A mixed-methods study of antibiotic use and prescribing dynamics in Indonesian hospitals: implications for antimicrobial stewardship



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Abstract

Antimicrobial resistance (AMR) is an accelerating public health problem, with antimicrobial agents, including their inappropriate use, being one of the key drivers. In Indonesian hospitals, there is a fragmented picture of antibiotic use and of the drivers of prescribing patterns. This thesis aimed to fill this knowledge gap by assessing patterns and quality indicators of antibiotic prescribing for hospitalised patients, mapping their drivers and dynamics, and exploring the factors influencing the implementation of antimicrobial stewardship (AMS) programmes.

Using an explanatory sequential mixed-method approach, data collection was conducted in six hospitals in Jakarta, between March 2019 and October 2020.

A quantitative survey found high proportions of hospitalised patients receiving systemic antibiotics, that guideline compliance was poor, use of blood cultures was low, and that prolonged surgical prophylaxis was common.

The qualitative findings revealed multidimensional social-cultural factors influencing antibiotic prescribing, such as disjunctions between drivers of AMR and day-to-day clinical practice, antibiotic prescribing as risk aversion vis-à-vis concerns of poor clinical outcomes, the ‘pull’ of conformity to

normative, suboptimal group prescribing practices, and suboptimal operations of microbiology and surgical facilities. Effective AMS programme implementation was challenged by ineffective resourcing and institutional buy-in, cost-prohibitive culture testing, entangled hospital priorities to generate profits, and a non-collegial communication approach to AMS execution.

Three identified areas of improvement are addressing hierarchical cultural norms in the medical profession, encouraging ownership of the AMR problem and solution among all stakeholders, and developing sustainable context-specific AMS strategies. Based on the complex adaptive system (CAS) concept, I formulated four recommendations: 1) identifying the agents of influence; 2) evaluating the problem using a CAS lens; 3) developing health system resilience; and 4) identifying leverage points.

In conclusion, this thesis contributed to the development of a conceptual framework showing how multilevel and multidimensional social-cultural factors interact to influence antibiotic prescribing and AMS implementation.

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Co-Authorship

The work presented in this thesis was primarily completed by me, under the supervision of Associate Professor Raph L. Hamers as my principal supervisor and Professor Alex Broom as my joint supervisor. I led day-to-day project management and coordination under the supervision of Associate Professor Raph L. Hamers and Dr. Erni J. Nelwan, the principal investigator. Dr. Nelwan helped coordinate with the study sites to obtain a hospital permit.

I performed and led the quantitative data collection with the assistance of a research assistant and a total of nine trained enumerators. I performed all components of qualitative data collection and analysis by myself, with the help of the hospital management, the heads of departments, and the antimicrobial stewardship team leaders from the participating hospitals who distributed the invitation to the study participants. I collected, managed, and analysed research data with the assistance of the people listed below.

Manzilina Mudia, MD, research assistant (2019–2020), assisted with the quantitative (point prevalence survey) data collection, enumerators' training, data entry, data cleaning, and data analysis (Chapter 4). Manzilina also assisted with the transcription and translation of some of the interviews (Chapter 5 and 6).

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Declaration

I, Ralalicia Limato, declare that other than the assistance outlined in the acknowledgements and co-authorship, the work described in this thesis is my own work and has not been submitted for a degree or other qualification to any other university.

Abbreviations and acronyms

AMR	Antimicrobial Resistance
AMS	Antimicrobial Stewardship
ATC	Anatomical Therapeutic Chemical
AWaRe	Access, Watch, Reserve
CAI	community-acquired infection
CAS	complex adaptive system
CDC	Centers for Disease Control and Prevention
DDD	Defined Daily Dose
DCF	Data Collection Form
DPJP	*Dokter Penanggung Jawab Pasien*/a specialist or consultant responsible for patient management during hospitalisation
ECDC	European Centre for Disease Prevention and Control
ESAC	European Surveillance of Antimicrobial Consumption
ESBL	extended-spectrum beta-lactamase
GAP	Global Action Plan
GP	general practitioner
HAI	hospital-acquired infection
HICs	high-income countries
ICU	Intensive Care Unit
IPC	Infection Prevention and Control
IT	Information and Technology
JKN	*Jaminan Kesehatan Nasional*/national health insurance

LMICs	low- and middle-income countries
LRTI	lower respiratory tract infection
MDR	multidrug resistance
MDRO	multidrug-resistant organism
MMR	mixed-methods research
MoH	Ministry of Health
MRSA	Methicillin-resistant *Staphylococcus aureus*
NAP	National Action Plan
PPS	point prevalence survey
SAP	surgical antibiotic prophylaxis
SSI	surgical site infection
WHO	World Health Organization

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Chapter 1
Introduction

1.1 Background

Antimicrobial resistance (AMR) is becoming increasingly recognised as a public health problem across many regions and countries. Global data estimated that AMR was responsible for 1.27 million deaths in 2019 and contributed to 4.95 million.[1] In addition, the problem of multidrug-resistance (MDR) and extensively-drug resistant bacteria has serious implications, leading to double or triple mortality rates.[2] In the hospital context, infections caused by resistant pathogens incur clinical consequences, such as treatment and prophylaxis failure, prolonged infections, and increased morbidity and mortality.[3,4] They also significantly increase economic burdens due to additional health expenditures by patients and hospitals to cover treatment, laboratory testing, specialist consultation, nurse care, and prolonged hospitalisation.[5–7] The resultant additional healthcare co-payments may force people into poverty.[8]

The unnecessary and suboptimal use of antibiotics has been well-recognised as one of the key drivers of emerging and accelerating antibiotic resistance.[9] Antibiotics are among the most commonly used drugs in healthcare. Their consumption has seen an increase globally of 65% between 2000 and 2015 and is projected to reach 200% by 2030.[10] In hospital settings, multi-country studies and a systematic review showed high use of broad-spectrum

antibiotics, third generation cephalosporins and fluoroquinolone, especially in Asian and African countries.[11,12] In addition, a systematic review and meta-analysis of studies across regions, mainly from high-income countries (HICs), estimated that patients with severe bacterial infection who received inappropriate empirical antibiotic treatment (based on antibiotic dose, route, and/or timing of administration) had double the chance of dying, compared to those receiving adequate, targeted, culture-guided treatment.[13] However, despite being disproportionally affected by AMR, low- and middle-income countries (LMICs) remain underrepresented in the global datasets published to date.

In Indonesia, surveillance data on AMR and antibiotic use are patchy, ad hoc, and not aggregated at the national level.[14] However, limited data suggests that AMR levels are high and on the rise. Results from the Regional Resistance Surveillance Programme in 12 Asia-Pacific countries collected in 2011 (only based on a limited number of hospital samples) showed concerning rates of extended-spectrum beta-lactamase (ESBL)-positive *E. coli* (71%) and *Klebsiella spp.* (64%).[15] The surveillance data collected by the Indonesian Clinical Microbiologist Association in 2021 from a total of 51 secondary and tertiary hospitals indicates alarming resistance rates, including among the WHO global priority pathogens.[16] For instance, results from blood samples showed a high prevalence of third generation cephalosporin resistance in *K. pneumonia* (72%) and *E. coli* (62%) and carbapenem resistance in *A. baumanii* (68%).[16]

Bacteria have resistance genes that provide protective and adaptive abilities to survive in unfavourable environments, including the ability to avert antibiotic agents.[17,18] This natural resistance mechanism can be intrinsic (always expressed in the species despite the absence of previous antibiotic exposure and/or horizontal gene transfer) or induced (only expressed after exposure to an antibiotic drug).[19] The development of antibiotic resistance is aggravated by complex factors surrounding antibiotic use. Systematic reviews and meta-analyses showed a positive association between antibiotic use and resistance, that increased antibiotic use will increase the resistance rate and vice versa.[20,21] Unnecessary use (i.e., extended duration, unnecessary prophylaxis, and duplicative use) and suboptimal use (i.e., poor drug choice, wrong route, incorrect dose, and poor timing) of antibiotics facilitates selective pressure because the exposure of pathogens to sub-inhibitory drug concentration can trigger gene mutation to be less or non-susceptible to antibiotics.[18]

Drivers of unnecessary and suboptimal antibiotic use are intertwined with a spectrum of complex structural, social, and health system factors. Many populations in LMICs do not have access to equitable basic infrastructure such as clean water, hygiene, and sanitation[22,23] which can create reservoirs for the spread of drug-resistant pathogens.[24,25] Furthermore, people from low-income families or who live in poverty are more susceptible to infection because of higher environmental exposure to pathogens, coupled with higher rates of underlying conditions such as malnutrition, metabolic diseases, and

chronic lung conditions.[23] Moreover, poverty may also become a barrier to accessing quality healthcare, which could result in, for example, prescriptions of poor quality antibiotics, partial dosing, and insufficient adherence to the prescribed drugs.[23] Additionally, in many settings, the adoption of preventable measures like vaccinations against common bacterial infections is suboptimal[9] and health systems struggle to provide access to optimal diagnostic testing and treatment.[23] In such contexts, antibiotics may be encouraged as a 'quick fix' to replenish the deficiency in these structural, social, and health governance areas.[22]

Rates of antibiotic prescribing as well as non-prescription antibiotic dispensing and self-medication have been reportedly higher in many LMICs, both in primary care and hospital care settings, compared to HICs. Data from the global point prevalence survey (Global-PPS) across 53 countries (mainly HICs) collected in 2015 found overall antimicrobial use among adult hospitalised patients at 34.4 %.[11] In comparison, similar PPS studies in LMICs in Asia and Africa (e.g., India, Pakistan, and Kenya) reported a prevalence that was twice as high.[12] In primary care settings, a meta-analysis of studies published between 2010 and 2020 found that the pooled proportion of patients in LMICs (mainly in Asia and Africa) receiving an antibiotic prescription was 52% (95% CI 51–53).[26] The same review also found a wide variation in the prevalence of inappropriate prescriptions between studies based on national or international antibiotic guidelines (7.9% reported by a Zambian study and 100% reported by two studies from China).[26] In the

community, lax or weakly enforced antibiotic regulations facilitate non-prescription antibiotic dispensing.[27] For instance, a systematic review of studies in LMICs between 2000 and 2017 (mainly from Asia) reported an overall pooled estimate of non-prescription antibiotic dispensing was 62% (95% CI 53–72).[28]

It is important to study antibiotic prescribing for hospitalised patients because the risks and unintended consequences of antibiotic use and drug-resistant infections are high in this context. In general, hospitalised patients have more severe medical conditions coupled with possibly reduced functioning of their immune system and the need for invasive medical procedures. These conditions make the patients more prone to contract hospital-acquired infections (HAIs) during hospitalisation which is associated with an increased risk of mortality.[29,30] Furthermore, more than 50% of HAIs are caused by gram negative bacteria from the ESKAPE-E group[31] (gram-positive bacteria *Enterococcus faecium* and *Staphylococcus aureus*; gram-negative bacteria *Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, *Enterobacter spp.*, and *Escherichia coli*), which have a high potential to induce multidrug-resistant strains correlated with broad-spectrum antibiotic use.[32,33]

1.2 AMR situation and research gaps in Indonesia

Indonesia is vulnerable to AMR due to persistent infectious disease burdens, including respiratory infections, diarrhoeal diseases, and tuberculosis, among

others,[34] coupled with low coverage of basic immunisation for children[*],[35] variable access to quality healthcare, and weakly enforced antibiotic policies.[14,34] Indonesia was ranked among the greatest risers in antibiotic consumption, at 29th out of 76 countries, in a comprehensive analysis of national pharmaceutical sales data between 2000 and 2015.[10] Within this period, Indonesia had seen an estimated 2.5-fold increase in nationwide antibiotic consumption, mostly driven by broad-spectrum penicillins, fluoroquinolones, and cephalosporins.[10] In hospital settings, as shown in a systematic review and meta-analysis of studies published between 2000 and 2021, broad-spectrum antibiotics, ceftriaxone and levofloxacin, were the most commonly consumed antibiotics in Indonesian hospitals.[36] The same review also found a twofold increase in hospital antibiotic consumption between 2016 and 2021, in comparison to the consumption between 2000 and 2015.[36]

Despite the fact that Indonesia has been estimated to have a high AMR burden, adequate and representative data on antibiotic use that contributes to AMR are lacking. There are no prior studies that have assessed hospital-wide antibiotic use, whereas studies to date have been limited to certain wards, clinical diagnoses, or patient types with variable quality.[37,38] Besides, at the start of my research, I found no previous published study exploring the factors influencing hospital physicians' antibiotic prescribing and decision-making,

[*] Children between 12-23 months (58% in 2018). In this report, basic immunisations for children are hepatitis B, DPT (diphtheria, tetanus, and pertussis), *Haemophilus influenza* type b (Hib), polio, and varicella.

even though they are important actors in antibiotic prescribing. Furthermore, there is also a dearth of published studies investigating the contextual socio-cultural factors driving antibiotic prescribing in Indonesian hospitals and the implications of these factors on the implementation of antimicrobial stewardship.

1.3 Aims and objectives

This research aims to assess antibiotic use patterns in hospitalised patients and to explore the contextual factors that may influence antibiotic decision-making and optimisation strategies in Indonesian hospitals. The three objectives of this research are as follows:

1. To assess the patterns and quality indicators of antibiotic prescribing;
2. To explore the social-cultural contexts and dynamics influencing antibiotic prescribing practices;
3. To explore the factors influencing antibiotic optimisation strategies through antimicrobial stewardship (AMS) programmes

1.4 Hypothesis and research questions

The main hypothesis for this thesis is that there is a high prevalence of broad-spectrum empiric antibiotic use in hospitalised patients in Indonesia, which is influenced by complex contextual social-cultural factors and dynamics. I formulated four research questions based on the three objectives.

1. What are the prevalence and patterns of antibiotic prescribing among hospitalised patients in Indonesia? (objective 1)
2. What are the quality indicators of antibiotic prescribing for hospitalised patients in Indonesia? (objective 1)
3. What are the social-cultural factors influencing antibiotic prescribing practices in Indonesian hospitals? (objective 2)
4. What are the contextual factors influencing the implementation of hospital AMS programmes in Indonesia? (objective 3)

1.5 Thesis overview

I will structure the thesis into seven chapters. **Chapter 1** presents the justification and significance of conducting the research and the research aims and objectives. **Chapter 2** comprises a review of literature summarising the existing evidence on antibiotic use in hospital settings, the conceptual framework I developed of the social-cultural factors influencing antibiotic prescribing and the implementation of antimicrobial stewardship programmes, and the context of Indonesia and Indonesian hospitals as the study setting. **Chapter 3** elaborates on the study methodology, which includes an approach to inquiry, the study setting, theoretical approaches, quantitative and qualitative designs, methodological justification, data collection, and data analysis. In **Chapter 4**, I present the quantitative findings of the patterns and quality indicators of antibiotic prescribing in Indonesian hospitals. **Chapter 5** comprises the qualitative findings, elaborating on the social-cultural factors

that influence antibiotic prescribing practices. **Chapter 6** elaborates on the contextual factors influencing AMS programme implementation in Indonesian hospitals. Finally, in **Chapter 7**, I present the synthesis and a discussion of the overall findings, referring to the conceptual framework, theoretical approaches, and previous studies. I highlight the identified areas for improvement, the actionable recommendations, the proposed future research, and the study conclusion.

1.6 Positionality statement

My positionality is an important aspect that influences how this research was conceptualised, conducted, and analysed. I am an Indonesian; I was born and raised in Indonesia. I studied medicine at an Indonesian university and was aware of the norms in the medical profession in the context of Indonesian hospitals. After graduating, I practiced medicine for five years before becoming a full-time researcher. I identify myself as a health systems and qualitative researcher with a background in medicine and public health. As a medical doctor, I believe that biological factors, e.g., age, genetics, and pathogenicity, are directly correlated with the occurrence of disease(s) in individuals or groups of individuals. Later, when I worked as a general practitioner (GP) in a government-owned community health centre, I observed first-hand the influence of socio-economic factors on health outcomes. For example, patients with a high frequency of clinic visits, especially for infectious disease management, often had a poor nutritional status, a low education

level, or came from low-income families. My interest in health systems research started during my postgraduate public health course. Later, I was involved in a five-year implementation health systems research programme focused on the work of close-to-community healthcare providers in maternal health in Indonesia. Through this positionality statement, I acknowledge that my world view in this research has been shaped by my background education, previous and current work, and research experiences.

Chapter 2
Review of the literature

In this chapter, I elaborate on the existing evidence from the literature with regards to antibiotic use in hospitals surrounding key thematic areas upon which this research is built. The main thematic areas explored through the review of the literature are:

1. Antibiotic use in hospitals covering indications for antibiotic use, prevalence, and patterns of antibiotic use in hospitals, quality indicators of antibiotic use, and the WHO AwaRe classification.
2. The conceptual framework of antibiotic prescribing in hospitals I developed covering the literature on social-cultural contexts and dynamics of antibiotic prescribing and antimicrobial stewardship programmes as strategies to optimise antibiotic prescribing.
3. The context of Indonesia as the research setting covering socio-demographics and government systems, healthcare organisation and financing, and hospital classifications.

I used PubMed MeSH and Scopus databases to search for relevant papers. I created a monthly alert to notify me whenever new papers were published. The applied key search terms relating to the main study areas were: ‘antimicrobial’ or ‘antibiotic’ or ‘anti-bacterial’ or ‘anti-bacterial agents’ or ‘antibiotic prophylaxis’ or ‘antibiotic treatment’ and ‘consumption’ or ‘use’ or

‘usage’ or ‘prescription’ or ‘prescribing’ or ‘prescribing practice’ or ‘awareness’ or ‘knowledge’ or ‘behaviour’ or ‘behavior’ or ‘influence’ or ‘cultural’ or ‘social factors’ or ‘social-cultural’ and ‘hospital.’ I applied the following filters: papers on ‘human’; published in English and Indonesian; and publication date from 1 January 2000, onwards. I included all quantitative and qualitative study designs, systematic reviews, and meta-analyses, and excluded conference papers and preprints. Regarding the quantitative papers on hospital antibiotic use, my review focused on global and multicountry studies and studies in the Asian and Southeast Asian regions, conducted at single and multiple hospitals.

In the database search, I included relevant publications, including reports, technical documents, and guidelines from the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC). I also included the policies, reports, and guidelines related to AMR, antibiotic use, and antimicrobial stewardship in the context of Indonesia.

2.1 Antibiotic use in hospitals

Antibiotics are valuable commodities for human health, providing positive clinical and health outcomes in regards to previously deadly and incurable infections. Antibiotic use can be traced back 2,500 years. Societies in ancient China, Egypt, Greece, and Rome used ‘natural’ antibiotics like mouldy bread and soybeans to treat skin infections.[39] However, the journey of antibiotic discovery in the modern era only started in the 17th century. The invention of

the microscope in 1590 and its use in medicine from 1653 onward, which led to the discovery of bacteria, established the foundation of antibiotic discovery.[40] Prior to the discovery of laboratory-based antibiotics, bacterial infections, such as pneumonia and tuberculosis, were the leading cause of death worldwide,[41] with people who contracted infections having a slim chance of survival. The discovery of penicillin in 1928 saved millions of lives, including during the Second World War, and became the cornerstone of wide antibiotic use in infection management and antibiotic mass production and commercialisation in the past century.[42]

2.1.1 Indications for antibiotic use in hospitals

In hospital settings, antibiotic prescriptions are indicated for two main purposes: to prevent and treat bacterial infections. Prophylactic antibiotics are indicated to prevent a future potential infection when a patient is in a vulnerable condition, for example, undergoing surgery (surgical prophylaxis) or in an immunocompromised state due to comorbidities or treatment that weakens the immune system (medical prophylaxis).[43] Antibiotic treatment is utilised in order to attenuate and prevent the multiplication of disease-causing bacteria while causing no or limited harm to the patient.

Two indications for therapeutic antibiotic use based on the context in which patients acquire an infection are community-acquired infection (CAI) and hospital-acquired infection (HAI). CAI is defined as an infection developed outside of a hospital or diagnosed within 48 hours of admission with no prior

healthcare encounter.[44] HAI is defined as an infection that occurs after hospital admission in a patient that was not present or incubating at the time of admission, as well as infections acquired in the hospital but manifesting after discharge.[45]

There are three main routes by which a patient can acquire a HAI. *First*, intervention-related infection occurs through invasive medical procedures during admission, including central line-associated bloodstream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), and ventilator-associated pneumonia (VAP).[30] *Second*, post-operative surgical site infection, or infection obtained from a surgical procedure that affects the surgical site and/or deeper tissues around the surgery site, occurs up to 90 days after surgery.[30] *Third*, cross contamination from other patients through healthcare providers (e.g., due to poor hand sanitation) and/or from hospital surfaces, for example, *Clostridioides difficile* (*C. difficile*) infection. *C. difficile* infection is a common HAI that can be transmitted during hospitalisation due to cross contamination.[46] Nonetheless, antibiotic use, mainly ampicillin, amoxicillin, cephalosporins, clindamycin, and fluoroquinolones, is the most important factor associated with an increased risk of *C. difficile* infection.[46,47]

The indication for antibiotic treatment based on the availability of microbiological evidence is divided into empirical and targeted (definitive) treatment. Empirical treatment is defined as antibiotics prescribed without microbiological evidence, based on previous clinical experience, the patient's

clinical presentation, and/or antibiotic guidelines based on local hospital susceptibility patterns.[11,43] When a patient is suspected to have an infection and a culture sample is taken, the result is usually available within the first 24–72 hours. Therefore, while waiting for the culture result, the common approach is to prescribe a broad-spectrum antibiotic to cover multiple possible disease-causing bacteria associated with the clinical syndrome, both for CAIs and HAIs.[43]

Targeted, or definitive, or culture-guided treatment is when antibiotics are prescribed based on the aetiology and antibiotic susceptibility of the disease-causing pathogen, derived from microbiological evidence from any relevant specimen, e.g., blood, urine, sputum, etc.[11] After receiving the microbiology result, prescribers are expected to change the broad-spectrum empirical treatment to the narrowest possible antibiotics based on the aetiology of the bacteria and antibiotic susceptibility.[43]

Surgical antibiotic prophylaxis (SAP) is aimed at preventing surgical site infection (SSI) both during and after surgery.[48] Concern regarding SAP prescribing is predominantly related to the unnecessary prolonged use, i.e., for more than 24 hours after the surgical procedure. Evidence from systematic reviews suggests that pre- and intra-operative SAP administration lowers the occurrence of postoperative SSI. However, prolonged SAP showed no conclusive protective benefit against SSI;[49,50] instead, it increased the risk of antibiotic resistance and *C. difficile* infection.[49]

2.1.2 Trends of antibiotic consumption

In the past two decades, there has been a shift in antibiotic consumption trends in HICs and LMICs. Global antibiotic consumption data obtained from hospital and/or retail pharmaceutical sales data in 76 countries between 2000 and 2015 revealed that in 2000, HICs, led by France, New Zealand, Spain, Hong Kong, and the US, had the highest antibiotic consumption rate.[10] In 2015, despite HICs persistently dominating the top 10 countries with the highest antibiotic consumption, four of these 10 countries were LMICs.[10] The same study reported a 65% increase in antibiotic consumption globally (21.1 to 34.8 billion defined daily doses (DDDs)) and a 114% increase in consumption in LMICs (11.4 to 24.5 billion DDDs) between these two periods.[10] Furthermore, this study found that between 2000 and 2015, there was a significant increase in consumption of cephalosporins (399%), quinolones (125%), and macrolides (119%) across LMICs; meanwhile, in HICs, the consumption of these antibiotic groups was decreasing by 18%, 1%, and 25%, respectively.[10]

In hospital settings, antibiotic consumption in some HICs has been showing a declining trend. The aggregated data from European hospitals showed that antibiotic consumption decreased from 2.1 DDD per 1000 inhabitants per day in 2016[51] to 1.6 DDD per 1000 inhabitants per day in 2020.[52] However, comparable surveillance data to track trends over time is lacking in many LMICs, including in Indonesia.

Available data on antibiotic consumption in Indonesia has been patchy, reported by individual hospitals or research groups. Therefore, our research group conducted a systematic review and meta-analysis of antibiotic consumption in Indonesia over the past 21 years, between 2000 and 2021.[36] We found a pooled antibiotic consumption among inpatients within this period of 134.8 DDD per 100 bed-days. There was a two-fold increase in antibiotic consumption between 2016 and 2021 (150.8 DDD per 100 bed-days), in comparison to the consumption between 2000 and 2015 (65.2 DDD per 100 bed-days). Within the same population, the most consumed antibiotic was ceftriaxone (a pooled estimate of 60 DDD per 100 bed-days), followed by levofloxacin (21.3 DDD per 100 bed-days), and ampicillin (18.7 DDD per 100 bed-days).[36]

2.1.3 Prevalence and patterns of antibiotic use in hospitals

Point prevalence surveys (PPS) have been used to provide information related to antibiotic use and the impact of antibiotic use optimisation across hospitals in different countries. The PPS method had been developed by various agencies, including the European Centre for Disease Prevention and Control (ECDC),[53] the WHO,[54] and the Laboratory of Medical Microbiology of the University of Antwerp (developed Global-PPS).[11] The description of the PPS method is in **Chapter 3**, section **3.4.1**.

PPS studies at the global, regional, country, and hospital levels showed variation in patterns in the prevalence of antibiotic use, the most commonly

prescribed antibiotics, and the reasons (diagnoses) and indications for prescription.

The prevalence of antibiotic use among hospitalised patients was higher in LMICs in comparison to HICs, as demonstrated by the following findings. The 2016–2017 European Surveillance of Antimicrobial Consumption (ESAC) PPS found 32.9% of inpatients received at least one antimicrobial agent, where antibiotics for systemic use (J01) accounted for 92.3% of antimicrobial prescriptions.[55] These figures were consistent with the 2015 Global-PPS findings from 53 countries (primarily HICs), with 34.4% of inpatients receiving at least one antimicrobial agent and 89.3% of antimicrobial prescriptions being systemic antibiotics.[11] In comparison, studies across hospitals in LMICs in the Southeast Asian region found a prevalence of antibiotic use among hospitalised patients that was twice as high, for example, 67.4% in Viet Nam,[56] 68.8% in Laos,[57] and 53% in Thailand.[58]

A high prevalence of broad-spectrum antibiotic prescribing for hospitalised patients has been reported across the world. The 2015 Global-PPS study reported that the most commonly prescribed antibiotic was the combination of penicillin and a beta-lactamase inhibitor, followed by cephalosporins and fluoroquinolones.[11] In line with this finding, the ESAC PPS conducted between 2016 and 2017 found that the most commonly prescribed antibiotics for CAI among European countries were combinations of penicillins and beta-lactamase inhibitors (23.2%), followed by third generation cephalosporins

(11.7%) and fluoroquinolones (11.1%).[55] Cephalosporins (mainly the third generation) were the most commonly prescribed antibiotic class for hospitalised patients, as reported by studies across LMICs in Southeast Asia: 70.2% in Viet Nam,[56] 41.2% in Thailand,[58] and 45.4% in Laos.[57] This finding is in accordance with our systematic review and meta-analysis of antibiotic consumption among inpatients in Indonesia, which found that ceftriaxone (third generation cephalosporin) was the most commonly prescribed antibiotic.[36]

There were similar patterns for the main reason (diagnosis) and indication for antibiotic prescribing across studies and settings. The most common diagnosis for antibiotic prescriptions was pneumonia or lower respiratory tract infection (LRTI) as reported by the ESAC PPS (31.8%),[55] the Global-PPS (19.2%),[11] as well as a study in Thailand (28.5%)[58] and Laos (12%).[57] Based on indications, antibiotic prescriptions for hospitalised patients were mainly indicated to treat CAI, including in European hospitals (49.5%),[55] hospitals in India (26.7%)[59] and Thailand (60.2%),[58] and globally (45.6%).[11]

2.1.4 Quality indicators of antibiotic use

Quality indicators are systematically defined measures based on literature reviews, expert input, and empirical evaluation to measure and evaluate the quality of key areas in organisations.[60] Quality indicators can provide information to identify areas that need improvement.[60] In hospital healthcare systems, they can be used as benchmarks to assess changes in clinical

practices and clinical outcomes.[61] In regard to antibiotic prescribing, quality indicators are aimed at identifying relevant problems in prescribing practices, finding suitable strategies for antibiotic use optimisation, and evaluating the effectiveness of antibiotic optimisation interventions.[62]

The methods to assess quality indicators of antibiotic use have been developed by different research groups using different approaches. In this review, I compare three methods to assess quality indicators of antibiotic use as presented in **Table** 2.1. *First*, the DRIVE-AB (Driving Reinvestment in Research and Development and Responsible Antibiotic Use) research consortium (2018)[62] and van den Bosch *et al*. (2015)[63] developed a list of quality indicators using a RAND-modified Delphi model[†]. *Second*, the Gyssens method uses a predefined set of six indicators to determine the quality of antibiotic prescribing. In this method, at least two experts in infectious disease assess the antibiotic prescriptions using a flowchart.[64] *Third*, the PPS method assesses the quality of antibiotic prescribing based on guideline compliance, clinical diagnosis and indication, documentation of the prescribing plan and stop/review, the use of microbial results, and drug choice, dose, and route (including intravenous to oral switch when available).

[†] A formal group consensus process that systematically and quantitatively combines expert opinion and evidence by asking panellists to rate, discuss, then re-rate items.

Table 2.1 A comparison of different methods assessing the quality indicators of antibiotic use

Method	A RAND-modified Delphi model[62]	Gyssens method[64]	Point Prevalence Survey (PPS)[11,54]
Approach	Retrospective	Retrospective	Cross-sectional (snapshot)
Indicators	Consists of a total of 51 process, structure, and outcome indicators, which are categorised into 19 themes.	Consists of six process indicators assessed in a sequential manner from indicator 1 to 6 using a pre-defined flowchart.	Assesses the process indicators (similar to the RAND-modified Delphi model) at the 'point' of the survey (snapshot).[11]
Process indicators	Assesses the decision-making process of antibiotic prescribing, for example: • Guideline compliance for empirical prescriptions • Targeted treatment based on culture and sensitivity results • Culture samples taken prior to antibiotic administration in patients suspected of infection • Adjustment of antibiotic dose based on renal function • Documentation of the antibiotic plan and stop/review • Route of administration	1. Data completeness (clinical and microbiology data) 2. Whether the prescribed antibiotic is indicated or not 3. The availability of an alternative antibiotic that is more effective, has less toxicity, is less costly, and has a narrower spectrum 4. Appropriateness of antibiotic duration 5. Appropriateness of antibiotic dose, interval, and route 6. Appropriateness of the timing of antibiotic administration	Some examples are: • Guideline compliance • Documentation of reason for antibiotic prescribing • Culture sample taken • Duration of surgical antibiotic prophylaxis
Structure indicators	Comprises of the availability of relevant structures for optimal antibiotic prescribing, including: • Antibiotic guidelines		

Method	A RAND-modified Delphi model[62]	Gyssens method[64]	Point Prevalence Survey (PPS)[11,54]
	• Antibiotic use surveillance and regular audits, • Antibiotic education for hospital staff, • AMS meetings • AMS accountability reports		
Outcome indicators	Comprises of clinical and microbial outcomes, including the rates of *C. difficile* infection.		
Data collection		A panel of infectious disease experts (at least two reviewers), sequentially evaluates each prescription based on local guidelines, and clinical and microbiological data.	• PPS provides a standardised data collection tool that facilitates homogenous data collection across wards, hospitals, and even countries. • The Global-PPS provides a web-based data collection tool that allows for global antibiotic use surveillance.[11]

The PPS method provides a standardised data collection tool, facilitating homogenous data collection across wards, hospitals, and even countries.[11,54]

In Indonesia, the Gyssens method has been widely used to assess the quality indicators of antibiotic prescribing in hospitals since the early 2000s.[36] According to a search of the literature, the only published studies using this method were from Indonesia. In our meta-analysis of studies conducted in Indonesia between 2000 and 2021, based on a pooled estimate from 18 studies, we found that only 35.3% of prescriptions were appropriate.[36] Based on the review of the literature, no study in Indonesia had used the PPS method when this research was started.

Quality indicators of antibiotic prescribing based on the PPS method

Literature showed that quality indicators of antibiotic prescribing varied between countries and regions. Based on the 2015 Global-PPS dataset, the overall prevalence of empirical antibiotic prescriptions complying with local guidelines (when guidelines are available) was 77.4% globally and 81.5% among Asian countries, predominantly HICs.[11] On the contrary, studies from LMICs in Southeast Asia showed a lower prevalence in comparison to the 2015 Global-PPS dataset. For example, a study in six hospitals in Laos (2017–2020) found only 26% of prescriptions complying with the local guidelines.[57] Similarly, a study in two hospitals in Myanmar found that the overall compliance was 31.9%.[65]

The quality indicator of targeted treatment was poor overall, globally, and between countries. According to the Global-PPS dataset, only 19.8% of patients on antibiotics received at least one targeted treatment, and 5.9% received at least one targeted treatment for MDROs.[11] Among therapeutic uses, only 20.9% of CAI prescriptions and 36.9% of HAI prescriptions were targeted.[11] Consistently, studies in LMICs in Southeast Asia also showed a low prevalence of targeted treatment. The results of a study in 41 hospitals in Thailand showed that only 20.8% of antibiotic prescriptions were targeted, and of these, 49.8% were indicated for HAI.[58] A retrospective study conducted in a tertiary hospital in Indonesia among sepsis patients found that, despite 49.9% of patients having blood cultures taken, only 3.4% received targeted treatment.[66]

The quality indicator of SAP duration, which is the proportion of prolonged SAP administration (>24 hours), was poorer in LMICs than in HICs. The ESAC PPS among 20 European countries found prolonged SAP duration in 57.3% of all patients who received SAP prescriptions.[67] Based on the 2015 Global-PPS dataset, 66.1% of the overall SAP prescriptions were prolonged for more than one day, with some differences between regions, e.g., 92.6% in Africa (predominantly low-income countries) and 26.5% in Western Europe (predominantly HICs).[11] In LMICs in the Southeast Asia region, studies reported the proportions of prolonged SAP as 70.3% in Thailand,[58] 78% in Myanmar,[65] and 100% in Laos.[57]

2.1.5 The WHO AwaRe classification

In 2017, the WHO developed the AwaRe (Access, Watch, Reserve) classification, aiming to monitor local antibiotic use and develop or update national antibiotic guidelines for infectious disease syndromes.[68] Using the traffic light system, this classification indicates different antibiotic categories based on their spectrum (narrow, broad), risk of resistance development (low, high), and utility in clinical practice (first choice, second choice, last resort).[69]

The Access group contains narrow-spectrum antibiotics that are recommended as first and second choices for most common clinical infection syndromes and are listed in the essential medicines and essential medicines for children. The antibiotics in this group should be widely available at an affordable price.[70]

The Watch group contains generally broader-spectrum antibiotic classes, corresponding to the highest priority agents on the list of critically important antimicrobial drugs for human medicine.[70] Watch antibiotics are still recommended as first- or second-choice treatments, but for a limited number of indications. Antibiotics in this category are more likely to be targets of antibiotic resistance and are thus prioritised as targets of antimicrobial stewardship programmes and monitoring.[69,71]

The Reserve group consists of ‘last-resort’ antibiotics for targeted use in multidrug-resistant infections or when other alternatives have failed (e.g., serious life-threatening infections due to MDR bacteria).[69,71] There are also

antibiotics classified as ‘not recommended’ as they are neither evidence-based nor recommended in high-quality international guidelines, hence not recommended for clinical practice. For example, antibiotics with fixed-dose combinations of multiple broad-spectrum antibiotics (e.g., amikacin/cefepime, azithromycin/levofloxacin, etc.).[72]

The AWaRe sets a national target of >60% of total Access antibiotic consumption by 2023.[73] Yet, data from the Global-PPS (2015, 2017, and 2018), collected from 664 hospitals in 69 countries among adult patients, showed substantial variations in AwaRe antibiotic use between countries.[74] Lower-middle and upper-middle income countries had the highest percentage of Watch antibiotic use (62–63%). Meanwhile, low-income countries, particularly those in sub-Saharan Africa, had the highest percentage of Access prescriptions (62%). Ceftriaxone (Watch antibiotic) was the most frequently prescribed therapeutic antibiotic, accounting for 13.3% of all prescriptions across the studied countries. Pneumonia treatment was the main reason for ceftriaxone prescriptions (20%), followed by prophylaxis for gastrointestinal infection (8.1%) and treatment for skin and soft tissue infection (6.7%).[74] When this research was started, there was no study in Indonesia assessing antibiotic use in hospitals based on the AwaRe classification.

2.2 The conceptual framework of factors influencing antibiotic prescribing and the implementation of antimicrobial stewardship programmes

The decision-making process in antibiotic prescribing is not only a matter of the presence or absence of infection. Complex social-cultural factors influence perceptions about antibiotic use and the practices of antibiotic prescribing. I developed a conceptual framework based on the current evidence of the social-cultural factors influencing antibiotic prescribing in hospitals and the interface between these factors and hospital antimicrobial stewardship (AMS) programmes (**Figure** 2.1).

The following subsections elaborate on each of the elements of the social-cultural factors influencing antibiotic prescribing (section **2.2.1**) and the AMS programmes as strategies to optimise antibiotic prescribing (section **2.2.2**).

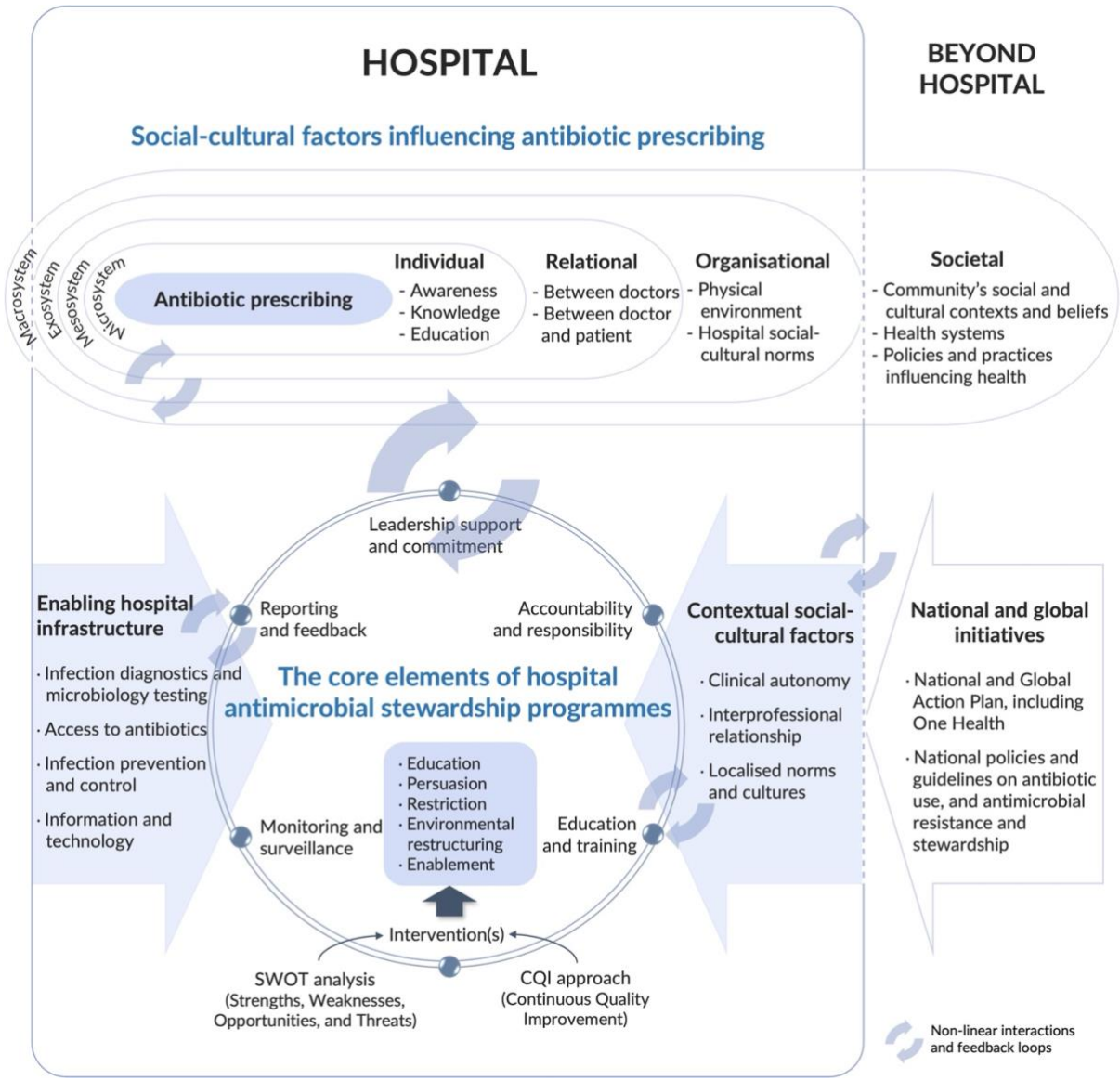


Figure 2.1 Conceptual framework of social-cultural factors influencing antibiotic prescribing and antimicrobial stewardship programmes in hospitals

2.2.1 Social-cultural factors influencing antibiotic prescribing

I used a four-level social-ecological model, adapted from Bronfenbrenner's ecological model,[75] to elaborate on multilevel and multidimensional social-cultural factors influencing antibiotic prescribing. The original concept of Bronfenbrenner's ecological model[75] proposes four dimensions affecting human development: 1) the microsystem (individuals as part of particular roles and/or activities in the setting); 2) the mesosystem (interaction between an individual and other people or groups of people); 3) the exosystem (institutional and social structures); and 4) the macrosystem (overarching cultural values and norms that can be manifested, for example, in political, legal, and educational systems).[75]

2.2.1.1 Individual level

The awareness of AMR among doctors and other healthcare providers is one of the most studied factors correlated with the decision to prescribe antibiotics. In a systematic review of studies (mainly from North America and Europe, up to 2014), 56% of 57 studies assessed clinicians' AMR awareness in relation to the significance of the problem and their prescribing practices.[76] This review showed a significantly high level of awareness concerning the AMR problem among hospital physicians. The majority of them consistently agreed that AMR is a serious problem (96%), and that broad-spectrum antibiotic use can drive antibiotic resistance (98%). However, there was a wide variation when asked if AMR was a problem in their local hospital. For

example, 97% of respondents in the US agreed or strongly agreed that AMR is a problem in their hospital, but only 45% in the West Indies.[76]

The perception of antibiotic practices contributing to AMR development was also explored in the literature. Studies have shown that doctors perceive AMR as driven by antibiotic practices 'out there' rather than their own practices.[77–80] For example, a 2012 study among 386 hospital physicians in Laos found that 75.9% of respondents agreed that antibiotics are overused in hospitals and the community, but only 47.1% agreed that antibiotics are overused in their own practice. However, 95.6% of respondents reported they prescribe antibiotics at least once a week, and 68.3% at least once a day.[77] Similarly, 95% of 689 hospital physicians participating in a Cambodian study in 2013 perceived that patients self-prescribe antibiotics before presenting to the hospital, and 81% reported that the community uses antibiotics inappropriately.[78] This component is significant since it pertains to who is responsible for the AMR problem and who should change antibiotic practices.

Suboptimal knowledge of infectious diseases and antibiotics, as well as the lack of antibiotic guidelines, can negatively influence the quality of prescriptions. A review of studies exploring the underlying factors of antibiotic prescribing in LMICs showed that the failure to diagnose infection-like syndromes or determine the infection's aetiology encourages doctors to prescribe broad-spectrum antibiotics to cover all possible aetiologies.[81] In settings where continuing medical education (CME) is inadequate or

unavailable, doctors continue to perform outdated antibiotic prescribing practices.[82,83] Besides the need for CME, it is also crucial to equip doctors with relevant information to make a well-informed decision, including the provision of up-to-date antibiotic guidelines. For example, a qualitative study in Pakistan found that doctors reported not knowing any local antibiotic guidelines in their hospitals.[84] Therefore, they looked for updated information from medical journals over the internet or received it from medical representatives.[84] This method can be used as a short-term fix, but the information may not match the local susceptibility pattern, and further, medical representatives have economic interests in increasing antibiotic sales.

2.2.1.2 Relational level

Relationship factors influencing antibiotic prescribing are mainly centred around two aspects: interpersonal relationships between doctors and doctor-patient relationships. Peers' practices can influence antibiotic prescribing, especially when it comes to the relationship between senior and junior doctors. This interpersonal relationship is entangled with hierarchy, culture, and norms in the medical profession. Studies in Australia, the UK, Sri Lanka, and South Africa found that junior doctors reported seeking advice from senior colleagues to make appropriate antibiotic decisions.[85,86] However, they also experienced challenges in improving their prescribing practices because they felt pressured to make similar decisions based on the seniors' preferences and expectations, irrespective of local antibiotic guidelines.[85,86]

The doctor-patient relationship is also crucial in the context of antibiotic prescribing. In healthcare, doctors have certain roles and responsibilities towards their patients. One of the most important responsibilities is to make every effort to aid the patient's early recovery through an objective and rational approach[87] (see further explanation related to the sick role in **Chapter 3**, section **3.3.1**).

As found by studies in both HICs and LMICs, despite awareness of the potential AMR threat, the fear of 'missing something', which has the consequence of poor clinical outcomes, encourages doctors to start antibiotics at the beginning of treatment, even without a clear indication.[85,86,88] Similarly, the fear of surgical site infection is mentioned as an argument to prolong the surgical prophylaxis prescriptions beyond the recommended duration and/or to prescribe broader-spectrum antibiotics even when it is unnecessary.[80,89]

Poor clinical outcome is a main concern for doctors because they are held responsible for it, and further, it can jeopardise their reputation.[83,85,88] This circumstance introduces the idea of 'anticipatory use of antibiotics' due to the anxiety surrounding the risk of poor patient outcomes.[90] However, the fear of 'potential' poor clinical outcomes must be distinguished from 'real' poor clinical outcomes. For example, a recent study in Zimbabwe discovered that when doctors withheld antibiotics, the same patients later seriously deteriorated.[90]

Yet, in this case, further context-specific exploration is required to understand the causative factors of this situation beyond the absence of antibiotics.

The fear of missing something can also be driven by diagnostic uncertainty. As found in qualitative studies, doctors reported that sometimes it is difficult to determine the differences between bacterial and non-bacterial infections based on the presenting symptoms.[90] Therefore, antibiotic prescribing is used as a risk-averse strategy to be safe rather than miss the bacterial infection diagnosis.[86,90]

Diagnostic uncertainty can also influence the selection of antibiotic type and spectrum, i.e., broad-spectrum antibiotic prescriptions to cover multiple possible disease-causing bacteria associated with the clinical syndrome.[43] For example, doctors from Sri Lanka participating in a qualitative study perceived that broad-spectrum antibiotics could provide a fast and effective clinical outcomes.[86] Doctors in a Cambodian study perceived that broad-spectrum antibiotics are more potent for hospitalised patients because pathogens are resistant to narrow-spectrum antibiotics as a result of unrestricted antibiotic access in the community.[91] In addition, diagnostic uncertainty is also influenced by limitations relating to hospital infrastructure, as described below (section **2.2.1.3**).

2.2.1.3 Organisational level

At the organisational level, antibiotic prescribing is influenced by the physical environment and the social-cultural contexts and norms of the workplace.

Regarding the physical environment, limitations in hospital infrastructure, such as infection prevention and control and diagnostic facilities, can have a negative impact on antibiotic prescribing in LMICs or low-resource settings. Doctors participating in qualitative studies across LMICs in Asia and Africa reported that antibiotic prescribing is driven by poor hygiene and sanitation, inadequate patient isolation facilities, and overcrowding and poor ventilation in patient management rooms.[84,91,92] Furthermore, hospitals frequently lack the resources to provide single-use sterile equipment. Therefore, when performing invasive procedures, the aseptic technique may not always comply with the standard operating procedure.[93] In such settings, antibiotics are used to prevent cross-infection within and between wards and patients[92] to cover structural vulnerabilities.[94]

The other challenges faced by doctors in LMICs are constraints in infection diagnostic testing and a paucity of local resistance data.[95] Timely and reliable microbiology testing is the gold standard for infection diagnosis. However, research in Asian and African LMICs found that doctors are hesitant to order culture tests due to concerns about sample contamination, which makes interpreting results difficult, or cultures being negative even when infections are highly suspected.[96] The other barriers to culture testing, for example, as reported by doctors in Ghana and Cambodia, are long turnaround times,[91,97] laboratories running out of specimen collection and processing materials, and high testing costs.[97] These factors have the implication that doctors frequently

lack essential information to guide their clinical decisions and, thus, lack confidence in not prescribing antibiotics.

Inadequate access to appropriate antibiotics also poses a challenge to optimum antibiotic prescribing. Studies across LMICs showed that restricted availability is one of the main barriers to the discrepancy between the intended and prescribed antibiotic agents.[81,90,96] Doctors reported they are forced to choose between treating with an antibiotic that might not work given an organism's susceptibility pattern and not treating at all due to a lack of access to antibiotic agents to which the organism seemed sensitive.[96] Furthermore, as found by a study in Zimbabwe, doctors prescribed broad-spectrum antibiotics because of their close expiration dates and to avoid waste.[90] In this case, the choice of antibiotics may depend on what antibiotics are available in the setting, which is sometimes inappropriate.

In addition to hospital infrastructure and access to appropriate antibiotics, the social environment, which encompasses the hospital's culture, norms, and interests, can also influence antibiotic prescribing practices. In regard to these aspects, there are some differences when comparing public and private hospitals, especially from the point of view of individual performance.

The findings from a study in Italy showed that individual performance in a public hospital is associated with clan or cooperative culture. However, in a private hospital, it is adhocracy, which is an entrepreneurial system that values innovative solutions, self-organisation, and risk-taking.[98] In line with

these findings, studies on antibiotic prescribing in Australia and South Africa reported that doctors in private hospitals, particularly treating specialists, have greater clinical autonomy in comparison to those in public hospitals.[99–101] The executives of private hospitals consider doctors as ‘partners’ rather than subordinates, and doctors independently practice as individual contractors and have more autonomy and ability to influence the working environment.[100,101] Furthermore, in private hospitals, doctors are also better incentivised and provided with better medical facilities.[101]

Financial incentives for doctors as antibiotic prescribers and hospitals as a result of antibiotic sales to generate income also play an important role in influencing antibiotic prescribing practices. Previous studies found that incentives from the pharmaceutical industry have a significant influence on doctors’ decisions to prescribe antibiotics in settings where therapeutic protocols are lacking[102] or doctors are not well-incentivised.[83] A review of studies on pharmaceutical sponsorship found an association between increased prescription rates of the sponsored drugs and incentives received by doctors, for example, to support continuing medical education through financial support to attend symposiums, including the lodging and travel costs.[103] Furthermore, as found in another systematic review of studies, the economic rationale of antibiotic prescription is especially strong in private settings where patients pay for services or have (private) health insurance coverage.[81]

Commercial considerations in antibiotic prescribing are also linked to the availability of hospital resources. For example, a study in six rural secondary hospitals in India found that antibiotic prescriptions are the main source of income for the hospital pharmacies.[83] The sale of antibiotics represented a significant portion of revenue for these smaller hospitals that focus primarily on treating acute diseases.[83]

Culture differences between departments in a hospital were explored by an ethnographic study in a UK hospital. This study found that antibiotic prescribing in medical wards is collectivist, where each team member is encouraged to participate and provide input, policy-driven, and oriented towards antibiotic de-escalation.[104] In contrast, the culture in surgery is individual and vertical, with the surgeons leading decision-making with less team input.[104] The organisational culture differences between hospitals and between departments can influence antibiotic prescribing, especially in relation to prescribing autonomy and opportunity in decision-making.

2.2.1.4 Societal level

Broader societal factors, such as healthcare systems, policies and practices beyond healthcare systems, and broader cultural beliefs, can also have an influence on antibiotic prescribing. Beyond hospitals, unnecessary use and overuse of antibiotics in the community, especially antibiotic self-medication, is a concerning problem in healthcare systems, which is commonly practiced in LMICs.[81,105,106] A global survey and studies in LMICs showed that antibiotic

self-medication is correlated with a lack of awareness and poor knowledge regarding AMR and the purpose of antibiotic use among the community; accustomed concepts, practices, and expectations of the local community about antibiotics; and poor access to healthcare services.[36,81,105,106] The WHO global AMR awareness survey among community members in 2015 found that a large proportion of respondents did not know that sore throats (70%) and colds and flu (64%) cannot be treated with antibiotics.[105] In certain local communities, antibiotics are perceived as preventive medicine, e.g., to prevent gastrointestinal symptoms among communities in Brazil and sexually transmitted diseases among communities in Zimbabwe and the Philippines.[81]

Antibiotic self-medication is encouraged by limited access to formal healthcare services or facilities, e.g., among rural communities. This finding is shown by studies in Nepal, Viet Nam, and Cambodia.[106–108] Meanwhile, the informal sectors, like drug shops and unofficial village health providers who provide antibiotics without prescriptions, have convenient proximity to the community.[106–108] This issue is further exacerbated by poor formal healthcare service delivery. For example, patients reported experiencing long waiting times in healthcare centres due to overcrowding, essential drug stockouts, and excessive costs to perform laboratory tests.[27,106] The doctor-patient hierarchical relationship in such settings discourages patients from being part of decision-making as they fear speaking to the doctor.[106,109]

Besides, antibiotic self-medication can also be influenced by the accustomed local practices in the settings where antibiotics can be purchased without prescriptions. Having a parent born abroad and being a first-generation immigrant are associated with a higher use of antibiotics in HICs. For example, in the US, antibiotic self-medication is more common in the Hispanic/Latino immigrant population (19-66%).[110] Chinese migrants in Australia (47%) reported having antibiotics stored at home, either as leftovers or from outside Australia.[111]

Health systems' vulnerabilities in regard to the power pull of the pharmaceutical industry influence a low priority to address the AMR problem in LMICs. Antibiotic sales drive profits and incentives for many parties, including drug companies, pharmacies, drug sellers, and prescribers. Despite the fact that the practices of non-prescription antibiotic dispensing and unethical antibiotic marketing have the potential to contribute to AMR development, they incur no or light penalties and are less addressed in the potential strategies to contain AMR.[112–114]

Falsified and substandard antibiotics also remain an unaddressed problem in some LMICs for several reasons, including high drug production costs[114] and low technical drug production capacity.[115] A recent study in Indonesia found that excessively low medicine prices (for the national health insurance scheme, *Jaminan Kesehatan Nasional,* or JKN scheme), as determined by the government, encourage pharmaceutical companies to produce

substandard drugs in order to maintain profitability (see section **2.3.2** for further explanation about the JKN scheme).[116]

Beyond antibiotic use in humans, antibiotic use in non-humans (livestock and agriculture) plays an important role in the emergence of antibiotic resistance and the transmission of drug-resistant bacteria through the food chain and the environment. All of the societal factors listed above do not only indirectly contribute to the acceleration of the AMR rate; they also indirectly influence antibiotic prescribing in hospitals. Hospitalised patients with drug-resistant bacteria will require higher generation and/or broader spectrum antibiotics, or even antibiotics from the Reserve group.

2.2.2 Antimicrobial stewardship programmes as strategies to optimise antibiotic prescribing

2.2.2.1 The core elements of hospital antimicrobial stewardship programmes

The term ‘antimicrobial stewardship’ (AMS) was introduced in 1996 as a concept to use antimicrobial drugs in a responsible manner concerning the scarcity of these drugs.[117] The two main goals of AMS are to prevent the emergence of AMR and to decrease already-established AMR.[118] In hospital settings, three main strategies to achieve AMS goals are AMR surveillance,[118] HAI prevention through infection prevention and control (IPC),[54] and ‘antibiotic prescribing control’ aiming to promote the appropriate selection of antibiotic regimens (type, dose, duration, and route) to ensure optimal efficacy of infection treatment.[118]

Implementing an AMS programme in a complex hospital system requires the support and participation of various stakeholders and infectious disease experts. It also entails the availability of six building blocks, or 'core elements', as recommended by the US CDC[119] and WHO[54]: 1) leadership support and commitment, 2) accountability and responsibility, 3) education and training, 4) interventions, 5) monitoring and surveillance, and 6) reporting and feedback (**Figure** 2.1).

Leadership support and commitment, especially from the hospital management and heads of departments, are critical to facilitate the allocation of resources (financial and other) and endorse the AMS action plan.[54,119] To run AMS programmes, a hospital needs an *accountable* AMS leader and team members who have expertise in infectious disease, pharmacy, and microbiology with clearly defined roles and responsibilities.[54,119] Further, the AMS leader and team members should be able to access AMS-related *education and training* to improve their competencies. For example, training on performing ward rounds and clinical case discussions. These abilities can aid the AMS leader and team in leading discussions and providing feedback to prescribers.[54]

AMS *intervention* (section **2.2.2.2**) should be customised to address the local problem(s).[119] The WHO[54] recommended that before executing an intervention, hospitals should perform a SWOT (strengths, weaknesses, opportunities, and threats) analysis to identify the potential barriers and

enablers of the intervention. The WHO also proposed that hospitals adopt the continuous quality improvement (CQI) model because it can provide a systematic approach for a tailored intervention.[54] *Monitoring and surveillance* of AMS programmes are crucial to measuring the impact of the intervention and tracking its progress.[119] The AMS leader or team then has to *report* the outcomes of the intervention and provide *feedback* to the stakeholders exposed to the programme, including physicians, pharmacists, nurses, clinical microbiologists, and hospital management.[119]

2.2.2.2 Antimicrobial stewardship interventions

Based on the Cochrane reviews,[120,121] AMS interventions can be classified as education, persuasion, restriction, environmental restructuring, and enablement (**Figure** 2.1).

1. *Education* strategies aim to improve knowledge related to AMR and antibiotic use, especially among prescribers and hospital clinical staff. Education is mainly provided through meetings, trainings, workshops, and the dissemination of educational material.[121]
2. The *persuasive* approaches are focused on strategies to stimulate targeted feelings and actions concerning AMR and antibiotic prescribing. For example, the AMS leader and team use a collegial approach instead of an instructive approach to communicate with prescribers.[121]
3. *Restriction* strategies employ actions to limit the prescribing freedom of certain antibiotics, often in the form of antibiotic pre-authorisation by infectious disease experts or the AMS team, a compulsory antibiotic order

form, selective reporting of microbiology susceptibilities, removing certain antibiotic choices from certain wards, or an automatic stop order.[120,121]

4. *Environmental restructuring* is aimed at tackling technical barriers to antibiotic prescribing, like shifting from paper-based to computerised medical records, providing pocket-size antibiotic guidelines, and introducing new technology like rapid laboratory testing that shortens laboratory result turnaround time.[120,121]
5. *Enablement* encompasses strategies to facilitate prescribers in making rational antibiotic decisions. They include guideline provision, audit and feedback, and computerised decision support systems.[121]

Davey *et al.* (2013)[120] and Dik *et al.* (2016)[122] presented five commonly used indicators for assessing the impact and effectiveness of an AMS intervention. First, *antibiotic use*. This indicator is intended to measure the frequency of antibiotic consumption or prescribing, the appropriateness of antibiotic choice (type, dose, route, and duration), and compliance with antibiotic guidelines or policies. Second, *clinical indicators*. They include hospital length of stay, mortality, surgical site infections, and hospital-acquired infections. Third, *microbial outcomes* such as the prevalence of drug-resistant pathogens and *C. difficile* colonisation or infection. Next are *unintended outcomes* of the intervention, such as delayed antibiotic administration due to the pre-authorisation process.[120,122] Preferably, all of the above outcome measures are quantified and transformed into monetary values or *financial outcome*

measures to assess the cost-effectiveness and cost-benefit of the intervention.[122]

In regard to the impact of AMS programmes, systematic reviews and meta-analyses (mainly from studies in HICs)[120,121,123] showed that *restriction* interventions have an immediate impact on antibiotic use, such as a significant decrease in the use of restricted antibiotics and a shorter length of stay. Meanwhile, there was no evidence that restriction interventions increase mortality.[120,121,123] A short-term restriction policy had shown positive microbial outcomes of increased susceptibility to fluoroquinolones[123–125] and broad-spectrum cephalosporins,[124,125] and decreased *C. difficile* infection.[125,126] On the other hand, there was a risk of creating the 'squeezing the balloon' phenomenon of increased non-restrictive prescriptions,[127] which was often ignored or not reported.[124] Furthermore, formulary restrictions with pre-authorisation raised some concerns, like delays in antibiotic administration and unsustainability without complementary enablement interventions.[121]

In Indonesia, our systematic review and meta-analysis of studies in the past 21 years found mixed results on the outcomes of AMS interventions. The majority of the reviewed studies implemented education interventions (trainings, seminars) or enablement interventions (the provision of antibiotic guidelines and feedback to prescribers). Single education and enablement interventions showed mixed positive and negative results on antibiotic consumption and prescribing appropriateness. Meanwhile, studies that

performed bundled education and enablement interventions showed favourable effects on antibiotic consumption, prescribing appropriateness, guideline compliance, blood culture samples taken, and HAI and mortality rates.[36] One study that applied pre-approval antibiotic restriction intervention found the consumption of restricted antibiotics decreased but the consumption of unrestricted narrow-spectrum antibiotics increased,[36] demonstrating the 'squeezing the balloon' phenomenon.[127] In this review, there is no study assessing the microbial or financial outcomes of AMS interventions.

Implementing an effective AMS programme in LMICs presents a number of challenges. A systematic review and a multi-country study in LMICs discovered that AMS in such settings often face economic and logistical barriers, with limited funds available for healthcare and limited access to diagnostic tests and essential and quality-assured antibiotics.[95,96] Furthermore, the execution of AMS is challenged by the low awareness and understanding of healthcare providers about the importance of the AMR problem and AMS programmes.[95] For example, a study among hospital physicians in Laos reported that they were often not aware that their prescribing practices could negatively impact the effectiveness of antibiotics.[77] Patients' perceptions and demands on antibiotic prescriptions may also have a negative impact on AMS in certain contexts. For example, a study in Indian hospitals reported that there is a perception among patients that an antibiotic prescription is standard care.[83] Therefore, patients expected antibiotics to be prescribed for every illness, regardless of the aetiology.[83] These factors can

lead to antibiotic overprescribing as well as difficulty implementing and sustaining AMS programmes in such contexts.

2.2.2.3 Enabling infrastructures and contextual social-cultural factors influencing antimicrobial stewardship implementation

Enabling infrastructure

AMS programmes cannot be implemented in isolation; they require enabling infrastructure in the hospital healthcare systems to achieve optimal, desirable outcomes. To support the execution of the AMS programmes, hospitals have to optimise infection diagnostic and microbiology testing, access to antibiotics, infection prevention and control (IPC), and information and technology (IT) systems (**Figure** 2.1). Often, in settings where these infrastructures are not available or operating at a minimum level, an effective and sustainable implementation of an AMS programme is unlikely to be achieved.

Reliable infection diagnostic tests and microbiology facilities are crucial elements in diagnostic stewardship to guide appropriate antibiotic choice.[118] The lack of access to these infrastructures eliminates the option of prescribing targeted, culture-guided treatment. Even when the testing facilities are available but are operated at a minimum level, prescribers are not confident enough to utilise the service,[95] for example, when cultures are negative, but infections are highly suspected.[96]

Another crucial element to supporting AMS implementation is *access to antibiotics,* which encompasses the availability and affordability of antibiotics

to ensure patients receive a rational course of treatment at the right time.[9] A study from three LMICs in Asia and Africa found that not having access to antibiotics as required by the susceptibility result and the inability to pay for antibiotics are barriers to AMS implementation and have the implication of delayed treatment in the settings.[96]

AMS and *IPC* are two sides of the same coin regarding AMR prevention and antibiotic use optimisation.[54] A well-executed IPC can prevent the spread of drug-resistant bacteria[54,118] which is important to make doctors feel confident that patients will not obtain a hospital-acquired infection during admission. The lack of or insufficient IPC puts doctors under pressure and therefore compensates for this limitation by prescribing unnecessary antibiotics,[93] which delimits AMS outcomes.

Hospital *IT systems* are another important aspect of hospital infrastructure. They can help the AMS team and doctors who prescribe antibiotics by providing them with relevant up-to-date information. For prescribers, integrated IT systems can shorten the antibiotic decision-making process by providing prompt access to antibiotic guidelines and microbiology test results.[128,129] Electronic antibiotic approval systems can help the AMS team review and give feedback on restrictive antibiotics in real time.[128,129] Furthermore, IT systems can assist with monitoring activities such as collecting and evaluating antibiotic prescribing with less time and human resources. These data help the AMS team develop a database and track

intervention progress, identify problems, prioritise or modify interventions, and generate feedback.[129]

Contextual social-cultural factors

Recognising the social-cultural factors in the setting, in addition to enabling infrastructure, is critical for a less resistant AMS execution. AMS interventions, especially the restriction strategies, may face resistance from prescribers[130] as doctors do not favour strategies limiting their autonomy.[131] To mitigate this barrier, studies showed that persuasive communication styles, i.e., collegial[132] and non-confrontational[133] approaches, are critical in reducing prescribers' resistance.

Localised norms and cultures set the tone for the interprofessional dynamics and priorities in the setting. A collaborative approach between different medical professions aids the AMS team members in performing their roles optimally.[132] However, this approach is limited by cultural aspects of the medical profession. Pharmacists[96,102] and nurses[102] who are not traditionally involved in antibiotic decision-making, have limited input in antibiotic use oversight due to concerns about stepping into clinicians' territory.[102]

2.2.2.4 National and global initiatives

Considering the complex and multifaceted problem and drivers of AMR, at the 2015 World Health Assembly, the WHO adopted a global action plan (GAP) on AMR to deliver the following objectives: 1) to raise AMR awareness and understanding through effective communication, education, and training; 2) to

strengthen the knowledge and evidence base of AMR through surveillance and research; 3) to decrease infection incidence through effective sanitation, hygiene, and infection prevention strategies; 4) to optimise antimicrobial use in human medicine and animal health; and 5) to provide an economic justification for long-term investment that considers the needs of all nations and to enhance investment in novel medications, diagnostic tools, vaccines, and other treatments.[134]

GAP urged countries to develop a context-specific national action plan (NAP) on AMR and to adopt a One Health approach. A NAP is aimed at guiding the key stakeholders and providing integrated responses against AMR through the identification of priority areas for work and collaboration.[134] Countries, including those in Southeast Asia, have begun to develop and implement NAPs.[135]

However, a recent synthesis of evidence of NAPs by Charani *et al.* (all available NAPs)[136] and Chua *et al.* (NAPs of Southeast Asian countries)[135] discovered challenges in the translation of NAPs' objectives from policies to practices. The NAPs from 16 least-developed countries recognised the role of the public in managing AMR.[136] Yet only a few NAPs had strategic and evaluation plans in place. There was also little to no recognition of the need to address the social-cultural drivers of health-seeking behaviours and antibiotic-providing practices.[136] All of the NAPs from Southeast Asian countries mentioned funding and resources, but only one country shared the budget it

had set aside for the activities listed.[135] Similarly, while 22% of NAPs across regions stated their commitments to invest in continuous antimicrobial supply, management, and procurement, these intentions were not followed through with explicit political or financial commitments.[136]

The national action plan on AMR and the milestone of hospital AMS programmes in Indonesia

Indonesia developed a NAP for 2017–2019,[137] which has just been extended for another four years, from 2020 to 2024.[138] The Indonesian NAP elaborated six strategic objectives, five of which are consistent with GAP objectives, and one additional objective, which is to develop an integrated governance and coordination system to curb AMR.[138] In recent years, international agencies and aid organisations have pushed for and supported the implementation of Indonesia's NAP at the national level, particularly AMR surveillance, for example, the Fleming Fund[139] and the WHO ESBL-E. coli Tricycle Project.[140] These initiatives aim to improve integrated AMR surveillance across human, animal, and environmental sectors by employing the One Health approach.[140]

At the hospital level, the AMS programmes have begun to receive significant attention among Indonesia's national priorities, with a NAP in place and increased political attention globally to push AMR containment. Hospital AMS initiatives in Indonesia were started in the early 2000s, yet their implementation was patchy during the first 15 years. Between 2003 and 2004, the AMRIN (Antimicrobial Resistance in Indonesia: prevalence and

prevention) study group conducted a multi-faceted AMS intervention in two tertiary hospitals.[141] This study found that the bundle AMS interventions (education, enablement, and environmental restructuring) were effective in optimising antibiotic prescribing. The findings of this study were used as an advocacy tool to push for a national policy on AMS. The following year, in 2005, the Ministry of Health (MoH) released a document to guide hospitals in performing a self-assessment on AMR, antibiotic use, and infection control measures.[142] However, it was not until 2015 that Indonesia reached an important milestone: the MoH endorsed a national policy on hospital AMS with the aim of pushing AMS implementation at the hospital level (**Figure** 2.2).[143] Since 2015, the national government has been releasing various national guidelines and policies to support AMS implementation, including a regulation that AMS programmes are mandatory for hospital accreditation since 2018.[144]

The national policy on AMS requires all hospitals in Indonesia to form an AMS team or committee, develop local antibiotic guidelines, and implement AMS strategies. The policy elaborates six fundamental elements to drive appropriate antibiotic use in hospitals: 1) to improve the knowledge and understanding of the clinical staff about prudent antibiotic use; 2) to foster the roles of infectious disease experts; 3) to develop and improve the function of the microbiology laboratory and other supported laboratories related to the management of infectious disease; 4) to improve the role of clinical pharmacists and pharmacology services to guide antibiotic use; 5) to enforce multidisciplinary and comprehensive infectious disease case management;

and 6) to perform antibiotic use and resistance surveillance and regular reporting.[143]

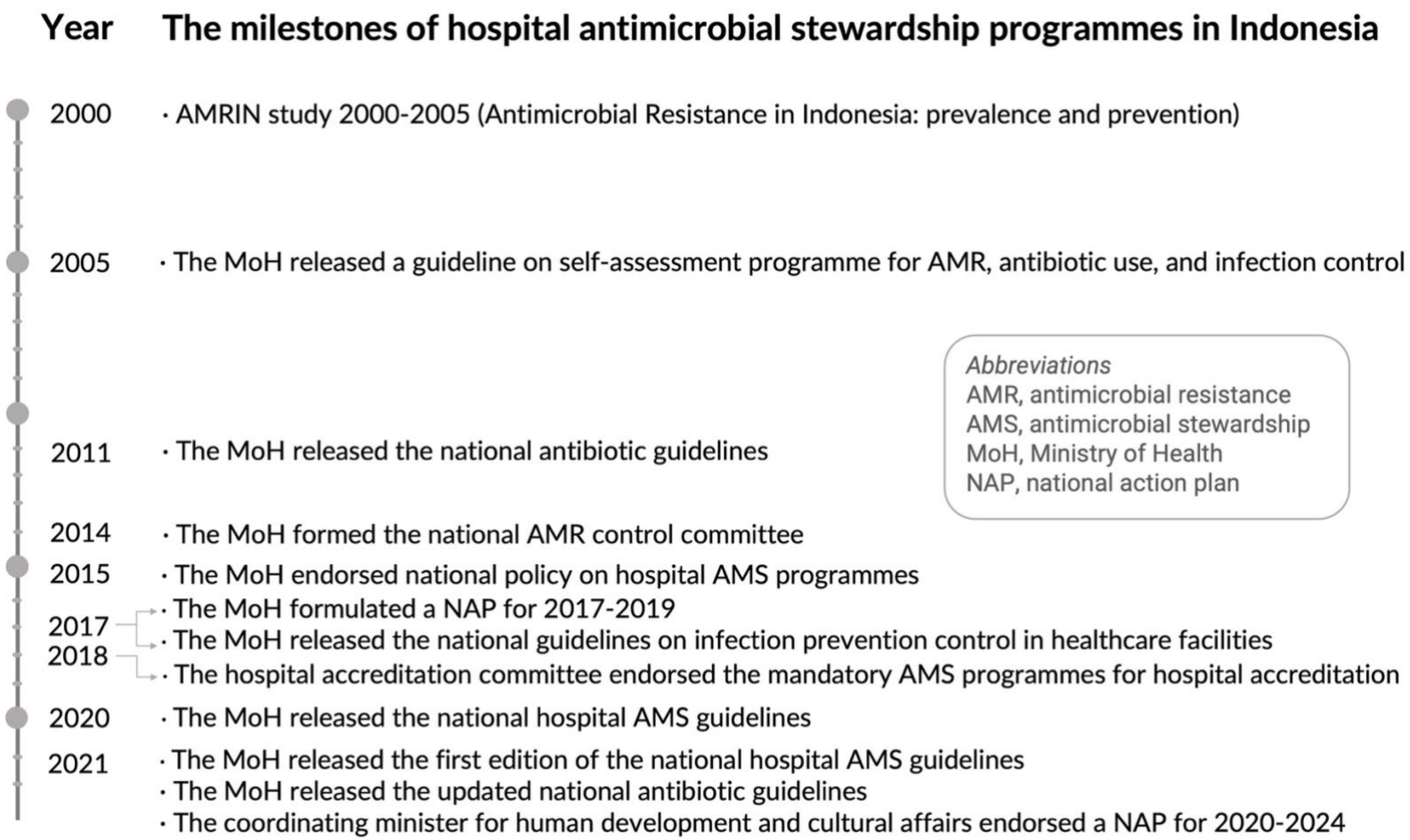


Figure 2.2 The milestones of the implementation of nationwide hospital antimicrobial stewardship programmes in Indonesia

To date, there has not been a national report on the progress of hospital AMS implementation in Indonesia. However, recent studies found some limitations in AMS execution across Indonesian hospitals. A study conducted across seven hospitals (five tertiary and two secondary) found limitations in regard to the availability of the core elements of AMS programmes. Four hospitals received leadership support from hospital management, only three had an AMS team and dedicated AMS funds, and the local antibiotic guidelines were available in only two hospitals.[145] Another study in a public hospital among doctors, pharmacists, and nurses found that the majority of respondents (64.1%) were unfamiliar with the term 'AMS programmes.' In the same study, respondents also reported concerns related to timely antibiotic administration (71.2%), potential conflicts with other clinical staff (74.2%), and prescribing autonomy (71.2%).[146]

2.3 Indonesia: the context of the research setting

2.3.1 Socio-demographics and government systems

Indonesia is the largest archipelago country that consists of five main islands and an estimate of 16,700 smaller islands across 1,916,906 km^2 (**Figure** 2.3).[147] Indonesia is a lower-middle-income country in Southeast Asia and the world's fourth-most populous country. In 2021, with a 1.2% population growth rate, the total population had reached 273 million people, with 60% living on Java Island.[147] The diverse Indonesian population consists of 1,331 ethnic groups, speaking more than 700 local dialects.[148] Jakarta is the capital of

Indonesia, located on the northwest coast of Java Island. There are 37 provinces and 514 districts in Indonesia.



Figure 2.3 Map of Indonesia

Indonesia is a constitutional republic led by a president and has a decentralised governance structure. Indonesia underwent a ‘big bang’ decentralisation in 1999, and effective since 2001, regional (provincial and district) governments have more significant power and important roles in local policy and decision-making.[149] This system also applies to the healthcare system, including the authority over hospital systems. Provincial and district governments have authority over the service management and budget allocation of the government hospitals at their respective tiers. The MoH has a coordination role in the execution and monitoring of the national health

programmes‡ and, when necessary, provides technical assistance to healthcare institutions (including hospitals) at the provincial and district levels (**Figure** 2.4).[149]

2.3.2 Healthcare organisation and financing

For-profit or private hospitals are Indonesia's most prominent curative providers, accounting for 65.4% of all hospitals in 2020.[150] In the 1960s, the national government started to allow the establishment of for-profit hospitals due to the shortage of public funds and as a response to the increasing demands for better healthcare services. Between the 1960s and 1990s, public health insurance was limited to civil servants, military personnel, and workers in formal unions. So, out-of-pocket payments became the largest portion of health expenditures.[149]

In 2014, the Indonesian government introduced the national health insurance scheme called *Jaminan Kesehatan Nasional* (JKN).[149] The JKN scheme adopted the concept of universal health coverage to provide equitable healthcare access for all people.[149] Since JKN's introduction, out-of-pocket spending has decreased from 51.6% in 2012 to 32.1% in 2019.[150] By 2021, 84% of the population had JKN coverage,[151] and 88.3% of hospitals provided health services under the JKN scheme.[152]

‡ Five national health programmes in Indonesian hospitals assessed in hospital accreditation (2022) are maternal and neonatal health, tuberculosis, HIV/AIDS, nutrition (with the main focus on stunting and wasting), and family planning.

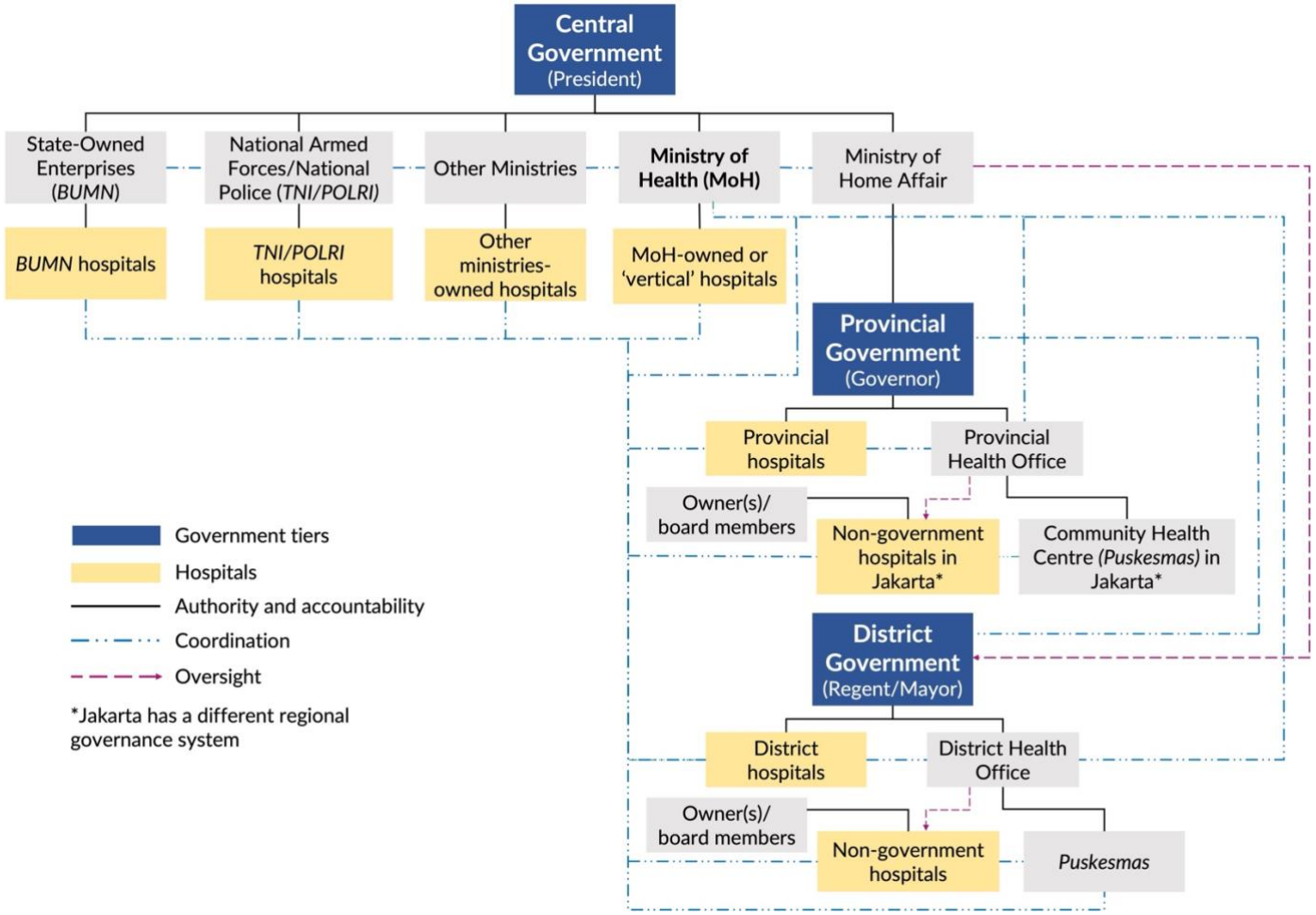


Figure 2.4 Indonesia's decentralised healthcare system

JKN applies two payment schemes: capitation and non-capitation. Capitation, or prospective payment, is applied for primary healthcare services, covering payments for consultation, basic medical procedures, and pharmaceuticals. Non-capitation payment, called Indonesia Case-Based Groups, or INA-CBGs (the term JKN uses for diagnosis-related groups) applies to all hospital services, for both outpatients and inpatients. Under the non-capitation payment scheme, hospital expenditures are reimbursed after service delivery. By law, healthcare centres operated by governments, including hospitals, are mandated to apply the JKN scheme. Private providers may join the scheme, subject to review and qualification.[153]

To guide JKN implementation, the MoH released a national formulary that provides a list of drug choices based on clinical indication, and drug availability based on healthcare tiers (primary, secondary, and tertiary care). Tertiary hospitals, which serve as referral centres, have the most comprehensive drug options, including antibiotics, whereas lower-tier hospitals have fewer options. There were also antibiotics not listed in the most recent (2019) formulary, including colistin.[154]

The JKN scheme offers ample benefits in health services, yet there are some challenges experienced by hospitals and healthcare providers within this scheme. In recent years, studies in various hospital types (public and private, different healthcare tiers) have discovered problems with rejected payment claims and delayed reimbursements. In 2018, a public hospital, for example,

had up to 21% of pending monthly reimbursements for payment claims among inpatient cases.[155] Another study assessing JKN claims among all hospitals applying the JKN scheme for one year between 2017 and 2018 found that among 57,475 claims, 40% were not reimbursed within a month.[156] These circumstances influenced hospital cash flow and operations, including delayed salary payments.[155,156]

2.3.3 Hospital classification

In Indonesia, hospital services are dominated by the private or non-government sectors. In 2020, there were 2,985 hospitals with a total of 379,548 beds operating in Indonesia,[150] classified based on service provision (82% general, 18% specialised), service management (34.6% public, 65.4% private), ownership (36.5% government, 63.5% non-government), and range of medical services (**Table** 2.2). Most government hospitals were owned by district governments (62.3%).[150]

In terms of hospital healthcare providers, in 2020, there were a total of 817,145 providers, mainly nurses (50.8%). General practitioners (GPs) and specialists/consultants only accounted for 4.3% and 4.6%, respectively. Most laboratories (83%) were also privately owned.[150]

Table 2.2 Hospital classification in Indonesia

Hospital classification	N=2,985 [a]	Characteristics
Service provision		
General	2,449 (82)	The hospital provides healthcare services covering medical, nursing, midwifery, medical support services,

Hospital classification	N=2,985 [a]	Characteristics
		and non-medical services (pharmacy, information and technology, forensics) for all types of health concerns and diseases.
Specialised [b]	536 (18)	The main service is based on one particular field or type of disease based on scientific discipline, age group, organ, or type of disease. This hospital type can provide other medical services outside of the specialised service with a maximum of 40% of total inpatient beds.
Service management		
Public	1,032 (34.6)	Healthcare services are non-profit.
Private	1,953 (65.4)	Healthcare services are for-profit.
Ownership		
Government	1,094 (36.5)	The hospital is owned by and under the authority of its respective government tier or government agency.
• Ministry of Health	35 (3.2)	
• Provincial government	150 (13.7)	
• District government	682 (62.3)	
• Indonesian National Armed Forces/ Indonesian National Police	166 (15.2)	
• State-owned enterprises and other ministries	61 (5.6)	
Non-government	1,891 (63.5)	The hospital is owned by either a corporate, religiously affiliated organisation, an individual, or a group of individuals.
Range of medical services		
Type A	60 (2)	The hospital has at least 250 inpatient beds for the general hospital and 100 beds for the specialised hospital. A general hospital provides at least four (4) basic specialties[c], twelve (12) other specialties[d], five (5) medical support specialties[e], and thirteen (13) subspecialties[f].

Hospital classification	N=2,985 [a]	Characteristics
Type B	436 (14.6)	The hospital has at least 200 inpatient beds for the general hospital and 75 beds for the specialised hospital. A general hospital provides at least four (4) basic specialties, eight (8) other specialties, four (4) medical support specialties, and two (2) subspecialties.
Type C	1,550 (51.9)	The hospital has at least 100 inpatient beds for the general hospital and 50 beds for the specialised hospital. A general hospital provides at least four (4) basic specialties and four (4) medical support specialties.
Type D	877 (29.4)	The hospital has at least 50 inpatient beds and at least two (2) basic specialties for the general hospital. There is no type D for a specialised hospital.
Not determined yet	62 (2.1)	

Data are expressed in number (percentage).

a. Total number of hospitals in 2020.[150]
b. Based on 2020 report,[150] there were 14 types of specialised hospitals: mother and child, cardiovascular, kidney, lung/chest, infectious disease, surgery, orthopaedics, brain, cancer, eye, head neck ear nose throat (ENT), dental and oral, psychiatry, and drug addiction.
c. The basic specialties comprise of internal medicine, paediatrics, surgery, and obstetrics/gynaecology.
d. Other specialties comprise of eye, ENT, neurology, cardiovascular, dermato-venerology, psychiatry, pulmonology, etc.
e. Medical support specialties comprise of anaesthesiology and intensive care, medical rehabilitation, radiology, and laboratories (clinical pathology, pathology anatomy, clinical microbiology, clinical parasitology).
f. Subspecialties comprise of 1) surgery sub-specialisation: digestive, oncology, vascular; 2) internal medicine sub-specialisation: gastroenterology-hepatology, tropical and infectious disease; and 3) paediatrics sub-specialisation: neonatology, emergency and intensive care.

Chapter 3
Methodology

In this chapter, I present the methodology of my research, which comprises the approach to inquiry, the study setting, theoretical approaches, quantitative data collection, and qualitative data collection.

3.1 The approach to inquiry

The objectives of this research are to assess the patterns and quality indicators of antibiotic prescribing for hospitalised patients; to explore the contextual social-cultural factors influencing antibiotic prescribing practices; and to explore contextual factors influencing antibiotic optimisation strategies through AMS programmes in Indonesian hospitals. To achieve these objectives, I used mixed-methods research (MMR), an approach to collecting and analysing quantitative and qualitative data in response to hypotheses and research questions. Creswell & Plano Clark[157] divided MMR into three designs based on the research intention: convergent, explanatory sequential, and exploratory sequential (**Table** 3.1). In this research, I used an explanatory sequential design.[157,158]

Table 3.1 Mixed-methods research designs

Design	Description
Convergent	The research uses parallel concepts and constructs of quantitative and qualitative methods. The intention of this design is to compare the quantitative and qualitative results and to provide complementary data that harnesses the strengths and offsets the weaknesses of both quantitative and qualitative methodologies.
Explanatory sequential	The research begins with the collection and analysis of quantitative data. Then, the specific results are followed up with subsequent qualitative data collection to help explain the quantitative results. The intention of this design is for the qualitative results to explaining the quantitative results.
Exploratory sequential	The research starts with collecting and analysing qualitative data, which is then used to create a hypothesis, an approach, or a tool that will be tested quantitatively. The intention is to develop and apply quantitative measures, tools, or variables that are grounded in the qualitative data. Therefore, the quantitative measures are based on the specific features of the research setting.

An explanatory sequential design (**Figure** 3.1) starts with a quantitative approach, followed by a qualitative approach. The quantitative approach in this research has adopted the positivism paradigm: one singular reality that can be identified and measured which takes an unbiased perspective, and maintains distance between the researcher and research subject.[159] My first research objective is to objectively assess the patterns and quality indicators of antibiotic prescribing. Therefore, quantitative methodology is the appropriate approach to addressing this objective. I selected a descriptive cross-sectional quantitative design using a point prevalence survey (PPS) as the method of data collection (further elaborated in section **3.4.1**). The PPS

results (presented in **Chapter 4**) provided numerical results on the prevalence of antibiotic prescribing patterns and quality indicators. However, they could not explain the 'why' and 'how' of the results.

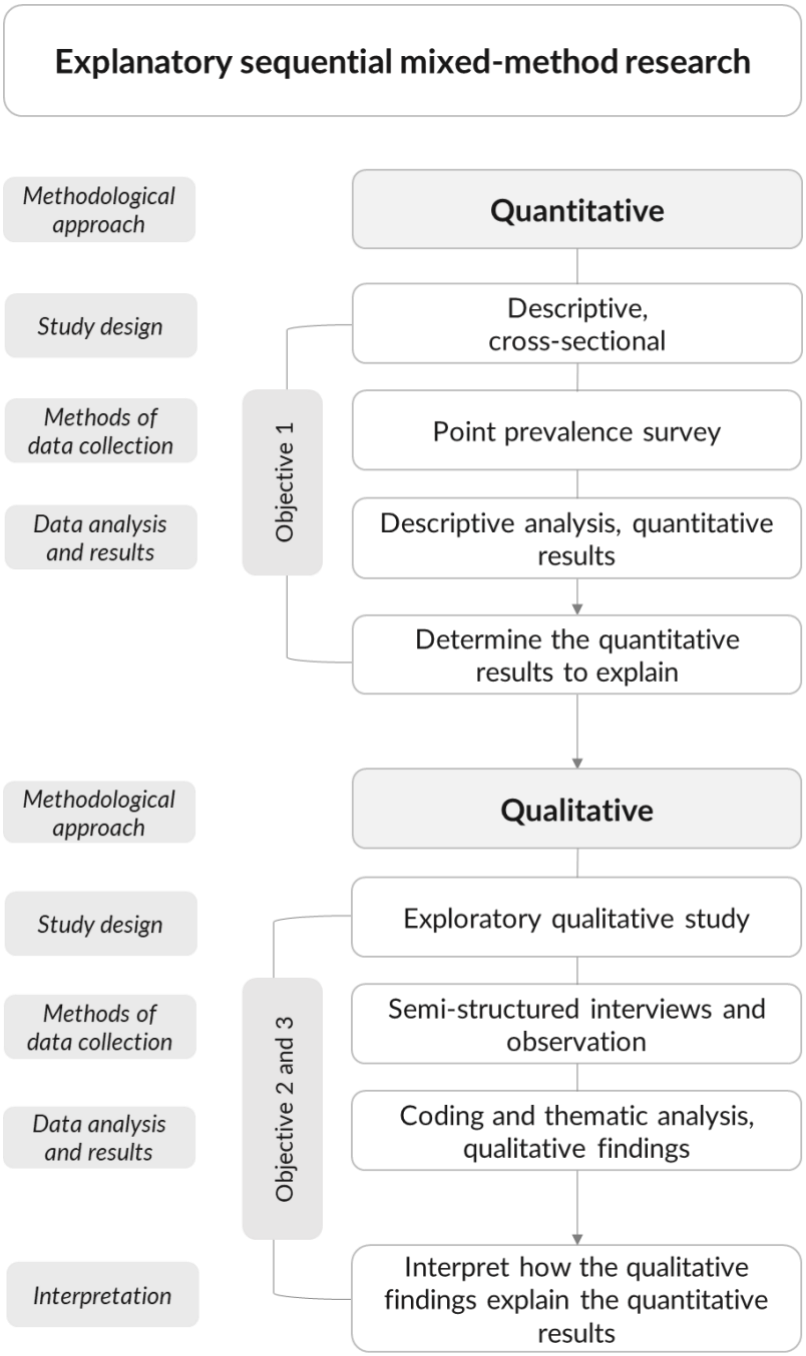


Figure 3.1 Explanatory sequential mixed-methods research design

Therefore, to address my second and third objectives, I followed-up on the PPS results using a qualitative approach. I adopted a naturalistic paradigm, which holds that multiple realities influence practices and that all aspects of the realities are interconnected.[160] This paradigm underlines the exploration of social-cultural contexts and dynamics that influence antibiotic prescribing practices and the factors that influence antibiotic optimisation strategies through AMS programme implementation. I chose an exploratory qualitative approach, employing semi-structured interviews and observation as the data collection methods. The naturalistic approach enables observation of people in their own territory and interacting with them in their own language on their own terms.[161] By using this design, I was able to explain the 'how' and 'why' of the quantitative findings through the findings of the qualitative data.

3.2 Study setting

This research was conducted in six hospitals in Jakarta, the capital of Indonesia. Jakarta is located on the northwest coast of Java Island and has a land area of 664 km^2. In 2020, Jakarta was recorded as the city with the densest population in Indonesia, with 16,000 people per km^2.[150] In 2022, Jakarta was ranked 29th among the global megacities, with a total population of 11 million people.[162] In 2020, there were a total of 193 hospitals in Jakarta (32.1% government and 67.9% non-government), accounting for 6.5% of all hospitals in Indonesia.[150]

Six hospitals, located in different geographic areas of Jakarta (**Figure** 3.2), participated in this research. These hospitals were purposively sampled to achieve diversity in geographic location, patient population (socio-economic status, disease patterns), hospital size, healthcare sector, and healthcare level. The participant hospitals were pragmatically selected based on existing collaborations, site willingness, and availability of study resources. The hospital samples comprised three public and three private hospitals, five general and one specialised hospital, two tertiary and four secondary level hospitals, four small (fewer than 500 inpatient beds) and two large (500 or more than 500 inpatient beds) hospitals.



Figure 3.2 Study sites

I collected relevant hospital information (**Table** 3.2) and relevant data regarding AMS programme implementation using an adopted instrument of the CDC's core elements of hospital AMS programmes[119] (**Chapter 2**, section **2.2.2.1**). The results of the core elements of hospital AMS programmes are presented in **Chapter 6**, section **6.1**. These data were collected at the beginning of the PPS data collection in each hospital, between March and August 2019.

Table 3.2 General information of the participant hospitals

Characteristics	Hospital					
	1	2	3	4	5	6
Service provision	General	General	General	Specialised	General	General
Level	Secondary	Tertiary	Secondary	Secondary	Tertiary	Secondary
Service management	Private	Public	Private	Public	Public	Private
Teaching hospital [a]	Yes	Yes	Yes	No	Yes	No
JKN scheme	No	Yes	Yes	Yes	Yes	No
Inpatient beds	159	767	300	145	853	134
Doctors [b]	101	255	143	55	1240	102
In-house microbiology services	Yes	Yes	Yes	Yes	Yes	Yes
On-site pharmacy opens 24/7 [c]	Yes	Yes	Yes	Yes	Yes	Yes
Computerised medical records	No	No	No	No	Yes	No
AMS programmes and team/ committee	Yes	Yes	Yes	Yes	Yes	Yes

Abbreviations: AMS, antimicrobial stewardship; JKN, *Jaminan Kesehatan Nasional*/national health insurance.

a. Had visiting interns and/or residents during the study period.
b. Doctors from all departments and hierarchy levels who prescribe antibiotics.
c. Serving prescriptions from inpatient and emergency wards.

3.3 Theoretical approaches

To address the thesis objectives, I explored the relevant theoretical frameworks and social theories. There are two validated theoretical frameworks that can aid in understanding 'the influence of practice' derived from the COM-B model (capability, opportunity, motivation, behaviour model): the Theoretical Domains Framework[163] and the Behaviour Change Wheel.[164] The main purpose of these frameworks is to identify behavioural determinants of practice (e.g., knowledge, motivation, beliefs, etc.)[163] to later inform targeted behaviour change interventions (e.g., restriction, persuasion, etc.).[164] In the context of implementation research, these frameworks are useful to elaborate on the undesirable (or desirable) behaviour elements in detail in order to facilitate researchers in designing a targeted intervention. However, both frameworks predominantly focus on individual aspects of practice.[163,164]

In **Chapter 2**, the existing findings from the literature, summarised in a conceptual framework (**Figure** 2.1), showed that antibiotic prescribing practice is influenced not only by individual behavioural determinants but also by broader multilevel and multidimensional social aspects, including cultural, economic, political, and ecological factors. This framework supports an exploration of how various social elements are interwoven within complex health systems. To explain how social-cultural factors influence antibiotic prescribing and AMS programmes implementation in hospitals I drew on four theories: 1) the sick role concept, 2) the theory of practice, 3) the social identity theory, and 4) the complex adaptive system. The first three theories

were selected at the beginning of the research, when I conducted the review of the literature. These theories explicitly and implicitly emerged in previous studies. I added the last theory during the final stage of data analysis to help explain the interaction between different factors influencing antibiotic prescribing and antimicrobial stewardship implementation.

3.3.1 Sick role

Talcott Parsons (1951)[87] introduced the concept of the sick role, which refers to the experience surrounding illness and the subsequent rights and obligations of the sick person (patient) and physician. From the perspective of a social system, health is defined as the functional needs of individuals as members of society. Therefore, illness involving temporary withdrawal from work is a potential threat to the functioning of the whole social system and positions the sick person into a relationship of dependency in which one needs to be taken care of by others. Accordingly, medical practice has a social function to maintain the optimum health of society.[87]

According to this theory, both the patient and the physician have two rights and two obligations. During sickness, a patient has a right to be exempted from one's societal responsibility, which has to be legitimised by a physician. The sick person also has a right not to be held accountable and to be taken care of. These rights were followed by two obligations: that the sick person must have a desire to 'get well' and thus seek technically competent medical help.[165] These two obligations serve as a bridge to the physician's rights and

obligations. A physician has the obligation to do everything possible to support the early recovery of the patient and to manage the illness in an objective and rational way.[87] These imply that the motivation for treatment should be centred around the patient's well-being and not personal or commercial interests.[166] In return, the physician, who is the expert in his field, has the right to work independently and to have access to private information and often the body of the sick person.[87]

This concept has been criticised for its applicability across a wide range of illness severity and medical practice. It was deemed to have the most applicability for sick people who require institutionalisation.[166] Moreover, it overemphasised the role of the physician while neglecting the immediate social support system, for example, family. Furthermore, the sick role concept may not be aligned with the patient-centred approach, where physician and patient share the best available evidence and options in clinical decision-making.[167]

Despite the fact that this patient-centred approach is fundamental to modern medical practices, it raises the question of its applicability in certain cultures and contexts. For example, in Pakistan, a physician is regarded as an authority figure, often being referred to as a 'senior family member' (mother, father, uncle, auntie), and a patient as the 'younger family member.' In this cultural context, the patient must respect or agree with the physician's decision.[168] Another example is a multicountry study among cancer patients in

Bangladesh, China, India, Sri Lanka, and Viet Nam found that 40-60% of patients were not involved in the treatment decision-making process, yet 73% agreed that the decision made by others (i.e., the physician, family members) was concordant with their preference.[169]

Therefore, the sick role concept is potentially still relevant in some settings and contexts, including Indonesia. Further, the sick role concept, as it mainly refers to illness that requires hospitalisation, also fits with the context of antibiotic prescribing practices in hospitalised patients, which include physicians' decision-making regarding patient treatment and the perceived patient expectation to immediately 'get well'.

3.3.2 Theory of practice

In many parts of the world, unnecessary and suboptimal antibiotic prescribing persists despite awareness of the AMR threat and efforts to improve practices, including the implementation of AMS programmes in hospital settings. To understand this disjunction, I included Pierre Bourdieu's theory of practice in this thesis. This theory provides an understanding of the dynamics of practice and how social order is reproduced. To understand practice, notions of *habitus*, *capital*, and *field* are intricately connected and cannot be separated: [(habitus) x (capital)] + field = practice[170]

Habitus is an embodied reality obtained through internalisation of external (social) concepts that later produce collective patterns of thoughts, beliefs, and actions without necessarily requiring rational or conscious reasoning.

Habituation is formed through social interactions and tends to persist in the future through the repetition of similarly structured practices.[171] *Habitus* is inflected by the forms of *capital* and functions as accumulated *capital*.

Capital refers to a range of resources or possessions that are acquired or inherited and displayed by an individual. Some examples are economic assets, knowledge, educational credentials, and social networks. *Capital* is part of the structuring process of *habitus* and is used by individuals within the *field* as a tool for gaining dominance and power.[171]

Field refers to a system (e.g., medical, judicial, academic, etc.) of social position where power relations play out within a set of rules and tend to be experienced as taken for granted (termed 'doxa'). An individual's position within the *field* is determined by one's *habitus* and *capital*. In a *field*, individuals engage, confront, or defend each other according to their position in the structure of the *field*. Individuals make adjustments based on the demands of the *field*, called 'feel for the game', which is produced by the experience of the game.[171]

A study by Broom *et al.* (2014),[88] applied this theory with regard to antibiotic prescribing practice in the hospital context. The findings of this study showed that antibiotic prescribing is less governed by AMS initiatives or therapeutic guidelines than by the practices produced within this particular *field*. The 'played game' of antibiotic prescribing is oriented towards immediate risk reduction, i.e., decreasing mortality and managing time pressures. Therefore,

antibiotic overtreatment prevails, as demonstrated by the practice of broad-spectrum antibiotic prescribing and initiating antibiotics without clear rationale. Antibiotic prescribing is also influenced by *habitus*—habitual antibiotic use of reproducing and internalising 'the way others do it,' which resonates with 'doxa'—the rules of the game. Antibiotic prescribing is not simply imposed on the lower player (prescriber) in the hierarchy, but rather determined by the strength of social *capital*—the norms and routines in the setting.[88]

3.3.3 Social identity theory

Social identity theory is a social psychology concept developed by Henry Tajfel and colleagues in the 1970s. Social identity is defined as the self-concept of a person as a member of social groups, mainly those who share the same values.[172] This theory examines group processes and emerges from an active process of categorisation or self-grouping, which corresponds to and underpins the distinguishing features of group behaviours.[173] The social identity theory can explain how and why elements of practice are learned.

In the context of medical training, during the apprentice phase, students (medical interns and residents) not only learn about theories, practices, and ethics in medicine, but they also have to adapt to the medical culture to obtain 'identity.'[174] Medical culture has developed and persists within a closed institution in which certain practices frequently go unquestioned, called the hidden curriculum. The hidden curriculum, encompassing emotional neutralisation, ritualised professional identity, and acceptance of hierarchy, is

instrumental in the enculturation process. Students learn how to cope with the group practices and norms to be accepted in the group, including refusal to challenge the practice of senior doctors to ‘survive in the game’.[174]

Obtaining social identity is followed by displaying the identity to fit the group prototype. Once the students have finished the training, obtained the group identity, and become members of the medical profession, it is important to display the performative elements of the identity. Doctors of different professions identify with their professional groups to different extents. This influences different attitudes among different medical professions.[173] For example, as described in **Chapter 2**, an ethnography study in a teaching hospital in the UK found different norms and cultures displayed by doctors in medicine (collectivist culture) and surgery (individualistic culture).[104] The self-categorisation explained how individuals conform to or enact group norms to correspond to the appropriate self-defining group prototype.[172]

3.3.4 Complex adaptive system

Complex adaptive system (CAS) is a complex system that has the capacity for adaptation where multiple agents interact and are interconnected in a dynamic, interdependent, and simultaneous manner, affecting and shaping the system.[175] CAS is the opposite of traditional linear ‘cause and effect’ models, which assume that addressing a past event or problem would result in predicted future outcomes.[175]

Most complex systems and organisation theorists agreed on the following four characteristics of CAS.[175–177]

1. Self-organisation and emergence

   Self-organisation is a process in which agents and system components constantly modify their behaviours to accommodate changing internal and external conditions.[176,177] *Emergence*, which is the appearance of results like new structures, behavioural patterns, or processes that are unexpected and unanticipated from the components that formed them, follows the *self-organisation* process.[177] *Emergence* is the core of CAS, which is an innovative pathway of governance. Therefore, the *emergence* of CAS results more from a *self-organisation* process than from a linear external control.[175–177]

2. Non-linear behaviours of agents

   CAS is characterised by the presence of a large number of interdependent agents and forces that engage in a non-linear interaction with one another. Small changes in variables can have a small impact at one time but a large impact in other circumstances.[175,177]

3. Unpredictable *emergence*

   Because of the multiple nonlinear interactions and feedback loops among the agents and forces, *emergent* properties cannot be predicted from the individual parts of a system.[175]

4. A resilient system

   CAS is resilient or robust, demonstrating the capacity to adapt to new information or conditions. Complex systems possess a spectrum of

> patterns that allow organisations to thrive in different conditions. In a case of disruption, the other agents or components are able to respond effectively to the altered agents or components due to the interdependency and interconnectedness between these elements.[175]

In the context of antibiotic prescribing, as outlined in section **2.2** of the study conceptual framework, there are multilevel social-cultural factors that are interconnected and drive antibiotic prescribing. Based on the concept of CAS, these factors form non-linear interactions and feedback loops so that a change in one part of the system can affect how the other parts of the system respond (**Figure** 2.1).

3.4 Quantitative data collection

3.4.1 Point prevalence survey

3.4.1.1 The justification for selecting the point prevalence survey method

The first objective of my thesis is to assess the patterns and quality indicators of antibiotic prescribing. I aimed to investigate 1) the prevalence of antibiotic use based on antibiotic class and name, reason for prescribing (diagnosis), clinical indication, and the AwaRe classification; and 2) the quality indicators of antibiotic prescribing, including compliance with the local antibiotic guidelines, culture-informed prescription, and documentation of reasons for prescribing and planned duration of prescriptions.

In Indonesia, the widely used quantitative method to measure antibiotic consumption in hospitals is the defined daily dose (DDD). DDD measures the average maintenance dose per day for a drug used for its main indication.[178] DDD cannot be used to assess antibiotic consumption in neonates and paediatric patients, and therefore, the consumption measurement for these population groups uses the days of therapy (DOT) method.[178] One DOT represents the use of a single agent on a given day, regardless of the number of doses.[179] The disadvantage of both methods is that they cannot provide patient-level antibiotic use or a realistic picture of the quality of antibiotic prescribing in day-to-day clinical practices.[179] Furthermore, interpreting DDD estimates can be difficult, especially when comparing across settings, because different studies or settings use different DDD indicators[§].

The Gyssens method has been used since the 2000s by hospitals in Indonesia to assess the quality indicators of antibiotic prescriptions. The Gyssens method evaluates the quality of individual prescriptions, which must be performed by at least two infectious disease experts (**Table** 2.1). Therefore, this method can be time-consuming (60–120 minutes per case or patient), is prone to the experts' subjective judgement, and is unlikely to be performed in hospitals where infectious disease experts are absent.[180] In Indonesia, DDD and the Gyssens method have been widely used as

[§] Some of the DDD's indicators: DDD per 1000 inhabitants per day, DDD per inhabitant per year, DDD per 100 bed-days, DDD per patient, and DDD per patient-days.

complementary methods to assess antibiotic consumption and the quality of antibiotic prescribing.[36]

The point prevalence survey, or PPS methodology, has been developed to bridge the limitations of the two methods above (**Table** 2.1). The PPS is able to measure both prevalence and patterns, as well as quality indicators, in an objective manner. PPS is less time-consuming,[180] which allows repeated data collection for surveillance purposes to monitor trends over time and the effectiveness of stewardship strategies.[181] PPS uses a standardised protocol that can be followed by trained medical staff, facilitating homogenous and objective data collection. The PPS method can also collect different levels of data, i.e., hospital-, ward-, patient-, and drug-level data. Therefore, in my research, I selected the PPS method to assess the patterns and quality indicators of antibiotic prescribing.

3.4.1.2 Design and setting

Following the Global-PPS protocol,[182] I conducted a cross-sectional survey of antibiotic use in all hospitalised patients across a sample of six hospitals in Jakarta (see section **3.2**) between March and August 2019. I also included additional items from the WHO PPS data collection tool.[54] PPS is a 'one-day' survey to collate medical record data on 1) antimicrobial prescriptions (type, dose, route, diagnosis, and indication) by inspecting treatment sheets; 2) patient demography information (sex, age, admission date); 3) relevant medical history (hospitalisation and surgery history); 4) comorbidities; 5)

relevant biomarkers (white blood count (WBC), c-reactive protein (CRP), procalcitonin); and 6) microbiology (bacterial culture) order and test results.

At the ward level, I included all inpatient wards (or departments). Prior to the survey, I made a ward list for each hospital to provide information related to the ward type (adult, paediatric, or neonatal) and main activity (medicine, surgery, intensive care, or mixed). There were four types of wards based on departments: 1) adult departments (medical wards including general, haemato-oncology, transplant, and pneumology; surgical wards; and intensive care unit (ICU)); 2) paediatric departments (medical wards, including general, haemato-oncology, transplant, and pneumology; surgical ward; and paediatric intensive care unit (PICU)); 3) neonatal departments (medical wards and neonatal intensive care unit (NICU)); and 4) other departments (other ward types not included in the previous list, e.g., adult neurology, adult dermato-venerology, etc.).

3.4.1.3 Population and sample size

The research population (numerator) was all inpatients (adults, children, and neonates) admitted to the ward before 8 a.m. who received ≥1 antimicrobial (antibiotics and other anti-infective agents, as presented in section **4.2**) on the survey day or surgical prophylaxis within 24 hours prior to the survey. The eligible patients were those who received antimicrobial agent(s), even if the drug was not administered on the survey day.

The denominator of the research population was the total number of admitted patients before 8 a.m. in the surveyed wards, including healthy infants in the case of maternity wards and those who had a bed in the ward but were currently in the operating room, recovery room, or diagnostic suite, e.g., undergoing haemodialysis, a CT (computed tomography) scan, or an MRI (magnetic resonance imaging) scan during the survey.

Patients in emergency and day-care wards, outpatient clinics, and those who were discharged ≤24 hours prior to the survey were excluded, including: 1) healthy mothers and babies in a maternity ward who will be discharged within 24 hours of admission following successful delivery; and 2) day-care haemodialysis and surgical patients.

3.4.1.4 Instrument

I, through a consultation process with my supervisor (RLH), developed paper-based data collection forms (DCFs) comprising three paper-based survey forms: ward, patient, and treatment sections (**Appendix 1**), modified from the Global-PPS[182] and the WHO PPS.[54] To support the enumerators (people completing the survey) and to ensure homogeneity of the collected data, I developed a data completion guideline that describes the definition of each item or question in all three DCFs. All DCFs were written in English and recorded the identification code of the hospital, ward, enumerator, and survey date.

Ward form

The following variables were recorded in the ward form: 1) ward name based on the name assigned by the hospital; 2) department type (medical, surgical, mixed medical-surgical, and ICU); 3) patient population (adult, neonatal, paediatric, and mixed adult-neonatal-paediatric); 4) total number of patients in the surveyed ward admitted before 8 a.m.; and 5) total number of beds in the surveyed ward present by 8 a.m.

Patient form

The patient form captured patient demographics, relevant laboratory test results, and the total antimicrobial treatment. The recorded patient demographics included the following variables: patient medical record identification number, admission date, the use of the JKN scheme, age and age category, weight, sex, surgery history in the past 90 days based on the National Healthcare Safety Network (NHSN) list (**Appendix 2**), hospitalisation history in the past 90 days, and transfer from another healthcare facility (hospital, non-hospital).

This patient form also recorded the relevant risk factors and comorbidities. These include patient catheter use (central vascular, peripheral vascular, urinary, intubation), comorbidities (malaria, tuberculosis, HIV, including documentation on CD4 and antiretroviral, malnutrition, chronic obstructive pulmonary disease, and diabetes mellitus), and McCabe score (a simple subjective method to assess underlying illness severity and classify patients

according to a prognosis of rapidly fatal (<1 year), ultimately fatal (1–4 years), and non-fatal (>5 years) (**Appendix 3**).

Relevant laboratory test results were recorded in this patient form. They include 1) infection-related biomarkers (white blood count, C-reactive protein, and procalcitonin) before antibiotics were started and the most recent values; 2) the most recent biochemistry (urea, creatinine, AST (SGOT), and ALT (SGPT)[**]); and 3) bacterial culture samples (sampling date and result reporting date, specimen type, and if the result was positive, the name of the microorganisms and susceptibility result). A photograph of all culture and susceptibility test results was taken with the personal identifiers in these microbiology reports removed. The total of prescribed antimicrobial drugs received by the patient was also captured in this form.

Treatment form

One patient could have more than one treatment form because one treatment form only records one antimicrobial drug received by the patient. For every treatment form, the recorded antimicrobial data were: 1) the generic name; 2) a code based on the 2018 WHO Anatomical Therapeutic Chemical (ATC) classification system;[183] 3) start date of antimicrobial administration; 4) a single unit dose per single administration; 5) a unit; 6) a dose per day; 7) route of administration; 8) intravenous-oral switch (if the route is oral); 8) diagnosis

[**] AST (SGOT), aspartate aminotransferase (serum glutamic-oxaloacetic transaminase); ALT (SGPT), alanine aminotransferase (serum glutamic-pyruvic transaminase*)*

(what the clinicians aimed to treat or the underlying diagnosis for antimicrobial administration) and the diagnosis code (**Appendix 4**); and 9) type of indication.

The types of indications were classified as follows: 1) CAI if symptoms were presented on admission or started less than 48 hours after admission; 2) HAI if symptoms started within or more than 48 hours after admission; 3) medical prophylaxis; 4) surgical prophylaxis, classified as single-dose, one-day, or longer than one day (>24 hours); 5) other, including pulmonary tuberculosis, HIV/AIDS (e.g., as prophylaxis for pneumocystis carinii pneumonia (PCP) and for neurotoxoplasmosis), and as motility agent; 6) unknown, was denoted when the indication is unclear.

The treatment form also captured data on the following quality indicators of antibiotic prescribing: 1) documentation of reason(s) for antimicrobial use, stop/review date, and duration of planned treatment or prophylaxis; 2) availability of and compliance with the local hospital antibiotic guideline in regard to drug choice[††] (if not available, this item was recorded as 'not assessable'); and 3) treatment type (targeted if the antimicrobial is prescribed in response to microbiology results and empirical for any other therapy or

[††] The assessment of guideline compliance was only for drug choice because not all guidelines (within and between hospitals) provided detailed information about the right dose, route, frequency, and length of treatment for certain clinical syndromes.

prophylaxis). I also developed a checklist for the enumerators to ensure data completeness in each DCF.

3.4.1.5 Data collection and management

I conducted the data collection with a research assistant (a medical doctor) based in OUCRU-ID. Depending on the hospital size, we were assisted by one to four trained enumerators (all medical doctors) who were based in OUCRU-ID, hospital-based general practitioners, and an internal medicine resident (only in one tertiary hospital). The research assistant and all enumerators received a one-day training and the DCFs' completion guideline.

One month before the PPS was started, I collected relevant hospital information (number of inpatient beds and ward type) to plan the data collection schedule and estimate the duration of data collection in each hospital. I also collected a copy of all relevant hospital antibiotic guidelines (if they were available) for the purpose of assessing the quality indicators of guideline compliance in the treatment form.

All wards of a single hospital were surveyed within 4 weeks, and each ward was completely surveyed within one day to minimise the effect of patient movements. The data collection was performed during the weekdays, except on national holidays.

On the survey day, I, the research assistant, and the enumerators arrived in the scheduled wards 30 minutes before 8 a.m. to inform the head nurse about the data collection activity. At 8 a.m., we first completed the ward form and

then continued to collect the data in patient and treatment forms. Any missing and/or unclear information, e.g., unclear writing, mismatch between diagnosis and antimicrobial treatment, or missing culture result, was clarified with the doctor in charge of the patient (a specialist or consultant), ward physician (a general practitioner), or ward nurse. All inpatient wards were surveyed only once on a single day in order to correctly calculate the denominator (number of admitted patients). Surgical wards (adult and paediatric) were surveyed on the day following the day when most elective surgeries took place or were planned. The purpose was to capture information about surgical prophylaxis in the previous 24 hours. For example, if a surgical ward mainly has operations planned on Tuesdays, the survey is performed on Wednesday. The daily data collection was concluded when the data collection of all eligible patients in the scheduled wards was completed.

The data from the paper-based DCFs was then entered into a study database (CliRes) by the research assistant. Later, a second person (one of the trained enumerators) performed a cross-check of the recorded data in the database. There were two stages of data verification. First, while completing DCFs in hospitals, any queries from the enumerators were directly consulted with me, and if I had a doubt, I consulted with my supervisor (RLH). Second, inconsistencies in the DCFs were checked against the source data in the medical records as needed. The collected data were securely saved in OUCRU-ID's data server, which could only be accessed by me and my supervisor (RLH).

3.4.1.6 Data analysis

Descriptive statistical analysis using Rstudio Version 1.3.1093 was performed to summarise the data, expressed as counts or percentages, by hospital, ward type, indication, and diagnosis. The analysis focused on antibiotics or antibacterials for systemic use (ATC code J01). J01 antibiotics were reported by drug names, chemical class (according to the 4th level of the WHO ATC classification), and the AwaRe classification.

3.4.1.7 Ethical considerations

I obtained two ethical approvals for this research: one from the research ethics committee of the Faculty of Medicine, Universitas Indonesia (1364/UN2.F1/ETIK/2018) and another from the Oxford Tropical Research Ethics Committee (OxTREC 559-18) (**Appendix 5**). I also obtained a written permit from all hospitals. The ethical approvals and hospital permits were applicable to all research components, both quantitative and qualitative. For the PPS data collection, the requirement for individual patient consent was waived.

3.5 Qualitative data collection

3.5.1 Justification for the qualitative data collection methods

In this research, I used semi-structured interviews (denoted as interviews) and observation as the qualitative data collection methods. The interviews in this research had the purpose of understanding people's perspectives on any topic of inquiry and allowed me, as a researcher, to capture the expressed

feelings and thoughts that cannot be obtained through observation.[184] Meanwhile, observation allowed me to encounter the first-hand experience of the studied phenomenon or practice in the participants' own territory and in the context in which people interact.[184] Observation bridges the gap between what is reported, i.e., through an interview, and what is actually done.[161] Observation also provides a context of reference for the observed dynamics, which is useful for asking probing questions in subsequent interviews.[184] Both methods were complementary, minimising the limitations of each method. In data analysis, the use of these two data collection methods helped me, as a researcher, to validate and triangulate the emerging findings from the other methods.[184]

3.5.2 Semi-structured interviews

3.5.2.1 Design and setting

All six hospitals participating in the PPS were included in the interviews. The data collection period was between January and October 2020, divided into two phases due to the COVID-19 pandemic. Phase 1 comprised face-to-face interviews conducted between January and March 2020 in three hospitals. Phase 2 comprised interviews conducted by online video call between June–July and September–October 2020 in two of the three remaining hospitals. One hospital withdrew from participating due to a high workload during the pandemic.

3.5.2.2 Participants

The interview participants were purposively selected among those who could provide rich information regarding decision-making in antibiotic prescribing and AMS programme implementation. I invited different types of participants to obtain different perspectives, 10–12 people from each hospital. The invited participants were doctors from medical and surgical departments, a clinical pharmacist, a clinical microbiologist, a representative of hospital management, the hospital AMS team leader or one of the senior members, and interns (medical students on the final year of clinical rotation or who had completed the rotation in at least three of the four major departments[‡‡]).

In addition to hospital-based participants, I also invited five national-level stakeholders who were involved in country-level AMR programme and nationwide AMS implementation. I also sought variation in terms of participants' stage of career, length of work in their current role, position in the department, and gender.

3.5.2.3 Instrument

The interview guides (**Appendix 6**) were developed in English based on the previous research of my supervisor (AB)[79,185] and the findings of relevant studies, including those that were conducted in similar contexts, such as hospitals in LMICs. I developed the probing questions based on the theories outlined in section **3.3**. I then translated the interview guides into Indonesian

[‡‡] Internal medicine, surgery, paediatrics, and obstetrics/gynaecology

after they were reviewed by the supervisors (RLH and AB). The Indonesian version was then back translated to English by an external translator to ensure the original meaning was detained.

The interview guides were piloted with five participants (an internist, a general practitioner, a clinical microbiologist, a clinical pharmacist, and an AMS leader) from non-participating hospitals that have similar characteristics to the participant hospitals. The purpose of this pilot was to obtain feedback about the clarity of the questions and the depth of the discussed topics.

The interview guides were aimed at exploring three main topics: perceptions of the AMR problem, decision-making in antibiotic prescribing, and AMS programme implementation. The first topic explored the perceptions of the AMR problem in the day-to-day (clinical) practice of the participants. The second topic explored antibiotic decision-making, with some probing related to drivers of antibiotic prescribing as found from the review of the literature (section **2.2.1**). The third topic explored the AMS implementation, including the usefulness of AMS, the facilitators and barriers of AMS programmes, and the impact of AMS programmes (section **2.2.2**).

3.5.2.4 Data collection and management

Access to potential participants was obtained through a ‘gatekeeper,’ who was either the hospital manager, a head of department, or the AMS team leader. This approach was requested by the participating hospitals. First, I discussed with the gatekeeper the characteristics of the desired participants,

as described above. Then the gatekeeper sent an invitation that I had formulated to the potential participants. Once the participants accepted the invitation and agreed to participate, the gatekeeper then sent their contact information to me. I and the research assistant followed-up to arrange the time and venue for the interview. For the national AMR stakeholders, I directly sent the invitation to the potential participants. I had no prior contact with the participants, except with a few participants who were also part of the observation (section **3.5.3.2**) and the gatekeepers, who were also included as the interview participants.

On the interview day, before starting the interview, I read the information for the participant about the study's objectives, confidentiality, and how the anonymous data would be handled. If the participant agreed, he or she signed a written consent (**Appendix 7**) to participate, including to audio-record the interview and to use the anonymised data for future approved research. For face-to-face interviews, all interviews were conducted in the hospital where the participants were working. For the online video call interview, I conducted the interviews from my home while the participants were at their home, hospital, or office.

The interview process was iterative. At the beginning of the interview, I briefly delineated the initial analysis of the aggregated PPS data from all participating hospitals. The aim was to provide context and evidence [of problems] from the Indonesian context to explore the 'why' and 'how' certain patterns and quality

indicators of antibiotic prescribing occurred. The interview was then conducted, with questions based on the interview guide and probing follow-up questions based on participant responses. During the interview, I also asked the interview participants about certain practices and phenomena that I found during the observation (section **3.5.3**), which preceded the interviews, to make sense of the observed practices.

One of the interview method's drawbacks is that participants may give social desirability answers or only report one side of the spectrum, such as all positive or all negative answers. Moreover, the interview participants in this research were invited by a gatekeeper, so there was a possibility that the gatekeeper only invited certain people who would give favourable answers. In order to minimise this potential bias, when I noticed this phenomenon, my strategy was to repeat the same questions in a different phrase later in the interview. The purpose was to verify whether the participant gave consistent answers. When asking sensitive topics or antagonising the participant, I used the 'devil's advocate' question approach in order to depersonalise the issue,[184] e.g., when asking about the economic drivers of antibiotic prescribing, such as incentives from the pharmaceutical industry.

I performed all the interviews in Indonesian. The interviews were audio-recorded, verbatim transcribed, and then translated to English. Some recordings were transcribed and then translated by a research assistant. I always checked the quality of all transcriptions and translations and made

revisions if necessary. I took field notes in all interviews to describe the physical setting, the non-verbal cues from the participants throughout the interview (e.g., gestures, facial expressions, and voice tone), and my own thoughts and feelings regarding the interview. Data collection was continued until no new findings emerged from the interviews.

All interviews were recorded using a voice recorder, not a smartphone or any device with an internet connection. The interview data (recordings, transcriptions, and translations) were stored in an anonymous manner using codes and securely saved in OUCRU-ID's data server, which could only be accessed by me and my supervisor (RLH) (see section **3.5.2.6** about confidentiality).

3.5.2.5 Data analysis

This section covers the data analysis of the qualitative approach, both interviews and observation. I used a thematic analysis approach using the following five steps: 1) data familiarisation; 2) thematic framework identification; 3) data coding into themes; 4) charting, rearranging coded data according to the thematic framework; and 5) data mapping and interpretation.[161] Data familiarisation consisted of reading and re-reading the data to identify initial themes or categories.

Because the interviews were interrupted due to the pandemic, I began familiarising myself with the data from the first three hospitals before resuming interviews in the next two hospitals. I systematically searched for recurring

themes and negative, atypical, and conflicting or contradictory cases. I then identified a thematic framework that drew on my understanding of the literature, study objectives, themes within the study instruments, and issues raised by the participants during interviews. The initial coding framework was subsequently refined as coding progressed. I coded all the data myself; hence, any changes to the coding framework were consistently incorporated as the data coding continued. Following coding, I conducted charting of the data in order to summarise the information while still retaining its context and essence. The Nvivo 12 software was utilised to manage and code data. I used the field notes to support the contextual analysis. The data analysis process was iterative, referring to the conceptual framework (**Figure** 2.1) and the four theories I included in this thesis (section **3.3**).

In order to ensure the credibility of the qualitative data analysis, I used the first three of the following four triangulation methods: 1) triangulation of *data sources*; 2) *analyst* triangulation; 3) *theory* triangulation; and 4) *methods* triangulation.[186] I used triangulation of *data sources* by comparing the consistency of information obtained through different qualitative methods, such as interviews and observation. I also compared the interview responses from different sources or participant types, e.g., doctors, clinical microbiologists, and national AMR stakeholders. Regarding *analyst* triangulation, I discussed the qualitative findings with the research assistant, and my supervisors (RLH and AB) to gain their perspectives on the interviews and observation data. Finally, I used four theories in the *theory* triangulation to

examine data from the perspectives of different participants concerning their roles within the research topic. For example, the sick role theory highlighted the role and obligation of doctors to ensure optimum clinical outcomes, which influenced their antibiotic prescribing practices. Meanwhile, the theory of practice highlighted the dynamics of practice, e.g., between senior and junior doctors, and how social order is reproduced, e.g., through the hierarchy in the medical profession. In this research, I did not use *methods* triangulation which involves collecting quantitative and qualitative data in parallel to answer the same hypothesis or research question.[186] The reason is that the purpose of the qualitative methodology in this research was to explain the quantitative findings.

3.5.2.6 Ethical considerations and confidentiality

Three ethical issues in qualitative research are anonymity, confidentiality, and consent to participate. Problems of anonymity may permeate every level of research, e.g., clues about the involved hospital and clues about the participants in the interview transcripts.[161] In this research, anonymity was ensured by concealing participants' names in any stored research data (recordings, transcriptions, and translations) and study reports and publications, and by inviting participants with similar roles or specialties from different hospitals to minimise the clue of hospital of origin. The only document that has the participant's name on it is the signed consent form, which is stored separately and coded differently from the research data.

The confidentiality of the interview was ensured at every stage of the research. Prior to the interview, I explained to the participant that the interview was going to take place in a closed, private room (including for online video interviews). On a few occasions, the face-to-face interviews were disturbed by a person entering the interview room unaware of the ongoing interview. In this case, I immediately paused the interview, and I resumed it only after the person had left the room. During the online video interviews, I was not able to verify that the interview participants were indeed sitting alone in a closed room. Under these circumstances, I took their words to mean that they were alone during the interview. As described in section **3.5.2.4**, the data was securely saved in OUCRU-ID's data server.

To compensate for the time spent on the interview, each interview participant was offered a monetary incentive (Rp. 150,000 or estimated US$ 10). For research ethical approvals, refer to section **3.4.1.7**.

3.5.3 Observation

3.5.3.1 Design and setting

My stance in the observation was 'peripheral membership role' or 'observer as participant.' This means that the observation activities were known to the observed participants, yet as an observer, I did not participate in the observed activities.[184]

My observation was focused on two main activities: antibiotic prescribing and AMS programme implementation. These two activities consisted of

observation related to the antibiotic prescribing decision-making process, the presence or absence of factors influencing the prescribing decision, contextual factors in the implementation of an AMS programme, and the behaviour of people in the observation settings.

My observations took place in the selected wards where antibiotics were mostly prescribed and in the venues or wards where AMS activities took place. In addition, I also observed the clinical rounds of the specialists, or consultants[§§], and residents. The observation activities were conducted between September 2019 and January 2020 in four of six hospitals—two public and two private hospitals.

3.5.3.2 Participants

Based on the PPS results, I applied a purposive sampling method to select the observed wards where antibiotics were most frequently prescribed. I purposefully chose to observe the clinical rounds of a specialist, consultant, or resident based on the specialties or departments that commonly prescribe antibiotics.

For the ward observation, I included the ICUs, adult medical-surgical wards, adult medical wards, adult surgical wards, and paediatric medical wards. The participants of the observation were any medical personnel involved in the ward's activities, including doctors, surgeons, residents, nurses, general

[§§] In the context of medical education and hospital systems in Indonesia, a consultant is referred to as a subspecialist.

practitioners, and medical interns. I also performed observations in the emergency wards, even though this type of ward was not included in the PPS data collection. The purpose was to understand the flow of decision-making in antibiotic prescribing from the first point of hospitalised patient presentation onward.

For the clinical rounds' observation, I selected participants from the specialties or departments that commonly prescribe antibiotics: internal medicine (including infectious diseases), surgery, and paediatrics. I considered variations regarding the prescriber's hierarchy, like resident, and specialist or consultant. During the ward observation, I found that certain doctors who were not from the department mentioned above, i.e., neurology, prescribed antibiotics for non-infection diagnoses. So, I added these prescribers as additional observation participants.

For AMS activity observation, the participants and settings were not predetermined because they were dependent on the activities performed during the observation period and the people who were involved in these activities.

3.5.3.3 Instrument

I used an adapted observation guide that contains six observation elements: the physical setting, the people in the setting, activities and interaction, conversation, the subtle factors (e.g., non-verbal communication, informal activities), and my own behaviour as an observer (**Table** 3.3).[184] The purpose

of the observation guide was not to limit the observation scope but rather to serve as a continuous reminder to myself to write in a descriptive manner and to minimise incomplete data collection based on the elements of interest that are important in the analysis. As I gained more familiarity with the studied phenomenon and its context, I adapted the questions in a more context-specific way.

Table 3.3 Observation elements

Elements	
1. The physical setting	– What is the physical environment (or ward) like? – What kinds of (antibiotic prescribing) behaviour is the setting designed for? For example, emergency versus non-emergency – What object, resource, technologies are in the setting (to help an optimal antibiotic decision)? – What is the anticipated behaviour towards the setting?
2. The people in the setting	– Who are in the scene (or ward)? – What are their roles (in antibiotic decision making)? – What are the relevant characteristics of the participants? – How people in this setting communicate (regarding antibiotic decision or AMS activities)? – What is the pattern and frequency of the communication (direct or indirect)? – What is the content of communication?
3. Activities and interactions	– What is the occurring activity? For example, clinical round, discussion between doctor and nurse or resident, doctor is ordering culture test, etc. – What is the definable sequence of activities, if any? – How do people interact with the activity? For example, pace of patient examination and antibiotic review. – How do people interact to one another? – How are people and activities connected? – What norms or rules structure the activities and interactions?
4. Conversation	– What is the content of conversation in this setting? – Who speaks to whom? – Who listens?

Elements	
	– Who initiates and ends the conversation?
5. Subtle factors	– Nonverbal communication and cues such as dress, physical space, hierarchy, voice tone during communication, and gestures. – Symbolic and connotative meanings of words. – Informal and unplanned activities. – What ‘does not happen’… especially if certain things out to happen or expected to happen.
6. Observer behaviour	– What is the observer role? – How is this role affecting the observation scene? – What thoughts are you having about what is going on?

3.5.3.4 Data collection and management

Observation data collection consisted of three stages: entry, data collection, and exit. At the entry stage, I introduced myself and my purpose for performing observation. At this stage, I described in brief the purpose of the observation, explained that I would make field notes during the observation, and stated that all collected data were anonymous. For the ward observation, I obtained permission from the head nurses. For the clinical rounds and AMS meetings or ward rounds, I obtained permission to observe from the respective participants. After obtaining verbal consent, I performed the observation without disrupting the activities that took place in the setting. For example, when I had questions related to the observed activities, I asked the participants at the end of the observation. Finally, the exit was the last stage of the observation. I thanked the participants for allowing me to conduct the observation.

The observation of ward activities and clinical rounds comprised observing the ward workflow with a focus on decision-making in antibiotic prescribing, including who made the decision to initiate or stop antibiotics and when and in what situation. I observed communication, i.e., the content of discussion and subtle cues related to antibiotics, between the doctor and other clinical staff, e.g., residents, nurses, and interns, and also between the doctor and patient. I also observed the presence or absence of elements to support doctors in making the decision to prescribe or not to prescribe antibiotics, e.g., the availability of the local antibiotic guidelines and consultation with an infectious disease physician or AMS team. The observation of AMS meetings and ward rounds focused on who was present, how they communicated, the content of the discussion, and any non-verbal cues.

At the beginning of the ward observation activities, I used a voice recorder to help me verbally record the observed phenomena along with field notes for later use in the data analysis. However, the hospital wards were usually so crowded that the quality of the recording was poor. Therefore, I did not use this method anymore in the rest of my observations.

I performed the observations in the selected wards during the weekdays and weekends between working hours (9 a.m. to 5 p.m.) and after working hours (between after 5 p.m. and 9 p.m.). The clinical round observations varied depending on the schedules of the respective participants, ranging from 6 a.m. to 7 p.m. Meanwhile, the AMS activities occurred during the working

hours, as did the observations. The observation duration ranged from two to four hours, with a total duration of 58 hours and 20 minutes.

Besides the ‘formal’ observation as explained above, I also informally observed the norms and dynamics during the PPS data collection and the engagements or meetings with the hospital ‘gatekeepers.’ My field notes included the availability of antibiotic guidelines in inpatient management wards, the roles of clinical staff (specialists/consultants, general practitioners, nurses, residents, and interns), the availability of AMS and clinical pharmacists’ rounds, and the hospital norms and dynamics between doctors and hospital management. I estimated the total duration of the ‘informal’ observation to be between three and six hours per hospital, depending on the duration of PPS data collection and the frequency of engagement or meeting with the ‘gatekeepers.’

All field notes were collected or written in English. I gave a specific code and completed the general information, i.e., date, time start and end, and hospital code. The observation data were securely saved on OUCRU-ID’s data server, and only I and my supervisor (RLH) can access the data (see section **3.5.2.6** about confidentiality).

3.5.3.5 Data analysis and triangulation

The data analysis of the observations was performed with interview data analysis, as described in section **3.5.2.5**. In the data analysis, the observation

data (field notes) were also used to triangulate the findings from the interviews.

3.5.3.6 Ethical considerations and confidentiality

Similar to the ethical considerations for the interviews, anonymity was ensured by replacing the hospital name with a code, and no name of the observed participants was mentioned in any reports. For the observation, I obtained verbal consent from the participants. For research ethical approvals, refer to section **3.4.1.7**.

3.5.4 Trustworthiness and reflexivity in the qualitative research

3.5.4.1 Trustworthiness

There are four aspects of trustworthiness in qualitative research: *credibility* (how well research findings match reality), *transferability* (to what extent research findings can be applied in other settings), *dependability* (to what extent the research findings can be replicated), and *confirmability* (or neutrality).[160]

I employed six strategies to strengthen trustworthiness and assure the quality of the collected data. First, I used triangulation of *data sources* (section **3.5.2.5**) that allowed cross-checking of data integrity by comparing the observed (observation) and reported phenomena (interviews).

Second, I used a purposive sampling approach to include participants who had the best understanding of the research topic. I also ensured the representation of different types of participants (roles, stages of career, length

of work in the current role, position in the department, and gender) to obtain as many different viewpoints as possible, which can enhance the breadth and depth of the analysis.

Third, the selected participating hospitals were highly variable in terms of healthcare sector and type to increase the transferability of the findings. Yet, the transferability of the findings to other types of hospitals, particularly those that are less resourced or rural, has to be further explored since they were not part of this research (further discussed in the research limitations in **Chapter 7**).

Fourth, I asked participants about a situation or experience that had previously been described by another participant to explore whether they had similar or contrasting perspectives.

Fifth, discussion with my supervisors (or *analyst* triangulation, section **3.5.2.5**) after the first several interviews to obtain feedback on the quality of the interviews and certain phenomena to explore in the following interviews. I also discussed the coded data and emerging themes with my supervisors throughout the data analysis. Last, I performed the interviews until data saturation was reached.

3.5.4.2 Reflexivity

Reflexivity is crucial in qualitative research to recognise my influence as a researcher in the research process that shaped the data collection, analysis,

and interpretation based on my prior assumptions and experiences and my relationship with the interview and observation participants.[161]

I am a medical doctor who completed my medical degree from a university in Indonesia. After my graduation, I never worked as a hospital physician; instead, I worked as a general practitioner in a government-owned community health centre (primary care) for three years. My experience with hospital clinical practice goes back 20 years to when I did my clinical rotation as a medical intern. I reflected that I have some degree of understanding about antibiotic prescribing practice in hospitals and social-cultural factors that can influence the practice. However, I was aware that my perspective might be limited due to my role as a medical intern at that time. In addition, certain practices and their influencing factors may have evolved over time during the last 20 years. These factors prompted me to try and detach my previous experience from the reality of the current data collection. I had no prior engagement with the participating hospitals or participants before conducting this research.

I also constantly reflected on how I introduced myself and behaved during data collection. I always introduced myself as a DPhil student conducting research about antibiotic prescribing who has a medical background. During the face-to-face interviews and observations, I always carried a name tag from the pertinent hospital, as this was mandatory. I also always wore a doctor's white coat and formal attire, i.e., no jeans or t-shirts. The purpose

was to blend in with the interview and observation participants and avoid attracting unnecessary attention from the patients, nurses, and observed and interviewed participants. From my self-reflection, this approach helped me to build trust with and give assurance to the study participants that I was also a part of the medical community. However, I was also aware that my identity and appearance could be intimidating for some participants, e.g., medical interns and clinical pharmacists, due to the (perceived) hierarchy in the medical profession. To minimise this, I took off the white coat before entering the interview room.

I reflected that there were two main limitations in the qualitative data collection. First, the AMS implementation observation. Second, the selection of the interview participants.

1. AMS implementation observation

   I reflected that there were two challenges when conducting observation of AMS programme implementation. The first challenge was the scarcity of AMS activities during the observation period, and the second challenge was the COVID-19 pandemic.

   During the observation data collection period, I managed to observe only four AMS activities, two meetings, one AMS round, and one clinical pharmacist round. The main reason was that the majority of AMS activities were incidental, which was mentioned by the AMS leaders at the beginning of this research and also reported by the interviews'

participants. Regarding the AMS meeting, I was only invited by a private hospital to attend two consecutive AMS meetings. There was no reported AMS meeting in the other five hospitals during the data collection period, despite the fact that I constantly communicated with the AMS leader or a senior team member. I could not rule out the possibility that I was not invited on purpose. The limited number of observations was also the consequence of the COVID-19 pandemic, which started during the qualitative data collection. Because of the prohibition to conduct any field work, i.e., visiting the hospitals, during this period, I had to discontinue my observation in two hospitals and could not perform any observation in the other two hospitals. The limited number of observations had the potential for bias in the data analysis.

2. Selection of the interview participants

I also reflected on a limitation in the selection of the interview participants. As noted in section **3.5.2.2**, the interview participants were purposively selected among those who could provide rich information regarding decision-making in antibiotic prescribing and AMS programme implementation. This process involved literature reading, consultation with my supervisors, and discussions with the AMS leader and hospital manager of the participating hospitals. In this research, I did not include nurses as interview participants because they were not traditionally involved in antibiotic decision-making nor played a central role in the AMS programmes in the context of Indonesian hospitals. However, they were

involved in the day-to-day inpatient management and the hospital IPC programmes. Therefore, I reflected that there is a potential future research area to be explored related to the potential cross-cutting roles of nurses in IPC programmes, antibiotic prescribing, and AMS implementation.

Chapter 4
The patterns and quality indicators of antibiotic prescribing in Indonesian hospitals

This chapter elaborates on the quantitative results from the PPS to address the first objective: to assess the patterns and quality indicators of antibiotic prescribing in Indonesian hospitals. The presented results cover: 1) hospital and patient characteristics; 2) prevalence and patterns of antimicrobial and antibiotic (ATC J01) use, including by diagnosis/reason, indication, and the AwaRe classification; and 3) quality indicators of antibiotic use based on documentation of antibiotic prescriptions, guideline compliance, administration route, duration of SAP, and culture samples taken.

The PPS results elaborated in this chapter have been published during the course of my DPhil in *JAC-Antimicrobial Resistance*.

Limato R., Nelwan E.J., Mudia M., de Brabander J., Guterres H., Enty E., Mauleti I.Y., Mayasari M., Firmansyah I., Hirzani M., and Hamers R.L. A multicentre point prevalence survey of patterns and quality of antibiotic prescribing in Indonesian hospitals. *JAC-Antimicrobial Resistance*, 3 (2), June (2021). [Link]

4.1 Hospital and patient characteristics

4.1.1 Hospital characteristics

The six participating acute care hospitals varied by healthcare level (two tertiary and four secondary), service provision (five general and one specialised in infectious disease), service management (three public and three private), and size (four small/with less than 500 inpatient beds, and two large/with 500 or more inpatient beds). During the PPS data collection period, hospital antibiotic guidelines were available in five of six hospitals.

On the day of the PPS data collection, there were a total of 238 surveyed inpatient wards: 87 medical, 31 surgical, 95 mixed medical-surgical wards, and 25 ICUs (including PICUs and NICUs), of which 123 were adult wards, 51 were paediatric-neonatal wards, and 64 were mixed adult-neonatal-paediatric wards (**Table** 4.1). During the PPS data collection, there were 2,358 active hospital beds for all hospitals (median 230, range 134-853 per hospital), which were occupied by 1,602 (67.9%) patients (median 149, range 51-625 per hospital) on the day of the survey.

Of 1,602 patients hospitalised on the day of the survey, 993 (62%) received ≥1 antimicrobials or 946 (59%) received ≥1 systemic antibiotics (J01). ICU patients received the highest antimicrobial prescriptions (83.6%, 107/128), followed by patients in mixed medical-surgical wards (64.5%, 401/622) and surgical wards (62.8%, 184/293).

Table 4.1 Hospital characteristics

Characteristics	Total	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Hospital 6
Service provision		General	General	General	Specialised in infectious diseases	General	General
Service management		Private	Public	Private	Public	Public	Private
Healthcare level		Secondary	Tertiary	Secondary	Secondary	Tertiary	Secondary
Hospital antibiotic guidelines		No	Yes	Yes	Yes	Yes	Yes
Inpatient wards [a]	238	19	74	30	14	79	22
By ward type							
Medical	87	4	27	15	6	30	5
Surgical	31	0	17	2	0	11	1
Mixed medical-surgical [b]	95	12	19	10	7	32	15
Intensive care unit	25	3	11	3	1	6	1
By ward population							
Adult	123	8	55	13	2	39	6
Paediatric and/or neonatal	51	5	12	6	3	21	4
Mixed adult-neonatal-paediatric [c]	64	6	7	11	9	19	12
Active inpatient beds [d]	2358	159	767	300	145	853	134
Admitted patients	1602 (67.9)	100 (62.9)	562 (73.3)	198 (66.0)	66 (45.5)	625 (73.3)	51 (38.1)
Admitted patients on ≥1 antimicrobials [e]	993 (62.0)	75 (75.0)	368 (65.5)	106 (53.5)	52 (78.8)	359 (57.4)	33 (64.7)
By ward type							
Medical	301 (30.3)	47 (62.7)	102 (27.7)	36 (34.0)	14 (26.9)	95 (26.5)	7 (21.2)
Surgical	184 (18.5)	0 (0.0)	87 (23.6)	24 (22.6)	0 (0.0)	73 (20.3)	0 (0.0)
Mixed medical-surgical [b]	401 (40.4)	23 (30.7)	135 (36.7)	37 (34.9)	35 (67.3)	147 (40.9)	24 (72.7)
Intensive care unit	107 (10.8)	5 (6.7)	44 (12.0)	9 (8.5)	3 (5.8)	44 (12.3)	2 (6.1)

Characteristics	Total	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Hospital 6
By ward population							
Adult	727 (73.2)	31 (41.3)	298 (81.0)	92 (86.8)	43 (82.7)	230 (64.0)	33 (100)
Paediatric	163 (16.4)	13 (17.4)	58 (15.7)	8 (7.5)	3 (5.7)	81 (22.6)	0 (0.0)
Mixed adult-neonatal-paediatric [c]	103 (10.4)	31 (41.3)	12 (3.3)	6 (5.7)	6 (11.6)	48 (13.4)	0 (0.0)
Admitted patients on ≥1 antibiotics [f]	946 (59.0)	75 (75.0)	362 (64.4)	103 (52.0)	50 (75.8)	329 (52.6)	27 (52.9)

Data shown reflect the hospital situation on the survey day, and are expressed as number (percentage), unless otherwise specified.
[a] Includes all inpatients wards in the hospital. Some wards were subdivided for the purpose of this survey.
[b] Wards that can admit both medical and surgical patients.
[c] Wards that can admit both adult, paediatric and neonatal patients.
[d] Available beds on the survey day.
[e] Includes antimicrobials for systemic use (J01, J02, J02, J04, J05, P01AB, A07A, P1B).
[f] Includes antibiotics for systemic use (J01).

All patients (100%) in the ICU for paediatric/PICU, neonate/NICU, and mixed adult-neonatal-paediatric received ≥1 antimicrobial drugs, while 74.4% (58/78) of patients in the adult ICUs were prescribed with ≥1 antimicrobials (**Appendix 8 Table 1**). The concurrent use of two or more antimicrobials was higher among patients in ICUs (58.9%, 63/107) than in non-ICU wards (37%, 328/886)

4.1.2 Patient characteristics

Of the 993 patients receiving ≥1 antimicrobial prescriptions, most were adults (78.8%, 782) and had JKN (74.8%, 743). The proportions of male and female patients were similar, 49.9% (496) and 50.1% (497), respectively. The median age was 43 years (IQR 22-58.5; range 1 day to 99 years) (**Table** 4.2).

Regarding a history of contact with healthcare, among patients receiving ≥1 antimicrobial agents (993), 37.1% (368) had surgery within 90 days, 30.1% (299) were hospitalised within 90 days, and 14.6% (145) were transferred from another hospital. The public hospitals had a higher proportion of patients with a history of transfers from other hospitals than the private hospitals.

In regard to catheter use, I found peripheral vascular catheter use was high across all participant hospitals (94.5%, 80.2–98.1%). Urinary catheter use was documented in 36.6% (363) of patients receiving ≥1 antimicrobial agents (993), followed by central vascular catheter use (13.3%, 132) and intubation (6.5%, 65).

One or more comorbidities were documented in 48.9% (486) of the surveyed patients (993). One third of these patients overall had malnutrition (33.7%, 335), which was higher in public hospitals (33.7-53.8%) than in private hospitals (0-16%). A low proportion of patients had diabetes mellitus (16.2%, 161), tuberculosis (12.1%, 120), HIV (4.4%, 44), or chronic obstructive pulmonary disease (1.1%, 11).

Using the McCabe score, the majority of patients (75.1%, 746) were classified as having a non-fatal condition (death ≥5 years), followed by an ultimately fatal condition (death 1-4 years) (21.9%, 217), and a rapidly fatal condition (death <1 year) (2.9%, 29).

4.2 Prevalence and patterns of systemic antibiotic use

4.2.1 Antimicrobial agents

A total of 1,666 antimicrobial agents were prescribed to 993 patients (median 1 per patient, range 1-12), with 60.6% of patients (602) receiving one antimicrobial agent, 25.6% (254) two, and 13.8% (137) three or more.

Of a total of 1,666 antimicrobial prescriptions, 76.4% (1,273) were antibiotics (ATC J01), 11.4% (197) were antimycobacterials (J04), 4.3% (72) were antivirals (J05), 3.7% (62) were antimycotics (J02), 2.6% (43) were intestinal antiinfectives (A07A), 0.8% (13) were antimalarials (P01B), and 0.4% (6) were nitroimidazole derivatives (P01AB).

Table 4.2 Characteristics of patients receiving ≥1 antimicrobial drugs

		Total N=993	Hospital 1 N=75	Hospital 2 N=368	Hospital 3 N=106	Hospital 4 N=52	Hospital 5 N=359	Hospital 6 N=33
Sex								
Male		496 (49.9)	34 (45.3)	182 (49.5)	45 (42.5)	30 (57.7)	184 (51.3)	21 (63.6)
Female		497 (50.1)	41 (54.7)	186 (50.5)	61 (57.5)	22 (42.3)	175 (48.7)	12 (36.4)
Median age (IQR) [a]		43 (22-58.5)	29 (20-55)	47 (25-60)	52 (33-66)	39.5 (28-59)	37 (8-53)	51 (28.5-65)
Neonates	<1 month	45 (4.5)	2 (2.7)	17 (4.6)	2 (1.9)	1 (1.9)	23 (6.4)	0 (0.0)
Paediatric	1-23 months	63 (6.3)	3 (4.0)	20 (5.4)	2 (1.9)	1 (1.9)	37 (10.3)	0 (0.0)
	2-17 years	103 (10.4)	12 (16.0)	24 (6.5)	6 (5.7)	4 (7.7)	57 (15.9)	0 (0.0)
Adult	18-29 years	131 (13.2)	21 (28.0)	47 (12.8)	7 (6.6)	8 (15.4)	39 (10.9)	9 (27.3)
	30-39 years	112 (11.3)	9 (12.0)	35 (9.5)	24 (22.6)	12 (23.1)	30 (8.4)	2 (6.1)
	40-49 years	145 (14.6)	7 (9.3)	55 (14.9)	7 (6.6)	8 (15.4)	63 (17.5)	5 (15.2)
	≥50 years	394 (39.7)	21 (28.0)	170 (46.2)	58 (54.7)	18 (34.6)	110 (30.6)	17 (51.5)
Patients with JKN [b]		743 (74.8)	0 (0.0)	329 (89.4)	24 (22.6)	50 (96.2)	340 (94.7)	0 (0.0)
History of contact with healthcare								
Transfer from other hospital		145 (14.6)	2 (2.7)	70 (19.0)	2 (1.9)	10 (19.2)	57 (15.9)	4 (12.1)
Hospitalisation within 90 days [c]		299 (30.1)	12 (16.0)	86 (23.4)	20 (18.9)	20 (38.5)	151 (42.1)	10 (30.3)
Surgery in the past 90 days [d]		368 (37.1)	3 (4.0)	162 (44.0)	41 (38.7)	8 (15.4)	142 (39.6)	12 (36.4)
Catheter use								
Central vascular		132 (13.3)	4 (5.3)	35 (9.5)	12 (11.3)	1 (1.9)	73 (20.3)	7 (21.2)
Peripheral vascular		941 (94.8)	69 (92.0)	357 (97.0)	85 (80.2)	51 (98.1)	347 (96.7)	32 (97.0)
Urinary		363 (36.6)	9 (12.0)	183 (49.7)	35 (33.0)	9 (17.3)	119 (33.1)	8 (24.2)
Intubation		65 (6.5)	3 (4.0)	21 (5.7)	7 (6.6)	1 (1.9)	30 (8.4)	3 (9.1)
Documented comorbidity		486 (48.9)	11 (14.6)	209 (56.8)	40 (37.7)	41 (78.8)	174 (48.5)	14 (42.4)
Malnutrition		335 (33.7)	0 (0.0)	165 (44.8)	17 (16.0)	28 (53.8)	121 (33.7)	4 (12.1)

	Total N=993	Hospital 1 N=75	Hospital 2 N=368	Hospital 3 N=106	Hospital 4 N=52	Hospital 5 N=359	Hospital 6 N=33
Diabetes mellitus	161 (16.2)	8 (10.7)	68 (18.5)	24 (22.6)	14 (26.9)	39 (10.9)	8 (24.2)
Tuberculosis	120 (12.1)	3 (4.0)	37 (10.1)	7 (6.6)	24 (46.2)	44 (12.3)	5 (15.2)
HIV	44 (4.4)	3 (4.0)	10 (2.7)	2 (1.9)	13 (25.0)	16 (4.5)	0 (0.0)
HIV on antiretroviral treatment	27 (2.7)	3 (4.0)	4 (1.1)	2 (1.9)	8 (15.4)	10 (2.8)	0 (0.0)
Chronic obstructive pulmonary disease	11 (1.1)	0 (0.0)	7 (1.9)	0 (0.0)	3 (5.8)	1 (0.3)	0 (0.0)
McCabe Score							
Rapidly fatal (death <1 year)	29 (2.9)	3 (4.0)	8 (2.2)	2 (1.9)	0 (0.0)	15 (4.2)	1 (3.0)
Ultimately fatal (death 1-4 years)	217 (21.9)	3 (4.0)	89 (24.2)	32 (30.2)	2 (3.8)	84 (23.4)	7 (21.2)
Non-fatal (death ≥5 years)	746 (75.1)	69 (92.0)	270 (73.4)	72 (67.9)	50 (96.2)	260 (72.4)	25 (75.8)
Unknown	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Prescribed antimicrobial drugs	1,666	114	630	158	98	622	44
Median (range) per patient	1 (1-12)	1 (1-12)	1 (1-9)	1 (1-7)	1 (1-6)	1 (1-10)	1 (1-4)
1	602 (60.6)	58 (77.3)	204 (55.4)	74 (69.8)	32 (61.5)	209 (58.2)	25 (75.8)
2	254 (25.6)	11 (14.7)	108 (29.3)	22 (20.8)	8 (15.4)	99 (27.6)	6 (18.2)
≥3	137 (13.8)	6 (8.0)	56 (15.2)	10 (9.4)	12 (23.1)	51 (14.2)	2 (6.1)

Abbreviations: HIV, Human Immunodeficiency Virus; IQR, interquartile range; JKN, *Jaminan Kesehatan Nasional*/national health insurance.
Data shown reflect the hospital situation on the survey day, and are expressed as number (percentage), unless otherwise specified.
[a] Median (interquartile range, IQR) age was 47 (28-60) years for adults, 7 (2-11) months for children <2 years, and 8 (3-14) days for neonates.
[b] National health insurance; Unknown for 4 (0.4%) patients.
[c] Before the current admission, the patient has been hospitalised within 90 days before the survey date.
[d] The patient underwent surgery in the past 90 days before the survey date, including surgery prior to and during the current admission.

The overall top five diagnoses for antimicrobial prescriptions (1,666) were pneumonia or lower respiratory tract infection (LRTI) (21.9%, 365), pulmonary tuberculosis (11.1%, 185), skin and soft tissue infections (6.6%, 110), prophylaxis for gastrointestinal infections (6.1%, 102), and gastrointestinal infections (5.0%, 84) (**Appendix 8 Table 2**).

4.2.2 Systemic antibiotic agents

The total of 1,273 antibiotic prescriptions covered 20 antibiotic classes documented. The overall top five antibiotic classes (accounting for 79.2%, 1008) were third generation cephalosporins (44.4%, 565), fluoroquinolones (13.5%, 172), carbapenems (7.4%, 94), imidazole derivatives (7.1%, 94), and penicillins with a beta-lactamase inhibitor (6.8%, 86) (**Figure** 4.1). There were 46 different prescribed antibiotic agents. The five most prescribed antibiotics (accounting for 56.5%, 720) were ceftriaxone (26.8%, 341), levofloxacin (10.7%, 137), metronidazole (7.1%, 91), meropenem (6.4%, 82), and cefotaxime (5.6%, 71). Based on the patient population, gentamicin was the most prescribed antibiotic for neonates (33.8%, 24/71), cefotaxime for paediatric patients (18.4%, 38/207), and ceftriaxone for adult patients (31.5%, 313/995). The prescriptions from two tertiary hospitals in this PPS accounted for 75.6% (963/1,273) of all antibiotic prescriptions.

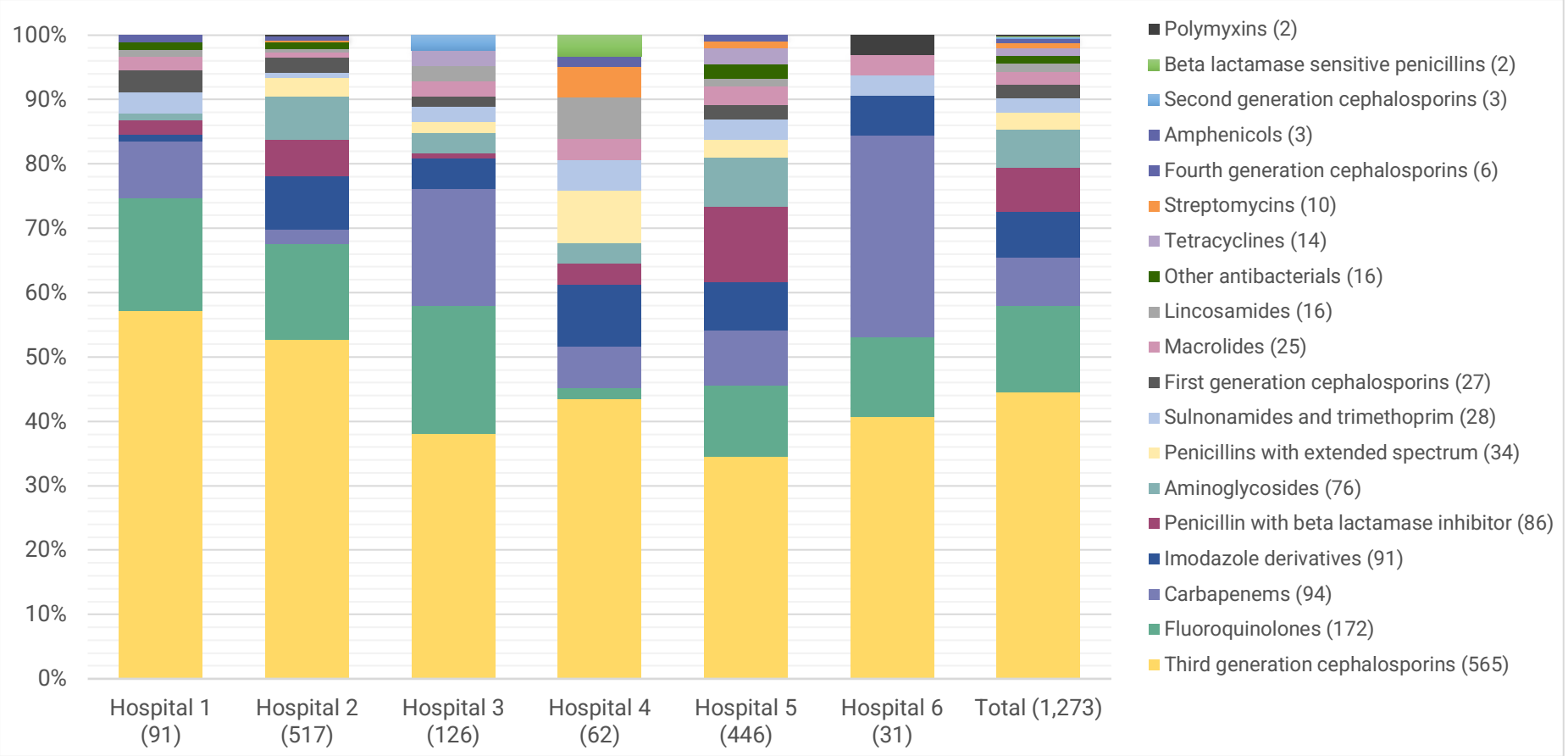


Figure 4.1 Systemic antibiotic use by antibiotic class, by hospital

4.2.3 Diagnosis/reason and indication of antibiotic prescriptions

4.2.3.1 Diagnosis of antibiotic prescriptions

Among 1,273 antibiotic prescriptions, the overall top five most common diagnoses (accounting for 49.4%, 629) were pneumonia or LRTI (27.7%, 353), skin and soft tissue infection (8.3%, 106), prophylaxis for gastrointestinal infection (7.9%, 101), gastrointestinal infection (5.4%, 69), and prophylaxis for bone and joint infection (4.6%, 58) (**Table** 4.3).

The majority of patients with pneumonia or LRTI were prescribed ceftriaxone (74%, 97/341) and levofloxacin (60.3%, 82/136). Ceftriaxone and levofloxacin were also frequently prescribed for patients with gastrointestinal infections, at 22.1% (29/341) and 8.1% (11/136), respectively. Metronidazole was mainly prescribed for skin and soft tissue infections (25.3%, 23/90). Meropenem was mostly prescribed for pneumonia or LRTI (48.8%, 40/82) and sepsis (13.4%, 11/82).

4.2.3.2 Indications of antibiotic prescriptions

The most common indication for antibiotic prescriptions (1,273) was CAI (42.6%, 542), followed by surgical prophylaxis (22.6%, 288), HAI (18.5%, 235), medical prophylaxis (9.6%, 122), unknown indication (4.6%, 59), and other indications (2.1%, 27) (**Table** 4.4).

Table 4.3 Top five systemic antibiotic use by diagnosis, by antibiotic name

Diagnosis	Ceftriaxone N=341	Levofloxacin N=136	Metronidazole N=90	Meropenem N=82	Cefotaxime N=71
Pneumonia or lower respiratory tract infection (LRTI)	97 (74.0)	82 (60.3)	2 (2.2)	40 (48.8)	18 (25.4)
Gastrointestinal infections	29 (22.1)	11 (8.1)	7 (7.7)	-	-
Prophylaxis for bone and joint infections	27 (20.6)	1 (0.7)	3 (3.3)	-	5 (7.0)
Skin and soft tissue infections	26 (19.8)	5 (3.7)	23 (25.3)	3 (3.7)	2 (2.8)
Unknown indication	25 (19.1)	3 (2.2)	1 (1.1)	2 (2.4)	5 (7.0)
Prophylaxis for obstetric or gynaecological infections	20 (15.3)	1 (0.7)	6 (6.6)	-	1 (1.4)
Other diagnosis	18 (13.7)	3 (2.2)	1 (1.1)	-	5 (7.0)
Medical prophylaxis general	14 (10.7)	1 (0.7)	1 (1.1)	-	1 (1.4)
Prophylaxis for ear, nose, and throat infections	12 (9.20	-	1 (1.1)	-	-
Prophylaxis for gastrointestinal infections	10 (7.6)	5 (3.7)	18 (19.8)	5 (6.1)	15 (21.1)
Central nervous system infections	9 (6.9)	1 (0.7)	-	-	3 (4.2)
Ear, nose, and throat infections	8 (6.1)	-	4 (4.4)	1 (1.2)	-
Prophylaxis for central nervous system infections	7 (5.3)	-	1 (1.1)	1 (1.2)	1 (1.4)
Lower urinary tract infections (cystitis)	5 (3.8)	5 (3.7)	-	1 (1.2)	-
Intra-abdominal infections	5 (3.8)	4 (2.9)	18 (19.8)	6 (7.3)	2 (2.8)
Prophylaxis for urinary tract infections (surgery or recurrent infection)	5 (3.8)	1 (0.7)	-	1 (1.2)	4 (5.6)
Upper urinary tract infections (incl. pyelonephritis)	5 (3.8)	3 (2.2)	-	5 (6.1)	1 (1.4)
Bone and joint infections	4 (3.1)	-	2 (2.2)	1 (1.2)	-
Upper respiratory tract infection	4 (3.1)	1 (0.7)	-	1 (1.2)	-
Sepsis	3 (2.3)	4 (2.9)	2 (2.2)	11 (13.4)	5 (7.0)

Diagnosis	Ceftriaxone N=341	Levofloxacin N=136	Metronidazole N=90	Meropenem N=82	Cefotaxime N=71
Prophylaxis for respiratory infections	2 (1.5)	-	-	-	1 (1.4)
Pyrexia of unknown origin	2 (1.5)	-	-	-	-
Cardiovascular infections	1 (0.8)	-	-	-	-
Obstetric/gynaecological infections	1 (0.8)	-	-	-	-
Prophylaxis for cardiac or vascular infections	1 (0.8)	1 (0.7)	-	-	-
Pyrexia of unknown origin in non-neutropenic haemato-oncology patients	1 (0.8)	-	-	-	1 (1.4)
Pulmonary tuberculosis	-	3 (2.2)	-	1 (1.2)	-
Acute bronchitis or exacerbations of chronic bronchitis	-	1 (0.7)	-		-
Febrile neutropenia	-	-	-	2 (2.4)	-
Bacteraemia	-	-	-	1 (1.2)	-
Prophylaxis for eye infections	-	-	-	-	1 (1.4)

Data are expressed as number (percentage).

Table 4.4 Systemic antibiotic use by hospital, by indication

Hospital	Total systemic antibiotics N=1,273	Therapeutic indication N=777				Prophylactic indication N=410		Other indication [a] N=27	Unknown indication N=59
		CAI empirical N=498	CAI targeted N=44	HAI empirical N=172	HAI targeted N=63	Medical prophylaxis N=122	Surgical prophylaxis N=288		
Hospital 1	91 (7.1)	59 (11.8)	2 (4.5)	3 (1.7)	1 (1.6)	9 (7.4)	4 (1.4)	1 (3.7)	12 (20.3)
Hospital 2	517 (40.6)	199 (40.0)	12 (27.3)	62 (36.0)	20 (31.7)	50 (41.0)	146 (50.7)	6 (22.2)	22 (37.3)
Hospital 3	126 (9.9)	61 (12.2)	4 (9.1)	14 (8.1)	6 (9.5)	4 (3.3)	31 (10.8)	1 (3.7)	5 (8.5)
Hospital 4	62 (4.9)	27 (5.4)	1 (2.3)	2 (1.2)	1 (1.6)	7 (5.7)	7 (2.4)	9 (33.3)	8 (13.6)
Hospital 5	446 (35.0)	139 (27.9)	23 (52.3)	90 (52.3)	32 (50.8)	50 (41.0)	93 (32.3)	10 (37.0)	9 (15.3)
Hospital 6	31 (2.4)	13 (2.6)	2 (4.5)	1 (0.6)	3 (4.8)	2 (1.6)	7 (2.4)	0 (0.0)	3 (5.1)

Abbreviations: CAI, community acquired infection; HAI, hospital acquired infection.
Data are expressed as number (percentage).
[a] Antibiotics were prescribed for other indications including pulmonary tuberculosis, HIV/AIDS (e.g., as prophylaxis for pneumocystis carinii pneumonia and neurotoxoplasmosis), and as a motility agent.

Out of the 235 antibiotics prescribed for HAI treatment, 70.2% (165) were indicated for hospital-acquired pneumonia (including other HAIs); 14.9% (35) for intervention-related infections (including catheter-related blood stream infection, ventilator-associated pneumonia, and catheter-related urinary tract infection); 13.6% (32) for post-operative surgical site infection; and 1.3% (3) for infection present on admission from another hospital or long-term care facilities. There was no *C. difficile*-associated diarrhoea documented.

Based on antibiotic agents, the most commonly prescribed antibiotics for HAI (235) were levofloxacin (18.7%, 44), meropenem (13.6%, 31), and ceftriaxone (9.8%, 23). Meanwhile, for CAI (542), they were ceftriaxone (32.8%, 178), levofloxacin (13.5%, 73), and metronidazole (8.1%, 44). For medical prophylaxis (122), the commonly prescribed antibiotics were ceftriaxone (28.7%, 35), cotrimoxazole (17.2%, 21), and gentamicin (10.7%, 13). For surgical prophylaxis (288), they were ceftriaxone (26.4%, 76), cefixime (11.5%, 33), and cefoperazone (11.1%, 32) (**Appendix 8 Table 3**).

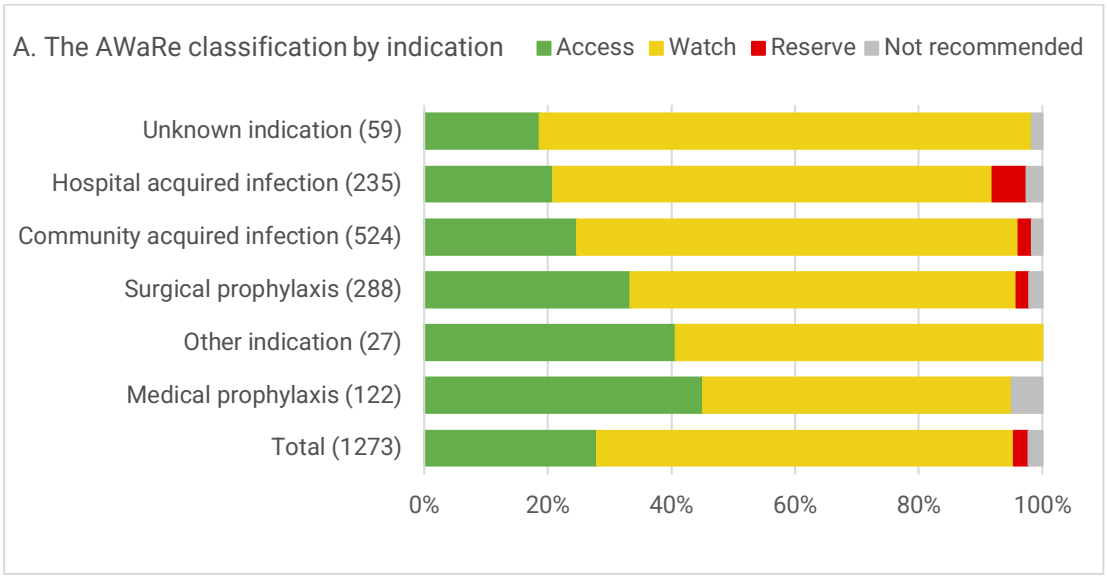
Of the 542 antibiotics indicated for CAI, the top three diagnoses were pneumonia or LRTI (42.6%, 231), skin and soft tissue infection (14.2%, 77), and gastrointestinal infection (12.2%, 66). The most common HAI (235) diagnoses were pneumonia or LRTI (51.9%, 122), skin and soft tissue infection (12.3%, 29), and intra-abdominal infections (11.9%, 28). For medical prophylaxis (122), the top three reasons to prescribe antibiotics were new-born risk factors (20.5%, 25), general medical conditions (19.7%, 24), and

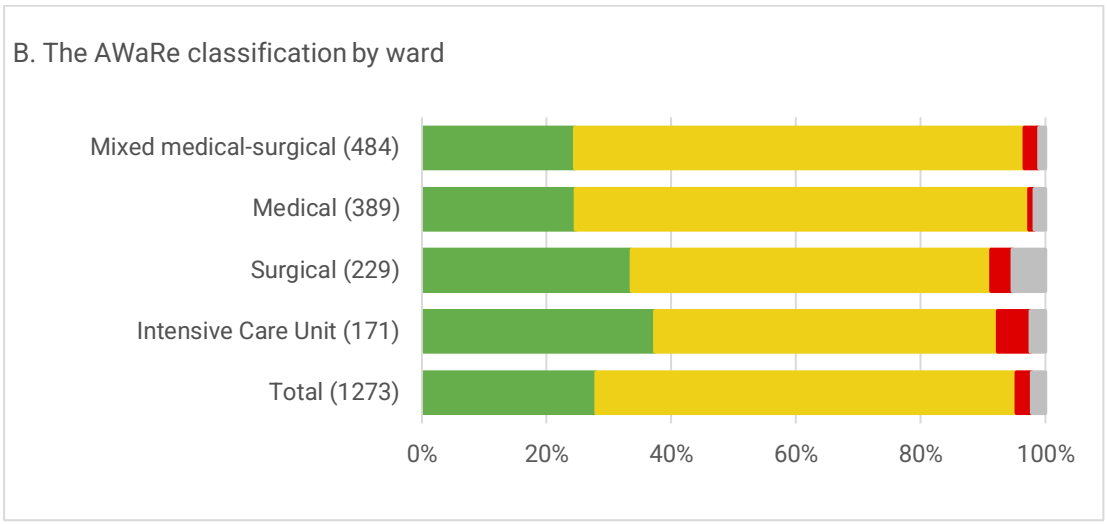
gastrointestinal infection (17.2%, 21). Surgical antibiotic prophylaxes were most commonly prescribed for gastrointestinal surgeries (27.8%, 80), followed by obstetrics/gynaecology procedures (20.1%, 58), and bone and joint surgeries (17%, 49).

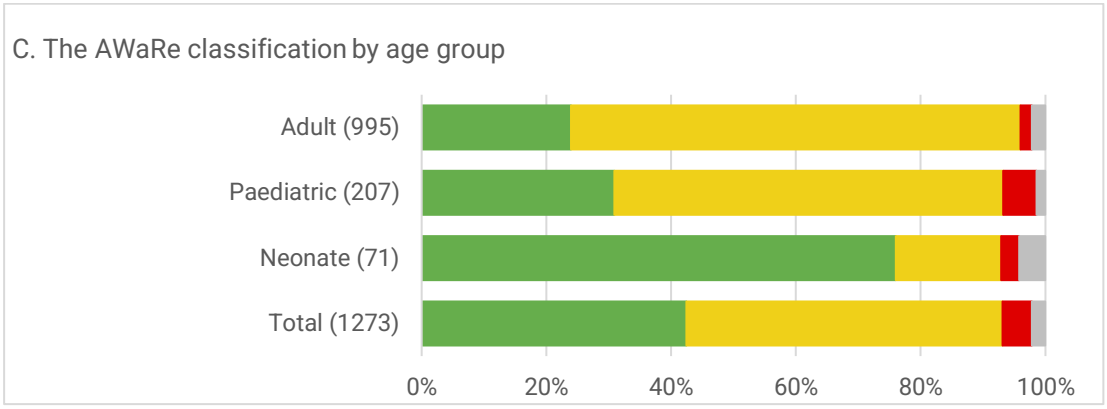
4.2.4 Systemic antibiotic use based on the AWaRe classification

The majority of antibiotic prescriptions (1,273) were classified as Watch antibiotics (67.4%, 858), followed by Access (28%, 356), Reserve (2.4%, 31), and Not recommended (2.2%, 28). This pattern was similar across indications (**Figure** 4.2 **A**) and ward types (**Figure** 4.2 **B**). Based on the age groups (**Figure** 4.2 **C**), adult and paediatric patients were mostly prescribed Watch antibiotics (72% and 62.3%, respectively), while the majority of neonates (76%) received Access antibiotics.

Watch antibiotics (858) were prescribed for the most frequent diagnoses, i.e., pneumonia or LRTI (34.4%, 295), gastrointestinal infection (6.6%, 57), and skin and soft tissue infection (5.8%, 50). Three diagnoses with the highest proportion of Access antibiotics were medical prophylaxis for new-born risk factors (96%, 24/25), cardiovascular system infection (85.7%, 6/7), and prophylaxis for respiratory infection (85%, 17/20). Reserve antibiotics (31) were infrequently prescribed; of these, 38.7% (12) were prescribed for pneumonia or LRTI, 19.4% (6) for prophylaxis of central nervous system procedures, and 12.9% (4) for skin and soft tissue infection (**Figure** 4.2 **D**).


A. The AWaRe classification by indication
Access
Watch
Reserve
Not recommended
Unknown indication (59)
Hospital acquired infection (235)
Community acquired infection (524)
Surgical prophylaxis (288)
Other indication (27)
Medical prophylaxis (122)
Total (1273)
0%
20%
40%
60%
80%
100%


B. The AWaRe classification by ward
Mixed medical-surgical (484)
Medical (389)
Surgical (229)
Intensive Care Unit (171)
Total (1273)
0%
20%
40%
60%
80%
100%


C. The AWaRe classification by age group
Adult (995)
Paediatric (207)
Neonate (71)
Total (1273)
0%
20%
40%
60%
80%
100%

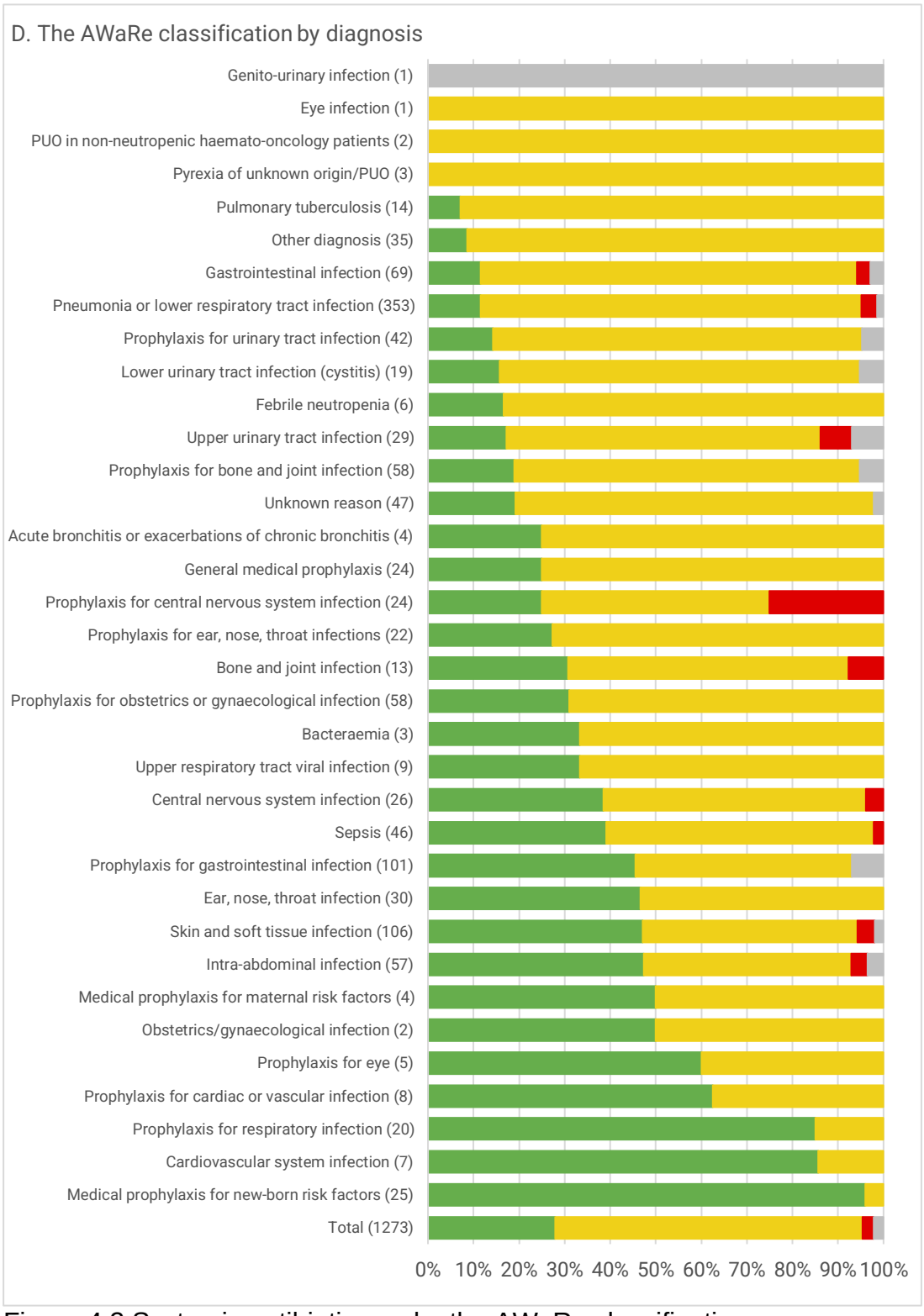


Figure 4.2 Systemic antibiotic use by the AWaRe classification

Based on antibiotic agents, the top three Watch antibiotics (858) were ceftriaxone (39.7%, 341), levofloxacin (15.8%, 136), and meropenem (9.6%, 82). The top three Access antibiotics (356) were metronidazole (25.3%, 90), ampicillin-sulbactam (12.4%, 44), and gentamicin (11.8%, 42). The top three Reserve antibiotics (31) were fosfomycin (48.4%, 15), tigecycline (41.9%, 13), and colistin (3.2%, 1). All of the Not recommended antibiotics (100%, 28) were cefoperazone/sulbactam.

4.3 Quality indicators of antibiotic use

4.3.1 Documentation of prescribing reasons and guideline compliance

The reason for antibiotic prescribing was documented for 63.5% (808/1,273) of all prescriptions. The documentation of diagnosis or reason for prescribing was better for therapeutic use (70.3%, 546/777) than prophylactic use (56.1%, 230/410), and in the ICU (72.5%, 124/171) than non-ICU (62%, 684/1102). Stop or review date (15.2%, 194/1,273) and planned treatment duration (9.8%, 125/1273) were poorly documented (**Table** 4.5).

Local hospital antibiotic guidelines were not available for 28.1% (358/1,273) of prescriptions overall, 27.9% (139/498) of empirical CAI prescriptions, 13.4% (23/172) of empirical HAI prescriptions, 28.5% (82/288) of prescriptions for surgical prophylaxis, and 76.2% (93/122) of prescriptions for medical prophylaxis.

Table 4.5 Quality indicators of antibiotic prescribing, by indication

Quality indicators	Total systemic antibiotics N=1,273	Therapeutic use N=777				Prophylactic use N=410		Other indication [a] N=27	Unknown Indication N=59
		CAI empirical N=498	CAI targeted N=44	HAI empirical N=172	HAI targeted N=63	Medical prophylaxis N=122	Surgical prophylaxis N=288		
Documentation of									
Reason for antibiotic prescribing	808 (63.5)	321 (64.5)	35 (79.5)	145 (84.3)	45 (71.4)	58 (47.5)	172 (59.7)	21 (77.8)	11 (18.6)
Stop/review date	194 (15.2)	69 (13.9)	7 (15.9)	43 (25.0)	18 (28.6)	15 (12.3)	38 (13.2)	2 (7.4)	2 (3.4)
Duration of antibiotic prescription	125 (9.8)	35 (7.0)	5 (11.4)	31 (18.0)	12 (19.0)	3 (2.5)	35 (12.2)	0 (0.0)	4 (6.8)
Guideline compliance [b]									
Yes	428 (36.7)	223 (44.8)	-	79 (45.9)	-	23 (18.9)	82 (28.5)	21 (77.8)	0 (0.0)
No	342 (29.3)	136 (27.3)	-	70 (40.7)	-	6 (4.9)	124 (43.1)	6 (22.2)	0 (0.0)
Indication unknown	59 (5.1)	0 (0.0)	-	0 (0.0)	-	0 (0.0)	0 (0.0)	0 (0.0)	59 (100.0)
Not assessable [c]	337 (28.9)	139 (27.9)	-	23 (13.4)	-	93 (76.2)	82 (28.5)	0 (0.0)	0 (0.0)
Route of administration									
Parenteral (IV)	1,084 (85.2)	444 (89.2)	42 (95.5)	150 (87.2)	58 (92.1)	92 (75.4)	237 (82.3)	10 (37.0)	51 (86.4)
Oral	183 (14.38)	52 (10.44)	2 (4.55)	22 (12.79)	5 (7.94)	30 (24.59)	51 (17.71)	13 (48.15)	8 (13.56)
IV-oral switch	48 (26.2)	6 (11.5)	1 (50.0)	9 (40.9)	1 (20.0)	1 (3.3)	28 (54.9)	0 (0.0)	2 (25.0)
Other [d]	6 (0.47)	2 (0.40)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	4 (14.81)	0 (0.00)
Surgical prophylaxis									
Single dose	-	-	-	-	-	-	43 (15.0)	-	-
1 day	-	-	-	-	-	-	26 (9.0)	-	-
>1 day/24 hours	-	-	-	-	-	-	219 (76.0)	-	-

Abbreviations: CAI, community acquired infection; HAI, hospital acquired infection; IV, intravenous.
Data are expressed as number (percentage).

[a] Other indication including pulmonary tuberculosis, HIV/AIDS (e.g., as prophylaxis for pneumocystis carinii pneumonia and neurotoxoplasmosis), and as a motility agent.
[b] Only for antibiotic choice and empirical prescriptions (N=1166).
[c] Hospital antibiotic guidelines were not available to assess compliance.
[d] Other systemic routes.

Guideline compliance for empirical prescriptions when guidelines were available (limited to antibiotic choice, but not the dose, route, and duration) was 51.6% (428/829) overall, 44.8% (223/498) for empirical CAI treatment, 45.9% (79/172) for empirical HAI treatment, 28.5% (82/288) for surgical prophylaxis, and 18.9% (23/122) for medical prophylaxis.

4.3.2 Administration route and surgical prophylaxis

The majority of prescriptions (85.2%, 1,084/1,273) were administered through the parenteral route, including 89.5% (486/542) for CAI, 88.5% (208/235) for HAI, 75.4% (92/122) for medical prophylaxis, and 82.3% (237/288) for surgical prophylaxis (**Table** 4.5).

Most prescriptions for surgical prophylaxis (288) were prolonged for more than one day (76%, 219), whereas single dose (15%, 43) or one-day (9%, 26) prophylactic prescriptions comprised about a quarter of prescriptions.

4.3.3 Culture samples taken

Among 619 patients with ≥1 antibiotic prescriptions for therapeutic use, 48.8% (302) had ≥1 samples taken for bacterial culture (total 831 samples, median 2, range 1-25 per patient). Of the total of 831 culture samples, results were available for 96% (798). Of the available results, 53.6% (428) yielded positive results.

One or more culture samples were taken in 44.3% (344/777) of therapeutic prescriptions. Blood cultures were taken in 95.8% (23/24) of patients with

sepsis, 68.4% (26/38) of patients with an intra-abdominal infection, and 57.1% (88/154) of patients with pneumonia or LRTI. Sputum cultures were taken in 61.7% (95/154) of pneumonias or LRTIs, and urine cultures were taken in 95.4% (21/22) of upper urinary tract infections.

Based on indication, targeted treatment accounted for 13.8% (107/777) of therapeutic prescriptions (CAI and HAI combined), 8.1% (44/542) of CAI prescriptions, and 26.8% (63/235) of HAI prescriptions. For CAI treatment, only 31.2% (169/542) of prescriptions had culture samples taken during admission, of which 50.3% (85/169) were taken within 24 hours, 17.7% (30/169) within 48 hours, and 32% (54/169) after 48 hours. For HAI treatment, 74.5% (175/235) of prescriptions had at least one culture taken during admission. The median time from culture specimen collection to reporting positive results of aetiology bacteria and antibiotic susceptibility was 4 (3-4) days for blood, 3 (2-4) days for sputum, and 3 (2-3) days for urine.

4.4 Discussion

The PPS method enables a systematic evaluation of patterns and quality indicators of antibiotic prescribing and offers a uniform data collection approach.

A high prevalence of broad-spectrum antibiotic use

This survey showed that the proportion of patients receiving at least one systematic antimicrobial agent (62%) in Indonesian hospitals is consistent with the findings of similar studies in LMICs in Southeast Asian countries: Viet

Nam (67.4%),[56] Laos (68.8%),[57] and Thailand (53%);[58] and was twice as high as the 2016–2017 ESAC PPS results from 29 European countries (32.9%),[55] as well as the 2015 Global-PPS findings across 53 countries (34.4%).[11]

Consistent with other studies across LMICs in Asia[57–59] and globally,[11] my research found that pneumonia or LRTI was the main reason for antibiotic prescribing, both for adult and paediatric patients. Furthermore, pneumonia or LRTI accounted for 51.9% of HAI antibiotic prescriptions. In this survey, the most commonly used antibiotic classes were third generation cephalosporins (mainly ceftriaxone), fluoroquinolones (mainly levofloxacin), and carbapenems (mainly meropenem), predominantly for pneumonia or LRTI among other diagnoses. Ceftriaxone was the most prescribed antibiotic across indications (CAI, surgical prophylaxis, and medical prophylaxis). Meanwhile, levofloxacin and meropenem were commonly prescribed for HAI. These findings were consistent with the widespread use of broad-spectrum antibiotics, primarily third generation cephalosporins, in Indonesia,[36] LMICs in Asia,[56–58,187] and globally.[11] This finding is concerning, as a global review of studies published between 1985 and 2018 identified the use of third generation cephalosporins as being associated with ESBL-producing pathogens.[33] Furthermore, resistance to third generation cephalosporins was also associated with longer hospital stays and an increased probability of mortality among hospitalised patients.[188]

According to the WHO AWaRe classification, this research identified a high proportion of the prescribed Watch antibiotics (67.4%, mostly ceftriaxone and levofloxacin). This figure was higher than that reported in two other studies in the region: 47.3% in 41 hospitals in Thailand[58] and 49% in six general hospitals in Laos.[57] The majority of adult patients (72%) in this survey were prescribed Watch antibiotics, which was slightly higher than the prevalence of Watch prescriptions (63.4%) in the 141 hospitals across 11 LMICs participating in the 2015–2018 Global-PPS survey.[74] In this survey, ceftriaxone was the most common antibiotic prescribed for Watch, which is consistent with the findings of the 2015–2018 AWaRE Global-PPS across 69 countries, mostly HICs and upper-middle income countries.[74] Meanwhile, the proportion of Access antibiotic prescriptions (28%) in this research was lower than the AWaRe's national target of >60% of total Access antibiotic consumption by 2023.[73]

Suboptimal quality indicators in antibiotic prescribing

In regard to quality indicators of antibiotic prescribing, the reasons for antibiotic prescriptions were documented in 64% of prescriptions. This was lower than the results of a study conducted in six general hospitals in Laos (88%) from 2017 to 2020,[57] but slightly higher than the results of a PPS study conducted in two tertiary hospitals in Myanmar (56.6%) in 2019.[65] In this research, the stop or review date of antibiotic prescriptions was only documented in 15.2% of prescriptions, substantially lower than the 2015 Global-PPS finding (38.3%) across 53 hospitals, mainly HICs.[11]

Guideline compliance was one of the most commonly used indicators in AMS interventions to assess changes in the quality of antibiotic prescribing.[123] In a previous systematic review and meta-analysis of studies up to 2014, mostly from HIC, guideline compliance was associated with a 35% relative risk reduction for mortality.[123] This survey found that hospital antibiotic guidelines were not available for 28.9% of empirical antibiotic prescriptions, with 51.6% compliance where available. These figures were lower than the Global-PPS findings across 53 countries, mainly HICs, 74.3% and 77.4%, respectively,[11] yet consistent with the results observed in other studies from LMICs in the region, like in Laos[57] and Myanmar.[65]

The majority (76%) of surgical prophylaxis prescriptions, aiming to prevent surgical site infections (SSIs), were administered for more than one day in Indonesian hospitals participating in this research. This finding was consistent with the findings of studies in LMICs and low-income countries, such as PPS studies in LMICs in Asia across 25 private hospitals in India (77%)[59] and 41 hospitals (mainly secondary and tertiary) in Thailand (70.3%).[58] In 2016, a cohort study of 343 hospitals in 66 countries assessed gastrointestinal surgery cases. The study found that patients in middle-income (80%) and low-income (85.6%) countries were more likely to be prescribed antibiotics after surgery than patients in HICs (46%).[48] However, the meta-analysis of this study found that, despite the higher prevalence of prolonged prophylaxis, patients in low-income countries had a higher incidence of SSIs (23.2%) in comparison to patients in HICs (9.4%).[48] Studies found that prolonged

surgical prophylaxis showed inconclusive evidence in reducing SSI; instead, it was sterilisation in operating rooms and surgical wards[189] and appropriate antibiotic choice, timing, duration, and route.[190]

The proportion of targeted prescriptions in this PPS accounted for only 13.8% of all therapeutic prescriptions, 8.1% of CAI prescriptions, and 26.8% of HAI prescriptions. These results were lower than the 2015 Global-PPS findings (26.6%, 20.9%, and 36.9%, respectively), which were mainly generated from studies in HICs.[11] In this research, bacterial culture samples were taken in 44.3% of therapeutic antibiotic prescriptions. Of all CAI prescriptions, only 21.2% had culture samples taken within the first 48 hours of admission, indicating that the majority of antibiotics were potentially administered before taking culture samples. Yet, previous studies have shown that antibiotic administration before taking culture samples, blood specimens in particular, reduces the number of positive culture results.[191,192]

A low prevalence of targeted treatment as well as culture samples taken may indicate a suboptimal diagnostic capacity and/or underutilisation of microbiology diagnostics, which leads to high empirical antibiotic prescribing. This situation might be influenced by the delayed reporting of positive culture and sensitivity results to prescribers, estimated at three to four days for blood specimens, two to four days for sputum samples, and two to three days for urine samples.

4.5 Conclusion

The point prevalence survey identified a high prevalence of antimicrobial prescribing, particularly broad-spectrum systemic antibiotics, in hospitalised patients across different hospital types and levels in Indonesia. Quality indicators of antibiotic prescribing with regard to documentation of reasons for prescription, stop or review date, planned duration, duration of surgical prophylaxis, targeted treatment, and culture samples taken were overall poor. Therefore, it is crucial to investigate the reasons behind these practices in order to optimise antibiotic prescribing in Indonesian hospitals.

Chapter 5
Social-cultural contexts and dynamics influencing antibiotic prescribing in public and private hospitals in Indonesia

This chapter elaborates on the qualitative findings from the interviews and observations to address the second objective, to explore the social-cultural contexts and dynamics influencing antibiotic prescribing practices in Indonesian hospitals. This chapter covers the findings from the qualitative methods: the characteristics of participants, the observed norms and practices of antibiotic prescribing, and the four identified themes from the analysis.

Some of the qualitative results presented in this chapter have been published during the course of my DPhil in *Antimicrobial Resistance & Infection Control (ARIC Journal)*.

Limato R., Broom A., Nelwan E.J., and Hamers R.L. A qualitative study of barriers to antimicrobial stewardship in Indonesian hospitals: governance, competing interests, cost, and structural vulnerability. *Antimicrob Resist Infect Control* 11, 85 (2022). [Link]

5.1 The characteristics of the interview and observation participants

5.1.1 Semi-structured interview

I performed a total of 51 interviews, 48 with participants from five hospitals and three with national AMR stakeholders. The participants comprised 26 doctors and surgeons from various medical and surgical departments (including specialists or consultants, residents, and general practitioners (GP)), four clinical microbiologists, five clinical pharmacists, three representatives of hospital management, five hospital AMS leaders or senior members, five medical interns, and three national AMR stakeholders. The majority of participants had been working for 1–5 years in their position (54.9%) and for 6–10 years (25.5%) in their respective hospitals (**Table** 5.1). Most of the interviews lasted for 60 minutes, with a range between 30 and 165 minutes. The variation in interview duration was mainly determined by the breadth and depth of the discussion, as well as the participants' time availability. The total interview time was 47 hours and 25 minutes.

Table 5.1 The characteristics of the interview participants

Interview participants		N=51 (100%)
Sex		
Female		28 (54.9)
Male		23 (45.1)
Participant type		
Doctors	Specialist or consultant [a]	10 (19.6)
	Resident	3 (5.9)
	General practitioner (GP)	2 (3.9)
Surgeons	Specialist or consultant [b]	9 (17.7)
	Resident	2 (3.9)

Interview participants		N=51 (100%)
AMR/AMS stakeholders	National AMR stakeholders	3 (5.9)
	Hospital AMS leader or senior member	5 (9.8)
Clinical microbiologist		4 (7.8)
Clinical pharmacist		5 (9.8)
Hospital executive		3 (5.9)
Interns		5 (9.8)
Length of work in the profession (year)		
<1		1 (2.0)
1-5		28 (54.9)
6-10		12 (23.5)
11-15		6 (11.7)
16-20		3 (5.9)
>20		1 (2.0)
Length of work in the hospital (year)		
<1		10 (19.6)
1-5		9 (17.7)
6-10		13 (25.5)
11-15		10 (19.6)
16-20		2 (3.9)
>20		4 (5.9)
Not applicable [c]		3 (7.8)
Hospital type		
Public		28 (54.9)
Private		20 (39.2)
Not applicable [c]		3 (5.9)

Abbreviations: AMR, antimicrobial resistance; AMS, antimicrobial stewardship; GP, general practitioner.
Data are expressed as number (percentage).
[a,b] A consultant is referred to a subspecialist.
[a] Internist, pulmonologist, haemato-oncologist, intensivist, paediatrician, neurologist.
[b] General surgeon, orthopaedic surgeon, neurosurgeon, urologist, plastic surgeon, digestive surgeon, obstetrician and gynaecologist.
[c] National AMR stakeholders.

5.1.2 Observation

I performed a total of 22 observations, comprised of six observations of ward activities, twelve observations of doctors' and surgeons' clinical rounds, one

observation of the clinical pharmacist's ward round, one observation of the AMS ward round, and two observations of the AMS meeting.

The observations of ward activities took place in the following six types of wards: the ICU, adult medical-surgical, adult medical, adult surgical, paediatric medical wards, and emergency room. The observations of doctors' and surgeons' clinical rounds were with two surgeons, two internists, three infectious disease consultants, two paediatricians, a neurologist, and two residents from internal medicine. Regular ward rounds of clinical pharmacists only occurred in one private hospital, and therefore, I conducted one observation in this hospital.

The AMS activities that occurred during the research period were two AMS meetings in a private hospital and one AMS ward round in a public hospital. The two AMS meetings were conducted consecutively in a private hospital. The first meeting was an internal meeting between the AMS team leader and members. The objective of this meeting was to plan the AMS strategy and develop tools to be discussed in the next meeting with the prescribers. The second meeting was a meeting between the AMS team and prescribers, aiming at elaborating on the AMS strategy to be implemented hospital wide. A representative of hospital management and specialists or consultants from various specialties and sub-specialties attended the meeting.

The ward round in a public hospital was attended by specialists and residents from the visited ward and the AMS team members (an infectious disease

consultant, a clinical microbiologist, a clinical pharmacist, and nurses). In this round, the appropriateness of antibiotic prescribing was retrospectively reviewed in the case of an ICU patient using the Gyssens method (**Table** 2.1).

The observations were mainly conducted in a public hospital (hospital 2) and a private hospital (hospital 1). I also conducted a few observations in hospital 5 (a public hospital) and 6 (a private hospital) just before the COVID-19 pandemic. Due to the regulations of the Indonesian government and OUCRU Indonesia, the remaining planned observations were cancelled.

5.2 Observed norms and practices around antibiotic prescribing

5.2.1 Authority and autonomy in antibiotic prescribing

Based on my observations across participating hospitals, the decision to prescribe antibiotics for hospitalised patients is under the authority of a specialist or consultant (a consultant is referred to as a subspecialist). In the context of Indonesian hospitals, this specialist or consultant is called a DPJP, or *Dokter Penanggung Jawab Pasien*.

When a patient came to the emergency ward, a GP on duty decided whether this patient would be discharged or admitted. When the GP decided to discharge the patient, this GP has the authority to prescribe oral antibiotics before patient discharge. When the GP decided to admit the patient, he or she then handed the patient management to a relevant DPJP based on the main clinical syndrome (Observation 7 and 16).

From my observations, I found that a DPJP has full responsibility for the entire patient management during hospitalisation and the authority to make clinical decisions, including medical and/or surgical procedures, laboratory and other diagnostic tests, and consultation with other specialists or consultants. In the case of patient consultation, a DPJP can accept or refuse advice from other specialists or consultants. As observed in ward activities, for complicated cases, even though patient management was shared between several specialists or consultants, the highest authority in clinical decision-making remained with the respective DPJP (Observation 7, 16, and 18).

Junior doctors, or non-specialists, had limited autonomy over antibiotic prescribing. As observed in the participating public hospitals, residents practised medicine under the supervision of the DPJP. They had to consult on any clinical decision with and obtain approval from the DPJP, including antibiotic prescribing (Observation 16 and 18). In the observed private hospitals, there were no residents present; instead, GPs staffed the wards. These GPs did not have autonomy in clinical decision-making, including antibiotic prescribing. Their main roles were to attend to patients' complaints, report the patient's condition to the DPJP, and, if necessary, write prescriptions as instructed by the DPJP (Observation 2, 3, and 5).

5.2.2 Antibiotic decision-making, antibiotic guidelines, and culture sample taking

As observed in both public and private hospitals, antibiotics for hospitalised patients could be prescribed as soon as the DPJP made a decision that the patient had to be admitted. For example, even when the patient was still in the emergency ward. However, in all observed hospitals, the prescribed antibiotic(s) could only be administered once the patient was in the inpatient ward. Yet, in certain circumstances, antibiotic administration was allowed in the emergency ward. For example, in a public hospital, a patient was stuck in the emergency ward for days due to overcrowded inpatient wards. Therefore, antibiotic administration had been started as instructed by the DPJP.

Different doctors (DPJP) used different justifications to prescribe antibiotics while patients were still in the emergency ward. Some of them waited for the white blood cell count result, aiming to judge the possibility of bacterial infection. Some immediately prescribed antibiotics based on the clinical presentation while waiting for the laboratory test result to be released. Often, the decisions by DPJP were based on the reports from the GPs examining patients in the emergency ward.

Written antibiotic guidelines and culture sampling procedures were not available in all observed wards, as well as in the ward computer, as confirmed by the nurses and/or the ward GPs (Observation 1, 7, 15, 16, 17, and 20).

Based on two observations, one in a public hospital and one in a private hospital, only patients showing signs of severe infections, e.g., sepsis or severe pneumonia, had their blood samples taken for culture tests while still in the emergency room (Observation 7 and 16). In a public hospital, I observed a nurse in an emergency room who was unclear about the culture sampling procedure as described in the following quote:

> A nurse to an emergency GP: *"Doc, I am about to take the culture samples from patient X [who was diagnosed with sepsis], but the antibiotics were administered two hours ago. Is that okay?" (Observation 16)*

5.2.3 Communication related to antibiotic prescribing

In most observations, communication about antibiotics was one-way, with a DPJP giving instructions to the other clinical staff (nurses, residents, or GPs). Communication between a DPJP and nurses, both in public and private hospitals, was limited to instructions to stop or initiate antibiotics, change antibiotic preparation, and adjust the antibiotic dose. There were no observed shared responsibilities around antibiotic prescribing, for example, discussion about the plan to review or stop antibiotic prescriptions (Observation 1, 5, 6, 11, 12, and 19).

Similarly, as I observed in a private hospital, communication between a DPJP and the ward GPs was limited to discussing the patients' clinical condition and giving instructions for follow-up. There was no observed discussion regarding, for example, reasons to prescribe antibiotics or an antibiotic de-escalation

plan. In this context, GPs did not have authority over antibiotic decisions for hospitalised patients (Observation 1, 5, and 6).

In my observations in two public hospitals (both are tertiary teaching hospitals), discussion between a DPJP and residents was limited to patients' clinical presentation and progress, laboratory results, and giving instructions related to patient treatment (Observation 17, 18, and 20). There was an exception in a clinical round with an infectious disease consultant in one tertiary teaching hospital where the discussion about antibiotics was salient. For almost every patient, this consultant and residents discussed the justification for antibiotic choice, the escalation or de-escalation plan, and the clinical response to antibiotic treatment, among others (Observation 19).

In all observed hospitals, both public and private, communication between a DPJP and patient was short and predominantly one-way, from the DPJP to the patient. In the observed two public hospitals, doctor–patient communication was frequently absent. In general, when it occurred, the discussion between a DPJP and patient was limited to clinical symptoms and progress, and there was barely a discussion about antibiotics. When a discussion about antibiotics occurred, it was mainly related to antibiotics' availability and cost (Observation 1–3, 5, 6, 8, and 12).

5.3 Social-cultural factors influencing antibiotic prescribing in Indonesian hospitals

5.3.1 Sentiment towards AMR and prioritisation of the problem

From the interviews, I found that the majority of the participants recognised the AMR problem as significant in their practice and were aware that overuse of antibiotics accelerates AMR. Clinical microbiologists from all participating hospitals reported that disease-causing bacteria were becoming less susceptible to commonly used antibiotics. Doctors and surgeons described their experience with AMR and its consequences for their clinical practices: difficult patient management and escalating poor clinical outcomes.

> *"I often receive referral patients with recurrent infections. When I ordered the culture test, the results often showed R (resistant) to all cephalosporins and quinolones, and only carbapenems that were still sensitive. This is frustrating." (P11 Obstetrician/Gynaecologist, female)*

> *"In this hospital, more than 70% of gram-negative bacteria are only susceptible to meropenem and colistin." (P18 Clinical microbiologist, female)*

> *"I've treated patients with multidrug resistance who were difficult to manage. For these patients, their clinical outcomes are not good. If they survive, the length of stay is long, and the cost of treatment is very high. So, AMR is very dangerous, and I am aware of the consequences." (P42 Internal medicine resident, female)*

The national AMR stakeholders had a different perspective on awareness of AMR in relation to prioritising actions to address the problem. Two of the three

participants mentioned that for prescribers, the immediate implication of antibiotic prescribing on antibiotic resistance is often invisible. Therefore, AMR was perceived as a 'potential' rather than 'immediate' problem that often received less attention.

> *"A different angle to look at the AMR problem is that AMR casualties are not directly seen by those who prescribe antibiotics irrationally. Doctors cannot immediately see the effects on all of their patients… Often we do not see the impact right away, so it does not become a priority." (P2 National AMR stakeholder, female)*

> *"The AMR problem is not a priority yet because it is not seen as an acute disease. It is similar to smoking. People won't get sick right away after smoking. When doctors prescribe antibiotics, that doesn't mean the bacteria will always be resistant right away. What happens is that there is a 'potential' for the bacteria to be resistant. In Indonesia and some parts of the world, when it is a 'potential', people won't bother with it." (P1 National AMR stakeholder, male)*

The invisibility of the AMR problem in relation to the antibiotic prescribing practices of hospital prescribers also emerged from a different perspective. Hospital-based interview participants perceived that AMR was driven by antibiotic practices outside the hospitals instead of antibiotic prescribing in hospitals. For example, unnecessary and inappropriate antibiotic use in the community, primary healthcare, and non-human settings like animal farms and agriculture.

> *I: "How significant is the AMR issue in comparison with the other concerns within the hospital context?"*

P: "In this hospital, this topic is not yet an important issue, especially with regard to the general public. Once I saw on social media that a healthcare worker was at a stall, and she showed that amoxicillin was sold in that shop. I texted her, 'Ma'am, do you educate the owner?' When people catch a cold, they Immediately try to treat themselves without doctor consultation, acting carelessly and being ignorant about self-prescribing antibiotics. Many people also don't know that poultry and fish farms use antibiotics to grow these food animals quickly… (P51 Senior AMS team member/clinical pharmacist)

I: "How do you perceive AMR in your day-to-day job?"
P: "…Some of my seniors have started to use meropenem for surgical prophylaxis. We are unaware that this practice will result in higher expenses, while patients' clinical conditions are not necessarily getting any better. However, there was also a big issue about antibiotics in our food back in 2016 or 2017. It was about livestock being given antibiotics to keep them healthy. This is a mess. So, even though we do not consume antibiotics in a drug form, a high AMR rate occurred because our foods are fed with antibiotics." (P31 AMS team leader/surgeon, female)

"Perhaps we need to fix the primary healthcare facilities such as private clinics and Puskesmas (community health centre) where doctors can easily prescribe antibiotics, or the orderlies and midwives can easily give antibiotics to patients…" (P29 Internist, female)

5.3.2 Diagnostic uncertainty, risk, and perceived quality of services

According to the findings of studies conducted in HICs and LMICs, diagnostic uncertainty and the fear of losing the patient can influence the decision to prescribe antibiotics.[79,86] The interview and observation participants, especially the DPJP (specialists and consultants), expressed concerns related to their responsibility for patients' clinical outcomes. This situation introduced

the fear of losing a patient under their responsibility. They justified antibiotic prescribing to avert the risk of poor patient outcomes, especially in cases of diagnostic uncertainty (e.g., difficulty differentiating bacterial from viral infection) and heightened risks such as comorbidities and/or an immunocompromised state.

> *"The way of thinking between clinicians and non-clinicians is different… For clinicians, if a patient has a fever, the fever must go RIGHT NOW! If possible, the patient can immediately recuperate and go home RIGHT NOW! We always make sure the patients don't die." (Observation 10 Internist, male)*

> *"When I have patients with a brain infection, for example, meningitis or encephalitis, I feel uncertain. Is this a bacterial infection or a non-bacterial infection like tuberculosis? Should I directly give antituberculosis? Or should I first prescribe antibiotics? Antituberculosis or antibiotic first? That is the most often-encountered uncertain situation. That's the confusion. So, I just prescribe antibiotics." (P23 Neuro-infectious disease consultant, male)*

> *"When fever occurs in a cancer or autoimmune patient, but the source of infection cannot be determined, it's difficult to decide whether or not to give antibiotics. Therefore, the decision to prescribe antibiotics is 'more loosely' because I concerned about the comorbidities or immunocompromised state. If I miss and treat the infection case as a non-infection case by not prescribing antibiotics, the result is poor patient outcomes. If I am too late in administering antibiotics because I have too many considerations, it will result in poor patient outcomes." (P44 Haemato-oncologist, male)*

The concerns about patients' clinical outcomes that influenced antibiotic prescribing were interwoven with the perceived quality of services. The

interview participants reported that, in the context of hospitalised patients, they barely experienced antibiotic demands from the patients or their families. This finding was in line with the finding of the observation, which was that the discussion about antibiotics between the DPJP and the patient was limited to drug availability and cost.

However, the interview participants reported that perceived patient expectations had a significant influence on the decision to prescribe antibiotics, particularly in the context of health service delivery in private hospitals by a specialist or consultant. As mentioned by participants, the cost of treatment in private hospitals was significantly higher than in public hospitals. In exchange, patients, particularly those with out-of-pocket payments or a co-payment scheme, expected the best care possible, such as prompt recovery. Therefore, doctors tried to meet this expectation in order to maintain their reputation and patient loyalty. These notions are shown in the quotations below from participants from private hospitals and their perceptions of doctors in private hospitals.

> *"When patients come to seek treatment, I want them to fully recover. Especially as a surgeon, the surgery I perform influences the satisfaction of my patients. So, I guard myself from the patient's perception of "Why is the treatment of this surgeon poor?" This factor plays a role in my antibiotic prescribing." (P8 General surgeon, male)*

> *"In our (Indonesian) culture, the indicator of a doctor's competency is immediate recovery from illness. Based on my observation, this often makes some doctors rush to prescribe antibiotics. Patients'*

expectations of 'high-level physicians' such as subspecialists are particularly high. They expect that with only one visit or a short period of treatment, they will immediately recover. Due to this expectation from patients and their families, doctors want to make sure that their patients can quickly recover to maintain loyalty." (P6 Hospital manager, female)

"Especially in private hospitals, doctors usually directly 'shoot' the patients with the third line antibiotics. … They tend to prescribe more aggressive antibiotics to the out-of-pocket patients, so the patients immediately recuperate. Perhaps there is a psychological effect where because the patients pay for the treatment, if they do not recover immediately, they will complain to the doctor." (P42 Internal medicine resident, female)

5.3.3 Habits, culture, and norms in the medical profession

The problem of suboptimal antibiotic practice continues and is embedded in the undulations of culture, norms, and habits in professional work.[88] Moreover, it is inflected by forms of hierarchy and ownership vis-à-vis what is instructed by best practice guidelines.[85,86] Specifically, and as also illustrated in my interviews, antibiotic prescribing practices follow the precedent rules of the game,[171,172] as much as following what is best, safest, or most effective. In line with the findings from the observations (section **5.2.1**), the interviews revealed that junior doctors (residents and GPs) have limited authority to prescribe antibiotics for hospitalised patients. Furthermore, the antibiotic prescribing practices of junior doctors are influenced by the teachings of their predecessors and the norms applied in the setting. The senior doctors

(specialists and consultants) reflected similar experiences when they were junior doctors.

> *"Honestly speaking, our antibiotic prescribing practice is definitely influenced by our teachers. When we were students, we copied our teachers. When the teachers did certain things, we followed their example. That's the reality of medical training." (P8 General surgeon, male)*

> *"Our prescribing habit has been shaped since we were in medical training. For example, we were taught to prescribe post-surgery antibiotics for a certain duration to prevent post-surgical wound infection." (P15 Neurosurgeon, male)*

> *I: "How do you choose which antibiotics to prescribe?"*
> *P: "Hmm we just follow the norms applied in hospital X (a teaching hospital). For example, if certain syndromes are treated with ampicillin sulbactam, we use the same antibiotics when we have a placement in other hospitals. Unless the local consultants disagree, we prescribe what they usually prescribe. I just follow the consultants' instructions." (P20 Obstetrics/Gynaecology resident, female)*

> *"This is what I call the 'p-drug', or personal drug. All physicians have their own beliefs and preferences based on their prescribing habits. That habit is usually passed down to the students, especially the residents. Residents then copy what they see in the practice of their role models. When I asked the residents [about their antibiotic decision], they said, "Oh because consultant A usually prescribes this antibiotic." (P2 National AMR stakeholder, female)*

Observing and reproducing habits were entangled with hierarchical medical culture. According to Bourdieu's theory of practice, acceptance of hierarchy, i.e., refusal to challenge the (deviated) practice of the seniors, is an

instrumental method to stay in 'the game'.[171,172] Junior doctors refused to challenge the senior doctors. This notion was also reported by the senior doctors, who had the same past experience as the residents.

However, there are nuances in regard to the hierarchical medical culture between surgery and medicine. Similar to the findings in a UK ethnographic study, my research found that the culture in surgery is individualistic, while doctors in medicine are collectivist.[104] In surgery, participants reflected that instructions from seniors must be followed. In medicine, despite its hierarchical culture, participants reported that there were more rooms for discussion, as reflected in the following quotes:

Surgery *"Oh, my God!!! I just follow the order. I never challenged them! I just go with the flow." (P14 Orthopaedic resident, female)*

"I don't dare do it! Back then as a resident, if I was being told to drown myself in the ocean, I just did that. I didn't ask many questions!" (P8 General surgeon, male)

"… When the seniors give instructions, just obey them! The same mistakes are repeated over and over again, but no one wants to change them. Why? Because a change is considered an anomaly, and the agent of change will be alienated! The wrong practice is never questioned because everyone is frightened!" (P11 Obstetrician/Gynaecologist, female)

Medicine *"When the antibiotic practice (of senior doctor) deviates from the guidelines, we will ask. At the very least, we want to know why that is the case. We usually get an explanation from our seniors*

or the specialists, "This is the reason why I prescribed this antibiotic." (P40, Internal medicine resident, female)

"The residents do not challenge me, but sometimes they give suggestions, or we have discussion, "How about this?" or "What do you propose?" (P23 Neuro-infectious disease consultant, male)

"The junior doctors can ask critical questions, for example, "Doc, why don't you prescribe this antibiotic?" The alert system can come from many directions, including nurses and GPs. I am open to discussion." (P27 Internist, female)

Interns reported they had limited knowledge and experience and therefore felt incompetent to challenge the senior doctors. Nonetheless, all stated that they had observed senior doctors deviate from the best practices taught in the pre-clinical stage in their antibiotic practices.

"I am afraid to ask questions because the consultants have more experience. My knowledge is only limited to the textbooks. If I question their practice, I'm afraid they'll become enraged and believe I'm second-guessing their decision." (P7 Intern, male)

"Based on the teaching from my pharmacology lecturers, antibiotic use must be based on the underlying disease. But the reality in practice, it is very different. There are some doctors whose antibiotic practice is not in accordance with what I was taught." (P22 Intern, female)

5.3.4 Vulnerability of hospital infrastructures

As reported by studies from LMICs or low-resource settings, antibiotic prescribing can be driven by 'vulnerable' hospital infrastructure. These include

poor infection prevention and control and the lack of or unreliability of infection diagnostic testing.[91–93,97] In such contexts, antibiotics are used as defensive medicine to compensate for structural vulnerabilities. From the interviews, I found that the barrier to prudent antibiotic prescribing was not so much a lack of infrastructure as it was a lack of funding flows to ensure standardised and high-quality operations to utilise infrastructures that were in fact available. This situation influenced doctors' decisions in antibiotic prescribing, including whether to prescribe broad-spectrum antibiotics.

The two main structural barriers, as reported by the participants, were surgical and microbiology facilities. Participants interviewed for this research reported barriers concerning reliable surgical facilities to prevent infection during and after surgical procedures. Surgeons from participating hospitals expressed reservations about the use of standard operating procedures to maintain sterility in operating rooms and surgical equipment. They also reported substandard infection prevention and control procedures in patient management wards. These limitations were used to justify prolonged SAP over concerns about surgical site infections.

> *"The sterility of the operating theatre cannot be guaranteed at 100%. Even though there is a protocol to sterilise the operating rooms, I don't trust whether the protocol is fully implemented or not. For example, I can still carry stuff from outside to the theatres. The operating rooms are also not completely isolated… So, even though the guidelines say that implant insertion doesn't need post-surgical antibiotic, I prescribe it due to fear of infection. Nosocomial infection is*

high in this type of hospital (a public hospital) and in Indonesia." (P25 Orthopaedic surgeon, male)

"The optimal condition of the operating rooms is the main factor in preventing infection. Surgical antibiotic prophylaxis is only a compliment. Often in Indonesia, the limitation is that aseptic and antiseptic procedures are not properly done. Not to mention the condition of the operating rooms, which I say in quotation marks, "unsterile." Because of these limitations, we, surgeons, back it up with prolonged surgical antibiotic prophylaxis just 'to be safe'." (P43 Urologist, male)

"…we know the appropriate antibiotic practice, but who dares to take a risk of patients contracting SSI? As far as I know, only the ICUs have complied with the protocol of infection and prevention control. But here (in the surgical ward), I immediately sneeze when I step my feet into this ward!" (P14 Orthopaedic resident, female)

Besides limitations in surgical facilities, predominantly in public hospitals, the interview participants expressed challenges related to microbiology testing. Some reported experience with ambiguous culture results due to unstandardised microbiology facilities and procedures, delayed reporting of culture results, as well as stock-outs of sample containers and antibiotic discs. In one public hospital, the microbiology laboratory was closed on weekends and public holidays, which resulted in delayed sample processing. These circumstances discouraged doctors and surgeons from being in favour of utilising and trusting microbiology testing.

"Well, specifically in this [public] hospital, the culture bottle for specimens is often out-of-stock or we have difficulty getting one… We

cannot take culture samples on the weekends. So, if a patient is admitted on the weekend, no specimens for a culture test is taken… The culture result often came out very late, sometimes it could take up to 3 to 5 days. The blood sampling procedures often did not meet the standard. For example, the laboratory staff took the blood sample with a volume that was less than requested. For instance, I asked for a 20-cc blood sample, but sometimes not even 10 cc of blood was taken. Maybe that's why we often get a false-negative result." (P17 Internal medicine resident, female)

"In the ICU, I often have arguments with the other specialists when they order blood cultures test. I said, "Of course we can order blood culture, but the results are often negative." The problem is the sampling technique is performed inaccurately. They ordered the nurses or lab staff to draw a small amount of blood, which was not in accordance with the standard. For instance, the blood sample must be 40 cc, but the specialists say, "Ah please don't draw too much blood, the patient's haemoglobin is low." … Furthermore, the culture results are available after 5 days, if not 7 to 8 days. Ouch!... Not to mention the broken refrigerator. Yes, the cooler. One time, I found that the culture result was 'funny'! So, I asked the lab doctor, and she said, "Oh, a couple days ago the temperature of the cooler was a bit warm." I mean, the lab staff have to inform me about this situation. The culture result might be unreliable since the laboratory condition was unstandardised when they were processing the samples." (P13 Intensivist, female)

5.4 Discussion

The findings from the interviews and observations identified several social-cultural factors influencing antibiotic prescribing in Indonesian hospitals. The emerging themes indicated some influencing factors and dynamics that have

also been found in other contexts, as well as situations that are specific to the Indonesian context. The findings showed how social-cultural factors within and beyond hospitals influence antibiotic prescribing, as pictured in the developed contextual framework (**Figure** 2.1) and the theories used in the thesis (section **3.3**)

Awareness and visibility of the AMR problem

This research found a disjunction between drivers and the visibility of AMR in day-to-day clinical practice. At the individual level, participants in this research were aware that AMR has poor implications for patients' clinical outcomes. Yet, similar to the findings in Australian[79] and Ethiopian[193] hospitals, participants deflected the drivers of the AMR problem to the antibiotic practices of 'others' outside the hospital, i.e., antibiotic self-prescribing in the community, liberal prescribing in primary healthcare, and uncontrolled antibiotic use in animal farms and agriculture. On one hand, this narrative demonstrated that there is an awareness of the complexity of the AMR problem and that antibiotic use in hospitals is only one node of the problem. On the other hand, this perspective implies the perceived 'externality of AMR', that is, participants acknowledged its significance but did not take ownership or responsibility. Therefore, reflecting the production of AMR as an externality, for example, a result of irrational antibiotic use elsewhere in communities or non-human sectors.

Evidence suggests that disease-causing bacteria can become antibiotic-resistant within a few days of antibiotic administration,[194] implying that antibiotic use during the current admission may contribute to antibiotic resistance. Therefore, it is important for hospital doctors to be aware of their practices of unnecessary and inappropriate antibiotic prescribing, including the decision to opt for broad-spectrum antibiotics and/or prolong the duration of surgical antibiotic prophylaxis. Otherwise, it would be difficult to promote and implement changes in antibiotic prescribing within hospitals.

Fear of poor clinical outcomes concerning professional responsibility and reputational risk

Regarding doctor-patient relationship, the fear of poor clinical outcomes is one important influencing factor for antibiotic prescribing in Indonesian hospitals. As reported in diverse other contexts,[83,88] a decision to prescribe antibiotics in the Indonesian hospital context is an expression of the doctor's responsibility as part of their professional role and identity. This is in line with the sick role concept, which states that when a patient has fulfilled the obligation to seek medical care, a doctor has an obligation to do everything possible for an early patient recovery.[87] Doctors perceived they might endanger their patients and did not put forth their best effort if they 'missed something' and failed to prescribe antibiotics. Meanwhile, the patients may also have comorbidities or be in an immunocompromised state, which can worsen the clinical outcomes. So, doctors are inclined to prescribe antibiotics when facing uncertainty around the aetiology of symptoms or when comorbidities occur.

The fear of clinical outcomes is also related to reputational risk, as perceived by participants in this study. As reported by Broom *et al.* (2017),[79] if a patient dies or has a poor outcome under their responsibility, it puts the doctors' reputation at stake. In this research, reputational risk is mainly the concern of doctors in private hospitals. As reported by two studies in Australian hospitals, doctors in private hospitals, particularly the treating specialists, independently practice as individual contractors and have more autonomy in decision-making.[100,101] The entrepreneurial elements,[98] e.g., maintaining and attracting 'customers', are important in this setting. Quick recovery, good clinical outcomes, and patient satisfaction have become the benchmarks of value for money. Therefore, doctors are pressurised to maintain their reputation, and one of the ways to achieve that was through more liberal antibiotic prescribing. This finding highlights a distinction in factors influencing antibiotic prescribing between public and private hospitals in Indonesia.

Vulnerable hospital infrastructure drives antibiotic prescribing

This research also found that, at the organisational level, vulnerable hospital infrastructure drives the fear of poor clinical outcomes. Studies in LMICs in Asia and Africa showed that the lack of or unreliability of infection diagnostic facilities increases the uncertainty in clinical diagnosis,[91,95–97] and the unreliable mechanisms of infection prevention and control increase the risks of contracting an infection during hospitalisation.[91–93]

In the context of this research, microbiology laboratories were available in all hospitals. However, hospitals (mainly public hospitals) faced operational challenges to ensure continuous availability of laboratory consumables as well as barriers to performing standardised culture specimen taking and handling procedures and delivering reliable and timely culture results. All of these factors have the consequences of ambiguous and delayed reporting of microbiology diagnostic results, which discourages doctors from ordering culture tests and/or trusting the results. This finding explains the PPS results (**Chapter 4**), which reported that culture samples were only taken for a small proportion of therapeutic antibiotic prescriptions (44.3%) and that only 13.8% of therapeutic antibiotic prescriptions were guided by culture results. Instead, the majority of patients prescribed with empiric, broad-spectrum antibiotics to cover all possible aetiologies (i.e., 67.4% of Watch antibiotics and 65.3% of combined third generation cephalosporins, fluoroquinolones, and carbapenems).

Besides microbiology facilities, another hospital structural challenge found in this research was inadequate infection prevention and control mechanisms concerning surgical facilities. Studies from Laos[91] and Thailand[93] reported that poor hygiene and sanitation in inpatient wards and unstandardised aseptic procedures encouraged antibiotic prescribing to cover structural vulnerabilities. In this research, structural limitations are mainly reported to be related to unstandardised procedures to ensure sterility in surgical facilities,

which were used to justify prolonged surgical antibiotic prophylaxis (76%) over concerns of surgical site infections (**Chapter 4**, section **4.3.2**).

Antibiotic prescribing habits are influenced by hierarchy and norms in the medical profession

The decision to prescribe antibiotics is intertwined with the hierarchy and norms in the medical profession. Junior doctors, i.e., residents, have varying degrees of autonomy in patient management across different contexts. In Indonesian hospital settings, the authority and autonomy for clinical decision-making around patient management rest fully with the treating specialists or consultants. Residents have limited decision-making autonomy, and final decisions are made by specialists or consultants. This finding contrasts with findings from other contexts. For example, a study in the US[195] and Canada[196] reported that residents learn during their training to make real, autonomous decisions and take responsibility for patient care, which has a real impact on their patients. Under such circumstances, junior doctors in the Indonesian context have to accept the hierarchy in decision-making and the practices of senior doctors.

This finding resonates with the social identity theory[174] and the theory of practice[171] where apprentices have to adapt to medical culture, including accepting hierarchy and coping with prevailing norms. Hierarchy in the medical profession, as well as the residency training systems in Indonesia, pushes the junior doctors to adjust their individual orientations (e.g., antibiotic

prescribing) towards the ‘played game’ in the *field* (i.e., the antibiotic practices of the specialists or consultants) or local settings (i.e., localised prescribing norms in hospitals).[171] Over time, junior doctors develop *habitus*[171]–habitual antibiotic prescribing practices, by reproducing and internalising ‘the way others do it.’.[88] The implication of such a culture in antibiotic prescribing is that junior doctors blindly follow the prevalent antibiotic practices without questioning. These practices, often unnecessary and inappropriate, are then carried out and passed down to the next generation of prescribers.

5.5 Conclusion

The high prevalence of prescribing broad-spectrum antibiotics and the poor performance on quality indicators of antibiotic prescribing in Indonesian hospitals are influenced by multilevel and multidimensional social-cultural factors: the externalisation of the AMR drivers, antibiotic prescribing as a risk aversion vis-à-vis concerns of poor clinical outcomes, the ‘pull’ of conformity to normative group prescribing practices, and unreliable microbiology and surgical infrastructures to cover structural vulnerabilities. Some influencing factors vary between public and private hospitals. The importance of identifying the local social-cultural contexts and dynamics is to develop suitable strategies in order to optimise antibiotic prescribing practices in Indonesian hospitals.

Chapter 6
Factors influencing antimicrobial stewardship implementation in public and private hospitals in Indonesia

This chapter elaborates on the qualitative findings from the interviews and observations to address the third objective: to explore the factors influencing the implementation of antimicrobial stewardship (AMS) programmes in Indonesian hospitals. This chapter covers the availability of core elements of AMS programmes from the participating hospitals and the emerging themes from interviews and observation data analysis.

Some of the qualitative results presented in this chapter have been published during the course of my DPhil in *Antimicrobial Resistance & Infection Control (ARIC Journal)*.

Limato R., Broom A., Nelwan E.J., and Hamers R.L. A qualitative study of barriers to antimicrobial stewardship in Indonesian hospitals: governance, competing interests, cost, and structural vulnerability. *Antimicrob Resist Infect Control* 11, 85 (2022). [Link]

6.1 The core elements of AMS programmes in Indonesian hospitals

The data on the core elements of AMS programmes in this research was collected using an adopted tool of the US CDC's core element of hospital antibiotic stewardship programmes (refer to section **2.2.2.1**).[119] At the time of data collection, all six hospitals had an AMS programme in place (limited to inpatients) with a designated coordinating team or committee, albeit at various stages of implementation and since inception (one to ten years). **Table** 6.1 presents the core elements of hospital AMS programmes, comprising the stages of implementation, interventions, and programme monitoring. The AMS team or committee from all hospitals received formal written support from hospital executive in the form of a decree. However, only one public hospital reported providing the AMS committee with a dedicated budget. In four of six hospitals, an infectious disease consultant was the AMS leader.

Various AMS intervention strategies were adopted by the participating hospitals (**Table** 6.1). *Education* strategies, i.e., training on the optimisation of antibiotic prescribing for prescribers, were provided in three of six hospitals. In terms of *enablement* strategies, the provision of hospital antibiotic guidelines was adopted by five of the six hospitals. Three of the six hospitals had an antibiotic documentation policy and an antibiotic review by a physician or pharmacist. However, only one of the six hospitals had antibiotic reviews within 48 hours and automatic alerts in situations where antibiotic therapy might be unnecessarily duplicative. The *restriction* approach to limit certain

antibiotic prescriptions through pre-approval authorisation was only adopted by all three public hospitals and not by private hospitals. No hospital has adopted time-sensitive automatic stop orders for specified antibiotic prescriptions.

The monitoring of AMS outcomes in all hospitals was limited to tracking antibiotic consumption using DDD, assessing the appropriateness of antibiotic use using the Gyssens method, and tracking local antibiotic susceptibility patterns. The adherence to the documentation policy and antibiotic guidelines was monitored only by one of six hospitals. However, as reported by participating hospitals, the monitoring of these outcomes was limited to a few selected cases, departments, or wards and only at certain times, for example, for hospital accreditation purposes.

None of the six hospitals monitored the clinical outcomes correlated with antibiotic prescribing, including the *C. difficile* infection rate, length of stay, and mortality rate. The tracking of financial outcomes, i.e., expenditure on antibiotic purchases, was also absent in all participating hospitals.

Table 6.1 The core elements of hospital AMS programmes

The core elements of hospital AMS programmes	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Hospital 6
Hospital type	Private	Public	Private	Public	Public	Private
AMS team/committee						
Format (team or committee) [a]	Team	Team	Team	Committee	Team	Team
Existence of the local AMS programme (by 2019)	1 year	3 years	2 years	2 years	10 years	4 years
AMS leader	Clinical microbiologist	Paediatric infectious disease consultant	Surgeon	Infectious disease consultant	Paediatric infectious disease consultant	Infectious disease consultant
Clinical pharmacists involved	Yes	Yes	Yes	Yes	Yes	Yes
Clinical microbiologists involved	Yes	Yes	Yes	Yes	Yes	Yes
Nurses involved	Yes	Yes	Yes	Yes	Yes	Yes
Infection Prevention and Control staff involved	Yes	Yes	Yes	Yes	Yes	Yes
Leadership support and commitment						
Written support statement from the hospital executive	Yes	Yes	Yes	Yes	Yes	Yes
Dedicated budget for the AMS programme	No	No	No	Yes	No	No
Interventions						
Education for prescribers and relevant clinical staff related to optimising antibiotic use	No	Yes	Yes	No	Yes	No
Enablement						

The core elements of hospital AMS programmes	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Hospital 6
Hospital antibiotic guidelines	Not yet [b]	Yes	Yes	Yes	Yes	Yes
Policy to document dose, duration, and indication for all antibiotic prescriptions	No	Yes	No	Yes	Yes	No
Review antibiotic course by a physician or pharmacist	No	No	No	Yes	Yes	Yes
Direct feedback to prescribers on how to improve antibiotic prescribing	No	Yes	No	No	Yes	No
Formal procedure to review antibiotic appropriateness within 48 hours	No	No	No	No	Yes	No
Automatic alerts in situations where antibiotic therapy might be unnecessarily duplicative	No	No	No	Yes	No	No
Restriction						
Restricted antibiotic list that needs approval	No	Yes	No	Yes	Yes	No
Time-sensitive automatic stop orders for specified antibiotic prescriptions	No	No	No	No	No	No
Monitoring and surveillance						
Antibiotic consumption outcomes						
DDD	Yes	Yes	Yes	Yes	Yes	Yes
DOT	No	Yes	No	Yes	No	No
Quality indicators						
Appropriateness of antibiotic use [c]	Yes	Yes	Yes	Yes	Yes	Yes
Adherence to documentation policy	No	No	No	No	Yes	No
Adherence to antibiotic guidelines	No	No	No	No	Yes	No
Clinical outcomes						

The core elements of hospital AMS programmes	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Hospital 6
C. difficile infection rate	No	No	No	No	No	No
Length of stay	No	No	No	No	No	No
Mortality	No	No	No	No	No	No
Microbial outcomes						
Local susceptibility patterns (antibiograms)	Yes	Yes	Yes	Yes	Yes	Yes
Financial outcomes						
Direct antibiotic expenditures (purchasing cost)	No	No	No	No	No	No
Reporting and feedback						
Reports on antibiotic use are shared with prescribers	No	Yes	No	Yes	Yes	No
Current antibiograms are distributed to prescribers	Yes	Yes	Yes	Yes	Yes	Yes

Abbreviations: AMS, antimicrobial stewardship; DDD, Defined Daily Dose; DOT, Days of Therapy.
[a] A 'committee' is eligible to have dedicated funding and has the discretion to run their own programmes, but not a 'team'.
[b] The AMS team was waiting for the hospital management to approve the final draft when this data was collected.
[c] Limited to a few selected cases, or departments, or wards. All hospitals used the Gyssens method.

6.2 Factors influencing antimicrobial stewardship implementation in Indonesian hospitals

6.2.1 National agenda and institutional buy-in

In 2015, the Indonesian Ministry of Health (MoH) enacted a national policy requiring an AMS programme to be implemented in all hospitals in Indonesia.[143] However, as evident in the interviews, observations, and reported AMS core elements, hospitals have not been able to fully implement the AMS programmes. This research identified that the highly decentralised health governance system challenged policy adaptation at the hospital level. Most public hospitals in Indonesia are under the authority of the regional (provincial and district) governments (**Table** 2.2).[150] Meanwhile, hospitals are not mandated by the regional governments because there is no policy for AMS implementation at these levels. As a result, in many cases, hospitals have been unable to allocate a dedicated budget to their AMS programmes. Participants from the private hospitals reported having little coordination with district health officials. As previously reported in the literature, private hospitals in Indonesia have not traditionally been partners in public health programmes.[197] This is a classic case of a mismatch between mandate and resources, governance, and implementation. To address this complex challenge, the MoH and national AMR stakeholders have made AMS programmes a required component of hospital accreditation since 2018, with the expectation that all hospitals will run AMS programmes with dedicated funding.

> *"…the hospitals didn't have the authority to provide the funds for the [AMS] implementation because most public hospitals are under regional governments' authority. These governments required a black on white (written) regulation that states, "This programme must be funded by the local government." (P2 National AMR stakeholder, female)*

> *"We collaborate with the hospital accreditation commission. After two years of lobbying, the accreditation committee was willing to adopt the AMS programmes as part of the accreditation assessment. The [accreditation] committee made it clear that "every hospital has to have an AMS team and programme if they want to pass the accreditation!" (P1 National AMR stakeholder, male)*

On the surface, accreditation appears to have aided hospital AMS implementation. Hospitals have been pushed to develop an AMS programme because it is one of the core requirements for hospitals to be accredited. Furthermore, as reported by participants from public hospitals, accreditation has pushed for a *restriction* strategy in the form of strict antibiotic dispensing.

> *"This policy makes it easier for us to enforce the programme. We can just say, "This is a regulation from the government." It prevents the clinicians from picking a fight with us. Without it, it is very challenging for us to implement the programme." (P31 AMS leader/surgeon, female)*

> *"I'm very excited that the AMR issue is included in the accreditation since it is one of the AMR control systems. It raises the awareness of hospital management and all related clinical staff to participate in AMR control." (P34 Surgeon, male)*

“Accreditation definitely influences antibiotic prescribing, especially in this [public] hospital. Antibiotic use is very strict. Even after the [empirical] antibiotic was approved, the AMS team strictly said, “Do not forget to take culture samples within x number of days.” (P40 Internal medicine resident, female)

However, at the national level, each of the national AMR stakeholders interviewed recognised that AMS programme implementation in most hospitals runs ineffectively and is done only to meet accreditation criteria.

“Even though an AMS programme is now mandatory because it is evaluated by the hospital accreditation commission, in reality, it ‘only exists’. The implementation has not gone as we expected. We can see that: “Oh, look! Now every hospital has an AMS programme!” Yes! However, the programme has not yet been fully implemented.” (P2 National AMR stakeholder, female)

“Although it was not stated in the official reports, AMS programmes are executed at full speed only to fulfil the national or international accreditation. But after passing these assessments, the support from hospital management for the programme decreased. Hospitals implement the AMS programme with the sole purpose of being accredited.” (P3 National AMR stakeholder, male)

At the hospital level, the hospital managers, AMS leaders, and AMS team members also mentioned similar issues, namely that AMS programme implementation is predominantly pushed for reasons of administrative compliance with accreditation standards.

I: “What is the purpose of forming an AMS team in this hospital?”
P: “The first reason is to meet the accreditation standard. Second, we thought that an AMS programme was necessary. But if it had not

been forced by accreditation, I think we would not have an AMS team." (P35 Hospital manager, female)

"Hospital management gives us (the AMS team) support in terms of, "Okay, we support (fund) you to attend AMS training." But the discussion about supporting this programme was only focused on accreditation. The AMS programme was used only as a tool to pass the accreditation." (P18 Clinical microbiologist/AMS team member, female)

The expectation that accreditation will enable budget provision for the development of an AMS programme and its effective implementation was met with disappointment. Despite the fact that all hospitals have written leadership support, only one hospital has already formed an AMS committee, which is able to receive a dedicated budget. Instead, five of the six hospitals in this research only have an AMS 'team' for which no dedicated funding is provided. Instead, they received incidental funding, for example, to attend AMS-related trainings and provide AMS programme-related logistics, mainly for accreditation interests.

"We, the hospital management, facilitate their (AMS team's) needs. But specific funding allocations, like how much money we allocated for the AMS programme, we don't have. We provide everything here, so they [AMS team] can use the available resources. For instance, if they want to hold a meeting, we provide the consumption." (P6 Hospital manager, female)

"We (the AMS team) are supported by [hospital] regulation because AMS is one of the national programmes. But we do not have any budget to run the programme because our structure is that of a 'team'

instead of a 'committee'. The funding for this programme is tied to other hospital programmes from different departments. For example, to provide AMS training, we have to tie our programme to the training agenda of the education and training department. We don't have any freedom to run the programme." (P12 AMS leader/paediatric infectious disease consultant, female)

6.2.2 Resourcing for diagnostic stewardship and the cost of antibiotics under the JKN scheme

Funding allocations for AMS programmes are also crucial to support diagnostic stewardship. A diagnostic stewardship approach encourages doctors to order diagnostic tests, especially bacterial cultures, to tailor the initial empirical antibiotic therapy to a targeted treatment.[198,199] However, in the context of public hospitals that implement the mandatory JKN scheme, the interview participants reported that the execution of this scheme was perceived as conflicting with diagnostic stewardship. Doctors considered culture testing to be expensive and exceptional—circa USD 27–34—while the insurance cover was minimum and variable. They expressed concerns that the JKN insurance would not cover the entire patient management if funds were spent on the diagnostic tests. In some hospitals, local JKN regulations discouraged doctors from ordering cultures, except in sepsis cases or when patients were not improving.

"For the ICU patients, in my experience, it is almost impossible to apply the JKN scheme. For example, a stroke case, the coverage for the entire patient management is limited to seven million rupiah (about USD 460). How come?!? Ventilator use, CVC (central vascular

catheter) insertion… they already cost almost four million rupiah (about USD 263). And sometimes patients are treated for weeks in the ICU. You do the math!" (P4 Intensivist/AMS team member, male)

"When I order a culture, it clashes with the JKN system. For example, when a patient is admitted with a urinary tract infection, I immediately order a culture, but the JKN system doesn't allow me to do so. So, I keep using the empirical antibiotic. When there is no sign of improvement on the third day, the culture test request is approved." (P29 Internist, female)

"There is a challenge, if doctors order cultures in the emergency room, they are not covered by the JKN scheme; ordering cultures is only allowed when the patient shows signs of sepsis. The base of this argument is that the emergency room is only for emergency cases, and an infection case is only considered an emergency when sepsis signs occur. Therefore, culture samples are taken later in the ward to prevent the JKN cap from being maxed out in the emergency ward." (P36 Surgeon/head of emergency department, male)

As such, AMS in practice is deeply connected to the nature of insurance cover, and the regulatory expectations of externalities (in this case, public insurers), rather than prescribers themselves. The normative health insurance does not accommodate diagnostics, and thus diagnostic stewardship best practices as part of AMS.

Another concern expressed by the interview participants is the availability and cost of antibiotics under the JKN scheme. In several instances, participants experienced an antibiotic stockout and unavailability. Doctors were also recommended by the stakeholders in the hospital to prescribe cheaper

antibiotics regardless of the spectrum over concerns of JKN reimbursement and insurance coverage. As a result, their prescriptions frequently do not correspond to susceptibility test results or antibiotic guidelines, nor do they favour more expensive, narrow-spectrum antibiotics.

> *"We are here bound by regulation to only prescribe medicines that are provided by the hospital from the JKN list." (P15 Neurosurgeon, male)*

> *"Drug varieties in the JKN scheme are limited. To prescribe antibiotics, we refer to the bacterial aetiology and its antibiotic sensitivity. However, often we are forced to use whatever antibiotics are available on the JKN list. So, sometimes the [antibiotic] review of the AMS team becomes useless." (P12 AMS leader/paediatric infectious disease consultant, female)*

> *"The JKN scheme covers everything, so, the prescription of antibiotics is not a problem. But the problem is that the recommended surgical antibiotic prophylaxis is cefazolin, a first-generation cephalosporin. It costs Rp. 40,000 (about USD 3) per vial, while ceftriaxone, a third generation cephalosporin, only costs Rp. 5,000 (about 35 cents). The JKN scheme has a package system, right? It means that the hospital tries to save as much money as possible. Because of this system, it is more profitable to spend Rp. 5,000 on ceftriaxone than Rp. 40,000 on cefazolin." (P19 Obstetrician/Gynaecologist, male)*

These specific situations demonstrate how AMS implementation is shaped by a range of fiscal and governance externalities, which can undermine effective antibiotic optimisation practices in hospitals.

6.2.3 Clinical autonomy and organisational priorities in private hospitals

Organisational priorities, which encompass doctors' autonomy and pharmaceutical sponsorship, had some degree of influence on AMS implementation in Indonesian hospitals, particularly in private hospitals. Similar to reports in other settings,[99–101] the interviews and observation analysis found that specialists or consultants working in private hospitals in this research own a status as 'partners' rather than subordinates or employees and therefore have a higher degree of clinical autonomy than those in public hospitals. As described above, doctors in public hospitals are bound by the mandatory JKN scheme and have to comply with its regulations. Therefore, the circumstances in private hospitals influenced the relationship between doctors and hospital management, as well as 'weaker' AMS enforcement in this setting. The hospital managers and the AMS team were apprehensive about enforcing the AMS programme as it is perceived as restricting the doctors' autonomy and creating fear that doctors would leave the hospital to practice elsewhere.

> *"Hospital management doesn't have the courage to enforce the AMS programme in this hospital. For instance, we, the AMS team, wanted to enforce a regulation that says surgical antibiotic prophylaxis is administered only once. But the surgeons always argue, "My collegium, my guidelines, my patients. I don't have to use the hospital guidelines..." The hospital management chose not to exercise an authoritarian approach, because some doctors are, in quotation marks, "hospital's source of income." They have many patients and bring a large number of patients to this hospital." (P9 AMS leader/clinical microbiologist, female)*

P: "If we want to execute an ideal stewardship scenario, we must do the pre-prescription authorisation approach. But there would be a war, and it is not good for doctors' comfort. We have a mutually beneficial relationship. We need them; they need us, especially the 'flagship' doctors."
I: "What do you mean by that?"
P: "The specialists who have many patients. If they leave their practice at this hospital, we are left with no patients." (P6 Hospital manager, female)

As reported by interview participants, an antibiotic restriction approach is seen as a threat to prescribers' clinical autonomy that could jeopardise the 'partnership' between doctors and hospital management. This situation is also reflected in the chosen AMS interventions (**Table** 6.1) in which no private hospital adopted restriction interventions. This power dynamic is also evident in my observation of two consecutive AMS meetings in a private hospital. The AMS team planned to initiate a pre-approval restriction strategy. However, the idea received pushback from the specialists and consultants attending those meetings (Observation 9 and 10).

Besides, in the context of private hospitals in Indonesia, participants recounted how hospital priorities to generate profits pose a barrier to AMS implementation. Pharmaceutical sponsorship for doctors and other healthcare providers has been identified as a barrier to AMS programmes, and this practice is common in LMICs where strict regulations are often not enforced.[83] In Indonesia, pharmaceutical sponsorship for doctors has been regulated in recent years,[200] and the interview participants reported that doctors are only

allowed to receive sponsorship in the form of knowledge or skill building, e.g., to attend conferences, seminars, or trainings. Therefore, the decision to prescribe or not to prescribe antibiotics is not necessarily influenced by the incentives per se, but rather by the choice of the antibiotic brand, which influenced the antibiotic selection concerning the antibiotic class or spectrum.

> *"If I have to prescribe antibiotics, and there are six choices of antibiotics with similar prices, of course, I choose to prescribe the drug from the company that supports me to attend seminars." (P27 Paediatrician, female)*

> *"I think sponsorship has an influence. For example, perhaps the patient didn't need meropenem but ceftriaxone. However, because the ceftriaxone from that brand was stocked out, the doctor replaced it with meropenem from the same brand." (P10 Clinical pharmacist/AMS team member, female)*

My research also found that pharmaceutical sponsorship influenced not only doctors as prescribers but also hospital management. Participants reported that hospitals also received pharmaceutical sponsorship, for example, by sponsoring health seminars for patients. This situation has some influence, which prevents the AMS team from running an effective programme. For example, the hospital management is reluctant to reduce antibiotic procurement from specific sponsors.

Nevertheless, implementing an effective AMS programme that serves the economic priorities of private hospitals is possible. As described by a national AMR stakeholder, some private hospitals in Indonesia have innovated their

AMS strategies by applying prudent and rational antibiotic prescribing. The goal of this strategy is to attract different patient segments by providing an appropriate antibiotic prescribing model.

> *"We can't deny that the hospital needs funding to run some programmes. We once proposed to stop antibiotic procurement from a pharmaceutical company. Then, we got feedback, "We can't cut off this one. They have sponsored us." There are some cases like that, and this complicates things. The expectation is that the sponsorship does not affect us, but it still happens, even though nowadays it is not as prominent as before. There are many interests involved, not only the doctors' and patients' but also the hospital management's." (P31 AMS team leader/surgeon, female)*

> *"Private hospitals don't like AMS programmes. The hospitals gain profits from antibiotic sales. As a result, they prefer clinicians to prescribe antibiotics. Therefore, it requires a context-specific approach. I was invited by a private hospital chain. Because this hospital wanted to attract foreign patients, antibiotic use was regulated based on the foreigners' standards. Westerners are aware that antibiotics are not supposed to be freely prescribed, like in Indonesia. This is how they control the antibiotic use in their hospital. Several big private hospitals have already implemented an AMS programme using this strategy." (P1 National AMR stakeholder, male)*

6.2.4 Interprofessional relationships and communication in AMS execution

In addition to issues surrounding the clinical autonomy of doctors in private hospitals, the level of doctors' clinical experience played a role in the acceptance and implementation of AMS policies in both public and private hospitals. The interview participants reported that senior doctors consider

themselves exempt from following policy and practice within a culture of perceived autonomous decision-making that relies more on personal knowledge and experience than formal policy. Restriction on prescribing specific antibiotics was viewed as a challenge to their expertise and judgment, stymieing the implementation of this approach. In two AMS meetings in a private hospital, I observed that the AMS leader, a young specialist, repeatedly said to the senior specialists and consultants attending the meetings that the proposed antibiotic restriction is not aimed at second-guessing their decisions but rather to contain AMR and implement a government programme (Observation 10).

> *"The funny thing is that there is one fresh graduate internist who was appointed as an AMS consultant. He has to answer the ICU antibiotic consultation, which, hmmm, I mean, he may not understand about the consulted case. I feel annoyed…" (P13 Intensivist, female)*

> *"Because AMS is a new programme, not everyone wants to accept it, especially the doctors who feel that they have more 'mileage' (experience). They often said, "This is a government programme, but I have more experience in treating my patients. This is my empirical therapy. How long have you been practicing as a doctor? I have been practicing medicine for as many years as your age!" (P6 Hospital manager, female)*

> *"The senior doctors usually dislike all regulations from the AMS team. I think, they are used to the old prescribing patterns. One senior doctor said, "If all antibiotics are regulated by the AMS team, there is no art to treating patients. Patients can get the same treatment from any doctor. I don't need to practice medicine anymore." The younger*

doctors, who have just practiced medicine for five or ten years, are more accepting of the AMS programme and its regulations. Perhaps they had less exposure to 'liberal' antibiotic prescribing since the beginning of their practice." (P31 AMS leader/surgeon, female)

The communication approach of delivering feedback to doctors as prescribers also has an influence on how these doctors perceive AMS programmes. The interview participants in two public hospitals where antibiotic restriction was implemented expressed opposing views on how the intervention was implemented and its implications for their day-to-day clinical practice.

In the first public hospital, the interview participants expressed dissatisfaction with the feedback strategies from the AMS team, which lacked a direct, two-way collegial communication manner. These participants also reported experiencing a lack of justification provided by the AMS consultants when their antibiotic requests were rejected and poor patient outcomes as a result. My observations in this particular hospital revealed that the antibiotic authorisation consultation from the specialists or consultants is not directly communicated to the AMS consultants, but instead through the nurses (Observation 14 and 17).

"The weakness in this hospital is that the AMS team doesn't sit together with us, the consultants. If there is a problem, they don't directly contact us and discuss it with us. Their job is only to approve or disapprove our antibiotic requests. Some of them are willing to provide a minimal suggestion like, "My advice is to increase the dose." But the others only say, "Approved!" or "Rejected!" (P15 Neurosurgeon, male)

“On Saturday, I visit all ICU patients, even though I am not the DPJP. Often, I found patients with poor clinical outcomes. I said, “Oh my God, why is this patient condition like this?” I mean, why did the DPJP let the patient in poor condition? When I asked the DPJP, my colleague said, “I already sought approval of this X antibiotic from the AMS team, but it was not approved!” (P13 Intensivist, female)

An ICU nurse to the observer: “When the intensivists request restricted antibiotics, one of us will make a consultation with an AMS consultant. After the antibiotic request is approved, we inform the pharmacist, and the pharmacist will release it.” (Observation 17)

On the other hand, the interview participants from the second public hospital reported positive experiences with the AMS team, which helped them make better antibiotic decisions by providing direction and justification for the recommendation. The AMS team also assisted prescribers with solutions to other AMS-related issues beyond antibiotic prescribing, for example, logistical issues. A senior AMS team member expressed that the AMS team applied direct communication with prescribers, a multidisciplinary approach, and a case-by-case assessment to provide recommendations.

“The AMS consultants are helpful and communicative. For instance, I proposed antibiotic A, then the AMS consultant suggested another antibiotic, “Doc, first try to evaluate this and this with these tests. We will re-evaluate once you get the results.” That is one example.” (P42 Internal medicine resident, female)

“When we faced logistical challenges, the AMS team was happy to facilitate them. For example, the laboratory ran out of culture disks. The AMS team said, “Oh okay, let us propose it to the director. We

will do the correspondence." Very helpful." (P39 Plastic surgeon, male)

"The [computer] system is set to ask for authorisation from the AMS team for the Watch and Reserve antibiotic prescriptions. First, one of us determines whether the prescription is appropriate or not. But do all AMS team members know everything? No, we don't. So, for the challenging cases, we discuss the cases in the [WhatsApp] group. We do this to avoid having a single person make the wrong decision. Then, we notify the doctor who requested the antibiotic, saying, "This decision was discussed among the AMS team" … We try our best to make sure not to delay the decision, especially when the antibiotic is urgently needed." (P49 Senior AMS team member/internist, male)

6.3 Discussion

Drawing on qualitative interviews with medical professionals and policymakers, and hospital-based observations, my research provided contextual evidence about factors influencing AMS implementation in Indonesian hospitals. The emerging themes indicated a considerable spectrum of challenges that delimit the effectiveness of AMS in this context in the areas of governance, resourcing, competing interests, and communication approach. This research also showed different barriers from within and beyond hospitals to implementing an AMS programme between public and private hospitals in Indonesia.

AMS programmes buy-in and resourcing under the JKN scheme

At the national level, the decentralised health system in Indonesia[149] limits the authority of the national-level government to enforce the AMS programme at

the hospital level, especially for hospitals to provide dedicated funding for an AMS programme, as reflected in the findings of this research. To address this barrier, national regulatory frameworks, like the mandatory AMS programme for hospital accreditation in Indonesia, were put in place with the expectation that they would motivate hospitals to adopt and implement AMS.[201] However, as demonstrated in this research, the 'separation of powers' between national and local priorities remains. Hospitals had developed local AMS programmes as reflected in the reported core elements, yet AMS implementation was often limited to merely meeting the national requirement rather than being purpose centred. Similar to the qualitative findings in other settings,[202] in the context of Indonesian hospitals, this situation encouraged hospital management to prioritise regulatory administration, i.e., passing hospital accreditation, over practice changes.

In regard to resourcing, this research illustrates the meaning of AMS in hospitals with a mandatory JKN scheme (mainly public hospitals in this research) as a cost-saving opportunity through postponing culture testing and opting for cheaper antibiotics. This finding demonstrates that low national health insurance coverage, while the cost of culture testing is high, positions AMS as not being able to be accommodated in reasonable care for the person (i.e., as a part of routine hospital practice and care). This situation has some impacts on the local regulations for culture testing and antibiotic choice. As a consequence, diagnostic stewardship that encourages culture-guided antibiotic treatment is less favoured. Meanwhile, previous studies showed that

diagnostic stewardship increases cost-effectiveness, i.e., decreases expenditures on treatment and hospitalisation.[193,203] Similarly, opting for cheaper antibiotics regardless of the spectrum was used as a strategy to prevent excessive medical costs beyond the JKN tariffs. As demonstrated in the PPS results in **Chapter 4**, these challenges have led to poor-quality indicators of antibiotic prescribing, i.e., a low prevalence of targeted treatment (13.8% of all therapeutic prescriptions).

Financial priorities as the challenge to implementing an AMS programme in private hospitals

Vested interests, especially in private hospitals, provide further energy behind continued antibiotic overuse, illustrating the power of enduring commercial ties in this context. In some LMICs,[83,204] including Indonesia,[200] policies prohibiting pharmaceutical sponsorship for commercial purposes are in place, yet monitoring and regulatory enforcement of such practices are often weak.[83,205] This research offered an example of a contextualised strategy to develop a stewardship 'model' that can work in a particular setting without jeopardising the quality of care. An alternative strategy was to shift revenue generation from antibiotic purchases to attracting different patient categories by offering an ideal antibiotic prescribing model.

Collegial communication approach to lower the resistance on AMS implementation

Clinical autonomy in the medical profession influenced the professional relationship between doctors and the AMS team, which in turn influences

effective AMS implementation. As elaborated in **Chapter 5**, clinical autonomy plays a crucial role in antibiotic prescribing, especially in private hospitals. A restriction strategy is perceived as challenging prescribers' autonomy. In this research, my findings showed that in one participating hospital implementing a pre-authorisation strategy, the AMS consultants were perceived by the prescribers as the 'antibiotic police' instead of a 'helping colleague.' Furthermore, antibiotic consultations between prescribers and the AMS consultants in this particular hospital were indirectly communicated through a nurse. In turn, these circumstances have implications of rejected antibiotic requests without any justification, which later result in poor patient outcomes.

On the other hand, another participating hospital in this research demonstrated a collegial communication approach that was perceived by prescribers to be helpful in their antibiotic decision-making. Previous studies in other settings demonstrated that a collegial[132] and non-confrontational[133] communication approach is the key to reducing doctors' resistance to AMS implementation. The AMS team should engage with the prescribers and not act in an authoritarian manner or as an expert. Instead, antibiotic consultation should be a platform for the AMS team and prescribers to work together to make sure patients get the best antibiotic treatment while minimising the risk of collateral damage.[206]

6.4 Conclusion

Antimicrobial stewardship has been implemented nationwide across Indonesian hospitals. The expectation of a national AMS policy enactment, supported by mandatory AMS programmes under hospital accreditation, was to push programme adoption by hospitals. Despite progress, the implementation of AMS programmes at the hospital level and a significant change in antibiotic prescribing practices have been challenged by ineffective resourcing and institutional buy-in regarding mandatory AMS under hospital accreditation, entangled priorities to generate profits in private hospitals, clinical autonomy, and a non-collegial approach in the execution of AMS interventions. A significant impact of current AMS models is likely to be limited, as evident in the patterns and quality indicators of antibiotic prescribing for hospitalised patients in Indonesia. In order to optimise the effectiveness of AMS implementation, it requires a context-specific approach, as different hospitals face different challenges in AMS execution.

Chapter 7
Discussion and conclusion

Unnecessary antibiotic use, in all its various forms, presents an increased risk of developing antibiotic resistance and thus presents a major global health problem. In the last few decades, global, regional, and local studies have shown a higher rate of broad-spectrum systemic antibiotic use in LMICs than in HICs, although such analyses simplify a range of structural, economic, political, and cultural dimensions that give rise to such trends.[11,56–58,65,74] Structural issues notwithstanding—and many of which have been explored in this thesis—Indonesia ranks among the highest consumers of antibiotics globally,[10] including broad-spectrum antibiotic use in hospitals.[36]

Over the past decade, as has been the trend elsewhere, national-level efforts in Indonesia to curb AMR have accelerated. The national Indonesian government had developed various action plans, released new regulatory controls, and further mandated hospitals to implement AMS programmes under the auspices of hospital accreditation.[143,144] However, to date, national surveillance data on hospital antibiotic use and progress reports on the outcomes of the nationwide AMS implementation are still limited. Data on antibiotic use in hospitals is patchy and limited to certain hospital types, wards, or patient groups.[36–38] Furthermore, at the time of writing, there was a lack of research to explore the contextual factors influencing antibiotic

prescribing, as well as how these sociocultural factors continue to influence the implementation of AMS programmes at the hospital level.

In response to this gap in understanding, using a mixed-method explanatory sequential design,[157,158] this thesis has addressed the following four research questions:

1. What are the prevalence and patterns of antibiotic prescribing among hospitalised patients in Indonesia?
2. What are the quality indicators of antibiotic prescribing for hospitalised patients in Indonesia?
3. What are the social-cultural factors influencing antibiotic prescribing practices in Indonesian hospitals?
4. What are the contextual factors influencing the implementation of hospital AMS programmes in Indonesia?

Patterns of antibiotic use among hospitalised patients

Antibiotic use can induce bacterial species to express resistance to antibiotic agents as part of their defence mechanisms.[17,18] The use of broad-spectrum antibiotics has a higher risk of selecting for resistance; prior exposure to these agents is strongly associated with infection with multidrug-resistant organisms in comparison to exposure to narrow-spectrum antibiotics.[33] My review of studies conducted in Indonesia[36] as well as previous studies in other LMICs in Southeast Asia[56–58] reported a higher use of systemic broad-spectrum

antibiotics in hospitals, compared with European countries and other HICs globally.[11,55]

In **Chapter 4**, using a quantitative approach, I presented the results of a PPS of antimicrobial use in six hospitals in Jakarta, Indonesia, collected in 2019. A key finding was that a high proportion (59%) of hospitalised patients in Indonesia received at least one systemic antibiotic, consistent with studies conducted in other LMICs in Southeast Asia.[56–58] Broad-spectrum third generation cephalosporins (mainly ceftriaxone), fluoroquinolones (mainly levofloxacin), and carbapenems (mainly meropenem) were the top three antibiotic groups commonly prescribed in these Indonesian hospitals. Commonly used broad-spectrum antibiotics in this research showed similar patterns across hospital types and levels, ward types, indications, and the most common diagnoses.

The high use of third generation cephalosporins for hospitalised patients in Indonesia, as found in this research is concerning. There is evidence that the use of third generation cephalosporins is associated with infection by ESBL-producing pathogens,[33] a prolonged hospital stay, and an increased probability of death during hospitalisation.[188] As presented in **Chapter 1**, limited available AMR data in 2021 from 51 hospitals in Indonesia have indicated alarming resistance rates to third generation cephalosporins in isolates of common gram-negative bacteria from blood cultures, for instance, 72% of *K. pneumonia* and 62% of *E. coli*.[16]

Quality indicators of antibiotic prescribing

Chapter 2 elaborated on quality indicators of antibiotic prescribing practices as an important element in setting a benchmark for antibiotic prescribing, clinical outcomes, AMR outcomes, and associated costs.[61,120,122] These indicators also enabled evaluations of the effectiveness of antibiotic optimisation interventions.[62] In my research, I assessed the quality indicators of antibiotic prescribing based on the PPS protocol described in **Chapter 3**.

Guideline compliance is an important quality indicator because it has been associated with a reduced risk of mortality in studies in HICs.[123] In my research in the six studied hospitals in Jakarta, I found that hospital antibiotic guidelines were not available for 28.9% of empirical antibiotic prescriptions, with 51.6% compliance where available. This finding of guideline availability is consistent with the results of studies from other LMICs in Southeast Asia,[57,65] but guideline compliance is lower than that reported for HICs.[11] The availability of antibiotic guidelines that are developed based on local antibiotic susceptibility patterns is important in providing doctors with relevant information to make a well-informed decision on empiric antibiotic therapy.

Another important quality indicator is the use of targeted, culture-guided treatment. Culture and susceptibility results can provide guidance for doctors to use the antibiotic with the narrowest spectrum to which the disease-causing bacterium has demonstrated susceptibility. The majority of systemic antibiotics in this research were indicated for therapeutic use (61%), and

69.7% of these prescriptions were aimed at treating CAI. However, as shown in **Chapter 4**, targeted treatment based on culture and susceptibility results only accounted for 13.8% of all therapeutic prescriptions, 8.1% of prescriptions for CAI, and 26.8% of prescriptions for HAI. These proportions were lower than the findings from the Global-PPS study, which mainly included HICs.[11] Furthermore, in my research, I found that bacterial culture samples were taken in only 44.3% of therapeutic prescriptions. In addition, of all CAI prescriptions, only 21.2% had culture samples taken within the first 48 hours of admission. These results may indicate a suboptimal diagnostic capacity and/or underutilisation of microbiology diagnostics, as reported by studies from LMICs in Asia and Africa.[91,96,97]

In my research, surgical antibiotic prophylaxis (SAP) was found to be the second most common indication (22.6%) for antibiotic prescriptions among hospitalised patients behind CAI (42.6%). As elaborated in **Chapter 4**, the top three antibiotics for surgical prophylaxis found in this research were broad-spectrum third generation cephalosporins, accounting for 49% of SAP prescriptions. Previous studies have shown that in some LMICs or low-resource settings, broad-spectrum antibiotic use, including in surgical procedures, is linked to poor sanitation, hygiene, and infection prevention measures, e.g., in regard to sterilisation of surgical instruments.[91,93] Furthermore, the majority (76%) of SAP prescriptions in this research were prolonged for more than one day, consistent with the PPS results from other LMICs in Asia[58,59] and globally.[48] Evidence from the literature presented in

Chapter 2 showed that prolonging the SAP duration is correlated with an increased risk of AMR and *C. difficile* infection.[49]

Social-cultural factors influencing antibiotic prescribing

The exploration of factors influencing antibiotic prescribing practices is crucial to understanding the underlying drivers of such practices in the local context. In my research, I used the exploratory qualitative methods of interviews and observation to explore such factors. The conceptual framework I developed and four theoretical approaches were used in an iterative manner in the qualitative analysis. As presented in **Chapter 5**, findings from the qualitative analysis showed multidimensional social-cultural factors at individual, relational, and organisational levels influencing antibiotic prescribing in Indonesian hospitals.

At the individual level, the interview participants in this research (i.e., doctors and surgeons as antibiotic prescribers, clinical microbiologists, clinical pharmacists, hospital AMS team, hospital management, interns, and national AMR stakeholders) were aware of antibiotic resistance and its consequences for patients' clinical outcomes. This finding is consistent with a review of studies conducted globally in which participants reported that they were aware that antibiotic resistance is a serious problem and that broad-spectrum antibiotic use can drive AMR.[76] However, participants in this research also perceived AMR as driven by antibiotic practices 'out there' rather than their own prescribing practices, in line with studies from other settings[77–80] as

presented in **Chapter 2**. This aspect is important because it reflects the ownership of the problem and the lack thereof: who is responsible for the AMR problem and who should change antibiotic practices.

At the relational level, interpersonal relationships between senior and junior doctors have a significant influence on shaping antibiotic prescribing practice as they are entangled with hierarchy, culture, and norms in the medical profession. In the context of Indonesian hospitals, I described in **Chapter 5** that only specialists and consultants have the authority to prescribe antibiotics for hospitalised patients. Participants, primarily specialists, consultants, and residents, reported that their prescribing habits have been shaped during residency training, following the practice norms of the senior doctors in the respective settings and contexts. One example is the common habit of extending SAP duration, as reported by surgeons.

The pressure to make antibiotic decisions based on the seniors' preferences and expectations, irrespective of local antibiotic guidelines, resonates with findings from studies in other settings.[85,86] This influencing factor is in line with the theory of practice and social identity theory, where apprentices have to adapt to medical culture, including accepting hierarchy and coping with prevailing norms, to 'stay in the game'.[171,174] To some degree, this factor can explain why around half of the prescribed antibiotics in this research did not comply with the local guidelines and more than 70% of SAP were prolonged for more than one day.

The doctor-patient relationship in the local context strongly influences fear of poor clinical outcomes. The interview participants in this research reported that the decision to prescribe antibiotics is part of their responsibility and professional role. They always make sure to do everything possible for an early patient recovery and not to die under their responsibility, which resonates with the sick role concept[87] and findings of studies in other contexts[83,88] elaborated in **Chapter 3** and **Chapter 2**, respectively.

Another aspect of the fear of poor clinical outcomes is related to reputational risk. Doctors' reputation is at stake if patients die or have poor outcomes under their responsibility.[79] The qualitative analysis of my research found that this influencing factor is more palpable in private hospitals, where entrepreneurial elements are crucial. In such contexts, doctors, as individual contractors[100,101] have to make sure the patients receive the best health service that is value for money, demonstrated by quick recovery, good clinical outcomes, and patient satisfaction.

At the organisational level, the decisions to prescribe broad-spectrum antibiotics, as well as the low adoption of culture-guided treatment, were influenced by the limitations of hospital infrastructure. As outlined in **Chapter 5**, in relation to culture sample taking, despite the fact that microbiology facilities were available, the research participants reported operational challenges, such as inadequate procedures for taking and handling culture samples and delays in reporting culture results to prescribers. Similar to the

findings in other settings,[91,97] these circumstances led to a lack of trust in culture results and a potential for delayed patient management, encouraging doctors to prescribe broad-spectrum antibiotics to cover all possible aetiologies.

Contextual factors influencing the implementation of antimicrobial stewardship

Antimicrobial stewardship (AMS), which aims at containing AMR,[118] has been implemented nationwide across Indonesian hospitals following a national regulation endorsed in 2015[143] and mandatory hospital accreditation since 2018.[144] In this research, I explored the contextual factors influencing its implementation using the exploratory qualitative methods of interviews and observation and the adapted US CDC's core elements checklist of hospital antibiotic stewardship programmes.[119] All hospitals in this research had been implementing AMS programmes for between one and ten years when the PPS data was collected in 2019. Despite this, the quantitative findings in **Chapter 4** showed suboptimal practices and quality indicators of antibiotic prescribing, including with regard to broad-spectrum antibiotic use, compliance with antibiotic guidelines, and utilisation of cultures for bacterial aetiology and antibiotic susceptibility.

The multilevel and multidimensional factors within and beyond the hospital not only influence antibiotic prescribing but also have implications for AMS implementation. As elaborated in **Chapter 6**, my research revealed a considerable spectrum of challenges in implementing AMS at the hospital

level. The qualitative analysis revealed that there was a ‘separation of powers’ between national and local priorities. The decentralised health systems in Indonesia[149] have a certain degree of influence on this factor, in which the national government was not able to enforce the AMS programmes due to a lack of authority over the majority of hospitals in Indonesia. As a result, according to the national AMR stakeholders interviewed, mandatory AMS under hospital accreditation was chosen as a solution to this barrier. However, the fact that the implementation of AMS programmes in hospitals was often limited to merely meeting the national requirement showed that this approach was ineffective. In this context, there was a lack of institutional buy-in, including providing dedicated funding for AMS programmes as recommended by the CDC[119] and WHO.[54] Therefore, hospital AMS leaders and team members reported struggling to execute AMS at an optimum level.

Another issue identified in my research was limited financial resourcing for microbiology diagnostic testing under the national health insurance (JKN) scheme. As presented in **Chapter 6**, participants in this research reported the JKN insurance scheme had a low threshold to cover the entire patient management during hospitalisation, which resulted in expenses for culture testing being prohibitive. This reality prevented doctors from ordering a culture test unless the patients were not improving, which explains the low adoption of culture samples taken and culture-guided treatment, as shown in the PPS results in **Chapter 4**. In addition, the JKN insurance scheme encouraged hospitals to save on treatment costs by mandating the use of cheaper

antibiotics. In some instances, broad-spectrum antibiotics were indeed cheaper than narrow-spectrum antibiotics, which contributes to the high rate of broad-spectrum antibiotic prescriptions.

In the context of private hospitals studied in my research, the two main factors challenging AMS implementation are related to prescribing autonomy and hospital interests in pharmaceutical sponsorship. As described in **Chapter 2**, previous studies found that the aspect of prescribing autonomy in private hospitals is intertwined with the doctors' position as partners rather than subordinates or employees.[99–101] In the context of private hospitals participating in my research, the implementation of restriction strategies in the AMS programmes was disfavoured by doctors and hospital management for this reason. Besides, participants also reported that pharmaceutical sponsorships for hospitals running certain hospital programmes were in conflict with the efforts to reduce the purchase of antibiotics from the sponsors.

However, my research also revealed an opportunity to implement AMS in this market-based setting. A national AMR stakeholder reported that some large private hospitals in Indonesia have innovated strategies to implement an AMS programme through shifting income generation from antibiotic purchases to attracting different patient segments by providing an appropriate antibiotic prescribing model.

In line with studies conducted in other contexts,[86,207] my research showed that antibiotic prescribing practices are influenced by complex, multidimensional social-cultural factors. However, as shown in the literature,[208,209] the solutions offered to address unnecessary or inappropriate antibiotic prescribing are one-sided, largely focusing on only one facet of the spectrum—identifying and 'fixing' the practice of individual prescribers. This situation is also evident in my research. For instance, the public hospitals implemented a restrictive antibiotic policy, demanding optimal individual prescribing practices. Meanwhile, the hospital infrastructure, like the microbiology laboratory and surgical facilities, was operated at a suboptimal level, as was the cost-prohibitive culture testing under the JKN scheme, preventing the intended optimal prescribing practices.

Globally used AMS models[54,119] as well as quality indicators to assess antibiotic prescribing in hospitals have been mainly[11,62] developed in the context of hospitals in HICs, where the basic hospital infrastructures like sanitation, hygiene, infection preventive measures, and microbiology testing meet high operational standards. Meanwhile, many hospitals in LMICs or low-resource settings are still struggling to provide these elements.

Applying the concept of a complex adaptive system and the identified areas for improvement

The conceptual framework I developed (**Figure** 2.1) and my research findings have contributed to the body of knowledge by showing how the complexity of

social-cultural factors influences antibiotic prescribing at different levels and dimensions. Furthermore, the interaction between these factors is evidently shaped by a complex adaptive system (CAS), as explained in **Chapter 3**. As demonstrated in **Chapter 5** and **Chapter 6**, the interactions of diverse agents (stakeholders from the individual to the national level) and pertinent system components (e.g., medical hierarchy, hospital infrastructure, and regulatory frameworks) in a CAS were non-traditionally linear in terms of 'cause and effect'. Certain agents in the system may pursue conflicting goals and interests, changing the dynamics in the systems, which has been described in the literature[175] and has also been demonstrated by a study applying CAS to explore drivers of antibiotic use in Iranian health systems.[176]

My research identified the CAS negative and positive feedback loops of antibiotic prescribing. For instance, in the context of public hospitals in this research, culture-guided antibiotic treatment was in conflict with the suboptimal operations of microbiology facilities as well as the cost-prohibitive diagnostic stewardship under the JKN scheme. These system components created a negative feedback loop: the agents (antibiotic prescribers) were encouraged to adapt their prescribing practices to these forces, such as in favour of prescribing empirical broad-spectrum antibiotics.

One example of a positive feedback loop was demonstrated in a participating public hospital related to an antibiotic restriction intervention. A restriction intervention often receives pushback from prescribers because it is

considered to limit their autonomy.[131] This is evident in a previous study[130] as well as in the context of private hospitals in my research. However, in this particular hospital, the AMS team provided feedback using a collegial, non-confrontational communication approach that resulted in positive feedback from prescribers. Prescribers reported that the feedback from the AMS team under this intervention is helpful in assisting them to make better antibiotic decisions. Furthermore, the AMS team made some efforts to facilitate the limitations of microbiology facilities. For example, in the case of laboratory consumable stockouts, the AMS team brought the issue to the attention of hospital management.

This research identified three main areas for improvement concerning antibiotic prescribing optimisation in the context of AMS strategies in Indonesian hospitals:

1. Addressing the hierarchical cultural norms in the medical profession, that influence the habit of antibiotic prescribing;
2. Promoting and encouraging ownership of the AMR problem and solution among all involved stakeholders;
3. Developing sustainable context-specific AMS strategies that are appropriate for and can address the local problems.

Research limitations

My research has contributed to the body of knowledge regarding antibiotic prescribing patterns and how multilevel, multidimensional social-cultural

factors influence antibiotic prescribing and AMS implementation in the context of Indonesian hospitals. However, this research has four main limitations, which can be further explored in future research.

1. The first limitation is the inherent limitation of the cross-sectional PPS design, and the fact that the data was only collected once means that the survey provided only a 'snapshot' of the antibiotic prescribing situation in the participating hospitals. Given that my research does not include any subsequent data collection, it is not possible to assess time trends in antibiotic prescribing patterns and quality indicators. The reasons behind this limitation are the limitations of the available resources and timelines to expand this research to that point.
2. The second limitation is that the quantitative and qualitative research data were collected from a convenient sample of six hospitals in urban Jakarta, which are potentially better resourced than many other hospitals in Indonesia. Therefore, the data is not necessarily representative of all hospitals in Indonesia in this context, which urged caution in extrapolating the presented antibiotic prescribing patterns and quality indicators in this research. Similar to the first limitation, the reasons behind this limitation are the limitations of available resources and timelines.
3. The third limitation is that the qualitative findings may not be transferable to other settings, which is an inherited limitation of qualitative methodology. Nonetheless, the fact that the main findings of this research corroborated findings from different countries and regions means that they

have, at least partially, broader applicability and relevance for other settings.

4. The fourth limitation is related to the qualitative data collection, as elaborated in section **3.5.4.2**. The number of observations is limited due to the scarcity of AMS implementation activities and the start of the COVID-19 pandemic during the observation period. Additionally, this research does not include nurses as interview participants, because they are traditionally not involved in antibiotic prescribing and AMS implementation in the context of Indonesian hospitals, yet they are part of day-to-day inpatient management and IPC. Future research should take the opportunity to explore the potential roles of nurses in these areas.

Recommendations and future research

Based on the above limitations and findings of this research, I propose four actionable recommendations and potential future research to optimise antibiotic prescribing and AMS implementation in Indonesian hospitals.

1. **Recommendations related to antibiotic use data collection and the PPS method**

   To address the first limitation, which is that the antibiotic use data using the PPS method was only collected once, my recommendation for future research is to conduct a longitudinal study that follows the patterns and quality indicators of antibiotic prescribing over time. For example, a prospective cohort study when there is no intervention or an interrupted time series (quasi-experimental) when an intervention is applied.

I also recommend hospitals adopt the PPS method as a monitoring and evaluation approach, which is one of the core elements of hospital AMS programmes. Hospitals with no infectious disease experts available or where these experts cannot be present at all times can benefit from this method because, unlike the Gyssens method, the PPS data can be collected by any clinical staff after minimal training.

Furthermore, to scale up nationwide hospital antibiotic use assessment, my recommendation is that all tiers of the Indonesian government, national AMR stakeholders, and relevant private healthcare sectors collaborate to create and sustain a national-level antibiotic use database, similar to the Global-PPS database, that can be used and accessed by all hospitals. This approach can simplify nationwide antibiotic use data collection, assessment, and reporting at a potentially lower cost.

2. Recommendations for future research settings

Regarding the second limitation, which is that my research only included hospitals in urban areas, my recommendation for future research is to include a larger variation of hospitals across Indonesia, including location (urban, sub-urban, and rural), resource availability (access to microbiology facilities and antibiotics), hospital ownership (different government tiers for public hospitals and various sizes of private hospitals), and availability of infectious disease experts. This recommendation is also applicable to the third limitation concerning the

transferability of the qualitative findings. Future research should explore the social-cultural contexts of antibiotic prescribing in hospitals with different organisational cultures, norms, and interests besides the aforementioned variations.

Furthermore, this research highlighted some differences regarding social-cultural factors influencing antibiotic prescribing and AMS implementation between public and private hospitals, including a 'non-conventional' AMS strategy in private or market-based hospitals. Therefore, for future research, it is important to explore which and how certain AMS strategies work or do not work in public and private hospitals, for example, through implementation research.

3. Recommendations on qualitative methods for future research

My third recommendation is related to the expansion of qualitative research in the areas of hospital antibiotic prescribing and AMS implementation in Indonesia. This research is the first to identify social-cultural factors influencing antibiotic prescribing in the context of Indonesian hospitals. Therefore, there are ample areas to be explored in future research, including the areas I identified in the fourth limitation: further exploration of the implementation of AMS strategies, the roles of nurses in day-to-day AMS implementation, the interface between hospital AMS and IPC programmes, and the utilisation of different qualitative methods like case studies and participatory action research.

4. Recommendations on the three identified areas for improvement concerning antibiotic prescribing in Indonesian hospitals

I propose four recommendations to improve the three identified areas elaborated above as found in the results based on the conceptual framework, the theoretical approaches used in this thesis, and the CAS best practices from the literature (**Table** 7.1).[210,211]

Table 7.1 Identified areas for improvement and recommendations

Identified areas for improvement	Recommendations
1. Addressing the hierarchical cultural norms in the medical profession, that influence the habit of antibiotic prescribing	a. Identifying the agents of influence, who are the senior doctors within the hierarchical culture, to create a safe environment for open discussions about antibiotic prescribing with junior doctors
2. Promoting and encouraging ownership of the AMR problem and solution among all involved stakeholders	b. Problem evaluation through the complexity lens of the CAS concept. This can encourage all relevant stakeholders to take ownership of the AMR problem and not the sole responsibility of doctors as antibiotic prescribers
3. Developing sustainable, context-specific AMS strategies	c. Developing resilient solutions, or AMS strategies, that are context-specific and that gain more stability with unpredictability, which have two main characteristics: flexibility and multiple functions
	d. The overarching, cross-cutting recommendation for the three areas for improvement is identifying the leverage points where the AMS strategies are able to address multiple issues within the context

a. *Identifying the agents of influence*

The agents of influence are individuals who work with and interact with one another on a regular basis and who have the greatest, most influential impact on the results of the system as a whole.[210,211] As depicted by the conceptual framework and the qualitative results of this research, in the context of Indonesian hospitals, senior doctors (specialists and consultants) are the agents of influence. In the hierarchical culture of the medical profession and hospital systems, they influence and shape the antibiotic practices of junior doctors.

The recommendation is to find and work with the senior doctors who have concern about the AMR problem, demonstrate good antibiotic prescribing practices, and are willing to create a safe environment for open discussions about antibiotic prescribing with junior doctors. This will create a positive feedback loop within the system as well as prudent prescribing habits that will be passed on to the next generation of prescribers.

b. *Problem evaluation through the complexity lens of the CAS concept*

Problem evaluation of antibiotic prescribing should take into account the complexity, dynamics, and interdependence of health systems, cultural factors, priorities, and resource availability in the respective setting and context. This could mean changing the approach to evaluation by asking a different set of questions.[210] Globally used

hospital AMS models[54,119] place emphasis on strategies to address the 'performance' of antibiotic prescribers, the AMS team, and the hospital. As demonstrated in this research and described in the literature,[210,211] these models pay little or no attention to the influencing social-cultural factors and dynamics that influence day-to-day antibiotic prescribing practices.[212]

My recommendation for AMS programme evaluation is to ask an additional set of questions involving all stakeholders to assess the CAS feedback loop through the lens of social-cultural aspects. For example, asking prescribers whether and how AMS strategies assist or do not assist them in making a better antibiotic decision. Further, ask the hospital management whether and how an AMS programme can serve the hospital's priorities and best interests. This recommendation has the purpose of encouraging all relevant stakeholders to take ownership of the problem and responsibility for actionable solutions that are relevant to day-to-day clinical practice. Additionally, it is anticipated that this strategy will assist these stakeholders in realising their significance as agents with the power to affect the dynamics of this complex system.

c. *Developing resilient solutions*

As elaborated in section **3.3.4**, one of the key characteristics of CAS is its unpredictability due to multiple nonlinear interactions and feedback

loops among the agents and system components.[175] In this context, it is critical to construct resilient systems that gain more stability with unpredictability, with changes in the systems having no effect on the overall outcomes.[210] Among others, two important characteristics of resilient systems are flexibility and multiple functions.[210,211] Complex systems possess a spectrum of patterns that allow organisations to thrive in different conditions. In a case of disruption, the other agents or components are able to respond effectively to the altered agents or components due to the interdependency and interconnectedness between these elements.[175]

Flexibility

The resilient systems in CAS should be flexible, with an emphasis on adaptation to emerging issues rather than rigid protocols and plans.[211] In this context, the globally used AMS tools[11,62] and models[54,119] have to be adapted to the local contexts and perceived as an iterative process guided by local responses to the interventions. Taking the results of this research as an example, an AMS intervention in public hospitals should look different from that developed for private hospitals, or between hospitals that apply the JKN insurance scheme and those that do not, or even between individual hospitals or departments. The emerging problems in each respective setting should be adapted to the existing evidence-based strategies for the specific local context.

Multiple functions

In the context of CAS, an intervention should be able to offer multiple functions. Using antibiotic restriction as an example, the approach of this intervention should tangibly help prescribers make better antibiotic decisions, feel more confident about those decisions, improve their patients' clinical outcomes, and prevent drug-resistant infections. At the same time, this intervention should also serve a financial purpose for the hospital and the health insurance system by reducing treatment and hospital expenditure costs. One of the strategies to achieve this is by identifying leverage points, which will be explained below.

d. Identifying the leverage points

Identifying the leverage points is an overarching, cross-cutting recommendation strategy for all three areas for improvement. Leverage points are the points where one part of the system overlaps with another,[210,211] or, in other words, the points where we can ‘kill two birds with one stone’. Addressing leverage points will yield better results than attempting to address smaller parts of individual systems (i.e., individual problems in the context of antibiotic prescribing and AMS programmes), and they can be better identified using the complexity lens of the CAS concept.[210,211]

In my research, one example of leverage points is strengthening hospital infrastructure by ensuring the application of standardised

structures and infection prevention and control protocols in all hospital wards, including surgical facilities. This leverage point overlaps with the above-mentioned antibiotic restriction intervention. This means that addressing this infrastructure will give doctors and surgeons confidence in holding antibiotic prescriptions and shorten SAP duration even when the restriction is applied.

My agenda is that hospitals in Indonesia, relevant government agencies, and AMR national stakeholders take into account the results of this research in national- and local-level policies, guidelines, and strategies to optimise antibiotic prescribing. The strategies to be employed as the first step to sharing these recommendations are to develop a policy brief and to share and present the research outcomes to the national AMR stakeholders.

Conclusion

In conclusion, the research presented in this thesis filled important knowledge gaps regarding the patterns and quality indicators of antibiotic prescribing as well as providing a conceptual framework showing how multilevel and multidimensional social-cultural factors influence antibiotic prescribing and AMS programme implementation in Indonesian hospitals in a non-linear approach. With the currently adopted AMS models, significant impact is likely to be limited in the Indonesian hospital context. Relevant stakeholders at the hospital and national levels need to know that the way forward for effective AMS outcomes requires approaches that are tailored to the local context and

that fully accommodate the complexity of AMR and antibiotic prescribing practices.

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Appendices

Appendix 1 PPS data collection forms

WARD FORM **(1 / 1)**

Study identifier **[ACS-JKT]** ☐☐☐ Hospital Identifier ☐☐☐ Unique Ward ID ☐☐☐ Completed by

1. Date of survey: ☐☐/☐☐/☐☐ (dd/mm/yy)

2. Ward name: (_____)

3. Department type

Paediatric departments
- ☐ Paediatric Medical Ward (PMW)
- ☐ Haemato-Oncology PMW
- ☐ Transplant PMW
- ☐ Paediatric Surgical Ward (PSW)
- ☐ Paediatric Intensive Care Unit (PICU)

Neonatal departments
- ☐ Neonatal Medical Ward (NMW)
- ☐ Neonatal Intensive Care Unit (NICU)

Adult departments
- ☐ Adult Medical Ward (AMW)
- ☐ Haemato-Oncology AMW
- ☐ Transplant AMW
- ☐ Pneumonology AMW
- ☐ Adult Surgical Ward (ASW)
- ☐ Adult Intensive Care Unit (ICU)

Other
- ☐ Other (_____)

4. Mixed department?
- ☐ Yes
- ☐ No
- ☐ Not applicable (N/A)

5. Activity *(In case of mixed department, tick all encountered activities)* ☐ Medical ☐ Surgical ☐ Intensive care ☐ N/A

6. Patient population:
- ☐ Male adult
- ☐ Female adult
- ☐ Mixed adult
- ☐ Neonatal/paediatric
- ☐ Mixed adult/neonatal/paediatric
- ☐ N/A

7. Total number of patients in this ward who were admitted before 08.00 a.m. ☐☐

8. Total number of active beds in this ward by 8 a.m. on the survey day ☐☐

9. Total number of patients with antimicrobials (AM) by 8 a.m. on the survey day ☐☐

PATIENT FORM **(1 / 3)**

Study identifier **[ACS-JKT]**	Hospital Identifier	Unique Ward ID	Completed by	Patient Unique ID
	☐☐☐	☐☐☐	☐☐☐	☐☐☐

A. DEMOGRAPHICS

1. Date of survey		☐☐/☐☐/☐☐ (dd/mm/yy)		
2. Ward name		(_____)		
3. Patient's medical record number		(_____)		
4. Admission date		☐☐/☐☐/☐☐ (dd/mm/yy)		
5. Jaminan Kesehatan Nasional (JKN)		☐ Yes	☐ No	☐ Unknown
6. Age recorded		☐ Yes	☐ No	
If yes, specify patient age category		☐ ≥ 2 years (_____) years	☐ 1-23 months (_____) months	☐ <1 month (_____) days
7. Weight		(_____) kg (at least 1 decimal)		☐ Unknown
8. Sex		☐ Male	☐ Female	☐ Unknown
9. Underwent surgery in the past 90 days (before or after admission) - *Refer to NHSN list.* ***If yes,***		☐ Yes	☐ No	☐ Unknown
	Surgery 1 (latest surgery)	☐ NHSN	☐ Non-NHSN	☐ Unknown
	Surgery 2	☐ NHSN	☐ Non-NHSN	☐ Unknown
	Surgery 3	☐ NHSN	☐ Non-NHSN	☐ Unknown
10. Hospitalisation within 90 days		☐ Yes	☐ No	☐ Unknown
11. Transfer from other health facility		☐ Yes	☐ No	☐ Unknown
If yes		☐ Hospital	☐ Non-hospital	☐ Unknown
12. Catheter	Central Vascular	☐ Yes	☐ No	☐ Unknown
	Peripheral Vascular	☐ Yes	☐ No	☐ Unknown
	Urinary	☐ Yes	☐ No	☐ Unknown
	Intubation	☐ Yes	☐ No	☐ Unknown
13. Comorbidities				
	Malaria	☐ Yes	☐ No	☐ Unknown
	Tuberculosis	☐ Yes	☐ No	☐ Unknown
	HIV	☐ Yes	☐ No	☐ Unknown
	On ART	☐ Yes	☐ No	☐ Unknown
	Recent CD4 count	(_____) cells/μL		☐ Unknown
	Malnutrition	☐ Yes	☐ No	☐ Unknown
	COPD	☐ Yes	☐ No	☐ Unknown
	Diabetes Mellitus	☐ Yes	☐ No	☐ Unknown
	McCabe Score	☐ Rapidly fatal (death <1 year)	☐ Ultimately fatal (death 1-4 years)	☐ Non fatal (death ≥5 years)
		☐ Unknown		

B. LABORATORY **(2 / 3)**

14. Biomarker	*Result*	*Unit*	*Sampling date*	
WBC (before antibiotic start)	(_____)	10^3/uL	☐☐/☐☐/☐☐	☐ Not done
WBC (most recent)	(_____)	10^3/uL	☐☐/☐☐/☐☐	☐ Not done
CRP (before antibiotic start)	(_____)	mg/L	☐☐/☐☐/☐☐	☐ Not done
CRP (most recent)	(_____)	mg/L	☐☐/☐☐/☐☐	☐ Not done
Procalcitonin (before antibiotic start)	(_____)	µg/mL	☐☐/☐☐/☐☐	☐ Not done
Procalcitonin (most recent)	(_____)	µg/mL	☐☐/☐☐/☐☐	☐ Not done

15. Biochemistry (most recent)				
Ureum	(_____)	mg/dL	☐☐/☐☐/☐☐	☐ Not done
Creatinine	(_____)	mg/dL	☐☐/☐☐/☐☐	☐ Not done
SGOT/AST	(_____)	U/L	☐☐/☐☐/☐☐	☐ Not done
SGPT/ALT	(_____)	U/L	☐☐/☐☐/☐☐	☐ Not done

16. Culture sample taken ☐ Yes ☐ No ☐ Unknown

If yes, specify for each relevant clinical sample

Specimen 1

Date — Sample taken ☐☐/☐☐/☐☐ ☐ Unknown; Results ☐☐/☐☐/☐☐ ☐ Unknown

Specimen type — ☐ Blood ☐ Urine ☐ Wound ☐ Sputum ☐ Sterile fluids ☐ Other (_____)

Results — ☐ Positive ☐ Negative ☐ Pending ☐ Not available

If Positive, Microorganism (_____)

Antibiotic susceptibility test results — ☐ Yes ☐ No ☐ Unknown

If yes Resistant phenotype (_____) (_____) (_____)

Specimen 2

Date — Sample taken ☐☐/☐☐/☐☐ ☐ Unknown; Results ☐☐/☐☐/☐☐ ☐ Unknown

Specimen type — ☐ Blood ☐ Urine ☐ Wound ☐ Sputum ☐ Sterile fluids ☐ Other (_____)

Results — ☐ Positive ☐ Negative ☐ Pending ☐ Not available

If Positive, Microorganism (_____)

Antibiotic susceptibility test results — ☐ Yes ☐ No ☐ Unknown

If yes Resistant phenotype (_____) (_____) (_____)

Specimen 3	Date	Sample taken Results	☐☐/☐☐/☐☐ ☐☐/☐☐/☐☐	☐ Unknown ☐ Unknown
	Specimen type	☐ Blood ☐ Sputum	☐ Urine ☐ Sterile fluids	☐ Wound ☐ Other (_____)
	Results	☐ Positive ☐ Not available	☐ Negative	☐ Pending
If Positive,	Microorganism	(_____)		
	Antibiotic susceptibility test results	☐ Yes	☐ No	☐ Unknown
If yes	Resistant phenotype	(_____) (_____) (_____)		
Specimen 4	Date	Sample taken Results	☐☐/☐☐/☐☐ ☐☐/☐☐/☐☐	☐ Unknown ☐ Unknown
	Specimen type	☐ Blood ☐ Sputum	☐ Urine ☐ Sterile fluids	☐ Wound ☐ Other (_____)
	Results	☐ Positive ☐ Not available	☐ Negative	☐ Pending
If Positive,	Microorganism	(_____)		
	Antibiotic susceptibility test results	☐ Yes	☐ No	☐ Unknown
If yes	Resistant phenotype	(_____) (_____) (_____)		

C. TREATMENT

17. Total number of active antimicrobial drugs ☐☐☐

For each given antimicrobial drug, please complete a separate treatment form. The number of treatment forms completed should be the same as the number of antimicrobial drugs given

TREATMENT FORM **(1 / 1)**

Study identifier **[ACS-JKT]** | Hospital Identifier ☐☐☐ | Unique Ward ID ☐☐☐ | Completed by ☐☐☐ | Patient Unique ID ☐☐☐ | Antimicrobial Drug # ☐☐☐

1. Antimicrobial drug (_____) Text (generic name)
   Refer to ATC classification list (_____) Code

2. Start date ☐☐/☐☐/☐☐ (dd/mm/yy)

3. Single unit dose (_____)

4. Unit ☐ g ☐ IU ☐ MegaUnit ☐ Other ☐ mg ☐ tablet ☐ Unknown _____

5. Doses per day ☐ 1x / day or per 24 hours ☐ 2x / day or per 12 hours ☐ 3x / day or per 8 hours ☐ 4x / day or per 6 hours ☐ STAT or immediately ☐ Unknown ☐ Other_____

6. Route ☐ Parenteral ☐ Rectal ☐ Unknown ☐ Oral ☐ Inhalation ☐ Other_____

7. If route is oral, IV-oral switch ☐ Yes ☐ No ☐ Unknown

8. Diagnosis (what the clinician aims at treating) *Refer to Diagnostic Code List* (_____) Text (_____) Code

9. Type of indication *Refer to Type of Indication code list* ☐ CAI ☐ HAI ☐1, ☐2, ☐3, ☐4, ☐5, ☐6 ☐ MP ☐ SP ☐1, ☐2, ☐3 ☐ Other ☐ Unknown

10. Reason documented in clinical notes at start of antimicrobial treatment ☐ Yes ☐ No

11. Stop/review date documented ☐ Yes ☐ No ☐ Not applicable

12. Duration of treatment documented ☐ Yes ☐ No ☐ Not applicable
    If yes, planned duration ☐☐ days

13. Guideline compliance ☐ Yes ☐ No ☐ Not assessable ☐ Indication unknown

14. Treatment type ☐ Targeted ☐ Empirical

Appendix 2 National Healthcare Safety Network (NHSN) list

Surgery is classified as NHSN or non-NHSN surgery, as defined by the National Healthcare Safety Network (NHSN) list below. Any surgery not included in this list is considered as non-NHSN surgery.[54]

NHSN		
Abdominal aortic aneurysm repair	Craniotomy	Pacemaker surgery
Abdominal hysterectomy	Exploratory laparotomy	Peripheral vascular bypass surgery
Appendix surgery	Gallbladder surgery	Prostate surgery
Bile duct, liver or pancreatic surgery	Gastric surgery	Rectal surgery
Breast surgery	Heart transplant	Refusion of spine
Cardiac surgery	Herniorrhaphy	Shunt for dialysis
Carotid endarterectomy	Hip prosthesis	Small bowel surgery
Caesarean section	Kidney surgery	Spinal fusion
Colon surgery	Kidney transplant	Spleen surgery
Coronary artery bypass graft with both chest and donor site incisions	Knee prosthesis	Thoracic surgery
Coronary artery bypass graft with chest incision only	Laminectomy	Thyroid and/or parathyroid surgery
	Limb amputation	Vaginal hysterectomy
	Liver transplant	Ventricular shunt
	Neck surgery	
	Open reduction of fracture	
	Ovarian surgery	

NON-NHSN	
Obstetrical procedures: peri-delivery/labour (one or more)	Any other operation where healing is by secondary intention
Dental extraction	Tonsillectomy
Transurethral resection of prostate	Application of external fixator/Olizarov
Incision and drainage of abscess with secondary closure	Extraventricular drain
Any diabetic forefoot amputation with healing by secondary intention	Hysteroscopic removal of fibroids; evacuation of retained products of conception

Appendix 3 McCabe score

McCabe score is a simple subjective method to assess underlying illness severity and classify patients according to a prognosis of rapidly fatal (<1 year), ultimately fatal (1–4 years) and non-fatal (>5 years). Examples of diseases for different McCabe score categories.[54]

Rapidly fatal (prognosis <1 year)
End-stage haematological malignancies (unsuitable for transplant, or relapsed)
Heart failure (EF < 25%)
End-stage liver disease (unsuitable for transplant with recalcitrant ascites, encephalopathy, or varices)
Multiple organ failure on intensive care unit – APACHE II score >30, SAPS II score >70
Ultimately fatal (prognosis 1 year to 4 years)
Chronic leukaemia, myelomas, lymphomas, metastatic carcinoma, end-stage kidney disease (without transplant)
Motor neuron disease, multiple sclerosis nonresponsive to treatment
Alzheimer's disease/dementia
Diabetes requiring amputation or post amputation
Nonfatal (prognosis >5 years)
Diabetes mellitus
Carcinoma/haematological malignancy with >80% 5-year survival
Inflammatory disorders
Chronic GI/GU conditions
Obstetrics
Infections (including HIV, hepatitis B and C – unless in above categories)

Abbreviations: APACHE, acute physiology and chronic health evaluation; EF, ejection fraction; GI/GU, gastrointestinal and urogenital; HIV, human immunodeficiency virus; SAPS, simplified acute physiology.

Appendix 4 Diagnostic code list

Code	Examples
CENTRAL NERVOUS SYSTEM (CNS)	
Proph CNS	Prophylaxis for CNS (neurosurgery, meningococcal)
CNS	Infections of the Central Nervous System
EYE	
Proph EYE	Prophylaxis for Eye operations
EYE	Therapy for Eye infections e.g., Endophthalmitis
EAR NOSE THROAT (ENT)	
Proph ENT	Prophylaxis for Ear, Nose, Throat (Surgical or Medical prophylaxis=SP/MP)
ENT	Therapy for Ear, Nose, Throat infections including mouth, sinuses, larynx
RESPIRATORY (RESP)	
Proph RES	Pulmonary surgery, prophylaxis for Respiratory pathogens, e.g., for aspergillosis
LUNG	Lung abscess including aspergilloma
URTI	Upper Respiratory Tract Viral Infections including influenza but not ENT
Bron	Acute Bronchitis or exacerbations of chronic bronchitis
Pneu	Pneumonia or LRTI (lower respiratory tract infections)
TB	Pulmonary TB (Tuberculosis)
CARDIAC VASCULAR (CVS)	
Proph CVS	Cardiac or Vascular Surgery, endocarditis prophylaxis
CVS	Cardio-Vascular System infections: endocarditis, endovascular prosthesis, or device e.g., pacemaker, vascular graft
GASTRO-INTESTINAL (GI)	
Proph GI	Surgery of the Gastro-Intestinal tract, liver or biliary tree, GI prophylaxis in neutropenic patients or hepatic failure
GI	Gastro-Intestinal infections (salmonellosis, Campylobacter, parasitic, *C. difficile*, etc.)
IA	Intra-Abdominal sepsis including hepatobiliary, intra-abdominal abscess, etc.
SKIN & SOFT TISSUE, BONE & JOINT (SSTBJ)	
Proph BJ	Prophylaxis for SST, for plastic, or orthopaedics surgery (Bone or Joint)
SST	Skin and Soft Tissue: Cellulitis, wound including surgical site infection, deep soft tissue not involving bone, e.g., infected pressure or diabetic ulcer, abscess

Code	Examples
BJ	Bone/Joint Infections: Septic arthritis (including prosthetic joint), osteomyelitis
URINARY TRACT INFECTION (UTI)	
Proph UTI	Prophylaxis for urological surgery (SP) or recurrent Urinary Tract Infection (MP)
Cys	Lower UTI
Pye	Upper UTI including catheter related urinary tract infection, pyelonephritis
GENITO-URINARY & OBSTETRIC GYNAECOLOGY (GUOB)	
Proph OBGY	Prophylaxis for Obstetric or Gynaecological surgery
OBGY	Obstetric/Gynaecological infections, Sexual Transmitted Diseases (STD) in women
GUM	Genito-Urinary Males + Prostatitis, epididymo-orchitis, STD in men
NO DEFINED SITE (NDS)	
BAC	Bacteraemia with no clear anatomic site and no shock
SEPSIS	Sepsis syndrome, or septic shock with no clear anatomic site
Malaria	
HIV	Human immunodeficiency virus
PUO	Pyrexia of Unknown Origin – Fever syndrome with no identified source or site of infection
PUO-HO	Fever syndrome in the non-neutropaenic Haematology–Oncology patient with no identified source of pathogen
FN	Fever in the Neutropenic patient
LYMPH	Infection of the lymphatics as the primary source of infection, e.g., suppurative lymphadenitis
Other	Antibiotic prescribed with documentation for which there is no above diagnosis group
MP-GEN	Drug is used as Medical Prophylaxis in general, without targeting a specific site, e.g., antifungal prophylaxis during immunosuppression
UNK	Completely Unknown Indication
PROK	Antimicrobial (e.g., erythromycin) prescribed for Prokinetic use
NEONATAL	
MP-MAT	Drug is used as Medical Prophylaxis for MATERNAL risk factors, e.g., maternal prolonged rupture of membranes
NEO-MP	Drug is used as Medical Prophylaxis for NEWBORN risk factors, e.g., VLBW (Very Low Birth Weight) and IUGR (Intrauterine Growth Restriction)

Appendix 5 Ethical approvals

Oxford Tropical Research Ethics Committee

University of Oxford
Research Services, University Offices
Wellington Square, Oxford OX1 2JD
Tel. +44 (0)1865 (2)82106
E-mail: oxtrec@admin.ox.ac.uk

Dr. Erni J Nelwan
Jl. Salemba Raya IV
Jakarta
Indonesia

23 January 2019

Dear Dr. Nelwan

Full Title of Study: Exploration of Antibiotic Consumption to Identify Targets for Quality Improvement in Indonesian Hospitals: A mixed method study

OxTREC Reference: 559-18

Thank you for your email of the 17 January 2019, and for your minimal risk application form.

I am pleased to confirm that approval has now been granted for this study. This is valid for the first five years and is subject to receiving the local ethical approval (if this approval has not yet been received).

The documents approved for this study are as follows:

Documents:	Version:	Date:
Minimal risk application form		
PIS/ICF – in-depth interview	V2.0	10/01/19
PIS/ICF – focus group discussion	V2.0	10/01/19
Questionnaire/survey/interview guide	V1.0	29/11/18

Any subsequent changes to the application must be submitted to the Committee as an Amendment. This should include a letter to give the reasons for the proposed modifications and all revised documents with changes tracked.

Please ensure that you submit a completed Annual Report form on every anniversary of this approval and a final End of Study Report. The relevant forms can be found on the OxTREC website: https://researchsupport.admin.ox.ac.uk/governance/ethics/apply/oxtrec.

Finally, please note the following **important information**:

Data safety—all studies
It is the responsibility of the PI to ensure that all data collected during the course of the study is stored and transferred safely and securely. Further guidance and advice is available from the Research Data Team.

Tel: +44 (0)1865 (2)82106
Email: oxtrec@admin.ox.ac.uk
Web: https://researchsupport.admin.ox.ac.uk/governance/ethics

Studies that will involve storing human tissue samples in Oxford
As you are planning to import the samples into England, you will need to make arrangements before the samples are transferred to store them under the governance of a Human Tissue Authority (HTA) licence. It is a legal requirement that any tissue or fluid made up of or containing human cells to be used for the purpose of research is stored on premises licensed by the HTA unless covered by an exemption. OxTREC approval is not a recognised exemption. Further information may be found on the University's human tissue governance web pages: https://researchsupport.admin.ox.ac.uk/governance/human-tissue.

Yours sincerely

Dr Rebecca Bryant
Research Ethics Manager, OxTREC

UNIVERSITAS INDONESIA
FAKULTAS KEDOKTERAN

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fk.ui.ac.id

Nomor : 1364 /UN2.F1/ETIK/2018

KETERANGAN LOLOS KAJI ETIK

ETHICAL APPROVAL

Komite Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Indonesia dalam upaya melindungi hak asasi dan kesejahteraan subyek penelitian kedokteran, telah mengkaji dengan teliti protokol berikut informasi yang diberikan kepada calon subjek yang berjudul:

The Ethics Committee of the Faculty of Medicine, University of Indonesia, with regards of the Protection of human rights and welfare in medical research, has carefully reviewed the research protocol including the information given to the potential subjects entitled:

"Explorasi Penggunaan Antibiotik di Rumah Sakit di Indonesia (Penelitian Explain): Penelitian dengan Metode Campuran (*Exploration of Antimicrobial Consumption to Identify Targets for Quality Improvement in Indonesian Hospitals (Explain Study): A Mixed Method Study*)".
No. protokol: 18-12-1483

Peneliti Utama / *Principal Investigator* : **dr. Erni Nelwan, Ph,D, SpPD-KPTI**

Nama Institusi / *Name of the Institution* : **Ilmu Penyakit Dalam FKUI-RSCM**

dan telah menyetujui protokol berikut informasi yang diberikan kepada calon subjek.
and approves the above mentioned protocol including the information given to the potential subjects.

Jakarta, 31 DEC 2018
a.n. Ketua
Wakil Ketua

dr. Nia Kurniati, SpA(K), MSc

* *Ethical approval* berlaku satu tahun dari tanggal persetujuan.
** Peneliti berkewajiban
1. Menjaga kerahasiaan identitas subyek penelitian.
2. Memberitahukan status penelitian apabila
   a. Setelah masa berlakunya keterangan lolos kaji etik, penelitian masih belum selesai, dalam hal ini *ethical approval* harus diperpanjang.
   b. Penelitian berhenti di tengah jalan.
3. Melaporkan kejadian serius yang tidak diinginkan (*serious adverse events*).
4. Peneliti tidak boleh melakukan tindakan apapun pada subyek sebelum protokol penelitian mendapat lolos kaji etik dan sebelum memperoleh *informed consent* dari subjek penelitian.
5. Menyampaikan laporan akhir, bila penelitian sudah selesai.
6. Cantumkan nomor protokol ID pada setiap komunikasi dengan KEPK FKUI-RSCM.

Semua prosedur persetujuan dilakukan sesuai dengan standar ICH-GCP.
All procedure of Ethical Approval are performed in accordance with ICH-GCP standard procedure.

UNIVERSITAS INDONESIA
FAKULTAS KEDOKTERAN

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NOTA DINAS
Nomor: ND-1498/UN2.F1/ETIK/PPM.00.02/2019

Kepada : Prof. Dr. dr. Dadang Makmun, SpPD-KGEH
Institusi : Kepala Departemen Ilmu Penyakit Dalam FKUI-RSCM
Dari : Komite Etik Penelitian Kesehatan FKUI-RSCM
Hal : Perpanjangan *Ethical Approval* dr. Erni Nelwan, Ph,D, SpPD-KPTI, PhD

Sehubungan dengan penelitian yang berjudul :
"Explorasi Penggunaan Antibiotik di Rumah Sakit di Indonesia (Penelitian Explain): Penelitian dengan Metode Campuran (*Exploration of Antimicrobial Consumption to Identify Targets for Quality Improvement in Indonesian Hospitals (Explain Study): A Mixed Method Study*)"
Peneliti Utama : dr. Erni Nelwan, Ph,D, SpPD-KPTI, PhD
No. Protokol Etik : 18-12-1483
No. Surat Lolos Kaji Etik : 1364/UN2.F1/ETIK/2018, tanggal 31 Desember 2018. .

Komite Etik Penelitian Kesehatan FKUI-RSCM telah menerima dan meninjau surat sejawat:

Tanggal	No. Surat	Perihal	Dokumen
26 Desember 2019	144/UN2.F1.D/IPD /PPM.00.00/2019	Permohonan perpanjangan Etik Penelitian	1. Salinan Surat Keterangan lolos kaji etik, 1 kopi 2. *Annual Progress Report*, 1 kopi

Komite Etik Penelitian Kesehatan FKUI-RSCM memberikan perpanjangan Surat Keterangan Lolos Kaji Etik (*Ethical Approval*) untuk pelaksanaan penelitian yang dimaksud selama satu tahun, terhitung dari **31 Desember 2019** sampai dengan **30 Desember 2020**.

Atas laporan dan kerjasamanya, kami ucapkan terima kasih.

30 Desember 2019
Wakil Ketua KEPK FKUI-RSCM

dr. Nia Kurniati, SpA(K), M. Sc.

Semua prosedur persetujuan dilakukan sesuai dengan standar ICH-GCP.
All procedures of Ethical Approval are performed in accordance with ICH-GCP standard procedure.

Appendix 6 Interview guides

Introduction

Since early 2019, I have been doing research on antibiotic use for hospitalised patients in six hospitals in Jakarta, including this hospital. Based on the initial analysis of the aggregated point prevalence survey (PPS) data from all participating hospitals, 62% of the total inpatients received one or more antimicrobials. Only 13.8% of all therapeutic antibiotics prescribed were targeted or based on a microbiology result. Broad-spectrum antibiotics, ceftriaxone, levofloxacin, and meropenem, were among the top five most commonly prescribed antibiotics. 76% of surgical antibiotic prophylaxis was prescribed for more than 24 hours; some were prescribed for up to two weeks. Compliance with the local guidelines accounted for 37.5% of prescriptions, while 28% could not be assessed due to a lack of local hospital guidelines.

Awareness of antimicrobial resistance (AMR)

- To start the interview, I want to know to what extent you are aware of antimicrobial resistance (AMR) in your day-to-day work.
- How significant is the issue of AMR compared to other concerns within the hospital context? Why do you think that is and has this changed over time?

Antibiotic use

<u>Prescribing decision</u>

Doctors

- In what situations is an antibiotic usually prescribed to a hospitalised patient? *Probe*: Who makes that decision? How is the decision made?
- How is the decision communicated among the medical staff?
- How do you decide to give certain antibiotics over others? For example, broad-spectrum are preferred over narrow spectrum antibiotics
- In what situations do you give extra antibiotics? To extend the duration of therapy? Deciding to use intravenous or oral antibiotics?
- How do you decide when to escalate, de-escalate, or stop giving antibiotics?
- What clinical situations are the most ambiguous or difficult for you with regards to antibiotic prescribing? *Probe*: What is the example? How did you manage uncertainty regarding prescribing?

- According to the findings of the PPS, the majority of antibiotic therapy was prescribed empirically or without regard for bacterial culture. What do you think the reason is?

Surgeons

- In what typical surgeries do you use antibiotics for surgical prophylaxis purposes?
  - How do you decide which antibiotic to use? *Probe:* Is there any difference in antibiotic choice for different types of surgery?
  - In general, how long do you use the surgical antibiotic prophylaxis? *Probe:* In what typical situation do you prescribe it for more than 24 hours (prolong prophylaxis)? Give extra antibiotics?
  - In the case of prolonged prophylaxis, how do you decide when to stop it?
- How about antibiotic administration via non-standard routes, e.g., topical antibiotics in the wound or operation area?
- Can you describe some cases when you might be worried about the outcome of a surgery? *Probe:* How does this impact how you use antibiotics?
- How do fears about infection or previous bad outcomes play a role in how you prescribe and use antibiotics prophylactically?

Doctors and surgeons

- How do your antibiotic decisions differ between the hospitals where you currently work? (If the participant works in multiple hospitals)

Clinical microbiologists and clinical pharmacists

- What are your roles in the context of antibiotic prescribing?
- What do you think about the level of authority you have in your current roles regarding antibiotic prescribing? *Probe:* To what extent do different types of responsibility play a role in the antibiotic decision?
- Are there any specific circumstances where you play a bigger role in advising antibiotic use? (For instance, polypharmacy for a clinical pharmacist or a drug-resistant infection for a clinical microbiologist)
- To what extent do you do ward rounds in a context where you are assisting or guiding a doctor’s or surgeon’s antibiotic decisions?
- To what extent do you conduct routine checks to see if prescribers follow your antibiotic advice?

Antimicrobial stewardship (AMS) team and hospital management

- To what extent do you play a role in antibiotic prescribing within the hospital context?
- Relative to other tasks, how important is this role?

Interns

- In what situations is an antibiotic usually prescribed to a hospitalised patient? *Probe*: How is the decision made? Who makes that decision?
- If the clinical round is performed in more than one hospital, to what extent does the antibiotic prescribing practice differ between hospitals? *Probe*: If so, what are the differences (between departments, between hospitals)? Why have these disparities arisen?
- To what extent has the reason for antibiotic use been discussed with you?
- To what extent do antibiotic guidelines differ or are similar between hospitals?
- To what extent do you agree or disagree about the discrepancy between the antibiotic practice taught in the classroom and the 'real practice' in the hospital? *Probe*: What are they? Give an example.
- What antibiotic practice have you learned during clinical rotations that you will put into practice once you become a doctor?

Factors Influencing Antibiotic Prescribing

All participants

- What are the Indonesian local conditions, e.g., environmental conditions and social factors, that influence your (the prescribers') decision to prescribe antibiotic? *Probe*: Do they align with broader guidelines for infection treatment (or prophylaxis)? Some argue that living in Indonesia's tropical climate and poorer environmental conditions makes it easier for people to contract infectious diseases, or that surgical wounds are more likely to become infected. What is your take on this notion?
- How do a patient's special conditions like immunosuppression, bad blood supply, diabetes, etc. play a role in your (the prescribers') antibiotic decision?
- To what extent does the national health insurance (JKN, *Jaminan Kesehatan Nasional*) play a role in your (the prescribers') antibiotic prescribing practice? *Probe*: How about private insurance and non-insurance patients?
- To what extent do the patients and/or patients' family play a role in your (the prescribers') antibiotic decision?
- In every context, including antibiotic prescribing, there are economic or financial drivers of practice. In some settings, the decision to prescribe antibiotics was also driven by pharmaceutical sponsorship or incentives from pharma companies. What is your take on this notion? *Probe*: To what extent does this practice occur in this hospital?

The role of diagnostic tests, clinical guidelines, and technology

All participants

- To what extent do the diagnostic markers play a role in your (the prescriber's) antibiotic decision?
- In what typical circumstances do you (the prescribers) ask for or not ask for a culture and sensitivity (microbiology) test? *Probe*:
  - To what extent and under what circumstances do you (the prescribers) rely on microbiology test results to guide antibiotic decisions?
  - Any reasons for not taking up the antibiotic advice based on the microbiology result?
  - To what extent do you (the prescribers) use or deviate from guidelines when prescribing antibiotics? *Probe*: Which guideline? How often is it updated? What is your faith in that guideline? How useful can it be in guiding your antibiotic prescribing?
- How much awareness and concern are there amongst your (the prescribers') colleagues about following the antibiotic guidelines?
- Is there any technology that helps you (the prescribers) optimise your (their) antibiotic decision, e.g., computer software, smartphone applications, etc.? *Probe*: To what extent does the availability or absence of this technology help or hinder antibiotic prescribing decisions? If not, what technology do you expect to have in the future to help antibiotic prescribing decisions?

Clinical microbiologists

- What method do you use in performing the culture test? Sensitivity analysis?
- How do you decide which antibiotics are to be included in the sensitivity test and to be reported back to the clinician?
- Is there any rapid microbiology testing that you use?
  - If yes, how helpful is this test to the doctors in their antibiotic prescribing?
  - If not, what rapid test do you suggest? How can this test help you and the doctors with antibiotic prescribing?

<u>Intra- and interprofessional relationships</u>

All participants

- What is the character of your interactions with other clinical staff within the context of antibiotic use and decision-making?
- In a situation where a patient management is handled by a multidisciplinary team, who makes the decision to prescribe antibiotics? Probe: To what extent is this decision communicated to the rest of the team.
- When any disagreement about antibiotic decision occurred between prescribers, how was this managed?

- In what circumstance is antibiotic decisions communicated with other clinical staff? For example, an infectious disease consultant, clinical microbiologist, clinical pharmacist, or AMS team? Probe: How?

Surgeons

- Drawing on your experience, can you think of any examples where there have been disagreements about antibiotics in the operating room? Who was involved, what mattered, how was it managed?
- How do the junior doctors in the ward find out about how long to continue antibiotic prophylaxis? How is the decision communicated?
- Can you describe some cases you had when a patient did not need a surgery but was prescribed antibiotics? To what extent do you consult these typical cases with other specialists?

Senior doctors (specialists and consultants from medicine and surgery)

- Were there any situations where junior doctors, e.g., residents or GPs, challenged or questioned your antibiotic decision? How was your response?
- Have you ever had a situation where your antibiotic decision was different from a clinical guideline? How do you communicate this to the junior team?
- To what extent does a clinical pharmacist play a role in terms of antibiotic prescribing, e.g., dose monitoring, alerting to restricted antibiotics, clarifying drug interactions? To what extent does it help or hinder you regarding antibiotic decisions and patient management?
- To what extent does a clinical microbiologist play a role in terms of antibiotic prescribing? To what extent does this help or hinder you in antibiotic prescribing and patient management?

Junior doctors (residents, general practitioners) and interns

- In a situation when you were aware that the prescribed antibiotic by a senior doctor/surgeon was not in line with antibiotic guideline, to what extent do you challenge or question this practice? *Probe*: If yes, how and give example. If no, why is that?

Antimicrobial Stewardship

All participants except interns

- From your perspective, what is the purpose of the hospital AMS programme?
- If any, what is your role in the hospital AMS programme?
- What strategies are used in hospitals to control or optimise antibiotic use? *Probe*: To what extent do these strategies effective?
- To what extent does the hospital's AMS programme help or hinder your daily work?

- Some doctors said that AMS takes away their prescribing autonomy and interferes with their clinical decision-making. How does this affect you (the prescribers)?
- To what extent do you (the prescribers) receive feedback related to antibiotic use? *Probe*: Who gives the feedback? How was it done? What was the content of the feedback?
- What type of collected evidence is needed to support the regulation of antibiotic use and prescribing, e.g., culture data, pharmacy data on antibiotic consumption? How are these dataset used? *Probe*:
  - How often are these data collected?
  - How is this information used to provide feedback to prescribers? If any, *probe*: How often AMR report is distributed? Are there any feedback sessions with prescribers and management? What actions had been taken?
  - Are these data reported to the higher-level health systems, e.g., the provincial health office or the ministry of health? If so, is there any feedback or follow-up?
- To what extent does hospital accreditation influence your (the prescribers') antibiotic prescribing practice?
- What is the most important aspect of the optimum implementation of the AMS programme?
- On balance, what impact do you think AMS has had in the hospital?
- On balance, what impact do you think it has on AMR in the hospital or society more broadly?
- What would be the best approach or strategy to establish the 'best practices' in antibiotic prescribing?

AMS team

- In terms of hospital guidelines (if any):
  - Who was involved in developing the guidelines for antibiotic prescribing?
  - How often are these guidelines updated?
  - Is there a formal mechanism to ensure guidelines are written and updated?
  - How is it being used?
  - What is the response of the prescribers to it?
- What are the supporting factors in the implementation of the AMS programme in this hospital?
- What are the barriers to the implementation of the AMS programme in this hospital?
- How and to what extent is the AMS programme funded? *Probe*: example of budget allocation for certain activities.

- To what extent does hospital accreditation influence the regulation of antibiotic use and prescribing?

Hospital management

- To what extent does the AMS programme benefit or disadvantage the hospital? *Probe*: From an economic perspective? From a patient safety perspective? From a quality assurance perspective?
- To what extent does the AMS programme put political pressure on the hospital management? In what terms?
- To what extent does the AMS programme influence the dynamics between clinical staff in this hospital? For example, between prescribers and the AMS team, or between prescribers and management?
- How is AMS viewed in the context of other competing resource demands in this hospital?
- In terms of resources and funding, to what extent does this hospital warrant dedicated funding for the AMS programme?
- To what extent does hospital accreditation influence the regulation of antibiotic prescribing?
- What are typical circumstances in which you are directly involved in the optimisation of antibiotic prescribing?
- What roles do you expect to have in facilitating the optimisation of antibiotic prescribing?
- To what extent do you engage in or give input related to antibiotic guideline development? The monitoring and evaluation of antibiotic use? Providing feedback to prescribers?

Interns

- To what extent are you aware of the hospital AMS programme? What is the purpose of AMS? What are the activities of the AMS programme?
- To what extent do you think it is important for you to be familiar with the hospital AMS programme? Why?
- To what extent does hospital accreditation influence antibiotic use in this hospital? Can you give an example?
- What would be the best approach or strategy to establish the ‘best practices’ in antibiotic prescribing?

Appendix 7 Participant information sheet and informed consent form

Participant Information Sheet

What is the purpose of this research?

You are invited to take part in a study that assesses the practices and perceptions of antimicrobial resistance (AMR), use, and stewardship among antimicrobial prescribers in Indonesian hospitals. This research is part of a broader research project that aims to explore antimicrobial consumption in hospitalised patients and identify targets for quality improvement of antimicrobial prescribing, using quantitative (observed use) and qualitative (reported experiences) measures.

Antimicrobial resistance (AMR) is the ability of microorganisms (like bacteria, viruses, and some parasites) to stop an antimicrobial (such as antibiotics, antivirals, and antimalarials) from working against it. As a result, standard treatments become ineffective, infections persist, and may spread to others. AMR is an emerging public health threat worldwide, with the overuse of antimicrobials as one of the main drivers. Understanding antimicrobial usage, and the underlying determinants, will provide guidance to develop further context-specific research on antimicrobial stewardship intervention strategies to improve prescribing practices, and in doing so contain AMR. This research will provide a feasible framework to design and assess stewardship interventions that aim at promoting prudent use of antimicrobials in Indonesia.

Why have I been invited to take part?

This research is aimed at health care professionals who prescribe antimicrobials in their daily practice, as well as the clinical pharmacists, the clinical microbiologists, the hospital's executives, and the AMS team or committee The inclusion criteria of the study are:

- Working in the participant hospital
- Male or female aged 18 or above

Do I have to take part?

No. Participation in the study is voluntary. You can ask questions about the study before deciding whether or not to participate. If you do agree to participate, you may withdraw yourself from the study at any time, without giving a reason and without penalty, by advising the researchers of this decision. All data collected from you will not be used as part of this research.

What will happen to me if I take part in the study?

If you are happy to take part in the study, you will be asked to give verbal consent and to sign a written consent form. Then, an interviewer will conduct an interview with a guidance from a pre-prepared question list. The interview will be audio-recorded. Some of the topics that will be covered in this interview are antimicrobial prescription for the inpatients, antimicrobial resistance, and the antimicrobial stewardship programme in the hospital. This process will take around 45 to 60 minutes.

Are there any potential risks in taking part?

There are no potential risks to taking part in this research. Your responses during the interview will not influence your job or career. To reduce the possibility that people outside the research team obtain the information you have provided, you are encouraged not to discuss your answers within the hospital.

Are there any benefits to taking part?

There will be no direct benefit to you from taking part in this research. However, this research can inform antimicrobial stewardship teams, health practitioners, and policymakers about the best possible ways to improve antimicrobial prescribing practices and contain AMR in Indonesia.

Expenses and payments

You will receive Rp. 150,000 to compensate for the time spent on this interview.

What happens to the data provided?

After the interview, the research data will be stored confidentially and anonymously using a unique code, so no one can identify the study participant. Later, it will be analysed using qualitative software, and the results will be written up in a report and other publications. All research data and records will be stored for a minimum retention period of 5 years after publication or public release of the research. We would like your permission to use your anonymised data in future studies and to share that data with other researchers (e.g., in online databases). All personal information that could identify you will be removed before files are shared with other researchers or results are made public. Responsible members of the University of Indonesia and the University of Oxford and funders may be given access to data for monitoring and/or auditing of the research to ensure we are complying with guidelines, or as otherwise required by law. The Universitas Indonesia and University of Oxford will be responsible for ensuring the safe and proper use of any personal information you provide, solely for research purposes.

Will the research be published?

The University of Indonesia and the University of Oxford are committed to the dissemination of research for the benefit of society and the economy. Research findings will be published in scientific journals, in reports to policymakers, and possibly as part of student theses.

Who is organising and funding the research?

The research is a collaboration between the Eijkman-Oxford Clinical Research Unit (EOCRU) and the Faculty of Medicine, Universitas Indonesia (FKUI). The funding comes from an Oxford University Clinical Research Unit (OUCRU) Strategic Committee Funding Award, as part of the Wellcome Trust core grant to OUCRU.

Who has reviewed this research?

This research has been reviewed and received ethical approval through the Research Ethics Committee of the Faculty of Medicine at Universitas Indonesia and the Oxford Tropical Research Ethics Committee.

Who do I contact if I have a concern about the study or I wish to complain?

If you have a concern about any aspect of this research, please speak to lead researcher dr. Ralalicia Limato (+62-81243-50-4004) or principal investigator dr. Erni J. Nelwan, Ph.D, SpPD-KPTI (+62-811-106-563) who will do their best to answer your query. The researcher should acknowledge your concern within 10 working days and give you an indication of how they intend to deal with it. If you remain unhappy or wish to make a formal complaint, please contact the relevant chair of the Research Ethics Committee of the Faculty of Medicine of the University of Indonesia and the Oxford Tropical Research Ethics Committee.

Further information and contact details

If you would like to discuss the research with someone beforehand (or if you have questions afterwards), please contact:

dr. Erni Nelwan, Ph.D., SpPD-KPTI
Email: ejnelwan@yahoo.com
Mobile: +62-811106563
Internal Medicine Department, Division of Infectious Diseases, Cipto Mangunkusomo Hospital (RSCM), Faculty of Medicine, Universitas Indonesia (FKUI); Infectious Disease and Immunology Research Cluster, Indonesia Medical Education and Research Institute (IMERI), Jakarta, Indonesia.

Informed consent form

I confirm that I have read and understand the information sheet for the above study. I have had the opportunity to consider the information, ask questions, and have had these satisfactorily answered.
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without any adverse consequences or academic penalty.
I understand that research data collected during the study may be looked at by designated individuals from Universitas Indonesia and the University of Oxford where it is relevant to my taking part in this study. I give permission for these individuals to access my anonymous data.
I agree to take part in this research
I agree ☐ / do not agree ☐ that the interview will be audio-recorded
I agree ☐ / do not agree ☐ that my anonymised data will be used and shared for future approved research

Participant's name	Date	Signature
Name of the person taking consent	Date	Signature

Appendix 8 Supplementary PPS results

Appendix 8 Table 1 Systemic antimicrobial use by ward type, by hospital

	Total	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Hospital 6
Wards	238	19	74	30	14	79	22
Wards with occupancy	213 (89.5)	14 (73.7)	70 (94.6)	27 (90.0)	11 (78.6)	76 (96.2)	15 (68.2)
Active bed	2358	159	767	300	145	853	134
Active bed in the occupied wards	2288	155	742	296	130	846	119
Admitted patients	1602 (67.9)	100 (62.9)	562 (73.3)	198 (66.0)	66 (45.5)	625 (73.3)	51 (38.1)
Patients on ≥1 antimicrobials [a]	993 (62.0)	75 (75.0)	368 (65.5)	106 (53.5)	52 (78.8)	359 (57.4)	33 (64.7)
Patients on ≥1 antibiotics [b]	946 (59.0)	75 (75.0)	362 (64.4)	103 (52.0)	50 (75.8)	329 (52.6)	27 (52.9)
By ward type [c]							
Medical ward							
Active bed	804	94	249	130	31	277	23
Admitted patients	559 (69.5)	57 (60.6)	167 (67.0)	96 (72.6)	19 (61.3)	210 (75.8)	10 (43.5)
Patients on ≥1 antimicrobial	301 (53.8)	47 (82.5)	102 (61.1)	36 (42.5)	14 (73.7)	95 (45.2)	7 (70.0)
Surgical ward							
Active bed	401	0	168	39	0	188	6
Admitted patients	293 (73.1)	0 (0.0)	119 (70.8)	32 (82.0)	0	141 (75.0)	1 (16.7)
Patients on ≥1 antimicrobial	184 (62.8)	0 (0.0)	87 (73.1)	24 (75.0)	0 (0.0)	73 (51.8)	0 (0.0)
Mixed medical-surgical ward							
Active bed	916	51	260	111	95	316	83
Admitted patients	622 (67.9)	38 (74.5)	215 (82.7)	60 (54.0)	44 (46.3)	227 (71.8)	38 (45.8)
Patients on ≥1 antimicrobial	401 (64.5)	23 (60.5)	135 (62.8)	37 (61.7)	35 (79.5)	147 (64.8)	24 (63.2)
Intensive Care Unit (ICU)							

	Total	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Hospital 6
Active bed	167	10	65	16	4	65	7
Admitted patients	128 (76.6)	5 (50.0)	61 (93.8)	10 (62.5)	3 (75.0)	47 (72.3)	2 (28.6)
Patients on ≥1 antimicrobial	107 (83.6)	5 (100.0)	44 (72.1)	9 (90.0)	3 (100.0)	44 (93.6)	2 (100.0)
By ward population [c]							
Adult ward							
Adult medical ward							
Active bed	601	43	199	112	14	210	23
Admitted patients	436 (70.7)	31 (72.1)	125 (62.8)	87 (77.7)	13 (92.9)	160 (76.2)	10 (43.5)
Patients on ≥1 antimicrobial	224 (51.4)	23 (74.2)	79 (63.2)	31 (35.6)	10 (76.9)	65 (40.6)	7 (70.0)
Adult surgical ward							
Active bed	300	0	145	39	0	110	6
Admitted patients	235 (78.3)	0 (0.0)	108 (74.5)	32 (82.1)	0 (0.0)	94 (85.5)	1 (16.7)
Patients on ≥1 antimicrobial	155 (66.0)	0 (0.0)	80 (74.1)	24 (75.0)	0 (0.0)	51 (54.3)	0 (0.0)
Adult mixed medical-surgical ward							
Active bed	639	15	202	65	78	196	83
Admitted patients	446 (69.8)	8 (53.3)	167 (82.7)	41 (63.1)	41 (52.6)	151 (77.0)	38 (45.8)
Patients on ≥1 antimicrobial	290 (65.0)	5 (62.5)	109 (65.3)	28 (68.3)	33 (80.5)	91 (60.3)	24 (63.2)
Adult ICU							
Active bed	101	7	50	16	0	37	7
Admitted patients	78 (77.2)	3 (42.9)	47 (94.0)	10 (62.5)	0 (0.0)	26 (70.3)	2 (28.6)
Patients on ≥1 antimicrobial	58 (74.4)	3 (100.0)	30 (63.8)	9 (90.0)	0 (0.0)	23 (88.5)	2 (100.0)
Paediatric ward							
Paediatric medical ward							
Active bed	160	33	50	5	5	67	0
Admitted patients	108 (67.5)	12 (36.4)	42 (84.0)	2 (40.0)	2 (40.0)	50 (74.6)	0 (0.0)

	Total	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Hospital 6
Patients on ≥1 antimicrobial	67 (62.0)	11 (91.7)	23 (54.8)	2 (100.0)	1 (50.0)	30 (60.0)	0 (0.0)
Paediatric surgical ward							
Active bed	60	0	23	0	0	37	0
Admitted patients	36 (60;0)	0 (0.0)	11 (47.8)	0 (0.0)	0 (0.0)	25 (67.6)	0 (0.0)
Patients on ≥1 antimicrobial	21 (58.3)	0 (0.0)	7 (63.6)	0 (0.0)	0 (0.0)	14 (56.0)	0 (0.0)
Paediatric mixed medical-surgical ward							
Active bed	127	0	41	38	17	31	0
Admitted patients	72 (56.7)	0 (0.0)	35 (85.4)	12 (31.6)	3 (17.60	22 (71.0)	0 (0.0)
Patients on ≥1 antimicrobial	41 (56.9)	0 (0.0)	14 (40.0)	6 (50.0)	2 (66.7)	19 (86.4)	0 (0.0)
Paediatric ICU							
Active bed	21	0	10	0	0	11	0
Admitted patients	19 (90.5)	0 (0.0)	10 (100.0)	0 (0.0)	0 (0.0)	9 (81.8)	0 (0.0)
Patients on ≥1 antimicrobial	19 (100.0)	0 (0.0)	10 (100.0)	0 (0.0)	0 (0.0)	9 (100.0)	0 (0.0)
Neonatal ward							
Neonatal ICU							
Active bed	18	3	5	0	0	10	0
Admitted patients	15 (83.3)	2 (66.7)	4 (80.0)	0 (0.0)	0 (0.0)	9 (90.0)	0 (0.0)
Patients on ≥1 antimicrobial	15 (100.0)	2 (100.0)	4 (100.0)	0 (0.0)	0 (0.0)	9 (100.0)	0 (0.0)
Mixed adult-neonatal-paediatric (A/N/P) ward							
A/N/P medical ward							
Active bed	43	18	0	13	12	0	0
Admitted patients	25 (58.1)	14 (77.8)	0 (0.0)	7 (53.8)	4 (33.3)	0 (0.0)	0 (0.0)
Patients on ≥1 antimicrobial	19 (76.0)	13 (92.9)	0 (0.0)	3 (42.9)	3 (75.0)	0 (0.0)	0 (0.0)

	Total	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Hospital 6
A/N/P surgical ward							
Active bed	41	0	0	0	0	41	0
Admitted patients	22 (53.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	22 (53.7)	0 (0.0)
Patients on ≥1 antimicrobial	8 (36.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	8 (36.4)	0 (0.0)
A/N/P mixed medical-surgical ward							
Active bed	150	36	17	8	0	89	0
Admitted patients	104 (69.3)	30 (83.3)	13 (76.5)	7 (87.5)	0 (0.0)	54 (60.7)	0 (0.0)
Patients on ≥1 antimicrobial	70 (67.3)	18 (60.0)	12 (92.3)	3 (42.9)	0 (0.0)	37 (68.5)	0 (0.0)
A/N/P ICU							
Active bed	11	0	0	0	4	7	0
Admitted patients	6 (54.5)	0 (0.0)	0 (0.0)	0 (0.0)	3 (75.0)	3 (42.9)	0 (0.0)
Patients on ≥1 antimicrobial	6 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)	3 (100.0)	0 (0.0)

Abbreviations: A/N/P, adult-neonatal-paediatric; ICU, Intensive Care Unit.

Data shown reflect the hospital situation on the survey day, and are expressed as number (percentage), unless otherwise specified.

[a] Includes antimicrobials for systemic use (J01, J02, J02, J04, J05, P01AB, A07A, P1B).

[b] Includes antibiotics for systemic use (J01).

[c] Wards with occupancy.

Appendix 8 Table 2 Systemic antimicrobial use by diagnosis, by hospital

Diagnosis	Total N=1666	Hospital 1 N=114	Hospital 2 N=630	Hospital 3 N=158	Hospital 4 N=98	Hospital 5 N=622	Hospital 6 N=44
Pneumonia or lower respiratory tract infection (LRTI)	365 (21.9)	16 (14.0)	155 (24.6)	42 (26.6)	17 (17.3)	129 (20.7)	6 (13.6)
Pulmonary tuberculosis	185 (11.1)	8 (7.0)	66 (10.5)	13 (8.2)	26 (26.5)	66 (10.6)	6 (13.6)
Skin and soft tissue infections [a]	110 (6.6)	4 (3.5)	45 (7.1)	10 (6.3)	7 (7.1)	42 (6.8)	2 (4.5)
Prophylaxis for gastrointestinal infections [b]	102 (6.1)	1 (0.9)	52 (8.3)	10 (6.3)	1 (1.0)	35 (5.6)	3 (6.8)
Gastrointestinal infections	84 (5.0)	26 (22.8)	13 (2.1)	10 (6.3)	1 (1.0)	27 (4.3)	7 (15.9)
Unknown indication	79 (4.7)	2 (1.8)	30 (4.8)	6 (3.8)	8 (8.2)	29 (4.7)	4 (9.1)
Central nervous system infections	69 (4.1)	0 (0.0)	23 (3.7)	3 (1.9)	9 (9.2)	30 (4.8)	4 (9.1)
Intra-abdominal infections [c]	66 (4.0)	0 (0.0)	36 (5.7)	2 (1.3)	0 (0.0)	27 (4.3)	1 (2.3)
Prophylaxis for bone and joint infections [d]	60 (3.6)	2 (1.8)	27 (4.3)	8 (5.1)	2 (2.0)	20 (3.2)	1 (2.3)
Prophylaxis for obstetric or gynaecological infections	58 (3.5)	1 (0.9)	39 (6.2)	9 (5.7)	3 (3.1)	6 (1.0)	0 (0.0)
Human Immunodeficiency Virus (HIV)	49 (2.9)	6 (5.3)	8 (1.3)	4 (2.5)	8 (8.2)	23 (3.7)	0 (0.0)
Sepsis	49 (2.9)	4 (3.5)	23 (3.7)	4 (2.5)	0 (0.0)	18 (2.9)	0 (0.0)
Prophylaxis for urinary tract infections (surgery or recurrent infection)	42 (2.5)	1 (0.9)	14 (2.2)	5 (3.2)	0 (0.0)	21 (3.4)	1 (2.3)
General medical prophylaxis	41 (2.5)	6 (5.3)	12 (1.9)	3 (1.9)	4 (4.1)	14 (2.3)	2 (4.5)
Ear, nose, throat infections [e]	40 (2.4)	5 (4.4)	9 (1.4)	4 (2.5)	4 (4.1)	18 (2.9)	0 (0.0)
Other diagnosis [f]	36 (2.2)	11 (9.6)	12 (1.9)	5 (3.2)	0 (0.0)	7 (1.1)	1 (2.3)
Upper urinary tract infections [g]	35 (2.1)	0 (0.0)	11 (1.7)	3 (1.9)	0 (0.0)	21 (3.4)	0 (0.0)
Medical prophylaxis for new-born risk factors	28 (1.7)	0 (0.0)	8 (1.3)	0 (0.0)	2 (2.0)	18 (2.9)	0 (0.0)
Prophylaxis for ear, nose, throat infections	26 (1.6)	3 (2.6)	12 (1.9)	1 (0.6)	0 (0.0)	7 (1.1)	3 (6.8)

Diagnosis	Total N=1666	Hospital 1 N=114	Hospital 2 N=630	Hospital 3 N=158	Hospital 4 N=98	Hospital 5 N=622	Hospital 6 N=44
Prophylaxis for central nervous system infections	25 (1.5)	3 (2.6)	13 (2.1)	0 (0.0)	0 (0.0)	9 (1.4)	0 (0.0)
Prophylaxis for respiratory infections	22 (1.3)	2 (1.8)	5 (0.8)	3 (1.9)	4 (4.1)	8 (1.3)	0 (0.0)
Lower urinary tract infections (cystitis)	20 (1.2)	4 (3.5)	3 (0.5)	7 (4.4)	0 (0.0)	5 (0.8)	1 (2.3)
Bone or joint infections [h]	13 (0.8)	1 (0.9)	5 (0.8)	0 (0.0)	0 (0.0)	7 (1.1)	0 (0.0)
Febrile neutropenia	11 (0.7)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	10 (1.6)	0 (0.0)
Upper respiratory tract viral infections [i]	9 (0.5)	7 (6.1)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (2.3)
Prophylaxis for cardiac or vascular infections	8 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	8 (1.3)	0 (0.0)
Cardiovascular system infections	7 (0.4)	0 (0.0)	2 (0.3)	0 (0.0)	0 (0.0)	5 (0.8)	0 (0.0)
Prophylaxis for eye operations	5 (0.3)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	4 (0.6)	0 (0.0)
Acute bronchitis or exacerbations of chronic bronchitis	4 (0.2)	0 (0.0)	3 (0.5)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
Medical prophylaxis for maternal risk factors	4 (0.2)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	3 (0.5)	0 (0.0)
Bacteraemia	3 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	1 (2.3)
Pyrexia of unknown origin	3 (0.2)	0 (0.0)	1 (0.2)	1 (0.6)	1 (1.0)	0 (0.0)	0 (0.0)
Malaria	2 (0.1)	0 (0.0)	0 (0.0)	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)
Obstetric/gynaecological infections [j]	2 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
Pyrexia of unknown origin in non-neutropenic haemato-oncology patients	2 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
Eye infections	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Genito-urinary infections [k]	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)

The table lists the most common reasons to treat adult inpatients with at least one antibiotic for systemic use (J01, J02, J02, J04, J05, P01AB, A07A, P01B). Data are expressed as numbers (percentage) and ranked by frequency. Patients recorded with more than one diagnosis were counted by number of diagnoses. Diagnoses were coded based on the Global-PPS 2018 diagnostic code list (Appendix 4).

[a] Including cellulitis, wound including surgical site infections, deep soft tissue not involving bone (e.g. infected pressure or diabetic ulcers, abscess).
[b] Including prophylaxis for surgery of the gastrointestinal tract, liver, or biliary tree, and prophylaxis in patients with neutropenia or hepatic failure.
[c] Including hepatobiliary, intra-abdominal abscess, etc.
[d] Including prophylaxis for surgical site infections, for plastic or orthopaedic surgery (bone or joint).
[e] Including mouth, sinuses, larynx.
[f] Antibiotic prescribed with documentation for which there is no above diagnosis group.
[g] Including catheter related urinary tract infection, pyelonephritis.
[h] Including septic arthritis, including prosthetic joint, osteomyelitis.
[i] Including influenza but not ear, nose, throat infections.
[j] Including sexually transmitted infections in women.
[k] Including sexually transmitted infections in men.

Appendix 8 Table 3 Systemic antibiotic use by indication

Systemic antibiotic (J01)	Total N=1273	CAI N=542	HAI N=235	Medical prophylaxis N=122	Surgical prophylaxis N=288	Other indication [a] N=27	Unknown Indication N=59
Ceftriaxone	341 (26.8)	178 (32.8)	23 (9.8)	35 (28.7)	76 (26.4)	0 (0.0)	29 (49.2)
Levofloxacin	136 (10.7)	73 (13.5)	44 (18.7)	3 (2.5)	8 (2.8)	3 (11.1)	5 (8.5)
Metronidazole	90 (7.1)	44 (8.1)	14 (6.0)	2 (1.6)	28 (9.7)	0 (0.0)	2 (3.4)
Meropenem	82 (6.4)	42 (7.7)	32 (13.6)	2 (1.6)	3 (1.0)	1 (3.7)	2 (3.4)
Cefotaxime	71 (5.6)	27 (5.0)	12 (5.1)	10 (8.2)	14 (4.9)	1 (3.7)	7 (11.9)
Cefoperazone	52 (4.1)	11 (2.0)	5 (2.1)	4 (3.3)	32 (11.1)	0 (0.0)	0 (0.0)
Cefixime	51 (4.0)	12 (2.2)	3 (1.3)	2 (1.6)	33 (11.5)	0 (0.0)	1 (1.7)
Ampicillin sulbactam	44 (3.5)	29 (5.4)	5 (2.1)	4 (3.3)	5 (1.7)	0 (0.0)	1 (1.7)
Gentamicin	42 (3.3)	17 (3.1)	3 (1.3)	13 (10.7)	7 (2.4)	0 (0.0)	2 (3.4)
Amikacin	32 (2.5)	10 (1.8)	15 (6.4)	0 (0.0)	6 (2.1)	0 (0.0)	1 (1.7)
Amoxicillin + clavulanic acid	31 (2.4)	8 (1.5)	5 (2.1)	1 (0.8)	16 (5.6)	0 (0.0)	1 (1.7)
Cefoperazone sulbactam	28 (2.2)	9 (1.7)	6 (2.6)	6 (4.9)	6 (2.1)	0 (0.0)	1 (1.7)
Co-trimoxazole	28 (2.2)	4 (0.7)	2 (0.9)	21 (17.2)	1 (0.3)	0 (0.0)	0 (0.0)
Ceftazidime	21 (1.6)	5 (0.9)	14 (6.0)	0 (0.0)	2 (0.7)	0 (0.0)	0 (0.0)
Ciprofloxacin	21 (1.6)	9 (1.7)	9 (3.8)	1 (0.8)	2 (0.7)	0 (0.0)	0 (0.0)
Cefazolin	18 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	18 (6.2)	0 (0.0)	0 (0.0)
Ampicillin	17 (1.3)	3 (0.6)	0 (0.0)	9 (7.4)	4 (1.4)	0 (0.0)	1 (1.7)
Amoxicillin	16 (1.3)	7 (1.3)	0 (0.0)	4 (3.3)	3 (1.0)	0 (0.0)	2 (3.4)
Azithromycin	16 (1.3)	9 (1.7)	6 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
Clindamycin	16 (1.3)	1 (0.2)	1 (0.4)	1 (0.8)	3 (1.0)	10 (37.0)	0 (0.0)
Fosfomycin	15 (1.2)	4 (0.7)	5 (2.1)	0 (0.0)	6 (2.1)	0 (0.0)	0 (0.0)

Systemic antibiotic (J01)	Total N=1273	CAI N=542	HAI N=235	Medical prophylaxis N=122	Surgical prophylaxis N=288	Other indication [a] N=27	Unknown Indication N=59
Moxifloxacin	13 (1.0)	8 (1.5)	3 (1.3)	0 (0.0)	2 (0.7)	0 (0.0)	0 (0.0)
Tigecycline	13 (1.0)	7 (1.3)	6 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Streptomycin	10 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (37.0)	0 (0.0)
Cefadroxil	9 (0.7)	4 (0.7)	0 (0.0)	0 (0.0)	4 (1.4)	0 (0.0)	1 (1.7)
Imipenem and cilastatin	7 (0.5)	4 (0.7)	2 (0.9)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Piperacilin tazobactam	7 (0.5)	1 (0.2)	5 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
Cefepime	6 (0.5)	4 (0.7)	1 (0.4)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Doripenem	5 (0.4)	0 (0.0)	4 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
Erythromycin	5 (0.4)	2 (0.4)	0 (0.0)	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
Sultamicillin	5 (0.4)	3 (0.6)	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Clarithromycin	4 (0.3)	1 (0.2)	2 (0.9)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Cefuroxime	3 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.0)	0 (0.0)	0 (0.0)
Chloramphenicol	3 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Vancomycin	3 (0.2)	1 (0.2)	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Penicillin procaine	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cefditoren pivoxil	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Colistin	1 (0.1)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Doxycycline	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.7)	0 (0.0)
Gentamicin	1 (0.1)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Levofloxacin	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Linezolid	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metronidazole	1 (0.1)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Netilmicin	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)

Systemic antibiotic (J01)	Total N=1273	CAI N=542	HAI N=235	Medical prophylaxis N=122	Surgical prophylaxis N=288	Other indication [a] N=27	Unknown Indication N=59
Ofloxacin	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.7)	0 (0.0)
Polymyxin B	1 (0.1)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Abbreviations: CAI, community acquired infection; HAI, hospital acquired infection.
This table includes antibiotics for systemic use (J01).
Data are expressed as numbers (percentage).
[a] Other indication including pulmonary tuberculosis, HIV/AIDS (e.g., as prophylaxis for pneumocystis carinii pneumonia and neurotoxoplasmosis), and as motility agent.