using more subjects than necessary, on the other hand, is costly and can delay completion of the study.

Curry and Nunez-Smith (2017b: 4) reported that sampling approaches in mixed method studies capitalise on the complementarity of purposeful and probability approaches. While the qualitative arm may or may not be concerned with transferability, the quantitative component aims for maximal external validity in terms of generalizability. Hence, the sample should be developed with consideration for both the quantitative component's representativeness to improve generalizability as well as the qualitative component's breadth and richness of data to enhance credibility.

The quantitative phase of this study was conducted in 10 public health centres selected from 5 of the sub-cities. This number constitutes about 10% (10/98) of the health centres found in the City. Given the objective of this phase of the study (mainly descriptive), probability sampling using the single population proportion formula (Daniel 2012: 9) was considered to determine the required number of prescriptions (sample size) to determine the rate and patterns of antibiotic prescribing.

$$\boldsymbol{n = z^2pq/e^2}$$

Where:

n = the sample size

z = the z score corresponding with the desired level of confidence or probability of error. A confidence level of 0.95 (95% confidence interval) was used which gives a z score of 1.96.

p = the estimated proportion in the population.

The most conservative estimate is 0.50 and this was used in this study.

q = 1 - p

e = the tolerable margin of error or precision of the estimate. 5% margin of error was used in this study.

Using these values, the sample size was then calculated to be:

$$n = (1.96)^2(0.5)(0.5)/(0.05)^2 = 384$$

Considering a design effect of 1.5 as the sampling involved multistage sampling, the sample size was 384*1.5 = 576.

This value suggested reviewing a total of 576 patient prescriptions across the selected healthcare facilities to describe the rate and patterns of antibiotics prescribing. The WHO (1993: 30, 2007: 38), however, recommends reviewing a total of at least 600 patient prescriptions to describe medicines use in a specific healthcare facility or group of healthcare facilities. To make comparison on medicine use patterns among healthcare facilities or prescribers, the WHO's recommendation is to review at least 100 prescriptions per healthcare facility or prescriber. Accordingly, to make comparison in relation to the prevalence of antibiotics prescribing among healthcare facilities possible and to appropriately describe the patterns of antibiotics prescribing, the researcher then reviewed 200 prescriptions from each health centre resulting in a total of 2000 prescriptions from the 10 health centres as presented in Table 3.1.

Table 3.1 Sample size determined for quantitative phase of the study.

Total number of sub-cities	Number of sub-cities selected for the study	Number of health centres selected	Number of prescriptions sampled from each health centre	Total number of prescriptions sampled from the 10 health centres
10	5	10	200	2000

Of the sampled prescriptions, all of the prescriptions containing one or more antibiotics were considered for the antibiotic-specific analyses conducted. Medical charts of all patients for whom one or more antibiotics were prescribed for respiratory tract infections were considered in determining appropriateness of the antibiotics therapy in reference to current clinical guidelines being used.

3.3.2.3 Sampling Procedures

Sampling procedures are used by researchers to select study units from a population. The time and effort invested in data collection and analysis can be wasted and result in false conclusions if the sampling processes are faulty (Fritz & Morgan 2012: 4). In creating a sampling plan for a mixed methods study, the common practice is to apply probability and purposeful techniques either interdependently or independently. A probability sampling approach is selected for the quantitative component of an independent mixed methods sampling plan, and a primary purposeful sampling technique is selected for the qualitative component. Although the component samples may still be linked or connected, the independent approach contains two distinct samples in the sampling plan. For instance, in a sequential design, researchers would be curious to discover a sample for the second component to respond to queries formulated based on findings of the first component.

Interdependent mixed methods sampling frames are built through the joint use of probability and purposeful techniques to create one or more samples for a particular research project. Researchers might decide to draw multiple samples from the defined sampling frame for participation in the different study components or to draw a single sample from the sampling frame that participates in both the quantitative and qualitative components of the research project.

Though both the quantitative and qualitative components of the study were conducted in the same public health centres, sampling frames of the two components were different. The sampling frame for the quantitative phase of the study were patient prescriptions and medical charts, whereas, the sampling frame for the qualitative component were the prescribers. Hence, the sampling procedure used in this study was an independent mixed methods sampling plan.

For the quantitative phase of the study, multistage sampling that involved cluster and random sampling methods was used. The first stage was selecting the five sub-cities. This was followed by selection of the health centres in which the study was to be conducted. In the third stage, the prescriptions from which the quantitative data was collected were selected.

Stage 1: Selecting the sub-cities

Considering the sub-cities as clusters, five clusters were selected by simple random sampling method using the Table of Random Numbers (Levine et al. 2008: 254,486). The list of sub-cities found in the City Administration and the public health centres under them was obtained from Addis Ababa City Administration Health Bureau. Using the list of the ten sub-cities obtained from the Health Bureau as a sampling frame, the ten sub-cities (clusters) were coded from 01 to 10. Then, the random sample was generated by reading the table of random numbers and selecting those sub-cities from the sampling frame whose assigned code numbers match with the digits found in the table. This resulted in selection of Addis Ketema, Gulele, Lideta, Nifas Silk Lafto and Yeka Sub-Cities as the five sub-cities (clusters) for the study.

Stage 2: Selecting the health centres

Once the Sub-cities were selected, the next step was selecting the 10 health centres from within those 5 sub-cities. Having the required sample of 10 health centres, the number of health centres to be selected from each sub-city was determined in proportion to the number of health centres found in each sub-city. The total number of health centres in the selected five sub-cities was 49 with the number of health centres per sub-city ranging from 6 (Lideta Sub-city) to 14 (Yeka Sub-city). Dividing the total number of health centres to be sampled by the total number health centres in these 5 sub-cities (10/49) gave the proportion (0.2) to be used in determining the number of health centres to be selected from each sub-city. Accordingly, the number of health centres to be selected from each sub-city was determined by multiplying this proportion by the number of health centres in each sub-city, rounding decimals to the nearest one digit number.

This process resulted in selection of 3 health centres from Yeka Sub-city, 2 health centres from each of Addis Ketema, Gulele and Nifas Silk Lafto Sub-cities and 1 health centre from Lideta Sub-city. Using the list of health centres found in each sub-city, the health centres were selected from each sub-city by simple random sampling method using the Table of Random Numbers. Table 3.2 presents the number and list of health centres selected for the study from the five sub-cities using the sampling method described above.

Table 3.2 Sub-cities and Health Centres selected for the quantitative study, Addis Ababa City Administration.

Name of selected Sub-city	Total number of health centres in the Sub-city	Number of health centres selected	Name of Health Centres selected for the study
1. Addis Ketama Sub-city	10	2	1. Kuas Meda Health Center 2. Millennium Health Center
2. Gulele Sub-city	10	2	1. Shiromeda Health Center 2. Tibeb Bekechene Health Center
3. Lideta Sub-city	6	1	1. Lideta Health Center
4. Nifas Silk Lafto Sub-city	9	2	1. Woreda 09 Health Center 2. Woreda 12 Health Center
5. Yeka Sub-city	14	3	1. Chefe Health Center 2. Entoto No. 1 Health Center 3. Yeka Health Center
Total	**49**	**10**	**10**

From Lideta Sub-city, Woreda 01 (Yehidase Fire) was the health centre selected for the study. While in discussion with the Sub-city Health Office when processing the support letter for the study, this health centre was found to be a COVID-19 Treatment Center. This health centre was then replaced by Lideta Health Center by applying simple random sampling technique on the remaining 5 health centres found in the sub-city.

Stage 3: Selecting the prescriptions from the health centres

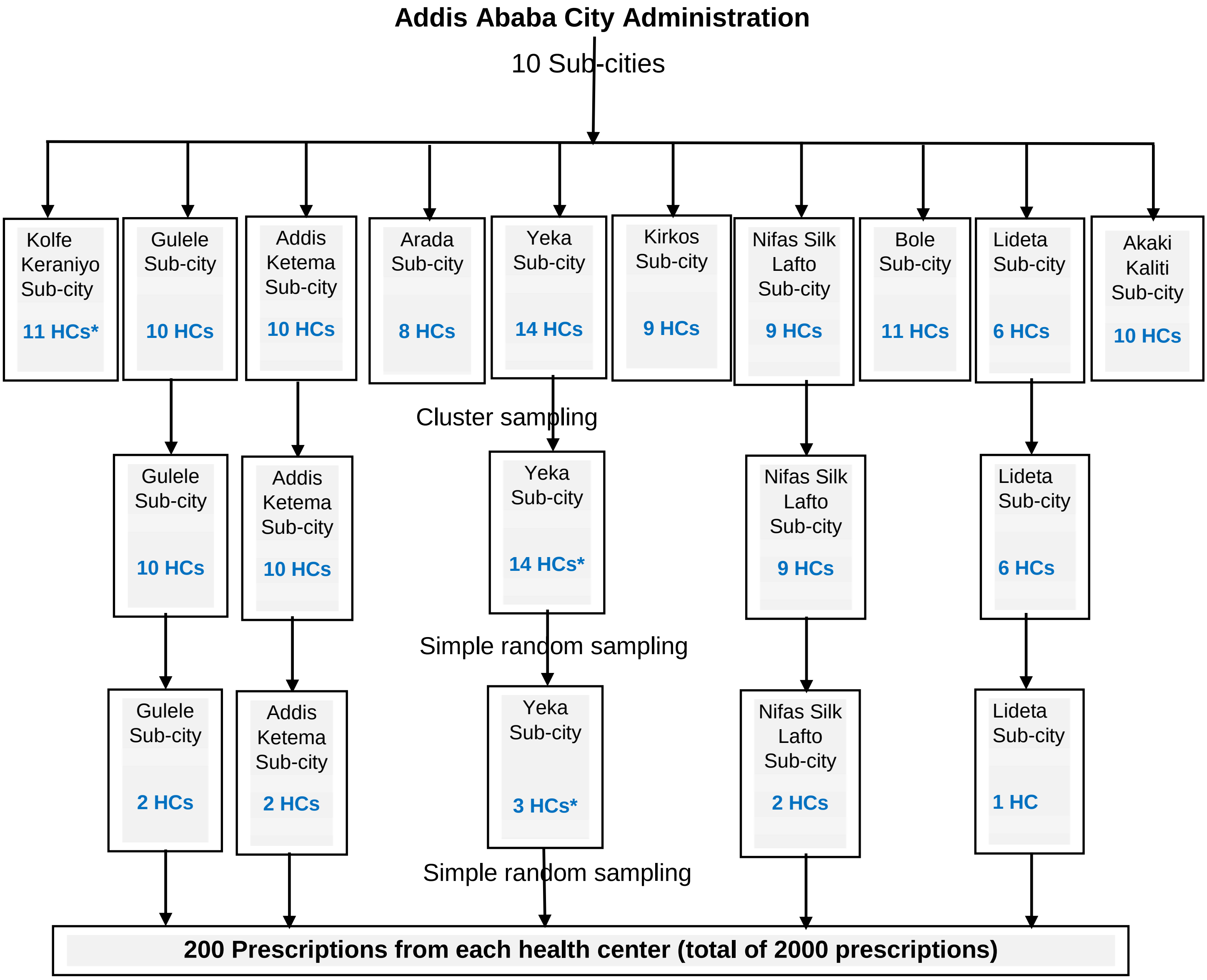
The WHO (2007: 16) recommends using a one year prescribing record in order to accommodate seasonal variations in the prescribing pattern. Accordingly, this study retrospectively reviewed prescriptions prescribed in a year period by selecting prescriptions using the Chronological Sampling Method recommended by the WHO (2007: 18). The total number of working days in the study year (September 1, 2019 – August 31, 2020) was determined by subtracting the number of holidays (13) and weekends (105) from the total number of days during the year (365) using a local calendar. Determining the number of working days was important since health centres provide regular service during working days and they only provide emergency service during holidays and weekends. Only prescriptions prescribed and dispensed during the regular working days and hours were included in this study.

The total number of working days during the study year were calculated to be 247 (365 – (105+13)). The sampling interval was calculated by dividing the number of working days (247) by the total number of prescriptions required for the study from each health centre (200): 247/200 = 1.24, which was rounded to 2. The working days (date/month/year) from September 01, 2019 to August 31, 2020 were listed chronologically and every other working day was selected till a total of 200 working days were selected.

Health centre dispensaries pack dispensed prescriptions on daily basis, label each pack by date (date/month/year) and store in cartons. At each health centre, packs of prescriptions dispensed during the selected working days were retrieved from the dispensary until 200 such packs were retrieved. When it was not possible to retrieve the prescription pack of a particular selected working day, the prescription pack of the next or previous working day (whichever came first) of the same month was taken. Similarly, when prescription packs of an entire month or part of a month were missing for any reason, the missing packs were replaced by prescription packs from working days of the previous and/or the next months that were not already included in the sample. This same procedure was followed for all of the 10 health centres.

Once the 200 prescription packs were retrieved, the prescriptions were unpacked, counted and coded using 2 or 3 digit numbers depending on the total number of prescriptions in the pack. When the number of prescriptions per pack were less than 100, the prescriptions were coded with two digit numbers that ran from 01 to the last number (e.g. 85). When the number of prescriptions in the pack were 100 or more, the prescriptions were coded with a three digit number that runs from 001 to the last number (e.g. 120). Then, one prescription was randomly picked from each sampled pack using a random number table.

Figure 3.3 shows schematic representation of the sampling procedures used in this study.



** HCs – Health Centers*

Figure 3.3 Schematic representation of the sampling procedures.

No sampling was done for prescriptions containing antibiotics and medical charts of patients with respiratory tract infections for whom antibiotics were prescribed. Of the sampled prescriptions, all of the prescriptions containing one or more antibiotics were considered in determining the patterns of antibiotic prescribing such as type of antibiotics prescribed, antibiotic class, diagnosis for prescribing antibiotics, AWaRe categories of the antibiotics prescribed, and the cost of antibiotics. Similarly, all patient medical charts that corresponded to the sampled prescriptions containing one or more antibiotics prescribed for respiratory tract infections were considered for the study to assess appropriateness of the antibiotics therapy.

3.3.3 Data collection

According to Creswell (2014: 239), the data collection in explanatory sequential mixed method approach proceeds in two distinct phases with rigorous quantitative sampling in the first phase and with purposeful sampling in the second, qualitative phase. The main idea is that the qualitative data collection builds directly on the quantitative results. In this study, the quantitative data was collected and were subjected to preliminary analysis before collection of the qualitative data and were used to inform the qualitative data collection.

3.3.3.1 Data collection approaches and methods

Data for the quantitative component of the study was collected from prescriptions and patient medical charts using data abstraction forms. The data collection was undertaken from 25th December 2020 to 30th January 2021. Details of the data collection tools and processes are described below.

3.3.3.2 Data collection instruments

Three data abstraction forms were used to collect the quantitative data from prescriptions and patient medical charts. In consultation with the research supervisor at Department of Health Studies, University of South Africa (UNISA), the data abstraction forms were developed in English language. The first form (Annexure A) was used to collect the data required to determine the prevalence (rate) of antibiotic prescribing and was developed based on the WHO Prescribing Indicator Form (WHO 2007: 133). Modifications were made on the WHO Form to include data on patient chart number just for reference purpose only, number of antibiotics prescribed, costs of the medicines and antibiotics prescribed, the number of antibiotics prescribed from the health centre's medicines list, and the qualification of prescribers.

In addition to these, the form was used to collect data on patient age and gender, date of prescribing, number of medicines prescribed, and whether the prescription has antibiotics or not. General information on the number of patients served by the health centre, annual budget allocated for pharmaceuticals during the budget year, July 2019 to June 2020 (2012 EFY), and the presence of functional Drug and Therapeutics Committee (DTC), health centre-specific medicines list and standard treatment guidelines was also collected using this form.

The second data abstraction form (Annexure B) was used to collect data on the patterns of antibiotics prescribing including the specific antibiotics prescribed, their dosage, the diagnosis for which the antibiotics were prescribed, the cost of each antibiotic prescribed, and qualification of the prescriber. The form was also used to collect information on the top ten diseases treated by each health centre during the budget year covered by the study (2012 EFY). This form was adapted from a tool that the researcher used during his previous study (Worku & Tewahido 2018: 4–5) and a tool used by a similar study conducted in Nigeria (Kpokiri et al. 2020: 3).

The third form (Annexure C) was used to collect data on the antibiotics prescribed for respiratory tract infections including, the indications, signs and symptoms, laboratory investigations conducted and appropriateness of the antibiotics prescribed in reference to updated clinical protocols. The unique patient identifier (Patient code) was used in all of the three data abstraction forms to ensure data accuracy and facilitated cross-checking of data between the three sets of data and between the hard and soft copies.

3.3.3.3 Pre-testing of data collection instruments

Prior to the actual data collection, each of the data collection instruments were pre-tested in two public health centres (Teklehaimanot and Abebe Bikila Health Centers) that were randomly picked from two of the sub-cities selected for the study (Addis Ketema and Lideta Sub-cities). These health centres did not form part of the sampled health centres. The data abstraction forms were pre-tested using 50 prescriptions and 10 patient medical charts (25 prescriptions and 5 patient medical charts from each health centre) sampled from prescriptions dispensed during a one month period in 2012 EFY (2019).

No modification was made on the first two data abstraction forms (Annexure A and Annexure B). Major modifications were made on the third data abstraction form (Annexure C) after the pilot-test. Columns were added for two additional parameters (antibiotics prescribed and pertinent diagnostic tests). The modifications made on the tools were reviewed and approved by the research supervisor. The research assistants have participated in the pilot-tests conducted in the two health centres.

3.3.3.4 Recruitment and training of research assistants

For the quantitative phase of the study, two research assistants were recruited from the School of Pharmacy at Addis Ababa University based on the criteria that they should be pharmacists with at least 5-year experience with a Master Degree in Clinical Pharmacy and experience in collecting quantitative data in relation to the prescribing and use of medicines in a healthcare setting. They were trained by the researcher for two days on the objectives of the study, the study setting, the type of data to be collected and their sources, the data collection tools, the sampling procedures and data collection techniques. From each health centre, one pharmacist (mainly the coordinator of the pharmacy team) was used as the focal person to facilitate the data collection process by locating and retrieving prescriptions to be sampled and by collecting and providing general health centre information required for the study.

Research confidentiality agreement (Annexure D) was signed with each of the research assistants using a form developed for this purpose. The form was adapted from Montague COBB Research Laboratory of Howard University (available at: *https://static1.squarespace.com/static/53dbcbd3e4b0ba1f9aa0693a/t/561d6764e4b06f8695a756a3/1444767588379/Researcher+confidentiality_Editiable.pdf).*

3.3.3.5 Reliability of data collection instruments

Reliability and validity are the two measures of quality in a quantitative study (Heale & Twycross 2015: 66). To ensure that the instruments and tests are adequate to measure the constructs, validation tests to assess the reliability and validity of the measurements are necessary (Leung & Shek 2018: 4). Reliability refers to the extent to which a research instrument consistently has the same results if it is used in the same situation on repeated occasions (Heale & Twycross 2015: 66).

In this study, the tools used for collecting the quantitative data were data abstraction forms developed based on a standard WHO tool and tools used by researchers in the area. Given the nature of the data collected and the data sources used in this study, there is no issue of subjectivity that can lead to variations in the nature of the data collected during repeated measurement in this component of the study. In order to enhance the reliability of the tools, the researcher pre-tested the data abstraction forms in a similar setting prior to the actual data collection. In addition, feedback received from the research supervisor was incorporated to enhance the reliability of the data collection tools.

3.3.3.6 Validity of data collection instrument

Validity refers to the extent to which the instrument adequately reflects what it is designed to measure. There are five approaches for assessing measurement validity: *face validity, content validity, criterion-related validity, construct validity, and factorial validity* (Leung & Shek 2018: 4–5). Of these approaches, face and content validity were applied in this study.

The instrument's content validity examines if it effectively covers every piece of information that should be included with regard to the variable. In other words, does the instrument cover the entire domain related to the variable, or construct it was designed to measure? (Heale & Twycross 2015: 66). In general, content validity involves evaluation of a new survey instrument in order to ensure that it includes all the items that are essential and eliminates undesirable items to a particular construct domain (Taherdoost 2018: 30).

Face validity refers to researchers' subjective assessments of the presentation and relevance of the measuring instrument as to whether the items in the instrument appear to be relevant, reasonable, unambiguous and clear. In order to examine the face validity, the dichotomous scale can be used with categorical option of "Yes" and "No" which indicate a favourable and unfavourable item respectively (Taherdoost 2018: 29).

In terms of content validity, the data abstraction forms were adapted from standardised data abstraction forms that are widely used as well as from tools previously used in the literature. The data abstraction forms have the necessary content to collect the data required to answer the research questions. The tools were developed to directly collect data that was available on the sampled prescriptions and patient medical charts. The tools were pre-tested in a similar setting prior to the actual study. In addition, feedback obtained from the research supervisor was incorporated to boost the content validity of the data abstraction forms. The tools were very relevant, clear, unambiguous and reasonable as the data collected using the tools was directly picked from prescriptions and patient medical charts.

3.3.3.7 Data collection process

To conduct the study in the selected setting, the researcher applied for ethical clearance to the City Administration Health Bureau's Research Ethical Clearance Committee by submitting hard and soft copies of the research proposal along with the Ethical Clearance Certificate (Annexure E) obtained from the Research Ethics Review Committee of the College of Human Sciences, UNISA (CREC Reference Number 64093352_CHS _CREC_2020) and a support letter from UNISA Addis Ababa Learning Center (Annexure F) with a cover letter signed by the researcher (Annexure G) that describes objectives of the study, the data to be collected, and list of the pilot and study sites. The Committee reviewed the proposal and granted permission to conduct the study by issuing an official letter to the Health Bureau and the selected five sub-cities (Annexure H). The sub-cities then wrote letters to the selected health centres under them, including the two pilot sites.

Having first obtained the official support letters from the sub-cities, the researcher visited each of the selected health centres and presented the letters to the Medical Directors. In each health centre, the researcher clarified the objectives of the study, the type of data to be collected from the health centre, the data sources, the method of data collection, who is going to collect the data, and the support required from the health centre. The Medical Director then forwarded the letter to the Medical Service Process Owner and Pharmacy Case Team to provide the necessary support during the data collection process. The Medical Service Process Owner and Pharmacy Case Team Coordinator were then briefed on the objectives of the study, the data to be collected and the data collection process for both the quantitative and qualitative phases of the study.

As per the researcher's request, the Pharmacy Case Team Coordinator or representative served as a focal person and provided support to the researcher and research assistants during the data collection process. In eight of the health centres, the Pharmacy Case Team Coordinators served as the focal person while in two of the health centres representatives from the pharmacy staff were assigned as focal person.

To maintain uniformity of the data collection across the health centres, the quantitative data from each health centre was collected by two research assistants working together with the researcher as a team. The pharmacist assigned to facilitate the data collection process assisted in making prescriptions ready for sampling and in facilitating the communication with the medical record unit to retrieve the patient medical charts for subsequent data collection following the administrative channel. Having a contact person enabled the researcher to have easy access to the prescriptions and patient medical charts for collection of the necessary data once permission was granted from the Health Centre's Medical Director and a directive forwarded to the record room through the Medical Service Process Owner. A room or corner was dedicated by the health centres for the researcher and research assistants to undertake the sampling and data collection.

To facilitate cross-matching of the information recorded on the data abstraction formats and the data entered into the statistical tool, a unique identifier (Patient code) was given for each sampled prescription and was made part of the data abstraction formats. This alphanumeric code contained 2 to 3 letters from the health centre's name followed by a three digit number starting from 001 to 200. These codes were used throughout the data collection process, including when collecting antibiotic related information from the corresponding patient medical charts.

From each sampled prescription, data on chart number, patient's age, gender, date of prescribing, numbers of medicines and antibiotics prescribed, costs of medicines, costs of the prescribed antibiotics, availability of the prescribed antibiotic(s) in the health centres medicines list, and qualification of the prescriber were collected using the data abstraction form developed for this purpose (Annexure A). Data related to the gender of prescribers was collected from only 5 of the health centres (CFHC, ENTHC, MLHC, TBHC and WD9HC), three of which were involved in the qualitative study. Information on whether there are upper respiratory tract cases for which an antibiotic was not prescribed was also collected from six of the health centres (CFHC, ENTHC, LDHC, MLHC, TBHC and WD9HC), four of which were involved in the qualitative phase of the study. For prescriptions that were dispensed free of charge, costs were determined by taking the costs of the same medicine availed for sale during the same or previous year.

For each sampled prescription, the unique identifier (Patient Code) was recorded prior to the recording of any other data. The medical chart number of the patient was used as a reference to retrieve the medical charts of those patients for whom one or more antibiotics were prescribed for the diagnoses selected to evaluate appropriateness of the antibiotics treatment for respiratory tract infections. The health system uses Patient Medical record numbers as a unique patient identifier in documenting and retrieving charts of patients.

Antibacterials belonging to the following categories of medicines in the List of Medicines for Health Centres in Ethiopia (3rd edition) were considered as antibiotics: *penicillins, other antibacterials, ophthalmic antibacterials, and topical antibacterials* (EFMHACA 2012a).

From prescriptions containing one or more antibiotics, information on the names of the antibiotics prescribed, dosage (dose, frequency and duration), routes of administration, cost of each antibiotic, the diagnosis for which the antibiotic was prescribed (whenever available), and qualification of the prescriber were recorded on the second data abstraction form (Annexure B). The AWaRe classification of each of the antibiotics prescribed was identified from the WHO database and made part of the data after data entry into the statistical tool.

For prescriptions that had antibiotics prescribed for respiratory tract infections, the medical chart numbers were recorded on a separate sheet of paper and provided to the medical record unit for the assigned officer to retrieve the medical charts. The researcher and research assistants counted and received the charts from the medical record unit, checked if the medical charts were the correct ones, and recorded the necessary data (diagnosis, laboratory investigation done, laboratory results, pertinent signs and symptoms) from each chart using Annexure C. The medical charts were then counted and returned back to the record unit.

Because dates are written on prescriptions and medical charts in the Ethiopian Calendar (E.C.) format, the data was collected following the E.C. The date was then converted from EC to Gregorian Calendar (G.C.) during data entry using a local calendar that shows both the E.C. and G.C. dates. To facilitate this, a list containing the working days in both E.C. and G.C. dates was prepared and used as a reference during data collection and entry.

Background information on number of prescribers in the facility (by profession), annual budget of the health centre for medicines, top ten diseases treated by the health centres during the previous year (2012 EFY), the presence of standard treatment guidelines (STG), presence of functional DTC and the presence of a facility-specific medicines lists were also collected from each health centre using the data abstraction forms by asking the Pharmacy Case Team Coordinator, and by observing and reviewing documents.

3.3.4 DATA MANAGEMENT

Both the researcher and research assistants had access to the hard copies of the collected data during the period of data collection. Only the researcher and supervisor have access to the data thereafter. Both the hard and soft copies of the collected data were kept secure in a lockable cabinet and a password protected file, respectively. Both copies of the data will be kept securely for 5 years and will be permanently destroyed through appropriate means thereafter. The researcher has attended UNISA seminars on quantitative and qualitative data analysis as part of the PhD study. In addition, series of YouTube video tutorials on data entry and analysis using Statistical Package for Social Sciences (SPSS) were watched to appropriately enter and analyse the quantitative data.

3.3.4.1 Data entry

Completeness of the data collected using each of the data abstraction forms was checked by the researcher on daily basis. Variables were defined and the data from each completed form was then entered into SPSS version 28 *(IBM SPSS Statistics 28, IBM Inc.)* which was downloaded online using UNISA's License Agreement with support from the UNISA-Ethiopia Learning Center*.* The variables included the name of the sub-city in which the health centre is found, name of the health centre (abbreviated), month of prescribing, patient age patient gender, number of medicines prescribed, number of antibiotics prescribed, cost of the medicines prescribed, cost of the antibiotics prescribed, qualification of the prescriber, name of the antibiotic prescribed, class of the antibiotic, duration of use, route of administration, the diagnosis for which the antibiotic was prescribed, AWaRe category of the prescribed antibiotic, and gender and qualification of the prescriber. Depending on nature of the variable (nominal, ordinal or scale), values of each variable were set as continuous, categorical or binomial, including a code for missing values.

After the data that corresponded to each of the 2000 prescriptions and selected patient medical charts was entered, the data inputted for each variable was carefully checked for accuracy. The necessary corrections were made when incorrect or omitted entries were identified using the hard copy data as a reference.

3.3.4.2 Data analysis

In an explanatory sequential mixed method approach, the quantitative and qualitative datasets are analysed separately. The quantitative results are used to plan the qualitative study. A mixed methods researcher interprets the follow-up results in a discussion section of the study. This interpretation follows the form of first reporting the quantitative, first-phase results and then the qualitative, second phase results (Creswell 2014: 272). In this study, the quantitative and qualitative data were collected and analysed separately and the findings brought together at the stage of interpretation and used to develop the intervention guidelines as per the first four phases of the theoretical framework (PRECEDE-PROCEED Model) selected for the study.

The quantitative data was analysed using SPSS versions 28. Descriptive statistics was used to determine the frequencies and percentages of occurrences of the study variables in the collected data. Independent variables such as gender and age of patients, qualifications of prescribers, gender of prescriber, period of prescribing, and dependent variables like number of medicines and antibiotics prescribed, costs of medicines and antibiotics prescribed, diagnosis for which antibiotics were prescribed, type and category of the antibiotics prescribed, and appropriateness of the antibiotics prescribed were determined using descriptive statistics.

After analysing the data for variables that applied to the whole dataset such as age and gender of patients, qualification and gender of prescribers, period of prescribing, average number of medicine per prescription, percentage of prescriptions with one or more antibiotics, costs of medicines, and percentage cost of antibiotics, the antibiotic-related SPSS data was extracted out and saved separately for further analysis.

Five key outcome indicators were determined from the quantitative data; the rate of antibiotics prescribing, percentage of antibiotics prescribed that are included in the health centres' medicines list, percentage of antibiotics that belong to the Access category of the WHO's AWaRe Classification of antibiotics, appropriateness of the antibiotics prescribed for respiratory tract infections, and percentage cost of the antibiotics prescribed. Of these, the major outcome measures are the rate (prevalence) of antibiotic prescribing and appropriateness of the antibiotics prescribed in terms of antibiotic selection and dosage. Table 3.3 presents purpose of the key outcome indicators and the formula used to calculate each indicator.

The fourth indicator, appropriateness of the antibiotics prescribed for respiratory tract infections, was determined for respiratory tract infections for which antibiotics were prescribed. A clinical protocol that was used as a reference standard to evaluate the antibiotic prescribing practices was developed by the research assistants. The protocol was developed using the Health centre clinical guidelines (EFMHACA 2014), the new primary healthcare clinical guidelines – PHCG (FMOH 2019) and other commonly used clinical guidelines. Each respiratory tract case was then evaluated against the standards set in terms of the antibiotic treatment and categorised as ‘appropriate’, ‘inappropriate’ or ‘difficult to evaluate’.

Table 3.3 Key outcome indicators measured in the study.

S/N	Outcome Indicator	Purpose	Calculation
1	Percentage of prescriptions with antibiotics prescribed	To determine the prevalence of use of these group of medicines	Calculated by dividing the number of prescriptions containing one or more antibiotics by the total number of prescriptions reviewed, multiplied by 100.
2	Percentage of antibiotics prescribed included in the health centres’ medicines list	To determine the extent of using the health facility specific medicines list in actual practice	Calculated by dividing the number of antibiotics prescribed that are included in the medicines list of the health centres by the total number of antibiotics prescribed, multiplied by 100
3	Percentage of antibiotics prescribed that belong to the Access category of WHO AWaRe Classification	To emphasise the importance of monitoring optimal uses and potential for antimicrobial resistance	Calculated by dividing the total number of antibiotics prescribed that belong to the Access category by the total number of antibiotics prescribed, multiplied by 100
4	Percentage of respiratory tract infections managed appropriately	To evaluate appropriateness of the antibiotics prescribed for	Calculated by dividing the number of respiratory tract infections appropriately managed by antibiotics by the total number of respiratory tract infection cases

S/N	Outcome Indicator	Purpose	Calculation
		respiratory tract infections	managed using antibiotics, multiplied by 100.
5	Percentage cost of antibiotics	To determine the contribution of antibiotics to the total cost of medicines prescribed	Calculated by dividing the total cost of antibiotics prescribed by the total cost of all medicines prescribed, multiplied by 100.

In addition to these key outcome indicators, indicators that show the antibiotics prescribing pattern-like percentage of each of the antibiotics prescribed, the commonly prescribed group of antibiotics, the number and percentage of infectious cases for which antibiotics were prescribed, and the percentage of antibiotics prescribed were also determined.

Association of demographic characteristics of patients (age and gender) and prescribers (gender and qualification), and period of prescribing (by quarter) with the major outcome variable (antibiotic prescribed or not prescribed) was tested using Chi-square test by setting the level of statistical significance at $p \leq 0.05$. The outcome indicators were compared with the WHO standards and findings of similar studies conducted at primary healthcare facilities in developing settings. The findings from this component of the study were also discussed in relation to findings of the qualitative study.

3.4 RESEARCH METHODS: PHASE II (QUALITATIVE)

This phase of the study was conducted through in-depth interviews of prescribers and key informants to explore the antibiotic prescribing problems and factors that affect the antibiotic prescribing decisions of prescribers, and identify the interventions that should be implemented to improve the prescribing of antibiotics in the study setting. Details of the study setting, study population, sample size determination and sampling techniques, the data collection tools and procedures used in the study are presented under this section.

3.4.1 Study Setting

This phase of the study was conducted in the same setting where quantitative phase of the study was conducted (Addis Ababa City. The qualitative study was conducted in five of the 10 health centers included in the quantitative phase of the study.

3.4.1.1 Study population

For the qualitative phase of the study, the study population was the healthcare providers who were involved in patient diagnosis and prescribing of medicines in the selected public health centres during the data collection period and office holders in the health centers, sub-cities and health bureau (May 1 – June 10, 2021). The inclusion and exclusion criteria used were the following:

Inclusion criteria:

- Healthcare providers working in the selected healthcare facilities who were involved in patient diagnosis and prescribing of medicines during the past, at least, 2 years;
- Healthcare providers who were on duty during the data collection period;
- Healthcare providers who were willing to take part in the study; and
- Office holders in the selected health centres, sub-cities and the Health Bureau.

Exclusion criteria:

- Healthcare providers who were not involved in patient diagnosis and prescribing of medicines;
- Healthcare providers who have not served in the facility for at least 2 years;
- Healthcare providers who were not on duty during the data collection period; and
- Healthcare providers who were not willing to participate in the study.

3.4.1.2 Sample Size Determination

Qualitative researchers often use a variant of purposive sampling, the specific type being dependent on the purpose of the research (Suter 2014: 36). It is reported that the goal of sampling in qualitative research is to obtain descriptive data by methods such as observations, interviews, or field notes to answer the how or why. Unlike quantitative studies, there are no statistical formulas for computing the required sample size needed to ensure generalization. There is less focus on generalizing findings from a sample to a large population and the focus is on selecting fewer participants who can best answer the research question (Suter 2014: 28). In this study, both groups of participants (prescribers and key informants) were selected purposively based on their role in the practice being investigated.

a) In-depth interview with prescribers

For the interview with prescribers, four prescribers were selected purposively from each of the five health centres. The prescribers included in the interview were those who fulfilled the inclusion criteria and were willing to participate in the study. With the support of the focal person from Pharmacy Team, prescribers with mix of profession and gender were selected from different clinical units. All of the twenty prescribers were interviewed, although towards the end, most of the information collected from those interviewed were just repetitions of what has been said by previous prescribers.

b) Key informant interview

These key informants were selected based on their direct roles in coordinating and supporting the provision of health services at health centres. Accordingly, Medical Directors and Pharmacy Case Team Coordinators of the selected five health centres, and Medical Service and Pharmacy Service and Logistics Team Coordinators of the Sub-city Health offices as well as Directors of the Medical Service and Pharmaceutical Service and Logistics Directorates of the City Administration Health Bureau were purposively included in the key informant interview as they are the ones who have the information about the antibiotic prescribing situation and related initiatives at the selected health centres.

3.4.1.3 Sampling Procedures

The qualitative component of the study was conducted in five of the ten health centres selected for the quantitative study. The qualitative study was conducted after preliminary analysis of the quantitative data, especially the rate of antibiotics prescribing. One health centre was selected from each of the five sub-cities using the rate of antibiotic prescribing as a general selection criteria. The ten health centres were grouped into three; high, medium and low rate of antibiotic prescribing according to their prescribing rate as determined by the quantitative study. Then, one health centre was randomly picked from each group until five health centres were selected without repeating a health centre from a specific sub-city.

The health centre with the lowest rate of antibiotic prescribing (TBHC), two health centres with the first (CFHC) and second (WD9HC) highest rate of antibiotics prescribing, and two health centres with a medium rate of antibiotic prescribing (KMHC and LDHC) were selected for the qualitative study. From each health centre, four prescribers that showed interest to participate in the study were purposively selected and interviewed. Effort was made to include prescribers from professional categories that are commonly involved in patient management at the health centres (Health Officer, Nurse). Consideration was also given to have prescribers from clinical units in which medicines are commonly prescribed (adult outpatient, paediatrics outpatient, and emergency). Gender was also considered in selecting prescribers for the study.

In the key informant interview, medical directors and pharmacy case team coordinators of the health centres, coordinators of the medical service and pharmacy service and logistics teams of health offices of the five sub-cities, and Directors of the Medical Service and Pharmacy Service and Logistics Directorates of the City Administration Health Bureau were selected purposefully.

3.4.2 Data collection

3.4.2.1 Data collection approaches and methods

The data required to answer the research questions related with factors influencing antibiotic prescribing and interventions to improve antibiotic prescribing were collected through in-depth interview of prescribers and key informants. The data was collected from 1st May to 10th June 2021 using interview guides developed for each participant group.

3.4.2.2 Data collection instruments

In this study, three in-depth interview guides were used to collect the necessary qualitative data required to answer the research questions. The interview guides were developed to gather information from prescribers and key informants with respect to antibiotic prescribing practices at health centres, the actions taken so far and ones that should be taken to improve their prescribing. This required developing three in-depth interview guides. The guides were developed based on the objectives of the study, phases of the theoretical model used and were informed by the preliminary findings of the quantitative study. Preliminary information generated from the quantitative data such as the rate of antibiotics prescribing, common prescribing of antibiotics for URTIs, and appropriateness of the antibiotics treatment for respiratory tract infections were taken into consideration when preparing the questions for the interview-guides.

For each guide, the questions were developed to understand the antibiotic prescribing practices, identify the predisposing, enabling and reinforcing factors that affect antibiotic prescribing, and identify interventions suggested by prescribers and key informants to improve antibiotics prescribing at health centres as per the 3rd and 4th phases of the PRECEDE-PROCEED Model that guides this study.

In consultation with the research supervisor at Department of Health Studies, University of South Africa (UNISA), the interview guides were first developed in English language and then translated to Amharic language through repeated checking and rechecking for consistency by the researcher and research assistant.

The guide used for the in-depth interview with prescribers (Annexure I) contained six main and a series of probing questions. The questions focused on the use of antibiotics, commonly used antibiotics and their indications, antibiotic resistance, use of narrow- and broad-spectrum antibiotics, problems associated with the prescribing and use of antibiotics, factors influencing antibiotic prescribing, the use of antibiotics for URTIs, the availability of information on antibiotics and resistance, the presence of monitoring and evaluation system on use of antibiotics, interventions implemented so far to improve antibiotic prescribing, interventions suggested to be implemented to improve the prescribing of antibiotics in the study setting, and challenges that might be faced in implementing the suggested interventions to improve antibiotic prescribing.

Six main and a series of probing questions were included in the guide used for the key informant interview at health centres (Annexure J). The questions were designed to get the views of the key informants on use of antibiotics and the issue of antibiotic resistance in general, prescribing of antibiotics at health centres, factors influencing antibiotic prescribing, interventions implemented so far, interventions that should be implemented, and anticipated challenges in implementing the suggested interventions.

For the key informants from sub-cities and the Health Bureau, the interview guide (Annexure K) included questions in relation to the inclusion of antibiotic and antibiotic resistance related issues in the annual plans, and performance reports and supportive supervision activities in addition to the basic questions on antibiotic prescribing, factors influencing antibiotics prescribing, interventions implemented so far, interventions that should be implemented to improve the prescribing of antibiotics at health centres, and implementation challenges.

3.4.2.3 Pre-testing of data collection instruments

Prior to the actual data collection, each of the data collection instruments were pre-tested in two public health centres (Teklehaimanot and Abebe Bikila Health Centers) that were randomly picked from two of the sub-cities selected for the study (Addis Ketema and Lideta Sub-cities). The in-depth interview guide used for the interview with prescribers was pre-tested with four prescribers from the two health centres where the data abstraction forms were pre-tested. The key informant interview guide was also pre-tested in these two health centres by interviewing the medical director of Abebe Bikila Health Center and the pharmacy team coordinator of Teklehaimanot Health Center. The research assistant has participated in the pilot-test conducted in the two health centres. The qualitative data collection was included in the Research Confidentiality Agreement (Annexure G) singed with the research assistant that supported the qualitative data collection, in addition to the quantitative data collection.

3.4.2.4 Recruitment and training of research assistants

For the qualitative phase, a two-day training was provided for the researcher and research assistants on qualitative study with a focus on in-depth interviews by a senior researcher and academician from the School of Public Health, Addis Ababa University who has a PhD in Public Health and long experience in qualitative research. Basics of qualitative studies, data collection, data management, coding, and data analysis using thematic content analysis with a focus on in-depth interviews were covered during the training. A demonstration on undertaking in-depth interviews with prescribers was also made using the interview guides, and the interview guides were reviewed in line with the study objectives and research questions. One of the research assistants who participated in the quantitative data collection was selected to assist the researcher in the qualitative data collection. The focal person from each health centre provided support in communicating with prescribers with respect to participation in the in-depth interviews.

3.4.2.5 Data collection

From a researcher's perspective, appropriate preparation; demonstration of respect for interviewees; intensive listening by the interviewer; development of thoughtful interview guides that include fewer questions; formulation of short, open-ended questions; flexibility on the part of the interviewer to deviate from prior plans when necessary; effective use of follow-up questions to elicit extended descriptions; and the ability to help participants tell their stories and the characteristics of ‘good’ interviewing practices (Roulston & Choi 2018: 10).

To allow free expression of ideas, the interview with both prescribers and key informants was conducted in Amharic. The Amharic language is a widely spoken local language and working language of the Federal Government of Ethiopia and of the City Administration in which this study was conducted. Unique identifiers that contained the interviewee profession (NU – Nurse and HO – Health Officer) for prescribers and role

(PS – Pharmacy Service and MS – Medical Service) for key informants plus a two digit number that shows the order of the interview for each category was used for each of the study participants (e.g., HO03 is the 3rd health officer interviewed). To ensure uniformity in the interview process, a checklist (Annexure L) that contained the key step-by-step actions that the interviewer was expected to undertake during the interview was developed and used by the researcher and research assistant.

The main questions asked to prescribers and key-informants were about the antibiotics prescribing and resistance situation, antibiotic prescribing and usage problems, factors influencing the antibiotic prescribing practices, measures taken so far to promote the prescribing of antibiotic at health centres, actions that should be taken to improve the situation, and challenges that might hinder implementation of the suggested interventions.

a) Interview with prescribers

Supported by the focal person from the five health centres selected for the qualitative study, prescribers with a mix of professions and genders from different clinical units (adult outpatient, paediatric outpatient and emergency units) that have served in the health centres for at least 2 years were approached by the researcher and research assistant. For prescribers willing to participate in the study, a briefing on the objectives of the study, the data to be collected, the method of data collection, and confidentiality of the information they would be providing was provided at their work place. Most of the interviews were conducted on the day of the visit to the health centre. Alternate dates and times were agreed upon with those prescribers who were not able to make the interview on the initial date of the visit. The interviews with prescribers were conducted in the examination rooms in which they provide healthcare service.

Prior to starting the one-on-one interviews, permission was requested and granted from each prescriber to audio record the interview to have full information for data analysis and presentation. Then, prescribers were asked to read the Participant's Information Sheet (Annexure M), ask questions if any, and sign the consent form (Annexure N) in duplicates; one copy for the researcher and one copy for the prescriber.

After collecting the copy of the signed consent form, the interviewer (researcher or research assistant) switched-on the audio recorder (personal mobile apparatus) and proceeded to asking the questions using the interview guide. Information on the age, gender, qualification, years of experience, and patient load per day was taken at the beginning of the interview. Each participant was allowed to talk freely on each area selected for the interview as per the guide. Probing questions were posed in between to solicit additional information on each issue under discussion. In addition to the audio record, field notes were taken as much as possible.

b) Key informant interview

In-depth interviews were conducted with key informants from the selected health centres, health offices of the five sub-cities, as well as the Medical Service, and the Pharmaceutical Service and Supply Directorates of the City Administration Health Bureau. The objectives of the study, the data to be collected as well as the data collection method and confidentiality of the data to be collected from them were explained to each key informant. An alternate date and time for the interview was agreed upon with each key informant who was not able to make the interview on the first date of visit. On the date of data collection, the researcher/research assistant met each key informant in his/her office where they were then asked to read the information sheet (Annexure O), ask questions if there were any, and sign the consent form (Annexure P) in duplicate.

After collecting a copy of the signed consent form, the interviewer switched on the audio recorder (mobile apparatus) and started asking the questions using the interview guide. The interview began by taking data on the age, gender, qualification, years of experience, and title of the key informant. Each participant was allowed to talk freely on each area selected for the interview as per the guide. Probing questions were posed in between to obtain more information on each issue under discussion. In addition to the audio record, field notes were taken as much as possible.

The researcher has attended UNISA seminars on quantitative and qualitative data analysis as part of the PhD study. In addition to that, the researcher has thoroughly read the ATLAS.ti 9 user manual and attended all the video presentations detailing how to create projects, coding transcripts, splitting, merging and renaming codes, generating a code book, and exporting quotations by theme and sub-theme.

3.4.3 DATA MANAGEMENT

3.4.3.1 Data entry

The data collected from the prescribers and key informants was first transcribed verbatim by the researcher and research assistant from the audio record to text form in Amharic. The transcribing began while data collection was underway. Each transcript was then translated to English by the researcher and were randomly checked by the research assistant. Each transcript was read at least twice to establish a general impression of the data contained in each transcript. Each transcript was then entered into ATLAS.ti 9 for coding and analysis. Two sets of projects were created on the ATLAS.ti 9; one for the data from prescribers and the other for data from key informants. Each transcript was entered as a word document identified by the unique identifier used for each prescriber and key informant. The ATLAS.ti 9 software was downloaded online using UNISA's License Agreement with support from the Information Technology Unit of UNISA-Ethiopia Learning Center.

3.4.3.2 Data analysis

The qualitative component of the study aimed predominantly at identifying the factors that affect the decision to prescribe antibiotics, potential interventions that participants of the study (both prescribers and key informants) think should be implemented, and the potential barriers and facilitators in implementing the suggested interventions. The data collected from prescribers and key informants was analysed separately by applying the same procedure. Once the data collection was over and all audios transcribed to text form and translated to English, the translated data was entered into and analysed through thematic content analysis using ATLAS.ti 9 software. Socio-demographic characteristics of the participants were analysed using Microsoft Excel.

According to Dawadi (2020: 62–63), thematic analysis is a qualitative research method that researchers use to systematically organise and analyse complex data sets. With the goal of searching for themes that can capture the narratives available in complex data sets, it involves the identification of themes through careful reading and re-reading of the transcribed data. A rigorous thematic analysis approach can produce insightful and trustworthy findings. Thematic analysis can be made both deductively (top-down) and inductively (bottom-up) way. In the inductive analysis, the data is coded without trying to fit the themes into a pre-existing coding frame. On the other hand, the deductive approach is explicitly researcher-driven allowing the researchers to analyse the data in relation to their theoretical interest in the issues being investigated.

The results of a thorough thematic analysis technique can be reliable and enlightening. There are two methods of analyzing a theme: deductive (top-down) and inductive (bottom-up). Without attempting to fit the themes into an already-existing coding framework or the researcher's beliefs about the research, the data is coded in an inductive approach. The deductive approach, on the other hand, is specifically geared toward researchers and enables them to analyze the data in light of their theoretical interest in the problems being investigated.

In this study, the thematic content analysis was conducted by applying the deductive (top-down) approach as the themes were already defined by the selected model. Guided by the research questions and the main questions of the interview guides which were developed based on the phases of the theoretical model used, the researcher prepared a code book that contained the major themes and sub-themes with definitions. Each of the transcripts were then coded thematically into the main themes which were later split into sub-themes by repeatedly going through the transcripts line by line. According to the ATLAS.ti 9 User Manual (https://doc.atlasti.com/ManualWin.v9/Codes/CodingData.html), coding distils data, sorts them, and gives an analytic handle for making comparisons with other segments of data. Coding is the strategy that moves data from diffuse and messy text to organised ideas about what is going on. Coding is a core function in ATLAS.ti that lets you tell the software where the interesting things are in your data.

The themes and sub-themes were grouped within the framework of the theoretical model into information about antibiotic prescribing and resistance, types of antibiotic prescribing and use problems, consequences of irrational antibiotic prescribing and resistance, factors influencing antibiotic prescribing (predisposing, enabling and reinforcing factors), interventions implemented so far to improve antibiotic prescribing, interventions to improve antibiotic prescribing, and the expected implementation challenges that should be considered in implementing the suggested interventions. Series of coding and recoding were undertaken by merging and splitting already created codes through a repeated process till the final themes and sub-themes emerged from each of the transcripts.

The themes and sub-themes generated from content analysis of the collected data are used to present findings of the qualitative study. While presenting the findings, each of the themes and sub-themes are supported by relevant quotes from participants indexed by the interviewee code. The qualitative findings are also discussed in relation to findings of the quantitative study.

3.5 ETHICAL CONSIDERATIONS

A researcher commits to a range of responsibilities when deciding to undertake research. All research involves ethical decisions. A responsible researcher need to afford the following considerations to the research participants (Nolan, Macfarlane & Cartmel 2019: 2–3):

- that they will be fully informed of the research process before making a decision on their involvement,
- that participation is voluntary (they have the right to withdraw without penalty or any ill-effects),
- that participants' rights will be upheld, and
- that information will be treated confidentially.

In this study, the researcher applied various techniques to ensure that ethical principles are maintained throughout the research process.

3.5.1 Ethical clearance

Ethical clearance was obtained from the Research Ethics Review Committee of the College of Human Sciences, UNISA with CREC Reference Number 64093352_CHS _CREC_2020 (Annexure E). Based on this clearance, ethical approval was obtained from the Research Ethical Clearance Committee of Addis Ababa City Administration Health Bureau (after reviewing the research proposal) with the reference number indicated on the attached ethical approval letter (Annexure H). Permission to conduct the study was granted through these official letters from the Ethics Committee addressed to the selected Sub-City Health Offices and then from the sub-cities to health centres. At facility level, permission was obtained from the Medical Directors of the selected health centres and heads of the sub-city health offices involved in the key informant interview after explaining objectives of the study, the type of data to be collected and the data collection procedures. Ultimate permission to access prescriptions and patient medical charts as a source of data were obtained from Medical Director of each health center as per the support letter from sub-city and brief discussion conducted with the researcher. In each health center, it was the Medical Director or his/her delegate who linked the researcher with Medical Record Unit and Pharmacy Unit for the necessary support to collect the data.

3.5.2 Informed consent

Informed consent is a formal agreement made by individuals willing to participate in research, having been fully advised of the potential benefits, risks, and the procedures or activities of research participation. Informed consent is considered an essential aspect of good research ethics practice (Parsons 2018: 2). In this study, informed consent was obtained from each of the prescribers (Annexure N) and key informants (Annexure P) prior to data collection after explaining purpose of the study and assuring confidentiality of the data obtained from them supported by Participant Information Sheets (Annexures M and O). Participation in this study was on voluntary basis and participants were informed that their participation was voluntary and that they had the right to discontinue their participation at any point during the interview if they so wished.

3.5.3 Confidentiality

Confidentiality of the data and reports generated from it were maintained by using codes in place of prescriber and patient names and other personal identifiers. Patient- and respondent-specific information such as names were not recorded and hence not used during data analysis. In addition, the collected data was kept secured from unauthorised individuals so as to ensure confidentiality of the information. To ensure confidentiality of patient-specific information, medical charts as well as prescriptions were handled with great care and all the data was collected within each health centre's compound.

3.5.4 Autonomy

Prior to data collection, information on the research and its objectives were given to participants by the researcher. Participants had the opportunity to ask questions related to the research undertakings before any data collection. Participants were also informed that they have the right to withdraw from the study if they so wished.

3.6 INTEGRATION OF THE FINDINGS

Each true mixed methods study has at least one "point of integration", also called the "point of interface" at which the qualitative and quantitative components are brought together. Having one or more points of integration is the distinguishing feature of a design based on multiple components. It is at this point that the components are "mixed", hence the label "mixed methods designs". In the design of mixed methods research, determining where the point of integration will be and how the results will be integrated, is an important decision. Some primary ways that the components can be connected to each other are as follows (Schoonenboom & Johnson 2017: 116):

1. merging the two data sets,
2. connecting from the analysis of one set of data to the collection of a second set of data,
3. embedding of one form of data within a larger design or procedure, and
4. using a framework (theoretical or program) to bind together the data sets.

In this study, the two data sets (quantitative and qualitative) were integrated using the theoretical framework selected for the study. The quantitative data was used to understand the antibiotics prescribing situation on the ground (Phase 1 and 2 of the Model) and preliminary findings of the quantitative data were used in designing the qualitative study. The qualitative data provided detailed information on the factors that influenced the antibiotic prescribing decision of prescribers that resulted in the observed prescribing behaviour (Phase 3 of the Model) and on actions that should be taken to shape the prescribing behaviour along with the anticipated challenges that should be taken into consideration in designing the interventions (Phase 4 of the Model).

At the point of interpretation, the findings from both phases of the study were brought together and discussed comprehensively by having the prescribing practice at the center. It was based on the integrated findings that the intervention guidelines to improve antibiotic prescribing were developed.

3.7 DEVELOPMENT OF INTERVENTION GUIDELINES (PHASE III)

Based on the findings of the quantitative and qualitative studies, the researcher developed intervention guidelines aimed at improving antibiotic prescribing in the study setting. The guidelines were developed mainly based on the interventions suggested by study participants, the antibiotic prescribing problems identified, the factors influencing the prescribing of antibiotics, and challenges that are expected to be faced while implementing the suggested interventions.

Depending on their nature, the guidelines were categorized into ten. Only high level description of the intervention guideline is provided with list of specific interventions under each of the guidelines. Though Phase I and Phase II of the study have their own purpose and research questions to be answered, ultimate purpose of the study was the development of intervention guideline to improve antibiotic prescribing at primary healthcare facilities. Figure 3.4 shows schematic representation of the whole research undertaking described above that ended up in developing the intervention guidelines as final goal of the study.

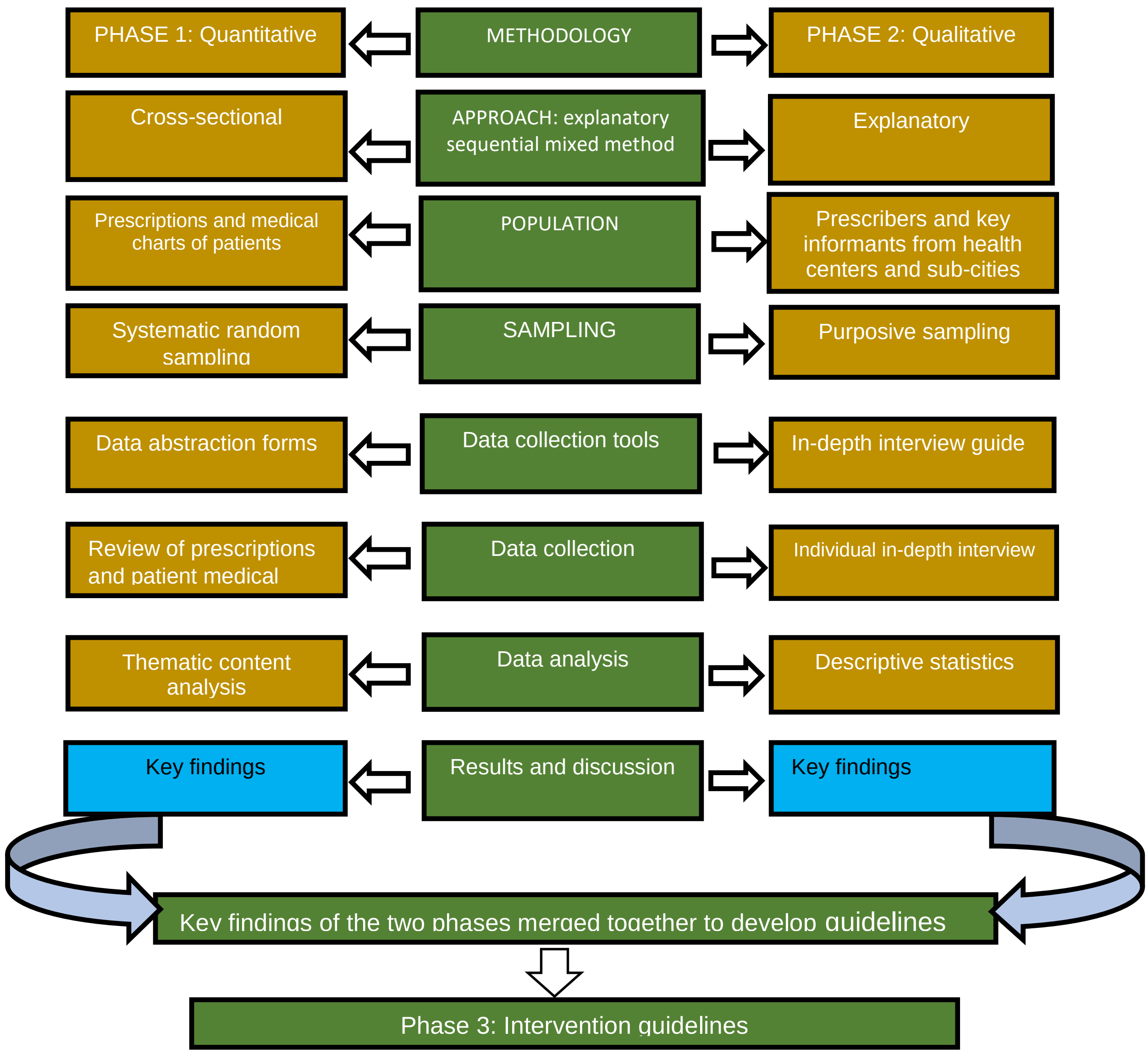


Figure 3.4 Schematic representation of the research undertaking.

3.8 CONCLUSION

This chapter covered the research design and methods used in the study. It gave detailed account of the study design, study setting, sample size determination, study population, sampling procedures, data collection instruments, validity and reliability of the data collection instruments, measures of trustworthiness, data collection, data entry and analysis methods. The techniques used by the researcher to maintain ethical principles in undertaking the study, integration of the quantitative and qualitative data sets and development of the intervention guidelines were also discussed. Findings of the study will be presented and discussed in the next chapter (Chapter 4).

CHAPTER 4: PRESENTATION AND DISCUSION OF THE RESULTS

4.1 INTRODUCTION

Chapter 3 presented research design and methodology of the study. The sampling, data collection and analysis methods used in the quantitative and qualitative phases of the study, the techniques used to ensure reliability, validity and trustworthiness of the data collected, and the ethical considerations in undertaking the study were discussed. In this Chapter, the researcher presents and discusses the findings from both phases of the study. The presentation and discussion will start with the quantitative findings and proceed to the qualitative ones. The findings are compared with available practice standards in the area and finding of similar studies conducted in primary healthcare settings locally and in other LMICs. Triangulation of findings of the quantitative and qualitative studies is conducted and is presented at the end of the chapter.

4.2 PHASE I: PRESENTATION AND DISCUSSION OF THE QUANTITATIVE RESULTS

Quantitative phase of the study focused on the first three research objectives;

- To determine the prevalence (rate) of antibiotics prescribing at primary healthcare facilities;
- To describe the antibiotics prescribing patterns at primary healthcare facilities;
- To assess appropriateness of the antibiotics prescribed to manage common cases at primary healthcare facilities;

As presented in Chapter 3, this phase of the study was conducted in 10 public health centres. The presentation of findings starts with background information of the health centres included in the study and sociodemographic characteristics of the patients and prescribers in relation to the prescriptions reviewed. It then proceeds to a presentation and discussion of the findings on the rate of antibiotic prescribing, antibiotic prescribing pattern and appropriateness of the antibiotics prescribed for respiratory tract infections. The findings are disaggregated by health centre, the sociodemographic characteristics of patients and prescribers as well as season of prescribing as much as possible. The findings are discussed in comparison to findings of similar studies conducted mainly at primary healthcare facilities in Ethiopia and other countries and in reference to available prescribing practice standards as applicable.

4.2.1 Background information of the health centres

As per the annual statistical report of the health centres during the year 2012 EFY (July 2019 to June 2020), the number of patients and clients served by the health centres during the budget year ranges from 20,195 (CFHC) to 474,311 (SMHC) with an average of 91,775 patients per health centre. It was observed that all of the health centres have the Primary Healthcare Clinical Guidelines (PHCG) in each examination room and their own updated medicines list. Pharmacy Case Team Coordinators of the health centres reported that they have functional DTC. As per the information obtained from the Pharmacy Case Team Coordinators, the annual budget allocated for the procurement of pharmaceuticals (medicines, medical supplies and laboratory reagents) during the budget year (2012 EFY) was within the range of Ethiopian Birr (ETB) 1,101,160 (TBHC) to ETB 2,184,166 (WD12HC) with an average of ETB 1,709,481 per health centre.

In terms of the professional mix of healthcare providers involved in patient diagnosis and prescribing of medicines, 9 of the health centres had 1 or 2 medical doctors and all of them had health officers, professional nurses and midwives as per data obtained from the Human Resource Management Units of the health centres during the time of data collection.

It was possible to obtain data on the 2012 EFY disease profile from nine of the health centres included in the study. According to data from the Health Management Information System (HMIS) of the nine health centres, infectious diseases accounted for about 61% of the top ten diseases during the budget year. This ranges from 23% in TBHC to 65% in WD9HC. URTIs, including tonsillitis, common cold and unspecified URTIs, were the first in the list accounting for 39% (range: 0 to 44%) of the top ten diseases and 63% (range: 0 to 71%) of the infectious diseases in the top ten list. In one of the health centres (TBHC), URTIs did not appear in the top ten disease list.

UTIs, typhoid, typhus, gastroenteritis and other unspecified bacterial infections were among the infectious diseases in the top ten diseases list of the health centres.

4.2.2 Patient and Prescriber related information of prescriptions

A total of 2000 prescriptions, corresponding to 2000 patients, were analysed during this phase of the study. The patient and prescriber related information refers to the age and gender of patients for whom the prescriptions were ordered and the qualifications and gender of prescribers who wrote the prescriptions as presented in Table 4.1. The majority of the patients (60.3%), were female with a male to female ratio of 1:1.5. The age group, 15-34 years accounted for the majority (43.0%) of the patients with about 22% of the patients in the paediatric age group (0 – 14 years). The number of females was greater than males across all age groups. Similar findings were reported by a study conducted in six health centres in Addis Ababa (Worku & Tewahido 2018: 3–4) where the majority (61.0%) of the prescriptions were prescribed for females and for patients in the age group of 15–34 years (41.7%).

Table 4.1 Patient and prescriber related information of prescriptions dispensed at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

Variable	Frequency	Percent
Patient's gender(n=1988)		
Female	1 198	60.3
Male	790	39.7
Patient's age in years (n=1981)		
0-14	434	21.9
15-34	852	43.0
35-54	442	22.3
$\geq$ 55	253	12.8
Prescriber’s gender(n=855)		
Female	483	56.5
Male	372	43.5
Prescriber’s qualification (n=1906)		
Health Officer	783	41.1
Midwife	36	1.9
Physician	192	10.1
Professional Nurse	895	47.0

With respect to prescribers, the majority (47.0%) of the prescribers were Professional Nurses followed by Health Officers (41.1%) with only 12% of prescriptions having been written by other professionals, medical doctors and midwives. The data related to the gender of prescribers was collected from only 5 of the health centres (CFHC, ENTHC, MLHC, TBHC, WD9HC) three of which were involved in the qualitative study. According to the data collected, 56.5% of the prescriptions were from female prescribers.

4.2.3 Antibiotic prescribing rate

Table 4.2 summarises the number of medicines and antibiotics prescribed per prescription. A total of 3731 medicines were issued from 2000 prescriptions. This gives an average number of medicines per prescription of 1.87 (95% CI: 1.83, 1.90) ranging from 1.71 (ENTHC) to 2.11 (WD9HC) among the health centres included in the study. This value is marginally lower than the value of 2.0 reported in a study conducted at six health centres in the city in 2017 (Worku & Tewahido 2018: 4). Unlike the findings of the 2017 study where the majority (45.3%) of the prescriptions contained two medicines, there was no that much difference between the number of prescriptions containing one medicine and those with two medicines, 38.2% and 40.8% respectively in the current study. Currently, 21% of the prescriptions contain three or more medicines which is lower than the 25% reported by the 2017 study. There were a limited number of prescriptions (0.4%) that contained up to 6 medicines.

At least one antibiotic was prescribed in 1049 of the prescriptions. This means that the percentage of prescriptions containing one or more antibiotics was 52.5% ranging from 41.5% at TBHC to 61.5% at CFHC. This is lower than the value reported in the 2017 study (Worku & Tewahido 2018: 4) where 56.0% of the prescriptions reviewed contained one or more antibiotics with the value ranging from 46.7% to 67.3% among the health centres included in that study. A total of 1138 antibiotics were prescribed on those 1049 prescriptions which gives an average number of antibiotics of 0.57 (95% CI: 0.54-0.59) out of the total number of prescriptions and 1.08 out of prescriptions containing one or more antibiotics.

In terms of total number of medicines prescribed, antibiotics accounted for 30.5% of the medicines prescribed which is similar to the value (30.8%) reported by the study conducted in 2017 (Worku & Tewahido 2018: 4). Of the prescriptions that contained one or more antibiotic, the majority (92.3%) contained one antibiotic with only 81(7.8%) of the prescriptions containing 2 or more antibiotics. It was shown that 99.6% of the antibiotics prescribed were included in the medicines lists of the health centres. From the health centres' own medicines' list it was azithromycin that was prescribed out of the list in four prescriptions (0.4%) from three of the health centres.

Table 4.2 Number of medicines and antibiotics prescribed per prescription at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

Category	Number of medicines or antibiotics per prescription	Number of prescriptions	Percent	Cumulative percent
All medicines (*n* = *2000*)	1	764	38.2	38.2
	2	816	40.8	79.0
	3	353	17.7	96.7
	4	60	3.0	99.7
	5	6	0.3	100.0
	6	1	0.1	100.0
Antibiotics (*n = 1049*)	1	968	92.3	92.3
	2	73	7.0	99.2
	3	8	0.8	100.0

The percentage of encounters with one or more antibiotic prescribed is one of the core prescribing indicators used to objectively measure the patterns of antibiotic prescribing. This indicator has been widely used to determine the prevalence of antibiotic prescribing at facility, region and country level. The WHO recommends that the percentage of encounters with one or more antibiotics prescribed should be less than 30% for general outpatients in primary healthcare facilities, with a higher percentage indicating a higher risk of antibiotic resistance (Ofori-Asenso et al. 2016: 2). In contradiction to this recommendation, most of the medicine use studies conducted at primary healthcare facilities in Ethiopia and other countries reported a far higher rate of antibiotics prescribing than the one recommended by WHO.

Various medicine use studies were conducted in different parts of Ethiopia most of which were general medicine prescribing studies (not antibiotic specific), conducted in hospitals with few studies conducted at primary healthcare level. A very high rate of antibiotic prescribing was reported from a study conducted in health centres found in the Somali Regional State, Eastern Ethiopia that reported a value of 82.5%. A relatively lower, but still high percentage of antibiotic prescribing was reported by a study conducted in primary healthcare facilities in Addis Ababa (Worku & Tewahido 2018: 4) which indicated an antibiotic prescribing rate of 56.0%. The findings from a primary healthcare facility in Bahir Dar City, Northwest Ethiopia showed a lower antibiotics prescribing rate (41.3%).

Three national pharmaceutical sector assessments have been conducted in Ethiopia during the last 20 years, in 2002, 2009 and 2016. According to the 2002 assessment (FMOH and WHO 2003: 23–24), the percentage of prescriptions with one or more antibiotics was 58%. Disaggregation by region showed that the antibiotic prescribing rate varied among the six regions included in the study between 44.2% (Benishangul-Gumuz) to 87.7% (Addis Ababa). By level of health facility, the average percentage of antibiotic prescribing rate was 55.4%, 62.3% and 57.3% for hospitals, health centres and health posts, respectively. This shows that the rate of antibiotic prescribing was the highest in Addis Ababa City Administration and health centres were the healthcare facilities with the highest rate of antibiotic prescribing.

The 2010 national assessment (FMOH and WHO 2010: 32) revealed a similar percentage of antibiotic prescribing rate (60%) indicating the persistence of a high level of antibiotic use in the country. The national pharmaceutical sector assessment conducted in 2016 (EFMHACA and WHO 2017: 31) reported an antibiotics prescribing rate of 30% which is far below the value reported by previous national assessments and studies conducted in healthcare facilities in different parts of the country.

Studies conducted at primary healthcare facilities in the country showed an antibiotics prescribing rate ranging from 41.3% (Bantie 2014: 1187) to 82.5% (Bilal et al. 2016). The study conducted in Addis Ababa City in 2017 (Worku & Tewahido 2018: 4) at primary healthcare facilities showed an antibiotic prescribing rate of 56.0% that falls somewhere in the middle of these extreme values with a wide variation among the health centres included in the study (range: 46.7% to 67.3%). The rate of antibiotic prescribing in the current study is a bit lower than the value reported in the 2017 study. Various factors might have contributed for the relative reduction in the rate of antibiotic prescribing in the current study as compared to the rate reported in the 2017 study in the same setting. Though not yet fully implemented, introduction of the new Primary Healthcare Clinical Guideline (PHCG) might have contributed to the reduction of antibiotic prescribing as all of the health centres included in the study have started implementing the guidelines.

The antibiotic prescribing rate in the current study is comparable with findings of similar studies conducted at primary healthcare facilities in other countries. More or less similar findings were reported from studies conducted at primary healthcare facilities in China (Yin et al. 2013: 2449), in six African countries (Richard Ofori-Asenso and Akosua Adom Agyeman 2015: 178), and by a systematic review of studies published from 2010 to 2019 that assessed antibiotic prescribing at primary healthcare facilities across many countries (Sulis et al. 2020: 9) with antibiotic prescribing rates of 50.3%, 51.5%, and 52%, respectively. The rate of antibiotic prescribing in the current study is higher than the one from a study conducted from 1995-2015 at primary healthcare facilities in the WHO African Region, 46.8% (Ofori-Asenso et al. 2016: 7) but lower than the findings of studies conducted at primary healthcare facilities in Ghana, 59.9% (Ahiabu et al. 2016: 5) and Nigeria, 55% (Adisa et al. 2015: 1323).

As shown in Table 4.3, majority of the prescriptions with one or more antibiotics (46.3%) were prescribed for patients in the 15 – 34 year age group followed by the paediatric age group of 0-14 years (27.1%). In the 2017 study (Worku & Tewahido 2018: 4), majority of the prescriptions (69.8%) with antibiotics were prescribed for patients in the paediatric age group. In terms of patient gender, most of the prescriptions with antibiotics (60.3%) were prescribed for females which is comparable with the 2017 study though the percentage is a bit higher in the current study. Female prescribers were shown to have prescribed more prescriptions with antibiotics (54.1%) than male prescribers (45.9%). Qualification wise, majority (50.6%) of the prescriptions containing antibiotics were ordered by Professional Nurses followed by Health Officers (41.1%).

Table 4.3 Prescriptions containing antibiotics by sociodemographic characteristics of patients and prescribers at primary healthcare facilities in Addis Ababa, Sept.1, 2019 to Aug.31, 2020.

Variable	Frequency	Percentage
Patient gender		
Female	628	60.3
Male	414	39.7
Total	1 042	100.0
Patient Age (Years)		
0 – 14	282	27.1
15 – 34	482	46.3
35 – 54	198	19.0
$\geq$ 55	78	7.5
Total	1 040	100.0
Prescriber's gender		
Female	258	54.1
Male	219	45.9
Total	477	100.0
Prescriber Qualification		
Health Officer	411	41.1
Midwife	8	0.8
Physician	75	7.5
Professional Nurse	505	50.6
Total	999	100.0

4.2.4 Antibiotic prescribing rate by season of prescribing

Figure 4.1 presents the rate of antibiotic prescribing by season of prescribing. The antibiotic prescribing rate showed a declining trend from quarter to quarter. The antibiotic prescribing rate was 57.1% during the first quarter of the data period (September 1 to November 30, 2019), declining quarter by quarter until the 4th quarter (June 1 to August 31, 2020) where it became 45.1%. This reflects an overall rate of decline of 21.0% from quarter 1 to quarter 4.

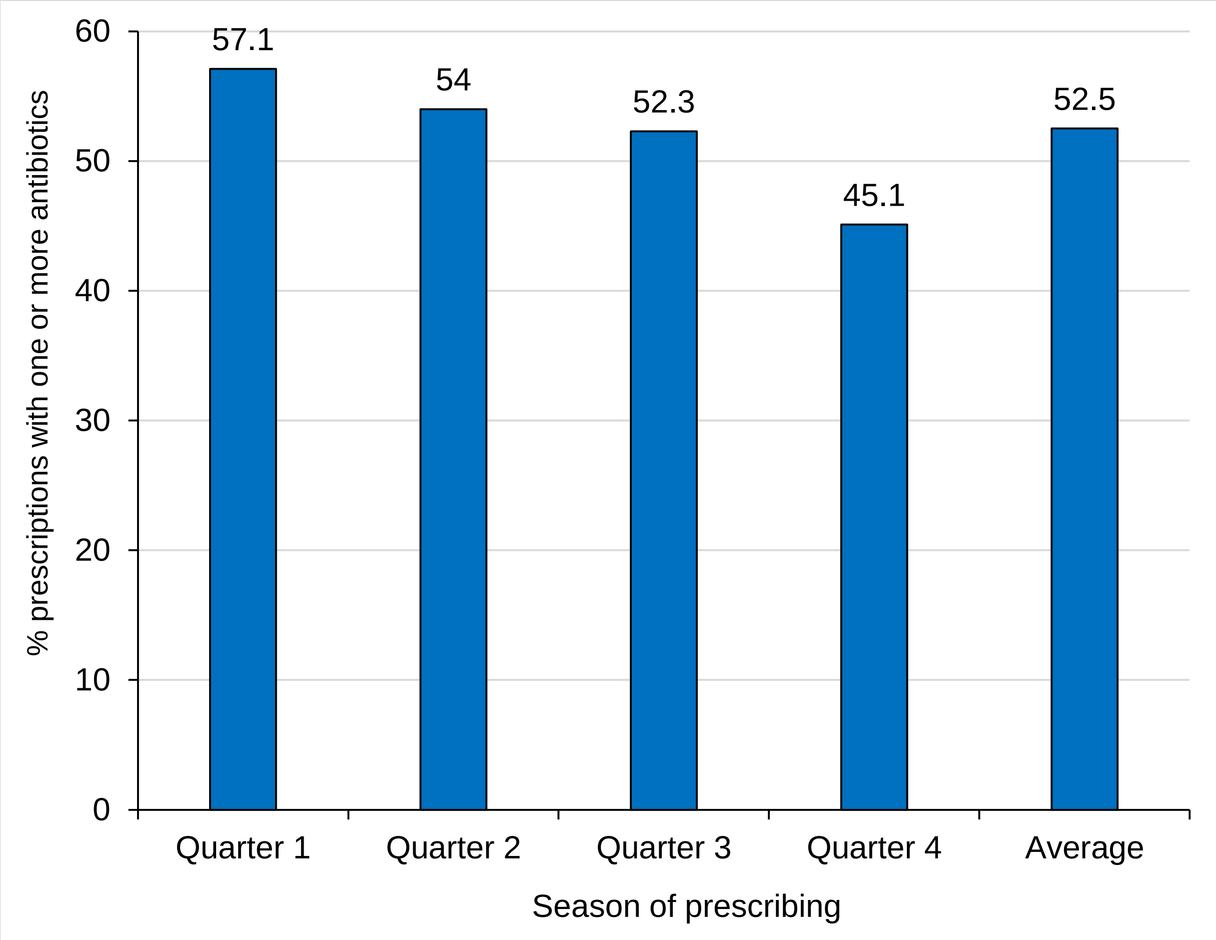


Figure 4.1 Antibiotic prescribing by season of prescribing at primary healthcare facilities in Addis Ababa, September 1, 2019 to August 31, 2020.

When aggregated into first and second halves of the year, the rate of antibiotic prescribing during the first half (September 1, 2019 to February 28, 2020) was 55.7%, whereas, it was 48.7% during the second half (March 1 to August 31, 2020) which shows an overall reduction of 12.6%. The second half of the data period was the time when the COVID-19 pandemic was reported in the country, with the first case reported on March 13, 2020. The serious protective measures taken during that time such as the use of face mask, maintaining physical distance and frequent hand-washing to prevent spread of the pandemic might have contributed for the reduction in the number of URTI cases and by extension the antibiotics that would have been prescribed for them. Fear of the pandemic had resulted in a significant reduction in the number of patients visiting health facilities during that time with people tended to visit health facilities only when they face serious health problems. This too might have contributed for the reduction in the number of URTIs and the antibiotics prescribed for these cases thereby for the overall reduction in antibiotic prescribing rate during second half of the data period.

This could be attributed to a reduced number of respiratory tract cases resulting from face mask usage and other preventive measures that were introduced during the pandemic. This might also be because patients with COVID-like symptoms are referred to COVID centres. It is also known that due to fear of contracting COVID, patients were not visiting health facilities during the pandemic unless they faced serious health problems. Patients with minor cases such as upper respiratory problems might not go to health facilities during this time, hence the reduction in the antibiotic prescribing rate. Implementation of the PHCG might have also contributed to the reduction in antibiotic prescribing during the pandemic.

When disaggregated by health centre, the antibiotic prescribing rate was lower during the second 6 months (March 01 to August 31, 2020) than during the first six months (September 01, 2019 to February 28, 2020) in eight of the health centres (Figure 4.2). The highest reduction was seen at WD9HC (from 67.3% to 48.4%) which is a reduction of 28.1% followed by ENTHC (64.5% to 51.6%), a reduction of 20%, followed by KMHC (from 53.3% to 43.0%) a reduction of 19.3%. The minimum reduction was observed at LDHC with a reduction of only 2.7% (from 48.6% to 47.3%). As discussed above, the overall average decline in rate of antibiotic prescribing was 12.6% (from 55.7% to 48.7%).

In two of the health centres(SMHC and WD12HC), the antibiotic prescribing rate has increased during the second six months as compared to the first six months by 10.8% (WD12HC) and 5.8% (SMHC). The reasons described above may justify the reduction in antibiotic prescribing rate in the majority of the health centres. For the two health centres in which the antibiotic prescribing rate has increased, it may be related to the PHCG implementation status.

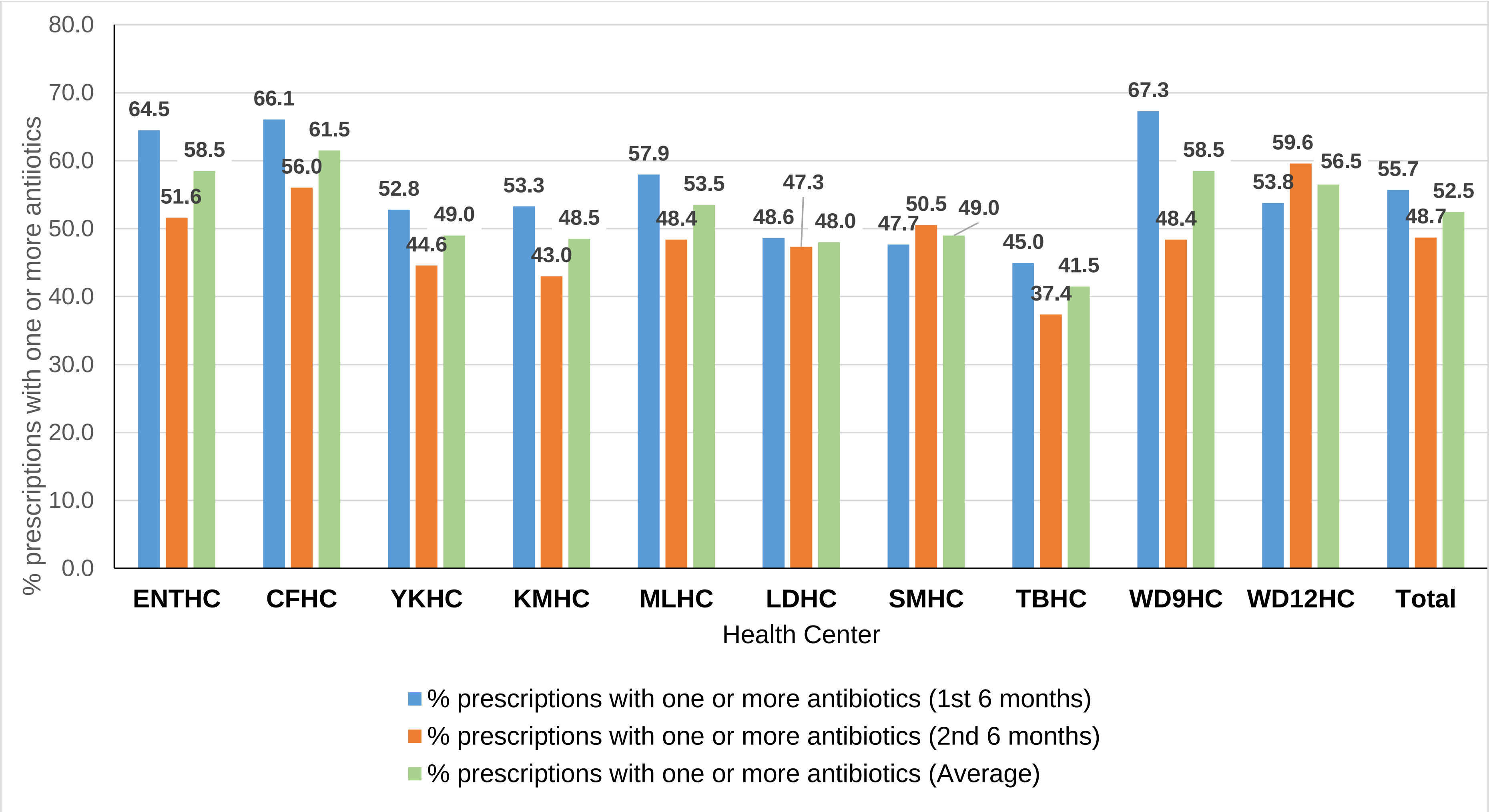


Figure 4.2 Antibiotic prescribing rate by health centre during the first and second 6-month of the year at primary healthcare facilities in Addis Ababa, Ethiopia, September 01, 2019 to August 31, 2020.

4.2.5 Antibiotic prescribing pattern

This includes identifying the common class and type of antibiotics prescribed, the diagnosis for which the antibiotics were prescribed, the common dosage forms of the prescribed antibiotics, AWaRe category of the prescribed antibiotics, and cost of the antibiotics. Unlike the rate of antibiotic prescribing, studies that assess antibiotics prescribing pattern at primary healthcare facilities are very limited.

4.2.5.1 Types of antibiotics prescribed

Twenty different types of antibiotics were prescribed in the 1049 prescriptions with a total antibiotic count of 1138 (Table 4.4). Amoxicillin was the most commonly (41.2%) prescribed antibiotic followed by ciprofloxacin (14.1%) and cloxacillin (9.6%). Amoxicillin-based antibiotics (amoxicillin and amoxicillin + clavulanic acid) accounted for about 45% of the antibiotics prescribed. Five antibiotics (amoxicillin, ciprofloxacin, cloxacillin, doxycycline and cotrimoxazole) accounted for nearly 80% of the antibiotics prescribed. Overall, ten of the antibiotics accounted for 94% of the antibiotics prescribed. Floxacillin (0.1%), procaine penicillin fortified (0.1%), clarithromycin (0.2%), erythromycin (0.3%) and ampicillin (0.4%) were the five least prescribed antibiotics.

Fifteen of the antibiotic prescribed in In the 2017 study conducted in by Worku & Tewahido (2018: 5), 15 different types of antibiotics were prescribed. The five antibiotics in the current study that were not reported in the 2017 study are ampicillin, benzathine penicillin, clarithromycin, floxacin and procaine penicillin fortified. These antibiotics accounted for 1.5% of the antibiotics prescribed. The remaining fifteen antibiotics are same as those reported in the 2017 study.

Amoxicillin and ciprofloxacin were the top two commonly prescribed antibiotics in the study conducted by Worku & Tewahido (2018: 5) at health centres in Addis Ababa with a rate that is not far from findings of the current study. There is a difference in the third top antibiotic between the two studies. In the current study, cloxacillin is the third one whereas in the previous study, the third one was cotrimoxazole. This could be as a result of the change in clinical protocol related to the introduction of the PHCG at health centres.

Table 4.4 Types of antibiotics prescribed at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

S/N	Name of antibiotic	Frequency	Percent	Cumulative percent
1	Amoxicillin	469	41.2	41.2
2	Ciprofloxacin	161	14.1	55.4
3	Cloxacillin	109	9.6	64.9
4	Doxycycline	86	7.6	72.5
5	Cotrimoxazole	76	6.7	79.2
6	Amoxicillin + Clavulanic acid	39	3.4	82.6
7	Norfloxacin	39	3.4	86.0
8	Metronidazole	33	2.9	88.9
9	Azithromycin	30	2.6	91.6
10	Ceftriaxone	28	2.5	94.0
11	Tetracycline	22	1.9	96.0
12	Chloramphenicol	10	0.9	96.8
13	Gentamycin	9	0.8	97.6
14	Benzathine penicillin	8	0.7	98.3
15	Cephalexin	7	0.6	98.9
16	Ampicillin	5	0.4	99.4
17	Erythromycin	3	0.3	99.6
18	Clarithromycin	2	0.2	99.8
19	Floxacillin	1	0.1	99.9
20	Procaine penicillin fortified	1	0.1	100.0

In terms of specific antibiotics, amoxicillin (including amoxicillin-clavulanic acid) was the most frequently prescribed antibiotic (47.5%) with about 50% of the amoxicillin prescribed for URTIs in the study conducted at primary healthcare facilities in Addis Ababa (Worku & Tewahido 2018: 5). Amoxicillin was the most frequently prescribed antibiotic in many other studies conducted in Ethiopia with a prescribing rate ranging from 16.4% to 44.4% (Yimenu et al. 2019; Sisay et al. 2017; Bilal et al. 2016; Bantie 2014; Desalegn 2013). Other commonly prescribed antibiotics include ciprofloxacin, cotrimoxazole (Yimenu et al. 2019: 4; Worku & Tewahido 2018: 4; Sisay et al. 2017: 3; Bilal et al. 2016: 4; Bantie 2014: 1188), and metronidazole (Yimenu et al. 2019; Bantie 2014: 1188).

4.2.5.2 Classes of the antibiotics prescribed

As presented in Table 4.5, the 20 antibiotics prescribed belong to nine antibiotic categories. Penicillins were the most commonly prescribed class of antibiotics prescribed in 632 (55.5%) of the prescriptions followed by fluoroquinolones and tetracyclines prescribed in 200 (17.6%) and 108 (9.5%) of the prescriptions, respectively. These three antibiotic categories accounted for about 83% of the antibiotics prescribed. Aminoglycosides and chloramphenicol were the least prescribed class of antibiotics.

Table 4.5 Class of antibiotics prescribed at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

S/N	Antibiotic class	Frequency	Percent	Cumulative percent
1	**Penicillins** ▪ Amoxicillin ▪ Amoxicillin + clavulanic acid ▪ Benzathine Penicillin ▪ Cloxacillin ▪ Floxacillin ▪ Procaine penicillin fortified	632	55.5	55.5
2	**Fluoroquinolones** ▪ Ciprofloxacin ▪ Norfloxacin	200	17.6	73.1
3	**Tetracyclines** ▪ Doxycycline ▪ Tetracycline	108	9.5	82.6
4	**Sulphonamides** ▪ Cotrimoxazole	76	6.7	89.3
5	**Cephalosporins** ▪ Ceftriaxone ▪ Cephalexin	35	3.1	92.4
6	**Macrolides** ▪ Azithromycin ▪ Clarithromycin ▪ Erythromycin	35	3.1	95.4
7	**Metronidazole**	33	2.9	98.3
8	**Chloramphenicol**	10	0.9	99.2
9	**Aminoglycosides** ▪ Gentamycin	9	0.8	100.0

Similar finding was reported by a study conducted at primary healthcare facilities in Addis Ababa (Worku & Tewahido 2018: 4) where penicillins were the most commonly prescribed (51.9%) class of antibiotics followed by fluoroquinolones (18.3%). The third antibiotic class in the current study is tetracyclines (9.5%), whereas, it was sulphonamides in the previous study with a prescribing rate of 11.2%. In both studies, antibiotics that belong to the first three categories accounted for over 80% of the antibiotics prescribed.

Studies from other countries reported similar findings on antibiotics prescribing pattern. According to studies conducted in Turkey (Mollahaliloglu, Alkan, Donertas, Ozgulcu & Akici 2013: 283) and Cameroon (Chem et al. 2018: 10), the most commonly prescribed group of antibiotics were penicillins accounting for 29.2% and 45.8% of the antibiotics prescribed, respectively. A similar finding was reported from Malaysia (Ab Rahman et al. 2016: 3) where penicillins were the most commonly prescribed group of antibiotics (30.7%) with cephalosporins and macrolides being the 2nd (23.6%) and 3rd (16.0%) frequently prescribed antibiotic groups.

Amoxicillin was the most commonly prescribed antibiotic accounting for 25.4%, 73.5%, and 29.3% of medicines prescribed in studies conducted at primary healthcare facilities in Nigeria (Adisa et al. 2015: 1324), Indonesia (Andrajati et al. 2017: 45) and Cameroon (Chem et al. 2018: 8), respectively. The second commonly prescribed antibiotic was cotrimoxazole in the studies conducted in Indonesia (Andrajati et al. 2017: 45) and Cameroon (Chem et al. 2018: 8) accounting for 17.4% and 19.1% of the antibiotics prescribed, respectively.

4.2.5.3 Route of administration of the antibiotics prescribed

Most of the antibiotics, 1048 (92.7%), were prescribed for oral administration. Antibiotics prescribed for topical application and injection accounted for 42 (3.7%) and 41 (3.6%) of the antibiotics prescribed, respectively. As presented in Table 4.6, of the antibiotics prescribed in injection form, ceftriaxone is the most frequently prescribed (68.3%) followed by benzathine penicillin (19.5%) and ampicillin (9.8%). There were four antibiotics prescribed for topical application. Tetracycline was the first contributing

52.4% of the antibiotics prescribed for topical application followed by gentamycin (21.4%).

Table 4.6 Route of administration of the antibiotics prescribed at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

Route of Administration	Antibiotic	Frequency	Percentage
Parenteral	Ceftriaxone	28	68.3
	Benzathine Penicillin	8	19.5
	Ampicillin	4	9.8
	Procaine Penicillin Fortified	1	2.4
	Total	**41**	**100**
Topical	Tetracycline	22	52.4
	Gentamycin	9	21.4
	Ciprofloxacin	8	19.1
	Chloramphenicol	3	7.1
	Total	**42**	**100**

In the 2017 study (Worku & Tewahido 2018: 4), most of the antibiotics prescribed were for oral administration (94.8%) followed by topical (2.7%) and parenteral (2.5%) routes. In that study, tetracycline, chloramphenicol, and gentamycin were the antibiotics prescribed for topical application, whereas, ceftriaxone was the only antibiotic prescribed for parenteral administration.

4.2.5.4 AWaRe classification of the prescribed antibiotics

The AWaRe Classification of antibiotics was developed in 2017 by the WHO as a tool to support antibiotic stewardship efforts at local, national and global levels. Antibiotics are classified into three groups, Access, Watch and Reserve, taking into account the impact of different antibiotics and antibiotic classes on antimicrobial resistance, to emphasise the importance of their appropriate use. The WHO 13th General

Programme of Work 2019–2023 includes a country-level target of at least 60% of total antibiotic consumption to be in the Access group of antibiotics (WHO 2021b).

Of the total 1 138 antibiotics prescribed, 875 (76.9%) belonged to the Access category and the rest 263 (23.1%) to the Watch category of the WHO AWaRe Categorization. Antibiotics that belong to the Reserve category were not prescribed in any of the prescriptions. The prescribing of antibiotics from the Access group meets the WHO target of at least 60% (WHO 2021b). A study conducted in the Police Hospital in Ghana (Darkwah et al. 2021: 4) reported comparable findings where 74% of the antibiotics prescribed were from the Access category and 24% from the Watch category with no antibiotics prescribed from the Reserve category. A study by Zhao (2022: 5) at primary healthcare facilities in China reported that 54.9% of the antibiotics prescribed were classified in the World Health Organization's Watch category which is not in line with the WHO's recommendation of at least 60% of the antibiotics prescribed should be from the Access category.

The specific antibiotics that belong to each of these categories and their proportion is presented in Table 4.7. Amoxicillin, cloxacillin and doxycycline were the top 3 antibiotics in the "Access" Category and ciprofloxacin, norfloxacin and azithromycin in the "Watch" Category. In terms of specific antibiotics, 14(70%) of the 20 antibiotics belong to the "Access" category and the rest 6 (30%) to the "Watch" category.

Disaggregated by health centre, the percentage of antibiotics that belong to the Access category ranges from 66.0% (TBHC) to 89.3% (ENTHC) and those that belong to the Watch Category ranges from 10.7% (ENTHC) to 34.0% (TBHC). Most (57.5%) of the antibiotics that belong to the Access category were prescribed by female prescribers. Male prescribers prescribed the majority (58.3%) of the antibiotics in the Watch category. In terms of prescribers' qualification, most (49.2%) of the antibiotics in the Access category were prescribed by Professional Nurses followed by Health Officers (42.3%). The same applies to the antibiotics in the Watch category where 55.5% were prescribed by Professional Nurses and 37% by Health Officers.

Table 4.7 AWaRe category of antibiotics prescribed at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

AWaRe category	Name of the Antibiotic	Frequency	Percentage
Access category (n = 875)	Amoxicillin	469	53.7
	Cloxacillin	109	12.5
	Doxycycline	86	9.7
	Cotrimoxazole	76	8.7
	Amoxicillin + Clavulanic acid	39	4.5
	Metronidazole	33	3.7
	Tetracycline	22	2.5
	Chloramphenicol	10	1.1
	Gentamycin	9	1.0
	Benzathine penicillin	8	0.9
	Cephalexin	7	0.8
	Ampicillin	5	0.6
	Procaine penicillin fortified	1	0.1
	Floxacillin	1	0.1
Watch category (n = 263)	Ciprofloxacin	161	61.2
	Norfloxacin	39	14.8
	Azithromycin	30	11.4
	Ceftriaxone	28	10.6
	Erythromycin	3	1.1
	Clarithromycin	2	0.8

4.2.5.5 Common diagnosis for prescribing antibiotics

The common diagnoses for which the top seven antibiotics and the commonly prescribed injectable antibiotic (ceftriaxone) were prescribed are presented in Table 4.8. Most of the amoxicillin was prescribed for URTI (44.7%) followed by tonsillitis (19.6%) and injury (9.0%). UTI (42.5%), gastroenteritis (12.4%) and AFI (11.8%) were the top three cases for prescribing of ciprofloxacin. The common diagnoses for prescribing of cloxacillin were topical infections (43.9%), injury (35.5%) and wound (15.9%). The majority of the doxycycline, cotrimoxazole and amoxicillin + clavulanic acid was prescribed for typhus (59.3%), gastroenteritis (36.8%) and URTI (33.3%), respectively. Almost all of the norfloxacin (97.4%) was prescribed for UTI and about

61% of the ceftriaxone (the commonly prescribed injectable antibiotic) was prescribed for STIs.

Table 4.8 Common diagnoses for the top antibiotics prescribed at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 30, 2020.

S/N	Antibiotic and common diagnoses	Frequency	Percent
1	**Amoxicillin**		
	▪ URTI	208	44.7
	▪ Tonsillitis	91	19.6
	▪ Injury	42	9.0
	▪ Dental infection	30	6.5
	▪ UTI	15	3.2
	▪ Topical infections	14	3.0
2	**Ciprofloxacin**		
	▪ UTI	65	42.5
	▪ Gastroenteritis	19	12.4
	▪ AFI	18	11.8
	▪ Topical infections	12	7.8
	▪ Diarrhoea	10	6.5
	▪ Typhoid	7	4.6
3	**Cloxacillin**		
	▪ Topical infections	47	43.9
	▪ Injury	38	35.5
	▪ Wound	17	15.9
4	**Doxycycline**		
	▪ Typhus	51	59.3
	▪ AFI	21	24.4
	▪ STI	7	8.5
5	**Cotrimoxazole**		
	▪ Gastroenteritis	28	36.8
	▪ diarrheal	16	21.1
	▪ Intestinal parasite	11	14.5
	▪ URTI	3	3.9
6	**Amoxicillin + Clavulanic acid**		
	▪ URTI	13	33.3
	▪ Topical infections	7	17.9
	▪ Injury	5	12.8
	▪ Tonsillitis	4	10.3
	▪ Pneumonia	3	7.7
	▪ Bronchial asthma	2	5.1
7	**Norfloxacin**		
	▪ UTI	38	97.4
8	**Ceftriaxone**		
	▪ STI	17	60.7
	▪ UTI	3	10.7
	▪ Typhus	3	10.7

Diagnosis was not recorded on 7 (0.7%) of the prescriptions containing one or more antibiotics. On the prescriptions with a diagnosis recorded, 1018 (96.9%) of the cases for prescribing antibiotics were single infections and the rest 32 (3.1%) were mixed infections. The total number of cases for prescribing of antibiotics in these 1042 prescriptions was 1072. Table 4.9 shows the top 15 cases that accounted for 91.1% of the total number of cases for prescribing of antibiotics. URTI was the most common (21.7%) diagnosis followed by UTIs (13.1%) and topical infections (9.7%). These three cases accounted for about 45% of the cases for prescribing one or more antibiotics. Ten of the cases accounted for over 80% of the total number of cases for prescribing antibiotics. All kinds of URTIs contributed for 33.8% of the antibiotics prescribed.

Table 4.9 Diagnoses for prescribing of antibiotics at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

S/N	Diagnosis	Frequency	Percent	Cumulative percent
1	Upper respiratory tract infection	233	21.7	21.7
2	Urinary tract infection	140	13.1	34.8
3	Topical (skin, eye, ear) infections	104	9.7	44.5
4	Tonsillitis	102	9.5	54.0
5	Injury	85	7.9	61.9
6	Typhus	58	5.4	67.4
7	Gastroenteritis	48	4.5	71.8
8	Acute febrile illness	45	4.2	76.0
9	Dental infections	36	3.4	79.4
10	Diarrhoea	26	2.4	81.8
11	Wound	25	2.3	84.1
12	Sexually transmitted infections (STIs)	21	2.0	86.1
13	Typhoid	19	1.8	87.9
14	Pneumonia	18	1.7	89.6
15	Bronchitis	17	1.6	91.1
	Total	**977**	**91.1**	

When disaggregated by season of prescribing, URTI cases showed an overall reduction of 41.9% from 26.5% during the first half of the year (September 2019 to February 2020) to 15.4% during the second half of the year (March to August 2020). Unlike URTI, most of the other cases showed an increase during the second half of the year when compared to the first half (Figure 4.3).

Among the top five cases, injury, topical infections, tonsillitis and UTI cases increased by a rate of 50.8%, 42.7%, 33.7 and 14.6%, respectively. The protective measures taken for COVID-19 and introduction of the PHCG might justify the reduction in the URTI cases during the second half of the data period.

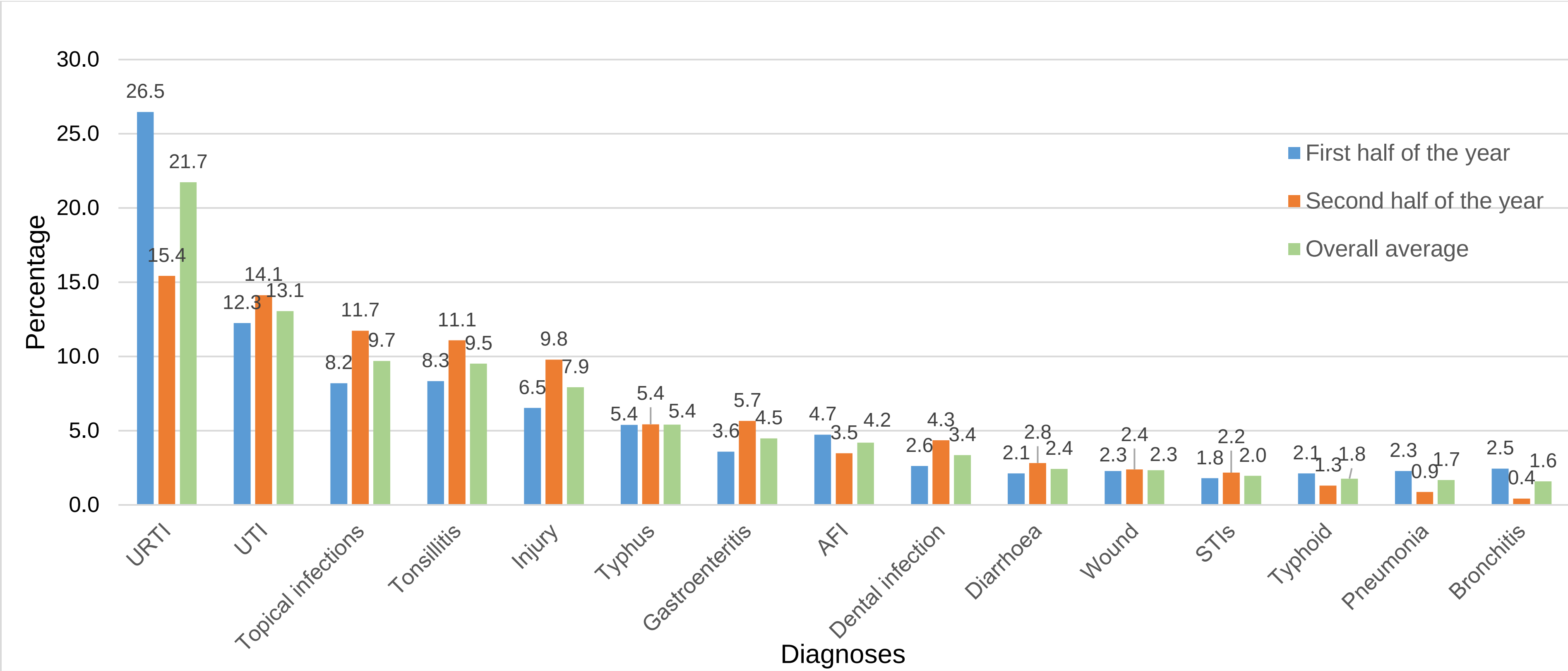


Figure 4.3 Figure 4.3 Percentage occurrence of top fifteen cases by season of prescribing at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

Overall, 401 (37.4%) of the cases for prescribing of antibiotics were respiratory tract infections. The majority of the respiratory tract cases were URTI (58.1%) followed by tonsillitis (25.4%) and pneumonia (4.5%). These three cases accounted for 88.0% of the respiratory cases (Table 4.10). Evidences show that most antibiotics (72% in 2018) are prescribed in general practice, largely for respiratory tract infections (RTIs) which are often self-limiting (Taxifulati et al. 2021: 2).

Table 4.10 Respiratory tract cases at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

S/N	Diagnosis	Frequency	Percent	Cumulative percent
1	URTI	233	58.1	58.1
2	Tonsillitis	102	25.4	83.5
3	Pneumonia	18	4.5	88.0
4	Bronchitis	17	4.2	92.3
5	Otitis media	15	3.7	96.0
6	Pharyngitis	5	1.2	97.3
7	Cough	4	1.0	98.3
8	Bronchial asthma	2	0.5	98.8
9	Respiratory tract infection	2	0.5	99.3
10	Sinusitis	1	0.2	99.5
11	Sore throat pain	1	0.2	99.8
12	Ear, Nose and Throat (ENT) infections	1	0.2	100.0
	Total	**401**	**100**	

When disaggregated by health centre, the percentage of respiratory tract cases per total number of infectious cases ranges from 32.5% to 51.3%. The highest percentage of respiratory tract cases were observed in ENTHC (51.3%) followed by KMHC (48.5%) and YKHC (38.8%). The lowest percentage of respiratory tract cases were observed in WD9HC and CFHC (32.5%). Figure 4.4 shows the proportion of respiratory tract cases at each health centre.

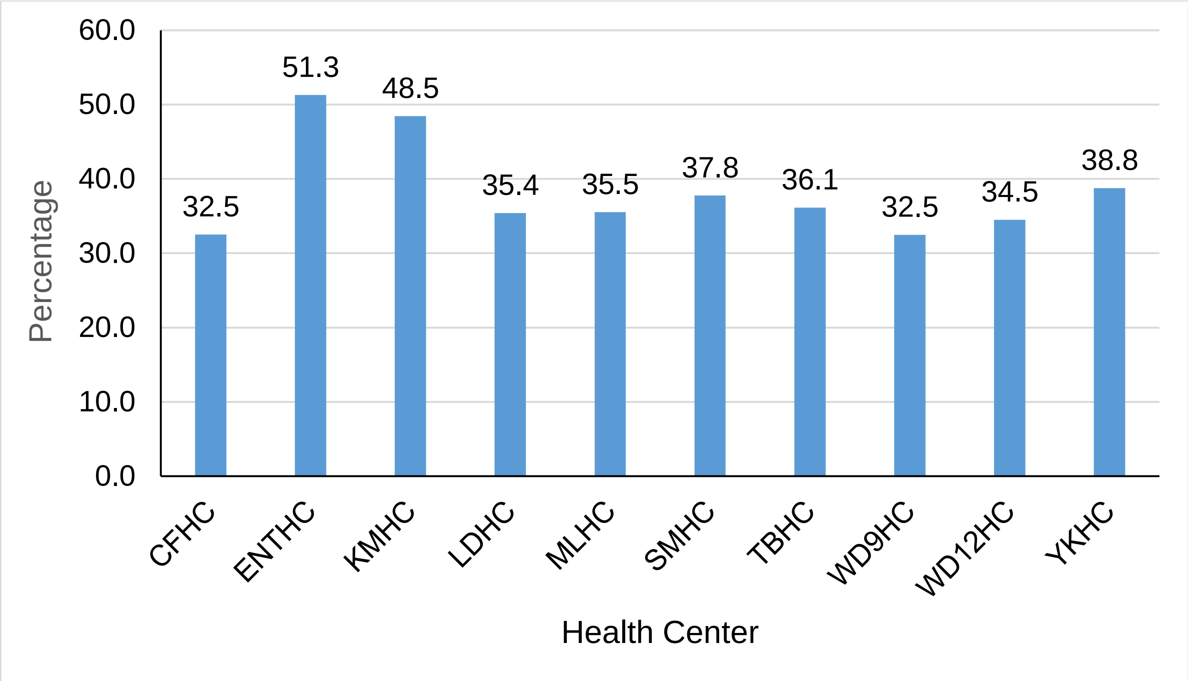


Figure 4.4 Percentage of respiratory tract cases per total number of infectious cases at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

Categorizing the respiratory cases into upper and lower respiratory cases (excluding the 2 cases labelled as “Respiratory Tract Infection”), 362 (90.7%) of the cases belong to upper respiratory and the rest 37 (9.3%) belong to lower respiratory. URTI and tonsillitis accounted for about 93% of the upper respiratory cases (Table 4.11). The data collected from six of the health centres to determine if there are URT cases that are managed without antibiotic showed that only 13 (8.9%) of the cases were managed without antibiotics implying that antibiotics were prescribed for about 91% of the URT cases. The cases managed without antibiotics were cough, common cold and unspecified URTI which were managed by cough syrup and/or analgesics.

Table 4.11 Proportion of upper and lower respiratory cases at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

Category	Diagnosis	Frequency	Percent	Cumulative percent
Upper respiratory tract cases (*n*=362)	URTI	233	64.4	64.4
	Tonsillitis	102	28.2	92.5
	Otitis media	15	4.1	96.7
	Pharyngitis	5	1.4	98.1
	Cough	4	1.1	99.2
	Sinusitis	1	0.3	99.4
	Sore throat	1	0.3	99.7
	Ear, Nose and Throat (ENT) infections	1	0.3	100.0
Lower respiratory tract cases (*n*=37)	Pneumonia	18	48.6	48.6
	Bronchitis	17	45.9	94.5
	Bronchial asthma	2	5.4	100.0

Evidences show that most respiratory tract infections are of viral origin, self-limiting, and do not require antibiotics for treatment (Taxifulati et al. 2021: 2; Chem et al. 2018). However, they account for the majority of antibiotics prescribed in primary health care facilities facilitating the development of antibiotic resistance. Respiratory tract infections were the main diagnosis (21.3%) for prescribing of antibiotics in a study conducted at primary healthcare facilities in Cameroon (Chem et al. 2018). RTIs are a leading cause of patient encounters in general practice. The common cold, acute sore throat, pharyngitis and tonsillitis, acute otitis media, rhinitis, acute sinusitis, laryngitis, and acute bronchitis are the most common acute RTIs. These are normally self-limiting, and since they often have a viral cause, they mostly improve without antibiotic therapy (Martínez-González et al. 2017).

4.2.5.6 Antibiotics prescribed for common cases

Table 4.12 shows the commonly prescribed antibiotics for the top 5 cases. Amoxicillin and Amoxicillin + Clavulanic acid were prescribed for many of the common cases for which one or more antibiotics were prescribed. The majority of the URTIs (87.1%), UTIs

(43.8%) and tonsillitis (90.1%) were managed with amoxicillin, ciprofloxacin and amoxicillin, respectively. Cloxacillin (44.2%), tetracycline (14.4%) and amoxicillin (12.5%) were commonly prescribed for topical infections, including eye and ear infections. Most injuries were managed by amoxicillin (47.1%) and cloxacillin (44.7%).

Table 4.12 Commonly prescribed antibiotics for common diagnosis at primary healthcare facilities in Addis Ababa, September 1, 2019 to August 31, 2020.

Diagnosis	Prescribed Antibiotic	Frequency	Percent	Cumulative percent
URTI	Amoxicillin	208	90.0	90.0
	Amoxicillin + Clavulanic acid	13	5.6	95.7
	Cotrimoxazole	3	1.3	97.0
	Erythromycin	3	1.3	98.3
	Azithromycin	2	0.9	99.1
	Cephalexin	2	0.9	100.0
UTI	Ciprofloxacin	68	48.6	48.6
	Norfloxacin	38	27.1	75.7
	Amoxicillin	16	11.4	87.1
	Cotrimoxazole	8	5.7	92.9
	Ceftriaxone	3	2.1	95.0
	Cephalexin	3	2.1	97.1
	Doxycycline	3	2.1	99.3
	Floxacillin	1	0.7	100.0
Topical infections	Cloxacillin	46	44.2	44.2
	Tetracycline	15	58.7	14.4
	Amoxicillin	13	71.2	12.5
	Ciprofloxacin	6	76.9	5.8
	Gentamycin	6	82.7	5.8
	Amoxicillin + clavulanic acid	5	87.5	4.8
	Amoxicillin/clavulanic acid + ciprofloxacin	2	89.4	1.9
	Chloramphenicol	2	91.3	1.9

Diagnosis	Prescribed Antibiotic	Frequency	Percent	Cumulative percent
	Amoxicillin + Gentamycin	1	92.3	1.0
	Cephalexin	1	93.3	1.0
	Ciprofloxacin + Amoxicillin	1	94.2	1.0
	Ciprofloxacin + Gentamycin	1	95.2	1.0
	Cloxacillin + Tetracycline	1	96.2	1.0
	Doxycycline + Tetracycline	1	97.1	1.0
	Azithromycin	1	98.1	1.0
	Cotrimoxazole	1	99.0	1.0
	Cotrimoxazole + Chloramphenicol	1	100.0	1.0
Tonsillitis	Amoxicillin	91	89.2	89.2
	Amoxicillin + Clavulanic acid	5	4.9	94.1
	Benzathine Penicillin	3	2.9	97.1
	Ciprofloxacin	1	1.0	98.0
	Azithromycin	1	1.0	99.0
	Procaine Penicillin fortified	1	1.0	100.0
Injury	Amoxicillin	40	47.1	47.1
	Cloxacillin	38	44.7	91.8
	Amoxicillin + Clavulanic acid	4	4.7	96.5
	Amoxicillin + Metronidazole	2	2.4	98.8
	Amoxicillin/Clavulanic acid + Metronidazole	1	1.2	100.0

4.2.5.7 Cost of the antibiotics prescribed

The total cost of medicines prescribed was ETB 74 809.47 with an average cost of medicines per prescription of ETB 37.40 (ranging from ETB 0.30 to 356.00). Among the health centres included in the study, the average cost of medicines per prescription ranges from ETB 29.26 in ENTHC to ETB 48.82 in WD9HC. The total cost of antibiotics was ETB 27099.45 which gives an average cost of antibiotics per prescription of ETB 13.55. Among the health centres, the average cost of antibiotics per prescription ranges from ETB 11.02 (TBHC) to 17.52 (WD9HC). For prescriptions containing one or more antibiotics, the average cost of antibiotics per prescription was ETB 25.83. Overall, antibiotics accounted for 36.2% of the total cost of medicines prescribed. This value is lower than the value (46.0%) reported in the study conducted by Worku & Tewahido (2018: 5) in Addis Ababa and findings of the study conducted in hospitals and primary healthcare facilities in Turkey (Mollahaliloglu et al. 2013: 283) that reported a percentage cost of antibiotics of 50.2%.

4.2.5.7.1 Cost of antibiotic by season of prescribing

Antibiotics prescribed during the first six months (September 2019 to February 2020) accounted for the majority (54.6%) of the cost of antibiotics. The percentage cost of antibiotics prescribed during the second six months (March to August 2020) was 45.4% which is a percentage reduction of 16.8% from the first six months. Similarly, the percentage cost of antibiotics per cost of medicines declined by a rate of 20.3% from 40.4% during the first six months to 32.2% during the second six months. This conforms with a reduction in the rate of prescribing of antibiotics during the second six months of the data period as reported and explained above. The preventive measures taken for the COVID-19 pandemic, the reduced patient flow to health facilities especially for minor cases such as URTIs and the introduction of PHCG may account for the reduction in the number of cases that would have resulted in the prescribing of antibiotics, hence the reduced cost of antibiotics during the second half of the data period.

The percentage of antibiotics per total number of medicines decreased by a rate of 10.9% during the second half of the year as compared to the first half from 32.1% to 28.6%.

4.2.5.7.2 Costs of specific antibiotics

Amoxicillin accounted for the majority (39.8%) of the cost of antibiotics followed by cloxacillin (15.7%) and ciprofloxacin (10.3%). Amoxicillin-based antibiotics (amoxicillin and amoxicillin + clavulanic) took 50% of the cost of antibiotics prescribed. Amoxicillin was the first antibiotic accounting for 43.5% in the 2017 study with amoxicillin-based antibiotics (amoxicillin, amoxicillin + clavulanic acid) accounting for 53.8% of the cost of antibiotics (Worku & Tewahido 2018: 5). In the current study, five of the antibiotics (amoxicillin, cloxacillin, ciprofloxacin, amoxicillin + clavulanic acid and cotrimoxazole) accounted for about 81% of the antibiotics prescribed. In the 2017 study (Worku &

Tewahido 2018: 5), five antibiotics (amoxicillin, amoxicillin + clavulanic acid, cotrimoxazole, ciprofloxacin and cloxacillin) consumed about 75% of the cost of antibiotics prescribed. Though the percentage contributions of the specific antibiotics vary, the five antibiotics that appear at the top by cost are the same in both of these two studies (Table 4.13).

Over 90% of the cost of antibiotics prescribed was taken up by eight of the antibiotics with the remaining 12 antibiotics contributing for less than 10% of the cost of antibiotics (Table 4.13). In the 2017 study (Worku & Tewahido 2018: 5), seven of the antibiotics

Table 4.13 Cost of antibiotics prescribed at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

S/N	Antibiotic	Total Cost (ETB)	Percent total cost	Cumulative percent total cost
1	Amoxicillin	10 791.45	39.8	39.8
2	Cloxacillin	4 257.50	15.7	55.5
3	Ciprofloxacin	2 787.60	10.3	65.8
4	Amoxicillin + Clavulanic acid	2 762.70	10.2	76.0
5	Cotrimoxazole	1 274.00	4.7	80.7
6	Ceftriaxone	1 085.10	4.0	84.7
7	Doxycycline	805.60	3.0	87.7
8	Azithromycin	728.25	2.7	90.4
9	Norfloxacin	571.60	2.1	92.5
10	Metronidazole	395.25	1.5	93.9
11	Cephalexin	271.15	1.0	94.9
12	Erythromycin	237.00	0.9	95.8
13	Chloramphenicol	232.20	0.9	96.7
14	Tetracycline	217.00	0.8	97.5
15	Clarithromycin	213.50	0.8	98.3
16	Ampicillin	149.30	0.6	98.8
17	Gentamycin	129.75	0.5	99.3
18	Benzathine Penicillin	126.00	0.5	99.8
19	Floxacillin	40.00	0.1	99.9
20	Procaine penicillin fortified	24.50	0.1	100.0

consumed about 90% of the cost of antibiotics with the remaining 8 antibiotics contributing nearly for about 10% of the cost of antibiotics.

Antibiotics that belong to the Access category cost ETB 21476.40 (79.3%) and those in the Watch category ETB 5623.05 (20.7%).

4.2.5.7.3 Cost of antibiotics by antibiotic class

Table 4.14 presents the cost of antibiotics by class. Of the 9 antibiotic categories, antibiotics that belong to the penicillins group accounted for the majority (67.0%) of the cost of antibiotics followed by fluoroquinolones (12.4%) and cephalosporins (5.0%). Overall, these three antibiotic categories accounted for nearly 85% of the cost of antibiotics.

Table 4.14 Cost of antibiotics by class at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

S/N	Antibiotic class	Total cost (ETB)	Percent total cost	Cumulative percent total cost
1	Penicillins	18 151.45	67.0	67.0
2	Fluoroquinolones	3 359.20	12.4	79.4
3	Cephalosporins	1 356.25	5.0	84.4
4	Sulphonamides	1 274.00	4.7	89.1
5	Macrolides	1 178.75	4.3	93.4
6	Tetracyclines	1 022.60	3.8	97.2
7	Metronidazole	395.25	1.5	98.7
8	Chloramphenicol	232.20	0.9	99.5
9	Aminoglycosides	129.75	0.5	100.0

4.2.5.7.4 Cost of antibiotics by route of administration

Of the total cost of antibiotics (ETB 27 099.45), the majority ETB 25142.35 (92.8%) was expended on antibiotics prescribed for oral administration. Injectable and topical antibiotics accounted for ETB 1354 (5.0%) and ETB 602.20 (2.2%) of the total cost of antibiotics prescribed, respectively. As shown in Table 4.15, ceftriaxone alone accounted for 80% of the cost of antibiotics prescribed in injection form. Among the antibiotics prescribed for topical application, ciprofloxacin accounted for 37% of the cost followed by tetracycline (36%).

Table 4.15 Cost of antibiotics by route of administration at primary healthcare facilities in Addis Ababa, Ethiopia, Sept. 1, 2019 to Aug. 31, 2020.

Route of Administration	Antibiotic	Value (ETB)	Percentage
Parenteral	Ceftriaxone	1 085.10	80.1
	Benzathine Penicillin	126.00	9.3
	Ampicillin	119.30	8.8
	Procaine Penicillin Fortified	24.50	1.8
	Total	1 354.90	100
Topical	Ciprofloxacin	223.45	37.1
	Tetracycline	217.00	36
	Gentamycin	129.75	21.5
	Chloramphenicol	32.00	5.3
	Total	602.2	100

4.2.5.7.5 Cost of antibiotics by diagnosis

Table 4.16 shows the top 15 cases by total value of antibiotics prescribed. These 15 cases accounted for ETB 24975.90 (92.2%) of the total cost of antibiotics prescribed. URTI is the top in the list accounting at 23.8% of the cost followed by wound and tonsillitis at 15.4% and 10.1% of the cost of antibiotics prescribed for these 15 cases, respectively. Overall, these three cases accounted for nearly 50% of the cost of antibiotics. Seven and ten of the cases accounted for nearly 80% and 90% of the cost of antibiotics prescribed for the top 15 cases, respectively.

In the study conducted by Worku and Tewahido (2018: 5) in Addis Ababa, URTI, UTI and tonsillitis were the top three cases responsible for 22.7%, 9.8% and 9.3% of the total cost of antibiotics prescribed, respectively. In the current study, wound is the second and UTI the fourth common case by value of antibiotics prescribed. The contributions of these three cases to the total cost of antibiotics is comparable with findings of the current study.

Table 4.16 Cost of antibiotics by diagnosis at primary healthcare facilities in Addis Ababa, Ethiopia, September 1, 2019 to August 31, 2020.

S/N	Diagnosis	Cost (ETB)	% Cost	Cumulative % cost
1	URTI	5 944.05	23.8	23.8
2	Wound	3 851.75	15.4	39.2
3	Tonsillitis	2 523.60	10.1	49.3
4	UTI	2 508.05	10.0	59.4
5	Injury	2 244.75	9.0	68.4
6	Topical infections	2 109.90	8.4	76.8
7	Typhus	962.80	3.9	80.7
8	STI	827.30	3.3	84.0
9	Gastroenteritis	783.20	3.1	87.1
10	Pneumonia	719.60	2.9	90.0
11	Dental infections	709.80	2.8	92.8
12	AFI	698.80	2.8	95.6
13	Diarrhoea	375.00	1.5	97.1
14	Typhoid	362.40	1.5	98.6
15	Bronchitis	354.90	1.4	100.0
	Total	**24 975.90**	**100**	

Of the total cost of antibiotics prescribed, antibiotics with a total value of ETB 10828.10 (40.0%) were prescribed for respiratory tract infections. Antibiotics prescribed for all kinds of URTs accounted for 35.3% of the total cost of antibiotics and 88.3% of the cost of antibiotics prescribed for respiratory cases. The cost of antibiotics prescribed for URTIs accounted for 27% and 16.5% of the total cost of antibiotics during the first and second six months of the data period, respectively. This implies a percentage decline of 38.9% from the first to the second six months of the data period. This correlates with the reduction in the percentage of URTI cases during the second half (15.4%) of the data period when compared with the first half (26.5%) reflecting a 41.9% reduction.

4.2.6 Appropriateness of the Antibiotics prescribed

Appropriateness of the antibiotics prescribed was evaluated for the most common diagnosis, respiratory tract infections. The evaluation was carried out according to the respiratory tract clinical protocol developed for this study. As presented above, most of the respiratory cases were URTI and tonsillitis. It was possible to retrieve the patient medical charts for 326 (81.3%) of the 401 respiratory tract cases. The diagnosis-related information for the remaining 75 (18.7%) cases was taken from prescriptions.

Of the patient charts retrieved, 24 (7.4%) contained no information about the diagnosis. Of the 401 prescriptions containing antibiotics prescribed for respiratory tract cases, 207 (51.6%) were found appropriate and 140 (34.9%) inappropriate. It was not possible to evaluate the appropriateness of the antibiotics prescribed for 54 (13.5%) of the respiratory tract cases either because the patient's medical chart was not found (83.3%) or the diagnosis related data was not recorded on the chart (16.7%). When those prescriptions that were found difficult to evaluate were excluded, 59.7% of the prescriptions were found appropriate and the remaining 40.3% inappropriate.

All kinds of upper respiratory cases accounted for nearly 88% of the inappropriately managed cases. Nearly 75% of the inappropriately managed upper respiratory cases were those diagnosed as URTI. All of the cases that were found difficult to evaluate appropriateness of their treatment were upper respiratory tract cases. Figure 4.5 shows the reasons for inappropriateness of the antibiotic treatment identified from evaluation of the respiratory tract cases. The most common one (53%) was "antibiotic initiation is not justifiable" followed by "high dose" (16%) and "need for additional antibiotic" (14%).

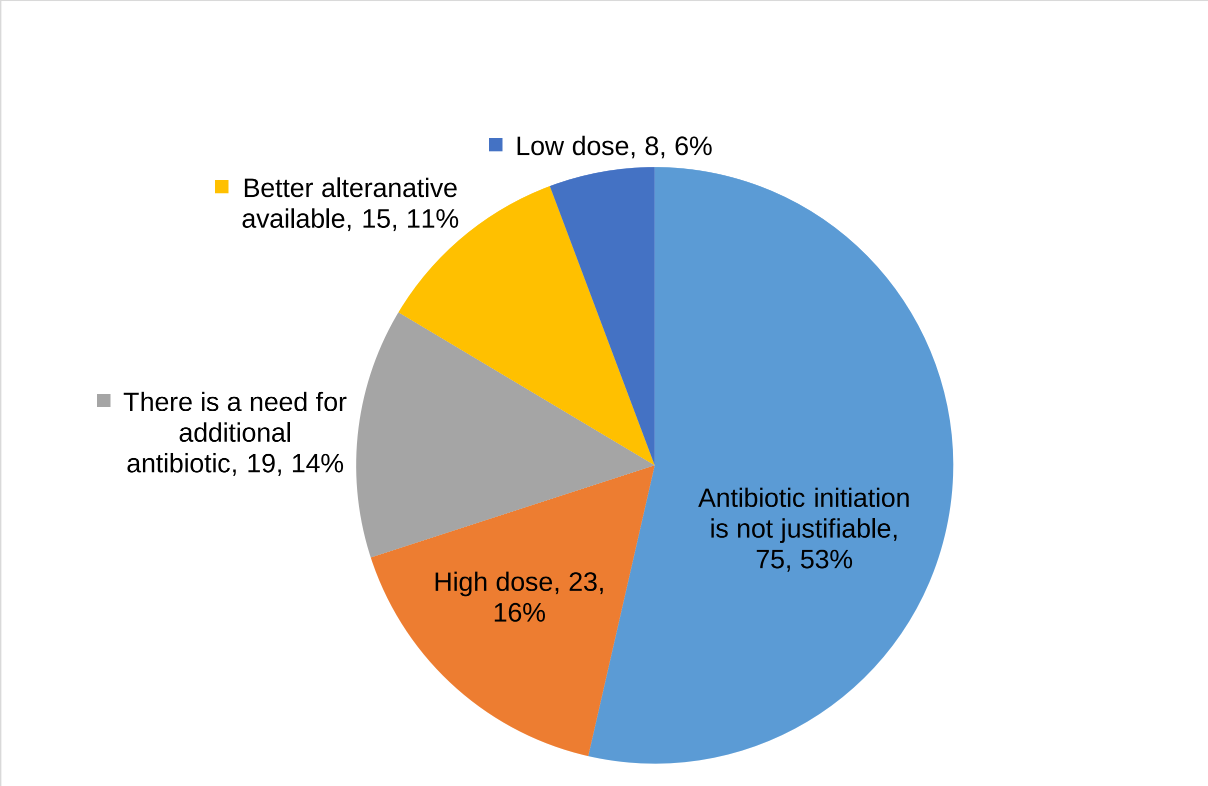


Figure 4.5 Reasons for inappropriateness of antibiotic treatment for respiratory tract infections at primary healthcare facilities in Addis Ababa, Ethiopia, Sept. 1, 2019 to Aug. 31, 2020 (n=140).

According to the study by Zhao (2022: 5) at primary healthcare facilities in China, 50.7% of the antibiotic prescriptions were inappropriate, 36.0% potentially appropriate and 13.3% were appropriate. The findings of the current study showed a better adherence to clinical guidelines though it is still low (59.7%).

Cost of antibiotics by appropriateness of treatment

Of the antibiotics prescribed for respiratory tract cases, cost of the antibiotics appropriately prescribed was ETB 5561.35 (51.4%). Whereas, the inappropriately prescribed antibiotics cost was ETB 3780.35 (34.9%). The cost of antibiotics on prescriptions for which evaluating appropriateness of the treatment was difficult was ETB 1486.40 (13.7%). Of the antibiotics prescribed for upper respiratory tract cases, a total of ETB 3172.50 (33.2%) was spent on inappropriately prescribed antibiotics. URTIs accounted for 59.3% of the value of all antibiotics prescribed inappropriately for respiratory tract cases. Furthermore, nearly 84% of the cost of antibiotics prescribed inappropriately were for upper respiratory cases.

4.2.7 Summary of key indicators by health centre

Table 4.17 presents the summary of the antibiotic prescribing indicators presented and described above disaggregated by health centre. The overall average of each indicator is shown in the last column. Each of these indicators are presented and discussed above and is presented here in summarised form to provide full picture on the key findings of the quantitative phase of the study.

Table 4.17 Summary of key indicators by health centre at primary healthcare facilities in Addis Ababa, Ethiopia, September 01, 2019 to August 31, 2020.

S/N	Indicator	Value of the indicator by Health Centre and average										
		KMHC	MLHC	SMHC	TBHC	LDHC	WD12HC	WD9HC	CFHC	ENTHC	YKHC	Overall average
1	Average number of medicines per prescription	1.98	1.75	1.77	1.85	1.74	2.02	2.11	1.81	1.71	1.92	**1.87**
2	Percentage of prescriptions with one or more antibiotics	48.5	53.5	49.0	41.5	48.0	56.5	58.5	61.5	58.5	49.0	**52.5**
3	Average number of antibiotics per prescription	0.52	0.57	0.53	0.47	0.53	0.60	0.63	0.70	0.60	0.54	**0.57**
4	Percentage of antibiotics per total number of medicines	26.6	32.4	29.7	25.4	30.7	29.6	29.9	38.3	35.2	28.4	**30.5**
5	Average cost of medicines per prescription (ETB)	43.16	36.65	34.51	39.14	31.03	41.67	48.82	34.54	29.26	35.26	**37.40**
6	Average cost of antibiotics per prescription (ETB)	13.15	13.36	13.06	11.02	12.06	15.59	17.52	15.44	12.87	11.42	**13.55**
7	Percentage cost of antibiotics per total cost of medicines	30.5	36.5	37.8	28.2	38.9	37.4	35.9	44.7	44.0	32.4	**36.2**
8	Percentage of antibiotics in Access category	82.9	71.7	66.7	66.0	78.3	82.5	80.2	74.8	89.3	73.4	**76.9**
9	Percentage of antibiotics in Watch category	17.1	28.3	33.3	34.0	21.7	17.5	19.8	25.2	10.7	26.6	**23.1**
10	Percentage of respiratory tract cases per total infectious cases	48.5	35.5	37.8	36.1	35.4	34.5	32.5	32.5	51.3	38.8	**38.2**

4.2.8 Testing association between variables

Chi-square test was conducted to check the association between the demographic characteristics of patients and prescribers as well as the season of prescribing with the rate antibiotics prescribing at level of significance of P≤0.05. As presented in the Table 4.18, antibiotic prescribing rate had statistically significant association with patient's age (p≤0.001), prescriber's qualification (p≤0.001) and the season of prescribing (p=0.001). However, the association between the prescriber's gender and antibiotic prescribing was not statistically significant and antibiotic prescribing has no association with patient's gender. The rate of antibiotic prescribing showed decline as age of the patient increases. In relation to season of prescribing, the antibiotic prescribing rate decreased consistently moving from the first to the fourth quarter of the data period. In a study conducted in Cameroon at primary healthcare facilities, a significant difference was observed in the exposure to antibiotics with respect to gender and age (Chem et al. 2018).

Table 4.18 Association of patient and prescriber characteristics, and season of antibiotic prescribing, September 01, 2019 to August 31, 2020.

Independent variable		Antibiotic prescribed, Number (%)		Chi-square value (Pearson)	P-value
		No	Yes		
Patient's gender	Female	570 (47.6)	628 (52.4)	0.00	0.995
	Male	376 (47.6)	414 (52.4)		
Patient Age (years)	0-14	152 (35)	282 (65)	90.92	< 0.001
	15-34	370 (43.4)	482 (56.6)		
	35-54	244 (55.2)	198 (44.8)		
	≥ 55	175 (69.2)	78 (30.8)		
Prescriber's qualification	Health Officer	372 (47.5)	411 (52.5)	32.653	<0.001
	Midwife	28 (77.8)	8 (22.2)		
	Physician	117 (60.9)	75 (39.1)		
	Professional Nurse	390 (43.6)	505 (56.4)		
Prescriber's gender	Female	225 (46.6)	258 (53.4)	2.535	0.111
	Male	153 (41.1)	219 (58.9)		
Prescribing season	Quarter 1	247 (42.9)	376 (57.1)	15.448	0.001
	Quarter 2	229 (46)	269 (54)		
	Quarter 3	221 (47.7)	242 (52.3)		
	Quarter 4	254 (54.9)	209 (45.1)		

4.3 PHASE II: PRESENTATION AND DISCUSSION OF THE QUALITATIVE RESULTS

Qualitative phase of the study was conducted to achieve the following research objectives:

- To explore and describe the factors that influence the prescribing of antibiotics at primary healthcare facilities;
- To identify interventions that should be implemented to improve antibiotic prescribing at primary healthcare facilities;

This study was conducted in five of the health centers (CFHC, KMHC, LDHC, WD9HC and TBHC) to obtain information on the antibiotic prescribing practices, the problems related to antibiotic prescribing and their use, factors influencing antibiotic prescribing decision, interventions to improve antibiotic prescribing at health centres, and implementation challenges. In this phase of the study, health centres with low, medium and high rates of antibiotic prescribing were included. From health centres with a high rate of antibiotic prescribing, CFHC (61.5%) and WD9HC (58.5%) were included. TBHC which has the lowest rate of antibiotic prescribing (41.5%) was considered. KMHC (48.5%) and LDHC (48.0%) with medium antibiotic prescribing rates were also included in this phase of the study. Starting with background information of the health facilities and study participants, findings of the qualitative study are presented and discussed supported by relevant quotations from the study participants.

4.3.1 Background information

4.3.1.1 Background information of the health centres

As per the annual statistical report of the health centres during the year 2012 EFY (July 2019 to June 2020), the number of patients and clients served by the health centres during the budget year ranges from 20,195 (CFHC) to 54,384 (WD9HC) with an average of 28,966 patients per health centre. It was observed that all of the health centres have the Primary Healthcare Clinical Guidelines (PHCG) in each examination room and their own updated medicines list. Pharmacy Case Team Coordinators of the health centres reported that they have functional DTC. As per the information obtained from the Pharmacy Case Team Coordinators, the annual budget allocated for the procurement of pharmaceuticals (medicines, medical supplies and laboratory reagents) during the budget year (2012 EFY) was within the range of Ethiopian Birr (ETB) 1,101,160 (TBHC) to ETB 2,000,000 (KMHC) with an average of ETB 1,420,232 per health centre.

In terms of the professional mix of healthcare providers involved in patient diagnosis and prescribing of medicines, all of the five health centers have 1 or 2 medical doctors and all of them had health officers, professional nurses and midwives as per data obtained from the Human Resource Management Units of the health centres during the time of data collection. According to data from the 2012 EFY Health Management Information System (HMIS) of the health centres, infectious diseases accounted for about 57.1% of the top ten diseases during the budget year ranging from 23% in TBHC to 65% in WD9HC. URTIs, including tonsillitis, common cold and unspecified URTIs, were the first in the list accounting for 29.3% of the top ten diseases and 51.4% of the infectious diseases in the top ten list. In one of the health centres (TBHC), URTIs did not appear in the top ten diseases list. UTIs, typhoid, typhus, gastroenteritis and other unspecified bacterial infections were among the infectious diseases in the top ten diseases list of the health centres.

4.3.1.2 Background information of the study participants

A total of 42 participants were involved in the in-depth interview. Depending on their role, the participants were categorised into two groups; prescribers and key informants. Twenty prescribers and 22 key informants were interviewed using three separate interview guides that had many questions in common. All of the 20 prescribers were from the health centres, whereas, the 22 key informants were from health centres (10), sub-city health offices (10) and the Health Bureau (2). Details of the background information about the two groups of participants is presented below.

Confirmation on correctness of the transcripts taken from the audio recording of each interview was obtained from 19 (95%) of the prescribers and 21 (95.5%) of the key informants that participated in the study with an overall confirmation rate of 95.2%. The participants confirmed that the information transcribed from the audio records was their own following the request for feedback sent to each one of them via telegram with the Amharic and English versions of their respective transcripts attached. The editorial comments provided by a few of the participants are addressed. It was not possible to obtain confirmation from one prescriber (not accessible) and one key informant (retired and hence didn’t respond).

The data collected from the prescribers and key informants was summarised into themes and sub-themes and presented in narrative form supported by relevant quotes from both groups. The data presentation and discussion follows the structure of the interview guides which were developed based on the queries that are expected to be answered with this phase of the study. Triangulation of the quantitative and qualitative findings, and identifying the key antibiotic prescribing problems and potential interventions for guideline development to improve antibiotic prescribing was done following the qualitative data presentation and discussion.

4.3.1.2.1 Background information of the prescribers

A total of 20 prescribers (4 from each health centre) participated in the in-depth interview from the five health centres selected for this phase of the study. The prescribers interviewed were from adult OPD, Under 5 OPD and the Emergency Unit. Twelve (60%) of the prescribers were females. Their age ranged from 24 to 55 years with an average age of 33.6 years. In terms of profession, of the prescribers who participated in the interview 10 were Health Officers and 10 were Nurses. Eighteen of the prescribers (90%) were degree holders and the other two (10%) were diploma holders (clinical nurses).

The total work experience of half of the prescribers was within the range of 5 to 10 years. In the facility they were working in during the data collection, half of them had provided service for five years and above. With regard to average daily patient load, about 58% of the prescribers provide service for over 25 patients per day. The average time taken to undertake for each in-depth interview was 34.7 minutes with a range from 22.1 minutes to 54.7 minutes. The majority of the interview (45%) took 31 to 40 minutes (Table 4.19). Almost all of the prescribers reported that they had not participated in any training related to antibiotics and antibiotic resistance during the past 2 years preceding the study.

Table 4.19 Background information of the prescribers interviewed at primary healthcare facilities in Addis Ababa, May 2021.

Variable	Number	Percent
Clinical Unit		
Adult OPD	7	35
Under 5	7	35
Emergency	6	30
Gender		
Female	12	60
Male	8	40
Age (Years)		
20 - 30	10	50
31 - 40	6	30
41 - 50	3	15
> 50	1	5
Profession		
Health Officer	10	50
Professional Nurse	8	40
Clinical Nurse	2	10
Total work experience (Years)		
< 5	5	25
5 - 10	10	50
> 10	5	25
Average daily patient load		
(Number)	5	26.3
< 20	3	15.8
20 - 25	11	57.9
> 25		

4.3.1.2.2 Background information of the key informants

A total of 22 participants from the five health centres (10), sub-city health offices (10) and Health Bureau (2) were involved in the key informant interviews. Thirteen (59.1%) of the participants were males and the other 9 (40.9%) were females. The age of the participants ranges from 29 to 58 years with an average of 36.5 years. Professionally, 11 (50%) of the key informants were pharmacists and the rest were Public Health Professionals (18.2%), Professional Nurses (18.2%), Health Officers (9.2%), and a Medical Laboratory Technologist (4.5%). The majority of the key informants (77.3%) were first degree holders (Table 4.20).

Table 4.20 Background information of the key informants interviewed at primary healthcare facilities in Addis Ababa, May to June 2021.

Variable	Number	Percent
Gender		
Female	13	59.1
Male	9	40.9
Age (Years)		
20 - 30	4	18.2
31 - 40	14	63.6
41 - 50	2	9.1
> 50	2	9.1
Profession		
Health Officer	2	9.1
Professional Nurse	4	18.2
Public Health	4	18.2
Pharmacist	11	50
Medical Laboratory Technology	1	4.5
Total work experience (Years)		
5 - 10	15	68.2
10 – 20	4	18.2
> 20	3	13.6
Responsibility		
▪ Health Center Medical Director	5	22.7
▪ Health Center Pharmacy Team Coordinator	5	22.7
▪ Sub-city Health Office Medical Service Team Leader	5	22.7
▪ Sub-city Health Office Pharmaceuticals and Medical Equipment Supply and Distribution Team Leader	5	22.7
▪ Health Bureau Medical Service Directorate Director Representative	1	4.5
▪ Health Bureau Pharmaceutical Supply and Pharmacy Service Directorate Director	1	4.5
Educational level		
First degree	17	77.3
Second degree	5	22.7

The total work experience of the key informants ranges from 5 to 37 years with an average of 12.7 years. In the facility they were working during the data collection, 14 (63.6%) of the key informants had served for at least three years with 6 (27.3%) for 5 years and more. In terms of responsibility, ten of the participants were Medical Directors (5) and Pharmacy Case Team Coordinators (5) of the five health centres. From the five Sub-city Health Offices, Medical Service Team Leaders (5) and Pharmaceutical and Medical Equipment Supply and Distribution Team Leaders (5) were involved. Representative of the Medical Service Directorate and a Director of the Pharmaceutical Supply and Pharmacy Service Directorate of the Health Bureau were also part of the interview. The individual interviews took an average of 43 minutes ranging from 21.7 minutes to 91 minutes.

4.3.2 Themes and sub-themes

Though main focus of the study was on exploring the antibiotic prescribing problems, the factors influencing antibiotic prescribing decision, and interventions to improve antibiotics prescribing, some more related themes emerged from the deductive thematic content analysis conducted using ATLAS.ti 9. Overall, the following seven themes were emerged from the thematic analysis:

1. Information about antibiotic prescribing and resistance,
2. Types of antibiotic prescribing and use problems,
3. Consequences of irrational antibiotic prescribing and resistance,
4. Factors influencing antibiotic prescribing decision,
5. Measures taken so far to improve antibiotic prescribing practices,
6. Recommended interventions to improve antibiotic prescribing practices, and
7. Challenges in implementing the recommended interventions.

These main themes were then split into subthemes as presented in Table 4.21. Each of the themes and subthemes are described and discussed subsequently with relevant quotes from the prescribers and key informants.

Table 4.21 Themes and sub-themes emerged from thematic analysis of the data collected from prescribers and key informants, May to June 2021.

Themes	Sub-themes
1. Information about antibiotic prescribing and resistance	1.1 Definitions of antibiotics
	1.2 Common antibiotics and cases
	1.3 Use of narrow- and broad-spectrum antibiotics
	1.4 Antibiotic prescribing trend
	1.5 Antibiotic resistance as a threat
2. Types of antibiotic prescribing and use problems	2.1 Prescriber-related antibiotic use problems
	2.2 Patient-related antibiotic use problems

Themes	Sub-themes
3. Consequences of irrational antibiotic prescribing and resistance	3.1 Consequences of irrational antibiotic prescribing
	3.2 Consequences of antibiotic resistance
4. Factors influencing antibiotic prescribing decision	4.1 Predisposing factors
	4.2 Enabling factors
	4.3 Reinforcing factors
5. Measures taken to improve antibiotic prescribing practice	5.1 PHCG implementation
	5.2 Undertaking medicine use study
	5.3 Undertaking morning sessions
	5.4 Information sharing
	5.5 Providing information through DIS
	5.6 Activities undertaken by DTC
	5.7 Undertaking supportive supervision
	5.8 Smooth communication between prescribers and dispensers
	5.9 Recognizing prescribers
	5.10 Assigning prescribers in OPDs in Team
	5.11 Providing health education to patients
	5.12 Providing written information to patients
6. Recommended intervention to improve antibiotic prescribing practice	6.1 Apply one protocol for public and private sector
	6.2 Properly manage minor cases
	6.3 Provide training for healthcare professionals
	6.4 Proper implementation of PHCG
	6.5 Undertake research and disseminate the findings
	6.6 Control the private sector
	6.7 Improve supply availability
	6.8 Provide follow-up and support
	6.9 Have M&E system
	6.10 Update knowledge
	6.11 Increase public awareness
	6.12 Proper patient counselling

Themes	Sub-themes
	6.13 Give attention to antibiotics and resistance
	6.14 Strengthen DTC and DIS
	6.15 Create discussion forum for healthcare providers
7. Challenges in implementing the recommended interventions	7.1 Shortage of professionals
	7.2 Lack of government commitment for change
	7.3 Shortage of medicines and laboratory reagents
	7.4 Professionals' resistance for change in implementing PHCG
	7.5 Financial constraint
	7.6 Profit motive of the private sector

4.3.2.1 Theme 1: Information about antibiotics prescribing and resistance

The information that prescribers and key informants have about antibiotics, antibiotic prescribing and resistance are covered under this theme. These include definitions of antibiotics, commonly prescribed antibiotics and the common diagnoses for which the antibiotics are prescribed, use of narrow and broad-spectrum antibiotics, and antibiotic resistance as a threat.

4.3.2.1.1 Sub-theme 1.1: Definition of antibiotics

Most of the prescribers defined antibiotics correctly as medicines used to prevent and treat bacterial infections. A Health Officer (HO01) defined antibiotics as *"Mostly antibiotics are used for bacterial infection and differs by case."*. Another Health Officer defined antibiotics as antibacterials by categorizing them into bactericidal and bacteriostatic.

> *"For me, antibiotics are curative medicines. When patients are infected with bacteria, we order bactericidals that kill the disease. There are also others that contain the infections what we call bacteriostatics that prevent further infection and transmission." (HO10).*

Nurse prescribers also defined antibiotics as antibacterials.

> *"Antibiotics are medicines that are used to treat diseases caused by bacteria." (NU02)*

"Antibiotic is a medicine we prescribe for bacterial diseases." (NU05)

Some of the prescribers defined antibiotics incorrectly as agents that can also be used for treatment of fungal and viral infections.

> *"Antibiotics means antibacterial medicine. It can also be antifungus. But, it is mainly antibacterial." (HO02)*
>
> *"Antibiotics are medicines that prevent infections that are caused by bacteria or virus." (NU01)*
>
> *"Well, antibiotics are medications that we prescribe for fungus, virus, bacteria to treat a disease or it is medication that we use by following guidelines." (NU10)*

The general definition of antibiotic is that antibiotics are agents used for the prevention and treatment of infections caused by bacteria (EFMHACA 2018: III). So, there is some misunderstanding on what antibiotics are which may have contributed to the overprescribing of antibiotics for minor cases such as URTIs as revealed by the quantitative study, which are mostly known to be of viral origin.

When asked to provide examples of antibiotics, all of them mentioned antibacterials such as amoxicillin, cloxacillin, ceftriaxone, azithromycin, cotrimoxazole and the likes. None of the prescribers mentioned other antimicrobials such as antifungals and antivirals as antibiotics. This implies that though some of the prescribers are confused about the causative agent for which antibiotics should be used, all of them are well aware of the medicines that belong to the antibiotic classes.

4.3.2.1.2 Sub-theme 1.2: Common antibiotics and cases

According to the prescribers, the most commonly prescribed antibiotics in the facilities in which they are practicing were amoxicillin (33.3%), cotrimoxazole (13.9%), cloxacillin (11.1%), ciprofloxacin (11.1%) and Augmentin (11.1%). Some of them have also mentioned cephalexin (5.6%), doxycycline (5.6%), norfloxacin (2.8%), ceftriaxone (2.8%) and azithromycin (2.8%) as commonly prescribed antibiotics. This conforms with the findings of the quantitative study where the five antibiotics mentioned by most of the prescribers were among the top six antibiotics commonly prescribed in the health centres. Except for cephalexin, the other antibiotics the prescribers mentioned were among the top ten antibiotics prescribed.

The common cases for prescribing of antibiotics, as reported by the prescribers, were URTI (32.1%), tonsillitis (14.3%), pneumonia (7.1%), skin infections (7.1%), typhoid (7.1%) and injury (7.1%). UTIs, AFI, otitis media, wound infection, diarrhoea, the common cold and typhus were also mentioned as common cases for prescribing of antibiotics, each of which accounted for 3.6% of the cases mentioned by the prescribers. Of these cases, URTI, UTI, tonsillitis, skin infections and injury were the top five cases for prescribing of antibiotics reported in the quantitative study.

4.3.2.1.3 Sub-theme 1.3: Use of narrow and broad-spectrum antibiotics

Most of the prescribers reported that they commonly prescribe broad-spectrum antibiotics.

> *“Mostly, we use broad-spectrum.” (HO07)*
>
> *“I personally use broad-spectrum ones.” (HO09)*

The reasons for the common use of broad-spectrum antibiotics varies from prescriber to prescriber. Some of them prescribe these category of antibiotics for the reason that broad-spectrum antibiotics are the ones made available at health centre level.

> *“As most of the antibiotics made available at health center level are broad-spectrum, we use them.” (HO04)*
>
> *“Since the ones made accessible here are these ones, we try to prescribe those available in the facility to reduce expenses of the patients. Because of this, we select broad ones.” (NU08)*

Other prescribers use broad-spectrum antibiotics because of a limitation in diagnostic capacity at health centre level to specifically identify the causative agent. They justify that in the absence of laboratory investigations to identify the causative agent, using broad-spectrum antibiotics is recommended to attack all kinds of bacteria that might be there.

> *“Sometimes, when unspecified, we prescribe broad-spectrum. When difficult to manage as specific, we treat it with broad. If identified by laboratory test, we treat it with specific. If not possible to identify, we use broad.” (HO05)*

"We are working in a health center where investigations may not be there as required. Under this condition, using broad-spectrum is recommended. Most investigations are not available." (NU02)

"There is a need for sophisticated laboratory that can identify the bacteria for us to use specific antibiotic. For example, culture may be important. So, if you use the broad-spectrum, it is expected to kill the bacteria that are not identified." (NU04)

Some prescribers prefer broad-spectrum antibiotics as they can cover all kinds of infections.

"Mostly, it is broad. I use broad-spectrum since I think that it can attack many infections." (HO06)

"For more cover." (HO07)

"Since they are broad and hence can treat all." (HO05)

Only one prescriber from the paediatric unit reported a preference for narrow-spectrum antibiotics.

"We commonly use narrow-spectrum antibiotics here. Why? Since they are children, we commonly use narrow-spectrum." (NU01)

Literatures indicate that clinical and commercial factors have driven the use of broad-spectrum agents for many years. The ability to treat infections quickly without waiting for a day or more for the identification of the disease-causing pathogen results in saving countless lives. Physicians have long been aware of the collateral damage that broad-spectrum antibacterial drugs have on the intestinal microbiome and the subsequent risks of adverse events. Besides the adverse events, broad-spectrum antibiotics support the emergence of resistance. As a result, narrow-spectrum antibiotics that act against specific species and do not generate resistance in other pathogens due to selection pressure have become an attractive alternative to combat resistance development (Alm & Lahiri 2020: 2–3).

The quantitative phase of the study indicated that most of the antibiotics prescribed are broad-spectrum antibiotics such as amoxicillin, cloxacillin, amoxicillin/clavulanic acid, ciprofloxacin, cotrimoxazole and doxycycline. Actually, most of the antibiotics that are made available at health centres are broad-spectrum ones.

4.3.2.1.4 Sub-theme 1.4: Antibiotic prescribing trend

When asked about the antibiotic prescribing trend, some of the prescribers indicated that the prescribing practices have changed as a result of the implementation of the new clinical guidelines, Primary Health Clinical Guideline (PHCG).

> *"Currently, each healthcare provider provides service using PHCG. As a result, the problem of resistance is expected to be less than before since there is better use. The necessary information is also being provided for the patient as per the guideline. So, it is better than before." (NU06)*

> *"In the past, antibiotics were prescribed for patients with cough of 2 or 3 days duration. Nowadays, what I appreciate about the guideline is that it tells you to properly diagnose the patient, counsel the patient to follow proper feeding style and send him/her back home. If the patient has no progress after 2 days or so, undertake further laboratory investigation and prescribe medication. This is better." (HU08)*

> *"It is good now. Especially after the PHCG for professionals who use the guideline though there is the question of "are all professionals using the guideline?" That is another issue. The PHCG is a good guideline that has brought everything into one. Because, it guides page by page about the disease, its signs and symptoms, are there related issues or not for professionals who use the guideline." (NU09)*

According to HO07, the feedback from pharmacy professionals and morning sessions contributes to the improvement in antibiotic prescribing practices from time to time.

> *"There are instances where you commit mistakes. While prescribing, you may miss the duration of treatment. Mostly, pharmacy professionals does not overlook these things. Most are addressed during morning sessions. Problems are there. There is a lot you share from fellow professionals like "this is your gap, do this and that". Direction is given during morning session to address identified gaps. There is improvement from time to time." (HO07)*

HO06 reported that prescribing antibiotics is increasing significantly which was also supported by NU02 and NU03. According to HO03, antibiotic prescribing is common in the facility and there are even complaints from Pharmacy Unit in relation to the inappropriate use of antibiotics.

> *"There are complaints coming from Pharmacy Unit "medicines are being prescribed inappropriately." The recommendation is 20%, but, it can be 80% if assessed now. So, the whole thing is antibiotics." (HO03)*

NU04 feels that the antibiotic prescribing practices has not improved by relating it with treatment outcome.

> *"There could be better antibiotics. But, I don't think the prescribing has improved. We can talk about improvement if we are able to treat our patients with the antibiotics we have at hand." (NU04)*

4.3.2.1.5 Sub-theme 1.5: Antibiotic resistance as a threat

Most prescribers feel that antibiotic resistance is a serious problem and is prevalent. They also feel that the necessary attention is not being given to it by the government and professionals and hence is neglected.

> *"As to me, it is very serious. First, there is nothing being done at this time. Antibiotics that were there while we were in school are still in use. It is only Fansidar for malaria that is taken out of market. Chloramphenicol is still in use though we were told that it has developed resistance. We were thought in 2002 E.C. that this antibiotic has resisted. But, it is still in use for both unresisted and resisted bacteria. My question is "is there study in this area?" There is no study." (HO03)*

> *"Very much. It is almost neglected. As a country, citizen and professional, resistance is the thing that we neglected much and I am deeply saddened with that. As I just told you, I am very much worried when I think about the future as it will be time where people who have money can be treated whereas rest of the people die. But, it is almost neglected. No one is considering it as an issue and it looks that there is no one who owns it. I am this much sensitive on the issue of resistance." (NU09)*

> *"Well, it is widespread. It is not a simple problem since it is not seen on a single individual. Resistance affects those who are not appropriately using medicines and those that are using properly once it develops. The burden is very huge. If you ask me "what level of attention is being provided?" I don't think the necessary attention is given based on my observation. But, the problem is very concerning." (NU08)*

One prescriber reported that there is no antibiotic resistance at health facility level where he is practicing as per his observation.

"In relation to resistance, so far I haven't received any complaint like "This medicine has resisted for me" or "I haven't got improvement with this medicine. It hasn't benefited me." The antibiotics that are made available by the facility are appropriate ones. If there was complaint related with resistance, it would have been evaluated. Hence, it is not there as a facility." (HO10)

Yet, there were prescribers who have come across resistant cases during their practice as per their suspicion from patient outcomes.

"Yes. I had a case where there was no improvement after using a specific medicines with proper dose and duration which is appropriate for the case. Not only in public, I have also faced in the private. It shows improvement when you use antibiotic that is not used repeatedly. So, there is resistance and I have faced it." (HO09)

"I would like to raise one case as an example. A mother whose child was repeatedly attacked by tonsillitis came to us and told me that "in the past, my child was cured after taking amoxicillin. But after some time, the tonsil relapses every fifteen days." What I understand from this is that previously there was no relapse of this case for up to 6 and 7 years. But now, the mother takes the amoxicillin, but does not complete the treatment. Then after, even if she gives the medicine every fifteen days, effectiveness of the medicine is reduced. There is a case that we referred to hospital for tonsillectomy after it failed to respond to a higher level antibiotic. I consider this as a drug resistance." (NU09)

Key informants were also asked about their views on antibiotic resistance. They see antibiotic resistance as a serious problem because of its devastating consequences on individuals, community and country.

"Now, the rate of resistance is very fast unlike the situation some years back. We were having back-up antibiotics when resistance was developed on antibiotics like penicillins. But now, we don't have that option." (MS01)

"Antibiotic resistance is a major concern. I am saying that because cases that can easily be cured can kill many people if the emergence of resistance continues. So, it is a big concern." (MS08)

"This is very concerning for the future. Unless this is addressed timely like by controlling prescribing, it will end up in loss of antibiotics. We may reach to a

level where people will not be cured due to resistance of bacteria to all antibiotics. When there is no antibiotic that can kill those bacteria, the final outcome is death." (PS04)

"We have been hearing about drug resistance since we were students. Now, when we see while practicing and reading journals, evidences show that the number of people that will be dying due to drug resistance in the coming years will be far more than the number of people that will die due to natural disaster and war." (PS06)

MS02 explained the problem of resistance by relating it to the country's economic situation and their inability to obtain high level antibiotics due the emergence of resistance on the existing ones.

"So, we have concern when we see it at country level. This is because we are a developing country. If resistance develops, it will be very difficult for us to move to other antibiotics in terms of economy and availing the medicine in sufficient quantity. So, the consequence is serious. Hence, all of us should work for change starting from health facility. I think that antibiotic resistance has serious consequences, especially for our country." (MS02)

PS08's concern arose from the time taken and processes required to discover new antibiotics to replace those antibiotics that are no longer effective because of misuse.

"When we think about the process required to discover a medicine and see our antibiotic misuse, I see difficult situation." (PS08)

Similar to the prescribers, the key informants also have concerns that the necessary attention is not being given to the issue of antibiotic resistance by professionals and the government.

"Antibiotics resistance has increased significantly. …. So, drug resistance is serious issue. My fear is how concerned the government is on the issue of resistance." (PS01)

"So, resistance is something that the professionals know but do not give attention to. I think the resistance situation is very shocking." (PS06)

"I think it is very concerning. As an individual, I think it is concerning. Since no action is being taken, it is concerning." (PS07)

When asked about any resistance cases participants may have come across during practice, a key informant shared the below case story about a resistant case confirmed by culture and sensitivity tests.

“Let me raise one of the cases that I came across while providing service. The necessary medication was ordered for a patient that came to the facility after undertaking the necessary medical examination. After taking the medication as ordered, the patient came back and reported that there is no improvement. Thinking over why there is no change, the questions of “has the patient taken the medication appropriately? has the patient completed the full course?” comes which leads to changing the medication to a higher level medication. Though the patient has taken the medication appropriately, there is no improvement. Moving to the next step, the next higher level antibiotic was prescribed. The patient came to pharmacy with the prescription and asked me what the prescribed medicine is. I showed her the medicine prescribed and counselled how to use the medicine. The patient knows the medicine by name and has taken it many times. As a result, she said “I will not take this medicine now.” Then, as a professional, I asked her when she took the medicine and she responded to me the time. When I tried to ask other questions related with the types of medicines she took, she listed down five to six medicines by name.

What is expected as a professional was discussing with the physician who provided medical service to her. The medicines she listed down were higher level ones. Having the failure to show improvement after taking these medicines in mind, I went to the physician and told him what I heard from the patient word by word. Through discussion, we agreed on the need to undertake drug sensitivity test prior to changing the medication. Agreeing on that, we sent the patient to undertake drug sensitivity test. When she came back with the result, her case has unexpectedly adapted to over ten medicines. This has first surprised us highly. Secondly, it has alerted all of us to put the antibiotic use situation under question. At that time, when the patient came back with result of the drug sensitivity test, we were shocked and disturbed due to the number of medicines resisted by the patient’s case.

Other than that, when we asked her, she has taken those medicines in different areas at different times. She was not showing any improvement after taking the medicines. So, what she was doing at that time was that she went to other facility and take another medicine when she felt that her case is not improving irrespective of the way she took the medicine. If still no improvement, she then go to another facility and get prescribed another medicine. It was through this process that the patient came to our facility. This is very serious situation. One individual adapted to over ten antibiotics is very difficult. The other shocking thing is that the patient was pregnant at that time. This shows how widespread *the problem is with one case even without undertaking research. This is what I came across." (PS02)*

This case story and the reports from the prescribers and key informants show that antibiotic resistance is evident in the study setting. It is alarming that the issue of resistance is not yet receiving the necessary attention from either the government or professionals as per the information from the study participants. Although the MOH and the City Administration Health Bureau are making an effort in that regard, it has not yet cascaded down to those primary healthcare facilities that provide services for the majority of the population. It is encouraging that the prescribers and key informants see antibiotic resistance as a concern and have general information about resistance and its consequences.

4.3.2.2 Theme 2: Types of antibiotic prescribing and use problems

Series of problems related to antibiotic prescribing and their use that are prevalent at the health centres were raised by prescribers and key informants. Although the focus of this study was on antibiotic prescribing, patient use-related problems are also presented since they have their own impact on prescribing practices, and prescribing practices have impact on use of antibiotics by patients.

The most frequently mentioned antibiotic use problems by the prescribers were the following:

- Discontinuing medication
- Repeated prescribing of the same antibiotic
- Not taking medication timely
- Prescribing antibiotics for minor cases
- Self-medication with antibiotics
- Jumping to higher level antibiotics

Most of the key informants mentioned the following antibiotic use problems occurring at health centres.

- Repeated prescribing of the same antibiotic
- Jumping to higher level antibiotics
- Over prescribing of antibiotics
- Discontinuing medication
- Prescribing antibiotics for minor cases

Most of the antibiotic use problems mentioned by the prescribers and key informants are similar These include discontinuing medication; repeated prescribing of the same antibiotic; prescribing antibiotics for minor cases; and jumping to higher level antibiotics. Categorised into prescriber- and patient-related, the antibiotic use problems mentioned by the prescribers and key informants are further explained below with quotations from both groups of study participants.

4.3.2.2.1 Sub-theme 2.1 Prescriber-related antibiotic use problems

Repeated prescribing of the same antibiotic

Both prescribers and key informants indicated that there is repeated prescribing of the same antibiotic. This was the top prescriber-related problem mentioned by prescribers.

> *"Here with us, there could be problems related with antibiotic prescribing. For instance, repeated prescribing of same antibiotic." (HO04)*

> *"Sometimes patients repeatedly come with same kind of disease for whom one medication is repeatedly prescribed without reviewing back history of the patient." (NU06)*

> *"What I think as a problem is repetition." (NU10)*

Most of the key informants indicated that repeated prescribing of the same antibiotic is a problems with prescribing of antibiotics.

> *"The first one we see during morning session is repeated prescribing of same antibiotic to patients. For example, prescribing amoxicillin for a patient who was on it for a week or two weeks but didn't show any improvement based only on patient complaint and laboratory investigation without reviewing the patient's past medical history." (MS01)*

"The second thing that concerns me is that I sometimes see patients taking same medicine repeatedly while I dispense. For example, same medicine is prescribed for a specific patient with 10 days or 15 days difference. What I think here is that the patient is not properly diagnosed and hence the case is not appropriately identified from the beginning. There is gap with the provider in reviewing what was prescribed and identifying where the problem is. Taking antibiotics repeatedly has its own problem. That is the first." (PS02)

Key informant MS07 indicated that same antibiotic is prescribed for a number of consecutive patients irrespective of the cases.

"For whatever case the patient comes, that same medicine is prescribed repeatedly. Be it typhoid, tonsil or so, same antibiotic is prescribed for each patient visit." (MS07)

PS06 corroborated this by saying;

"First, what we see in our health centers and in private pharmacies that are under our catchment is that a specific prescriber can prescribe the same antibiotic such as cipro on 7 to 8 consecutive prescriptions. We see this sometimes in dispensaries." (PS06)

According to MS04, healthcare providers are even nicknamed by the antibiotic they repeatedly prescribe;

"At times, we hear that when new providers come, they are named by the medicine they frequently prescribe. For instance, a provider named as "Amoxicillin" is known by always prescribing amoxicillin. Such kind of providers prescribe amoxa for every infectious case coming to them." (MS04)

PS03 linked the repeated prescribing of same antibiotic with the limited number of antibiotics that can be prescribed at health centre level;

"Second, they repeatedly prescribe the antibiotic that they think can be available in the health center. This is because we have medicine list that is available in every OPD which contains medicines that can be prescribed at health center level. As a result, they prescribe antibiotics repeatedly." (PS03)

Prescribing antibiotics for minor cases

Using antibiotics for minor cases was among the most frequently mentioned antibiotic prescribing problems. Prescribers indicated that antibiotics are being prescribed unnecessarily for minor cases such as coughs and other viral cases.

> *"We prescribe antibiotics for those that does not need antibiotic. Mostly, viral cases can be easily managed and prevented. It comes and go by itself. We also order antibiotic for allergic condition." (NU03)*

HO01 connected this with the pressure from patients having CBHI coverage.

> *"Currently, people are coming to health facilities frequently. This may be due to CBHI (Community-Based Health Insurance). There should be something for the community while advocating this thing. People are coming to health facility even for minor cases. They are not willing to go back home without having medicine. I have concern on this. Antibiotics are highly prescribed even for minor cases. Antibiotic can be prescribed for a patient with cough that was diagnosed with same thing two months back." (HO01)*

Antibiotics are even repeatedly prescribed for minor cases as reported by HO01;

> *"Antibiotic can be prescribed for a patient with cough that was diagnosed with same thing two months back." (HO01)*

When asked about the prescribing of antibiotics for upper respiratory tract cases which are the common cases for the prescribing of antibiotics in the quantitative study, the key informants highlighted the practice of overprescribing of antibiotics for these cases. Prescribing of antibiotics for minor cases that can be managed without antibiotics such as the common cold and other upper respiratory cases is irrational. PS01 indicated that

> *"For upper respiratory tract infection, there are cases for which antibiotics are prescribed and there are cases for which antibiotics are not prescribed." (PS01)*

MS03 supported this idea by giving specific examples,

> *"There are instances where they should not be prescribed. Take common cold. Unless the condition persists for 2 to 3 days and the case become serious, antibiotic should not be prescribed for a case that can be managed at home by*

advising the patient. Prescribing amoxa for everything like for sneezing and others is difficult." (MS03)

But, the actual prescribing practices show prescription of antibiotics for almost all kinds of upper respiratory cases. As per the information from most of the key informants, antibiotics such as amoxicillin, Augmentin, ciprofloxacin and erythromycin are prescribed for upper respiratory cases.

"By the way, there is misuse especially on antibiotics use where they use antibiotics for all cases. For example, they use amoxicillin for cases like common cold and other upper respiratory tract infections. The major problem is with us. Antibiotics are prescribed for most upper respiratory tract infections even for patients that have just running nose." (PS01)

"Antibiotics are prescribed for most upper respiratory cases, especially amoxicillin, and when the patient comes repeatedly, a higher antibiotic like Augmentin and erythromycin are prescribed. Now, we are teaming up our professionals to work in one OPD for them to support each other. After identifying whether it is bacteria or virus, antibiotic prescribing may be a must if it is bacteria despite the resistance. The major thing is looking at the history. After reviewing the history and deciding on whether it is viral or bacterial or other case, there could be antibiotic prescribing." (MS02)

"Starting from amoxa, many antibiotics are prescribed for upper. Amoxa is commonly prescribed. Cipro, erythromycin and Augmentin are also prescribed. In addition to cough syrup, antibiotics are commonly prescribed." (PS03)

The quantitative study showed that URTI is the most common case (21.7%) for the prescribing of antibiotics. Of the respiratory tract cases, URTI accounted for about 58% of the cases for antibiotic prescribing. Cost wise, antibiotics prescribed for URTIs accounted for nearly 24% of the total cost of antibiotics.

Jumping to higher level antibiotics

Not prescribing antibiotics following their levels (first-line, second-line and third-line) was mentioned by some of the prescribers and key informants as one of the problems related to antibiotics prescribing. Prescribers were quoted saying;

"Normally, there are situations where we leave first-line drugs and jump to third generation." (HO07)

"There is serious problem in relation to not following the antibiotics level. For a patient who hasn't taken any antibiotic, there are instances where we jump to third and fourth levels." (NU05)

The key informants indicated that some prescribers jump directly to higher level antibiotics instead of starting from first level antibiotics.

"Sometimes, professionals jump-up and prescribe the higher level broad-spectrum antibiotics. We always advise professionals to monitor the treatment and change it accordingly in terms of dose or antibiotic category. But, there is a trend of prescribing higher level antibiotics for both minor and complicated cases." (MS05)

"Yes, there is problem. There is practice of using second and third generations instead of first generation. Moving to high generations prior to using first generation affects the patient cost wise. Second, it causes irrational medicine use." (PS05)

MS06 shared this view by comparing the current prescribing practices with the past;

"If we see antibiotic use in the past and today, in the past any professional be it senior or junior, starts from first generation. But now, be it senior or junior, almost all give third generation to get fast relief." (MS06)

Overprescribing of antibiotics

Overprescribing was the other antibiotic prescribing problem commonly cited by the key informants. The key informants feel that antibiotics are being over prescribed. MS05 explained the overprescribing of antibiotics by relating it to the medicines' budget consumed by the procurement of antibiotics.

"Though we don't have antibiotic use data, it is estimated that antibiotics are prescribed in three-fourth of the prescriptions written by professionals. The medicines procurement data also shows that majority of the budget is being taken up by antibiotics. Leaving the use related issues for later discussion, in general antibiotics staring from the low level up to the higher ones like Augmentin and ceftriaxone are availed and used in the health center."

This claim corresponds with the findings of the quantitative study where 52.5% (from a range of 41.5% to 61.5%) of the prescriptions contained one or more antibiotics, and antibiotics accounted for about 37% of the total cost of medicines prescribed.

PS04 and PS06 reinforced this idea by indicating the practice of prescribing two to three antibiotic together.

> *"But mostly, those who are not that much competent professionals and don't have adequate knowledge on medicines prescribe two to three antibiotics together." (PS04)*

> *"Second, there is practice of prescribing 2 to 3 antibiotics on a prescription." (PS06)*

In addition to the above common prescriber-related problems, some prescribers indicated the practice of prescribing the wrong antibiotic and antibiotic prescribing just to satisfy the patient.

> *"The antibiotic that should be prescribed may not be prescribed for the patient. For example, prescribing antibiotics for a case that requires Cotri or prescribing cotri for a parasite." (NU03)*

> *"… antibiotic use problem is caused by the professionals. Why? Because we prescribe antibiotics for all clients that come to the facility just to satisfy the client." (NU03)*

4.3.2.2.2 Sub-theme 2.2 Patient-related antibiotic use problems

As indicated above, common patient-related problems raised by the study participants were discontinuation of medication, not taking the medication timely and self-medicating with antibiotics. Keeping medicines at home and sharing medicines were also cited by some of the participants.

Discontinuing medication

Discontinuation of medication was mentioned by most of the prescribers as a patient-related antibiotic use problem. Patients mostly discontinue medication as soon as they feel some kind of relief.

> *"There are also patients that discontinue their medication after taking it for 2 days or so when they feel some kind of cure." (HO03)*

> *"In addition, they discontinue after taking it for a day or two when they feel some improvement." (NU01)*

> *"Our patients stop taking the medicine when they see some improvement in the symptoms." (NU04)*

> *"The patient will not also take the full course. There is discontinuing the medication when feels some improvement. Because of these things, I don't think there is rational use." (MS08)*

Not taking medication timely

Some prescribers reported that patients do not take their medications timely.

> *"Things like not taking timely, taking only once a medication that was prescribed to be taken three times a day, not taking medications due to fasting and so on are common." (HO07)*

> *"There are also problems related with not taking medicines appropriately contributing for resistance." (NU02)*

> *"What patients commonly do is they take during breakfast, lunch and dinner without maintaining the 8 hours interval between doses." (NU04)*

Self-medicating with antibiotics

Taking antibiotics by one's own decision (self-medication) rather than consulting a medical professional was another antibiotic use problem mentioned by some of the prescribers.

> *"The public has become very familiar and is purchasing by its own by calling names of specific antibiotic. The public has become very familiar with antibiotics." (HO06)*

> *"Using a specific medicine repeatedly and taking medicine by own decision." (NU10)*

In addition to the aforementioned common problems, keeping medicines at home and sharing of medicines were also mentioned by some of the prescribers as patient-related problems.

4.3.2.3 Theme 3: Consequences of irrational use of antibiotics and antibiotic resistance

Participants were asked to talk about the consequences of irrational use of antibiotics and antibiotic resistance. The consequences reported by the study participants are summarised as follows.

4.3.2.3.1 Sub-theme 3.1: Consequences of irrational antibiotic use

According to the participants, the following are the consequences of irrational use of antibiotics:

- Drug resistance
- Shortage of medicines
- Drug toxicity
- Wastage of resources, and
- Death

Drug resistance

The emergence of antibiotic resistance was mentioned by almost all of the prescribers as a consequence of irrational prescribing and inappropriate use of antibiotics.

> *"If you prescribe antibiotics assuming bacterial infection, it will first lead to drug resistance." (HO03)*

> *"The major one is drug resistance. Inappropriate use of medicines will cause drug resistance." (HO07)*

> *"If we don't use appropriately, the first problem is resistance." (NU04)*

Among the key informants, MS08 pointed out resistance as an obvious consequence of irrational use of antibiotics.

> *"That is clear. It causes antibiotic resistance. This is because antibiotic is given for bacteria. If they are not taking that appropriately, that will lead to resistance like the one we see on TB. That can happen in all antibiotics and that is the danger." (MS08)*

MS11 tried to estimate the rate of occurrence of antibiotic resistance emerging as a result of inappropriate use;

> *"Based on what we see in relation to rational drug use, since we are not using appropriately, I guess that such case is there 60 to 80%. Since there is misuse, if every person is checked for the presence of resistance, it is there. There are instances where we take a specific medicine and shift to another medicine when we fail to get cure by saying that "this medicine is not for me"."*

PS08 and PS10 further explained resistance as a consequence of inappropriate use of antibiotics by giving examples.

> *"At the end, there will be drug resistance. That means a patient that can be easily treated with amoxa will not be treated with amoxa." (PS08)*

> *"Resistance will develop. A case that can be managed simply will require high level antibiotic which will increase the resistance. The patient will also adapt to the drug. Since there is also dispensing without prescription in some areas, there will be adaptation. Once adapted, it will require new medicine to manage it some other time. Resistance will develop to the medicine that we were using." (PS10)*

Shortage of medicines

Two nurses mentioned medicine shortage as a consequence of inappropriate use of antibiotics.

> *"That also affects the supply; one person take it and discontinue; the other person suffers due to lack of the same medicine." (NU01)*

> *"It will also cause medicine shortage which will be difficult to avail medicines for those in need." (NU03)*

MS07 and PS01 mentioned stock-out of antibiotics as a result of irrational prescribing.

> *"It will also lead to stock-out of medicines due to unnecessary use which is wastage and make the medicine not to be available for those in need of that medicine." (MS07)*

> *"Since prescribers use for viral cases, the consumption is high and there is stock-out." (PS01)*

Drug toxicity

Two Health Officers indicated that inappropriate use of antibiotics can lead to toxicity.

> *"Yes, misuse has consequence since it is medicine. Burdening our liver and kidneys as filtering organs for cases that can be managed at home level." (HO01)*
>
> *"Second, it can cause organ failure. If antibiotics prescribed for 7 days are taken within 3 days, it will cause toxicity. That means organs like liver and kidneys will fail which in turn will expose us to complicated diseases." (HO03)*

Wastage of resources

Wastage of resources was mentioned by NU01 as a consequence of inappropriate use of antibiotics;

> *"Second, wastage by itself is one problem. Since they discontinue and take another one next time that is one problem." (NU01)*

Death

NU10 indicated that inappropriate use of antibiotics can lead to deaths;

> *"Till research is undertaken and new medication found, many can die if available medicines are not used appropriately." (NU10)*

4.3.2.3.2 Sub-theme 3.2: Consequences of antibiotic resistance

All of the prescribers see antibiotic resistance as a threat because of its chain of events and eventual impact. The following were the most frequently mentioned consequences of resistance.

- Economic impact
- Having no option
- Treatment failure
- Complication of cases

Of these consequences, economic impact and having no option were also mentioned by the key informants.

Economic impact

Economic impact was mentioned as a consequence of resistance by many prescribers. They indicated that resistance has economic impact on the patient, health system and country.

> *"So, drug resistance has impact on the community, professional and country in many ways. The economic impact is in two ways. First, if the person stays at home and unable to work which will lead to economic failure. Second, the person at home will demand care giver who too will stay at home." (HO03)*

> *"From a facility perspective, there will be economic wastage. It also affects the patient economically since putting a patient that can be treated with a low cost first generation on third generation may not take the patient's economic status into consideration. If the prescribed third generation is not available in the facility, the patient will go out to get it. In the private, the patient is exposed to high expense, I think." (HO10)*

> *"That has economic impact. When we go from first to second and third level antibiotics, their price increases. The patient may not afford that. When we go up, the cost increases for the patient. The medicine may not even be available in the country. So, it may require dollar or so. So, it has economic impact." (NU05)*

Key informants too indicated economic impact as consequence of resistance.

> *"If we continue as such, I think it will have high economic and public health impact." (MS01)*

> *"If resistance develops, it will be very difficult for us to move to other antibiotics in terms of economy and availing the medicine in sufficient quantity." (MS02)*

> *"It has also impact on the country. It will force the country to shift its capital from important investments to the procurement of expensive medicines." (MS05)*

Having no option

Almost half of the prescribers indicated that antibiotic resistance will lead to a situation where there will be no alternative medicine to manage infectious cases.

> *"Hence, drug resistance is great threat for both the patient and healthcare provider. The major concern now is what to use as an alternative if resistance develops to ceftriaxone." (HO03)*

“When we prescribe high level antibiotics, we will end up having no alternative to use for our patients. We don’t have now above third generation. There will be risk of failure to manage our patients.” (HO07)

“As a professional, I am highly worried of what to use in the future.” (NU03)

“Second, the public may end up in having no option to treat their cases till new ones are manufactured. Till research is undertaken and new medication found, many can die if available medicines are not used appropriately.” (NU10)

Some of the key informants considered the antibiotic resistance situation as alarming by relating it with the problem of having no option to manage patients.

“Now, the rate of resistance is very fast unlike the situation some years back. We were having back-up antibiotics when resistance was developed on antibiotics like penicillins. But now, we don’t have that option.” (MS01)

“The consequence of this is serious at the end. It impacts the country, community and medicine supply will be difficult for us.” (MS03)

“You will end up in a situation where you have no treatment option. Second, if the case is not treated at this level, you need to look for high level antibiotics that may be very difficult to avail.” (MS05)

Treatment failure

The other consequence mentioned by prescribers was treatment failure.

“There will be risk of failure to manage our patients.” (HO07)

“That medicine may not treat them if they take it again. That means, we should use the second line.” (NU01)

“This leads to failure of that medicine to treat that disease which requires using the next higher level medicines.” (NU10)

Complication of cases

Antibiotic resistance was also reported by some prescribers as leading to complication of cases.

“A simple case can be complicated. You may not be cured at all for a simple case that was used to be managed at lower level.” (HO03)

> *"A case that can be managed by a simple antibiotic can be complicated and become difficult to treat even with higher level antibiotic." (NU10)*

PS06 mentioned large numbers of deaths due to resistance;

> *"We have been hearing about drug resistance since we were students. Now, when we see while practicing and reading journals, evidences show that the number of people that will be dying due to drug resistance in the coming years will be far more than the number of people that will die due to natural disaster and war." (PS06)*

In addition to these, the following were also mentioned as consequences of antibiotic resistance by some of the prescribers.

- Repeated visit to health facility
- Drug wastage
- Impact on professionals
- Increased pill burden
- Increased side effect
- Increased susceptibility to infection
- Increased patient's doubt on providers

4.3.2.4 Theme 4: Factors influencing antibiotics prescribing decision

The specific factors presented in Table 4.22 emerged from the main theme of "Factors influencing antibiotic prescribing decision". In this Table, the factors are presented by being categorized into prescriber-, patient and system-related factors.

Table 4.22 Factors influencing antibiotics prescribing at primary healthcare facilities in Addis Ababa, May to June 2021.

Category	Specific factors
Prescriber-related factors	▪ Not updating oneself ▪ Competency problem ▪ Not taking patient history ▪ Not taking AMR into consideration ▪ Prescriber’s negligence ▪ Misconception about antibiotics
Patient-related factors	▪ Patient pressure ▪ Low community awareness ▪ Lack of respect from patients
System-related factors	▪ Impact of the private sector ▪ CBHI membership ▪ Availability of antibiotics ▪ Availability of laboratory tests ▪ Lack of updated AMR information ▪ Not engaging pharmacy professionals ▪ Inadequate capacity building ▪ Lack of accountability ▪ Inadequate support and follow-up ▪ Lack of guidelines ▪ Patient load

These factors were further categorized into predisposing, enabling and reinforcing factors to fit the findings into Phase 3 of the theoretical framework guiding this study. These categories of factors are taken as sub-themes to present and discuss the findings (Table 4.23). The specific factors under each of the sub-themes are presented supported by relevant quotations from the prescribers and key informants.

Table 4.23 Factors influencing antibiotic prescribing categorized into predisposing, enabling and reinforcing factors at primary healthcare facilities in Addis Ababa, May to June 2021.

Theme	Sub-themes	Specific factors
Factors influencing antibiotics prescribing decision	Sub-theme 1: Predisposing factors	▪ Patient pressure ▪ Not updating oneself ▪ Competency problem ▪ Not reviewing patient history ▪ Not taking AMR into consideration ▪ Prescriber's negligence ▪ Low community awareness ▪ CBHI membership ▪ Misconception on antibiotics
	Sub-theme 2: Enabling factors	▪ Lack of updated AMR information ▪ Inadequate capacity building ▪ Impact of the private sector ▪ Availability of antibiotics ▪ Availability of laboratory tests ▪ Not engaging pharmacy professionals ▪ Lack of guidelines ▪ Patient load
	Sub-theme 3: Reinforcing factors	▪ Inadequate support and follow-up ▪ Lack of accountability ▪ Lack of respect from patients

4.3.2.4.1 Sub-theme 4.1: Predisposing factors

Predisposing factors are factors connected to knowledge and attitude which can promote or inhibit a specific behaviour (Lundborg & Tamhankar 2014: 128). The factors identified from the in-depth interview with the study participants and are categorized under this sub-theme are presented and discussed below supported by relevant quotes.

Patient pressure

Patient pressure was the most commonly mentioned factor for irrational prescribing of antibiotics. Patients coming to health facilities want specific antibiotics during each health facility visit and push providers for that. They do that even for minor cases. Convincing patients to manage minor cases at home as per the guidelines is not easy as that has not been the practice in the past.

“Let me tell you one thing. Everyone who comes to this facility wants to get medicines. If you say “this antibiotic is not necessary”, you can be accused and the case can be taken to office. There are people who use medicines as ‘snk’ (food prepared for future use while on mission). Even after you teach and counsel, there are patients who tries to take medicines through others.” (HO03)

“Patients want to have antibiotic for any flu case since they used to get that from private health facilities. I have personal observation in the private related with flu. For a case that you think requires hot drinks and home-based management, they prescribe ceftriaxone.” (HO04)

“It is very common. Since I am now working in chronic clinic, patient pressure is not common. Even here, chronic patient come to me when they come to the health center for other cases and ask me to prescribe a specific antibiotic. When I try to tell them the right thing that should be done, they just don’t accept. This emanates from the misconception in the community that they want to get a specific medicine. It is after long discussion that we kind of agree with them. There is interest from patients to get a specific medicine.” (HO08)

The prescribers indicated that the patient pressure is to the extent that healthcare providers prescribe antibiotics for the patient just to avoid conflict with the patient and subsequent grievance.

“Even those that are not users of CBHI, do that. For example, when ORS is prescribed for a patient with diarrhoea or when a patient with common cold is advised and sent back home without medicine, that creates pressure. The professional may simply prescribe antibiotic to avoid the debate with the patient. He may prescribe amoxa or cotri for simple cough. We should make the public aware of such issues.” (NU03)

“Most patients will be very happy if you give them ceftriaxone injection instead of amoxicillin. I think most professionals are coming to say that “why should I quarrel with the patient?” and intend to prescribe as per the patient’s interest.” (NU05)

Some prescribers indicated that although there is patient pressure, they do not change their prescribing decision.

“Especially these days since there is community health insurance most people come to health facilities and everyone wants to have medicines prescribed. They complain when you tell them that medicine is not required. But, we don’t prescribe though they push us to do that.” (HO04)

“They do. There are patients who come to me to get specific medicines. But, I don’t order. I try to convince him. If he is not willing to listen, I tell him that he cannot come here and he can buy and use by his own.” (NU05)

Key informants indicated that patients complain for not getting the medicine they want.

> *"There are patient who say "I prefer the injection" kind of thing. We have also meetings with the community every quarter. Though not confirmed, there are issues that the public complains like "it is always amoxicillin that is prescribed to us." It was also point of debate at Woreda Council in a session I was part. Such kind of complaints are there." (MS01)*

> *"…the client who come to health center wants to take some kind of bottle for his/her children or get injection for himself/herself and do not want to listen to your advice for home treatment like "do this, use hot drink" and respond to you "I know that, I am here not for that, give me tablet." Then, you order antibiotic just to satisfy the patient's need. This is very common. This will become trend." (MS05)*

> *"Yes, there are such kinds of things from patients. They may not know the medicine when it is prescribed. But, when they come to pharmacy and see the medicine physically, they say "I don't need this one" and so on and complain. The other thing we are facing from patients is that if they have taken amoxa for some kind of case and is prescribed again for another case they complain by saying "how can I take this again for this case?" assuming that it is used for a specific case only. There is such kind of problem." (PS04)*

A study conducted in Cameroon (Chem et al. 2018) at primary healthcare facilities revealed that time constraint, providers' perception of patients' expectation for antibiotics, patient expectation and direct patient access to antibiotics (non-prescription use of antibiotics) were among the factors that affected the antibiotic prescribing decision of primary healthcare providers. It was shown that general practitioners and other primary healthcare providers working in highly pressurized clinical environment managing high patient volumes were more likely to prescribe antibiotics for acute respiratory tract infection.

General practitioners and other primary care providers were also more likely to prescribe antibiotics to patients who expect them or whom they believe expect them. Patient expectation was also reported as a factor affecting antibiotic prescribing in a study conducted at primary healthcare facilities in Australia (Lum et al. 2018). In the current study, the prescribers have reported the presence of patient pressure that arises from the expectation to get a specific antibiotic.

Not updating oneself

The other factor raised by key informants affecting antibiotic prescribing is in relation with the prescribers themselves, and not keeping themselves updated.

> *"What I see on professionals is not updating oneself timely. For instance, when guidelines are issued but not used appropriately, the practice will continue with old knowledge. Based on research findings, guidelines are issued with increased or decreased dose. We see overdosing and underdosing due to inappropriate use of standards. This is the gap on professionals, not updating oneself regularly in relation to medicines." (MS08)*

> *"In addition to that, there is practice of prescribing antibiotics for everything assuming that it can manage everything due to lack of updating oneself through continuous reading." (MS07)*

> *"What I think as contributing factor for misuse is that the providers don't update themselves. Once started, they continue prescribing same thing for long." (PS01)*

Some of the key informants related the problem of not updating oneself with the failure to use available information resources such as DIS and not applying the feedback provided by pharmacy professionals.

> *"Even if we give information to OPDs about the available alternative antibiotics and those that are about to be stock-out, no one refers that and apply." (PS01)*

> *"There is DIS, but, there is no one coming and requesting information. There is information here with us about antibiotics. But, most people do not use and there is information gap. This contributes for drug resistance." (PS01)*

According to PS09, DISs of health centres are not providing the services they are expected to provide. As a result, professionals and patients are not receiving medicine related information.

> *"To be honest, I think DIS is there just as a sample. I don't think it is playing its expected roles. The professionals and patient should get information on resistance or any other medicine-related problem from the DIS. But, that is not happening when we see it. Even, some health centers are not able to arrange space for it. ……. There are some health centers that do not have internet. There are also others that do not have some of the books. It is 50:50 and is not as such. But, the knowledge is there. They know how useful it is if available. It will be good if all concerned carry out their responsibilities to strengthen it." (PS09)*

Competency problem

Competency of those professionals involved in the prescribing of medicines was the other factor affecting prescribing practices. Key informants reported that there are professionals that are not competent enough to manage patients and hence prescribe medicines. Some of the key informants linked this competency problem with educational system of the country which is not appropriately preparing graduates for the intended practice, especially in the private sector. The responses from MS06 and MS04 focuses on the educational system contributing to the skills gap of professionals.

> *"The major cause for this is the educational system. First is the educational system. You may ask me why the educational system. We all see at universities and colleges. For instance, here in Addis, a private college trains students. But, there is no practical training at hospitals. Government also trains. It has no adequate space for training. I can say this with full confidence. In the past, nurses move around to have clinical practice. Physicians and pharmacists do the same. There was coaching while practicing. That time, if a coach is assigned for 10 students, it was said that the number of students is high and blamed as not providing appropriate training. But today, one coach handles 70 to 80 students. How can he/she train all these students?" (MS06)*

> *"The cause is clear. Previously, physicians who graduated from public university with high grade were assigned to health facilities. So, they know very well when assigned. These days, there are many private colleges. Recently, their number is declining. We know them. We are looking at instances where people are getting from diploma up to master level qualification without attending any class. Simply pay monthly payments and then receive the degree. Professionals who are having problems even to prescribe antibiotics are upgraded from diploma to degree by simply getting the paper following registration. From degree to masters has also become easy now and people get masters as paper is also done by paying money to someone. But, there are situations where they can't properly respond when they are asked title of their masters paper. So, skill gaps are observed at times." (MS04)*

MS11 related the failure to realise health facility-based skill laboratory for the observed competency problem.

> *"The thing that we mostly propose but is not made practical yet is that we want every facility to have skill lab. Skill lab means before a professional starts managing a patient, it is important to equip him/her to have skill on holistic approach."*

According to PS04, the competency issue come from the decision on who should prescribe given educational preparation of the professionals. This key informant suggested that prescribers should be physicians or health officers.

"I have already said that. From the beginning, the question of "who should prescribe?" Nurses are prescribing. But, nurses should focus on administration instead of prescribing. Prescribers better be HO or physician. Mostly, will be good if prescribers are physicians from what we see. Since there are also writing-related problems, Nurses better be involved more on injection, dressing and treatment. So, the issues are I think related with educational preparation."

Not reviewing patient history

Failure to review the patient's past medical history can lead to irrational prescribing. Both prescribers and key informants reported such malpractice as a contributing factor for irrational prescribing of antibiotics.

"Sometimes patients repeatedly come with same kind of disease for whom one medication is repeatedly prescribed without reviewing back history of the patient. This is a prescribing gap that arises from failure to review previous medical records of the patient." (NU06)

"When there is upper respiratory on both paediatric and adult patients, there could be failure to properly review back history. For a paediatric patient that is repeatedly attacked by upper respiratory and took antibiotics repeatedly, the medication should be changed or the patient should be referred for better care. Hence, not reviewing patient history sheets is a gap." (NU10)

"The first is that there is gap from the provider side to go back and review patient's medical history. There is a problem to look at previous history and its impact on the current complaint." (MS01)

Even if the provider wants to review the patient's past medical history, it is also difficult to get patient history sheets.

"The second is loss of history sheets. History sheets are lost even in medical record room. Sometimes, medical records of patients that were in use for long time don't have history sheets inside. Disorganization of the card room, lack of computerized recording system and time constraint are also factors." (NU10)

"Patients repeatedly come to healthcare providers with new charts as they frequently loss their card number. Hence, the provider cannot check the patient's history on what the diagnosis was and what was prescribed which can lead to repeated prescribing of amoxicillin." (MS03)

MS01 related the problem with patients who fail to reveal past medical history to healthcare providers.

"There is also problem from the patient side by not revealing past medical history and the medication that was prescribed in other health facilities in addition to the current complaint." (MS01)

Not taking AMR into consideration

Not considering the issue of resistance during prescribing was another factor affecting antibiotic prescribing problem raised by key informants. When asked about their view on the practice of taking AMR into consideration during prescribing, MS01 responded;

> *"I think there is gap on that. I think there is gap in thinking about the long-term implications beyond undertaking the daily routines. I consider that as a gap in the facility."*

This was supported by MS02, PS01 and PS05.

> *"Antibiotics are commonly prescribed and there is gap in taking resistance as a concern during prescribing." (MS02)*

> *"Normally, they don't as such worry about drug resistance." (PS01)*

> *"I don't think. It is the pharmacy professional who is somehow concerned about resistance. I don't think such kind of thing is there with the prescribers, nurses and HOs. There may be some. I think great effort has to be made on alerting and training them. Their focus is on prescribing and may not take the issue of resistance into consideration by reviewing background data and understanding how many times has this patient visited this facility? has he taken this medicine before? for how long? and so on and reach on decision to prescribe or not to prescriber it." (PS05)*

MS03 and PS04 indicated that prescribers take antibiotic resistance into consideration during prescribing.

> *"Yes. After looking at the cause and condition of the disease, they may not prescribe first line. They may go to third generation based on the history. The case may become chronic in addition to the resistance issue." (MS03)*

> *"Though not possible to say all, there are some prescribers who say "This medicine was prescribed for this patient. But, I haven't seen any improvement. So, there could be something. Let culture test be done." There are competent ones. Most of them google and refer and hence there is improvement. When a medicine fails to treat a case repeatedly, there are prescribers who order culture test. There are also patients for whom medicine is changed." (PS04)*

Prescribers were asked if they have any mechanism(s) by which they can identify the emergence of antibiotic resistance. Three of the prescribers reported that it is difficult to know resistant cases for the reason that there is no full information about the patient's past medication history and the local antibiotic resistance pattern.

> *"That is not there because what you know is what the patient tells you about the medicines he/she took in the past. Sitting at OPD as a physician, you provide*

the service and don't see who took which medicine and which medicine resisted kind of things." (HO10)

"No, I don't. Because the clients that come to me at different times are different and are not same. A patient that come to me today will go to another provider next time even if resistance occurred. So, how can that be tracked?" (HO10)

"It is after diagnosing the patient that we decide on what to prescribe. There is no information on which bacteria are resistant for which of the antibiotics. If the case is not severe, we can prescribe first-line antibiotics. If it is severe one, we may go to higher level antibiotics." (HO01)

Other prescribers reported that they suspect antibiotic resistance based on lack of improvement, repeated visit, cure with other antibiotic, and patient medical history.

Prescriber's negligence

The negligence from providers was mentioned by some prescribers as a factor for the irrational prescribing of antibiotics.

"What I think as a problem is negligence. If a patient treated with a specific antibiotic shows no improvement, we should think one step up instead of down. This patient has taken this antibiotic, but showed no improvement. If the patient gets no improvement after taking the medicine for 3 to 4 days, he/she will come to us. That implies that there is no improvement." (HO08)

"There are instances where due to inappropriate use, lack of knowledge on how to use them or due to negligence, we repeatedly prescribe them or jump to third generation while we are expected to start from first generation." (HO10)

"I don't think there is lack of information. The professionals know about resistance since they hear about resistance and there is orientation. Even if not oriented, I don't think they haven't heard about it through social media and other means. Some health centers have even focal persons. So, it is not lack of awareness. Rather, it is lack of attention." (PS06)

Low community awareness

The community's awareness about antibiotics and resistance was another common factor mentioned by prescribers that affected prescribing of antibiotics.

"The other thing is the community. We are having a community that is not yet relieved from cultural influence. Unless injected with a medication, the community does not consider as treatment. As a result, there are many who come here and request injections." (HO02)

"When I talk from the perspective of my unit in relation to patients, patients believe with medicines. Especially on paediatrics, there are cases that require

medicines and there are cases that can be management by reassurance. Patients don’t trust that and they depend on medicines. This arises from lack of awareness.” (HO09)

“I think it is related with lack of awareness of the public on the issue.” (NU02)

The key informants shared the concern of prescribers and said the following.

“The first is awareness. The community’s awareness is low. Patient’s focus is on getting fast relief and there is a problem of not thinking about the long-term complications related with the misuse.” (MS01)

“I think the major one is knowledge gap. It is the knowledge gap that is there throughout the community.” (PS07)

One key informant raised the lack of public awareness on implementation of the new guidelines, PHCG.

“But, the patient is not familiar with the things in the PHCG. As per the PHCG, there are cases that are sometimes managed without medication and requires only counselling. The patient is not familiar with this kind of management. The usual practice was prescribing at least a painkiller or some other medicine for a patient. Since that is the practice that the patient knows, there is interest to get medicines not to go back home without medicine. As a result, there are questions being raised by patients like “Is this the only medicine? Is this the medicine?” and so on. There are cases that can be managed using painkillers as per the new guideline. Patients raise questions when their case is managed with painkiller. They raise issue of not being satisfied.” (PS02)

CBHI membership

The Community-Based Health Insurance (CBHI) membership status of patients was reported as a factor affecting the antibiotic prescribing decisions of prescribers. One prescriber indicated that prescribers are very reluctant to prescribe medicines if the patient is a CBHI member due to fear of accountability.

“Since there is CBHI (Community-Based Health Insurance), we don’t prescribe much. All prescribers take great care while prescribing for patients who are CBHI members. From the beginning, we ask clients “Are you CBHI or paying patient?” If the client is paying one, we are not afraid of writing medications. If CBHI, professionals send the patient mostly with no medication. This is because there is audit and recording on finance.” (HO01)

Other prescribers reported that patients who are members of CBHI scheme want to be given medicines at every visit considering it as their right in compensation for the premium they are paying for the insurance scheme. It is a form of patient pressure on providers backed by CBHI membership.

> *"Especially these days since there is community health insurance most people come to health facilities and everyone wants to have medicines prescribed. They complain when you tell them that medicine is not required." (HO04)*

> *"Now, it is also related with Health Insurance. When a person has health insurance card, he thinks that he should get medicines even for common cold. There is thinking of "I have already paid for the service and hence I have to get medicine" as a compensation for the paid premium. This is very common here. It is even a cause for conflict between the patient and provider. When the conflict become serious, we order placebo to calm the situation." (HO09)*

Key informants also raised concerns with the increase in prescribing of antibiotics due to the CBHI scheme in that patients are visiting health facilities more frequently and are taking medicines at every visit.

> *"In our health facilities, what is coming as a new problem related with medications is Community-Based Health Insurance. When prescriptions are audited and observed in various ways, we are identifying that unnecessary medications are being prescribed for clients. The number of patients receiving antibiotics is increasing and patient are visiting health facilities repeatedly due to the feeling they have that "I have paid" or "it is paid for me"." (MS07)*

> *"My fear is how concerned the government is on the issue of resistance. Since the community has health insurance, they come to health facility and take medicines over and over just to compensate for the premium they pay to the insurance system." (PS01)*

Misconception on Antibiotics

A key informant indicated that there is some kind of misconception among professionals on the use of antibiotics.

> *"There is some kind of thinking on antibiotics that they are broad-spectrum and hence can treat other infections that may be there."* (PS02)

4.3.2.4.2 Sub-theme 4.2: Enabling factors

Enabling factors are individual or organizational factors that facilitate an action (Lundborg & Tamhankar 2014: 128). Series of factors that belong to this category were identified from the interview with study participants.

Lack of updated AMR information

When asked about the availability of updated and compiled information on the local antibiotic resistance situation, most of the key informants reported that there is a lack of updated information on the local antibiotic resistance situation. Though some of the key informants from the Health Bureau and sub-city health offices reported that they are sharing various information via telegram, including about AMR, most of the key informants from the health centres remarked on the lack of updated information on AMR. One key informant from sub-city health office reported that;

> *"In relation to awareness, we don't believe that there is awareness problem. This is because most are professionals and hence have the knowledge. But, since looking at updates is important, what we do is when there are updates like in relation to drug resistance, we collect leaflets and other information sources (if available) and distribute to them for awareness creation. In addition, if there are online information, effort is made for all to have knowledge on that. Though the knowledge is there, it is not believed that the knowledge is fully applied since there are things that we observe." (MS09)*

The response from most of the other key informants does not support this idea. MS01 indicated that the only opportunity he had to hear about antibiotic resistance was on a workshop organised by the Health Bureau.

> *"I don't think I have seen that. But, there was orientation organized by Addis Ababa Health Bureau Medicine and Medical Equipment Logistics Directorate for health center heads and pharmacy heads. In addition to pharmacy and DTC, one of the topic was on drug resistance which covered the current global and national situation and actions that should be taken in the future. There is no information other than this."*

This was supported by other key informants who indicated the difficulty in obtaining updated resistance information.

> *"We know about the problem from discussion. But, I haven't seen any document that specifically shows the resistance situation in a specific facility or in the city supported by figure." (MS11)*

> *"There is gap in updating the staff with information. Once you are assigned here, you always do the same thing without getting any updated information." (PS01)*

“It is not possible to get compiled resistance data as far as I know. I haven’t got such kind of information. I haven’t got that since such kind of study is not conducted, I think. This area is not yet assessed.” (PS02)

A key informant explained that the focus is on obtaining medicines and the issue of resistance is ignored.

“The current focus is only on procuring and selling medicines and there is nothing on updating knowledge. The only thing that can be cited is there is orientation for relevant professionals working on ART when new combinations come. Otherwise, there is nothing that is coming to update professionals in relation to antibiotics. That is difficult and possible to say that it is ignored.” (MS05)

Inadequate capacity building

Problems associated with the capacity building of professionals on antibiotic use and resistance was the other factor commonly mentioned by the study participants. It is reported that training is not common in the area of medicine use in general, and on antibiotics and resistance in particular, as a country although there is training in other areas. Prescribers were quoted saying the following in relation to capacity building on antibiotics and resistance;

“What I see as a problem is related with updating oneself as a gap for myself since there is no new training.” (HO05)

“The things that can be causes are lack of refreshing the professionals on regular basis.” (HO10)

“Is proper training being given on curative aspect? As you see, there is no training on curative aspect. The focus is on disease prevention. Will be good if both are addressed equally. When we participate in meetings, the agenda is on how to prevent diseases. It is also just to utilize some kind of fund secured. There is no discussion on issues like "this bacteria might have resisted this antibiotic and so on" even via pharmacy though the training gap is obvious.” (HO03)

Key informants supported the claim from prescribers. MS01 indicated that there was no training for prescribers.

> *"To be honest, other than the one I mentioned before, I don't think there was training especially for prescribers who provide services in OPDs. I don't remember any event other than that workshop." (MS01)*

According to MS04, training on antibiotic use is not common despite the presence of training in other areas.

> *"The other thing is that many training opportunities are given to capacitate the provider. But, training on antibiotics use and overall on medicines use are not common even as a country." (MS04)*

Other key informants also indicated that capacity building on antibiotic use has not been available for several years.

> *"Nothing. Let alone two years, it was not there even before that." (MS03)*

> *"What I want to raise here is that I haven't ever seen training or recap kind of things related with medicines after graduation. I think that is the problem. Why? If a professional is providing service for six or seven years using the knowledge and skill he/she gained from school, I think that has problem." (PS02)*

> *"There is nothing I remember in relation to antibiotics." (MS10)*

PS08 from sub-city health office complained about the absence of capacity building training for pharmacy professionals when compared to other professionals.

> *"What we see in other areas is that they have frequent training. If we see prescribers, they have frequent update. Even, if we see the medical team and disease prevention team here, they have regular updating system. Pharmacy professional has no update other than the basic thing from school." (PS08)*

One key informant indicated that the capacity of focal persons at sub-cities is not built on antibiotics and antibiotic resistance and on what should be done at health facility level to provide the necessary support and follow-up. As a result, they are not providing the necessary support as per the expectation.

> *"It is not that much strong. There was plan to provide orientation on AMR. It was included in the reporting checklist. But, there is nothing shared in the form of document on how health facilities should work. It was only in the checklist that a question "what have you done on antimicrobial resistance?" was included for health facilities. Other than that, they don't know what to do. I myself don't know. What I did is I took out the question from the checklist since I don't have answer if they ask me "what should we do?" I have no answer for this question. Since I myself don't have the information, asking them this question is meaningless. I cannot guide them on how to do it. For instance, if the issue is on how to strengthen IPLS (Integrated Pharmaceuticals Logistics System), I have things to say. But, on antimicrobial resistance, it is what I gained from school which has vanished. So, I deleted the questions from the checklist since I have nothing to guide health facilities on that." (PS08)*

Two of the key informants indicted that there was training on medicine use.

> *"At least once per year, we hear that professionals go for training in relation to medicines use. It may be once per year or once per 2 years. It may be the pharmacy head. Training is not common in this area. Professionals are working with what they gained from school." (MS04)*

> *"During the past almost three years, there has been many gaps in relation to training. This is because we don't get training as required due to budget related national issues. But, our professionals participate on training organized by the health bureau. As per the quota they allocate for us, we send one or two professionals to participate. This year, for example, training was provided by us twice. Though we cannot say that the training is provided focusing on drug resistance, it is included in the pharmacy service part. Though not provided separately, we have tried to incorporate it in the training we provided." (MS09)*

Impact of the private sector

Impact of the irrational prescribing of antibiotics from the private sector on the prescribing practice of the public sector was mentioned by almost all of the study participants. The prescribers complained that private health facilities put patients on unnecessarily high level antibiotics which makes patient management, as per the new clinical guidelines, difficult at health centre level. This is because returning a patient who was on second or third line antibiotic back to first-line as per the guidelines is difficult and is challenging for prescribers in the public sector.

> *"The other big issue now is that private health facilities put patients on ceftriaxone from the beginning. Since they put them on high level antibiotics, managing it with amoxa is not easy when the patients come to the health center." (HO03)*

> *"In addition, there is the private sector. I don't think the private sector is aware of the presence of amoxicillin as a medicine. They directly go for Augmentin or cephalexin. I think this is also one of the contributing factors." (NU03)*

A nurse prescriber reported the following in relation to impact of the private sector's prescribing practices on the public sector's practices.

> *"I don't see as such exaggerated kind of thing in this facility though my experience is short. When you see the situation in private clinics, it is very worrisome. This is because the practice in the private has contribution for the patients that come here. So, though I think that the problem is not that much in our facility, I also think that burden of the malpractice in the private will come to us." (NU08)*

Key informants shared the concerns of prescribers on the prescribing of antibiotics in the private sector and its impact on public health facilities.

> *"There is still problem in the private sector that should be investigated appropriately. That is creating problem on health centers. When patients go to private hospitals, prescribing starts from high level antibiotics like Augmentin and ceftriaxone and even more than that." (MS05)*

“Patients mostly come after visiting private health facilities. As a result, they come to us after reaching third generation. When they come to us, we may put them on first line. Bringing them down to first line will compromise the healing. At times, it is very confusing for us. We kind of say “Go and finish there. We go step-by-step. You have already used that medicine there and the medicine we are going to prescribe may not benefit you.”” (MS03)

According to the study conducted on the prescribing pattern of private health facilities in Addis Ababa (Asmamaw, Ejigu, Tewihubo & Ayenew 2022), 63.8% of the prescriptions were found to have one or more antibiotics which is higher than findings of the current study (52.5%) in public primary healthcare facilities in the City.

In addition to the private health facilities that prescribe antibiotics (private hospitals and clinics), private pharmacies were also mentioned by many prescribers as having impact on the prescribing of antibiotics at health centres.

“If you go to community pharmacy and ask for sale of any quantity of medicine, you can get it. The patient comes to you with the medicine after taking all or some doses of that medicines and fail to get improvement.” (HO03)

“The things that I think is that there are patients who without visiting a healthcare provider directly go to private pharmacy and ask medicines like any shop for salt or sugar “Give me amoxicillin, I have cough.” I see patients saying “give me ampicillin.” The professionals in the pharmacy are retailers, businessmen. They give the medicine as per the client’s request. The patients themselves tell us about that “I have taken amoxicillin”. When we ask them who prescribed that for them, they say “I myself purchased it from pharmacy.” Things like this highly contribute for drug resistance.” (HO10)

Though none of the antibiotics are part of the Over-The-Counter (OTC) List of Medicines for Ethiopia (EFMHACA 2012b), dispensing of antibiotics without prescription at private pharmacies and drug stores is very common. A study conducted in private pharmacies and drug stores in Addis Ababa (Koji et al. 2019) indicated that 63.4% of the simulated visits ended up by over-the-counter (without prescription) dispensing of requested antibiotics with only 36.6% of the simulated antibiotic requested denied on grounds of not having a prescription.

PS06 related the prescribing problem in the private sector with lack of standard treatment guidelines

> *"We don't get the standard treatment guideline when we go to the private sector. We don't get it when we go there for work or other purpose. They don't use it. The prescriber prescribes whatever he thinks appropriate and there is no first line, second line kind of things. Will be good if there is reference for that." (PS06)*

MS08 reported another private sector influence on the public sector where pharmaceutical companies influence prescribing by bringing their own protocol while promoting their products.

> *"Sometimes, there is a problem where pharmaceutical companies apply their own approach. They train professionals from the public sector and demand prescribing of their products. When we bring this to the guideline, we may not use their product as first-line though they put it as such." (MS08)*

Availability of antibiotics

The availability of antibiotics in the facility was the other common factor that affects prescribing practices. Two nurse prescribers indicated that the availability of antibiotics in the facility has effect on their prescribing practices since they prescribe what is made available in the facility.

> *"When we prescribe, we consider access. While I am working here, professionals consider the available medicines." (NU08)*

> *"Yes, especially when the medicines that we want to prescribe are out of stock and the patient does not afford buying from private pharmacies, we are forced to change the medicine. It depends on the medicines made available here." (NU10)*

Some prescribers indicated that they prescribe the antibiotic that is required for the patient's case irrespective of availability of the antibiotic in the facility for the patient to buy from private or public community pharmacies if not available in the facility.

> *"The issue is not on prescribing, rather on availability. For example, now there is common practice of sending patients to buy their prescribed medicines from outside. I don't think the problem is on prescribing." (HO05)*

> *"Medicines that the PHCG requires are not available. Even if prescribed, they are purchased from outside." (NU06)*

> *"Especially after we started using the guideline, our cases are guideline related and we don't hesitate to prescribe as per the guideline. Getting the medicine is up to the patient. If not available here, the patient should purchase it from outside so as to get cure. We prescribe the medicine." (HO07)*

Key informants also indicated that the availability and shortage of antibiotics affects the prescriber's decision.

> *"What is concerning is the antibiotic supply interruption that is there as a country. As a result, if the first line is not available, pharmacy informs prescribers to use alternative drug. So, if the flow is not consistent, prescribing decision of professionals will depend on the health facility's supply. Apart from the supply problem, I think the prescribing and use is good so far." (MS01)*

> *"The major problem is here. Supply problem is the major one and is above all the issues we raised. The whole responsibility to supply medicines for public institutions is given to PFSA, now called EPSA. But, when we go there, we cannot get 10 out of 100 items requested. Then, you can only procure after getting stock-out confirmation from EPSA. There was also delay in giving stock-out confirmation by saying "it is on the way." Now, they have started giving stock-out confirmation immediately. Even after getting stock-out confirmation, you cannot get the medicine from the private sector. As a result, it is becoming difficult to serve the public coming here. There is serious supply problem." (PS04)*

According to PS04, healthcare providers prescribe whatever is required for the patient irrespective of product availability in the facility as was also reported by some of the prescribers.

> *"It may not have that much effect on prescribers. They prescribe and send. If not available in the facility, they send the patient to procure from outside. The problem is on us. When the patient comes, we try not to say "not available" by recommending second choice which requires the prescriber's decision. If the patient says "this is what I need", we don't change that. We inform them to procure that from outside." (PS04)*

Availability of laboratory tests

The availability of laboratory tests was reported as a factor affecting antibiotic prescribing at health centres. There are shortages in the supply of laboratory reagents and hence tests that are necessary to confirm the diagnosis are not undertaken as required in the facilities. A nurse prescriber reported that the unavailability of laboratory tests affects their prescribing practices.

> *"Laboratory mostly affects us when we try to manage by ourselves. At times, when we have patient that don't afford undertaking laboratory test outside, we prescribe based on signs and symptom. The supply is not adequate as per the PHCG." (NU06)*

A key informant from a health centre reinforced this by explaining that the overuse of antibiotics is due to lack of laboratory investigation.

> *"Normally, they manage clinically based on sign and symptom. But, the antibiotic prescribing decision would have been based on laboratory result. It is due to unavailability of that. It is due to the lack of laboratory investigation that there is overuse of antibiotics. If laboratory investigation is available, it would have been possible to identify viral infections which is characterized by the presence of neutrophils which does not need antibiotics and can be managed with analgesics. There are instances where they prescribe antibiotics for viral infection." (PS01)*

A key informant from sub-city health office reported that over half of the laboratory investigations required at health centre level as per the PHCG are not available due to shortages of laboratory reagents and chemicals. He further pointed out that health facilities may stop providing services if the supply problem continues.

> *“The PHCG requires about 30 laboratory tests and the standard is 43. If you go to health facilities, you cannot get more than 20. The reason is that EPSA is not supplying. If you go to the private to buy through tender, the budget you have and the expense does not match and hence is not feasible. If things continue this way, facilities may stop providing service. So, that is the major problem. Hence, a lot should be done on the supply of medicines and reagents.” (MS07)*

Another key informant reported that supply is very low despite the follow-up from office holders and political leaders who are more concerned on availability of products than antibiotic use and resistance issues.

> *“It is difficult, especially on reagents. What the office holders here, council members and political leaders want is availability. They don’t even worry much about antibiotic resistance. But, they want the availability since it is availability that the patient can directly speak about and since complaints come on that. Now, availability is very low and difficult.” (PS08)*

HO07 and NU07 reported that patients are sent to other facilities when the laboratory tests are not available in the health facility. This indicates that there are prescribers who do not change their prescribing decisions based on the availability of laboratory tests in the facilities.

> *“For us, it is like the medicine. As far as the case requires laboratory investigation, we encourage the patient to have the test in other facilities if not available here.” (HO07)*

> *“Same is true for laboratory reagents. Urine and stool tests are mostly unavailable and hence patients go outside for these tests.” (NU07)*

In relation to ordering culture and sensitivity tests, a key informant complained about the delay in getting back culture results to make decision.

> *"We order culture to be undertaken. We send to Pasteur, Arsho and others. But, getting the result takes long time. The patient may not even come back to you. We commonly face this. Hence, we may not know the outcome." (NU10)*

Not engaging pharmacy professionals

Almost all of the key informants with a pharmacy background complained that there is a problem in that pharmacy professionals are not engaged in the implementation of new initiatives in which pharmacists can play critical role. One of the key informants said the following;

> *"Mostly, I don't think pharmacy professional is seen as a professional by the government. But, everything is with the pharmacy professional. The knowledge, task and logistics is with this professional. When something comes, they should update pharmacy professionals together with other health professionals. This is because it is the pharmacist that has direct contact with the medicines and the public. We have raised that in different meetings "Pharmacist is a health professional" since they are not thinking that way. Most people up there on leadership position are either physician, HO or nurse. As a result, they consider pharmacy as a non-professional. When something comes, pharmacy is not included and hence not updated on that. But, the key is with pharmacy who comes in direct contact with the patient. In general, this should be changed as to me. The challenge is not being considered as a health professional, not participating on key issues and hearing from other professionals." (PS04)*

Most of the complaints were raised in relation to implementation of the PHCG. According to the key informants, pharmacy professionals were not part of the PHCG although the guidelines have brought many changes in the management of cases that pharmacy professionals must know how to properly evaluate the appropriateness of the prescription and counsel the patient. They also indicated that a similar complaint was there during the introduction of the Integrated Management of Neonatal and Child

Illness (IMNCI) Guideline. The issue is that only prescribers (physicians, health officers and nurse) are trained without including pharmacy professionals in the training.

> *“One thing that I always complain is that, especially in paediatrics, when there is training, the nurse go and take the training. But, the pharmacist knows nothing. This brings about change in regimen and prescribing leading to conflict on correctness of the prescription. For example, they prescribe amoxa b.i.d. for pneumonia. They have taken training, but, most health professionals are not trained. This leads to conflict among professionals.” (PS01)*

> *“But, here as a complaint, training was given only for physicians and prescribers when the PHCG was introduced. It would have been good if pharmacy professionals were included. There was disagreement at the beginning when the guideline was introduced. Since we were not aware of it, we were debating with prescribers when they prescribe amox q.i.d. instead of the usual t.i.d. that we know. So, it will be good if drug-related things are first introduced to pharmacy professionals. There was also disagreement when IMNCI was introduced for paediatrics as it says amoxa b.i.d. Conflict on every issue coming as new. So, better introduce new documents issued by government to pharmacy professionals.” (PS04)*

Even pharmacy professionals working at sub-city level coordinating pharmaceutical supply and service activities that are expected to support the health centres were not trained on the PHCG. Some of them were not even at least made aware of it as a member of the sub-city management.

> *“I myself don’t know the PHCG. I don’t know it as a system. I hear about it as a member of the management when it is evaluated and so on. But, I don’t know what its components are, to be honest. I had the chance to take the IMCI guideline training. Orientation was provided for selected health centers. But, it was not accessible to all and many professionals don’t know about it. We know nothing about the PHCG.” (PS08)*

> *“I don’t know about that. It is by my own effort that I know about the PHCG. I haven’t taken training. I don’t think those at health center have taken training.*

Mostly, it includes nurses, HOs and others, and I don't think pharmacy professionals are included. What I want to tell you is that there were medicines that are there in the PHCG but not in the drug list. I think direction is now given for health centers to develop their drug list based on the PHCG." (PS09)

The key informants from sub-cities witnessed that pharmacy professionals working at health centres were not trained on the PHCG and that was a challenge for implementation of the guidelines at the beginning.

"It is important. But, when it comes from the higher level, pharmacy was not considered. As a country, it has ignored pharmacy. When some kind of study is undertaken, pharmacy is not included." (PS07)

"They haven't engaged pharmacy as such on that. Other departments have participated on that. There was problem on that. There was complaint "new dosing has come that we don't know". We have tried to convince the professionals on that." (PS10)

The key informants from the Health Bureau indicated that the gap in involving pharmacy professionals in the PHCG training was due to the guidance from MOH to train those involved in case management (physicians, health officers and nurses) and there was no direction to include pharmacy and laboratory professionals in the training. Later on, the gap was identified once implementation had started and these professionals were included in the onsite training provided at health centres together with rest of the healthcare teams.

A Health Officers indicated that there is poor communication between prescribers and pharmacy professionals which is an obstacle for the rational use antibiotics that requires the active involvement of prescribers, pharmacy professionals and patients.

"All pharmacy professionals are not the same. While prescribing, you may commit mistake. There are some pharmacy professionals who don't interact with prescribers in a positive way. As a result, we don't have much courage to discuss with pharmacy professionals." (HO01)

Lack of guidelines

The lack of clinical guidelines that are seriously enforced at each level in the past was mentioned as a contributing factor.

> *"Second, we have seen that there was gap in providing similar care for similar clients due to lack of guideline." (MS01)*
>
> *"Guideline was not available. Now, we are providing service using the PHCG. It was started about 6 months back." (MS03)*
>
> *"Implementation of the guideline was started a year ago. This guideline has restricted the use of antibiotics." (HO03)*

Prescribers indicated that they haven't fully adhered to the new clinical guidelines, PHCG, as it requires time given the high patient load.

> *"It is difficult to say that we adhere to it fully or 100%. There are working days where patient flow is high and days where patient flow is low. There are also instances where you work alone or in a team of two. So, it is difficult to say that we are managing every case as per the PHCG." (HO07)*
>
> *"It requires time. For example, you may start from page 89. Then, you go to page 90. Then after, it tells you to go back to page 60 to manage a single case. It would have been better if it is arranged page to page for ease of use while communicating with our patients. As there are interrupting things in it, patients cannot have confidence on us and may say "why don't I go to pharmacy and buy medicine if they are managing this way." Nowadays, patients have some awareness as they are informed about the guideline. They are told while in the waiting area about the guideline that they should not worry if they see the healthcare provider reading a document while treating them. Now, things are better, but still difficult. Even with that, things are still hard." (HO08)*
>
> *"But, it may not mostly apply for emergency. If it is OPD or cold case, you can use the guideline. But, if it is emergency, since you cannot have time to go page by page, you provide what you think is appropriate." (NU02)*

Patient load

The mismatch between the number of providers and patients that need services at health center level was raised by both prescribers and key informants as a factor affecting prescribing practices.

"The first thing is that there is mismatch between the number of patients coming to health facilities and the number of professionals that health facilities have. As a result, there are instances where patients may not be told clearly what their case is after undertaking investigation." (MS09)

"First, during the past two years, there was high staff shortage since we were not able to hire. There is what we call Family Health Team. Part of the team serves outside and one professional remains in the facility. Only one professional in that OPD. This shows the high workload which has impact to serve the patients that visit that OPD for care." (MS01)

With many patient lined-up waiting for service, it is difficult for prescribers to properly diagnose cases and prescribe appropriate antibiotics as per clinical guidelines.

4.3.2.4.3 Sub-theme 4.3: Reinforcing factors

Reinforcing factors are rewards or punishments that follow a particular behaviour (Lundborg & Tamhankar 2014: 128).

Inadequate support and follow-up

The key informants feel that support and follow-up from upper to lower level in relation to promotion of the rational use of medicines is inadequate. One key informant raised the issues about not getting any response for the requests the sub-city health office presented to the Health Bureau on the resources required to establish DIS at health centres.

"As a challenge, one is the inadequate support and follow-up starting from the higher level. What we mean by that is, for instance, we were expecting good things from DIS implementation if done properly. But, many of the requests we made, especially those related with infrastructure/construction kind of things are not addressed and hence we haven't yet implemented DIC in most of our facilities." (MS09)

The other key informant did not remember any remedial action with respect to antibiotics being taken in relation to support and follow-up from the Health Bureau.

This key informant reflected on the inadequate support and follow-up to health centres with the shortage of human resources in the sub-city.

> *"There is nothing done as such specifically for antibiotics. There is no support and follow-up for us from health bureau. What is there is we support health centers together with them. The number of pharmacy professionals in the sub-city and the number of health centers under the sub-city does not match. For instance, we are two. But, the number of health centers in the sub-city are fifteen. Though the structure requires 6 professionals, what is currently available is only two. Additional staff is going to be assigned." (PS10)*

One key informant indicated that the only support they were receiving was on PHCG implementation as there were no other activities that required support.

> *"They were supporting us in a better way in relation to implementation of the PHCG. Since there are no other things undertaken other than that, I don't think there is area to be supported on. Will be good if the structure is there up to the higher level." (MS10)*

Lack of accountability

Despite prescribing being a very sensitive professional role, accountability is not yet ensured. Although there is a legal provision that controls the prescribing of medicines, it is not yet as such enforced. There are standards that prescribers are expected to fulfil while writing prescriptions, including their name, signature, qualification and professional registration number. But, prescribers often fail to provide full information on prescriptions especially their professional registration number to ensure accountability.

> *"Prescribing medicines has issue of accountability in it. But, there are instances where prescriptions are sent without signature. The rights and obligations of professionals in relation to prescriptions is not as such known. … As I was saying, while prescribing, the prescriber should be known as per FMHACA's standard which indicates that the prescriber's registration number should be written on the prescription. But, it is not there practically. Even, there are prescribers who do not sign on prescriptions." (MS11)*

Lack of respect from patients

One of the prescribers raised the ethical problem of patients affecting and influencing the prescribing practices.

> *"The respect given to professionals in the past is different from the current one. Just imagine how you manage the next patient after being insulted by a patient and passed through unnecessary conflict. So, one is the ethical problem related with patients." (HO03)*

4.3.2.5 Theme 5: Measures taken to improve antibiotic prescribing practices

Study participants were asked to talk about measures taken so far to improve the antibiotic prescribing practices. Most of the prescribers responded that there are no measures taken that they know.

> *"I haven't participated in such kind of sessions. There are no implemented interventions that I know." (HO07)*
>
> *"There is nothing related with medicines and antibiotics." (NU07)*

Other prescribers mentioned that the following interventions are implemented to improve the prescribing of antibiotics thereby prevent antibiotic resistance.

- PHCG implementation
- Undertaking medicine use study
- Undertaking morning session
- Providing health education to patients
- Posting and distributing medicine information to patients

The interventions that were mentioned by many of the key informants are the following:

- PHCG implementation
- Undertaking medicine use study
- Information sharing
- Providing information through DIS
- Supportive supervision
- Providing health education to patients
- Activities undertaken through the DTC

In addition to these commonly mentioned measures, there were other measures reported by some of the study participants. The measures taken so far mentioned by the prescribers and/or key informants are summarised below with relevant quotations.

4.3.2.5.1 Sub-theme 5.1: PHCG implementation

Implementation of the PHCG was mentioned by both prescribers and key informants as the most important intervention to improve antibiotic prescribing practices. A prescriber described the PHCG as an important intervention to prevent antibiotic resistance.

> *"What I think as a good thing done is preparation of the PHCG. Now, antibiotics are not taken for long time, rather taken for short time. If no improvement with the first, it guides us to go to the next. So, it is major intervention in terms of preventing drug resistance." (NU06)*

For HO08, the training on PHCG and its implementation was the only intervention implemented so far.

> *"There was no training. There is nothing other than the PHCG and its training." (HO08)*

Introduction of the PHCG was mentioned by almost all of the key informants as the main intervention implemented so far at health centres to improve antibiotic prescribing. The key informants hope that the PHCG will significantly improve antibiotic prescribing thereby contribute for the reduction in antibiotic resistance. MS04 hopes that the guidelines can address the medicine use problems.

> *"We expect that the recently introduced guideline called Primary Healthcare Guideline (PHCG) that is guiding the practice will rectify the problem. Medicines are prescribed as per the guideline." (MS04)*

According to MS09, the guidelines can address the problems related to antibiotic prescribing and use.

> *"There can be change in the antibiotics use too since the PHCG limits the prescribers not to jump to higher level." (MS09)*

Other key informants explained about the benefits of the new guidelines being implemented at health centres.

> *"The measure taken by the health bureau and sub-city is very good, the PHCG. This has enabled all to have similar knowledge, even if no similar knowledge, similar use pattern since they prescribe by looking at the guideline. No one can prescribe from his own experience. It is only what the guidelines says. I think that has brought one key solution in relation to resistance and medicines for patients. Instead of prescribing antibiotic for viral case and exposing him for resistance, no medicine is required for this patient when you follow the guideline, only counselling. He can send the patient by antipain and advise only. So, it has made professionals to prescribe same thing though their level of knowledge may differ. This has great benefit for the health center." (PS04)*

> *"As I said, professionals are now prescribing step-by-step. When patient comes, the provider reviews the chart to see what was prescribed before. It is good after implementation of the guideline. Before that, there could be many faults from the professionals' side like prescribing same medicines repeatedly. I think things are improved by following the guideline. The guideline is good for providers. It is there in front of them and they can work by reading it page by page. I think that has resolved the problem." (MS03)*

Though there were clinical guidelines in the past, PHCG is unique in the way it is applied in practice. It is being implemented with serious monitoring and evaluation where providers are expected to follow strictly.

> *"Previously, there were guidelines. Normally, those were used as a reference for the provider to check as necessary on medication, dose, diagnosis and so on while managing patients to update himself/herself. The current guideline is not something that we see when we want. It requires following each and every step in diagnosing the case till the medication to be prescribed. Using this guideline is the patient's right. The patient has to be there while we are using the guideline. It will not be possible to prescribe out of the guideline once full implementation is started. The currently available system is the new guideline." (MS02)*

The monitoring and evaluation system that is established as part of implementation of the PHCG was also mentioned by prescribers as an important intervention to improve antibiotic prescribing at health centres.

> *"As I just said, it is not only for antibiotics. In general, to minimize overuse and other things, patient charts are sometimes reviewed by Quality Team. Patient charts are retrieved, reviewed and they send written feedback to us if there is problem. This is for all cases and not specific to antibiotics. Antibiotics are part of the review process. They provide feedback on unnecessary medicine use." (HO04)*

> *"Here, if a patient comes to the facility 2 or 3 times per month, his back history is reviewed in addition to the chief complaint. According to the evaluation system, what was given to the patient is evaluated against the guideline, including the proper use of antibiotics. No one can manage cases out of the guideline by his/her own philosophy, experience or so. The guideline will be seen. Patient cards are collected and evaluated by technical working group against the guideline. Measures are taken on providers not practicing as per the guideline. So, cases are managed by the set guideline. A provider who prescribes antibiotics without pertinent physical examination, laboratory findings and history will be accountable for that." (NU04)*

This was supported by the key informants who indicated that the monitoring and evaluation system is contributing for effective implementation of the new guidelines.

> *"The gap previously was that there was no such kind of monitoring and evaluation system. Implementation of this PHCG has its own technical team that monitors its implementation. Accordingly, patient charts seen in every service delivery point are audited on weekly basis against the treatment guideline. The technical team go to service delivery points and randomly pick and see 5 patient charts from each, check the cases managed according to the guideline and also those referred to other health facilities if that is as per the guideline. As I said, the previous one had no such monitoring system. It was only relying on clinical audit. This is the good part of this guideline. Even the team undertakes baseline assessment on medicines and laboratory supplies quarterly. It undertakes audit on quarterly basis. It provides feedback to healthcare providers on the basis of the findings." (MS01)*

> *"There is a PHCG Technical Working Group that evaluates this. There is mentoring team that mentors this. The mentoring team undertakes clinical audit that is expected to be conducted every other week. Currently, it is undertaking every month. During clinical audit, sample is taken and the number of cases managed as per the guideline and those not managed as per the guideline are identified and feedback on strengths and weakness are provided to each OPD." (MS04)*

Following introduction of the PHCG, a Family Health Team is established at health centres to provide health information and service at household level. Key informants indicated that the Family Health Team is providing community-based health service as much as possible though the shortage of human power is challenging effective implementation of the initiative.

> *"Probably, there is one thing that we think has brought some change. The reason for the change is the Family Health or the establishment of PHCG Unit Team in each health facility. What this Family Health Team do is that they go to the community. People are not expected to come to facility for every case. For minor cases, people are managed at home through psychological therapy or using medicines for them not to come to facility. They go to homes and ask if there are ill persons, see the person, and follow what medicine the person is taking, in addition to health extension workers. They undertake follow-up and counsel on appropriate use of the medicine. They have been doing these for the last 2 years. It has almost 3 years since the PHCG implementation started. There are some improvements. But, this undertaking is not continuing consistently due to shortage of professionals and other things. That is discussed in different sessions and I hope will be addressed. If not, it is difficult. The past two years, especially before COVID, there were changes where patients were taking their medicines appropriately and not visiting health facilities repeatedly. There were good things." (MS09)*

To encourage facilities in implementation of the new guidelines, key informants indicated that staff from better performing facilities in PHCG implementation are involved in supportive supervision activities organised by sub-cities in collaboration with the Health Bureau.

> *"Furthermore, when we want professionals for supervision and other activities we undertake with health bureau, we take professionals from health canters that have better performance in PHCG implementation. This by itself is one encouragement. We encourage facilities using the opportunities we get. We post the information that we get from better performing health facilities to motivate others for better performance. We show ranks of those who are not performing well and write letter through the office for them to correct that." (MS07)*

There were challenges faced in implementing the PHCG. According to the key informants, the challenges are related to both the professionals and the patients. Professionals complain that using the guidelines takes time as it requires going page by page while the patient is in front of you. They also complain that patients may feel that the professional is not competent to manage their case if they have to refer to the guidelines in the presence of the patient.

> *"One thing I would like to repeat is PHCG. There are challenges that professionals raise like "it takes time", "the clients reaction is not good while we read the guideline" and so on. To address that, we have prepared and posted banner for the community to know ahead of time that professionals treat each patient by reading book. We are working on that. The major challenge was the professionals' non-acceptance. It is being addressed through time. We print picture of the guideline on the banner and we are working in each facility on informing the community that professionals manage patients by reading the guideline page by page. This is to make the community aware that the professional will be using a book while managing him/her. The professionals are accepting it when they become familiar through time. The professional that was taking ten to twenty minutes before is able to manage same case with less time. As a result, they are accepting it." (MS07)*

> *"Yes, actually the PHCG is introduced recently. We all have taken the training. Professionals use it. To be honest, it is time-consuming and is challenging them. This is because they need to see many pages to manage a case. They should go many steps." (PS03)*

> *"One thing I would like to repeat is PHCG. There are challenges that professionals raise like "it takes time", "the clients reaction is not good while we read the guideline" and so on. To address that, we have prepared and posted banner for the community to know ahead of time that professionals treat each patient by reading book. We are working on that. The major challenge was the professionals' non-acceptance. It is being addressed through time. We print picture of the guideline on the banner and we are working in each facility on informing the community that professionals manage patients by reading the guideline page by page. This is to make the community aware that the professional will be using a book while managing him/her. The professionals are accepting it when they become familiar through time. The professional that was taking ten to twenty minutes before is able to manage same case with less time. As a result, they are accepting it." (MS07)*

The other complaint raised by key informants was the failure to involve pharmacy professionals in the PHCG training.

> *"But, here as a complaint, training was given only for physicians and prescribers when the PHCG was introduced. It would have been good if pharmacy professionals were included. There was disagreement at the beginning when*

the guideline was introduced. Since we were not aware of it, we were debating with prescribers when they prescribe amox q.i.d. instead of the usual t.i.d. that we know. So, it will be good if drug-related things are first introduced to pharmacy professionals. There was also disagreement when IMNCI was introduced for paediatrics as it says amoxa b.i.d. Conflict on every issue coming as new. So, better introduce new documents issued by government to pharmacy professionals. Other than that, I think the guideline has benefited a lot and provided solution for resistance and related things." (PS04)

"I don't know about that. It is by my own effort that I know about the PHCG. I haven't taken training. I don't think those at health center have taken training. Mostly, it includes nurses, HOs and others, and I don't think pharmacy professionals are included." (PS09)

4.3.2.5.2 Sub-theme 5.2: Undertaking medicine use studies

Undertaking medicine use studies is the starting point to address medicine use problems. Medicine use studies include prescription review and medicine use evaluation. Some of the prescribers reported the practice of carrying out medicine use evaluations in their facilities as a measure taken to improve antibiotic prescribing.

"Prescription evaluation was initiated by DTC. The Pharmacy head was very active. I am not sure why he become weak now. There is nothing that came to us. He might have done it in there. But, the practice of coming together and getting feedback on appropriateness of prescriptions is not there currently." (HO03)

"I think there is. This is because there is prescription evaluation which I think is planned." (NU08)

The information from the key informants indicated that health centres are expected to undertake prescription review and medicine use evaluation though this is not conducted uniformly in all health centres as would be expected.

"There is checklist from health bureau prepared for supportive supervision. The checklist requires health centers to undertake drug use evaluation and prescription review. It also request them to analyse the data and report the status. When we go for supportive supervision, we ask them if they have conducted the review and evaluation. If they say "yes", we then ask them what the findings are and the measures taken. As a result, we are observing improvements. For example, there were situations where ceftriaxone received today become stock-out within 3 days. Now, that trend is becoming less and

less. I think it is good. Though not possible to say it as fully addressed, it is improving." (PS10)

There were health facilities that have undertaken prescription review and medicine use evaluation focusing on antibiotics. Key informants from health centres indicated that they have undertaken medicine use evaluation and prescription review aimed at improving antibiotic prescribing using their DTCs. Once the problems are identified, interventions are planned to address them.

"One of the activities related with antibiotic resistance in the Drug and Therapeutics Committee's action plan is undertaking prescription review. We always undertake that from prescriptions. We have prepared plan to undertake this at least twice per year. So, from the sampled prescriptions, we see how the prescribing of antibiotics is? Does the prescribed antibiotic go with the diagnosis? How many antibiotics are prescribed per prescription? How many injections? Second, we also see if they are using specific drug list of the health center while prescribing medicines." (PS02)

"We did prescription evaluation twice when I was head of the health center. The clinical audit was also conducted every six months. We have tried to undertake the clinical audit till the first six months to see the progress. I think we did prescription evaluation twice in 2012 EFY. We also did patient knowledge assessment as a health center and proceeded to prescription evaluation. The gaps identified were discussed on DTC and agreed on the need to provide orientation. Contents of the training were selected with the pharmacy head. It is part of the plan." (MS01)

"Normally, all management members are members of the Drug and Therapeutics Committee. Because of that, we see together where we are through the committee. So, when prescription review is done twice a year, we sit together and randomly pick prescriptions and see the use pattern together. Based on that, we see where we are? Which medicines are being prescribed frequently? Which ones are slow-moving? and decide on which medicines should be availed more." (MS02)

PS04 reported that the feedback provided to prescribers based on the finding of the medicine use studies have brought improvement in antibiotic prescribing practices as compared to the practices in previous years.

"There are improvements on that. As there is prescription review and providing feedback for the prescribers based on the review, they have improved many of

the things starting from prescription neatness. There is assessment starting from drug therapy and what is needed. There is drug use evaluation and prescription review. Since we are telling them the actual rate of antibiotic prescribing in the facility and the reference standard based on the review, they are improving their practice even the prescribing of antibiotics for simple cases like common cold. Now, that is decreasing and there are instances where patients are returned back home with antipain and counselling. So, there is change now as compared to the previous practice." (PS04)

There are also quarterly follow-ups from sub-city health offices for health centres to undertake prescription review and medicine use evaluation on antibiotics. Key informants from both health centres and sub-city health offices mentioned the practice.

"There is quarterly evaluation, BSC. The BSC asks for drug use evaluation and prescription review on antibiotics. BSC is one of the means we are evaluated every three months on what we performed. It is done four times per year. Those coming from higher level also evaluates us. We do that not just for the evaluation, but, it is something that should be done. The plan contains targets for the rate of antibiotic prescribing." (PS04)

"There is quarterly support and follow-up for health centers to undertake prescription evaluation as per the WHO standard. We see that when we go for support and follow-up. Other than that we don't request to send it to us. Since we request them, the health centers do that at least every six months. They present the findings to the management there. They also present on morning sessions and discuss. That is determined by the professional's and case team coordinator's commitment." (PS08)

Some of the key informants indicated that medicine use studies are not being undertaken in all of the health centres on a regular basis.

"Though not continuous, it is there. We have DTC, but it is not continuous. I cannot say that we are doing perfectly. … Not done. It is not something that I can speak with confidence." (MS03)

"Such kind of things are not there at health center level." (PS08)

4.3.2.5.3 Sub-theme 5.3: Undertaking morning session

Morning sessions provide the opportunity for healthcare providers to discuss real cases and learn from each other thereby improve the practices. Some of the prescribers and key informants mentioned the morning sessions as one of the interventions being implemented to improve antibiotic prescribing practices. Prescribers stated the following.

> *"There is always morning meeting to narrow this gap." (HO02)*

> *"As a plan, morning session by itself is good since it also addresses antibiotics. This is because it gives us the opportunity to learn from each other. Morning session is a very important learning session for us to correct our mistakes." (HO10)*

Similarly, key informants witnessed the presence of morning sessions as a very important learning platform for health professionals at health centres.

> *"In addition to that, we discuss on morning sessions for all to be capacitated. Selected cases are presented. This is how we tried to build the capacity of professionals. We have morning session on daily basis for about 30 minutes." (MS04)*

> *"Though may not be considered as a measure, we have created the forum for the staff to learn during morning sessions by presenting cases that are not managed properly. Through this forum, we are able to present the cases that have problems for the professionals to see their practices and others to learn from the cases." (MS05)*

> *"There is also morning session at health centers where they discuss on cases about the pathophysiology, drug reaction and the nursing care. There are health centers that implement morning session though we cannot say all." (MS06)*

4.3.2.5.4 Sub-theme 5.4: Information sharing

The other intervention that was mentioned by key informants as implemented was the sharing of medicine related information to healthcare professionals. Information is shared though various means. The first means of disseminating antibiotic and resistance related information to professionals and concerned bodies was through organizing workshops and orientation as reported by MS01, PS07 and PS11.

“As I said, we have tried to address the gaps in taking into consideration patients’ past medical history. We have also provided orientation to the professionals in 2012 EFY based on findings of the clinical audit undertaken on history taking.” (MS01)

“A one-day workshop was organized on resistance. At health center level, orientation was provided for the staff in 2012 EFY.” (PS07)

“In terms of awareness creation, we have celebrated the world AMR day at bureau level in collaboration with MOH and EFDA in the presence of Deputy Head of the Bureau with awareness creation sessions. This is because the issue should get attention not only at facility level but also by the leadership. These are among the activities we conducted. Similar awareness creation activities are also undertaken at sub-city level to be owned by the leadership.” (PS11)

MS09 and PS11 reported sharing of information by distribution of different materials on antibiotics and antibiotic resistance.

“Last time, there was a document sent from EFMHACA to pharmacy and medical service on the WHO list of drugs that are resisted. We have attached that for them. Next to that, there was the one issued by our Food and Medicine. We have similarly attached that on this telegram page and they have tried to see that. The question that immediately came to us was “the medicines in the list you sent to us are available at our hand”. We informed them that it is just to create awareness and not to dispose the medicines they have. All have posted the data on which antibiotics are resisted by what. It is national data plus WHO global data.” (MS09)

“It is one of the findings that we got from the ROSS and taken as a gap. After the gaps related with antimicrobial resistance are identified, we have prepared references that the drug information center should have and we are distributing those. We, in collaboration with EFDA, have distributed different brochures and guideline that can be used to promote rational drug use. The documents are available at lower level. This is one of the interventions that we work with EFDA and ROSS initiative in relation to antimicrobial resistance.” (PS11)

Another mechanism used for dissemination of information on antibiotics and resistance was using telegram.

“Sometimes, some facilities through their DISs post information through their telegram channel. But, that is not as such. For instance, I have the post released by one of our health centers on its DIS page.” (PS08)

"When new things come like new algorithm, medicine use, the responsible professionals post that on the health center's telegram page. Professionals read that. In addition to that, sometimes pharmacy unit prepares brochures. There are also brochures prepared by other units. We use all these." (MS04)

"Beyond that, I have my own telegram pages that I use as one platform. One of the pages has 712 members where medical directors and chief executives officers are part. Level "A" health centers have Chief Executive Officer in addition to medical director. On this page, we have shared 503 files. We share links, different things including antimicrobials, letters and videos. Health facilities have created their own telegram page to share information with each other. Many staff of the facilities are members of these telegram pages." (PS11)

PS10 indicated that there is no system to properly update professionals on antibiotics and resistance issues.

"There is no proper flow of information. That means, there is no system to update the professionals on details of a specific medicine, its side effects, what to do and so on." (PS10)

4.3.2.5.5 Sub-theme 5.5: Providing information through DIS

The information provided to health professionals through their DIS was reported as one of the interventions implemented to improve antibiotic prescribing and reduce resistance.

"Normally, we provide updated information about antibiotic resistance through the DIS. As you can see here, there is everything on the poster we post periodically. It can change many things. But, people do not come and read. We also post there when there are new things as you can see." (PS01)

"What we do on this is that there is Drug Information Center that is taken as one standard for all health facilities. We are working on that. We are trying to provide information for prescribers and patients. So, there is practice of providing different updates, including new things, changes made, things that are made obsolete, along with their references. Information is provided for the patient in the form of health education using appropriate methods like in picture or written form. In relation to professionals, we have adequate references in both hard and soft copy form. As a professional, we always provide updates by our own and as per the written request from them." (PS02)

"As I said, what I do is identifying the commonly prescribed medicines while undertaking prescription review, preparing details about these medicines in the form of flyer and distributing that to professionals." (PS02)

Key informant PS03 indicated that professionals do not use DIS as such. There is also gaps from the DIS side where drug information service is not provided on regular basis.

"The practice of coming to the DIS to get information is not that much. There is also gap from our side. We may not provide information regularly. When we meet like during night duty, we communicate information. Otherwise, there is nothing different." (PS03)

PS06 supported the idea raised by PS03 with respect to the drug information service interruption and added that health centres are not sending complete DIS reports regularly to the sub-city health office.

"There are activities. But, only few health canters perform as per the DIS's plan. Most are not operating regularly, there are interruptions in between, and queries are not completed properly. We require monthly DIS report from health centers that shows the number of users, type of users (professionals, clients, administrative staff) and for what purpose. This report does not come to us regularly. There is gap in DIS." (PS06)

4.3.2.5.6 Sub-theme 5.6: Activities undertaken by DTC

Key informants mentioned activities that were undertaken at health centres through the DTC. DTCs work on both supply management and medicine use.

"But, the problem is becoming less and less from time to time. Why? There are interventions being done by Pharmacy through the DTC. That has enabled the prescribers to improve their prescribing." (MS02)

"Now, the major thing is that the DTC provides comment on the annual procurement of medicines. Discussions are held on issues like the type of medicines to be procured based on the clinical characteristic of the medicines." (MS05)

"The other, DTC is there in all health centers. Since the medical director and most of the management is there, it is believed that it can contribute in addressing medicine related problems. They are working on that and are getting results, we think. Now, there are good things and there are changes as a result of it. We think that it has addressed our medicine use issues to some extent.

Not only for use, it has also contributed for the accumulation of medicines. But, their functionality vary from facility to facility." (MS09)

"As I said, I think the support and follow-up is beyond the requirement. But, when you go down, you face many challenges. DTC is functional in all health facilities. Except one health which is COVID center, all the others are functional. Though I am not sure on whether they discuss on antimicrobial resistance as a topic, the DTC is functional in all facilities." (PS07)

PS04 and PS06 indicated that most of the DTC activities are left for the Pharmacy Team due to the misconception of considering DTC solely as a Pharmacy issue. This contradicts the multidisciplinary nature of the Committee which involves all kinds of health professionals.

"DTC is also well performing. But, on DTC, it is the pharmacy that is working more. Mostly, DTC is considered as if it belongs to pharmacy. The major burden is on us. It is more on Medical Director and Pharmacy." (PS04)

"There is gap on that. What is DTC? Once DTC is established, I can tell you for sure that 100% of the activities are performed by pharmacy head or may be with the storeman. To the extent that it looks a burden damped on the pharmacy team, they just discuss few things and take meeting minutes just for formality. On the technical activities, it is only the pharmacy unit that operates. It is like that in most health centers. Not only on health center, we also see that in hospitals. When we go there, they tell us that it is only the pharmacy that is working on DTC." (PS06)

4.3.2.5.7 Sub-theme 5.7: Undertaking supportive supervision

One of the interventions that was implemented to improve antibiotic prescribing and reduce resistance was supportive supervision at health facilities. Although there is no separate checklist prepared to undertake supportive supervision on antibiotics prescribing and resistance, the key informants indicated that this is somehow addressed in the comprehensive checklist used for the supportive supervision at health centres from the Health Bureau and sub-city health offices.

"We don't have separate checklist prepared for drug resistance. There is also no health facility visit organized for drug resistance alone. What we did is there is reform checklist which is used every six months. There are 14 points listed in relation to medicines. One of them is on medicines use. So, we were following

using that. The other is the one we go down with checklist and follow every quarter. There is one component on medicines use in that. We follow using that. Otherwise, there is no separate checklist on drug resistance designed and provided to us." (MS09)

"We go for supervision every quarter. We try to see the pharmacy appropriately when we go for supervision every quarter. We also try to take sample prescription and see. We see the registers we provided to them. We see the list of medicines on the register. We see how many times has a specific antibiotic been prescribed? is that correct? At the end, we provide written feedback. We discuss with the health centers management and provide feedback based on the findings. We agree on timeframe to address the gaps identified."(PS06)

"There is nothing that we organized in workshop form or so. Other than raising the issue when we go for supportive supervision, there is nothing we did or any invitation for a workshop organized by health bureau or MOH on resistance. It is possible to say that there is no discussion about resistance. It is based on what we learnt from school that we try to." (PS09)

PS08 indicated that antibiotic prescribing and resistance is not as such covered under supportive supervision. PSO9 revealed that there is no such supportive supervision at sub-city level from the Health Bureau.

"It was included in the reporting checklist. But, there is nothing shared in the form of document on how health facilities should work. It was only in the checklist that a question "what have you done on antimicrobial resistance?" was included for health facilities. Other than that, they don't know what to do. I myself don't know. What I did is I took out the question from the checklist since I don't have answer if they ask me "what should we do?" I have no answer for this question. Since I myself don't have the information, asking them this question is meaningless. I cannot guide them on how to do it. For instance, if the issue is on how to strengthen IPLS (Integrated Pharmaceuticals Logistics System), I have things to say. But, on antimicrobial resistance, it is what I gained from school which has vanished. So, I deleted the questions from the checklist since I have nothing to guide health facilities on that." (PS08)

"Normally, what is there is requesting information and reports through telephone. Other than the one or two on medicines management, I haven't seen any supportive supervision to us from health bureau on resistance as far as I am here. No one has come for supportive supervision on that." (PS09)

4.3.2.5.8 Sub-theme 5.8: Smooth communication between prescribers and dispensers

Strengthening the role of the pharmacy professionals in prescription evaluation and providing medicine related information to prescribers was cited as one of the interventions implemented to improve antibiotic prescribing at health centres.

> *"We haven't taken measures that can bring radical change. Related with the changes made on the IMCI guideline, we have tried to strengthen the communication between prescribers and pharmacy professionals. For pharmacy professionals not to be limited to dispensing of whatever prescription come to them, but to communicate with prescribers. Though the decision is up to the prescriber, we were enforcing during case presentations to have smooth communication with pharmacy professionals." (MS01)*

> *"Second, as diagnosis is also written on prescriptions, there is a system where the pharmacist can evaluate the prescription and work with the prescriber. There is a possibility by which the pharmacist can correct what is ordered by the prescriber thereby reduce the emergence of resistance. If there is mismatch, they discuss and agree on what to do for that patient." (MS02)*

> *"When clinical pharmacist are on duty and provide feedback during dispensing like this is overdose, the duration is much, why two similar antibiotics, the professionals start reading and prescribe appropriately. Many things are corrected through communication with pharmacy. When that staff resigns, the practice returns back. So, it is also related with the retention or resigning of staff. Since the practice improves when there is professional that can defend them, it is on and off and is not consistent." (PS05)*

4.3.2.5.9 Sub-theme 5.9: Recognizing prescribers

Two key informants from one of the health centres reported that prescribers were rewarded with official certification for using the DIS established in the health centre to update their knowledge in relation to medicines.

> *"There is drug information service request form that is used by prescribers to request different kinds of medication-related information like "can this medicine create reaction with that one?" "can this be prescribed for this?" and so on. This is part of our plan. The pharmacy section provides detailed response for the request. As health is very wide and not possible to have information on all issues, professionals who presented request for pharmacy section and got response accordingly were awarded with certificate in recognition for their good practice." (MS02)*

“Probably, as I said before, professionals are developing themselves by information after establishment of the drug information center. What we see as a recognition now is the one being done for professionals who update themselves in relation to medicines and resistance. There are professionals who frequently send drug information queries for the drug information center. We are providing official certificate to these professionals. In addition, we are also working with the management for this certificate to be part of the efficiency evaluation of professionals taking it as one criterion.” (PS02)

Another key informant indicated that there is a recognition system at sub-city level for health centres in relation to the PHCG implementation. They suggested that health facilities can use this practice to identify and reward better performing professionals.

“There is system in relation to the guideline, not only on prescription. As I said before, we have telegram channel. We share the performance of every health center through this telegram page to all health centers by ranking them as first, second and third. In addition to that, we have recognized health facilities for their better performance during the third quarter. Health facilities can take that down to identify and recognize better performing professionals.” (MS07)

The same key informant (MS07) reported that professionals working in health centres that are recognised as better performing in PHCG implementation are considered to be part of the sub-city health office team in undertaking supportive supervision activities at health centres as a means of recognition.

“Furthermore, when we want professionals for supervision and other activities we undertake with health bureau, we take professionals from health centers that have better performance in PHCG implementation. This by itself is one encouragement. We encourage facilities using the opportunities we get. We post the information that we get from better performing health facilities to motivate others for better performance. We show ranks of those who are not performing well and write letter through the office for them to correct that.” (MS07)

PS06 on the other hand reported that although not specifically focused on antibiotics and resistance, there is a ranking of health centres based on their performance in different programmatic areas (including pharmacy services) following the quarterly supportive supervision conducted by the sub-city.

“Though not specifically on this, there is reform where we visit health facilities every quarter. There is also supportive supervision. We assess health centers using a checklist. Pharmacy is one team and biomedical is also one team. Based on the supportive supervision, the scores are added with other programs of the health centers and recognition is given to health centers as Sub-city health office by ranking them first, second and third.” (PS06)

Key informants PS02 and MS04 indicated that there was no formal recognition system beyond providing feedback on the basis of prescribing performance.

“Normally, this is not experienced so far. When we do prescription analysis, we provide feedback to all. Though there is no reward for better performers, we provide feedback after analysing the evaluation data. If such kind of system is there, professionals can be motivated for better performance. But, it is not there here so far.” (PS01)

“There is no such system. A system of rewarding professionals on the basis of prescribing and educating others is not there. What is there is providing feedback based on findings of the clinical audit and staff presentation. If such system is in place, there could be corresponding accountability on that. We don’t simply say this is weak and that is strong. While we reward or recognize good performers, we should take action on those who have weak performance as the decision is being made on human life.” (MS04)

4.3.2.5.10 Sub-theme 5.10: Assigning prescribers in OPDs in team

Some of the key informants indicated that there is the practice of pairing experienced and less experienced healthcare providers together in OPDs as an intervention to improve the prescribing practices. According to the key informants, this arrangement has provided the opportunity for the healthcare providers to learn from each other and appropriately manage cases.

“In addition to that, we have tried to team-up experienced and less experienced professionals during rotation to work together for them to learn from each other.” (MS01)

“Now, we are teaming up our professionals to work in one OPD for them to support each other. After identifying whether it is bacteria or virus, antibiotic prescribing may be a must if it is bacteria despite the resistance. The major thing is looking at the history. After reviewing the history and deciding on whether it is viral or bacterial or other case, there could be antibiotic prescribing.” (MS02)

“If we assign two clinical nurses together, there will be problem. If we assign relatively weak professionals, there will be gap in handling patients at OPD. To address this gap, we assign senior professionals with junior professionals.” (MS04)

4.3.2.5.11 Sub-theme 5.11: Providing health education to patients

Prescribers reported that medicine related issues are addressed during the health education provided to patients every morning.

“… there is health education to the public every morning. Every Friday, Pharmacy professionals provide health education on appropriate use of medicines like not to take medicines unless it is prescribed for them, not to borrow medicines from neighbours.” (NU04)

“Nowadays, education is provided. Previously, health education was provided by professionals who were on duty during the previous night. Now, laboratory and pharmacy professionals are also involved. The pharmacist educates about medicines, their handling. The laboratory professional discusses on issues related with laboratory investigation since there are people who complain when they are asked to give or bring sample for laboratory test.” (NU09)

Some of the key informants also indicated that health facilities provide health education in the morning while patients wait for service.

“Furthermore, for the community to have awareness on resistance, every morning before daily duty is started, pharmacy professionals together with professionals from OPD and medical record unit orient patients. Effort is made to orient them with focus on medicines use to create awareness.” (MS09)

“We are trying to address this through the regular morning health education. For instance, I myself have program once per week. On that program, we try to inform patients about the case management process for them to be familiar and avoid unnecessary complaints.” (PS02)

4.3.2.5.12 Sub-theme 5.12: Providing written information to patients

In some of the health facilities, pharmacy units prepare, post and distribute medicine use related information materials to patients. A key informant from one of the health centres described such practice by saying;

"There could be patients that want to finish the medical process and go back home quickly. We support that by providing written information to increase their awareness." (PS04)

Two prescribers supported such practices at health centres.

"Pharmacy unit posts some information like the meaning of taking medicines three times a day, every 12 hours. Sometimes three times a day looks taking the medicine during breakfast, lunch and dinner time. They have posted information on taking medicines every 8 hours and every 12 hours. But, that is not as such done seriously." (NU03)

"Pharmacy has information paper that they give to the patient during dispensing. The paper contains information on why the prescribed medicine is taken, the meaning of three times a day." (NU04)

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4.3.2.6 Theme 6: Recommended interventions to improve antibiotic prescribing

The other common question presented to all of the prescribers and key informants was the interventions they recommend to be implemented at various levels to improve antibiotic prescribing at health centres. Most of the prescribers recommended the following interventions.

- Apply the same clinical protocol for public and private sector
- Proper management of minor cases
- Having a M&E system
- Increase public awareness
- Provide proper counselling
- Provide Training for health professionals
- Update knowledge
- Provide health education
- Conduct research and disseminating findings
- Proper implementation of the PHCG
- No dispensing without prescription

The interventions recommended by most of the key informants are the following.

- Provide training for health professionals
- Provide health education to the public

- Conduct research and disseminate the findings
- Control the private sector
- Improve supply availability
- Provide follow-up and support
- Provide proper patient counselling
- Proper implementation of the PHCG
- Assign AMR focal person
- Strengthen DTC
- Apply the same one protocol for public and private sector

4.3.2.6.1 Sub-theme 6.1 Apply the same clinical protocol for public and private sector

Standardizing the prescribing practices in both the public and private health sector was the most common intervention suggested to improve the prescribing of antibiotics and reduce antibiotic resistance. Most prescribers indicated that the prescribing practices in the private sector is not governed by clinical guidelines. They recommended implementing the PHCG in the private sector too.

> *"This guideline is not implemented in the private sector. It is good that the guideline is implemented in government health centers. Drug resistance cannot be stopped by working on the public sector alone. It can be stopped if both sectors are guided by this guideline. If it develops resistance in the private sector, giving the medication of your choice when the patient comes to you has no meaning." (HO03)*

> *"The focus should not only be on the public sector. It is only few people that are coming to public health facilities. Most people go to the private sector. Will be good if same guideline is given for all professionals and system is created to monitor that." (HO04)*

> *"When government issues directions, it should consider the private sector as its own and address the whole health sector. The professionals serving in private health facilities are those working in the public sector. Hence, we should provide the same service. To provide similar service, there should be same guideline for both to guide the service and its implementation should be monitored and evaluated. This is because we are providing service for the same community. We are providing service for a human being. Whether I serve in the public or private sector, there should be unique law. Health service should not be left as free market and there should be unique law that governs the service in the public*

and private sector equally. If that is done, I think we can decrease drug resistance." (NU04)

"Currently, the medicines prescribed at private and public health facilities are quite different. It is the professional working in public health facilities that follows the steps. As we see the private as a patient or accompanying family members, the practice is different in the private. If there is a guideline that can be used by both the public and private health facilities and if measures are taken on those who don't adhere to the guideline, I think it can be resolved." (NU05)

Having one standard for both the public and private sector in the management of cases was also suggested by the key informants as an intervention to improve antibiotic prescribing. Currently, practices in the public and private sector are different due to lack of common protocol applied to both sectors.

"Effort should be made to reconcile this. There will be better practice if this is reconciled and a standard that can be used by both the public and private sector is developed. Now, it is different. Even in our health centers, pharmaceutical companies provide their own training, bring their own medicine use protocol which confuses us since it contradicts with what is known in the public sector. It contradicts and creates confusion on which one to use. Will be good for all if there is only one protocol." (MS08)

"For the time-being, the PHCG clinical care guideline is started at health centers. When we discuss on the issue, there was consensus on the benefits of implementing this initiative in hospital setting so that hospitals can support health centers in relation to PHCG implementation. Accordingly, one quality focal was trained from hospitals. Even the practice among public hospitals is no similar. For the same case, what is prescribed by different physicians vary. If we strongly work on that and start the initiative at hospital level, there will be no problem in taking it to the private sector. Though I cannot put specific percentage, most of the professionals working in the private on part time basis are those working in the public sector. So, if we can make it practical in the public sector, I think the private will be corrected." (MS11)

"I hope it will be possible to reduce these problems if the government, community and private sector work in a coordinated manner and apply some kind of standard." (MS11)

4.3.2.6.2 Sub-theme 6.2 Properly manage minor cases

Not prescribing antibiotics for minor cases such as viral infections was suggested by many prescribers as an intervention to improve antibiotic prescribing and prevent antibiotic resistance. They suggested managing minor cases with home remedies and/or pain-relievers and delaying the use of antibiotics.

> *"If it is viral, we should manage it following the protocol used for the management of viral cases by prescribing paracetamol and advising the patient to drink warm water and not by prescribing antibiotics." (HO03)*

> *"The first option is home treatment. If not improved by home treatment and if the case complicates, I think antibiotic is vital." (HO07)*

> *"Many cases are coming especially related with the current COVID-19. Patients come even when there is sneezing. We don't give antibiotic for this. To prescribe antibiotics, there are things to be fulfilled that we learnt at school. Antibiotic is not commonly given for upper respiratory tract infection. For instance, if you take common cold with chest finding and runny nose kind of things, we prescribe antihistamines. Besides that, we advise home remedies like taking Vitamin C and more fluid and hot drinks." (HO04)*

> *"For instance, if it is common cold with low severity, I don't prescribe antibiotics mostly. I advise them to manage with food like adding "nech shinkurit/white onion" and honey in their food. Cough can stay up to 14 days in paediatric patients. If there is no fever and it is only cough, I advise the mother to give breast milk repeatedly if the baby is less than one year and give honey (one teaspoon) if the child is above one year. If the child has started additional food, we also advise the mother to give orange at least 3 times a day. So, we also focus on nutrition and we don't simply prescribe antibiotic due to fear of resistance. When that baby become seriously sick next time, he/she will use the antibiotic. So, we strongly advise on nutrition." (HO06)*

> *"If it is common cold, the guideline orders home treatment with tea and honey and then follow-up. We tell them the signs of pneumonia for them to quickly take to a health facility when the child has fast breathing and fever, and how to manage the case at home. When there is congestion in the nose, we advise them to use steam and fumigate the house with salt and boiled water. If it is progressing well, we send back with no antibiotic. That trend is there. Then after, we follow the progress during follow-up." (NU03)*

> *"But, for simple upper respiratory cases like common cold and others that are viral in nature, even if there is cough, if there is no chest finding and no fever, I counsel and send the patient back home." (NU05)*

Prescribers were asked under what condition they prescribe antibiotics for URTIs. Though they mentioned different criteria, the common one was the presence of a repeated cough with a duration of over 3 days and a productive or wet cough.

> *"One is cough with duration of five days or more. Fever can be additional one. In addition, if there is no improvement while on home remedy, the case is decided not to be viral case and is considered as bacterial case for which antibiotic is prescribed. We counsel patients to take hot things if they haven't taken that. If there is no improvement with that, it is one criteria." (HO09)*

> *"When there is cough with duration of over 7 days and when there is fever, we prescribe antibiotic." (NU01)*

> *"A patient with upper respiratory problem may have cough. If there is productive cough, I will give antibiotic without the need for any further investigation. The new guideline recommends a patient who has productive cough to be on antibiotics while waiting result for TB. If there is fever in addition to the productive cough, I order antibiotics." (NU04)*

> *"If there is repeated cough, that requires antibiotic. Cough that persisted for 3 and 4 days. The presence of repeated cough is serious for paediatric patients. Hence, antibiotic is recommended for repeated cough in paediatric patients that persisted for 3 days or more." (NU07)*

The presence of fever and chest finding were the other criteria mentioned by prescribers for the prescribing of antibiotics for URTIs.

> *"If there is very high fever, we suspect infection and go for antibiotics." (NU06)*

> *"I consider antibiotic as a choice when there is high grade fever since that is expected to be bacterial most of the time." (NU08)*

> *"Antibiotic is a must if the patient has fever, chest finding and fast breathing. There are many types of pneumonia. Of these, if it is febrile pneumonia with fever, chest finding and fast breathing, this patient requires antibiotic." (HO04)*

For cases that are suspected to be of bacterial origin, the prescribers indicated the need for antibiotics.

> *"For instance, if a patient comes with sinusitis, I add antibiotic since there is infection. Cases like simple rhinitis or common cold may not require antibiotic. We manage such case through counselling and prescribing anti-pains and*

antihistamines as necessary. Some patients are returned back home without any medicine. That does not mean that we prescribe antibiotics for every upper respiratory tract infection as to me. I don't know what others are doing." (HO02)

"The guideline recommends antibiotic for rhinitis. But, how severe is it? and which one should come first? is left for your professional decision. If you see tonsillitis, does it have exudate, pus, fever? If it is bacterial, it will have severe fever and exudate. You cannot simply leave this. This is not something you manage it by advising the patient to do this and that. Rather, the patient must get antibiotic. Prescribing antibiotic for simple and viral cases is irrational." (HO03)

"But, for cases like tonsillitis in the presence of swelling, redness plus pus, even if it is exudated tonsillitis, I think antibiotic is important." (NU08)

The other criteria that prescribers use to prescribe antibiotics for URTIs is when the condition shows no improvement with home treatment.

"In my view, if they are not able to treat with home medication and anti-inflammatory and if the patient has cough with 4 to 5 days duration, then since that is going to advance to lower respiratory tract infection, there is trend of putting on first generation antibiotic. I manage that way." (HO10)

Evidences show that a well-documented strategy for reducing antibiotic prescriptions for respiratory tract infection is the use of delayed prescriptions. Delayed prescriptions are valid prescriptions issued at the time of the consultation. The healthcare provider usually negotiates with the patient that they are not to be used immediately but only if the patient feels that their symptoms deteriorate or do not improve as expected. There is substantial evidence that the use of delayed prescriptions has been associated with reduced antibiotic use (O'Connor, O'Doherty, O'Regan & Dunne 2018).

4.3.2.6.3 Sub-theme 6.3: Provide training for healthcare professionals

Capacitating healthcare providers through training on antibiotics use and antibiotic resistance was suggested by prescribers as an intervention.

"The professional should update himself/herself. It may be difficult to update oneself given the salary. For this to happen, there should be system whereby professionals can get update like in the form of training, brochures, leaflets. This

can help the professional to restore his/her mind and support financially. The initiation that will come through this will lead to better performance." (HO08)

"As a health center, training should be there and there should be monitoring and feedback system for professionals to improve their practice by learning from their mistakes." (NU01)

"In the future, if the professional is updated through training and capacitated, it will be big intervention." (NU06)

One prescriber further suggested that the training should be provided to relevant healthcare providers who can apply the knowledge and skill gained to improve practices.

"What I suggest based on the knowledge I have is that medicine-related training should be given for the relevant professional. Sending irrelevant professionals for training should be stopped and the necessary attention should be given for this issue. If the training is for pharmacist, then the pharmacist should go for it. If it is for nurses such as paediatrics and youth, the professional working on paediatric and youth health should be the one to attend. This should be strictly followed so that the concerned professionals can get the training. When we do that, the trained professionals will share the knowledge he/she gained and apply the knowledge and skill in practice." (NU09)

Most of the key informants suggested updating professionals through training as one of the interventions to improve antibiotic prescribing and reduce resistance.

"The first and most important is proving training for professionals to reduce the use of antibiotics." (PS07)

"The major action that should be taken is that training should be provided to professionals on antibiotic resistance and related issues." (PS09)

"The major thing is that a person could commit mistake intentionally or unintentionally. Since it may be due to lack of updating oneself, training is important. Professionals should be trained. Practicing for 3 to 4 years with the knowledge he/she gained from school is very difficult." (MS05)

MS03 added the need to train professionals practicing in the private sector to make them responsible for their patients rather than for their business.

"First, update the professionals working in OPDs through training. Second, provide training at government level for physicians working in the private sector for them to be responsible for patient than for their business." (MS03)

According to MS05, antibiotic use and resistance issues are almost neglected as there is no training on that; most of the available training is on disease prevention.

"It is possible to say that there is no training on this issue. Most of the trainings available are only on disease prevention. There are many things neglected in relation to medical service. The pharmacists and professionals should get appropriate training on antibiotics and others on regular basis. Capacity building is very important. I think this is almost neglected as I see it. Government's focus and direction is only on those supported by CDC like HIV, TB and related things." (MS05)

MS08 justified the need to build the capacity of healthcare providers on use of antibiotics and resistance on a regular basis by relating it with the continuous changes in the healthcare sector.

"What I am thinking actually is providing onsite training on medicines use for healthcare providers, especially for professionals delivering service at health facilities. This is because, health requires continuous reading. The knowledge is volatile and you cannot use it for long unless you update it regularly. Professionals should take training and orientation on medicine use and resistance to keep them updated." (MS08)

This was supported by PS02 who indicated the need to be aware of current advances in the area.

"Hence, there should always be updated and continuous training and alerts on antibiotics. I think the professional should be aware of current advances in the area through alerts, trainings and workshop organized on regular basis based on well-prepared program. Otherwise, we will face a problem." (PS02)

Due to the focus on theoretical issues, having practical sessions in capacity building training was suggested by MS11 to address the skill gaps of professionals.

"First, awareness creation sessions should be organized for the professionals. If possible, the awareness creation sessions should have practical sessions.

> *Mostly, our training become theoretical and the practical part like counselling become difficult." (MS11)*

Providing training for all concerned professionals at a time when different clinical protocols are developed and disseminated for use was suggested by PS03. According to this key informant, the training will give healthcare providers the opportunity to be aware of changes and the rationale behind those changes.

> "*The other is providing training for the staff when different protocols are developed and disseminated for use. In addition, protocols contradict each other at times. This should be reconciled or make the professionals aware of the differences. I think there will be better thing if people from the* health bureau *do that." (PS03)*

PS04 suggested that training should be provided to prescribers on the global, national and local antibiotic resistance situation based on evidence.

> *"Even after the prescribers become physicians, continuous training should be provided. Updating professionals on the global, national and local situation based on evidence on things like which antibiotics became out of market due to resistance." (PS04)*

4.3.2.6.4 Sub-theme 6.4: Proper implementation of PHCG

Both prescribers and key informants hope that the correct implementation of PHCG can improve the prescribing of antibiotics and reduce antibiotic resistance. Prescribers explained this as follows:

> *"Implementation of the guideline has significantly improved our antibiotics use. This is because the guideline has reduced the duration of treatment from 10 and 7 days to 3 days which is not boring for patients. So, the guideline has become good for patients as well as for healthcare providers as it is very indicative." (HO05)*

> *"But, we are coming to it. Other than that, I believe we should use the guideline. It is very important and we must use it. If human resource is made available, we should 100% adhere to the guideline. I think we must use the guideline by informing the patient during health education." (HO07)*

> *"Currently, each healthcare provider provides service using PHCG. As a result, the problem of resistance is expected to be less than before since there is better*

use. The necessary information is also being provided for the patient as per the guideline. So, it is better than before." (NU06)

Most of the key informants hope that PHCG can address the antibiotic prescribing and resistance problems. As a result, most of them have suggested proper implementation of the PHCG as one of the interventions to improve antibiotic prescribing and reduce resistance.

"What I think as a good thing on this is that the government has already identified the gap. The PHCG is developed by assuming skill gap as one of the gaps. Hence, this guideline should be implemented for all patients. Currently, the direction is to apply it for 50% of the clients. We are recently informed to go for 100% thereby apply the guideline for all clients." (MS04)

"Probably, there is one guideline issued recently. I think the prescribing as per this guideline has minimized the differences. I think practicing as per the guideline has somehow limited the antibiotic use though there are some issues that should be corrected as to me. But, I think there are some changes in the prescribing of antibiotics. There is no prescribing left and right. This should be strengthened. But, the threat will continue if this is applied only on government health facilities. As a guideline, it should I think be applied in private and others similarly. The use is better after the guideline is issued." (PS02)

"The other thing I want to say is that it is a solution for all if the guideline is implemented appropriately. Both professionals and users benefit from the guideline. It will contribute for the reduction in resistance as it will bring things to a common standard. So, applying the guideline is key for all. If we keep on updating it, discuss on it, it can even be used for medium clinics. Like this one, if something is done for hospitals to standardize their practice, the problems will lessen from time to time." (MS02)

4.3.2.6.5 Sub-theme 6.5: Undertake research and disseminate the findings

This intervention is related with generating evidence and disseminating the findings to all concerned to improve antibiotic prescribing. The need to first identify the problems in the prescribing practices was suggested by HO02. NU01 indicated that interventions should be designed and implemented to address the problems identified.

"The first thing is identifying the problem, where is the problem?" (HO02)

"…after identifying the problems, interventions should also be designed and implemented." (NU01)

As per the suggestion from HO07, this involves not just undertaking research, but making the findings available for healthcare providers on the ground.

> *"In addition to that, from higher level, study should be conducted on drug resistance and the findings made available for healthcare providers. It should come down to the professionals. Studies are conducted, but the findings does not reach to the lower level. Since resistance is affecting our country and community, the healthcare provider should have information. I think this can be a big input for the professionals." (HO07)*

HO03 raised similar issues in connection with this study and in making the findings accessible to professionals in practice. According to this prescriber, unless the findings are utilised to improve practices, undertaking research has no benefit or value. Hence, the relevant government body should disseminate the findings for the professionals to be made aware and take the necessary action to improve practices.

> *"You are the first to undertake this kind of study. There may be other studies. But, looking at finding of the studies and evaluating where we are should be the responsibility of the concerned government bodies at each level. Unless we utilize the findings, simply undertaking research and shelfing the reports is useless. It will help you to graduate. But, it should go beyond graduation and the findings contribute some value for the country. It will be difficult if the concerned government body does not take the findings down to the practice and make the prescribers aware of the findings and actions to be taken." (HO03)*

The key informants indicated that interventions taken to improve antibiotic prescribing practices need to be based on evidence to bring tangible change in practice.

> *"To achieve better results, interventions should be supported by evidence. If the actions are evidence-based, we can bring tangible changes and thereby improve quality of the service to the community. Now, things are being done arbitrarily. I hope the study will address this." (MS07)*

> *"Since studies are evidences, they can bring change if conducted in each area. Saying this and that based on what we know will not get acceptance since that is not study. When studies are conducted, if they are conducted by going down to the community and professionals, it will be possible to address the problems based on evidence." (MS08)*

Knowing the antibiotic resistance situation at national and local level requires undertaking studies. Such kind of information is very important to appropriately update the guidelines that govern the prescribing practices.

> *"Undertaking research is also important. This is because we should know which antibiotics are being resisted in the city so that we can update guidelines accordingly." (MS01)*

> *"Study should be conducted on the resistance status of the existing antibiotics. Most of the antibiotics available here are said to have resisted. You cannot get that in the form of study. You get it in the form of rumour. It will be good for the physician and all others if the information on resistance situation on specific antibiotics like ampicillin, tetracycline, and amoxa is based on research. I think it will be good if things are supported by evidence to contain the emergence of resistance." (PS04)*

The importance of having data on local antibiotic resistance patterns was also suggested by HO07. According to this prescriber, having such data can guide prescribers which antibiotics to use and which ones not to use.

> *"The Health Bureau should work on this to identify which antibiotics to use and which ones not to use." (HO07)*

MS09 feels that the new clinical guideline (PHCG) has included antibiotics that are already resisted due to the lack of information on the local antibiotic resistance pattern. This key informant suggested that the list of antibiotics that are resisted should be made available to the public and professionals in the form of publication.

> *"For example, the recently issued guideline has included antibiotics that are already resisted. The guideline we are using, PHCG, has included those medicines. So, when such guidelines are developed, they should appropriately incorporate recommendations of professionals and be evidence-based. The list of medicines that are resisted be made public to the community and health professionals by issuing a publication. That can increase awareness and build trust. Now, there is nothing that has reached to the professional other than the rumour of this and that has created resistance. If these things are published and reach to the professional, it will help address the resistance problem. Will be good if that is worked out." (MS09)*

PS07 stressed on the need to disseminate findings of the studies conducted in relation to antibiotics and resistance to professionals and other concerned bodies. The key informant further explained that having local antibiotic use and resistance data is very important and budget should be allocated to undertake such kind of study to have local data that can be presented to healthcare providers at health facilities.

> *"If results of the assessment is briefed to the providers, there will be the motivation. This is because the action should be started from assessment to have detailed data which can be presented to concerned bodies and professionals instead of talking about resistance without local evidence. So, budget should be allocated for the assessment to have data that can be presented to providers at facilities, I think." (PS07)*

PS03 suggested that information on antibiotic use by healthcare providers should be part of the routine reporting system.

> *"Undertaking research on antibiotic use by the healthcare providers and making it part of the routine reporting system with proper follow-up." (PS03)*

MS07 suggested the need to encourage researchers to undertake studies in the areas of antibiotic use and resistance. According to this key informant, the area of antibiotic use and resistance is not yet well investigated.

> *"One is encouraging researchers undertaking study in this area since it is not yet touched. There may be no much studies conducted in this area as a country and city administration. It is important to take the necessary steps at bureau level to encourage researchers to undertake study in this area. Both the community and professionals are applying as per the knowledge they have. Though the implementation will take some time, if studies are conducted and guidelines are updated accordingly, I believe the practice will be improved." (MS07)*

PS11 focused on the need to increase research capacity to undertake detailed investigation on antibiotic use and resistance. Effort should be made to expand research institutions and build capacity to make the necessary evidence accessible to providers and decision-makers in relation to antibiotic use and the resistance situation in the country.

> *"I think it is important to increase research capacity. Now, we are talking about prescribing trend in general. We should talk at individual level. Even individual strain and make-up has its own factor. We can access this if we expand research institutions. Their decision should be based on the findings. Capacity should be increased to do that. So, it is based on evidence that it is possible to decide prescribing or not prescribing. Undertaking coordinate research is important." (PS11)*

4.3.2.6.6 Sub-theme 6.6: Control the private sector

Most of the key informants indicated that controlling the private sector is a key intervention to improve the antibiotic prescribing practices at public health facilities. This is because of the impact that the malpractice in the private sector has on the prescribing practices of the public sector. They suggested that the regulatory body, EFMHACA, should also regulate the antibiotic prescribing and dispensing practices in the private sector.

Some of the key informants focused their suggestions on regulating the prescribing practices in private clinics by enforcing the use of clinical guidelines. Some of the key informants even suggested implementation of the PHCG in the private sector in order to make the practices uniform.

> *"EFMHACA should control the private clinics to improve antibiotic prescribing and use. It is important to ensure that the professionals are certified and prescribe medicines following some kind of guideline." (MS01)*

> *"Will be good if the PHCG is comprehensive and applied throughout the country and be accessible to private health facilities." (MS07)*

> *"The issues are many and can be beyond what you said. We have raised the idea of implementing the PHCG for all, including private clinics. In terms of inspection, support and follow-up, it is not done by health office, but by FMHACA. So, I think effort should be made to address that by engaging FMHACA. Since it is FMHACA that undertakes the follow-up and support, their profile can only be found there. It will be good if uniform and similar standard is followed. The issue of "there should be similar and uniform practice" is a question of all." (MS07)*

According to PS06, the regulatory body should control both the private and public health facilities with respect to antibiotic use and resistance.

“In addition, there will be better thing if the government or regulatory body establishes strong system to control private and public health facilities in relation to antibiotic use and resistance.” (PS06)

The majority of the key informants strongly recommended the need to stop the dispensing of antibiotics without prescription in private pharmacies.

“The other thing that we should focus on is reducing the irrational use of antibiotic without prescription. Here in the health center, we dispense medicines based on prescription. When we go out of this facility, antibiotics are given without prescription in pharmacies, clinics and drug stores just by looking at the leftovers from previous course. Private pharmacies should know that dispensing antibiotics without prescription is irrational and something should be done to limit the dispensing of antibiotics based only on prescription in private pharmacies. I think the resistance can be reduced if FMHACA strengthens its control on that.” (MS04)

“When we go to the private facilities, FMHACA should strengthen its regulatory activities. There should be regulation that can stop pharmacies from selling antibiotics without prescription.” (PS08)

“Second, I will be happy if antibiotics are not sold without prescription by private pharmacies. The practice is that any person can go to private pharmacies and get antibiotics without prescription. He/she can get whatever he/she wants, full dose, 3 pills or 5 pills. This is very common. There should be strict controlling system where the antibiotic prescriptions are retained with the pharmacies after the prescriptions are filled. Prescriptions are retained in public facilities since there is registration. But, private pharmacies return the prescription back to you.” (PS10)

Most prescribers blame the private pharmacies for dispensing antibiotics without prescription as it impacts the prescribing practices at health centres. Accordingly, they strongly suggested stopping the dispensing of antibiotics without prescription altogether as an intervention to improve antibiotic prescribing and reduce antibiotic resistance.

“First, private pharmacies should not dispense antibiotics without prescription. Antibiotics should not be sold without prescription. Government institutions cannot sale without prescription as there is audit. As this is very common in the private sector, something has to be done.” (HO08)

> *"I will be happy if we can avoid that. The people going to private pharmacy are more than those going to clinic or health center. People go to pharmacy with signs and symptoms and ask "I have such complaint. What shall I do?" and the professional there provides antibiotic. This should be corrected."* (NU03)

> *"Second, no medicine should be sold without prescription in pharmacies since medicines that are being sold without prescription are killing many people. The government has to develop policy and properly work on that since many children and pregnant mothers are being affected highly."* (NU10)

MS11 emphasised the need to have guidelines that show medicine that can be dispensed with prescription and those that require a prescription to be dispensed.

> *"There are many pharmacies and the access is there to use. As a government, there should be some kind of guideline that limits the medicines to be dispensed with prescription and those that can be dispensed without prescription. The practice now is that the community can go to any pharmacy and get any medicine by telling signs and symptoms." (MS11)*

Ethiopia actually has a list of Over-The-Counter (OTC) Medicines (EFMHACA 2012c) that lists those medicines that can be dispensed without prescription. Medicines not included in this list are then prescription only medicines. None of the antibiotics are part of the OTC medicines list and hence all antibiotics are prescription only medicines in the Ethiopian context.

PS02 went further and suggested the need to design some kind of mechanism to control the rational dispensing of antibiotics in the private sector as per legal prescriptions.

> *"Second, as I said, I should be responsible for the antibiotics I handle as pharmacy professional working in a private pharmacy or owner of a private pharmacy. Regulatory bodies like FMHACA should appropriately control if the medicines are being dispensed as per legal prescription. To do this, for example, what quantity was received? If 10 packs of amoxicillin were received, then there has to be 10 packs or prescriptions that matches with the quantity. Hence, I have to record and keep those prescriptions. This is one of the control means. Second, FMHACA has different professionals working on medicines and related issues. These professionals should undertake emergency inspection." (PS02)*

4.3.2.6.7 Sub-theme 6.7: Improve supply availability

Improving the availability of medicines and laboratory reagents was among the interventions suggested by most of the key informants to improve antibiotic prescribing and reduce resistance. Having the necessary laboratory investigations will enable the providers to reach the proper diagnosis and prescribe the right medicine if its availability is ensured.

> *"The other most important thing is improving the diagnostic capacity of health facilities for the diagnosis to be laboratory-based by availing the necessary reagents. Currently, the shortage of reagents is common. The other problem at this time is that antibiotics are not available as required. Out there, the medicines commonly available are from black market. If diagnostic capacity of health facilities is increased, there will be no misdiagnosis that will lead to resistance. If diagnosis is done appropriately, reagents are made available through the government, and cases are managed appropriately as per the guideline, I think it will be possible to prevent the irrational use of antibiotics and emergence of resistance." (MS04)*

> *"As a public institution that serves the low and middle income community, I think supply should be fulfilled through the government supply agency." (PS02)*

> *"The necessary resources like laboratory tests and alternative medicines should be made available." (PS03)*

> *"Not having the prescribed medicine at the end nullifies all the effort made for that patient. Patients hope that they will get medicine at the end of the process. Hence, government should work hard on that over other things." (PS04)*

Beyond acquiring supplies, PS11 recommended increasing the laboratory capacity of health centres for them to undertake proper investigation of samples.

> *"The other, as I said, the laboratory capacity should be increased." (P11)*

In relation to increasing diagnostic capacity, HO10 suggested equipping health centres with imaging facilities. Currently, imaging facilities are not available and hence patients are sent to the private sector for that.

> *"In addition to that, if imagings are made accessible to all as I said before. One of the complaints that clients have is related with imaging "go to the private and have x-ray". So, it will be better if facilities are equipped with imaging facilities." (HO10)*

MS05 strongly suggested the need to enter into contract with private suppliers to ensure the continuous availability of medicines since EPSA is not able to meet the needs of health facilities.

> *"We are not getting the medicines we need. I have raised this issue many times. We should expand our scope. For example, Kenema Pharmacy has deal with many wholesalers. It enters into contract with different wholesalers. An item that is not available in one can be available in the other. This means their stock is always good and hence you can get what you want including antibiotics. But, the only one that the health center has is EPSA. It is after you get written stock out confirmation from EPSA that you can go to the private sector. When you go to the market, the businessmen sets the price they want leaving you with option of either buying or not buying. Instead of this, it will be good if the government or Ministry of Health discuss on that to have a system whereby we can sign annual agreement with strong pharmaceutical wholesalers. There will be no problem if we enter into contract with 3, 4 or 5 wholesalers. Our role will be placing request for them to deliver the product to us. This will give us the possibility of getting antibiotics from different sources." (MS05)*

4.3.2.6.8 Sub-theme 6.8: Provide follow-up and support

Providing support and follow-up to sub-cities and health centres can improve antibiotic prescribing, according to the study participants. The progress being made in implementation of interventions to improve antibiotic prescribing and reduce resistance need to be monitored and the necessary support provided on regular basis.

> *"There should be a system for follow-up and support on what has been done so far. "Where are we now in terms of achieving targets?" kind of things have to be there. We will become strong when the follow-up and support is strong. Hence, that should be there." (MS02)*

> *"We also need support. I will be happy if the ones at higher level come in the form of supervision and support us on this issue." (PS09)*

> *"Second, it is important to undertake regular follow-up as expected. Undertaking continuous follow-up and awareness creation activities is important. There was budget constraint to undertake this." (PS11)*

According to MS07, capacitating the staff that are involved in support and follow-up is key for them to effectively provide the necessary support and follow-up at lower levels.

"Role of the staff working at bureau is support and follow-up. Since he/she supports by going down to the lower level to capacitate others, it will be better if he/she undertakes that by having the necessary knowledge and skill to properly capacitate others. If he/she has no information in the area, going down for support will be meaningless." (MS07)

Follow-up and support was also suggested for proper implementation of the various protocols that are developed and distributed to health facilities to improve clinical practices.

"Second, there are protocols that are issued by Ministry of Health in relation to AMR. If these protocols are made accessible to all professionals and follow-up and support is seriously provided to ensure proper implementation and professionals' adherence to the guidelines, I think there will be improvement." (MS11)

4.3.2.6.9 Sub-theme 6.9: Have an M&E System

The prescribers suggested that having a monitoring and evaluation system on antibiotic prescribing practice can improve antibiotic prescribing and reduce resistance.

"There should be monitoring in the facility. Institutions include sub-cities who are the ones to develop updating plan that is just for planning purpose. For the purpose of monitoring drug resistance, it will be good if committee is established at all levels since things start from there. It will be good if monitoring and evaluation system is created." (HO09)

"… there should be monitoring and feedback system for professionals to improve their practice by learning from their mistakes." (NU01)

"The health center should monitor the medicines that are prescribed." (NU05)

4.3.2.6.10 Sub-theme 6.10: Update knowledge

Antibiotic prescribing practices can be improved if healthcare providers update themselves on issues of antibiotics and resistance.

"The other thing is that healthcare providers should update themselves. Now, it is good that we have internet access in the health center for us to update ourselves. If someone has the knowledge, he/she can prevent unnecessary

wastage of medicines and share information to others, I think. Knowledge is the first. Hence, work on knowledge." (HO05)

"As a professional, the professionals should be updated on the service he/she is providing to address the problem. I am updating by myself. A professional should update by himself/herself as much as possible. Next, the health facility should update professionals. The updating from the health facility will encourage professionals to update by themselves." (HO09)

Among the key informants, MS02 and MS03 indicated that keeping oneself updated on the issue of antibiotics and resistance can improve antibiotic prescribing.

"We should adapt ourselves with new things and consider national problems as our own problems." (MS02)

"The provider should appropriately practice by updating himself/herself since this is a life issue. This is because science always requires updating. We cannot practice with the knowledge we gained last year." (PS03)

Increasing access to medicine information through the internet and the library was the suggestion by HO10 to improve antibiotic prescribing practice.

"There is no internet access. In addition to that, there is a need for library." (HO10)

4.3.2.6.11 Sub-theme 6.11: Increase public awareness

Increasing public awareness on antibiotics and resistance was another suggested intervention to improve antibiotic prescribing practice.

"The other thing is identifying the community's awareness problem and working with government to address it." (HO02)

"There should be system whereby adequate time can be given to make the public aware of antibiotics. It should be made part of the service provision and be performed seriously as to me. Otherwise, I cannot convince all the patients that come to me on daily basis since I am a human being. Patients would like to get their treatment quickly and get back home. So, I think there should be system for the awareness creation." (HO06)

“For the public, awareness creation activities should be implemented for them not to use medicines by simply buying from pharmacies by their own and to appropriate take the medicines prescribed to them.” (NU02)

“The public should not undermine the issue and should be more attentive. The public does not give the necessary attention to it unless it is deadly one. For instance, people are afraid of COVID as it is considered as a killer. The public should give similar attention to antibiotics and be aware of it and give the necessary attention.” (HO06)

NU03 suggested proper use of the Family Health Team for raising public awareness as the team goes out to the public on daily basis.

“There is Family Health Team on daily basis. Since we go to the community house-to-house 4 days per week, we should use that as well to create public awareness. If we are able to do that, I think we can change many things.” (NU03)

HO04 suggested the use of mass media for public awareness creation in addition to Family Health Team.

“It is also important to use the Family Health Team, Medias and MOH program for awareness creation. MOH should sponsor awareness creation sessions through media like the time being taken for advertisement. More effort should be made on using the media to educate the public on use of medicines since this is a common problem that affects everyone.” (HO04)

Using mass media to educate the larger community was also suggested by some of the key informants. Using the media is reported as key to increase awareness of the public about antibiotics and resistance. Different awareness creation platforms should be organised for the community through available media on a regular basis.

“There should be continuous and regular awareness creation forums through available media, including mass media, for the public on what resistance is and how it emerges. If the community’s awareness is increased, the community itself will refuse taking antibiotic if asked to do so which will I think reduce the risk.” (MS11)

“As a country, the major measure that should be taken is using the media. Using the media which is easily accessible to the community to create awareness about medicines for the public will enable us to address the problem. The health sector should work on drug resistance by giving due attention to it. The issue of

drug resistance is not as such raised in our health sector. It is possible to say that the awareness on antibiotic resistance starting from the higher levels is low. So, if appropriately done on these, it will be possible to solve the problem." (MS09)

Using the media for public awareness creation was suggested by HO08. This prescriber cited the example of media use when creating awareness for TB and HIV.

"The other thing is that there are many advertisements on media like for TB, HIV and so on. There should be awareness creation on benefits of antibiotics, consequences of misuse using media." (HO08)

Providing health education to the public was suggested by many of the key informants as a means to improving antibiotic prescribing and reduce resistance. The key informants believe that it is lack of knowledge that results in the community inappropriately using antibiotics and hence the solution is to educate them on correct antibiotic use and resistance.

"It is due to knowledge gap that the public is using antibiotics inappropriately. It can be corrected by health education." (MS03)

"Then after, the user/community is the major one and hence should be educated on antibiotic resistance and related issues." (PS09)

Some of the key informants suggested facility-based health education;

"The health facility should educate the community on medicines use using mass media. If proper orientation is provided, I think we can reduce the number if not possible to stop it." (MS01)

"In all instances that we get the community (during diagnosis, dispensing and morning waiting area), we should educate them on medicines, especially by pharmacy section." (MS02)

"We should appropriately educate the community on drug resistance at health center level. I think there should be education on drug resistance." (PS01)

"In government health institutions, any kind of medicine including antibiotics cannot be dispensed without prescription. It will be good if this is applied in other sectors too. I would like to suggest that the service should be seen from human life aspect than business aspect and medicines, especially key medicines,

should not be dispensed without prescription. We should inform to the patient during health education that he/she should first go to health facility, undertake diagnosis and know the case prior to seeking medicines. This is important to address the patient's thinking of getting medicines from private facilities easily." (PS02)

Other informants suggested community level health education, addressing antibiotics and resistance by health extension workers and family health teams at the health centres.

"The public should get health education by health extension workers on issues of drug resistance, not to buy antibiotics from pharmacies by themselves unless it is prescribed for him/her after proper diagnosis. Make them understand the benefits and risks associated with antibiotics. The public may not understand that. It is possible to provide health education by area since there are health extension workers in each area. There is Family Health Team. They should provide health education to the community when they go to the community to provide service." (MS03)

"When we go down, one of the mechanism is health extension. There is what we call PHCU (Primary Healthcare Unit). In addition to health extension workers, health professionals of the health center go to the community every week. When they go to the community, they take medicines with them. There is education that they give." (MS07)

"We are now working mainly at institution level. This should go to the community. Going to the community like through the health extension workers for them to have the AMR awareness and be part of the initiative." (PS11)

One key informant suggested the need to work more closely with universities and for them to educate the public on antibiotic use and resistance.

"In relation to this, what we are thinking that can bring about significant change is that the relationship between academia and health bureau should be strong. For instance, our universities are not close to the community. As you can see, many studies are conducted. The awareness on AMR was there at different levels for long time starting from universities. But, the awareness in the pharmaceutical sector did not go to the ground level for the community. There should be interventions at community level. For that, we should work with academic area in a coordinated manner. Universities have the expertise and the government may have resource. So, coordinating these is important. We know what health extension brought about in this country. This is as a result of the

work done at community level. Nothing else. So, our universities should go down and work on the community. For instance, I know that there is community-based activities in Jimma University. There are many universities here in Addis. So, these universities should work on the community." (PS11)

PS03 suggested that there should be media dedicated to medicine usage;

"So, there should be media that works on medicines use since that is key."

4.3.2.6.12 Sub-theme 6.12: Proper patient counselling

Proper counselling by healthcare providers (prescribers and pharmacy professionals) was the other commonly suggested intervention to improve antibiotic use and reduce resistance. Prescribers suggested as follows;

"Healthcare providers should provide health education, and counsel the patient on the consequences of inappropriate use. Not being responsible and failure to counsel and teach the patient on the benefits and side effects of the medication. The patient even give his/her medication to others in the form of lending. Patients should be educated not to share medicines with others. I mostly address this issue while providing health education to patients." (HO05)

"As I said, the client should be appropriately counselled by the prescriber on benefits of the medicine, on the need to take the medicine appropriately, and the need to attentively listen to the counselling provided by pharmacy professionals to reduce resistance." (NU06)

Key informants indicated that the counselling practice has problems and should be improved. Both prescribers and dispensers should counsel patients on taking prescribed medicine correctly. Some also indicated that patients taking antibiotics need more counselling than patients taking other medicines.

"We professionals are the ones who can take responsibility and stop that starting from pharmacy unit by educating patients on use of the medicine, for how long the medication should be taken, the fact that the medicine is prescribed for him/her and should not be shared to anyone. As resistance has serious consequences, the prescriber should also counsel the patient on how to take the medication which will be later strengthened by the pharmacy professionals." (MS02)

"… I think the patient should get more counselling on antibiotics than other medicines, including not to discontinue the medicine, the number of days the medicine should be taken, the number of doses to be taken per day and the time. Just to take an example, if an antibiotic is prescribed to be taken three times a day, the patient commonly takes during breakfast, lunch and dinner if not properly counselled by the provider. This is a problem from the provider's side. When a medication is ordered to be taken three times a day, the patient should be appropriately counselled that the medication should be taken every eight hours like at 7:00 a.m., 3:00 p.m. and 11:00 p.m. The patient should be informed that the medication should be taken every eight hours." (PS02)

"Lack of proper counselling and not giving adequate time for counselling. Also, the burden and the low number of professionals available. We focus on sending the patient by saying "morning 1, noon 1, night 1" without much concern about the side effects. The counselling time is too short. I think it will be good if we take time for counselling." (PS09)

One of the key informants indicated the need to give written information to patients in addition to the counselling provided during dispensing.

"In addition to that, I think it is good to give written information as there is a possibility of forgetting the information provided orally." (PS02)

4.3.2.6.13 Sub-theme 6.13: Give attention to antibiotics and resistance

Study participants indicated that antibiotics and antibiotic resistance should get the attention of government, professionals and the public. Both prescribers and key informants feel that the necessary attention is not being given to the issue and recommended various interventions that should be implemented for antibiotics and resistance to get the necessary attention in the health system.

Assign an AMR focal person

Assigning a focal person that can coordinate antibiotic use and resistance issues at sub-city and health centre level was suggested as an intervention by some of the key informants to improve antibiotic prescribing and reduce resistance. The MOH has established an AMR team to coordinate AMR prevention and containment activities at national level. The Health Bureau also has an AMR focal person. But, sub-cities and health centres do not have an AMR focal person.

“What I want to say is that there are normally many programs that are expected to be undertaken at health facility level. It can be done if it has its own focal who oversees the activities. First, there should be owner while the DTC is there. Though that may increase the number of focals, will be good if it can have its own focal given its seriousness.” (MS02)

“… focal person should be there at all levels.” (PS08)

Include antibiotics and resistance issues in action plan

The key informants believe that antibiotic and resistance issues need to be addressed by making them part of the action plan at each level.

“To start with, the issue is big. But, no that much attention is given to it beyond availing, ordering medicines and managing patients. Pharmacy case team might have worked on that. But, having joint work plan as health office and health center is good. In addition, undertaking follow-up on health facilities is good. But, I think the structure starting from higher level is a gap.” (MS10)

“Probably, I would like to thank you for giving us the opportunity to see what can be done in addition to supply of medicines coordinated by pharmacy sections since it is the activity to which we haven’t given the necessary attention. It is planning season.” (MS10)

“We also think that having it in the plan is one important thing. This is because something that is not part of the plan and hence not owned by the political leadership is valueless. So, it is important to have these things in the plan and implement accordingly since there will be gap if not done that way.” (PS11)

Develop Project on AMR

One key informant suggested developing a project on AMR to appropriately address the issues on antibiotic usage and resistance.

“As intervention, I think there should be one project if possible. First basis of the project should be ethics. It should work on people’s mind. Money can buy many things. But, it cannot buy identity. So, the project is building on the existing good things.” (MS06)

Guidelines on antibiotic use

The need to have guidelines that focus on antibiotics was suggested as an intervention to improve antibiotics prescribing. The guidelines are expected to address the case management as well as promoting the rational use of antibiotics.

> *"There should be control when medicines are distributed. Without any difference between private and government, there should be some kind of regulation that enables managing the practice appropriately and uniformly. It will be good if separate guideline is prepared based on evidence of current resistance pattern (this antibiotic is resisted) and that clearly shows which antibiotic should be first-line for which case. I think it is due to inaccessibility of such information that professionals repeatedly prescribe same antibiotic for all kinds of cases or start prescribing from high level antibiotics." (MS07)*

> *"If the awareness is there on how to perform and implement practically, I think the sub-city can work collaboratively with health centers and influence. But, there should be uniform guidance as a country on how that can be done. When I go to health center, instead of saying "do this one, don't do that one", there should be details on "what should be done and how" that can be applied uniformly and the health center can accept." (PS08)*

Among the prescribers, NU02 and NU08 suggested the need for antibiotic–specific guidelines.

> *"Will be good if antibiotic-specific guidelines are developed." (NU02)*

> *"There may also be need to prepare guidelines. We cannot say that people don't read without preparing and availing customized guidelines. If guidelines are prepared and updated training provided, I think the professionals can bring about change." (NU08)*

A time-series study conducted at primary healthcare facilities in Spain (Fernández-Urrusuno et al. 2020) showed that publication of antimicrobial therapeutic guideline and subsequent interventions carried out to improve adherence to the guide or to improve antibiotic use by other mechanisms, such as financial incentives, were followed by a significant reduction in rates of antibiotic prescribing. The researchers concluded that implementing multifaceted interventions following the introduction of antimicrobial guide, with strong institutional support could lead to sustained improvement in antibiotic prescribing in primary care.

Collaborative effort and attention

Some of the key informants suggested the need to work in conjunction with others by giving the necessary attention to the issue of resistance. According to them addressing the issue of antibiotics and resistance requires the collaborative effort of all concerned bodies.

> *"I hope it will be possible to reduce these problems if the government, community and private sector work in a coordinated manner and apply some kind of standard." (MS11)*

> *"On top of that, the government, regulatory body, and health bureau of Addis Ababa should work hard on resistance. I think there is a lot to be done by all of us here at sub-city and health center level." (PS06)*

According to PS06 and PS10, professionals should give due attention to antibiotics and work towards rationalising prescribing and reducing resistance without expecting any push from a higher level.

> *"Yes, first is on the professional. Unless the professional is committed and take action and reduce/stop it within a limited period of time, for sure after few years we will have no option. So, the professional without expecting anything from higher level should be committed. No one can correct that other than the health professionals. We should give due emphasis and correct that." (PS06)*

> *"The first is that professionals should give the necessary attention for antibiotics. Professionals should see antibiotics as something different by giving high weight to it. Professionals should not see antibiotics like other medicines." (PS10)*

PS11 compared the attention given to AMR and the recent COVID-19 pandemic and the ultimate consequences of the two. According to this informant, far more attention has been given to COVID-19 than has been given to AMR though its impact is less than AMR.

> *"If we see the case of COVID, COVID does not influence more than AMR. But, if we compare the attention we give to COVID and AMR, it is as we know. Hence, the attention and engagement of all sectors is important for antibiotics too." (PS11)*

HO06 and NU10 indicated the need for government and professionals to give the necessary attention to issues of antibiotics and resistance.

> *"First, attention should be given for it. Government as Ministry of Health should give attention to it since the majority are antibiotics." (HO06)*

> *"The first thing is that the healthcare provider should be cautious. Properly reviewing back history, getting patient feedback on whether he has previously taken the medicine or not." (NU10)*

Encouraging better performance

HO03 and HO07 suggested that encouraging better performance can improve antibiotic prescribing practices.

> *"At health center level, maintaining the case presentation and encouraging better performers." (HO03)*

> *"Not only in this health center, recognizing good performers and encouraging others for better performance is not there in the health sector as a whole as to my understanding. No appreciation. This is big intervention area." (HO07)*

4.3.2.6.14 Sub-theme 6.14: Strengthening DTC and DIS at health facilities

Key informants think that strengthening the DTCs and DISs of the health facilities can improve antibiotic prescribing practices. The key informants stressed the need to strengthen them.

> *"At the back of the PHCG, first the DTC is very important. The Committee has to continue as it has many tasks. One of the tasks is on antibiotic resistance. It should be performed on continuous basis without interruption." (MS02)*

> *"The other thing we think should be done as city administration is continuing strengthening projects designed. For example, if projects like DIC and others are implemented appropriately, I think it will be possible to solve the problem." (MS09)*

> *"DIS should be strengthened. It is an area we can do a lot." (PS06)*

PS11 further indicated that there is a practice of leaving out initiatives under implementation when new initiatives come by citing DTC as one of such initiatives.

“The other thing we observed is that there is trend of leaving out initiatives when new initiatives come. For instance, DTC is one of the initiatives that we think that can appropriately address things. It is important to strengthen DTCs. What we identified as a gap here is that it is not financially supported. This is because if it is not financially supported, it is difficult to continuously organize discussion forums on AMR and related things. If we are not able to create the system to conduct consultative sessions with different bodies, it is still a gap. I think we should use that as one of the initiatives.” (PS11)

4.3.2.6.15 Sub-theme 6.15: Create discussion forum for healthcare providers

Having a discussion forum which all healthcare professionals can attend on regular basis was suggested by the prescribers as a possible intervention to improve antibiotic prescribing practices. HO06 and HO10 suggested maintaining the existing morning session as a discussion forum.

“We, the professionals, have morning brief where we discuss cases of the previous day every morning. We discuss on cases and comment on the medicines prescribed, why that medicine is prescribed, raise alternative management options and medicines, the need for better antibiotics and the use of one antibiotic that can treat all cases instead of prescribing 2 or 3 antibiotics. This way, we learn from each other.” (HO06)

“As a plan, morning session by itself is good since it also addresses antibiotics. This is because it gives us the opportunity to learn from each other. Morning session is a very important learning session for us to correct our mistakes.” (HO10)

The suggestion from HO03 focused on establishing a discussion forum (in the afternoon) at health centre level where all healthcare professionals can regularly meet and discuss on antibiotic and resistance issues. According to this prescriber, the discussion in the morning sessions focus only on specific cases managed and does not engage all health professionals.

“Other than that, we can stop drug resistance if professionals properly discuss on medicines prescribed like hospitals through morning sessions that should be organized in the afternoon instead of morning. That will enable the professionals to build their capacity through experience sharing. As I said, you can debate on issues like on prescribing or not prescribing antibiotics for viral infections. Professionals should regularly meet and discuss to prevent drug resistance. For

this to happen, management commitment is key. The current morning session is simply discussing on what case was managed and is not being attended by all healthcare providers. In the past, there was a session organized once per month in the presence of all healthcare providers." (HO03)

HO07 supported the suggestion made by HO03 by saying;

"We can bring change if professionals have discussion groups through which they can discuss on drug resistance, read on it, and identify own gaps. There should be participation on everything." (HO07)

4.3.2.7 Theme 7: Implementation challenges

Identifying the challenges that can affect implementation of the suggested interventions is important. Study participants were asked about the challenges they anticipate in implementing the suggested interventions. Some prescribers reported that they do not anticipate any challenges in the implementation of the suggested interventions. Other prescribers and key informants mentioned the following challenges that could be faced during implementation.

- Shortage of professionals
- Lack of government for change
- Shortage of medicines commitment and laboratory reagents
- Resistance to change
- Financial constraint
- Profit motive of the private sector

4.3.2.7.1 Sub-theme 7.1: Shortage of professionals

One of the challenges that prescribers anticipated was shortage of professionals to provide the necessary services at health centres.

"The first thing is assigning adequate number of professionals. As far as there are many OPDs and guidance is given on how to provide quality service, the load will be reduced. The challenge may be on assigning adequate number of professionals." (HO06)

One key informant indicated that health centres have a shortage of staff to appropriately provide the necessary services. Human resource demands are not yet fulfilled.

> *"The challenges are many. Human power by itself is one challenge for our health centers. The health centers do not have human power as per their need. In the presence of a very limited human power, health centers may have only two functional OPDs while implementing the guideline at pilot level by closing other OPDs. Human power may not be there for various reasons. To start with, they don't have human power as per the approved structure. So, one is human power." (MS08)*

4.3.2.7.2 Sub-theme 7.2: Lack of government commitment for change

HO10 indicated that lack of government commitment for change can be a challenge.

> *"There will be no challenge. I am saying that because if there is change-driven attitude, there will be no challenge. A government official should appropriately transform the institution. If the official is committed for change, I think that will be possible. The problem is lack of commitment." (HO10)*

4.3.2.7.3 Sub-theme 7.3: Shortage of medicines and laboratory reagents

A shortage of medicines and/or laboratory reagents was mentioned by some of the prescribers as a challenge in implementing the suggested interventions.

> *"As a challenge, stock-out is common here at health center level. That creates serious problem. As I said, patient will say "they don't have it" and fuels the problem. Supply is serious issue for patients." (NU01)*

> *"One is supply. That means in public health facilities, stock of medicines does not last for more than one or two weeks. It will soon be stock-out. If you prescribe that medicine to buy from the private, it will be expensive, may be 2 or 3 fold. So as to use the medicines available in the facility, you may change the medicine. That means you may violet the antibiotic level in consideration of cost for the patient. So, I think shortage of medicines is a challenge." (NU05)*

Supply shortage was also mentioned as a challenge by key informants.

> *"The second challenge is the unavailability of medicines and diagnostic facilities as per the requirements of the PHCG." (MS08)*

“As I said before, the medicine supply problem of PFSA will I think continue in the future too. When we say that there is 60% availability at health centers, which means 40% is procurement from the private.” (MS10)

4.3.2.7.4 *Sub-theme 7.4: Professionals’ resistance* for change in implementing PHCG

Resistance to change was another challenge mentioned by prescribers. They indicated that changing the professionals’ minds away from the traditional prescribing practices can be a challenge.

“… bringing providers into the new system can be a challenge.” (NU02)

“First, we may not be able to out of the tradition we have been in. There was challenge to accept the changes made with the new guideline like changes in dosage, physical examination. That is due to our familiarity with the previous practice. We don’t want to quickly adapt new things and there will be some challenges. Second, the private ones may not accept the measures. They may not consider the issue as a threat. So, these things will be there.” (NU04)

According to the key informants, there are provider and patient related challenges in implementing the new guidelines.

“The first one I want to raise is that the healthcare provider may resist since there is traditional prescribing practice that is common for many of us. We may refuse to change that practice. Even there are things that are prescribed, but not there in the guideline. The chronic staff may resist to come to the common standard.” (MS02)

“One thing I would like to repeat is PHCG. There are challenges that professionals raise like “it takes time”, “the clients reaction is not good while we read the guideline” and so on.” (MS07)
“There are professionals who are implementing the guideline despite the gaps the guideline itself has. Especially, since awareness of the patients and the community is low, managing a patient by following a guideline is considered as incompetence. There are still professionals that resist using the guideline for this reason.” (MS09)

4.3.2.7.5 Sub-theme 7.5: Financial constraint

Prescribers raised budget constraint as a challenge to implement the interventions.

> *"As I said, there could be some financial problem. In our facility, there will be no challenge. It is attitude. There could be challenge in building manufacturing plants, getting medicine plants and professionals." (NU03)*

Budget constraints of both health centres and the sub-city health offices for capacity building and follow-ups on antibiotics and resistance was raised as a challenge by key informants.

> *"We may not be able to get budget to provide training. Hence, will be better if the training is organized by the Health Bureau. There will be budget constraint to provide training. Organizing training will I think be difficult for us." (MS03)*

> *"Since there is no budget for this office, you cannot give training on these things. But, the health bureau provides that training. There are instances where professionals from health facilities get training. But, our office has no budget and hence cannot provide training as before. We work with the Bureau in recruiting professionals for the training." (MS07)*

> *"At our level, there are some financial challenges that we will address through discussion with our head of office. Most of the things are there at health center level. What is left is internet access in some health centers. There is better thing." (PS06)*

4.3.2.7.6 Sub-theme 7.6: Profit motive of the private sector

The challenge raised by PS02 was in connection with the private sector's motive for profit which could prevent standardising of practices.

> *"Speaking the truth, the challenge will be that these private facilities are established for profit. So, the decision not to dispense medicines without prescription may affect their business. I also hear from different bodies saying that it affects their business. So, that can be considered as a challenge. Comparing this with human life puts the practice under question mark. There are medicines that can be dispensed without prescription. I think these are enough. Effort should be made for other medicines, including antibiotics, to be dispensed with prescriptions only." (PS02)*

4.4 INTEGRATING THE QUANTITATIVE AND QUALITATIVE FINDINGS

This section describes the integration of the two studies that were conducted sequentially to answer the research questions. The studies were designed to achieve different, but related objectives of the research which when combined together helped in developing the intervention guidelines that can address the problem of antibiotic prescribing at primary healthcare facilities. The studies were integrated at two points; in developing tools for data collection and at outcome level:

i. Tools for data collection: The data collection tools used in both phases of the study were developed based on the research objectives. Preliminary findings of the quantitative study were used in designing the in-depth interview guide used for data collection during second phase of the study (qualitative).
ii. Outcomes: The outcomes of Phases 1 and 2 studies were combined to develop guidelines aimed at improving antibiotic prescribing at primary healthcare facilities.

Although the quantitative data was collected from prescription and medical charts of patient served from 01 September 2019 to 31 August 2020, the in-depth interviews with prescribers who were part of the practices during those years was conducted during May and June 2021. This has shed light on the quantitative data and provided detailed information to understanding the antibiotic prescribing practices at the primary healthcare facilities included in this study.

The PRECEDE-PROCEED model was used as a theoretical framework to guide the undertakings of this study. The first two phases of the Model focus on understanding the health problem that affects the community. In this study, the health problem is inappropriate and over-prescribing of antibiotics at primary healthcare facilities. Findings of both the quantitative and qualitative components of the study indicated that there is irrational and over-prescribing of antibiotics where the rate of antibiotic prescribing was shown to be at 52.5%, far higher than 30% for outpatients at primary healthcare facilities. Prescribing antibiotics for minor cases such as URTIs is common. The majority of the commonly prescribed antibiotics and the cases for which the antibiotics were prescribed reported by prescribers during the in-depth interviews are similar to those identified through the prescription review during quantitative phase of the study.

Most prescribers feel that antibiotic resistance is a serious problem and is prevalent. They also feel that the necessary attention is not being paid to it by the government and professionals and hence is neglected. Key informants also see antibiotic resistance as a serious problem because of its potentially devastating consequences on individuals, community and country. Like the prescribers, the key informants also have concerns in that professionals and the government are not giving the necessary attention to the issue of antibiotic resistance. Though the MOH and Addis Ababa City Administration Health Bureau are making effort in this regard, this has not yet cascaded down to those primary healthcare facilities that provide services for the majority of the population.

The qualitative component enabled identification of antibiotic prescribing and use problems in the study setting. Further, the qualitative study revealed the views of the prescribers and key informants on the consequences of irrational prescribing of antibiotics and their resistance. Hence, the quantitative and qualitative findings are integrated in providing the evidence necessary to understand the prevailing antibiotic prescribing problems and the consequences as perceived by prescribers and key informants who are involved in day-to-day service provision and service management. The identified multifaceted problems in the existing antibiotic prescribing practice deserves designing interventions to improve the prescribing practice. Designing interventions requires identifying the factors influencing the antibiotic prescribing decisions of prescribers and getting the views of those involved in the practice on interventions that have been and should be implemented to improve antibiotic prescribing at primary healthcare facilities. Accordingly, with active involvement of the study participants, it was possible to identify the factors influencing antibiotic prescribing and the interventions that should be implemented to improve the practices as per Phases 3 and 4 of the theoretical model used in this study. The factors that affect the prescribing of antibiotics that were identified from the qualitative phase of the study were categorised into predisposing, enabling and reinforcing factors.

The intervention guidelines to improve antibiotic prescribing were developed by systematically organizing the interventions that are reported by study participants as being implemented in healthcare facilities and those interventions suggested to be implemented. The interventions suggested by the study participants were contextualised and systematically grouped into ten guidelines that can be implemented at national, city administration, sub-city and/or healthcare facility levels. The challenges that can be faced in implementing the suggested interventions and hence the intervention guidelines developed were also identified.

Table 4.24 Summarises the integration of the quantitative and qualitative findings in answering the research questions aligned with the first four phases (Planning Phase) of the theoretical model.

Table 4.24 Integration of quantitative and qualitative findings aligned with the four planning phases of the theoretical model.

Research questions	Main source of data and Phase of the study	Key findings	Alignment with phases of the PRECEDE – PROCEED Model
How prevalent is the prescribing of antibiotics at primary healthcare facilities?	Quantitative data (Phase I)	There is high rate of antibiotic prescribing	Phase 1 and Phase 2
What does the pattern of antibiotics prescribing look like at primary healthcare facilities?	Quantitative data (Phase I)	Antibiotics are being commonly prescribed for minor cases such as URTIs	Phase 1 and Phase 2
How appropriate is the prescribing of antibiotics for selected cases at primary healthcare facilities?	Quantitative data (Phase I)	There is gap in prescribers adherence to clinical guidelines while prescribing antibiotics	Phase 1 and Phase 2
What are the factors that influence the prescribing of antibiotics at primary healthcare facilities?	Qualitative data (Phase II)	Various factors influence prescribers' decision in prescribing antibiotics	Phase 3
What interventions should be implemented to improve antibiotic prescribing at primary healthcare facilities?	Qualitative data (Phase II)	Various interventions suggested that should be implemented at primary healthcare facilities to improve antibiotic prescribing	
What interventions should be developed to improve antibiotics? prescribing at primary healthcare facilities?	Qualitative data (Phase III)	Intervention guidelines that can be used to improve antibiotic prescribing at primary healthcare facilities developed	Phase 4

The findings of the two components of the study provided the necessary evidence on what the antibiotic prescribing practices at primary healthcare facilities look like, the factors that contribute to the observed antibiotic prescribing practices, and the interventions that should be implemented to improve the prescribing practice thereby contribute to the effort being made at national and global level to prevent and contain AMR. As to the knowledge of the researcher, this is the first qualitative study conducted at primary healthcare level in the country that explored the factors related with antibiotic prescribing and developed intervention guidelines based on the information gathered from those directly involved in the practice and relevant key informants.

4.5 CONCLUSION

This chapter presented and discussed the findings of the quantitative and qualitative studies that were conducted sequentially. The presentation and discussion of the quantitative findings covered the rate and patterns of antibiotic prescribing, and prescribers' adherence to clinical guidelines in prescribing antibiotics for the management of respiratory tract infections. Supported by relevant quotes from prescribers and key informants, the presentation and discussion on the qualitative findings mainly focused on antibiotic prescribing and use problems, factors influencing antibiotic prescribing, interventions implemented so far to improve antibiotic prescribing, suggested interventions to improve antibiotic prescribing, and implementation challenges. Integration of findings of the two studies in addressing the research objectives and in developing the intervention guidelines were discussed at the end of the Chapter. The findings revealed that there is high rate of antibiotic prescribing and many factors influence the prescribing decision of prescribers. Various interventions were suggested by the study participants that need to be implemented to improve the prescribing practice. This requires developing intervention guidelines by systematically organizing suggestions of the study participants. The next chapter will present the intervention guidelines developed to improve antibiotic prescribing at primary healthcare facilities.

CHAPTER 5: GUIDELINES TO IMPROVE ANTIBIOTIC PRESCRIBING IN PRIMARY HEALTHCARE FACILITIES

5.1 INTRODUCTION

The previous chapter presented and discussed the findings of the quantitative and qualitative findings, and how these findings were linked together to answer the research questions and led to the development of intervention guidelines to improve antibiotic prescribing. Building on the findings presented in the previous chapter, this chapter presents the intervention guidelines developed to improve antibiotic prescribing at health centres. The development process, purpose and use of the guidelines, and the guidelines developed to address the prescribing problems are covered in this chapter.

5.2 THE GUIDELINE DEVELOPMENT PROCESS

This third phase of the study was aimed at developing intervention guidelines that can be used to improve antibiotic prescribing at primary healthcare facilities. To develop these guidelines, the researcher has undertaken two consecutive studies. The first phase of the study was designed to determine the rate and patterns of antibiotic prescribing at primary healthcare facilities. This phase of the study also provided information on the appropriateness of antibiotic treatment for the management of respiratory tract infections. This part of the study answered the “what” aspect of antibiotic prescribing at the health facilities.

Building on the findings of the quantitative study, the qualitative phase of the study was undertaken to gather information on the “why” and “how” aspects of antibiotic prescribing to understand actual prescribing problems, the underlying factors influencing prescribing, measures taken so far to improve prescribing, the recommended interventions to improve prescribing, and challenges that can be expected during implementation of the interventions.

Although conducted sequentially, the two studies are related and the findings complement each other in achieving the research objectives and answering the research questions. Since the ultimate objective of this study was to develop intervention guidelines that can be used to improve antibiotic prescribing at primary healthcare facilities, guidelines are developed based on the identified gaps and interventions that were suggested by the study participants. Integration of the qualitative and quantitative findings has provided the necessary information on what the prescribing problems are, the underlying factors for the observed prescribing practice and the interventions that should be implemented to improve the practice as viewed by the study participants. The researcher has made effort to systematically group the interventions suggested by the study participants into manageable guidelines with specific interventions mentioned under each guideline.

5.3 PURPOSE AND USE OF THE GUIDELINES

The guidelines are developed to improve the antibiotic prescribing practices at primary healthcare facilities. The guidelines provide broad interventions that all stakeholders responsible for ensuring the provision of quality health services at healthcare facilities can use as a reference document to develop tailored and detailed interventions aimed at improving the prescribing of antibiotics. In this regard, Addis Ababa City Administration Health Bureau, Sub-city Health Offices, the regulatory body, and health centres are at the forefront. Professionals involved in training, providing supportive supervision and follow-up, prescribing and dispensing of medicines are also expected to use the guidelines to improve the antibiotic prescribing practices at health centres.

The MOH and other Regional Health Bureaus can also adapt these guidelines for use in primary healthcare facilities found in other regions. Researchers can use the guidelines to test the effectiveness of one or more of the intervention guidelines developed in improving antibiotic prescribing.

5.4 THE INTERVENTION GUIDELINES

The specific intervention guidelines developed to improve antibiotic prescribing by integrating findings of the quantitative and qualitative findings are presented as follows.

5.4.1 Guidelines for effective implementation of PHCG

Majority study participants hope that effective implementation of the PHCG will significantly improve antibiotic prescribing practices. Based on their practical experiences, study participants strongly recommended the PHCG as one of the interventions to improve antibiotic prescribing. There are various actions that should be taken to appropriately implement the guidelines thereby improving prescribing practices. The following interventions should be implemented to effectively implement the PHCG:

- Strengthen the clinical audit being undertaken to check adherence of prescribers to the guidelines;
- Design and implement interventions to facilitate use of the PHCG by healthcare providers, including availing it in electronic form and undertaking workload analysis;
- Increase awareness of patients and parents on the new clinical guideline (PHCG) and its application in practice; and
- Engage all concerned health professionals in PHCG training to facilitate its implementation.

5.4.2 Guidelines to capacitate healthcare providers on antibiotics and antibiotic resistance

The lack of training for prescribers' capacity building on antibiotics and resistance was mentioned as a common factor for the irrational prescribing of antibiotics at health facilities. Capacity building training in the areas of medicine use in general and antibiotics use in particular are rarely available. As a result, the majority of the study participants recommended provision of training for prescribers on antibiotics and their resistance. In relation to this, the following interventions should be taken into consideration:

- Develop and provide competency-based training on antibiotic use and resistance to all categories of health professionals;
- Develop and implement guidelines on appropriate management of minor cases such as URTIs ;

- Introduce a system and provide support and follow-up to professionals to appropriately apply knowledge and skills gained from training; and
- Develop system for the healthcare team to engage in undertaking medicine use studies that can be used to improve practice.

5.4.3 Guidelines to increase the awareness of patients and the public on antibiotics and AMR

Patients and the community play critical roles in healthcare. Low patient and community awareness on antibiotics and resistance was raised by many of the study participants as a cause of irrational prescribing of antibiotics. The pressure that patients and parents place on providers to prescribe specific antibiotics; the lack of patience and loss of trust in the provider with the efforts that the provider is making to manage cases as per the guidelines; the practices of CBHI members frequently visiting health facilities to collect medicines; and self-medication with antibiotics are all consequences of a lack of awareness. The following actions are recommended to address the awareness problem with patients and the community.

- Develop standard materials in different languages that can be used to educate the public on antibiotics use and resistance;
- Use available media outlets to educate the public on antibiotics use and resistance in a planned way, including spot messages, drama and film that can alert the public to the consequences of inappropriate use of antibiotics;
- Strengthen the provision of health education to patients and the community at health facilities; and
- Capacitate and exhaustively utilise Health Extension Workers and the Family Health Team to provide health education within the community.

5.4.4 Guidelines to institutionalise antibiotic use and resistance into the healthcare system

The study participants feel that the issue of antibiotics and resistance is not receiving the necessary attention by government and some of them even considered it as being ignored. As a result, they recommended various interventions to prominently raise AMR as a serious public health threat. Institutionalising antibiotic use and resistance within each and every undertaking of the health system as part of the routine can address this gap. To this end, the following interventions are suggested:

- Develop and implement evidence-based antibiotic-specific clinical guidelines that can guide the prescribing practice and promote rational use of antibiotics;
- Develop and implement evidence-based, problem-solving projects on promoting the rational use of antibiotics and prevention of antibiotic resistance;
- Make antibiotics and resistance related activities continuous by properly addressing antibiotic use and resistance issues in strategies, annual action plans, supportive supervision, and M&E activities at all levels of the healthcare system;
- Establish a system to generate and regularly share updated antibiotic use and resistance information to all health professionals in a coordinated manner;
- Implement tailored antimicrobial stewardship program at health centres by networking them with hospitals for the necessary support; and
- Organise experience-sharing events for health centres and sub-city health offices to share experiences with each other on the promotion of the rational use of antibiotics.

5.4.5 Guidelines to improve availability of antibiotics and laboratory reagents

The availability of medicines and laboratory reagents play a critical role in the provision of health services. It was reported by the study participants that there was shortage of medicines and laboratory reagents which affected antibiotic prescribing practices. To address these gaps, the following interventions should be implemented:

- Establish a system to ensure the continuous availability of antibiotics and laboratory reagents at health centers as per the new PHCG;
- Introduce a system by which health centres can have alternative sources of supply for the procurement of medicines and laboratory reagents that are in short supply from the public pharmaceutical procurement agency; and

- Increase diagnostic capacity of health centres to undertake the required laboratory tests as per requirements of the PHCG.

5.4.6 Guidelines to establish and strengthen platforms for health professionals to discuss antibiotic use and resistance

Having a discussion forum to provide the opportunity for prescribers and other professionals to learn from each other can positively contribute to antibiotic prescribing practices. The discussion forum should not be limited to health centres as professionals working at the Health Bureau and sub-city health officers also require updates. The interventions that should be implemented in this regard are:

- Strengthen existing learning platforms such as morning sessions at health centres;
- Establish regular discussion forums on antibiotic use and resistance at the Health Bureau, sub-city health office and health centre levels for all health professionals; and
- Encourage professionals to actively engage in professional discussions using virtual platforms via telegram and other electronic means.

5.4.7 Guidelines to strengthen DTC and DIS at health centres

The DTC and DIS are important tools for the promotion of the rational use of antibiotics at health facilities. The majority of the health centres have DTCs and DISs. But, the expected activities are not being carried out consistently, particularly in relation to DIS; there is wide variation among the health centres in terms of functionality. Hence, the following interventions are recommended to enable DTCs and DISs to play an active role in the promotion of the rational use of antibiotics and prevention of AMR.

- Strengthen DISs through staff capacity building and availing reference materials;
- Network the DISs of health centres with each other and the DISs of nearby hospitals to support each other;
- Strengthen DTCs of the health centres to undertake their roles appropriately in the promotion of the rational use of medicines with a focus on antibiotics; and

- Monitor and evaluate the performances of DTCs and DISs of health centers.

5.4.8 Guidelines to undertake research on antibiotic use and resistance

Undertaking research is key to identifying and rectifying medicine use problems. A variety of studies can be undertaken in relation to antibiotic usage and resistance, including prescription review, medicine use evaluation, and antimicrobial sensitivity testing. Studies such as prescription review and medicine use evaluation can be undertaken by researchers in the field without the need for major resources from the health centre itself. Antimicrobial sensitivity testing requires a well-organised antimicrobial laboratory, expertise and finance and therefore can be undertaken by hospital laboratories, regional laboratories and research institutions. The following interventions are recommended in relation to this guideline.

- Build the capacity of the Health Bureau, sub-city health office and health centre staff to enable them to undertake medicine use studies with a focus on antibiotics, including prescription review and medicine use evaluation;
- Encourage and support researchers to undertake studies on antibiotics use and resistance at health centres and in the community;
- Coordinate the research undertakings of researchers and students to avoid duplication of effort and guide their studies so they will be useful for practice improvement; and
- Establish a mechanism and build capacity to obtain reports of studies conducted on antibiotic use and resistance in the city administration, triangulate the findings, extract data that is useful for practice and disseminate summary of the findings to all concerned.

5.4.9 Guidelines to improve antibiotic prescribing and dispensing in the private sector

The impact of irrational prescribing and dispensing of antibiotics without prescription from private pharmacies on the prescribing practices of public health facilities was raised repeatedly by the study participants who recommended the need to control the sector. The following interventions should be implemented to address the antibiotic prescribing and dispensing problems in the private sector.

- Enforce implementation of clinical guidelines in private sector health facilities;
- Apply a strict controlling mechanism to stop the dispensing of antibiotics without prescription in private pharmacies;
- Implement behavioural change interventions for private sector prescribers and facility owners to prioritise the public over their business; and
- Support the private sector in developing and implementing intervention to promote the ration use of antibiotics.

5.4.10 Guidelines to strengthen the planning, monitoring and evaluation system

Planning is the starting point for any undertaking, while monitoring and evaluation are necessary to track progress and take corrective measures timely. The information obtained from the study participants indicated that medicine use activities in general, and antibiotics in particular, are not appropriately incorporated into action plans to be monitored and evaluated. Some indicators in connection with the use of medicines and antibiotics are known to be included in work plans, but, activities that should be implemented to meet those targets are not planned appropriately. Hence, there is a need to strengthen the planning, monitoring and evaluation system by implementing the following interventions.

- Appropriately address antibiotics and resistance related issues on annual action plans at all levels as part of promoting the program on rational use of medicines;
- Organise performance review meetings at the Health Bureau and sub-city health office level focusing on medicines supply and use on a quarterly basis; and
- Strengthen the M&E system to track the progress of implementation of planned activities in relation to antibiotics through regular routine reporting of standardized indicators at each level.

5.5 CONCLUSION

This chapter discussed the intervention guidelines developed to improve the prescribing of antibiotics at the primary healthcare facilities. The development process, purpose and uses of the intervention guidelines were presented first. Then, the ten intervention guidelines developed based on suggestions of the study participants were described and the key interventions that should be implemented mentioned under each guideline. The next chapter presents the conclusion, recommendations, the study's contribution to knowledge and limitations of the study.

CHAPTER 6: CONCLUSIONS, RECOMMENDATIONS, CONSTRIBUTION TO KNOWLEDGE, AND LIMITATIONS

6.1 INTRODUCTION

The previous chapter presented development of the intervention guidelines to improve antibiotics prescribing at primary healthcare facilities which was the ultimate goal of the study. In this last chapter, the conclusions drawn from the findings and the recommendations made by the researcher are presented. In addition, contribution of the study to knowledge and the limitations of the study are also described. The chapter ends by providing overall conclusions of the study.

The purpose of this study was to develop intervention guideline to improve the prescribing of antibiotics at primary healthcare facilities. To this end, the study was conducted in three phases with each phase having inter-related objectives. First phase of the study (qualitative) was undertaken to determine the prevalence of antibiotic prescribing, describe the antibiotic prescribing pattern and evaluate appropriateness of the use of antibiotics for common infectious cases. Exploring and describing the factors influencing antibiotic prescribing decision, and identifying the interventions that should be implemented to improve antibiotic prescribing were addressed by second phase of the study. Integrating findings of the two phases, intervention guidelines were developed in the final (Phase III) of the study.

6.2 CONCLUSIONS

The study has achieved all of the research objectives and answered the research questions. Integrating findings of the quantitative and qualitative findings guided by the selected theoretical model (PRECEDE-PROCEED Model) provided comprehensive information on the antibiotics prescribing situation, the underlying factors influencing the practice and interventions that should be implemented to improve the practice. This led to the development of intervention guidelines to improve antibiotic prescribing at the healthcare facilities (phase III) as ultimate goal of the study. The selected theoretical model has helped the researcher to properly structure the study starting from the selection of study design up to development of the intervention guidelines. It was following the first four phases of the theoretical model that the quantitative and qualitative phases of the study were undertaken and the intervention guidelines developed.

Below are the conclusions drawn from the findings:

- The prevalence (rate) of antibiotic prescribing was high with wide variations between the primary healthcare facilities;
- Almost all of the antibiotics prescribed were included in the medicines list of the healthcare facilities;
- Upper respiratory tract infections were the most common diagnosis for prescribing of antibiotics and only five antibiotics accounted for nearly 80% of the antibiotics prescribed;
- Over three-quarters of the antibiotics prescribed belong to the Access category of the WHO AWaRe categorization of antibiotics;
- Antibiotics accounted for over one-third of the total cost of medicines prescribed with over one-third of the cost taken-up by antibiotics prescribed for upper respiratory tract infections;
- Prescribers' adherence to clinical guidelines in using antibiotics for the management of respiratory tract infections was about 60%;
- The prevalence (rate) of antibiotic prescribing was shown to have significant association with patient age, qualification of prescribers and season of prescribing;
- There were various types of prescriber-, patient- and system-related antibiotic prescriber and use problems at the primary healthcare facilities;
- The prescribing decision of healthcare providers is influenced by several predisposing, enabling and reinforcing factors that are related with the healthcare providers, patients and the community, and the healthcare system;
- Based on findings of the study, ten categories of intervention guidelines that can be used to improve the prescribing of antibiotics at the health centres were developed. The guidelines are related with capacitating prescribers, increasing awareness of patients and the community, controlling and supporting the private sector, and institutionalizing the issue of antibiotics and antibiotic resistance in the health system; and
- The anticipated challenges that should be addressed to effectively implement the interventions are also identified.

6.3 RECOMMENDATIONS

The recommendations are based on the conclusions of the study and are focused on areas for future research and application of the intervention guidelines in practice.

6.3.1 Recommendations for future research

The findings of the study highlighted the following areas for further research in relation to the prescribing of antibiotics at primary healthcare facilities.

- Investigate the actual effect of implementing PHCG on the prevalence (rate) and patterns of antibiotic prescribing using the findings of this study as baseline data;
- Undertake medicine use evaluation focusing on URTIs using the PHCG as a reference standard to evaluate its impact;
- Undertake a comparative study on the CBHI scheme and its effect on the prevalence (rate) and patterns of antibiotic prescribing;
- Conduct a study on the effectiveness of the proposed intervention guidelines in improving the prescription of antibiotics at primary healthcare facilities by applying phases 5 to 8 (PROCEED PART - implementation and evaluation phases) of the PRECEED-PROCEED Model;
- Undertake a systematic review on initiatives implemented so far to promote the rational use of antibiotics in the city administration and their effectiveness;
- Conduct medicine usage studies (prescription review and medicine use evaluation) in private clinics to provide evidence and baseline data to promote the rational prescribing of antibiotics in the private sector;
- Explore the underlying factors for the irrational dispensing of antibiotics without prescription in private pharmacies and how it can be addressed; and
- Undertake a feasibility study on using standard treatment guidelines such as the PHCG at private clinics that are providing primary healthcare service.

6.3.2 Recommendation to apply the intervention guidelines in practice

Under the leadership of the MOH and Addis Ababa City Administration Health Bureau, effective implementation of the intervention guidelines requires the collaborative effort of all stakeholders including health professionals, health system managers, researchers, development partners and the community. Above all, commitment of the government represented by the health system managers and the different decision-making bodies at all levels is key. In this regard, the following recommendation are forwarded:

- The Health Bureau should play a central role in the implementation of the guidelines to improve the rational prescribing of antibiotics at health centres by coordinating the efforts of all stakeholders;
- The findings of this study and the proposed intervention guidelines should be widely disseminated to all concerned in the form of presentations and publications;
- The findings of the study should be used as baseline data to evaluate the effectiveness of interventions that will be implemented to improve antibiotic prescribing at health centres in the City Administration, including the interventions proposed in this study;
- Combinations of two or more interventions should be implemented to realise change in prescribing of antibiotics;
- The effectiveness of the guidelines should be tested at small-scale in selected health centres with proper documentation of prescribing practices at baseline and during implementation phase;
- The guidelines should be contextualized and incorporated into policy documents, guidelines and strategies developed to promote the rational use of medicines in general and antibiotics in particular; and
- The identified challenges that are expected to be faced during implementation of the guidelines should be addressed to facilitate implementation of the proposed interventions.

6.4 CONTRIBUTION OF THE STUDY TO NEW KNOWLEDGE

This study was aimed at developing intervention guidelines to improve antibiotic prescribing at primary healthcare facilities. Guided by the PRECED-PROCEED Model, the study has described the prevalence (rate) and patterns of antibiotic prescribing, explored the underlying predisposing, enabling and reinforcing factors influencing antibiotic prescribing, and the interventions that should be implemented to improve antibiotic prescribing in the setting selected for the study. Intervention guidelines were developed by integrating findings of the quantitative and qualitative phases of the study.

There is a paucity of information on the prevalence (rate) and patterns of antibiotic prescribing, factors influencing prescribing practices and interventions that should be implemented to improve those practices at primary healthcare facilities, especially from developing countries. Hence, this study contributes to the existing body of knowledge by providing such comprehensive antibiotic prescribing data from a developing setting by applying a theoretical model as a guide. Moreover, interventional studies on improving antibiotic prescribing at primary health care facilities are rare in general, and from developing countries in particular. As to the knowledge of the researcher, this is the first study that explored the factors influencing the prescribing of antibiotics and developed interventions to improve the practice at primary healthcare facilities in Ethiopia in general and in the City Administration in particular.

The guidelines developed in this study are new additions to the existing body of knowledge that can be tested, contextualized and implemented to promote the rational prescribing of antibiotics at primary healthcare facilities in this country and beyond. The findings of the study are also useful additions to the existing data on the prevalence (rate) and patterns of antibiotic prescribing which will serve as baseline data to evaluate the effectiveness of interventions that will be implemented to improve antibiotic prescribing at primary healthcare facilities in the City Administration.

6.5 LIMITATIONS OF THE STUDY

This study has encountered methodological and literature availability limitations as summarised below.

a) Methodological limitations

Sampling limitations

- Only ten health centres from five of the ten sub-cities are involved in the quantitative phase of the study which might affect generalisability of the findings to all of the health centres found in the City Administration; and
- Although there were few physicians and midwives involved in the prescribing of medicines at the health centres, only health officers and nurses were involved in the qualitative phase of the study. These categories of professionals might have different views on factors influencing the prescribing of antibiotics than the ones included in the study.

Data collection limitations

- The clinical protocol used to determine prescribers' adherence to clinical guidelines for respiratory tract infections was developed using the PHCG, the STGs for Health Centres and other clinical guidelines as a reference due to the absence of a uniformly used guidelines during the data period. The findings may have under- or over-estimated actual adherence of the prescribers to the recent PHCG or the previous health centre STG;
- Obtaining reliable data on when the ten health centres included in the study actually started implementation of PHCG made it difficult to assess its effect on the rate and patterns of antibiotic prescribing;
- There were difficulties in retrieving some patient medical charts and extracting the necessary information from the medical charts for medicine use evaluation on the use of antibiotics for respiratory tract infections. This has limited the number of cases available for the evaluation on prescribers' adherence to clinical guidelines; and
- Due to time and financial constraints, the intervention guidelines developed were not reviewed by the study participants or a team of experts in the field.

b) Literature availability limitations

- The limited availability of literatures on antibiotic prescribing at primary health care facilities has made comparison of the findings in the areas of cost of antibiotic, commonly prescribed antibiotics, common diagnoses and AWaRe category of the prescribed antibiotics limited;
- The limited availability of interventional studies on antibiotic prescribing at primary healthcare facilities has constrained the effort made to support the proposed interventions with evidences from the literature.

6.6 CONCLUSION

In this final chapter, conclusions of the study drawn from the findings, the recommendations for future research and application of the intervention guidelines in practice are presented. In addition, contribution of the study to the existing body of knowledge and limitation of the study are described. The references used in this study and annexures to this study are presented in the next sections.

REFERENCES

Ab Rahman, N, Teng, CL & Sivasampu, S. 2016. Antibiotic prescribing in public and private practice: A cross-sectional study in primary care clinics in Malaysia. *BMC Infectious Diseases*. 16(1):1–8. doi.org/10.1186/s12879-016-1530-2.

Abd, R, Mohamed, R & Khaton, SE. 2017. The Effect of an Educational Intervention Based on the PRECEDE- PROCEED Model on Knowledge , Behaviors and Attitudes of Adolescent Students Regarding Drug Abuse and Addiction. *IOSR-JNHS*. 6(4):14–27. doi.org/10.9790/1959-0604051427.

Abdullah Ramdhani , Muhammad Ali Ramdhani, AS. 2014. Writing a Literature Review Research Paper: A step-by-step approach. *International Journal of Basic and Applied Science*. 3(1):47–56.

Acheson, A. 2012. Sample Size. In: *Encyclopedia of Research Design*. N.J. Salkind, Ed. Thousand Oaks: SAGE Publishing, Inc. doi.org/10.1201/9780429275067-8.

Adisa, R, Fakeye, TO & Aindero, VO. 2015. Evaluation of prescription pattern and patients' opinion on healthcare practices in selected primary healthcare facilities in Ibadan, South-Western Nigeria. *African Health Sciences*. 15(4):1318–1329. doi.org/10.4314/ahs.v15i4.35.

Africa Union. 2018. *Africa CDC framework for Antimicrobial Resistance-Regional guide for governments in Africa.*

Ahiabu, MA, Tersbøl, BP, Biritwum, R, Bygbjerg, IC & Magnussen, P. 2016. A retrospective audit of antibiotic prescriptions in primary health-care facilities in Eastern Region, Ghana. *Health Policy and Planning*. 31(2):250–258. doi.org/10.1093/heapol/czv048.

Akl, OA, El Mahalli, AA, Elkahky, AA & Salem, AM. 2014. WHO/INRUD drug use indicators at primary healthcare centers in Alexandria, Egypt. *Journal of Taibah University Medical Sciences*. 9(1):54–64. doi.org/10.1016/j.jtumed.2013.06.002.

Alemayehu, T, Ali, M, Mitiku, E & Hailemariam, M. 2019. The burden of antimicrobial resistance at tertiary care hospital, southern Ethiopia: A three years' retrospective study. *BMC Infectious Diseases*. 19(1):6–13. doi.org/10.1186/s12879-019-4210-1.

Alm, RA & Lahiri, SD. 2020. Narrow-spectrum antibacterial agents—benefits and challenges. *Antibiotics*. 9(7):1–8. doi.org/10.3390/antibiotics9070418.

Andrajati, R, Tilaqza, A & Supardi, S. 2017. Factors related to rational antibiotic prescriptions in community health centers in Depok City, Indonesia. *Journal of Infection and Public Health*. 10(1):41–48. doi.org/10.1016/j.jiph.2016.01.012.

Asmamaw, G, Ejigu, N, Tewihubo, D & Ayenew, W. 2022. Assessment of private health sector prescribing patterns and adherence to prescription format using World Health Organization core drug use indicators in Addis Ababa, Ethiopia. *Journal of Pharmaceutical Policy and Practice*. 15(1):1–10. doi.org/10.1186/s40545-022-00408-0.

Awad, AI & Aboud, EA. 2015. Knowledge , Attitude and Practice towards Antibiotic Use among the Public in Kuwait. *PLoS ONE*. 10(2):1–15. doi.org/10.1371/journal.pone.0117910.

Ayukekbong, JA, Ntemgwa, M & Atabe, AN. 2017. The threat of antimicrobial resistance in developing countries: Causes and control strategies. *Antimicrobial Resistance and Infection Control*. 6(1):1–8. doi.org/10.1186/s13756-017-0208-x.

Bantie, L. 2014. Assessment of Prescribing practice pattern in Governmental Health Centers of Bahir. *World Journal of Pharmaceutical Sciences*. 2(10):1184–1190. Available from: http://www.wjpsonline.org/.

Biezen, R, Roberts, C, Buising, K, Thursky, K, Boyle, D, Lau, P, Clark, M & Manski-Nankervis, JA. 2019. How do general practitioners access guidelines and utilise electronic medical records to make clinical decisions on antibiotic use? Results from an Australian qualitative study. *BMJ Open*. 9(8):1–8. doi.org/10.1136/bmjopen-2018-028329.

Bilal, AI, Osman, ED & Mulugeta, A. 2016. Assessment of medicines use pattern using World Health Organization's Prescribing, Patient Care and Health facility indicators in selected health facilities in eastern Ethiopia. *BMC Health Services Research*. 16(1):0–7. doi.org/10.1186/s12913-016-1414-6.

Borek, AJ, Campbell, A, Dent, E, Butler, CC, Holmes, A, Moore, M, Walker, AS, McLeod, M, et al. 2021. Implementing interventions to reduce antibiotic use: a qualitative study in high-prescribing practices. *BMC Family Practice*. 22(1):1–11. doi.org/10.1186/s12875-021-01371-6.

Boum, Y, Mwanga-Amumpaire, J, Orikiriza, P, Muhindo, A, Ampaire, L & Bebell, L. 2016. A review of antimicrobial resistance in East Africa. *African Journal of Laboratory Medicine*. 5(1):1–6. doi.org/10.4102/ajlm.v5i1.432.

BSAC. 2018. *Antimicrobial Stewardship from Principle to Practice*. British Society for Antimicrobial Chemotherapy. Available from: http://www.bsac.org.uk/antimicrobialstewardshipebook/BSAC-AntimicrobialStewardship-FromPrinciplestoPractice-eBook.pdf.

Catherine J. Binkley and Knowlton W. Johnson. 2014. Application of the PRECEDE-PROCEED Planning Model in Designing an Oral Health Strategy. *J Theory Pract Dent Public Health*. 1(3):1–18.

Central Statistical Agency. 2013. Population Projection of Ethiopia for All Regions At Wereda Level from 2014 – 2017. *Journal of Ethnobiology and Ethnomedicine*. 3(1):28. doi.org/10.1186/1746-4269-3-28.

Chem, ED, Anong, DN & Akoachere, JFKT. 2018. Prescribing patterns and associated factors of antibiotic prescription in primary health care facilities of Kumbo East and Kumbo West Health Districts, North West Cameroon. *PLoS ONE*. 13(3):1–18. doi.org/10.1371/journal.pone.0193353.

Costelloe, C, Metcalfe, C, Lovering, A, Mant, D & Hay, AD. 2010. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: Systematic review and meta-analysis. *BMJ (Online)*. 340(7756):1120. doi.org/10.1136/bmj.c2096.

Creswell, JW. 2014. *Researh Design: Qualitative, Quantitative, and Mixed Methods Approaches*. Fourth ed. California: SAGE Publicaitons, Inc.

CSA. 2013. Population Projections for Ethiopia 2007-2037. *Central Statistical Agency Population, Ethiopia*. (July):188.

Cuevas, C, Batura, N, Wulandari, LPL, Khan, M & Wiseman, V. 2021. Improving antibiotic use through behaviour change: A systematic review of interventions evaluated in low- And middle-income countries. *Health Policy and Planning*.

36(5):754–773. doi.org/10.1093/heapol/czab021.

Curry, L & Nunez-Smith, M. 2017a. Definition and Overview of Mixedd Methods Designs. In: *Mixed Methods in Health Sciences Research: A Practical Primer*. Thousand Oaks: Sage Publishing, Inc. doi.org/10.4135/9781483390659.n2.

Curry, L & Nunez-Smith, M. 2017b. Sampling and Data Collection in Mixed Methods Studies. *Mixed Methods in Health Sciences Research: A Practical Primer*. 203–228. doi.org/10.4135/9781483390659.n8.

DACA. 2009. Antimicrobial use, Resistance and Containment baseline survey. 1-160 pp.

Dadgostar, P. 2019. Antimicrobial resistance: implications and costs. *Infection and Drug Resistance*. 12:3903–3910. doi.org/10.2147/IDR.S234610.

Daniel, J. 2012. Choosing the Size of the Sample. In: *Sampling Essentials: Practical Guidelines for Making Sampling Choices*. Thousand Oaks: SAGE Publishing, Inc. doi.org/10.4135/9781452272047.n7.

Darkwah, TO, Afriyie, DK, Sneddon, J, Cockburn, A, Opare-Addo, MNA, Tagoe, B & Amponsah, SK. 2021. Assessment of prescribing patterns of antibiotics using national treatment guidelines and world health organization prescribing indicators at the ghana police hospital: A pilot study. *Pan African Medical Journal*. 39. doi.org/10.11604/pamj.2021.39.222.29569.

Dawadi, S. 2020. Thematic Analysis Approach: A Step by Step Guide for ELT Research Practitioners. *Journal of NELTA*. 25(1–2):62–71. doi.org/10.3126/nelta.v25i1-2.49731.

Desalegn, AA. 2013. Assessment of drug use pattern using WHO prescribing indicators at Hawassa University teaching and referral hospital, south Ethiopia: A cross-sectional study. *BMC Health Services Research*. 13(1). doi.org/10.1186/1472-6963-13-170.

Ebadifard Azar, F, Solhi, M, Nejhaddadgar, N & Amani, F. 2017. The effect of intervention using the PRECEDE-PROCEED model based on quality of life in diabetic patients. *Electronic Physician*. 9(8):5024–5030. doi.org/10.19082/5024.

EFDA. 2019. *Rational Medicine Use Control Directive.pdf*. Addis Ababa.

EFMHACA. 2012a. *List of Medicine for Health Centers*.

EFMHACA. 2012b. *OVER – THE - COUNTER MEDICINES LIST FOR ETHIOPIA SECOND EDITION Food , Medicine & Health Care Administration & Control Authority of Ethiopia*. Second ed. Addis Ababa: Ethiopian Food, Medicine and Healthcare Administration and Control Authority.

EFMHACA. 2012c. *OVER – THE - COUNTER MEDICINES LIST FOR ETHIOPIA*. Second ed. Addis Ababa: Ethiopian Food, Medicine and Healthcare Administration and Control Authority. Available from: www.fmhaca.gov.et/documents/.

EFMHACA. 2014. *STG for Health Centers in Ethiopia*. Addis Ababa.

EFMHACA. 2015. *Strategies for the Prevention and Containment of Antimicrobial Resistance for Ethiopia 2015-2019*. Addis Ababa: Ethiopian Food, Medicine and Healthcare Administration and Control Authority.

EFMHACA. 2018. *A Practical Guide to Antimicrobial Stewardship Program in Ethiopian Hospitals.* Addis Ababa: Ethiopian Food, Medicine and Healthcare Administration and Control Authority.

EFMHACA and WHO. 2017. *Pharmaceutical Sector Assessment in Ethiopia*. Addis Ababa.

Ethiopian Public Health Institute. 2019. *Ethiopia Antimicrobial Resistance Surveillance Annual Report 2nd Year (September 2018 - October 2019)*. Addis Ababa. Available from: http://www.ephi.gov.et.

Fernández-Urrusuno, R, Meseguer Barros, CM, Benavente Cantalejo, RS, Hevia, E, Martino, CS, Aldasoro, AI, Mora, JL, Navas, AL, et al. 2020. Successful improvement of antibiotic prescribing at Primary Care in Andalusia following the implementation of an antimicrobial guide through multifaceted interventions: An interrupted time-series analysis. *PLoS ONE*. 15(5):1–16. doi.org/10.1371/journal.pone.0233062.

FMOH. 2019. *Ethiopian primary health care clinical guidelines*. Addis Ababa.

FMOH and WHO. 2003. *Assessment of the Pharmaceutical Sector in Ethiopia*. Addis Ababa.

FMOH and WHO. 2010. *Assessment of the Pharmaceutical Sector in Ethiopia*. Addis

Ababa.

Founou, RC, Founou, LL & Essack, SY. 2017. Clinical and economic impact of antibiotic resistance in developing countries: A systematic review and meta-analysis. *PLoS ONE*. 12(12):1–18. doi.org/10.1371/journal.pone.0189621.

Friedman, ND, Temkin, E & Carmeli, Y. 2016. The negative impact of antibiotic resistance. *Clinical Microbiology and Infection*. 22(5):416–422. doi.org/10.1016/j.cmi.2015.12.002.

Fritz, BAE & Morgan, GA. 2012. Sampling. In: *Encyclopedia of Research Design*. N.J. Salkind, Ed. Thousand Oaks: SAGE Publishing, Inc.

Frost, I, Laxminarayan, R, McKenna, N, Chai, S & Joshi, J. 2018a. *Antimicrobial resistance and primary health care*. Available from: https://apps.who.int/iris/bitstream/handle/10665/326454/WHO-HIS-SDS-2018.56-eng.pdf%0Ahttps://www.who.int/docs/default-source/primary-health-care-conference/amr.pdf?sfvrsn=8817d5ba_2.

Frost, I, Laxminarayan, R, McKenna, N, Chai, S & Joshi, J. 2018b. *Antimicrobial resistance and primary health care*. Geneva: World Health Organization. Available from: https://apps.who.int/iris/bitstream/handle/10665/326454/WHO-HIS-SDS-2018.56-eng.pdf%0Ahttps://www.who.int/docs/default-source/primary-health-care-conference/amr.pdf?sfvrsn=8817d5ba_2.

Fujita, AW, Werner, K, Jacob, JT, Tschopp, R, Mamo, G, Mihret, A, Abdissa, A, Kempker, R, et al. 2022. Antimicrobial Resistance Through the Lens of One Health in Ethiopia: A Review of the Literature Among Humans, Animals, and the Environment. *International Journal of Infectious Diseases*. 119:120–129. doi.org/10.1016/j.ijid.2022.03.041.

Gasson, J, Blockman, M & Willems, B. 2018. Antibiotic prescribing practice and adherence to guidelines in primary care in the cape town Metro district, South Africa. *South African Medical Journal*. 108(4):304–310. doi.org/10.7196/SAMJ.2018.v108i4.12564.

Gebresilasie, YM, Tullu, KD & Yeshanew, AG. 2018. Resistance pattern and maternal knowledge , attitude and practices of suspected Diarrheagenic Escherichia coli among children under 5 years of age in Addis Ababa , Ethiopia : cross sectional study. *Antimicrobial resistnace and Infection Control*. 7:4–5.

Gillies, MB, Burgner, DP, Ivancic, L, Nassar, N, Miller, JE, Sullivan, SG, Todd, IMF, Pearson, SA, et al. 2022. Changes in antibiotic prescribing following COVID-19 restrictions: Lessons for post-pandemic antibiotic stewardship. *British Journal of Clinical Pharmacology*. 88(3):1143–1151. doi.org/10.1111/bcp.15000.

Heale, R & Twycross, A. 2015. Validity and reliability in quantitative studies. *Evidence-Based Nursing*. 18(3):66–67. doi.org/10.1136/eb-2015-102129.

Hellen, G, Molly, M-P, Pantsumanth, G, Jordan, L, Devra, B, Andrea, WhiteANDREA, W & Ramanan, L. 2015. *State of the World's Antibiotic Situation 2015*. Washington, D.C.

Hoa, NQ, Lan, PT, Phuc, HD, Chuc, NTK & Lundborg, CS. 2017. Antibiotic prescribing and dispensing for acute respiratory infections in children: Effectiveness of a multi-faceted intervention for health-care providers in Vietnam. *Global Health Action*. 10(1). doi.org/10.1080/16549716.2017.1327638.

Hussen, S, Mulatu, G & Yohannes Kassa, Z. 2019. Prevalence of Shigella species and its drug resistance pattern in Ethiopia: A systematic review and meta-analysis. *Annals of Clinical Microbiology and Antimicrobials*. 18(1):1–11. doi.org/10.1186/s12941-019-0321-1.

Iwu-Jaja, CJ, Jaca, A, Jaja, IF, Jordan, P, Bhengu, P, Iwu, CD, Okeibunor, J, Karamagi, H, et al. 2021. Preventing and managing antimicrobial resistance in the African region: A scoping review protocol. *PLoS ONE*. 16(7 July):1–9. doi.org/10.1371/journal.pone.0254737.

Jasovský, D, Littmann, J, Zorzet, A & Cars, O. 2016. Antimicrobial resistance — a threat to the world ' s sustainable development. 121(3):160. doi.org/10.1080/03009734.2016.1195900.

Kefal Gelaw, B, Feyissa, A & Tegegne, GT. 2015. Prescription Pattern of Injection at Out Patient Pharmacy Department of Adama Hospital Medical College, Adama, Ethiopia. *Clinical Pharmacology & Biopharmaceutics*. 04(04):308–314. doi.org/10.4172/2167-065x.1000146.

Koji, EM, Gebretekle, GB & Tekle, TA. 2019. Practice of over-the-counter dispensary of antibiotics for childhood illnesses in Addis Ababa, Ethiopia: A simulated patient encounter study. *Antimicrobial Resistance and Infection Control*. 8(1):4–9. doi.org/10.1186/s13756-019-0571-x.

Kpokiri, EE, Taylor, DG & Smith, FJ. 2020. Development of antimicrobial stewardship programmes in low and middle-income countries: A mixed-methods study in nigerian hospitals. *Antibiotics*. 9(4):1–11. doi.org/10.3390/antibiotics9040204.

Lee, CR, Lee, JH, Kang, LW, Jeong, BC & Lee, SH. 2015. Educational effectiveness, target, and content for prudent antibiotic use. *BioMed Research International*. 2015. doi.org/10.1155/2015/214021.

Lee, TH, Wong, JGX, Lye, DCB, Chen, MIC, Loh, VWK, Leo, YS, Lee, LK & Chow, ALP. 2017. Medical and psychosocial factors associated with antibiotic prescribing in primary care: Survey questionnaire and factor analysis. *British Journal of General Practice*. 67(656):e168–e177. doi.org/10.3399/bjgp17X688885.

Lenjisa, JL & Fereja, TH. 2014. A Retrospective Analysis of Prescribing Practices through WHO Prescribing Indicators at Four Selected Hospitals of West Ethiopia. *Journal of Bioanalysis & Biomedicine*. 06(02):29–32. doi.org/10.4172/1948-593x.1000105.

Leung, JT & Shek, DT. 2018. Quantitative Research Methods. In: *The SAGE Encyclopedia of Educational Research, Measurement, and Evaluation*. B.B. Freyfrey, Ed. Thousand Oaks: SAGE Publicaitons, Inc. 79–95. doi.org/10.1057/978-1-137-59146-3_5.

Levine, DM, Stephan, DF, Krehbiel, TC & Berenson, ML. 2008. *Statistics for Managers Using Microsoft ® Excel*. Fifth ed. New Jersey: Prenice Hall. doi.org/10.1198/tech.2001.s615.

Liu, C, Liu, C, Wang, D & Zhang, X. 2019a. Intrinsic and external determinants of antibiotic prescribing: A multi-level path analysis of primary care prescriptions in Hubei, China. *Antimicrobial Resistance and Infection Control*. 8(1):1–12. doi.org/10.1186/s13756-019-0592-5.

Liu, C, Liu, C, Wang, D & Zhang, X. 2019b. Knowledge, attitudes and intentions to prescribe antibiotics: A structural equation modeling study of primary care institutions in Hubei, China. *International Journal of Environmental Research and Public Health*. 16(13). doi.org/10.3390/ijerph16132385.

Low, M, Almog, R, Balicer, RD, Liberman, N, Raz, R, Peretz, A & Nitzan, O. 2018. Infectious disease burden and antibiotic prescribing in primary care in Israel. *Annals of Clinical Microbiology and Antimicrobials*. 17(1):1–8. doi.org/10.1186/s12941-018-0278-5.

Lucas, PJ, Ingram, J, Redmond, NM, Cabral, C, Turnbull, SL & Hay, AD. 2017. Development of an intervention to reduce antibiotic use for childhood coughs in UK primary care using critical synthesis of multi-method research. 1–10. doi.org/10.1186/s12874-017-0455-9.

Lum, EPM, Page, K, Whitty, JA, Doust, J & Graves, N. 2018. Antibiotic prescribing in primary healthcare: Dominant factors and trade-offs in decision-making. *Infection, Disease and Health*. 23(2):74–86. doi.org/10.1016/j.idh.2017.12.002.

Lundborg, CS & Tamhankar, AJ. 2014. Understanding and changing human behaviour — antibiotic mainstreaming as an approach to facilitate modi fi cation of provider and consumer behaviour. (January):125–133. doi.org/10.3109/03009734.2014.905664.

Manga, MM, Mohammed, Y, Suleiman, S, Fowotade, A, Yunusa-Kaltungo, Z, Usman, M, Abulfathi, AA & Saddiq, MI. 2021. Antibiotic prescribing habits among primary healthcare workers in Northern Nigeria: a concern for patient safety in the era of global antimicrobial resistance. *PAMJ - One Health*. 5. doi.org/10.11604/pamj-oh.2021.5.19.30847.

Martínez-González, NA, Coenen, S, Plate, A, Colliers, A, Rosemann, T, Senn, O & Neuner-Jehle, S. 2017. The impact of interventions to improve the quality of prescribing and use of antibiotics in primary care patients with respiratory tract infections: A systematic review protocol. *BMJ Open*. 7(6):1–8. doi.org/10.1136/bmjopen-2017-016253.

Mason, T, Trochez, C, Thomas, R, Babar, M, Hesso, I & Kayyali, R. 2018. Knowledge and awareness of the general public and perception of pharmacists about antibiotic resistance. *BMC Public Health*. 18(1):2. doi.org/10.1186/s12889-018-5614-3.

McDonagh, MS, Peterson, K, Winthrop, K, Cantor, A, Lazur, BH & Buckley, DI. 2018. Interventions to reduce inappropriate prescribing of antibiotics for acute respiratory tract infections: summary and update of a systematic review. *Journal of International Medical Research*. 46(8):3337–3357. doi.org/10.1177/0300060518782519.

Ministry of Health. 2021. *Health Sector Transformation Plan II 2020/2021-2024/2025*.

Ministry of Health & Ministry of Agriulture. 2019. *ANTIMICROBIAL RESISTANCE PREVENTION AND CONTAINMENT STRATEGIC PLAN: THE ONE HEALTH APPROACH*. Addis Ababa: Ministry of Health, Ministry of Agriculture, and Environment, Forest and Climate Change Commision.

MOH. 2020. *Health and Health-Related Indicators 2013 EFY (2020/2021)*. Addis Ababa. Available from: https://e-library.moh.gov.et/library/wp-content/uploads/2021/11/Health-and-health-related-indicators-_2013-EFY.pdf.

Mollahaliloglu, S, Alkan, A, Donertas, B, Ozgulcu, S & Akici, A. 2013. Assessment of antibiotic prescribing at different hospitals and primary health care facilities. *Saudi Pharmaceutical Journal*. 21(3):281–291. doi.org/10.1016/j.jsps.2012.10.004.

Muhie, OA. 2019. Antibiotic Use and Resistance Pattern in Ethiopia: Systematic Review and Meta-Analysis. *International Journal of Microbiology*. 2019. doi.org/10.1155/2019/2489063.

Munn, Z & , Micah D. J. Peters, Cindy Stern, Catalin Tufanaru, AM and EA. 2018. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach Zachary. *BMC Medical Research Methodology*. 18(143):1–7. doi.org/10.1186/s12874-018-0611.

Murray, CJ, Ikuta, KS, Sharara, F, Swetschinski, L, Robles Aguilar, G, Gray, A, Han, C, Bisignano, C, et al. 2022. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet*. 399(10325):629–655. doi.org/10.1016/S0140-6736(21)02724-0.

Nathwani, D. 2018. Overview of Antimicrobial Resistance. In: *Antimicrobial Stewardship From Principles To Practice*. Birmingham: British Society for Antimicrobial Chemotherapy. 12–26. doi.org/10.1007/s00134=015-3978-8.

Nolan, A, Macfarlane, K & Cartmel, J. 2019. Guiding the Research Journey: Ethical

Considerations. In: *Research in Early Childhood*. 55 City Road: SAGE Publicaitons, Inc. doi.org/10.4135/9781526490728.n6.

O'Connor, R, O'Doherty, J, O'Regan, A & Dunne, C. 2018. Antibiotic use for acute respiratory tract infections (ARTI) in primary care; what factors affect prescribing and why is it important? A narrative review. *Irish Journal of Medical Science*. 187(4):969–986. doi.org/10.1007/s11845-018-1774-5.

O'Neill, J. 2014. *Antimicrobial Resistance : Tackling a crisis for the health and wealth of nations*. doi.org/10.1038/510015a.

Ofori-Asenso, R, Brhlikova, P & Pollock, AM. 2016. Prescribing indicators at primary health care centers within the WHO African region: A systematic analysis (1995-2015). *BMC Public Health*. 16(1). doi.org/10.1186/s12889-016-3428-8.

Parsons, S. 2018. Informed Consent. In: *The SAGE Encyclopedia of Educational Research, Measurement, and Evaluation*. B.B. Frey, Ed. Thousand Oaks: SAGE Publicaitons, Inc. doi.org/http://dx.doi.org/10.4135/9781506326139.

Phillips, JL, Rolley, JX & Davidson, PM. 2012. Developing Targeted Health Service Interventions Using the PRECEDE-PROCEED Model: Two Australian Case Studies. *Nursing Research and Practice*. 2012:1–8. doi.org/10.1155/2012/279431.

Porter, CM. 2015. Revisiting Precede-Proceed : A leading model for ecological and ethical Revisiting Precede – Proceed : A leading model for ecological and ethical health promotion. *Health Education Journal*. (December). doi.org/10.1177/0017896915619645.

Prestinaci, F, Pezzotti, P & Pantosti, A. 2015. Antimicrobial resistance: A global multifaceted phenomenon. *Pathogens and Global Health*. 109(7):309–318. doi.org/10.1179/2047773215Y.0000000030.

Reta, A, Bitew Kifilie, A & Mengist, A. 2019. Bacterial Infections and Their Antibiotic Resistance Pattern in Ethiopia: A Systematic Review. *Advances in Preventive Medicine*. 2019(Cdc):1–10. doi.org/10.1155/2019/4380309.

Richard Ofori-Asenso and Akosua Adom Agyeman. 2015. A review of injection and antibiotic use at primary health care (public and private) centers in Africa. *J Pharm Bioallied Sci.* 7(3).

Robertson, F, Jagers, SC & Rönnerstrand, B. 2018. Managing sustainable use of antibiotics-the role of trust. *Sustainability*. 10(1):1. doi.org/10.3390/su10010143.

Roulston, K & Choi, M. 2018. Qualitative Interviews. In: *The SAGE Handbook of Qualitative Data Collection*. U. Flick, Ed. London: SAGE Publicaitons, Inc. doi.org/10.1002/9780470750841.ch2.

Schoonenboom, J & Johnson, RB. 2017. How to Construct a Mixed Methods Research Design. 107–131. doi.org/10.1007/s11577-017-0454-1.

Sisay, M, Mengistu, G, Molla, B, Amare, F & Gabriel, T. 2017. Evaluation of rational drug use based on World Health Organization core drug use indicators in selected public hospitals of eastern Ethiopia: A cross sectional study. *BMC Health Services Research*. 17(1):1–9. doi.org/10.1186/s12913-017-2097-3.

Snyder, H. 2019. Literature review as a research methodology: An overview and guidelines. *Journal of Business Research*. 104(March):333–339. doi.org/10.1016/j.jbusres.2019.07.039.

Spellberg, B, Srinivasan, A & Chambers, HF. 2016. New societal approaches to empowering antibiotic stewardship. *JAMA - Journal of the American Medical Association*. 315(12):1229–1230. doi.org/10.1001/jama.2016.1346.

Sulis, G, Adam, P, Nafade, V, Gore, G, Daniels, B, Daftary, A, Das, J, Gandra, S, et al. 2020. Antibiotic prescription practices in primary care in low- And middle-income countries: A systematic review and meta-analysis. *PLoS Medicine*. 17(6):1–20. doi.org/10.1371/journal.pmed.1003139.

Summoro, TS, Gidebo, KD, Kanche, ZZ & Woticha, EW. 2015. Evaluation of trends of drug-prescribing patterns based on WHO prescribing indicators at outpatient departments of four hospitals in southern Ethiopia. *Drug Design, Development and Therapy*. 9:4551–4557. doi.org/10.2147/DDDT.S83588.

Suter, WN. 2014. *Sampling in Research*. Thousand Oaks: SAGE Publishing, Inc. doi.org/10.4018/978-1-5225-0007-0.ch006.

Tadesse, BT, Ashley, EA, Ongarello, S, Havumaki, J, Wijegoonewardena, M, González, IJ & Dittrich, S. 2017. Antimicrobial resistance in Africa : a systematic review. *BMC Infectious Diseases*. 17:1. doi.org/10.1186/s12879-017-2713-1.

Taherdoost, H. 2018. Validity and Reliability of the Research Instrument; How to Test the Validation of a Questionnaire/Survey in a Research. *SSRN Electronic Journal*. (September). doi.org/10.2139/ssrn.3205040.

Tarrant, C, Colman, AM, Chattoe-Brown, E, Jenkins, DR, Mehtar, S, Perera, N & Krockow, EM. 2019. Optimizing antibiotic prescribing: collective approaches to managing a common-pool resource. *Clinical Microbiology and Infection*. 25(11):1356–1363. doi.org/10.1016/j.cmi.2019.03.008.

Taxifulati, Y, Wushouer, H, Fu, M, Zhou, Y, Du, K, Zhang, X, Yang, Y, Zheng, B, et al. 2021. Antibiotic use and irrational antibiotic prescriptions in 66 primary healthcare institutions in Beijing City, China, 2015–2018. *BMC Health Services Research*. 21(1):1–9. doi.org/10.1186/s12913-021-06856-9.

Teixeira Rodrigues, A, Ferreira, M, Roque, F, Falcão, A, Ramalheira, E, Figueiras, A & Herdeiro, MT. 2016. Physicians' attitudes and knowledge concerning antibiotic prescription and resistance: Questionnaire development and reliability. *BMC Infectious Diseases*. 16(1):1–8. doi.org/10.1186/s12879-015-1332-y.

Terfa Kitila, K, Taddese, BD, Hailu, TK, Sori, LM, Geleto, SE, Mengistu, GZ, Tesfaw, DD, Gebeyehu, CS, et al. 2018. Assessment of Bacterial Profile and Antimicrobial Resistance Pattern of Bacterial Isolates from Blood Culture in Addis Ababa Regional Laboratory , Clinical Microbiology : Open Access. *Cliinical Microbiology: Open Access*. 7(2):2–3. doi.org/10.4172/2327-5073.1000312.

Tuem, KB, Gebre, AK, Atey, TM, Bitew, H, Yimer, EM & Berhe, DF. 2018a. Drug Resistance Patterns of Escherichia coli in Ethiopia: A Meta-Analysis. *BioMed Research International*. 2018. doi.org/10.1155/2018/4536905.

Tuem, KB, Gebre, AK, Atey, TM, Bitew, H, Yimer, EM & Berhe, DF. 2018b. Drug Resistance Patterns of Escherichia coli in Ethiopia : A Meta-Analysis. *Bomed Research International*. 2018:5–9.

Turnidge, J, Binns, P, Cruickshank, M, Firman, J, Heaney, A & McKenzie, D. 2016. *AURA 2016: first Australian report on antimicrobial use and resistance in human health*.

Wang, J, Wang, P, Wang, X, Zheng, Y & Xiao, Y. 2014. Use and prescription of antibiotics in primary health care settings in China. *JAMA Internal Medicine*. 174(12):1914–1920. doi.org/10.1001/jamainternmed.2014.5214.

Wangai, FK, Masika, MM, Lule, GN, Karari, EM, Maritim, MC, Jaoko, WG, Museve, B & Kuria, A. 2019. Bridging antimicrobial resistance knowledge gaps: The East African perspective on a global problem. *PLoS ONE*. 14(2):1–12. doi.org/10.1371/journal.pone.0212131.

Wei, X, Zhang, Z, Walley, JD, Hicks, JP, Zeng, J, Deng, S, Zhou, Y, Yin, J, et al. 2017. Effect of a training and educational intervention for physicians and caregivers on antibiotic prescribing for upper respiratory tract infections in children at primary care facilities in rural China: a cluster-randomised controlled trial. *The Lancet Global Health*. 5(12):e1258–e1267. doi.org/10.1016/S2214-109X(17)30383-2.

WHO. 1993. *How to investigate drug use in health facilities - selected drug use indicators*. Geneva: Workld Health Organization.

WHO. 2007. *WHO Operational package for assessing , monitoring and evaluating country pharmaceutical situations Guide for coordinators and data collectors*. Geneva: Workld Health Organization.

WHO. 2014. *Antimicrobial resistance global report on Surveillance*.

WHO. 2015a. *Global action plan on antimicrobial resistance*.

WHO. 2015b. *Global Action Plan on Antimicrobial Resistance*. Geneva: Workld Health Organization. doi.org/10.1128/microbe.10.354.1.

WHO. 2015c. *Antibiotic resistance: multi-country public awareness survey*. Geneva.

WHO. 2015d. *Antibiotic resistance: multi-country public awareness survey*. Geneva.

WHO. 2016. *WHO Fact Sheet on Antibiotic Resistance*. Geneva.

WHO. 2017. *Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics*. Available from: WHO_global_priority_antibiotic_resistant_bacteria_17.pdf.

WHO. 2018. *WHO Report on Surveillance of Antibiotic Consumption 2016 - 2018*. Available from: http://apps.who.int/iris%0Ahttps://apps.who.int/iris/bitstream/handle/10665/277359/9

789241514880-eng.pdf.

WHO. 2019a. *Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries: a WHO practical toolkit*. Geneva: World Health Organization. doi.org/10.1093/jacamr/dlz072.

WHO. 2019b. *WHO releases the 2019 AWaRe Classification Antibiotics*. Available from: https://www.who.int/news/item/01-10-2019-who-releases-the-2019-aware-classification-antibiotics.

WHO. 2021a. *Global antimicrobial resistance and use surveillance system (GLASS) report 2021*. Available from: http://www.who.int/glass/resources/publications/early-implementation-report-2020/en/.

WHO. 2021b. *AWaRe Classification*.

WHO, FAO & OIE. 2019. *Monitoring and evaluation of the global action plan on antimicrobial resistance*.

Wilkinson, A, Ebata, A & Macgregor, H. 2019. Interventions to reduce antibiotic prescribing in LMICs: A scoping review of evidence from human and animal health systems. *Antibiotics*. 8(1). doi.org/10.3390/antibiotics8010002.

Williams, SL & Mummery, KW. 2015. We can do that ! Collaborative assessment of school environments to promote healthy adolescent nutrition and physical activity behaviors We can do that ! Collaborative assessment of school environments to promote healthy adolescent nutrition and physical. *Health Education Research*. (February). doi.org/10.1093/her/cyv007.

Worku, F & Tewahido, D. 2018. Retrospective Assessment of Antibiotics Prescribing at Public Primary Healthcare Facilities in Addis Ababa, Ethiopia. *Interdisciplinary Perspectives on Infectious Diseases*. doi.org/10.1155/2018/4323769.

World Bank. 2016. Drug-Resistant Infections: A Threat to Our Economic Future. *World Bank Report*. 2(September):1–132. doi.org/10.1007/s11947-009-0181-3.

Yao, L, Yin, J, Huo, R, Yang, D, Shen, L, Wen, S & Sun, Q. 2020. The effects of the primary health care providers' prescription behavior interventions to improve the rational use of antibiotics: a systematic review. *Global Health Research and Policy*. 5(1). doi.org/10.1186/s41256-020-00171-2.

Yimenu, DK, Emam, A, Elemineh, E & Atalay, W. 2019. Assessment of Antibiotic Prescribing Patterns at Outpatient Pharmacy Using World Health Organization Prescribing Indicators. *Journal of Primary Care and Community Health*. 10. doi.org/10.1177/2150132719886942.

Yin, X, Song, F, Gong, Y, Tu, X, Wang, Y, Cao, S, Liu, J & Lu, Z. 2013. A systematic review of antibiotic utilization in china. *Journal of Antimicrobial Chemotherapy*. 68(11):2445–2452. doi.org/10.1093/jac/dkt223.

Zhao, H, Wang, S, Meng, R, Liu, G, Hu, J, Zhang, H, Yan, S & Zhan, S. 2022. Appropriateness of Antibiotic Prescriptions in Chinese Primary Health Care and the Impact of the COVID-19 Pandemic: A Typically Descriptive and Longitudinal Database Study in Yinchuan City. *Frontiers in Pharmacology*. 13(April):1–15. doi.org/10.3389/fphar.2022.861782.

ANNEXURES

ANNEXURE A: DATA ABSTRACTION FORM FOR ANTIBIOTICS PRESCRIBING RATE

PART I: GENERAL INFORMATION

Name of Health Center __________________ Sub-City ___________________

Number of prescribers in the health center (by profession): _____ Medical Doctors; ______ Health Officers _____ Nurses

Is there functional Drug and Therapeutical Committee (DTC)? ____ Yes ____ No

Is the Standard Treatment Guideline for Health Center available? ____ Yes ____ No

If Yes, is a copy available in every examination room? ____ Yes _____ No

Does the health center have medicines list? ____ Yes _____ No

If Yes, when was it developed/revised? ______________________

How many patients does the health center serve annually? __________

What was annual budget allocated for the procurement of pharmaceuticals (ETB) during the previous budget year? ____________

PART II: MEDICATION RELATED INFORMATION AS ABSTRACTED FROM PRESCRIPTION PAPER

____________________ *Health Center*

Patient code	Card number	Date of prescribing (dd/mm/yy) in E.C.	Patient's Age (Years)	Patient's Gender(M/F)	Number of medicines prescribed	Cost of medicines prescribed (ETB)	Number of Antibiotics Prescribed	Cost of antibiotics prescribed (ETB)	Number of antibiotics available on the HC's Medicines List	Qualification of the Prescriber (MD, HO, Nurse)*

***** *MD – Medical Doctor, HO – Health Officer*

ANNEXURE B: DATA ABSTRACTION FORM FOR ANTIBIOTICS PRESCRIBING PATTERN

PART I: GENERAL INFORMATION

Name of Health Center __________________ Sub-City ___________________

Top ten diseases (with percentage) for the year 2012 E.C. (July 2019 – June 2020):

S/N	Disease category (as per the HMIS	Percentage
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		

PART II: DISEASE AND MEDICATION INFORMATION AS ABSTRACTED FROM PATIENT MEDICAL CHART

_______________________ *Health Center*

Patient code	Name of the antibiotic(s) prescribed, the dosage for each (dose, frequency) and route of administration	Duration/ Quantity	Diagnosis	Qualification of the prescriber (MD, HO, Nurse)*	Result of the Laboratory Investigation	Cost of the antibiotic (ETB)	AWaRe Classification (Access, Watch, Reserve)

** MD – Medical Doctor, HO – Health Officer*

ANNEXURE C: DATA ABSTRACTION FORM FOR APPROPRIATENESS OF ANTIBIOTICS PRESCRIBED FOR RESPIRATORY TRACT INFECTIONS AS ABSTRACTED FROM PATIENT MEDICAL CHART

___________________ *Health Center*

Patient code	**Diagnosis**	Medicines prescribed and dosage (Antibiotics)	Pertinent diagnostic tests conducted	Appropriateness of therapy and justifications

ANNEXTURE D: CONFIDENTIALITY AGREEMENT WITH RESEARCH ASSISTANTS

Department of Health Studies, University of South Africa

I, ____________________, agree to assist the Researcher with this PHD study ***"Guidelines to Improve Antibiotics Prescribing at Primary Healthcare Facilities in Ethiopia"*** in *collecting the quantitative data, developing clinical protocols and undertaking evaluation on appropriateness of the antibiotics prescribed for respiratory tract infections, and collecting and transcribing the qualitative data*. I agree to maintain full confidentiality when performing these tasks.

Specifically, I agree to:

1. Collect data from records and research participants with full adherence to the research protocol;
2. Keep all research data I come across confidential by not discussing or sharing the information in any form or format (with anyone other than the researcher;
3. Hold in strictest confidence the identification of any individual that may be revealed during the course of performing the research tasks;
4. Not make copies of any raw data in any form or format, unless specifically requested to do so by the researcher;
5. Keep all raw data that contains identifying information in any form or format (e.g., disks, tapes, transcripts) secure while it is in my possession. This includes:
    a. keeping all digitized raw data in computer password-protected files and other raw data in a locked file;
    b. closing any computer programs and documents of the raw data when temporarily away from the computer;
    c. permanently deleting any e-mail communication containing the data; and
    d. using closed headphones in transcribing recordings; give, all raw data in any form or format to the researcher when I have completed the research tasks;
6. Destroy all research information in any form or format that is not returnable to the researcher (e.g., information stored on my computer hard drive) upon completion of the research tasks.

Name of research assistant: ________________________

Address: _______________________

Telephone number:________________

Signature of research assistant______________________ Date __________

Name of the researcher: _____________________

Signature of the researcher _____________________ Date_________

ANNEXURE E: ETHICAL CLEARANCE CERTIFICATE FROM UNISA

UNISA university of south africa

COLLEGE OF HUMAN SCIENCES RESEARCH ETHICS REVIEW COMMITTEE

11 November 2020

Dear FIKRU WORKU ALTAYE

NHREC Registration # : Rec-240816-052
CREC Reference # : 64093352_CHS _CREC_2020

Decision: Ethics Approval from 10 October 2020 to 31 August 2024

Principal Researcher(s): FIKRU WORKU ALTAYE (email: 64093352@mylife.unisa.ac.za)

Supervisor: Gb Thupayagale-Tshweneagae (email: tshweg@unisa.ac.za)

New Title: Guidelines to Improve Antibiotic Prescribing Practice at Primary Healthcare Facilities in Ethiopia

Degree Purpose: Doctor of Philosophy in Public Health

Thank you for the application for research ethics clearance by the Unisa College of Human Science Ethics Committee. Ethics approval is granted for three years.

The **Low-*Risk application was reviewed*** by College of Human Sciences Research Ethics Committee, on **29 November 2020** in compliance with the Unisa Policy on Research Ethics and the Standard Operating Procedure on Research Ethics Risk Assessment.

The proposed research may now commence with the provisions that:

1. The researcher(s) will ensure that the research project adheres to the values and principles expressed in the UNISA Policy on Research Ethics.
2. Any adverse circumstance arising in the undertaking of the research project that is relevant to the ethicality of the study should be communicated in writing to the College Ethics Review Committee.

University of South Africa
Preller Street, Muckleneuk Ridge, City of Tshwane
PO Box 392 UNISA 0003 South Africa
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3. The researcher(s) will conduct the study according to the methods and procedures set out in the approved application.
4. Any changes that can affect the study-related risks for the research participants, particularly in terms of assurances made with regards to the protection of participants' privacy and the confidentiality of the data, should be reported to the Committee in writing, accompanied by a progress report.
5. The researcher will ensure that the research project adheres to any applicable national legislation, professional codes of conduct, institutional guidelines and scientific standards relevant to the specific field of study. Adherence to the following South African legislation is important, if applicable: Protection of Personal Information Act, no 4 of 2013; Children's act no 38 of 2005 and the National Health Act, no 61 of 2003.
6. Only de-identified research data may be used for secondary research purposes in future on condition that the research objectives are similar to those of the original research. Secondary use of identifiable human research data require additional ethics clearance.
7. No fieldwork activities may continue after the expiry date **(31 October 2024)**. Submission of a completed research ethics progress report will constitute an application for renewal of Ethics Research Committee approval.

Note:

The reference number **64093352_CHS _CREC_2020** should *be clearly indicated on all forms of communication with the intended research participants, as well as with the Committee.*

Disclaimer : The initial certificate was issued Under the Following title: A Model to Empower the Community on Antibiotic Use and Resistance.

Yours Sincerely,

Signature :

Signature :PP

Dr. K.J. Malesa
CHS Ethics Chairperson
Email: maleskj@unisa.ac.za
[illegible]

Prof K. Masemola
Executive Dean : CHS
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ANNEXURE F: SUPPORT LETTER FROM UNISA REGIONAL LEARNING CENTER, ADDIS ABABA

UNISA | university of south africa

23 November, 2020

UNISA-ET/KA/ST/29/23-11-2020

Addis Ababa City Administration Health Bureau

Public Health Research and Emergency Management Core Process

Addis Ababa

Dear Madam/Sir,

The University of South Africa (UNISA) extends warm greetings. By this letter, we want to confirm that Mr. Fikru Worku Altaye (student number 64093352) is a PhD student in the Department of Health Studies at UNISA. Currently, he is about to go out for data collection on his doctoral research entitled "***Guidelines to Improve Antibiotic Prescribing Practice at Primary Healthcare Facilities in Ethiopia***".

This is therefore to kindly request your cooperation in assisting the student by giving hin in-country ethics clearance. We would like to thank you in advance for all the assistance that you would provide to the student. Attached, please find the ethical clearance that the student has received from the Department.

Sincerely,

Dr. Tsige GebreMeskel Aberra

Director

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ANNEXURE G: LETTER OF REQUEST FOR LOCAL ETHICAL CLEARANCE

Date: November 25, 2020

Addis Ababa City Administration Health Bureau

Public Health Research and Emergency Management Core Process

Addis Ababa

Subject: Application for Ethical Clearance

I am Fikru Worku Altaye a Public Health PHD student at the University of South Africa (UNISA) with student number 64093352 under the Department of Health Studies. I have got ethical clearance from the University to undertake my PHD research on the topic ***"Guidelines to Improve Antibiotic Prescribing Practice at Primary Healthcare Facilities in Ethiopia***". The aim of this study is to assess the antibiotic prescribing practice and explore the underlying factors with the ultimate goal of developing guidelines to improve antibiotics prescribing in the study setting.

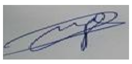
The study will be conducted from December 1, 2020 to January 31, 2021 in 5 sub-cities and 10 public health centers selected from 5 of the sub-cities found in Addis Ababa. Both qualitative and quantitative data will be collected. In addition to the sub-cities and health centers, the Health Bureau will also be included in the qualitative study. The selected sub-cities and health centers are the following:

Name of selected Sub-city	Name of Health Centers selected for the study
1. Addis Ketama Sub-city	1. Kuas Meda (Woreda 9) Health Center 2. Millennium Health Center
2. Gulele Sub-city	1. Shiromeda Health Center 2. Tibeb Bekechene Health Center
3. Lideta Sub-city	Woreda 1 (Yehidase Fire) Health Center
4. Nifas Silk Lafto Sub-city	1. Woreda 9 Health Center 2. Woreda 12 Health Center
5. Yeka Sub-city	1. Entoto No. 1 Health Center 2. Woreda 8 Health Center 3. Yeka Health Center

Prior to the actual study, the data collection tools will be pre-tested in two health centers: Abebe Bikila Health Center (Addis Ketama Sub-city) and Tekle Haimanot Health Center (Lideta Sub-city).

I am kindly requesting your office to grant me ethical clearance for this study. I have attached the ethical clearance certificate and support letter from UNISA, hard and soft copies of the research proposal and my CV for your reference.

With best regards,



Fikru Worku Altaye

PHD Candidate, UNISA

ANNEXURE H: LETTER OF PERMISSION FROM ADDIS ABABA CITY ADMINISTRATION HEALTH BUREAU RESEARCH ETHICAL CLEARANCE COMMITTEE

አዲስ አበባ ከተማ አስተዳደር ጤና ቢሮ
City Government of Addis Ababa Health Bureau

Ref.N.o. 2/ጤ/ጠ/ A542/22

Date 25/3/13

TO:

- GULELLE SUB-CITY HEALTH OFFICE
- NIFAS SILK LAFTO SUB-CITY HEALTH OFFICE
- LDETA SUB-CITY HEALTH OFFICE
- ADDIS KETEMA SUB-CITY HEALTH OFFICE
- YEKA SUB-CITY HEALTH OFFICE
- ADDIS ABABA HEALTH BUREAU

Subject: Request to access Facilities to conduct approved research

The letter is to support **FIKRU WORKU ALTAYE** of "**GUIDELINES TO IMPROVE ANTIBIOTIC PRESCRIBING PRACTICE AT PRIMARY HEALTH CARE FACILITIES IN ETHIOPIA.**" The study proposal was duly reviewed and approved by Addis Ababa Health Bureau IRB, and the principal investigator is informed with a copy of this letter to report any changes in the study procedures and submit an activity progress report to the Ethical Committee as required. Therefore we request the facility and staffs to provide support to the principal investigator.

With Regards

Ethical Clearance Committee

Cc

- FIKRU WORKU ALTAYE
- **To Ethical Clearance Committee**

ANNEXURE I: IN-DEPTH INTERVIEW GUIDE FOR PRESCRIBERS

Date of data collection ___________

Background Information:

Code: __________

Gender: ____ Male ____ Female Age (in years) ___________

Professional qualification ____________ Educational level ___________

Total years of service as a prescriber___________

Years of service as a prescriber in this health center ____________

Any training taken during the past 2 years on antibiotic use and resistance: ____

The Unit/Department you are working in _____________________

The number of patients you treat per day ____________

Interview questions:

Introductory Questions	Probing Questions
Tell me about antibiotic use	o How do you describe the current use of antibiotics (Globally, Nationally and locally particularly in your setup)? o Do you think that inappropriate use of antibiotics is a problem? How and why? o What kind of antibiotics use problems are more common in your setting? o How do you see the trend in the antibiotic use problem over time? o Do you have concern in the way antibiotics are prescribed and used today? o What factors contribute for the overuse of antibiotics? o How do you see the use of broad versus narrow spectrum antibiotics? o Do prescribers tend to prescribe broad-spectrum antibiotics empirically and/or overprescribe antibiotics? o What are the potential reasons for the preference of broad-spectrum antibiotics?
What is your understanding on antibiotic resistance?	o How do you describe the current status of antibiotic resistance (global, national and local level)? How serious is the problem? o Should healthcare professionals be worried of this problem? Why? o Do you face any challenge in your daily practice as a result of antibiotic resistance? How does it affect you? How does it affect the patient?

Introductory Questions	Probing Questions
	○ What factors do you think are contributing for the increasing emergence and spread of antibiotic resistance? Which of these factors apply in your setup? ○ How do you describe the utilization of laboratory findings in the diagnosis of infections?
Tell me about your antibiotic prescribing practice	○ How do you decide on antibiotic prescribing? ○ Do you know the local/national antibiotic resistance pattern? ○ What are the common ailments for which you prescribe antibiotics? What are the antibiotics you commonly prescribe? ○ How do you describe patients' pressure to prescribe antibiotics? ○ Does patient pressure affect your antibiotic prescribing decision? ○ How confident are you in prescribing antibiotics? ○ Have you made any change in your antibiotic prescribing in recent years? Why and how? ○ How do you evaluate your antibiotic prescribing practice? ○ How do you see the antibiotic prescribing practice in your facility? ○ What resources do you use to support your antibiotic prescribing decision? ○ Availability of system for rewarding good practice and discouraging/punishing malpractice in relation to antibiotic prescribing? ○ Availability of audit and feedback system? ○ Availability of opportunities to update knowledge on antibiotic use and resistance?
How do you see the use of antibiotics for upper respiratory tract infections?	○ How beneficial are antibiotics for URTI? ○ What are the common complaints to prescribe antibiotics for URTI? ○ What are the evidences/basis for prescribing antibiotics for URTI? ○ What are the antibiotics that you commonly prescribe for URTIs? ○ How do you evaluate the practice of prescribing antibiotics for URTI in the facility? ○ How do you evaluate your practice of prescribing antibiotics for URTIs?
What measures have been taken to improve the prescribing of antibiotics?	○ What actions/interventions have been taken during the past two years to improve the prescribing of antibiotics? ○ How do you evaluate effectiveness of the interventions implemented? ○ What were the factors that contributed for the success/failure of the interventions implemented? ○ Are there interventions that are being implemented?

Introductory Questions	Probing Questions
What measures/interventions do you suggest to improve the prescribing of antibiotics?	○ What initiatives do you know that are being implemented to prevent and contain AMR? (global, national, local) ○ Do you think you can influence the problems of antibiotic use? If yes, in what ways? ○ What possible interventions do you recommend for better antibiotic resistance prevention and containment at national and local level, in your facility? (Prioritize the interventions by level of importance.) ○ Who should do what? ○ From your experience, what potential factors might influence the antibiotic resistance containment practice in your setup? ○ What should be your role in promoting the appropriate use of antibiotics and prevention of AMR?

Is there anything else about antibiotic prescribing that we haven't discussed which you think would be useful for me to know about? ___________________________________

____

Thank you for participating in this study!

ANNEXURE J: IN-DEPTH INTERVIEW GUIDE FOR KEY INFORMANTS (HEALTH CENTER)

Date of data collection ___________

Background Information:

Code: _________

Gender: ____ Male _____Female Age in years _________
Position ________________________________
Professional qualification ________________ Educational level ___________
Total years of service ________ Year of service in this position ________

Interview questions:

Introductory Questions	Probing Questions
Tell me about antibiotic use	○ How do you describe the current use of antibiotics (Globally, Nationally and locally particularly in your setup)? ○ Do you think that inappropriate use of antibiotics is a problem? How and why? ○ How do you see the trend in the antibiotic use problem over time? ○ Do you have concern in the way antibiotics are being prescribed and used today? ○ What factors contribute for the overuse of antibiotics? ○ How do you see the use of broad versus narrow spectrum antibiotics? ○ Do prescribers tend to prescribe broad-spectrum antibiotics empirically and/or overprescribe antibiotics? ○ What are the potential reasons for the preference of broad-spectrum antibiotics?
What is your understanding on antibiotic resistance?	○ How do you describe the current status of antibiotic resistance (global, national and local level)? How serious is the problem? ○ Should healthcare professionals be worried of this problem? Why? ○ What are the causes and consequences of antibiotic resistance? ○ What factors do you think are contributing for the increasing emergence and spread of antibiotic resistance? Which of these factors apply in your setup? ○ How do you describe the utilization of laboratory findings in the diagnosis of infectious diseases?

Introductory Questions	Probing Questions
Tell me about the antibiotic prescribing practice at health centers	○ Do you know the local/national antibiotic resistance pattern? ○ How do you see the prescribing of broad-spectrum versus narrow-spectrum antibiotics? ○ How do you see the antibiotic prescribing practice at health centers? ○ What resources do prescribers use to support their antibiotic prescribing decision? ○ Availability of system for rewarding good practice and discouraging/punishing malpractice in relation to antibiotic prescribing? ○ Availability of audit and feedback system? ○ Availability of opportunities to update knowledge on antibiotic use and resistance?
How do you see the use of antibiotics for upper respiratory tract infections?	○ How beneficial are antibiotics for URTI? ○ What are the antibiotics that you commonly prescribe for URTIs? ○ How do you evaluate the practice of prescribing antibiotics for URTI in the facility?
What measures have been taken to improve the prescribing of antibiotics?	○ What actions/interventions have been taken during the past two years to improve the prescribing of antibiotics? ○ How do you evaluate effectiveness of the interventions implemented? ○ What were the factors that contributed for the success/failure of the interventions implemented? ○ Are there interventions that are being implemented?
What measures/interventions do you suggest to improve the prescribing of antibiotics?	○ What initiatives do you know that are being implemented to prevent and contain AMR? (global, national, local) ○ Do you think you can influence the problems of antibiotic use? If yes, in what ways? ○ What possible interventions do you recommend for better antibiotic resistance prevention and containment at national and local level, in your facility? (Prioritize the interventions by level of importance.) ○ Who should do what? ○ From your experience, what potential factors might influence the antibiotic resistance containment practice in your setup? ○ What should be your role in promoting the appropriate use of antibiotics and prevention of AMR?

Is there anything else about antibiotic prescribing that we haven’t discussed which you think would be useful for me to know about? ________________________________
____

Thank you for participating in this study!

ANNEXURE K: IN-DEPTH INTERVIEW GUIDE FOR KEY INFORMANTS (SUB-CITY AND HEALTH BUREAU)

Date of data collection ___________

Background Information:

Code: _________

Gender: ____ Male _____Female Age in years _________
Position ________________________________
Professional qualification ________________ Educational level ___________
Total years of service ________ Year of service in this position ________

Interview questions:

Introductory Questions	Probing Questions
About antibiotic use	○ The current use of antibiotics (Globally, Nationally and locally particularly in your setup) ○ Irrational use of antibiotics as a problem? How and why? ○ Specific concerns in the way antibiotics are being prescribed and used ○ Factors that contribute for the irrational use of antibiotics
Antibiotic resistance	○ The current status of antibiotic resistance (global, national and local level)? ○ How serious is the problem? (national, health center, healthcare providers, patients and the community) ○ Factors contributing for the emergence and spread of antibiotic resistance
Antibiotic prescribing practice at health centers	○ Antibiotic prescribing at health centers over time ○ Issues in the prescribing of antibiotics at health centers ○ References that prescribers use to support their antibiotic prescribing decision? ○ System for rewarding good practice and discouraging/punishing malpractice in relation to antibiotic prescribing

Resources	○ Available policies, directives, strategies, guidelines, manual and other resources that governs antibiotics use and antibiotic resistance
	    ○ Good prescribing practice manual
	    ○ Good dispensing practice manual
	    ○ AMR strategy
	    ○ PHCG/IMNCI Guideline
	○ Any training/workshop organized to familiarize these resources
	○ Adherence of prescribers on the PHCG and IMNCI Guidelines
	○ Supply of antibiotics and laboratory reagents and supplies
	○ Support from development partners

Measures taken to improve the prescribing of antibiotics?	○ Interventions implemented during the past two years to improve antibiotics use at health centers ○ Effectiveness of the interventions implemented ○ Interventions planned to be implemented in 2013 EFY and their implementation status ○ Inclusion of antibiotic use and resistance issues in:

Introductory Questions	Probing Questions
	◦ Annual planning at each level ◦ Health education to patients and the community in the facility and at community level through the Urban HEP ◦ Supportive supervision and mentoring ◦ Performance review meetings ◦ Experience sharing events ◦ Regular performance reports ◦ Performance appraisal and recognition of healthcare providers ◦ Roles being played by DTC and DIS to promote the rational use of antibiotics ◦ Promoting the rational use of antibiotics in the private sector through working with the Addis Ababa City Administration FMHACA and other concerned bodies ◦ Assigning focal person to coordinate antibiotic use and resistance related activities ◦ Undertaking/supporting studies to identifying antibiotic use problems and antibiotic resistance pattern ◦ Interventions taken as per findings of the studies conducted ◦ Utilization of research findings to improve antibiotic use ◦ System to avail up-to-date information to healthcare professionals on antibiotic use and resistance ◦ Challenges
Measures/Interventions to improve the prescribing of antibiotics	◦ Interventions that should be implemented to improve the rational use of antibiotics and prevent antibiotic resistance (national, City Administration, Sub-city, Health Center level)? ◦ Your office's role in promoting the rational use of antibiotics and prevention of antibiotic resistance ◦ Anticipated challenges to implement the proposed interventions

Anything else about antibiotic prescribing that we haven't discussed which you think would be useful for me to know about ____
____

Thank you for participating in this study!

ANNEXURE L: CHECKLIST TO CONDUCT THE IN-DEPTH INTERVIEW

University of South Africa
Department of Health Studies
PHD in Public Health

Checklist to conduct the in-depth interview

- Get the selected Interviewee at the agreed quiet place;
- Introduce yourself to him/her (name, qualification and role in the research undertaking);
- Provide the Information Sheet and Consent Form to the Interviewee and summarize the information contained in the information to him/her; with focus on objectives of the study and anonymity of the information that is going to be collected from him/her;
- Inform him the need to read and sign the Consent Form;
- Inform him/her that the interview will take about 40 - 50 minutes and the whole session will be recorded to ensure that no information is missed;
- Allow him/her to ask questions regarding the interview;
- Allow him/her to read and sign the Consent Form in two copies;
- Take a copy of the signed form and retain the second to the Interviewee;
- Inform him/her not to mention his name, names of others and the health facility's name during the interview;
- Inform him/her that you are about to begin the interview with recording;
- Turn on the recorder and ask the interview questions as per the interview guide;
- Take the necessary notes while maintaining eye contact;
    - Record the date of interview, interviewee unique identifier and background information
- Frequently check if the recording is going well;
- Thank the Interviewee for participating in the study;
- Save the recorded interview with the unique code used for the interviewee;
- Transfer the recorded data to PC.

ANNEXURE M: PARTICIPANT INFORMATION SHEET FOR PRESCRIBERS

Dear Prospective Participant,

My name is *Fikru Worku Altaye* and I am doing research with *Professor G Thupayagale-Tshweneagae*, a Professor in the Department of Health Studies, towards a Doctor of Philosophy in Public Health at the University of South Africa. We are inviting you to participate in a study entitled ***"Guidelines to Improve Antibiotic Prescribing Practice at Primary Healthcare Facilities in Ethiopia."***

WHAT IS THE PURPOSE OF THE STUDY?

This study is expected to collect important information on the practice of antibiotics prescribing and associated factors that will be used to develop intervention guidelines. The guideline developed will be used to promote the prudent use of antibiotics at primary healthcare facilities thereby contribute for the reduction in the emergence and antibiotic resistance in Ethiopia and beyond.

WHY AM I BEING INVITED TO PARTICIPATE?

The Health Center you are providing service is selected as one of the study sites among the health centers found in Addis Ababa City Administration. All healthcare professionals in the selected health centers that are involved in prescribing of medicines are target groups of this study. A total of at least 30 prescribers will participate in this qualitative study.

WHAT IS THE NATURE OF MY PARTICIPATION IN THIS STUDY?

In this study, you will be asked on your antibiotics prescribing practice and factors associated with it for you to talk in length in a one-to-one interview. The main questions you will be asked focuses on your view of the antibiotics prescribing practice in your health center, your antibiotic prescribing practice, the factors influencing your antibiotic prescribing decision, and interventions that you would like to suggest to implemented to improve the practice. The interview will take about 45 minutes and the whole session will be recorded not to miss important information from the discussion.

CAN I WITHDRAW FROM THIS STUDY EVEN AFTER HAVING AGREED TO PARTICIPATE?

Participating in this study is voluntary and you are under no obligation to consent to participation. If you do decide to take part in this study, you will be given this information sheet to read and understand, and be asked to sign a written consent form. You are free to withdraw any time without giving a reason.

WHAT ARE THE POTENTIAL BENEFITS OF TAKING PART IN THIS STUDY?

This study aims at developing guidelines to promote the rational prescribing of antibiotics at primary healthcare facilities. The guidelines will be used as a reference material to promote the rational prescribing of antibiotics at primary healthcare facilities in Addis Ababa and other parts of the country thereby contribute for optimizing the use of antibiotics and reducing the emergence of antibiotics resistance. Hence, you are contributing your part for the national and global effort on antibiotic resistance prevention and containment by providing this prescribing information.

ARE THERE ANY NEGATIVE CONSEQUENCES FOR ME IF I PARTICIPATE IN THE RESEARCH PROJECT?

As this study aims at understanding the antibiotics prescribing practice and associated factors through in-depth interview, there will be no harm to the participant. It will require the participant's time to give the necessary information at the participant’s work place.

WILL THE INFORMATION THAT I CONVEY TO THE RESEARCHER AND MY IDENTITY BE KEPT CONFIDENTIAL?

Your name and any personal identifier will not be recorded anywhere in the notes taken during the discussion and the audio records and no one will be able to connect you to the answers you give. Your answers will be given a unique code and you will be referred to in this way in the data, the thesis, any publications, or other research reporting methods such as conference proceedings.

The anonymous data you provided may be used for other purposes, such as a research report, journal articles and/or conference proceedings. A report of the study may be submitted for publication, but individual participants will not be identifiable in such a report.

HOW WILL THE RESEARCHER(S) PROTECT THE SECURITY OF DATA?

The researcher will store hard copies of your answers for a minimum period of five years in a locked cupboard/filing cabinet at home for future research or academic purposes; electronic information will be stored on a password-protected computer. Future use of the stored data will be subject to further Research Ethics Review and approval if applicable. Hard copies will be shredded and burnt, and electronic copies will be permanently deleted from the hard drive of the computer and backup devices through the use of a relevant software programme.

WILL I RECEIVE PAYMENT OR ANY INCENTIVES FOR PARTICIPATING IN THIS STUDY?

Participation in this study will not have any financial or other forms of gain.

HAS THE STUDY RECEIVED ETHICS APPROVAL

This study has received written ethical approval from the Research Ethics Review Committee of the Department of Health Studies, University of South Africa and has got ethical clearance from the Research Ethical Review Committee of Addis Ababa City Administration Health Bureau. The health center management has granted permission for the study to be conducted. A copy of the approval letters from both institutions can be obtained from the researcher, when necessary.

HOW WILL I BE INFORMED OF THE FINDINGS/RESULTS OF THE RESEARCH?

The findings will be accessible for 5 years after the study. Should you require any further information or want to contact the researcher about any aspect of this study, please contact the researcher at fikruworku114@gmail.com or call at +251 921 878528.

Should you have concerns about the way in which the research has been conducted, you may contact Prof G Thupayagale-Tshweneagae at tshweg@unisa.ac.za. You can also contact the research ethics chairperson of the Research Ethics Committee of Addis Ababa City Administration Health Bureau Dr. Yohannes at +251911384599 and the ethics chairperson of the Department of Health Studies at the University of South Africa at Maritje@unisa.ac.za.

Thank you for taking time to read this information sheet and for participating in this study!

Fikru Worku Altaye
PHD student, UNISA

ANNEXURE N: CONSENT FORM FOR PRESCRIBERS

I, __________________, confirm that the person asking my consent to take part in this research "***"Guidelines to Improve Antibiotic Prescribing Practice at Primary Healthcare Facilities in Ethiopia"*** has told me about the nature, procedure, potential benefits and anticipated inconvenience of participation.

I have read (or had explained to me) and understood the study as explained in the information sheet.

I have had sufficient opportunity to ask questions and am prepared to participate in the study.

I understand that my participation is voluntary and that I am free to withdraw at any time without reason.

I am aware that the findings of this study will be processed into a research report, journal publications and/or conference proceedings, but that my participation will be kept confidential unless otherwise specified.

I agree to the recording of the discussion.

I have received a signed copy of the informed consent agreement.

Participant Name & Surname…………………………………………

Participant Signature…………………………..Date…………………

Researcher's Name & Surname: Fikru Worku Altaye

Researcher's signature…………………………………………..Date…………………

ANNEXURE O: PARTICIPANT INFORMATION SHEET FOR KEY INFORMANTS

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WHY AM I BEING INVITED TO PARTICIPATE?

The institution you are working in is a key stakeholder in promoting the ration use of antibiotics and you are selected as a key informant for the study because of your position in the organization in relation to the area being investigated in this study.

WHAT IS THE NATURE OF MY PARTICIPATION IN THIS STUDY?

In this study, you will be asked about the antibiotic prescribing situation at primary healthcare facilities in the City, the problem of antibiotic resistance, factors associated with the practice and potential interventions for you to talk in length in a one-to-one interview. The interview will take about 45 minutes and the whole session will be recorded not to miss important information from the discussion.

CAN I WITHDRAW FROM THIS STUDY EVEN AFTER HAVING AGREED TO PARTICIPATE?

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Thank you for taking time to read this information sheet and for participating in this study!

Fikru Worku Altaye
PHD student, UNISA

ANNEXURE P: CONSENT FORM FOR KEY INFORMANTS

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I have read (or had explained to me) and understood the study as explained in the information sheet.

I have had sufficient opportunity to ask questions and am prepared to participate in the study.

I understand that my participation is voluntary and that I am free to withdraw at any time without reason.

I am aware that the findings of this study will be processed into a research report, journal publications and/or conference proceedings, but that my participation will be kept confidential unless otherwise specified.

I agree to the recording of the discussion.

I have received a signed copy of the informed consent agreement.

Participant Name & Surname…………………………………………

Participant Signature…………………………..Date…………………

Researcher's Name & Surname: Fikru Worku Altaye

Researcher's signature…………………………………………..Date…………………