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PATTERNS AND QUALITY OF ANTIBIOTIC PRESCRIBING: RESULTS FROM A MULTICENTRE POINT PREVALENCE SURVEY IN GOVERNMENT HOSPITALS IN PERAK, MALAYSIA

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ABSTRACT

A point prevalence survey (PPS) is used to collect data on antimicrobial prescribing and assess a set of quality indicators associated with antimicrobial use. This study aimed to describe patterns and quality indicators of antibiotic prescribing among government hospitals in Perak, Malaysia. Data was retrospectively reviewed data from a PPS conducted from 1st to 14th December 2021 in 5 specialist and 10 non-specialist hospitals. All hospitalised patients on the day of the survey formed the study population. Those who had received at least one active systemic antibiotic by 8.00 a.m. or surgical prophylaxis within 24 h of the survey day were eligible for PPS. Data on pattern and quality indicators of prescribing (documentation of indication, guideline compliance and appropriateness of surgical prophylaxis) were analysed with descriptive evaluation. Of 2,386 hospitalised patients, 40% were prescribed antibiotics, mainly from the 'Access' category (52.3%). Antibiotic prevalence was highest in the intensive care unit (ICU) (90.8%). The predominant antibiotic class was beta-lactam/beta-lactamase inhibitor (32.6%), corresponding to community-acquired pneumonia (CAP) (19.8%) being the most common diagnosis. Intravenous administration was ordered in 79.4%, while empirical therapy constituted 84.5%. Documentation of indication within 24 h and guideline compliance were 88.2% and 69.8%, respectively. Inappropriate choice of antibiotics and improper dose/frequency were identified as important non-compliance issues. Of the surgical prophylaxis prescriptions, 35.6% were administered for more

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than 24 h. The findings have helped identify critical areas for antimicrobial stewardship interventions. Efforts are needed to reinforce compliance, documentation and improve surgical prophylaxis prescribing practices.

Keywords: Antibiotic prescribing, Point prevalence survey, Antimicrobial stewardship, Government hospitals

INTRODUCTION

The development of antimicrobial resistance (AMR) is a threat to public health. The global burden associated with drug-resistant infections in 2019 was an estimated 4.95 million deaths, of which 1.27 million deaths were directly attributable to drug resistance. Highest AMR-related death rates were noted in sub-Saharan Africa and South Asia which are low- and middle-income countries (LMICs). Resistance to fluoroquinolones and beta-lactam antibiotics (i.e. carbapenems, cephalosporins and penicillins) accounted for more than 70% of deaths attributable to AMR across pathogens (Murray *et al*. 2022).

Preventing and containing the spread of resistance requires accurate surveillance of antimicrobial use and AMR. The 2021 Global Antimicrobial Resistance and Use Surveillance System (GLASS) reported median resistance rates for third-generation cephalosporins between 40% and 50% for *Klebsiella pneumoniae* bloodstream infections (BSIs) and urinary tract infections (UTIs) caused by both *Escherichia coli* and *K. pneumoniae*. Notably, the high rates of resistance in pathogens causing BSIs against last resort antimicrobial drugs, such as carbapenems, are worrying. The median carbapenem resistance of 65.5% in BSIs caused by *Acinetobacter* spp., an emerging pathogen in hospital-acquired infections, depicts a dire scenario (World Health Organization 2021).

In Malaysia, the percentage of carbapenem resistance for *Acinetobacter baumannii* BSIs had increased, ranging from 68% to 70% in 2021 compared with 59% to 60% in 2020. For *E. coli* and *K. pneumoniae*, average resistance rates to third-generation cephalosporins (e.g. ceftazidime and cefotaxime) were comparable between both years but increased for carbapenems (e.g. imipenem and meropenem) in UTIs (0.4%–1.4% and 2.9%–4.9%, respectively) and BSIs (0.7%–1.2% and 3.5%–8%, respectively) (Hassan *et al*. 2023).

Antimicrobial stewardship (AMS) programme is an intervention designed to optimise the use of antimicrobials. It remains one of the key actions of the WHO Global Action Plan to contain AMR (World Health Organization 2015). The programme acts through concerted efforts to promote the selection of the appropriate antimicrobial regimen, including dose, duration of therapy and method of administration. In addition, AMS helps to improve and monitor the proper use of antibiotics (Fishman 2012). Initiatives have been taken by the Ministry of Health (MOH) Malaysia through establishing a protocol on AMS for all healthcare facilities (hospitals and primary care) and the mandatory implementation of the AMS programme in such facilities since 2014 (Ministry of Health Malaysia 2014).

A point prevalence survey (PPS) is a validated tool to measure the success or progress of an AMS programme while identifying targets for intervention. It can help to collect information related to the antimicrobial prescribing practices and management of infectious diseases among hospitalised patients; complementary to the surveillance of antimicrobial consumption (World Health Organization 2018). Additionally, this PPS has adopted the AWaRe (Access, Watch and Reserve) classification of antibiotics proposed by WHO as a tool to support monitoring of antibiotic prescribing and inform AMS programmes (World Health Organization 2019a). Several studies of the applicability and benefits of PPS showed their value in a range of hospitals in different settings and geographical regions. Prevalence of antibiotic prescribing varied between 32% and 62% (Cai *et al.* 2017; Limato *et al*. 2021; Ministry of Health Malaysia 2017; Panditrao *et al*. 2021; Thamlikitkul *et al*. 2020; Versporten *et al*. 2018; Xie *et al*. 2015), while the rate of guideline compliance ranged from 50% to 81% (Jamaluddin *et al*. 2021; Limato *et al*. 2021; Versporten *et al*. 2018). The documentation of indication rates (77%–84%) (Jamaluddin *et al*. 2021; National Centre for Antimicrobial Stewardship and Australian Commission on Safety and Quality in Health Care 2021; Singh *et al*. 2019; Vandael *et al*. 2020; Versporten *et al*. 2018) and proportion of surgical prophylaxis extending beyond 24 h (30%–66%) (Jamaluddin *et al*. 2021; National Centre for Antimicrobial Stewardship and Australian Commission on Safety and Quality in Health Care 2021; Versporten *et al*. 2018) were other important findings which helped raise awareness of inappropriate antimicrobial prescribing and provide tangible, quantifiable quality indicators to improve antibiotic prescribing at the hospital level (Versporten *et al*. 2018).

We have initiated this multicentre study as part of various activities related to AMS (World Health Organization 2019b). It aims to evaluate the data of antibiotic PPS done in all government hospitals in the state of Perak, Malaysia in 2021 in terms of the pattern and quality of prescribing.

METHODS

Study Design and Setting

This cross-sectional study utilised data obtained retrospectively from a PPS, which was conducted over 14 days (1 December–14 December 2021, excluding weekends and public holidays) simultaneously across 5 specialist and 10 non-specialist hospitals under the MOH in the state of Perak, Malaysia. The PPS is a yearly exercise commissioned by the MOH to be carried out in government-funded hospitals nationwide (Antibiotic Committee 2021).

Study Population

All hospitalised patients on the day of survey were sampled. Those who had received at least one active (i.e. currently ongoing) systemic antibiotic (oral or injection) by 8.00 a.m. on the survey day or surgical prophylaxis within 24 h of the survey were eligible for PPS. We excluded patients in emergency and day-care wards, outpatient clinics, those receiving outpatient parenteral antibiotic therapy (OPAT), on outpatient dialysis, inpatients who were discharged before or admitted after 8.00 a.m. and patients whose antibiotic therapy was stopped before 8.00 a.m. or initiated after 8.00 a.m. on the day of the survey. Antibiotics used for tuberculosis, non-tuberculous mycobacterium and others such as trimethoprim/sulfamethoxazole for pneumocystis pneumonia (PCP), clindamycin for toxoplasmosis and dapsone for PCP/toxoplasmosis were also excluded.

Data Collection and Consolidation

The PPS methodology was adapted from the Global-PPS (Versporten *et al*. 2021) and WHO-PPS (World Health Organization 2018) protocols by the Pharmacy Division, MOH, Malaysia (Antibiotic Committee 2021). Before the survey, a user manual was developed and discussed via web conferencing with all the study centres. A central PPS committee was established to impart training to all the pharmacist team members in each hospital. In addition, technical and clinical support was available through group text messaging with the state-appointed PPS committee. Importantly, relevant stakeholders at the hospital had been informed about the survey, such as the hospital director, head of clinical departments, ward managers and the AMS team.

Data collection by appointed PPS pharmacists in each hospital was done using two paper data collection forms: one for ward-level data to record the denominators, i.e. the total number of in-patients on the ward and one for patient-level data to record numerators. For patient-level data, information was obtained from medical records and treatment charts in electronic or manual formats. If further clarification was required, the information was obtained from the primary management team from any doctor (Medical Officer, Specialist or Consultant). Each patient was only surveyed once despite being moved between wards and the survey was done within a specific time limit of one calendar day or over several days. Anonymised individual-level data from all hospitals were transcribed into a study database. These were uniformly cleaned to avoid repeat entries, collated and summarised into secondary data for final analysis. Details of the workflow and data collection were included in Appendix (Figure S1).

Statistical Analysis

IBM Statistical Package for Social Science (SPSS) software version 24.0 (IBM Corp., Armonk, NY, USA) was used for descriptive analysis (percentage and frequency).

The following parameters were analysed:

(1) Prevalence of patients on antibiotic
(2) Types, class and WHO AWaRe (Access, Watch, Reserve) classification of antibiotics
(3) Types of infectious diseases
(4) Route of administration
(5) Documented indication of antibiotic
(6) Proportion of antibiotics used empirically, prophylactically or definitively
(7) Guideline compliance
(8) Description of antibiotic issues in guideline non-compliance

Ethical Consideration

The study was registered with the National Medical Research Register (NMRR) (NMRR ID-22-01527-LQY [IIR]) and ethical approval was obtained from the Medical Research and Ethics Committee (MREC) of Malaysia. Due to the observational nature of the survey, the need for informed consent was waived.

Definitions

Antibiotic prevalence rate was expressed as a percentage of all patients on an ongoing antibiotic(s) prescription at 8.00 a.m. on the survey day (numerator) over all in-patients present in the ward at 8.00 a.m. on the survey day (denominator) (Antibiotic Committee 2021).

Compliance assessment was based on hospital antibiotic guideline, National Antimicrobial Guideline 2019 (Lee *et al*. 2019) and Paediatric Protocol 4th edition (Muhammad Ismail *et al*. 2019). A Guide to Antimicrobial Therapy in the Adult ICU 2017 (Chan *et al*. 2017) was used to assess cases in the intensive care unit (ICU). Guideline compliance is defined as prescribing the preferred or alternative agent, route, dose and frequency according to the above guidelines, and evaluation was done based on the information written in patient records (Antibiotic Committee 2021).

The WHO AWaRe classification acts as a tool to support antibiotic stewardship efforts at local, national and global levels. Antibiotics are classified into three groups: Access, Watch and Reserve, considering the impact of different antibiotics and antibiotic classes on AMR, and to emphasise the importance of their appropriate use (World Health Organization 2019a).

(1) Access: Antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups. Selected Access group antibiotics are recommended as first or second choice empiric treatment options for infectious diseases.

(2) Watch: Antibiotic classes that have higher resistance potential and include most of the highest priority agents among the Critically Important Antimicrobials for Human Medicine (World Health Organization 2019c) and/or antibiotics that are at relatively high risk of selection of bacterial resistance. Selected Watch group antibiotics are recommended as first or second choice empiric treatment options for a limited number of specific infectious syndromes.

(3) Reserve: Antibiotics and antibiotic classes that should be reserved for the treatment of confirmed or suspected infections due to multi-drug-resistant organisms. Reserve group antibiotics should be treated as 'last resort' options when all alternatives have failed or are not suitable.

RESULTS

Overview of Hospital Characteristics

The 5 specialist and 10 non-specialist hospitals which participated in the 2021 PPS had a combined total of 3,601 active hospital beds (range 46–1,117 per hospital), 158 inpatient wards (range 3–51 per hospital) and 2,386 admitted patients (range 18–764 per hospital) (in Appendix Table S1). Specialist hospitals differed from non-specialist facilities by having permanent or resident specialists to provide services, including medicine, surgery and other specialty services, to meet the medical and surgical needs of the community. Laboratory services (e.g. microbiology lab) for specialised pathological analysis and dedicated imaging units are also available. All hospitals have an established AMS programme.

Prevalence of Patients on Antibiotics

A total of 2,386 hospitalised patients were identified during the survey period; 954 (40.0%) patients received at least one antibiotic, with the lowest and highest prevalence being 8.8% and 55.9%, respectively (in Appendix Table S1). Table 1 shows the percentage of antibiotic prescribing by discipline. The top 5 disciplines with the highest proportion of patients on antibiotics were intensive care unit (ICU), neurosurgical, plastic and reconstructive surgery, orthopaedic and burn units.

Table 1: Percentage of patients on at least one antibiotic based on discipline of prescriber.

Discipline	***n* (%)**
ICU[a]	69 (90.8)
Neurosurgical	21 (80.8)
Plastic and reconstructive surgery	7 (77.8)
Orthopaedic	88 (66.2)
Burn	3 (60.0)
General surgical	97 (50.5)
Otorhinolaryngology	3 (50.0)
Medical[b, c]	452 (42.8)
Paediatric[c]	63 (33.9)
Ophthalmology	2 (33.3)
NICU	52 (24.5)
O&G[c]	67 (24.4)
Others[c]	28 (14.9)
Palliative and rehabilitation[c]	2 (13.3)

Notes: [a]Includes general ICU and COVID ICU; [b]Includes general medical, rheumatology, nephrology, haematology, COVID general adults, cardiology, dermatology; [c]These are the only disciplines in non-specialist hospitals; COVID = Coronavirus; ICU = intensive care unit; NICU = neonatal intensive care unit; O&G = Obstetrics and Gynaecology.

Types and Classes of Systemic Antibiotics

There were 1,248 antibiotics administered during the period of PPS, with an average of 1.3 antibiotics per patient. Beta-lactam/beta-lactamase inhibitors (*n* = 407, 32.6%), second-generation cephalosporins (*n* = 157, 12.6%) and third-generation cephalosporins (*n* = 151, 12.1%) constituted the top three antibiotic prescriptions (Figure 1). In Appendix, Figure S2 further details antibiotic prescription by class in different hospital settings.

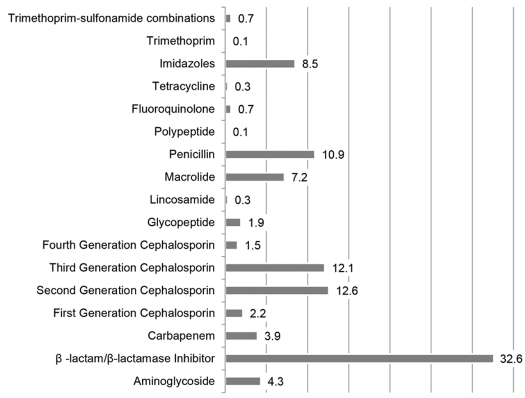

Figure 1: Percentage of antibiotic prescription by class.

Figure 2 categorises antibiotics according to WHO AWaRe classification. The top three Access group antibiotics were amoxycillin/clavulanate (*n* = 225, 34.5%), metronidazole (*n* = 106, 16.2%) and ampicillin/sulbactam (*n* = 87, 13.3%). Cefuroxime (*n* = 157, 26.4%), piperacillin/tazobactam (*n* = 95, 16.0%) and azithromycin (*n* = 83, 14.0%) constituted the top three Watch group antibiotics. The Reserve antibiotic was colistin (*n* = 1, 100%). The proportion of AWaRe antibiotic prescriptions based on hospital setting is shown in Appendix Figure S3.

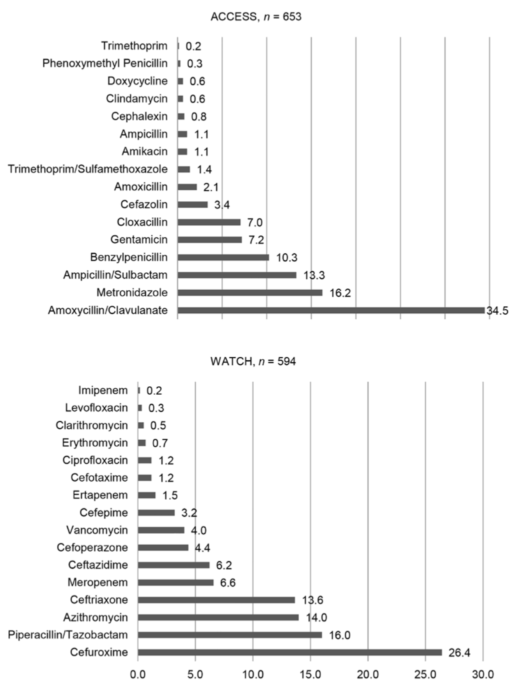

Figure 2: Percentage of antibiotics prescribed under AWaRe categories. Only one Reserve antibiotic prescription, colistin, was audited during the survey period in a specialist hospital.

Infectious Diseases Diagnosis

In the survey, the most common diagnosis was respiratory infections, predominantly community-acquired pneumonia (CAP) (*n* = 189, 19.8%), and hospital-acquired pneumonia (HAP) (*n* = 98, 10.3%). Other infectious diseases were presented in Figure 3 and in Appendix Figure S4.

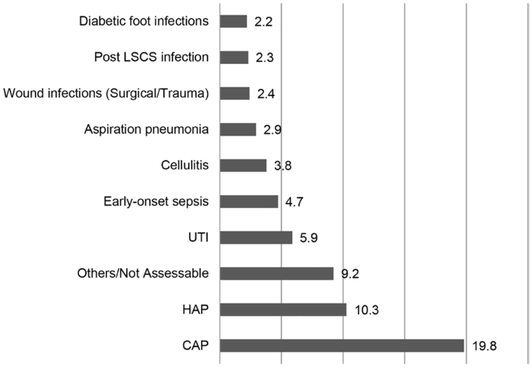

Figure 3: The 10 most frequently encountered infectious diseases in percentage.
CAP = community-acquired pneumonia; HAP = hospital-acquired pneumonia; LSCS = lower segment Caesarean section; UTI = urinary tract infection.

Route of Antibiotic Administration and Indication

Approximately 80% of antibiotic prescriptions were administered parenterally, almost four times the proportion of oral antibiotics (Table 2). The intraperitoneal and intramuscular routes of administration were reported in specialist hospitals (in Appendix Table S2). Additionally, 84.5% and 11.5% of antibiotics were prescribed for empiric and definitive therapy, respectively, while the remainder were for surgical and non-surgical prophylaxis.

Table 2: Route of antibiotic administration and indication of treatment.

Route	***n* (%)**
IV	991 (79.4)
PO	253 (20.3)
IP	3 (0.2)
IM	1 (0.1)
Indication category of antibiotic prescriptions	***n* (%)**
Empiric	1,055 (84.5)
Definitive	143 (11.5)
Surgical prophylaxis	45 (3.6)
Non-surgical prophylaxis	5 (0.4)

Note: IV = intravenous; PO = per oral; IP = intraperitoneal; IM = intramuscular

Documentation of Antibiotic Plan

The indication of antibiotics was documented in most of the prescriptions within 24 h of initiation (88.2%) (Table 3). By discipline, neonatal intensive care unit (NICU), burn, ophthalmology, and palliative and rehabilitation all recorded 100% documentation of the reason for antibiotic use (in Appendix Figure S5). A comparison between specialist and non-specialist hospitals is shown in Appendix Table S3.

Table 3: Quality indicators for antibiotic prescriptions.

Documentation of antibiotic indication within 24 h	***n* (%)**
Yes	1,101 (88.2)
Guideline compliance	***n* (%)**
Compliant	720 (69.8)
Not compliant	311 (30.2)
Not applicable[a]	217
Description of non-compliance issues	***n* (%)[b]**
Indication does not require any antibiotic treatment	20 (6.2)
Inappropriate choice	136 (42.0)
Inappropriate dose/frequency	94 (29.0)
Antibiotic spectrum too broad	16 (4.9)
Antibiotic spectrum too narrow	40 (12.3)
Antibiotic spectrum overlapping	2 (0.6)
Surgical prophylaxis given for > 24 h[c]	16 (4.9)

Notes: [a]Not included for compliance assessment: Definitive treatment, indication not available in guidelines, not assessable; [b]Some antibiotic prescriptions may contain more than one non-compliance issue; [c]Among the surgical prophylaxis orders, 16 out of 45 prescriptions (35.6%) had been prescribed for longer than 24 h post-surgery.

Antibiotic Compliance

The PPS showed that approximately 70.0% of antibiotic prescriptions complied with the national guideline recommendations. The major non-compliance issues were inappropriate choice of antibiotics (42.0%) and improper dose/frequency (29.0%) while 35.6% of surgical prophylaxis orders were prescribed for longer than 24 h post-surgery (Table 3). By discipline, guideline compliance was highest in the ICU (84.4%) and lowest in the burn unit (in Appendix Figure S6). The differences in compliance rates and issues between different hospital settings are reported in Appendix Table S3.

DISCUSSION

Perak state hospitals' overall antibiotic prevalence of 40% conformed to a previous nationwide PPS completed in 2016, which reported that 32.7% to almost 60% of inpatients in individual state and tertiary hospitals were prescribed antibiotics (Ministry of Health Malaysia 2017). This figure was comparatively lower than the prevalence observed among hospitals in Southeast Asian nations such as Singapore (51%) and Thailand (51.5%) (Cai *et al*. 2017; Limato *et al*. 2021; Thamlikitkul *et al*. 2020). Prevalence of antimicrobial consumption in other PPS studies varied between different regions; 50.3% in India, 56% in China and 34.4% from the Global-PPS data collected across 53 countries (Panditrao *et al*. 2021; Versporten *et al*. 2018; Xie *et al*. 2015).

High antibiotic prevalence was noticed in ICU (general and COVID ICU). Previous reports support the high antibiotic prescribing rate in ICU, with 80% in a Malaysian tertiary hospital, 83.1 % in Indonesian hospitals, 86% in Ethiopian hospitals and 89.6% in Chinese hospitals (Fentie *et al*. 2022; Jamaluddin *et al*. 2021; Limato *et al*. 2021; Xie *et al*. 2015). Compared with other specialties, patients in critical care unit had higher prevalence of severe infections with resistant organism and may be complicated with co-existing medical conditions, thus necessitating the initiation of antibiotics (Jamaluddin *et al*. 2021).

In this survey, amoxicillin/clavulanate, a beta-lactam/beta-lactamase inhibitor, was the main antibiotic prescribed in Perak hospitals. The result concurs with studies by Versporten *et al*. in 53 countries, Cai *et al*. in Singapore and Jamaluddin *et al*. in a Malaysian tertiary centre (Cai *et al*. 2017; Jamaluddin *et al*. 2021; Versporten *et al*. 2018). Consistent with other surveys in Asia (Limato *et al*. 2021; Singh *et al*. 2019; Thamlikitkul *et al*. 2020) and globally (Versporten *et al*. 2018), CAP was the most common disease for antibiotic prescription in all Perak hospitals, which explains the high prescribing rate of amoxycillin/clavulanate.

This survey reported minimal prescription of broad-spectrum antibiotic groups like third-generation cephalosporin, carbapenems, fluoroquinolones and polypeptides (vancomycin). High prescribing rates of third-generation cephalosporin and fluoroquinolones in other Asian countries (Limato *et al*. 2021; Panditrao *et al*. 2021; Thamlikitkul *et al*. 2020; Xie et al. 2015) may suggest that at least a proportion of these prescriptions were unnecessary or inappropriate (Versporten *et al*. 2018). Other contributing factors include possible differences in AMR patterns and empirical antimicrobial treatment recommendations between the countries (Abubakar 2020).

The WHO AWaRe classification considers the impact of different antibiotics and antibiotic classes on AMR, and emphasises the importance of their appropriate use. Access antibiotics have activity against a wide range of commonly encountered susceptible pathogens while showing lower resistance potential than antibiotics in Watch and Reserve categories (World Health Organization 2019a). For all hospitals in this survey, most antibiotic prescriptions (> 50%) were in the Access category, followed by Watch antibiotics. The significant number of Access antibiotic prescriptions indicates the prescribers' awareness to abstain from unnecessarily prescribing broad-spectrum antibiotics. However, the value was below the country-level target of at least 60% set by the WHO (World Health Organization 2021). On the contrary, other surveys showed that Watch antibiotics (> 50%) were the most prescribed and a considerable number under Reserve (> 2.0%) (Limato *et al.* 2021; Panditrao *et al*. 2021). The minimal prescription of broad-spectrum antibiotic groups in Perak hospitals could be attributed to the concerted effort of the AMS team in the respective hospitals, sufficient levels of national antimicrobial guideline implementation and prescription habits (Xie *et al*. 2015).

Similar to other studies, the predominant route of antibiotic administration was intravenous (Limato *et al*. 2021; Xie *et al*. 2015). Parenteral therapy is inevitable in patients admitted with severe and life-threatening infections, with considerations for impairment of oral route, age, type of lesion (particularly deep-seated lesions), microorganism susceptibility and availability of dosage form (Jamaluddin *et al*. 2021). In view of the high prevalence of intravenous antimicrobial use, factors related to inappropriate prescribing reported in other studies like prescribers' preference to use injections out of fear of litigation or complaints if patient expectations are not met, limited opportunities for de-escalation and belief in the superiority of intravenous antibiotics are worthwhile to be further explored and addressed accordingly (Broom *et al*. 2016). Timely conversion from intravenous to oral therapy should routinely be practiced after assessing the patient's clinical condition as it reduces the treatment costs, resistance rates, intravenous line-related problems and the length of hospital stay (Shrayteh *et al*. 2014).

Empiric antibiotic prescriptions were much higher than nationwide PPS findings in 2016 (78.2%) (Ministry of Health Malaysia 2017), a Malaysian tertiary care university hospital (65.5%) (Jamaluddin *et al.* 2021), Indonesian hospitals (52.6%) (Limato *et al*. 2021) and Indian tertiary care centres (40.1%) (Panditrao *et al*. 2021), but comparable to Singaporean hospitals (83%) (Cai *et al*. 2017). Empirical therapy is usually initiated based on clinical judgement and experience, with choice and regimen guided by local or national guidelines. Several factors were reported to influence high empiric antibiotic prescriptions, e.g. lack of fully equipped microbiology laboratories in the facilities (Panditrao *et al*. 2021). In Perak non-specialist hospitals, the samples need to be outsourced to their affiliated referral centres which led to delays in obtaining formal results. With prompt microorganism identification and antimicrobial susceptibility testing, accurate diagnosis can guide clinical decisions for definitive antibiotics, de-escalation or early discontinuation, thus shortening the duration of and unnecessary use of empirical antibiotics (Saini *et al*. 2022).

Documentation of antibiotic indication is one of the quality indicators of antibiotic use. Proper documentation serves as a communication tool between prescribers and other healthcare providers for diagnosis and subsequent therapy plan (Jamaluddin *et al.* 2021). The documentation rates in Perak hospitals were comparable to previous studies ranging from 76.9% to 84.2% (Jamaluddin *et al*. 2021; National Centre for Antimicrobial Stewardship and Australian Commission on Safety and Quality in Health Care 2021; Singh *et al*. 2019; Vandael *et al.* 2020; Versporten *et al*. 2018). Further investigation is needed to evaluate the reasons contributing to delayed documentation (24 h after the antibiotic was prescribed) or missing indication (requiring clarification from the prescriber).

Overall compliance rate in Perak hospitals was higher than the findings from a Malaysian tertiary care university hospital (50.4%) and Indonesian hospitals (52.2%) (Jamaluddin *et al*. 2021; Limato *et al.* 2021). However, it was lower compared to other countries in the East and Southeast Asia region (81.5%) as reported by Versporten and colleagues (Versporten *et al*. 2018). The rate in this survey was also far from the targeted 90% proposed by an international antibiotic policy (Vandael *et al*. 2020; Versporten *et al.* 2018). Evidence from systematic review and meta-analysis has shown that guideline adherence was associated with a relative risk reduction for mortality of 35% (Schuts *et al*. 2016). This survey did not investigate the reason for low guideline compliance, especially those pertaining to antibiotic choice and dosage regimen, but it could be multifactorial. We postulate that the experience of prescribers, senior colleagues' influence, clinical uncertainty, and fear of treatment failure could be some reasons for non-compliance (Versporten *et al*. 2018; Skodvin *et al*. 2015). Further studies are needed to validate these reasons, especially in disciplines with low national guideline adherence.

The rate of 36.4% for surgical prophylaxis extending beyond 24 h in Perak specialist hospitals was lower than the figures reported by a Malaysian tertiary hospital (50%) and 303 hospitals in 53 countries (66.1%) (Jamaluddin *et al*. 2021; Versporten *et al*. 2018). Increasing the duration of prophylaxis was associated with a higher risk of AMR, acute kidney injury and *Clostridium difficile* infection. However, it did not lead to additional postoperative infection reduction (Allegranzi *et al*. 2016; Branch-Elliman *et al*. 2019). These findings suggest that restriction of the surgical prophylaxis period can reduce adverse events without increasing surgical site infections. Further stewardship efforts may be considered by referring to other countries like Australia which sets a target of < 5% antibiotic prescriptions with prolonged surgical prophylaxis as one of its key performance indicators in the national antimicrobial policy after their national antimicrobial prescribing survey showed that 30% of surgical prophylaxis orders were continued inappropriately (National Centre for Antimicrobial Stewardship and Australian Commission on Safety and Quality in Health Care 2021).

One of the strengths of our study is the insight it provides into the prevalence and quality of antibiotic use in Perak government healthcare facilities with different settings. Data can be used to evaluate the AMS programme's effectiveness and identify the gap for 'low-hanging fruit' interventions. In addition, the use of standard forms for data collection, the simplicity of the protocol and data entry templates, the lack of need for intensive training, ease of access to supporting materials in cloud storage (e.g. user manual and frequently asked questions) and availability of technical and clinical support by group text messaging, have allowed all hospitals with different resource settings to participate in the survey successfully (Versporten *et al*. 2018).

Similar to other PPS, the study limitation lies in the cross-sectional nature of the survey, whereby only prevalence values were reported and patients were not followed-up in time. In addition, other factors influencing antibiotic trends were not controlled, namely, patient case mix (number and types of patients), disease incidence, the prevalence of different types of infections, variations in microorganism resistance or institutional factors (Versporten *et al*. 2018). In cases with unclear medical notes documentations (e.g. antibiotic prescribed for a patient with documented diagnosis of traumatic brain injury post-motor vehicle accident, while the indication to cover for central nervous infection was not written), interpretation by individual surveyor was practiced, potentially leading to assessment discrepancies (Jamaluddin *et al*. 2021). However, these were minimised as much as possible through discussions between surveyors and prescribers in the decision-making process. Informing relevant hospital stakeholders beforehand on PPS can potentially introduce bias. As these data were obtained from the government healthcare facilities, caution should be exercised when extrapolating the observed patterns to private centres.

CONCLUSION

The prevalence of antibiotic use in Perak government hospitals was 50%, with more than half of the antibiotic prescriptions having narrow spectrum coverage and low AMR risk (Access category). The survey also revealed high rates of empirical and intravenous antibiotic prescribing. These with key quality indicators of prescribing, such as guideline compliance and surgical prophylaxis, can suggest important areas for implementing AMS interventions tailored to each hospital setting.

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APPENDIX

Table S1: Hospital characteristics and antibiotic prevalence.

	Total	HRPB	HT	HTI	HSM	HSR	HBUK	HBG	HKK	HPB	HSS	HTP	HS	HK	HG	HCM
Level of health service	–	S	S	S	S	S	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Total no. of beds	3,601	1117	561	485	274	160	236	139	105	101	93	81	72	68	63	46
Total no. of wards surveyed	158	51	26	20	11	8	7	7	4	4	4	3	3	4	3	3
Admitted patients	2,386	764	529	322	205	90	147	70	53	45	36	29	18	32	27	19
Antibiotic prevalence, *n* (%)	954 (40.0)	327 (42.8)	196 (37.1)	180 (55.9)	82 (40.0)	46 (51.1)	13 (8.8)	18 (25.7)	22 (41.5)	15 (33.3)	7 (19.4)	11 (37.9)	9 (50.0)	10 (31.3)	10 (37.0)	8 (42.1)

Notes: [a]Specialist hospital: Presence of permanent or resident specialists to provide services, including medicine, surgery, and other specialty services, to meet the medical and surgical needs of the community. Laboratory services (e.g. microbiology lab) for specialised pathological analysis and dedicated imaging units are available; [b]Non-specialist hospital: Absence of permanent or resident specialists and specialty services. Limited laboratory and imaging services are available for general analysis.

HRPB = Hospital Raja Permaisuri Bainun; HT = Hospital Taiping; HTI = Hospital Teluk Intan; HSM = Hospital Seri Manjung; HSR = Hospital Slim River; HK = Hospital Kampar; HBG = Hospital Batu Gajah; HPB = Hospital Parit Buntar; HTP = Hospital Tapah; HKK = Hospital Kuala Kangsar; HCM = Hospital Changkat Melintang; HSS = Hospital Sungai Siput; HG = Hospital Gerik; HS = Hospital Selama; HBUK = Hospital Bahagia Ulu Kinta; S = specialist[a]; NS = non-specialist[b]

Table S2: Route of antibiotic administration and indication of treatment.

	Specialist hospital	Non-specialist hospital
Route of administration, *n* (%)		
IV	886 (80.3)	105 (72.9)
PO	214 (19.4)	39 (27.1)
IP	3 (0.3)	0
IM	1 (0.1)	0
Indication category of antibiotic prescriptions, *n* (%)		
Empiric	927 (84.0)	128 (88.9)
Definitive	129 (11.7)	14 (9.7)
Surgical prophylaxis	44 (4.0)	1 (0.7)
Non-surgical prophylaxis	4 (0.4)	1 (0.7)

Notes: IV = intravenous; PO = per oral; IP = intraperitoneal; IM = intramuscular

Table S3: Quality indicators for antibiotic prescriptions.

	Specialist hospital	Non-specialist hospital
Documentation of antibiotic indication within 24 h, *n* (%)		
Yes	967 (87.6)	134 (93.1)
Guideline compliance, *n* (%)		
Compliant	630 (69.7)	90 (70.9)
Not compliant	274 (30.3)	37 (29.1)
Not applicable[a]	200	17
Description of non-compliance issues, *n* (%)[b]		
Indication does not require any antibiotic treatment	12 (4.2)	8 (21.1)
Inappropriate choice	122 (42.7)	14 (36.8)
Inappropriate dose/frequency	79 (27.6)	15 (39.5)
Antibiotic spectrum too broad	16 (5.6)	0
Antibiotic spectrum too narrow	40 (14.0)	0
Antibiotic spectrum overlapping	1 (0.3)	1 (2.6)
Surgical prophylaxis given for > 24 h	16 (5.6)	0

Notes: [a]Not included for compliance assessment: Definitive treatment, indication not available in guidelines, not assessable; [b]Some antibiotic prescriptions may contain more than one non-compliance issue; [c]Among the surgical prophylaxis orders in specialist hospitals, 16 out of 44 prescriptions (36.4%) had been prescribed for longer than 24 h post-surgery, while none was encountered in non-specialist hospitals.

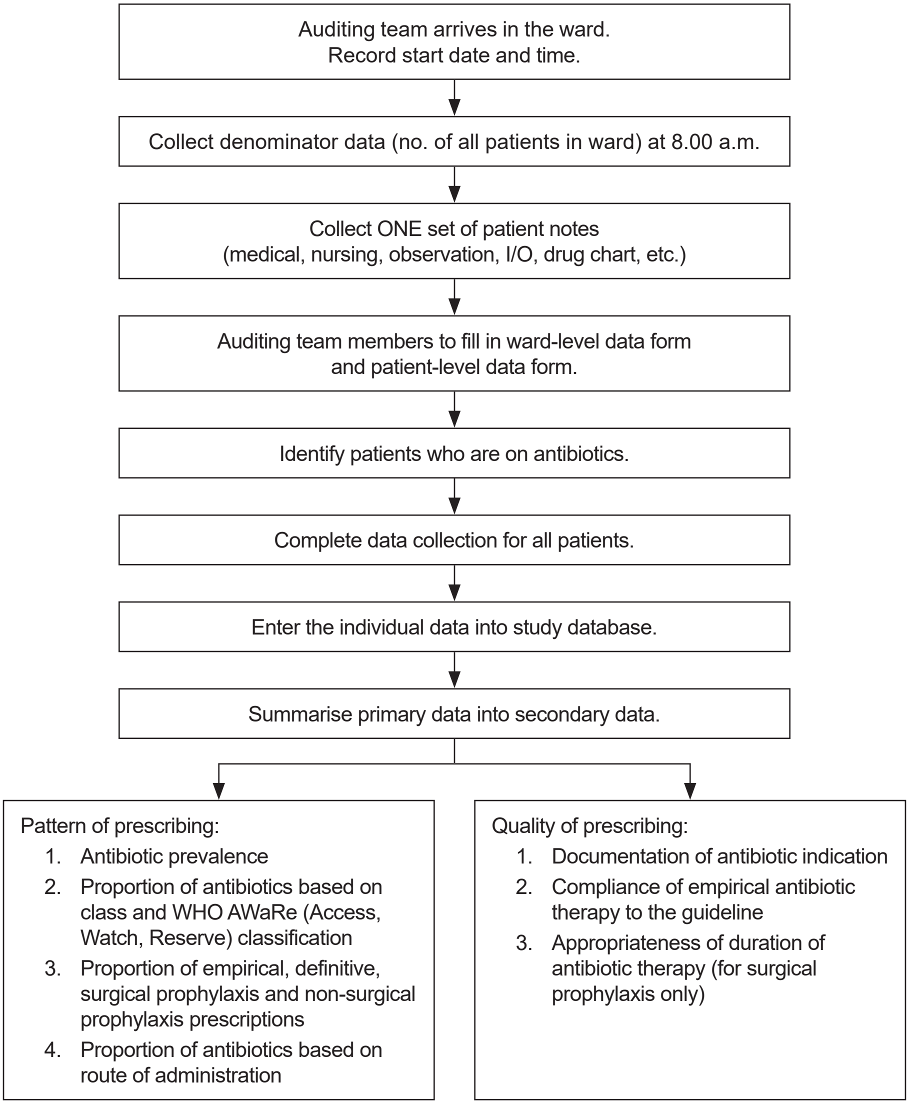

Figure S1: Workflow and data collection.

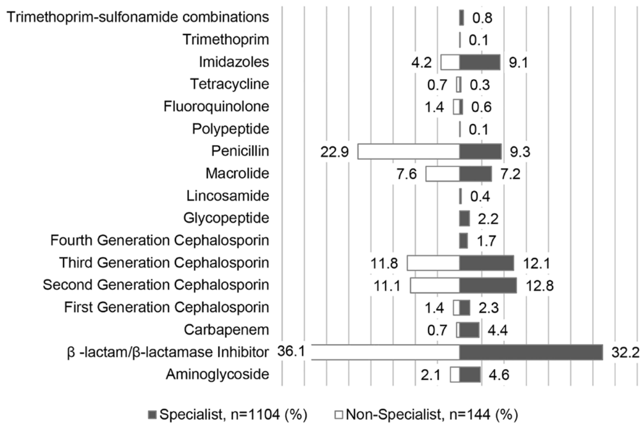

Figure S2: Percentage of antibiotic prescription by class according to hospital setting.

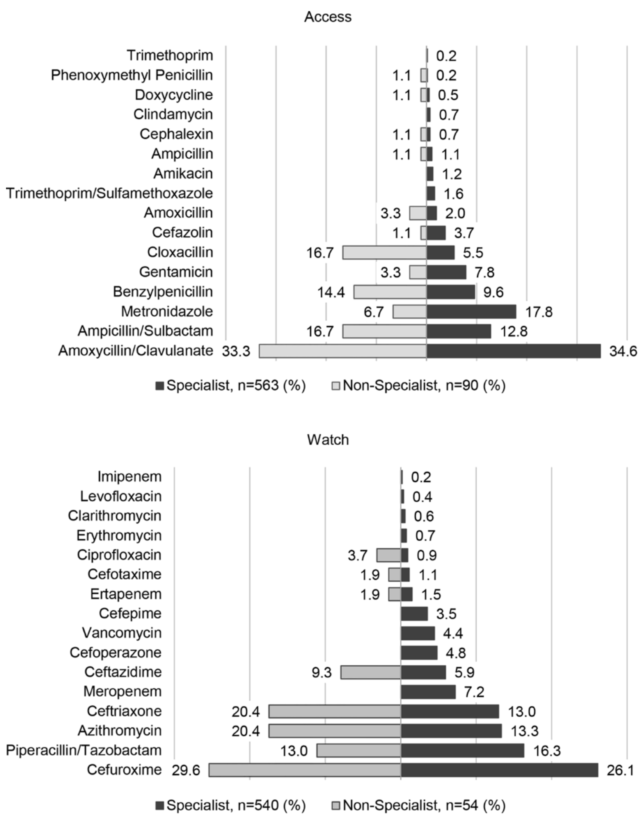

Figure S3: Percentage of antibiotics prescribed under AWaRe categories based on hospital setting. Only one Reserve antibiotic prescription, colistin, was audited during the survey period in a specialist hospital.

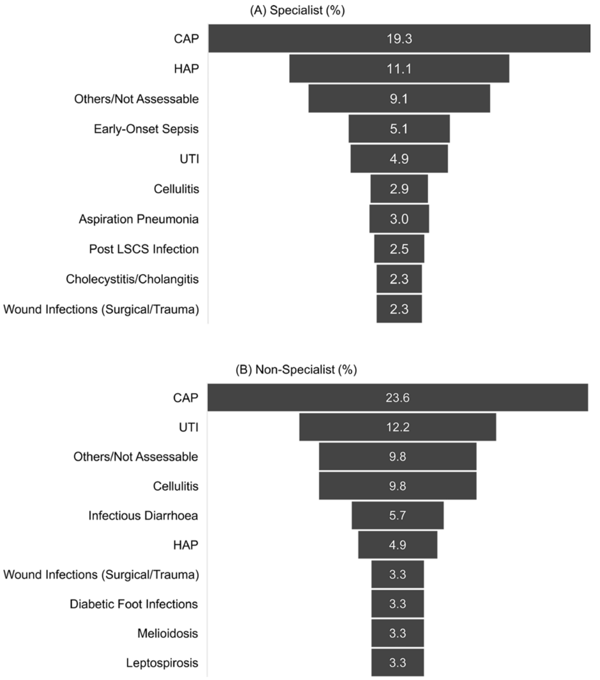

Figure S4: Types of infectious diseases in specialist (A) and non-specialist hospitals (B). The 10 frequently encountered diagnoses were presented here.

CAP = community-acquired pneumonia; HAP = hospital-acquired pneumonia; LSCS = lower segment Caesarean section; UTI = urinary tract infection

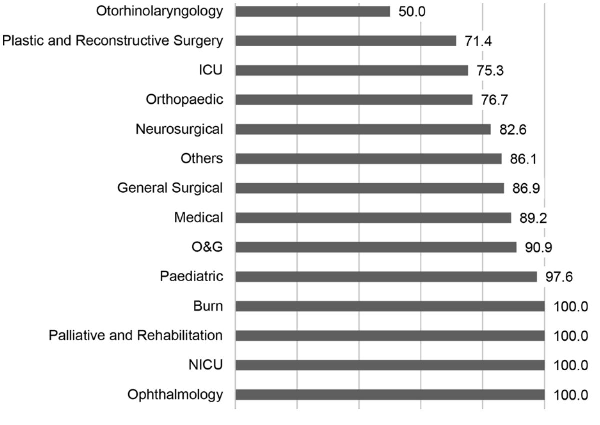

Figure S5: Percentage of antibiotic prescriptions with reason for use documented within 24 h of initiation.

ICU includes both general ICU and COVID ICU. Medical includes general medical, rheumatology, nephrology, haematology, COVID general adults, cardiology and dermatology. Medical, paediatric, others, O&G, and palliative and rehabilitation are the only disciplines in non-specialist hospitals. COVID = Coronavirus; ICU = intensive care unit; NICU = neonatal intensive care unit; O&G = Obstetrics and Gynaecology

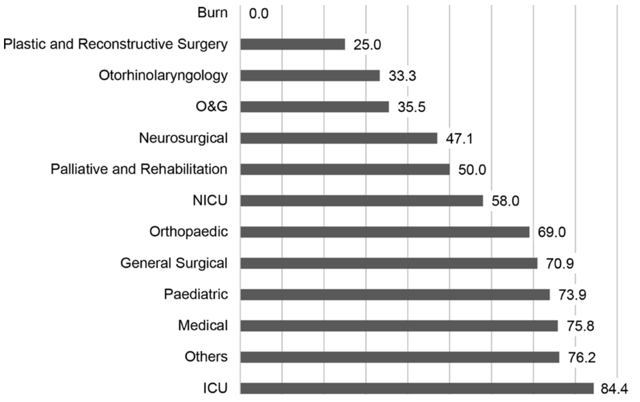

Figure S6: Guideline compliance in percentage by discipline based on 1,031 prescriptions. As there were only two antibiotic prescriptions from the ophthalmology speciality, adherence was not assessed due to the absence of indication in guidelines.

ICU includes both general ICU and COVID ICU. Medical includes general medical, rheumatology, nephrology, haematology, COVID general adults, cardiology and dermatology. Medical, paediatric, others, O&G, and palliative and rehabilitation are the only disciplines in non-specialist hospitals. COVID = Coronavirus; ICU = intensive care unit; NICU = neonatal intensive care unit; O&G = Obstetrics and Gynaecology