ASSESSING KNOWLEDGE, ATTITUDES, AND PRACTICES REGARDING ANTIBIOTIC USE AND RESISTANCE: A COMPREHENSIVE STUDY AMONG PRIVATE PRIMARY CARE PROVIDERS AND THE PUBLIC IN NORTHERN MALAYSIA

DEEBADARISHANI A/P SATHASIVAN

UNIVERSITI SAINS MALAYSIA

2024

ASSESSING KNOWLEDGE, ATTITUDES, AND PRACTICES REGARDING ANTIBIOTIC USE AND RESISTANCE: A COMPREHENSIVE STUDY AMONG PRIVATE PRIMARY CARE PROVIDERS AND THE PUBLIC IN NORTHERN MALAYSIA

by

DEEBADARISHANI A/P SATHASIVAN

**Thesis submitted in fulfilment of the requirements
for the degree of
Master of Science**

November 2024

ACKNOWLEDGEMENT

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AMR	Antimicrobial Resistance
AMS	Antimicrobial Stewardship
ART	Antiretroviral Treatment
CRE	Carbapenem-resistant Enterobacterales
COVID-19	Coronavirus Disease 2019
DDD	Defined Daily Doses
GLASS	Global Antimicrobial Resistance Surveillance System
GPs	General Practitioners
HIV	Human Immunodeficiency Virus
KAP	Knowledge, Attitudes, and Practices
MDR-TB	Multidrug-Resistant Tuberculosis
MINDEF	Ministry of Defence
MRSA	Methicillin-Resistant Staphylococcus Aureus
MOH	Ministry of Health
MOHE	Ministry of Higher Education
NSAR	National Surveillance of Antimicrobial Resistance
NSAU	National Surveillance on Antibiotic Utilization
URTI	Upper Respiratory Tract Infection
TB	Tuberculosis
WHO	World Health Organization
XDR-TB	Extensively Drug-Resistant Tuberculosis

LIST OF APPENDICES

x

PENILAIAN PENGETAHUAN, SIKAP DAN AMALAN MENGENAI PENGGUNAAN DAN RINTANGAN ANTIBIOTIK: KAJIAN KOMPREHENSIF DALAM KALANGAN PETUGAS KESIHATAN PRIMER SWASTA DAN ORANG AWAM DI UTARA MALAYSIA

ABSTRAK

Rintangan antimikrobial (AMR) dianggap sebagai ancaman kesihatan global oleh WHO, dan malangnya Malaysia, seperti setiap negara lain di dunia, tidak terlepas daripada bahaya ini. Kajian telah menunjukkan bahawa preskripsi antibiotik dalam penjagaan primer Malaysia adalah lebih tinggi di klinik swasta berbanding di klinik awam, dan pengetahuan tentang antibiotik dalam kalangan pengamal am hanya sederhana. Ini amat membimbangkan kerana penggunaan antibiotik yang tidak sesuai membawa kepada rintangan antibiotik pada manusia dan seterusnya telah terbukti membawa maut. Penyedia penjagaan kesihatan utama bertanggungjawab untuk menetapkan dan mendispens antibiotik kepada pesakit untuk pelbagai tanda kesihatan. Oleh itu, mereka memainkan peranan penting dalam memastikan penggunaan antibiotik yang betul di kalangan orang ramai, selari dengan usaha kerajaan untuk mencegah rintangan antimikrobial. Kajian ini dijalankan untuk mengisi jurang pengetahuan, sikap dan amalan dalam kalangan pengamal am di klinik swasta. Tinjauan keratan rentas menggunakan soal selidik yang dilengkapkan sendiri telah dijalankan di kalangan tiga populasi kajian berbeza iaitu pengamal am, ahli farmasi dan orang awamdi negeri utara Malaysia, termasuk Perlis, Kedah, Pulau Pinang dan Perak. Ini adalah penyelidikan deskriptif yang dijalankan semasa norma baharu pandemik Covid-19. Soal selidik telah dilengkapkan oleh doktor, ahli farmasi dan orang ramai sendiri semasa kerja lapangan. Setiap soal selidik mengandungi 30 soalan yang boleh

mengambil masa sehingga 10-15 minit untuk dijawab. Soal selidik yang dikembalikan telah disemak untuk kesempurnaan dan diminta menjawab mana-mana bahagian yang hilang. Data yang diperolehi dianalisis secara statistik menggunakan SPSS untuk analisis statistik dan inferensi. Secara keseluruhannya, tahap pengetahuan, sikap dan amalan untuk pengamal penjagaan kesihatan dan orang awam didapati memuaskan. Mengenal pasti pengetahuan dan persepsi penggunaan antibiotik dalam kalangan penyedia penjagaan kesihatan boleh mewujudkan rangka kerja yang sesuai untuk memerangi rintangan antimikrob dengan berkesan. Hasil kajian ini boleh menjadi mekanisme penting untuk menyelamatkan banyak nyawa, meningkatkan kualiti hidup dan mengurangkan beban ekonomi yang disebabkan oleh AMR.

ASSESSING KNOWLEDGE, ATTITUDES, AND PRACTICES REGARDING ANTIBIOTIC USE AND RESISTANCE: A COMPREHENSIVE STUDY AMONG PRIVATE PRIMARY CARE PROVIDERS AND THE PUBLIC IN NORTHERN MALAYSIA

ABSTRACT

Antimicrobial resistance (AMR) is considered a global health threat by the WHO, and unfortunately Malaysia, like every other country in the world, is not immune to this danger. Studies have shown that antibiotic prescribing among primary care in Malaysia is much higher in private clinics than in public clinics, and that knowledge of antibiotics among general practitioners is only moderate. This is of particular concern as the inappropriate use of antibiotics leads to antibiotic resistance in humans and subsequently has been shown to be fatal. Primary health care providers are responsible for prescribing and dispensing antibiotics to patients for various health indications. Therefore, they play an important role in ensuring the correct use of antibiotics among the public, parallel with government efforts to prevent AMR. This study was conducted to fill the gaps of knowledge, attitudes and practices among healthcare providers in the private sector and the public. A cross-sectional survey using self-completed questionnaires was conducted among three different study populations of general practitioners, pharmacists and the general public in the northern states of Malaysia, including Perlis, Kedah, Pulau Pinang and Perak. This descriptive research was conducted during the new norm of the Covid-19 pandemic. The questionnaires were completed by the doctors, pharmacists and the public themselves during the fieldwork. Each questionnaire consisted of 30 questions that could take up to 10-15 minutes to answer. The returned questionnaires were checked for completeness and

respondents were asked to answer any missing sections. Data obtained were statistically analyzed using SPSS for both statistical and inferential analyses. Overall, the KAP level for healthcare practitioners and the public is found to be satisfactory. Identifying the knowledge and perception of antibiotic use among healthcare providers can create an appropriate framework to effectively combat AMR. The results of this study could be an important mechanism to save countless lives, improve quality of life and reduce the economic burden caused by AMR.

CHAPTER 1

INTRODUCTION

1.1   Research Background

From the moment the antibiotic was discovered in the late 1920s, antibiotics have been a magic pill in the treatment of infectious diseases caused by bacteria (Ribeiro et al., 2019). Alexander Fleming discovered penicillin, a revolutionary discovery that saved the lives of many soldiers during the First World War. However, the discoverer himself warned that one day, when the antibiotic is freely available, it will be deadly because bacteria will develop resistance due to people's negligence by exposing themselves to the antibiotic at lower than intended doses (Aslam et al., 2020). Antibiotics are agents that kill bacteria by inhibiting their growth through various mechanisms of action, including inhibiting the synthesis of the bacterial cell wall, protein synthesis and DNA synthesis (Kapoor & Elagovan, 2017). After saving lives for decades, antibiotic resistance has become an alarming global threat in the current millennium and requires immediate action to combat this natural phenomenon arising from the misuse of this powerful drug (Aslam et al., 2020).

Antimicrobial resistance (AMR) is emerging around the world and is one of the greatest threats to global health today. It threatens the treatment of infectious diseases and undermines many other advances in health and medicine. Antimicrobial drugs can be classified according to the microorganisms they mainly target. For example, antibiotics are used against bacteria and antifungals are used against fungi. The World Health Organisation (WHO) defines AMR as "the resistance of a microorganism to an antimicrobial drug that was originally effective in treating infections caused by it" (WHO, 2014).

Antibiotic resistance occurs when bacteria acquire the ability to fight off the effectiveness of an antibiotic by adapting to the environment in the presence of the drug and continuing to grow (Baym et al., 2016). This condition affects not only bacteria but also all other microbes such as fungi, viruses and parasites, which is why it is also known as antimicrobial resistance (Baym et al., 2016). Admittedly, antimicrobial resistance is nothing new, dating back to the 1980s when no new antibiotics were discovered due to the advancement of medicine focusing on other non-communicable diseases (Dewi et al., 2021).

AMR occurs naturally, but misuse of antimicrobials in humans and animals accelerates this process. Consequently, AMR leads to longer hospital stays, higher medical costs and mortality rates, as well as the possibility of adverse drug reactions and the promotion of expanded AMR among pathogens in the community. The alarming spread of drug-resistant infections currently causes 700,000 deaths annually and, if left unaddressed, is expected to cause 10 million deaths per year by 2050, with a cumulative economic cost of US$100 trillion (O'Neill, 2016).

1.2   Problem Statement

Rational use of antimicrobials started with the recognition that their inappropriate use is the main cause of resistance development, such as unnecessary prescriptions and inappropriate use (inappropriate dosage, wrong duration) (Salam et al., 2023). Malaysia has a dual public-private health system with 871 public primary careclinics and 5198 private primary care clinics (Hwong et al., 2014; Jaafar et al., 2012).Research has shown that antimicrobial prescribing rates in Malaysian primary care aremuch higher in private clinics as compared to public clinics, whereby private clinics contributed to 87% of the total antimicrobials prescribed in primary care.

General practitioners reportedly prescribe 90% of antimicrobials (Jamaluddin et al.,2021; Ab Rahman, Teng & Sivasampu, 2016).

The occurrence of superbugs causing resistance to antimicrobials is difficult totreat, as some cases are almost impossible to treat and lead to death (Ventola, 2015). This situation is made worse by people's behaviour and practices. Health professionals are considered the custodians of medicines. They are highly educated and trained to use all kinds of medicines ethically and only for their intended purpose. It is well known that general practitioners and other health professionals have good knowledge regarding theuse of antibiotics (Salcedo et al., 2022). In a study conducted by Ab Rahman, Teng and Sivasampu (2016), data from a nationally representative sample of Malaysian primary care clinicsshowed high levels of antibiotic prescribing, with at least one in five encounters resulting in a prescription for an antibiotic. The WHO and numerous national recommendations, such as those in Singapore and other neighbouring countries' protocols emphasised on completing antibiotic courses even after improvised symptoms, to avoid the emergence of resistant bacteria (Chua et al., 2023). Thus, it is important that health professionals have a sound knowledge of antibiotic use so that patients can get the full benefit of their treatment.

In emerging countries, access to healthcare and medicines has improved in parallel with economic progress, but with the disadvantage of a high prevalence of inappropriate use of antimicrobials. In countries such as China, Chile, Malaysia and Vietnam, dispensing antimicrobials without prescription/medical consultation is also a common practice (Haque et al., 2019; Jacobs et al., 2019; Nguyen et al., 2022; Zhang et al., 2023).

Self-medication is widespread and is often described as the cheapest and most convenient method of treatment (Nguyen et al., 2023). It is reported that in many

developing and developed countries, the pharmaceutical industry incentivises general practitioners to promote the sale of medicines, including antimicrobials (Tiong, Loo & Mai, 2016). This is exacerbated by the lack of a legal framework that separates prescribing and dispensing of medicines to create an effective system of checks and balances in health systems (Ofori & Agyeman, 2016). Mutair et al. (2021) urged that drug safety be monitored and measured using a consistent organisational structure, as encouraging reporting, monitoring, and open discussion of pharmaceutical mistakes is critical to developing a safety culture. The system will improve as more data is entered; these may be known mistakes, previously ignored faults, or even new errors (Mutair et al., 2021).

Despite pharmacies' increased enforcement measures, the lack of effective deterrents, particularly harsh penalties, may encourage pharmacists to take the risk (Kho et al., 2017). Pharmacists seem to admit that accommodating customers' demands is the only pragmatic choice for their survival (Xuan et al., 2023). The widespread prevalence of this practice in developing countries points to a systemic flaw in current pharmacy laws, particularly the lack of segregation of dispensing of medicines (Fovargue & Neal, 2021). The controversy over the separate dispensing of medicines continues to dominate the Malaysian pharmacy landscape and inhibits the further growth of existing pharmacy practices. Malaysian pharmacists currently have exclusive jurisdiction over a narrow range of medicines that are only available in pharmacies, which does not give them a sufficient competitive advantage. The professional organisations of Malaysian pharmacists, including the Malaysian Pharmaceutical Society (MPS) and the Malaysian Community Pharmacy Guild (MCPG), are continuously fighting for the separate dispensing of medicines (Kho et al., 2017). Unfortunately, recent developments indicate that the current arrangement

continues to be favoured by the Malaysian authorities (Loo et al., 2020). Thus, the lack of segregation of dispensing of medicines in Malaysia may contribute to the unchecked prescription of antibiotics to the patients.

Similarly, insufficient public awareness of the rational use of antimicrobials is an important causal factor in the over-prescription of antimicrobials by physicians under pressure from patients, as well as the worrying culture of antimicrobial sharing and lack of compliance (Haque et al., 2016; Islahudin, Tamezi & Shah, 2014).

1.3   Study Rationale

The Antimicrobial Stewardship Programme (ASP) has emerged as one of the WHO's key strategies to minimise the development of resistance and maintain antimicrobial efficacy as there are fewer and fewer antimicrobial candidates in the pipeline (Baroudi et al., 2015). It focuses mainly on improving patient outcomes by reducing the morbidity and mortality of infections and optimising antimicrobial therapy by promoting the prudent use of antimicrobials, optimising the selection, dosage, administration and duration of antimicrobial therapy to maximise clinical cure or prevent infections (De Waele & Dhaese, 2019).

The Ministry of Health Malaysia (MOH) has made great efforts to improve ASP in Malaysia, and while improvements have been seen in public hospitals, the private sector is still lagging (Nwagbara & Rasiah, 2015). Fortunately, private hospitals in Malaysia have also started implementing ASP as they are aware of this global problem and have been encouraged by the MOH. Unfortunately, private clinics run by general practitioners and community pharmacies run by pharmacists are not officially involved in ASP as their practice is not directly linked to the MOH (Lim et al., 2024a).

Another factor that also plays an important role in this problem is the public itself. Due to lack of awareness and education regarding the use of antibiotics, some patients believe that antibiotics are the answer to all ailments, hence, insist on getting antibiotics from private healthcare practitioners such as community pharmacists and general practitioners (Bhatt et al., 2023; Mason et al., 2018; Saliba et al., 2021). In a study conducted by Bhatt et al (2023), a misconception among respondents were observed that sore throats, fevers, colds, and flu can be treated with antibiotics. Other studies have also reported the similar findings (Chow & CY, 2020; Islahudin, Tamezi & Shah, 2014; WHO, 2015).

With this perspective, knowledge and awareness regarding AMR and the correct use of antimicrobials are essential to ensure that attitudes and practices in the use and consumption of antimicrobials are correct among health professionals and the public. This study aims to identify gaps in addressing the issue of antibiotic overuse among general practitioners, community pharmacists, and the public, which the Ministry of Health (MOH) has not adequately addressed. This study supports the MOH's efforts in government settings by directing on private-sector healthcare providers and establishes the foundation for future strategies to prevent antibiotic misuse in private primary care.

1.4   Research Questions

The research questions for this research are as the following:

1. What is the level of knowledge, attitudes, and practices (KAP) level regarding the use of antibiotics and resistance in the private setting among primary care providers (general practitioners and community pharmacists) and the public in the northern Malaysian states of Penang, Perak, Kedah and Perlis?

2. What are the driving factors for irrational use of antibiotics among healthcare practitioners and public in Northern Region of Malaysia?

3. Do the sociodemographic factors have any influences toward knowledge, attitudes and practices (KAP) level regarding antibiotics usage and resistance among healthcare practitioners and the public in Northern Region of Malaysia?

4. What is the relationship between knowledge, attitudes and practices towards antibiotic usage among healthcare practitioners and public in Northern Region of Malaysia?

1.5 Research Objectives

1.5.1 General Objective

The general objective of this study is to assess the knowledge, attitudes and practices (KAP) level regarding the use of antibiotics and resistance in the private setting among primary care providers (general practitioners and community pharmacists) and the public in the northern Malaysian states of Penang, Perak, Kedah and Perlis.

1.5.2 Specific Objectives

The specific research objectives of this study are as the following:

1. To determine the driving factors for irrational use of antibiotics among healthcare practitioners and public.

2. To identify the influence of sociodemographic factors toward knowledge, attitudes and practices (KAP) level regarding antibiotics usage and resistance among healthcare practitioners and the public.

3. To analyse the relationship between knowledge, attitudes and practices towards antibiotic usage among healthcare practitioners and public.

1.6   Study Hypotheses

H1: The level of knowledge, attitudes and practices among healthcare practitioners and the public have significant differences.

H0: The level of knowledge, attitudes and practices among healthcare practitioners and the public have no significant difference.

H2: Several driving factors for irrational use of antibiotics among healthcare practitioners and public can be identified in this study.

H0: No driving factors for irrational use of antibiotics among healthcare practitioners and public can be identified in this study.

H3: Some sociodemographic factors are statistically significant when compared to knowledge, attitudes and practices among healthcare practitioners and the public.

H0: Some sociodemographic factors are not statistically significant when compared to knowledge, attitudes and practices among healthcare practitioners and the public.

H4: There are some correlations between knowledge, attitudes and practices towards antibiotic usage among healthcare practitioners and the public.

H0: There are no correlations between knowledge, attitudes and practices towards antibiotic usage among healthcare practitioners and the public.

1.7   Operational Definition

Private primary care providers are healthcare practitioners and entities that provide primary care services outside of the government-funded or public health

system. These providers work in private clinics, independent practices, or in privately controlled healthcare facilities (Mackintosh et al., 2016). They include general practitioners (GPs), community pharmacists, and other healthcare professionals who provide outpatient services such as medical consultations, treatment plans, and medication prescriptions. Private primary care providers typically provide faster access to medical treatments than overcrowded public facilities and play an important role in fulfilling patients' needs, educating the public, and maintaining continuity of care within the private healthcare sector (Chua & Fried, 2024; Ong et al., 2022).

Community pharmacists are more approachable and stand as the first line mediator to public regarding medical information (El-Kholy et al., 2022). They are often approached for simple ailments and advises. The role of pharmacists is not limited only to dispensing but also in educating the public or consumers on the medicines and products utilized. In private setting, general practitioners and community pharmacists work side by side in exchanging patients who require medical attention and vice versa (Saw et al., 2015).

Public becomes a major component in this study as they are the one who are affected by antibiotic resistance (McCullough et al., 2016). It is vital to reason on this prior to resolving this global issue.

CHAPTER 2

LITERATURE REVIEW

2.1   Causes of Antimicrobial Resistance (AMR)

The advocacy of rational use of antimicrobials began forthwith the recognition of their inappropriate use being the key driver of resistance development, such as unnecessary prescriptions as well as inappropriate use (inadequate dosing, wrong duration) (Ayukekbong et al., 2017). In most instances, 80%–90% of antimicrobials are given to patients outside of hospitals, with the remaining used for those who are hospitalized. Reports also indicate that 90% of antimicrobials are prescribed by general practitioners (GPs). State-sponsored research in the United States has estimated that 50 out of 150 million outpatient prescriptions for antimicrobials are not evidence-based. It has also been found that up to 50% of antimicrobials are utilized without a valid scientific reason, and antimicrobials were prescribed that were unnecessary or questionable (Haque et al., 2016; Lockhart et al., 2019).

Access to healthcare and drugs has grown in parallel with economic success in developing nations, yet there is a high rate of improper antibiotic usage. This is obvious from a recent study that highlighted the high rates of antibiotic prescribing in Malaysian primary care settings, even for self-limiting diseases (Ab Rahman, Teng & Sivasampu, 2016). Similarly, antimicrobial dispensing without prescription or medical consultation is also a common practice as can be seen in countries like China, Chile, Malaysia, and Vietnam. Self- medication is rampant, often being dubbed the most affordable and convenient mode of treatment (Nguyen et al., 2023; Tiong et al., 2016). The pharmaceutical industries in numerous developing- and developed-nations have been reported to incentivize health practitioners for pushing the sales of drugs including antimicrobials (Tiong et al., 2016).

This is worsened by the absence of a regulatory framework that separates prescribing and dispensing to elicit an effective system of checks and balances in the healthcare systems of this part of the world (Redmond et al., 2018). Therefore, rational prescribing of antimicrobials maybe precluded by the monetary gains derived from the sales of drugs. Likewise, the under-addressed low level of public awareness pertaining to rational use of antimicrobial is an important causative factor for patient-pressured antimicrobial over-prescribing among general practitioners as well as the worrisome culture of antimicrobial sharing and lack of compliance (Islahudin et al., 2014; Haque et al., 2016; Ab Rahman, Teng & Sivasampu, 2016).

2.2   Status of Antibiotics in Malaysia

According to the Ministry of Health Malaysia's Report on Antibiotic Utilisation in Malaysian Hospitals 2008-2017, antibiotics are among the most often used medications in Malaysian healthcare settings, along with antidiabetic, antihypertensive, and lipid-lowering medications (Ministry of Health, 2020). As per Malaysian Statistics on Medicines 2018-2022, the utilization of antibacterials for systemic use is measured in Defined Daily Doses (DDD) per 1,000 inhabitants per day. The data reveals that the public sector has an antibiotic utilization rate of 2.4069 DDD/1,000 inhabitants/day, while the private sector shows a significantly higher rate of 7.3153 DDD/1,000 inhabitants/day indicating that antibiotic use in the private sector is much higher compared to the public sector (Lim et al., 2024a; Ministry of Health, 2024).

The most commonly used antibiotic in both private and public settings is Cephalosporin, specifically cefepime, which is the fourth generation of the Cephalosporin group (Che Hamzah et al., 2019). The report also highlighted the use of vancomycin as the main choice to treat patients with Methicillin Resistant

Staphylococcus aureus (MRSA) (Che Hamzah et al., 2019). Emphasis must be given to revise the use of antibioticamong the public as higher number of resistance cases are being reported. Khan et al. (2018) reviewed various data on AMR to conclude that the most frequent antibiotic resistance profiles in Malaysia were observed by ampicillin, piperacillin, ceftazidime, and tetracycline. A study by Noordin et al. (2016) managed to profile molecular typed methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from a teaching hospital in Malaysia where they found that the dominant strains were ciprofloxacin, erythromycin and gentamicin resistant which are typical characteristics of Malaysian MRSA strains isolated in the years 2003 to 2009 (Noordin et al., 2016).

Researchers agreed that antimicrobial resistance is a "constant threat and challenge for clinicians" in Malaysia, and therefore is a cause of highest concern in Malaysian communities due to the negative impact on public health (Majumder et al., 2020; Mariappan et al., 2021; Salam et al.,2023). Although the MOH has been issuing antimicrobial use guidelines for more than two decades, compliance with these guidelines was found to be lacking (Cheong et al., 1994). Therefore, National Antibiotic Guidelines was officially launched in 2019 by MOH as an initiative to enhance appropriate prescribing and avoid dubious indication and inappropriate duration in line with the Protocol on Antimicrobial Stewardship (AMS) Program in healthcare facilities (Lim et al, 2021).

2.3   Clinical Patterns and Implications of AMR

When the deadly coronavirus disease 2019 (COVID-19) spread in late 2019 and remains unrelenting two years later, millions of lives worldwide have been lost to this deadly and unstoppable virus (Sheng & Sheng, 2022). In the same vein, there were an estimated 4.95 million (95% UI, 3.62–6.57) deaths associated with bacterial AMR in

2019, including median of 1.27 million (95% UI, 0.911–1.71) deaths attributable to bacterial AMR could have been prevented, ranking behind COVID-19 death tolls and tuberculosis in terms of global deaths from an infection (Murray et al., 2022; Laxminarayan, 2022). The extensive literature review discussed by Murray and team interprets the global estimates of the burden of bacterial AMR involving a comprehensive set of pathogens and pathogen-drug combinations using consistent methods in which drug-resistant infections would be replaced by susceptible infections or by no infection in a scenario,in which all drug resistance would be eliminated. This estimation may function as critical key insights for policy makers to support informed and site-specific policy decisions, particularly with regard to infection prevention and control programmes, access to key antibiotics, and research and development of new vaccines and antibiotics (Murray et al, 2022).

Ironically, a separate paper stressed that the burden of AMR can be huge than the estimated as without effective antibiotics, modern treatment options such as major transplant surgeries and chemotherapies will go in vain as AMR patients may succumb from infections (Laxminarayan, 2022; Dadgostar, 2019). The WHO GLASS (2018) combined global AMR data for seven common bacterial pathogens (*Escherichia coli (E. coli), Klebsiella, Staphylococcus aureus (S. aureus), Streptococcus pneumonia, non-typhoidal Salmonella, Shigella spp. and Neisseria gonorrhoeae*) (WHO, 2018). In Thailand, it is anticipated that Thailand would have 111,295 fewer AMR cases and 48,258 fewer fatalities per year if AMR bacteria were completely eradicated (Phodha et al., 2019). A separate study in Malaysia confirmed that *methicillin-resistant Staphylococcus aureus* (MRSA) was present in 10-20% of the hospitals surveyed (Che Hamzah et al., 2019). The first Malaysian case of MRSA was reported in 1978, isolated from patients at a major hospital in Kuala Lumpur (Cheong et al., 1994). The high prevalence of MRSA in hospitals was stated as mainly due to the difficulty in

maintaining an adequatelevel of hygiene in a very large and crowded tertiary hospital (Zainudin, 1994; Soe et al., 2021). Another important factoris cross-infection from the large number of staff who may be asymptomatic carriers of MRSA (Soe et al., 2021).

Another commonly reported AMR is from the *Enterobacteriaceae,* which is resistant to carbapenems (Low et al., 2017). Colistin is the last resort treatment for life-threatening infections caused by carbapenem-resistant *Enterobacteriaceae* (Mondal et al., 2024). However, resistance to colistin has recently been detected in several countries and regions, making infections caused by the bacteria untreatable (Mondal et al., 2024).

Klebsiella pneumonia is a major cause of hospital-acquired infections such as pneumonia, bloodstream infections, including infections in newborns and intensive-care unit patients (Ferri et al., 2017). In some countries, due to the resistance, carbapenem antibiotics do not work in more than half of the people treated for Klebsiella pneumoniae infections (Pitout, Nordmann & Poirel, 2015). The WHO has also updated the treatment guidelines for gonorrhoea to address emergingresistance besides the existing AMR pathogens (WHO, 2014).

Surveillance on Antibiotic Utilization in Malaysia has been conducted in selected hospitals since 2001 (Bakon et al., 2023; Mariappan et al., 2021; Rezal et al., 2015). Hospitals under the Ministry of Health (MOH), Ministry of Higher Education (MOHE), Ministry of Defense (MINDEF) and private hospitals are also included under the surveillance, later renamed as the National Surveillance on Antibiotic Utilization (NSAU) (Mariappan et al., 2021). By July 2015, the program had expanded to include primary care (MOH Health Clinics) (Mariappan et al., 2021).

Carbapenem-resistant Enterobacteriaceae (CRE) surveillance in 2016 reported an alarming increase in the number of cases when it rose from 28 cases in 2011 to more than 800 cases in 2016 (El-Sayed et al., 2020). Analysis showed that 95%

of thepatients had a history of antibiotic exposure, while 50.6% had antibiotic exposure of more than 7 days (Mariappan et al., 2021). Polymyxin resistance was also reported among *Carbapenem-resistant Enterobacterales* (CRE) cases linked to 21.7% fatalities in 2016 (Jia et al., 2023).

In the most recent National Surveillance of Antimicrobial Resistance (NSAR) Report (2020), a total of 660,348 isolates were reported from 45 hospitals and one public health laboratory. However, based on the first isolate per patient, only 238,270 isolates were analysed for NSAR 2020 (NSAR, 2021; Ismail et al., 2024). The proportionof *S. aureus* isolated from blood in 2020 was 22.4%, slightly higher than in 2019 (20.2%). As for *S. aureus*, a decrease in resistance rates was observed for penicillin, clindamycin, erythromycin, gentamicin, and rifampicin in 2020 compared to 2019 (NSAR, 2021). There was also a decrease in MRSA rates from 15.0% in 2019 to 14.9% in 2020. A decreasing trend in resistance was observed for all antibiotics tested (NSAR, 2021).

Multidrug-resistant tuberculosis (MDR-TB) is a disease caused by *Mycobacterium tuberculosis* that is resistant to first-line anti-tuberculosis drugs rifampicin and isoniazid (Prasad, Gupta & Banka, 2018). According to estimates by the WHO, some 470,000 people fall ill to MDR-TB every year with 180,000 deaths. Globally, 105 countries with representing data reported that 20% of patients with MDR-TB developed extensively drug-resistant TB (XDR-TB). The emergence of MDR-TB and XDR-TB hampers the fight against diseases such as HIV and malaria. Some countries have recently reported levels at or above 15% amongst those starting HIV treatment and up to 40% among people re-starting the treatment (Dodd, Sismanidis & Seddon, 2016). It is a dire situation requiring urgent attention. Since September 2015, the WHO has recommended that everyone living with HIV start antiretroviral treatment (ART) (Kazanjian, 2017). Greater use of ART is expected

further to increase ART resistance in all regions of the world. It is essential to continue monitoring resistance to minimize its further emergence and spread among HIV patients to maximize the long- term effectiveness of first-line ART regimens (Kazanjian, 2017).

Resistance to the first-line treatment for *Plasmodium falciparum (P. falciparum)*, which causes malaria has been confirmed in five Southeast Asian countries, namely, Thailand, Indonesia, Myanmar, Cambodia and Vietnam. Along the Cambodia-Thailand border, where *P. falciparum* has become resistant practically for all available antimalarial medicines, treatment has become more challenging, and the need for close monitoring (Amato et al., 2018). This is a tangible risk as multidrug resistance may likely emerge in other parts of the sub-region as well. The interconnection of resistance in influenza and superbug is not novel (Adegoke et al., 2016). The new coronavirus is no exception, as some studies have found that one in seven patients hospitalized with Covid-19 acquired a dangerous secondary bacterial infection where 50% of the fatalities had such infection (Garcia et al., 2021; Li et al., 2020). The challenges of AMR could become an enormous force of additional sickness and death across our health system as the toll of coronavirus pneumonia stretches critical care units beyond their capacity (De Vries, Hofstraat & Spaan, 2020).

2.4   The Use of Antibiotics among the Public

A study on the usage of antibiotics in a community in Malaysia revealed that the percentage of non-compliance was highest among males compared to females and up to 80% never obtained antibiotics without a doctor's prescription (Fatokun, 2014). However, the alarming issue which requires much attention is that up to 55% of the public stopped taking their antibiotics once their symptoms were gone (Fatokun et al. 2014). A cross- sectional study conducted by Ab Halim et.al (2018) recorded poor

antibiotics knowledge among the local community in Penang. The study found that up to 80% of the respondents were unaware of the purpose of antibiotics and 76% of them had a misconception that antibiotics could cure viral fever (Ab Halim et al., 2018). The public also believed that antibiotic would work for all kinds of infections, and it would speed up recovery from adisease. Hence, this urges for the need to better educate the public on the understandingand consumption of antibiotics. Ying et al. (2018) studied the pattern of self-medicationwith antibiotics among the public in Alor Setar, Kedah and it was found that the publictended to self-medicate themselves as they perceived their conditions as simple illnessand did not require examination from the general practitioners (Ying et al., 2018).

Another study by Hassali et al. (2017) found that the antibiotics knowledge level in young adults was slightly higher yet their attitudes towards handling antibiotic was poor (Hassali et al., 2017). Many respondents of the survey reasoned high consultation fee and inconvenience to visit a doctor channelling them to obtain medications from the community pharmacies (Mohamad Azmi et al., 2016). More than half of the respondents also agreed that it was important to provide education regarding antibiotic for the public in order to tackle AMR.

2.5   Understanding AMR from the Perspectives of Healthcare Professionals

Healthcare professionals are perceived as the guardians of medications. Besides their medical knowledge to diagnose and treat, they are also expected to practice good medications ethics, especially on the use of antibiotics. Despite this perception, a study conducted by Ab Rahman, Teng and Sivasampu (2016) found that national sampling data of Malaysian primary care clinics showed a high level of antibiotic prescriptions, with at least one in every five encounters involving an antibiotic prescription. It is noteworthy that half of all antibiotics prescribed were for

upper respiratory tract infections (URTIs) which are primarily viral in nature (Ab Rahman, Teng & Sivasampu, 2016). Results from this finding suggest that antibiotics are not clinically indicated and are therefore overused in primary care clinics in Malaysia.

In various studies, many general practitioners (GPs) reported that their patients expected antibiotics to be prescribed (Alabid et al., 2013; Sivanandy & Loh, 2020). Approximately 36.7% GPs reported that when it was not prescribed, patients would demand for it even though more than one-fifth of the responding GPs clearly believed that antibiotics were not specifically required as in the case (Hassali et al., 2015). This study concludes that there is an urgent need for educational interventions to address the irrational use of antimicrobials and AMR among all healthcare stakeholders, including the patients themselves (Hassali et al., 2015).

Other studies investigating knowledge on antibiotics and resistance among medical students found that more than 50% of the student's respondents had low levels of knowledge on the usage of antibiotics, including some having outdated health beliefs (Haque et al.,2019; Tiong & Chua, 2020). Another cross-sectional study conducted by Sivanandy and Loh (2020) on 113 medical students, the findings showed most were aware that antibiotics could only be used to kill bacteria, treat bacterial infections, and not meant for viral infections (Sivanandy & Loh, 2020). Surprisingly, half of the respondents believed antibiotics can be used to treat sore throats, a conclusion that suggests that some prescribers were less knowledgeable on the proper prescribing of antibiotics. Another study found a gap between theoretical input and clinical practices (Haque et al., 2016). The study's authors further commented that clinical competence in antibiotic prescribing during the students' internship largely resulted from learning by imitating senior colleagues and suggested this method should be corrected (Haque et al., 2016). Tan et al., (2015) identified that general practitioners have a middling

level of expertise of antibiotics, yet they frequently prescribe them. Bundan (2020) found that although the general practitioners working in emergency department (ED) had a negative attitude towards antimicrobial stewardship (AMS), their general knowledge and practices level were good. Years of ED experience and the frequency of antibiotic prescriptions were the indicators of positive attitudes towards AMS (Bundan, 2020).

2.6   Antimicrobial Stewardship Program (ASP) in Malaysia

The development of AMR strains in hospitals is exacerbated by the high use of antimicrobials and the concentration of patients with multiple pathogens require concerted action be taken. Antimicrobial stewardship program (ASP) is a coordinated systematic approach designed to heighten appropriate use of antimicrobial agents by promoting the selection of optimal antimicrobial drug regimens focusing primarily on improving patient outcomes through reduced morbidity and mortality from infections while optimizing antimicrobial therapy by promoting the judicious use of antimicrobials, optimizing selection and dosage, and administering and duration of antimicrobial therapy to maximize clinical cure and prevent infections for existing and future patients (Majumder et al., 2020). A detailed chronology of AMR strategic action in Malaysia and the establishment of ASP are illustrated in Figure 2.1.
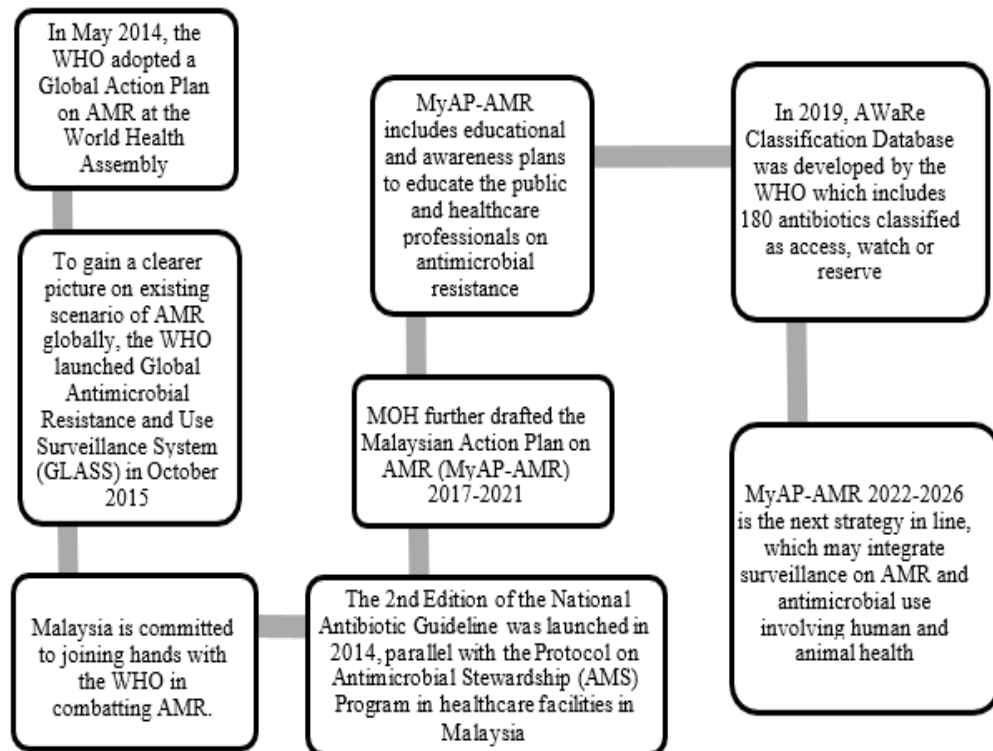
Figure 2. 1 Chronology of the establishment of ASP in Malaysia (MOH, 2017)

Ongoing surveillance and prospective audits have shown improved patient care and the reduction of unnecessary antimicrobial use (by 22% - 36%), AMR, and pharmacy spending. The program which is a governance of multidisciplinary teams of all Malaysian hospitals incorporate various activities including the developments of local antibiotics guidelines and clinical pathways to standardize prescribers' approaches, surveillance on antimicrobial prescription and consumption behaviour to aid therapy decisions. The program assesses the consequences of antimicrobial misuse on public health and evaluates impact resistance containment interventions along with prospective audits and restrictions or pre-authorization of certain antibiotic usage by designing antimicrobial order tool to encourage clinicians to review basic clinical and laboratory information as well as categorize antimicrobial use as prophylactic, empirical and therapeutic. Education is one of the pillars to optimize this program nationwide which are introduced in the form of newsletters, continuous medical education and prescribing aids for healthcare practitioners.

Comprehensive surveillance is generally lacking in most sectors since ASP focuses primarily on hospital settings. A study reported that 87% antibiotics prescriptions in Malaysia came from private primary care reflecting the contraindicating structure of surveillance bias to public healthcare settings in Malaysia (Ab Rahman, Teng & Sivasampu, 2016). However, it must be conceded that the ASP program is still in infancy stage, but with time and stringent implementation, it should efficiently combat AMR in Malaysia.

2.7   Role of General practitioners

In a recent study by Lim et al. (2024b), it is identified that inappropriate selection of antibiotic is still occurring even after the introduction of National Antibiotics Guideline in 2014. A review of prescriptions in the government hospital setting in Kedah, Malaysia also showed that prescribers tended to initiate irrelevant defined daily dosage when compared to the maximum suggested defined daily dose in the guidelines (Jean et al., 2023). This shows that the efficacy in adhering to guidelines was still minimal among the prescribers, so there should be a well-planned approach to modify the antibiotic prescribing practices among general practitioners in the northern region of Malaysia. Tan et al. (2015) emphasized the need to educate the medical officers as there was a significant association between frequency of antibiotic prescribing and awareness of AMR in their daily lives. The study also exhibited the confidence level of general practitioners in prescribing antibiotic was high as only 18.0% of them consulted or referred to their colleagues prior to prescribing antibiotics and up to 62% of the respondents were confident in prescribing antibiotics.

In a report to the WHO on antibiotic prescribing and resistance by Pearson & Chandler. (2019), it is found that healthcare providers especially general practitioners were concerned about under- treatment in absence of antibiotic prescribing. Though

the awareness of resistance exists among the prescribers, the call over risks of non-treatment remains while infrastructure to allow follow-up, provide confidence in hygiene standards, and ensure adequate time to investigate each patient remains poor in the private setting (Muteeb et al., 2023). As the main prescribers who guarantee the appropriate and responsible use of these drugs, general practitioners are crucial to the use and stewardship of antibiotics (Ha, Haste & Gluckstein, 2017). Since antibiotics only work against bacterial illnesses, their first task is to correctly diagnose infections in order to identify whether they are viral or bacterial. Another crucial component of a doctor's job is keeping an eye on how well antibiotics are working. Beyond clinical practices, some clinicians conduct research to analyse antibiotic resistance trends, assess the efficacy of new antibiotics, and look at alternative therapies (Muteeb et al., 2023).

2.8   Role of Pharmacists

In a study conducted among public in Penang, it was found that customers walk into pharmacies to purchase antibiotics without prescriptions (Irawati et al., 2019). This suggests the poor practices of community pharmacists in handling antibiotics without a prescription. In addition, Siltrakool (2018) identified the high KAP in antibiotic handling among community pharmacists in Thailand, yet the cross-sectional study suggested that competency is the main reason for pharmacists to prescribe antibiotic without a prescription (Sitrakool, 2018).

Khan et al. (2016) identified that the role of pharmacist in ASP was not well established as more than half of the respondents were neutral about incorporating the program to community pharmacy setting. Though most of them believed that ASP would help healthcare providers to improve patient care, yet they felt that the key role of pharmacist in the program was still questionable as lesser number of involvements

were noted for antimicrobial awareness campaigns by pharmacists. This calls for an intervention to bridge the gap between perception and practices among community pharmacists. Educational interventions targeting community pharmacists can improve their practices.

In Thailand, patients can obtain antimicrobials from community pharmacies without a prescription, as the legislation permits pharmacists to dispense them without requiring a doctor's order as an initiative to include community pharmacists in promoting public health and disease preventions (Sitrakool et al., 2021). These businesses often operate on a model driven by medicine sales and maintaining customer satisfaction for competitiveness. While the practices of Thai pharmacists often align with the local guidelines and could be seen as "good practices," they do not necessarily equate to good antimicrobial stewardship. As irrational antimicrobial use is a significant contributor to AMR, pharmacists hold an important role in promoting appropriate use and maintaining the effectiveness of antibiotics while advancing antimicrobial stewardship (Sitrakool et al., 2021).

International Pharmaceutical Federation (FIP) 2015 expressed that pharmacists have a unique position in the healthcare system and act as an entry gate to the system on the account of their easy accessibility by the public. Pharmacists hold the standing where they can reassure patients if they need antibiotics and correct any misunderstandings. Therefore, the role of a pharmacist is pivotal in advising patients on minor ailment and referring to physicians for further diagnosis when required.

2.9   Directing Awareness towards the Public

Several small-scale studies have been conducted across Malaysia to obtain the public's perspectives on usage of antibiotics (Aslam et al., 2020; Irawati et al., 2019; Qamar et al., 2014). One study identified critical gaps in the attitudes and practices of

the Cheras community (a city in the capital Kuala Lumpur) towards antibiotic use (Hassali et al., 2017). The study reported that up to 55% of the respondents who were prescribed antibiotics in clinics stopped taking them once their symptoms improved. Another study conducted among patients in a hospital outpatient setting found that patients (22.3%) discontinued their antibiotics once their symptoms were gone (Fatokun, 2014). The same study also found the respondents generally lack knowledge and awareness on antibiotics use and purposes and are significantly linked to poor compliance of antibiotic therapy. This study has identified important knowledge and attitudes gaps as well as 'at risk' individuals in relation to antibiotic treatment. Taking steps to improve the knowledge and attitudes of the public concerning antibiotic usage together with appropriate measures to regulate availability of antibiotics and developing targeted antibiotic education and patient counselling campaigns will play an important role to promote effective use of antibiotics in the community. Most of the findings in studies conducted in Malaysia pertaining antibiotic usage exhibited a pattern of awareness among the consumers depending on their socio-economical background. In a study done by Qamar et al. (2014), a self-administered cross-sectional survey was conducted among 380 respondents using a pre-validated questionnaire at public places in Shah Alam, Malaysia. The survey analysis found that 43% of the respondents had good knowledge about antibiotics. Most of the respondents knew that antibiotics were used for bacterial infections. However, 40% of the respondents had the misconception that antibiotics were for viral infections. Half of the respondents said they could differentiate antibiotics from other medications. Although it can be concluded that public knowledge on antibiotics was generally acceptable, greater awareness on the importance of correct antibiotic use and a change in their attitudes towards antibiotic use should be encouraged.