Reducing bacterial resistance with

IMPACT

Interhospital Multi-disciplinary Programme on Antimicrobial ChemoTherapy

Sixth Edition

Edited by P.L. Ho & T.C. Wu

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Reducing bacterial resistance with IMPACT –

Interhospital **M**ulti-disciplinary **P**rogramme on **A**ntimicrobial **C**hemo**T**herapy

Editors: HO Pak Leung & Tak Chiu, WU

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Table of Contents

List of Tables

List of Figures

Foreword

Antimicrobial resistance (AMR) is a formidable challenge that continues to threaten global public health. The World Health Organization (WHO) identified AMR as one of the top ten global public health threats in 2019. The health impact of AMR is far-reaching — an estimated 1.14 million deaths were attributable to bacterial AMR globally in 2021. In Hong Kong, the WHO projected over 18,000 AMR-related deaths in 2020 to 2030. The rise of AMR not only compromises the effectiveness of treatments but also jeopardises the sustainability of our healthcare system.

The first Hong Kong Strategy and Action Plan on Antimicrobial Resistance, launched in 2017, called for coordinated efforts across sectors and laid a solid foundation for a multi-faceted approach to halt AMR. Building on this foundation, the second Action Plan was launched in 2022, mapping out priority interventions and target indicators. One of the key strategic interventions was to review, update and promote evidence-based guidelines for antimicrobial prescription among healthcare professionals.

The sixth edition of these guidelines is a testament to the Government's commitment to ensuring that antibiotics are prescribed judiciously to preserve their efficacy, in an effort to curb AMR. I would like to express my gratitude to all the experts and professionals who have generously contributed their time and insights to this important initiative.

The IMPACT guidelines provide a strong foundation for antimicrobial stewardship in Hong Kong and are integral to our larger initiatives against AMR. Their success, however, rests on widespread adoption and sustained commitment by both the public and private healthcare sectors. I encourage all healthcare practitioners to fully utilise this invaluable resource and integrate it in their daily medical practice.

Prof. LO Chung Mau, B.B.S., J.P.
Secretary for Health
The Government of the Hong Kong Special Administrative Region
May 2025

Foreword

My heartfelt congratulations to the Interhospital Multi-disciplinary Programme on Antimicrobial ChemoTherapy (IMPACT) Editorial Board on the publication of the sixth edition of IMPACT. With the ever-rising global threat of antimicrobial resistance (AMR), the issuance of the new edition could not be more opportune.

In recent years, not only do we encounter a sustained high level of methicillin-resistant *Staphylococcus aureus* (MRSA), but also an uprising trend of carbapenem-resistant *Escherichia coli* (CRE) and a re-emergence of vancomycin-resistant *enterococcus* (VRE). Outbreak of *Candida auris* in hospitals, an emerging multidrug-resistant fungus, has further increased overwhelming burdens to our hospitals. The local threat of AMR is dire in which the necessity for antibiotic stewardship is greater than ever. The sixth edition of IMPACT reflects the most recent local statistics on antibiotic resistance, along with guidelines for selected antimicrobial use, as well as treatment recommendations for specific infections and pathogens. The content has been revised, taking reference from international guidelines and up-to-date scientific research, as well as local disease epidemiology and the latest susceptibility data from local surveillance network. Besides, a new part on Outpatient Parenteral Antimicrobial Therapy (OPAT) has been developed highlighting key issues for this treatment modality. I am confident that the sixth edition of IMPACT would contribute profound values to the management of various infections.

I would like to express sincere gratitude to all those who worked tirelessly to bring the sixth edition of IMPACT to fruition, especially the Editors and Members of the Editorial Board. The Editorial Board truly encompassed a multifaceted spectrum with leading experts and representatives from hospitals of the private and public sector, universities, professional bodies, the Hospital Authority, and the Department of Health. I am also grateful to the continuing contribution of the Infection Control Branch of the Centre for Health Protection (CHP) in analysing the local epidemiology of AMR, coordinating the editing work, and developing an e-Book and a mobile app, both equipped with clinical calculators and antibiograms, to optimise usability for healthcare professionals. Through close collaboration with local experts across sectors, the CHP will continue to dedicate its utmost to stave off the advance of AMR.

Dr. TSUI Lok Kin, Edwin, J.P.
Controller, Centre for Health Protection, Department of Health
The Government of the Hong Kong Special Administrative Region
May 2025

Foreword

It gives me a great pleasure to write the foreword for the sixth edition of the Interhospital Multi-disciplinary Programme on Antimicrobial ChemoTherapy (IMPACT).

Antimicrobial resistance (AMR) is a major and rising global challenge across healthcare spectrum as a result of inappropriate use of antimicrobials which accelerates the emergence of newer resistant strains of microorganisms. AMR jeopardises the effectiveness and limits the choices of treatment, attributes to prolonged illness and hospitalisation, increases mortality among vulnerable patients as well as healthcare and social costs.

Collaborative effort from all stakeholders is critical in combating AMR, as underlined and advocated by the Hong Kong Strategy and Action Plan on AMR (2023–2027). With this, the Hospital Authority (HA) is working in partnership with the Government to turn the tide against AMR.

Since 2005, the HA has introduced the Antibiotic Stewardship Programme (ASP) to promote appropriate use of antimicrobials in hospitals. Seizing the opportunity arising from technological development, the HA brings ASP to a next level and progressively launched the SmartASP beginning from early 2024 onward, which is a protocol-driven tool sending reminder prompts on potentially inappropriate use of broad-spectrum antibiotic.

The IMPACT guideline is a cornerstone and reference tool to guide health professionals on appropriate choices of antimicrobials for treating various types of infections based on the latest clinical and scientific evidence. The IMPACT and SmartASP programme are complementary with each other and would achieve synergies.

The IMPACT Editorial Board, comprising leading experts from major medical disciplines, especially in the field of antimicrobial use, has rendered invaluable guidance to this new edition. I wish to express my sincere thanks and congratulations to the successful launching of the sixth edition of IMPACT, which would definitely further safeguard the health of our community.

Dr. KO Pat Sing, Tony
Chief Executive
Hospital Authority
May 2025

Preface

Antimicrobial resistance (AMR) is a formidable challenge that threatens global health security. Defined as the ability of microorganisms to adapt and withstand the effects of antimicrobial agents, AMR poses a grave threat to modern medicine. The impact of AMR is starkly evident, with a rising number of lives lost to untreatable infections. In Hong Kong alone, projections indicate a staggering 18,433 deaths related to AMR, costing US$4,300 million from 2020 to 2030.

For over a quarter of a century, IMPACT has been at the forefront of efforts to combat AMR by promoting the judicious use of antimicrobial agents. As we unveil the sixth edition of IMPACT, our commitment to providing evidence-based guidance tailored to the unique epidemiological landscape of Hong Kong remains unwavering. This edition involved and is supported by the Hospital Authority, Centre for Health Protection, University of Hong Kong, Chinese University of Hong Kong, Hong Kong Medical Association, and Hong Kong Private Hospital Association.

I extend my heartfelt appreciation to the dedicated experts whose invaluable insights have shaped this publication. Special thanks are due to the Centre for Health Protection for their unwavering support in facilitating the production and dissemination of IMPACT. It is my sincere hope that this guideline will serve as a useful reference tool for healthcare professionals in optimizing antibiotic use and safeguarding the efficacy of these crucial therapeutics.

Dr. HO Pak Leung, J.P.
Chairman, IMPACT Editorial Board
May 2025

Part I: Antibiotic Resistance (AMR) - Global and Local Epidemiology

1.1 Global Burden of Antimicrobial Resistance (AMR)

1. A global disease burden study has estimated that in 2021 there were 4.71 million deaths associated with bacterial AMR, including 1.14 million deaths attributable to bacterial AMR, and forecasts show that an estimated 1.91 million deaths attributable to AMR and 8.22 million deaths associated with AMR could occur globally in 2050. [1]
2. The World Bank estimates that AMR could result in US$1 trillion additional healthcare costs by 2050, and US$1 trillion to US$3.4 trillion gross domestic product (GDP) losses per year by 2030. [2]
3. According to the 2022 Global Antimicrobial Resistance and Use Surveillance System (GLASS) report published by the World Health Organization (WHO), the median reported rates in 76 countries for third-generation cephalosporin-resistant *Escherichia coli* and methicillin-resistant *Staphylococcus aureus* (MRSA) were 42% and 35% respectively. [3] Besides, *Klebsiella pneumoniae* also showed elevated resistance levels against critical antibiotics including carbapenems across multiple regions. [3]
4. The AMR situation of AMR worsened during the Coronavirus Disease 2019 (COVID-19) pandemic. A systematic review of 30 studies revealed increased rates of MRSA, vancomycin-resistant enterococci (VRE), carbapenem-resistant *Acinetobacter baumannii* (CRAB) and carbapenem-resistant Enterobacterales (CRE) during this time. [4]

1.2 Local Situation of AMR

1. The emergence of AMR has jeopardised the effective treatment of patients with infections. [5–9]
2. AMR leads to higher drug costs, prolonged hospital stay, and adversely affects patient's outcome. [10]
3. The WHO estimates that AMR-related infections in Hong Kong from 2020 to 2030 resulted in 18,433 excess deaths and incurred a total economic cost of US$4.3 billion. [11]

4. Resistance to all classes of antibiotics has developed to various extents among common and important nosocomial pathogens (Table 1.1, Table 1.2, Table 1.3).
5. In Hong Kong, MRSA, extended-spectrum β-lactamase (ESBL)-producing *E. coli* and *Klebsiella* spp., carbapenem-resistant *Acinetobacter* spp. are the most common multidrug-resistant organisms. Carbapenemase-producing Enterobacterales (CPE) has emerged during the COVID-19 pandemic while VRE resurges again in recent years after the epidemic occurred in 2013–2014.
6. Factors contributing to the rapid rising and high prevalence of AMR in Hong Kong include. [12]
    - Hospital: overcrowding, manpower shortage, lapse in infection control measures, inappropriate use of antibiotics, environmental contamination, lack of transparency of surveillance data and lack of incentive in healthcare administration.
    - Community: misuse of antimicrobials, including in animal husbandry, lack of awareness, and inadequate food and personal hygiene.
7. The COVID-19 pandemic has worsened AMR by disrupting the hospital infection control practice, resulting in more secondary bacterial infections, and increasing the utilisation of antibiotics for in-patients. [13,14]
8. In the Hong Kong Strategy and Action Plan on AMR 2023 to 2027, promoting antibiotic prescription according to evidence-based guidelines for doctor is one of the key strategic interventions to combat AMR (Strategic intervention 5.2). [15]

Table 1.1: Top Ten Bacterial Organisms Isolated From Different Clinical Specimens in 2023. Data From the Hospital Authority.

Blood			Lower Respiratory Specimens*			Urine†	
Organism	Non-ICU/ HDU	ICU/ HDU	Organism	Non-ICU/ HDU	ICU/ HDU	Organism	Non-ICU/ HDU
	Rank (%)	Rank (%)		Rank (%)	Rank (%)		Rank (%)
Escherichia coli	1 (34%)	2 (17%)	*Pseudomonas aeruginosa*	1 (21%)	3 (14%)	*Escherichia coli*	1 (52%)
Klebsiella spp.	2 (12%)	3 (11%)	*Staphylococcus aureus*	2 (18%)	2 (16%)	*Klebsiella* spp.	2 (14%)
Staphylococcus aureus	3 (11%)	4 (10%)	*Klebsiella* spp.	3 (14%)	1 (16%)	*Enterococcus* spp.	3 (9%)
Staphylococcus, coagulase negative	4 (9%)	1 (23%)	*Acinetobacter baumannii*	4 (6%)	5 (6%)	*Proteus mirabilis*	4 (7%)
Proteus mirabilis	5 (4%)	8 (2%)	*Haemophilus influenzae*	5 (5%)	9 (2%)	*Pseudomonas aeruginosa*	5 (3%)
Enterococcus spp.	6 (4%)	5 (5%)	*Stenotrophomonas maltophilia*	6 (5%)	4 (7%)	*Citrobacter* spp.	6 (3%)
Pseudomonas aeruginosa	7 (2%)	6 (3%)	*Escherichia coli*	7 (5%)	6 (5%)	*Staphylococcus aureus*	7 (2%)
Enterobacter spp.	8 (2%)	-	*Enterobacter* spp.	8 (3%)	7 (4%)	*Streptococcus agalactiae*	8 (2%)
Acinetobacter baumannii	9 (1%)	7 (2%)	*Corynebacterium striatum*	9 (2%)	8 (3%)	*Morganella* spp.	9 (1%)
Streptococcus agalactiae	10 (1%)	-	Alpha-haemolytic *streptococcus*	10 (1%)	10 (2%)	*Staphylococcus*, coagulase negative	10 (1%)

*Lower respiratory specimens include: Bronchial biopsy; Bronchial trap; Bronchial washing; Bronchoalveolar lavage; Lung biopsy; Sputum; Bronchial/Endotracheal/Tracheal/Tracheostomy/Transbronchial/Transtracheal aspirate.

†Only isolates from urine specimens with a bacterial count greater than 10^5 CFU/mL are included.

Mycobacterium spp. and *Candida* spp. are excluded from the analysis.

Table 1.2: Intrinsic and Associated Resistance to Antimicrobial Agents Among Five Nosocomial Pathogens

Bacteria	Intrinsic resistance	Associated resistance
MRSA	All β-lactams[1], β-lactam/β-lactamase inhibitor combinations	Common: erythromycin, clindamycin, aminoglycosides, cotrimoxazole, fluoroquinolones
VREfm	Glycopeptides, cotrimoxazole, clindamycin, aminoglycosides	Common: ampicillin, carbapenems, fluoroquinolones, high level aminoglycoside resistance
ESBL-E	All cephalosporins including third-generation cephalosporins, (variable activity against fourth-generation cephalosporins), all penicillins and monobactams	Common: fluoroquinolones, aminoglycosides, cotrimoxazole
CRE	All β-lactams including carbapenem (except monobactam)	Common: fluoroquinolones, aminoglycosides, cotrimoxazole
CRAB	Cross-resistance to other β-lactams is common	Common: fluoroquinolones, aminoglycosides, cotrimoxazole

[1] Except anti-MRSA cephalosporins such as ceftaroline.
CRAB, Carbapenem-resistant *Acinetobacter baumannii*; CRE, Carbapenem-resistant Enterobacterales; ESBL-E, extended-spectrum-β-lactamases-producing Enterobacterales; VREfm, vancomycin-resistant *Enterococcus faecium*

Table 1.3: Non-Susceptibility of Common Bacterial Isolates From Blood Specimens in HA Hospitals in 2023

Organisms	% Non-susceptible*																							
	Minocycline	Penicillin	Ampicillin	Cloxacillin	Ampicillin-sulbactam	Amoxicillin-clavulanate	Piperacillin-tazobactam	Cefuroxime (parenteral)	Cefotaxime	Ceftazidime	Cefoperazone-sulbactam	Cefepime	Meropenem	Ertapenem	Imipenem	Cotrimoxazole	Erythromycin	Clindamycin	Gentamicin	Amikacin	Ciprofloxacin	Levofloxacin	Vancomycin	Fusidic acid	Rifampicin
Escherichia coli	-	-	79	-	-	30	9.8	34	32	15	-	18	-	0.6	-	-	-	-	26	3.4	-	36	-	-	-
Klebsiella spp.	-	-	99	-	-	23	16	22	18	12	-	11	1.4	1.5	-	-	-	-	7.8	2.0	-	16	-	-	-
Proteus spp.	-	-	74	-	-	35	2.9	28	24	4.0	-	9.5	-	0.0	-	-	-	-	25	2.6	-	48	-	-	-
Pseudomonas aeruginosa	-	-	-	-	-	-	8.5	-	-	5.0	12	3.3	8.6	-	13	-	-	-	-	0.3	7.8	17	-	-	-
Enterobacter spp.†	-	-	-	-	-	96	20	36	25	18	-	5.3	1.4	5.3	-	-	-	-	3.3	1.1	-	5.2	-	-	-
Acinetobacter spp.	15	-	-	-	49	-	57	-	-	28	49	57	61	-	57	22	-	-	30	21	52	57	-	-	-
Enterobacter aerogenes‡	-	-	-	-	-	97	47	49	40	29	-	4.4	0.0	1.8	-	-	-	-	5.1	1.7	-	8.7	-	-	-
Staphylococcus aureus	-	-	-	46	-	-	-	-	-	-	-	-	-	-	-	0.2	23	22	19	-	-	-	0.0	9.2	0.8
Viridans group streptococci	-	16	-	-	-	-	-	-	-	-	-	-	-	-	-	-	29	21	-	-	-	5.4	0.0	-	-
Enterococcus spp.§	-	-	44	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	34	-	-	55	1.9	-	-

Non-susceptible percentages from less than 70% of the total isolates tested for susceptibility to that drug are not reported.

*Non-susceptible is defined as an isolate tested as Intermediate, Resistant to that particular drug.

†Excluding *Enterobacter aerogenes*

‡Formerly known as *Klebsiella aerogenes*

§Excluding viridans group streptococci

Table 1.4: Estimates of Microorganisms Significantly Associated With AMR, Hong Kong, 2019–2023

Antibiotic-resistant microorganism	Specimen Type	Number of cases by year§				
		2019	2020	2021	2022	2023
MRSA	Blood only	806	793	879	843	824
ESBL-producing *E. coli*	Blood only	1,881	1,805	1,684	1,465	1,726
ESBL-producing *Klebsiella* spp.	Blood only	381	381	353	388	373
Carbapenem-resistant *Acinetobacter* spp.	Blood only	91	112	101	145	122
MRSA	All clinical specimens	12,742	11,617	12,612	14,527	17,680
ESBL-producing *E. coli*	All clinical specimens	16,651	14,997	16,092	15,188	16,999
ESBL-producing *Klebsiella* spp.	All clinical specimens	5,092	4,714	4,776	4,508	5,916
Carbapenem-resistant *Acinetobacter* spp.	All clinical specimens	3,340	3,366	3,858	5,074	5,416
Ceftazidime-resistant *Pseudomonas aeruginosa*	All clinical specimens	977	993	1,106	1,060	1,143
Vancomycin-resistant *Enterococcus* spp.*	All clinical specimens	15	16	129	296	310
Erythromycin-resistant *Streptococcus pyogenes*†	All clinical specimens	555	231	159	119	199
Clostridioides difficile‡	Stool only	-	2,665	3,246	3,164	3,242

*VRE isolated from stool and rectal swabs, as well as High Risk Screening on Haemodialysis and VRE Targeted Screening on Admission, are excluded. The majority of these isolates are vancomycin-resistant *Enterococcus faecium* (95%).

†Erythromycin-resistant strains are also resistant to other macrolides, such as clarithromycin and azithromycin.

‡Previously known as *Clostridium difficile*. Figure for year 2019 is not available.

§ The annual number of cases was estimated by using microbiological results from all HA laboratories. Each patient was counted only once in the calculation. The figures for *Clostridioides difficile* were extracted from the Standard Report of the Hospital Authority *Clostridioides difficile* Surveillance Programme. [613]

1.3 Methicillin-resistant *Staphylococcus aureus* (MRSA)

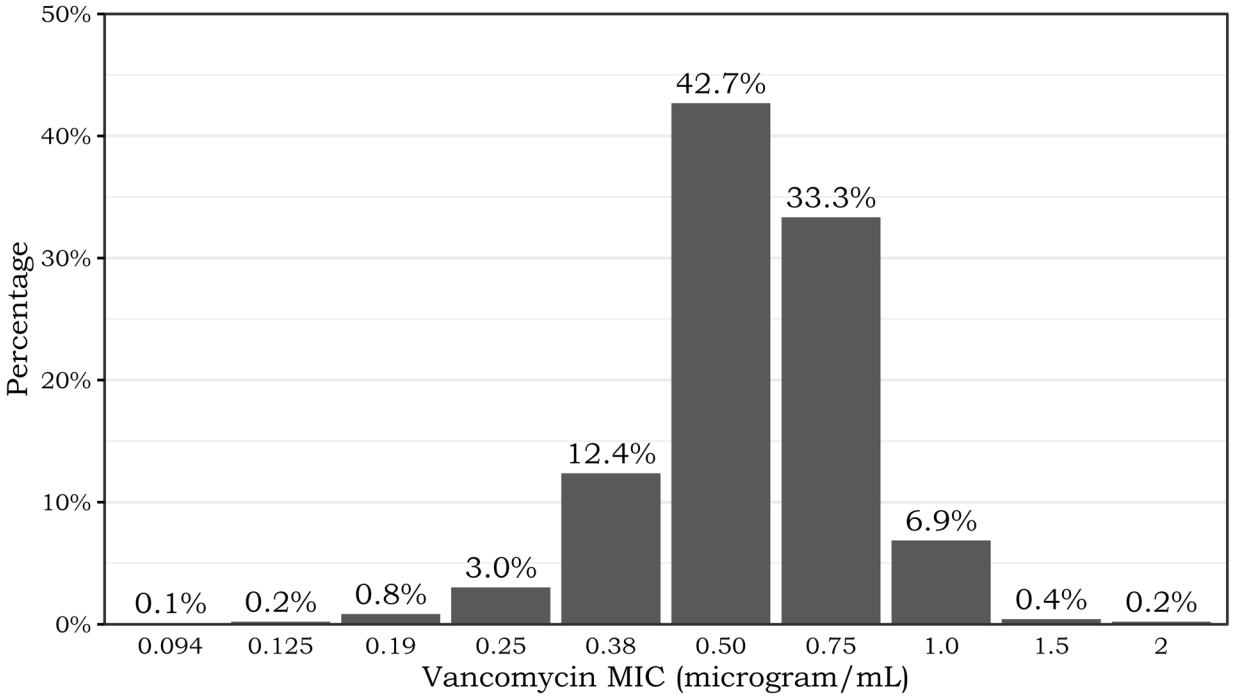
1. MRSA are resistant to penicillins (including cloxacillin and flucloxacillin), β-lactam/β-lactamase inhibitor combinations, cephalosporins, and carbapenems due to alterations in penicillin binding protein. Only the new anti-MRSA β-lactams (e.g. ceftaroline) remain effective against MRSA. However, reduced susceptibility to ceftaroline has recently been reported both *in vitro* and *in vivo*. [16,17]
2. MRSA is classified into healthcare-associated (HA-MRSA) and community-associated (CA-MRSA). The United States Centers for Disease Control and Prevention (CDC) classification, which is the most widely accepted, classified HA-MRSA and CA-MRSA epidemiologically. [18] However, the border between the two is becoming blurred and surveillance using epidemiological criteria alone has become insufficient.

HA-MRSA

1. Vancomycin is less effective than anti-staphylococcal β-lactams for methicillin-susceptible *S. aureus* (MSSA) infections. [19] However, vancomycin remains the treatment of choice for infections caused by MRSA. The efficacy of vancomycin may be compromised by factors such as the lower potency of generic formulations, suboptimal dosing, limited tissue penetration, slow bactericidal activity, and strains of MRSA with reduced susceptibility to the drug. [19–21]
2. The susceptibility profile is not a distinguishing factor between HA-MRSA and CA-MRSA. Local hospitals have seen a rise in multi-susceptible MRSA prevalence in recent years. These MRSA are classified as HA-MRSA and are linked to the spread of the ST45/t1081 clone carrying SCC*mec* type IV or V. About 75% of these isolates were identified in residents of elderly care facilities, suggesting a potential for increased transmission among this population, serving as a reservoir. [22]
3. In 2011, a local study on MRSA carriage at admission to 15 acute medical units showed that the overall carriage rate was 14.3%. [23] Risk factors include MRSA history within the past 12 months, old age home residence, and bed-bound state. Molecular typing revealed that ST45/t1081 is a major clone circulating among the patients. [23]

4. A study conducted locally between 2015 and 2018 revealed that 2.1% of patients were carriers of gastrointestinal MRSA upon admission screening, with ST45 being the predominant sequence type. [24]
5. A 2021 local study discovered that 48.7% of elderly home residents carried MRSA at any body site, while 8.5% of staff members were nasal MRSA carriers, predominantly of the ST1047 lineage 1. [25]

Figure 1.1: Distribution of MIC for Vancomycin Against 963 MRSA Isolated from Blood Cultures in KCC, KEC and HKWC, 2020–2023



Note: KCC refers to Kowloon Central Cluster, KEC refers to Kowloon East Cluster, and HKWC refers to Hong Kong West Cluster.

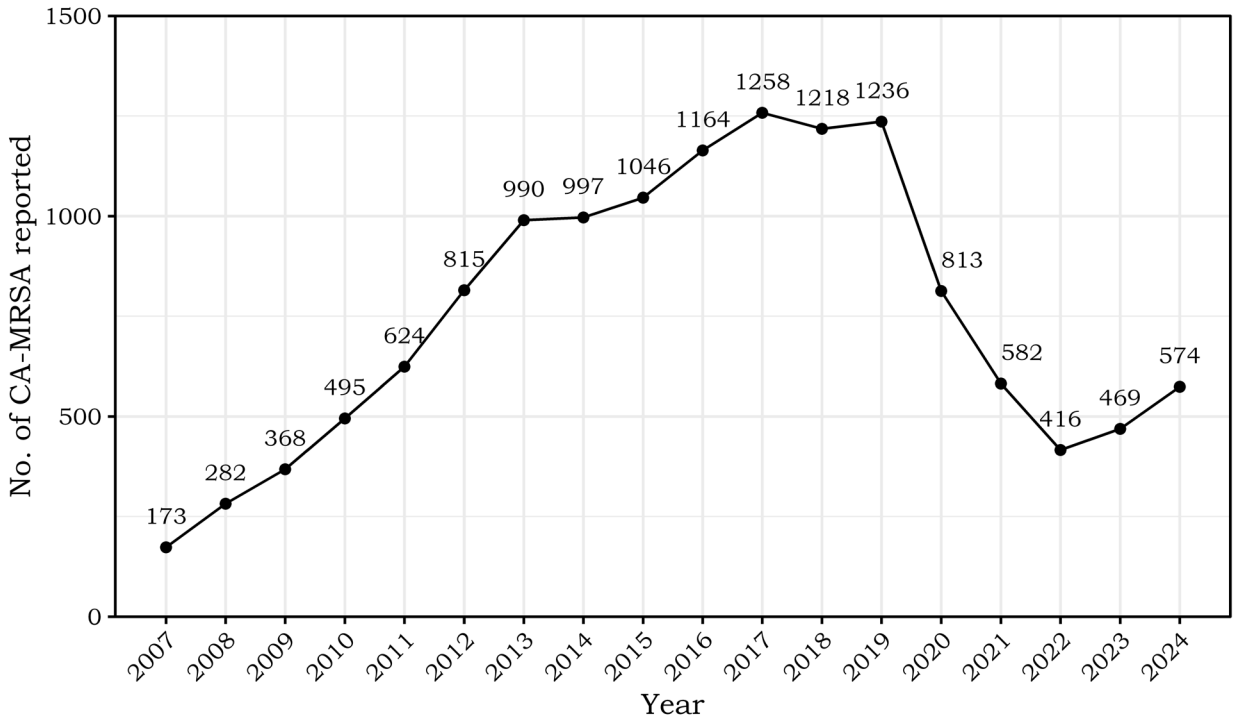
6. The vancomycin MIC of 3 public hospitals between 2020–2023 showed that majority of the isolates had MIC ≤1 microgram/mL.

CA-MRSA

1. CA-MRSA was initially documented in Hong Kong in 2001 and has shown rapid emergence over the past two decades. It has been designated as a notifiable disease, necessitating reporting to the Department of Health (DH) since January 2007 (Figure 1.2). The number of cases has steadily risen to over 1,000 per year, with a subsequent decrease during the COVID-19 pandemic. [26]
2. It is responsible for 10.4% of purulent cellulitis and 5% of cutaneous abscess in the Accident & Emergency setting. [27]

3. During the period from January 2012 to October 2015, 3,650 cases of CA-MRSA were documented, of which 98% were uncomplicated skin and soft tissue infections, and 2% were invasive CA-MRSA infections, resulting in four fatalities. [28]
4. Patients infected with CA-MRSA do not have the usual risk factors associated with HA-MRSA. Locally, case control studies revealed that ethnic minority and sharing of personal items with other persons were risk factors for CA-MRSA while frequent hand washing was protective against CA-MRSA infection. [29,30]
5. Panton-Valentine leukocidin (PVL) toxin is a pore forming cytotoxin that is capable of destroying human monocytes and neutrophils. PVL toxin has been associated with virulence and transmissibility of CA-MRSA. While presence of PVL toxin in MRSA is used as a criterion for reporting of CA-MRSA in Hong Kong, it has been shown that some of the CA-MRSA causing skin and soft tissue infection were PVL negative. [29]
6. Other than skin and soft tissue infections, PVL toxin is also associated with necrotising pneumonia, necrotising fasciitis and meningitis. CA-MRSA has also been reported to co-infect with influenza resulting in fulminant pneumonia. [31–33]

Figure 1.2: Number of CA-MRSA Reported to the CHP From 2007–2024



CA-MRSA has been notifiable since January 5, 2007.

1.4 Vancomycin-resistant Enterococci (VRE)

1. VRE were first reported in Europe in 1986. Since then, this resistant organism has spread throughout the world and has become a major nosocomial pathogen. Currently, *Enterococcus faecium* is the most important vancomycin-resistant species. In the United States and some European countries, vancomycin-resistant *Enterococcus faecium* (VREfm) has disseminated widely in the hospitals and old age homes. [34]
2. The first case of VREfm in Hong Kong was identified in 1997, involving a patient returning from the United States. From 1997 to 2008, VRE occurrences were sporadic, resulting in occasional small clusters (<5–10 cases) of nosocomial transmission. There has been no sustained transmission within our healthcare system. In the mid-2000s, two ad hoc studies revealed that VRE was carried by less than 0.1% of patients in high-risk areas. [35,36]
3. A prolonged outbreak of VREfm occurred in our public hospitals starting in 2011, but through the enforcement of directly observed patient hand hygiene and other infection control measures, the outbreak was successfully contained by 2015. During this period, a total of 4,060 new cases of VREfm were reported in local public hospitals. [37]
4. The resistance of enterococci to vancomycin is mediated by mobile genetic elements. The *vanA* gene is carried in transposon Tn1546, while *vanB* is encoded in Tn1547. These transposons are mobile and capable of spreading the resistant gene to other highly virulent organisms like *S. aureus*. Consequently, although VRE may have low pathogenicity, they can serve as a source of mobile resistance genes. [38]
5. Hospital outbreaks caused by VRE have been increasingly reported globally. Molecular epidemiology studies using multilocus sequence typing have revealed that this increase is linked to the dissemination of a specific genetic lineage of *Enterococcus faecium* known as clonal complex 17 (CC17). [38,39] Research indicates that CC17 has been circulating in U.S. hospitals since the early 1980s. [38] Currently, CC17 is the predominant clone associated with hospital outbreaks worldwide. [40–44] The prolonged VREfm outbreak in Hong Kong's public hospitals from 2011 to 2015 also involved strains belonging to the CC17 lineage. [37]

Table 1.5: Characteristics of Vancomycin-Resistant *Enterococcus faecium*, CC17

Characteristics of vancomycin-resistant *E. faecium*, CC17	
1.	Multidrug-resistant, including resistance to: a. Ampicillin b. Fluoroquinolones
2.	Contains a putative pathogenicity island and the *esp* gene which encodes for a protein involved in colonisation and biofilm formation
3.	An association with hospital outbreaks

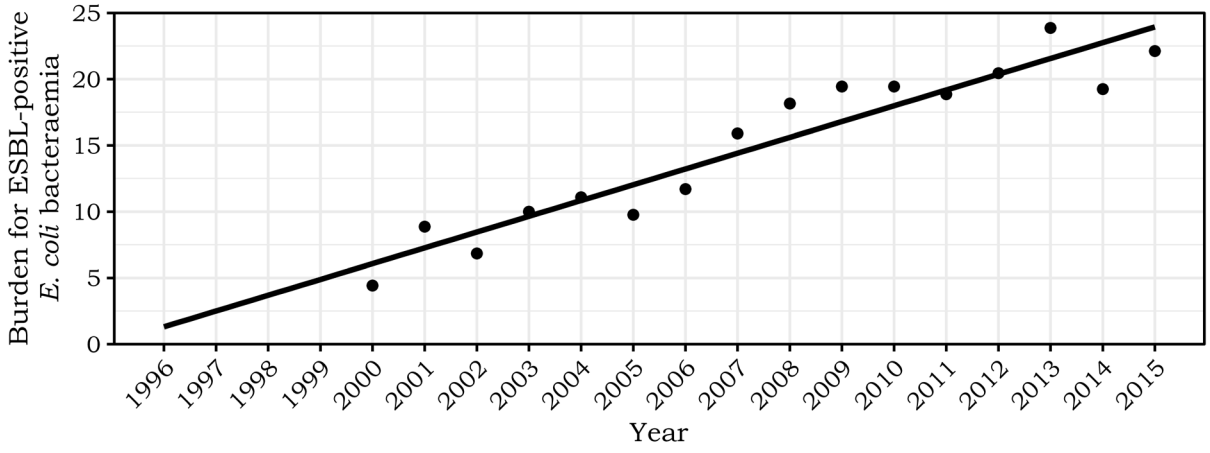
6. While the majority of CC17 VREfm isolates are typically susceptible to linezolid, resistance to this antibiotic can develop through the acquisition of *cfr* and *optr* genes, or mutations in the chromosomal 23S rRNA gene. [42,45]

1.5 Extended-spectrum β-lactamase producing Enterobacterales (ESBL-E)

1. ESBLs are enzymes capable of hydrolysing penicillin, first-, second- and third-generation (extended-spectrum) cephalosporins and aztreonam (except the cephamycins and carbapenems). Most ESBLs can be inhibited by β-lactamase inhibitors such as clavulanate and tazobactam (Table 1.6). [46] TEM, SHV and CTX-M are the three most common families of ESBLs seen worldwide.
2. In Hong Kong (Figure 1.3), >90% of strains with an ESBL phenotype produced CTX-M type enzymes. [47,48] There is a high rate of resistance towards non-β-lactam antibiotics, particularly fluoroquinolones, cotrimoxazole and aminoglycosides. [47,48] The high rate of resistance to non-β-lactam antibiotics therefore limits the choice for management of patients in outpatient setting.
3. ESBL-E has been considered to be a hospital pathogen in the past. However, community-onset infection has been described in different countries including Hong Kong in recent years. Most of the patients presented with lower urinary tract infection, other presentations include bacteraemia and intra-abdominal infection. [49–52]

4. In a local population-based study in 2017, ESBL-E was detected in 52.8% of stool samples in healthy individuals. [53] Food animals are a major reservoir of ESBL-producing *E. coli*. [54,55] Local surveillance data by the Centre for Health Protection revealed presence of ESBL-E in 77.8% of beef, 80.7% of pork and 99.7% of chicken. [56] It is also worth noting that ESBL-E is also commonly found in ready-to-eat (RTE) foods such as *siu mei*, *lo mei*, sashimi, sushi, RTE vegetables and cut fruits. [57]
5. In Hong Kong, the burden of ESBL-E is highest among the elderly population, especially those aged 75 years and above. [58]
6. For two decades, ESBL-E were considered to be clinically resistant to all cephalosporins. Accordingly, all laboratories are advised to edit the results for ceftazidime, ceftriaxone and cefepime to resistant, irrespective of the *in vitro* inhibition zone diameters or MIC values. [59]
7. Recently, the laboratory testing advisory bodies in the United States and Europe have revised their advice and argued that with the lowered cephalosporin breakpoints that both organisations now adopted, it is unnecessary to edit susceptibility categories if an ESBL is found. [60,61] A group of international experts in this field considered such advice is misguided. [59] Therefore, it is prudent to continue to test for the presence of ESBLs directly and to avoid cephalosporins as treatment.
8. In Hong Kong, if we apply the new ceftazidime breakpoint, three-quarters of the ESBL-producing isolates would be re-classified from resistant to susceptible to ceftazidime. [62] Caution with this approach is necessary whilst clinical data are limited. [59]

Figure 1.3: Burden for ESBL-Producing *Escherichia coli* Bacteraemia in a Regional Hospital in Hong Kong



Incidence density, number of episodes per 100,000 patient days was used as an indicator.
R^2 for fitted line = 0.89 ($p<0.001$)

Reference: [58]

Table 1.6: Characteristics of ESBL and AmpC β-Lactamases

	ESBL	AmpC β-lactamase
Bush-Jacoby-Medeiros functional class	2be	
Ambler molecular classification	A	C
Plasmid mediated	Almost always (responsible for the spread)	Most are chromosomal Plasmid increasingly reported
Inhibition by clavulanate, tazobactam, sulbactam*	Inhibited	Not inhibited
Cephamycins - cefoxitin - cefmetazole	Not hydrolysed	Hydrolysed
Oxyimino-β-lactams - cefotaxime - ceftriaxone - ceftazidime	Hydrolysed	Hydrolysed
Cefepime	Variable	Not hydrolysed
Carbapenem	Not hydrolysed	Not hydrolysed
Examples	TEM, SHV and CTX-M	*Enterobacter*, *Citrobacter* and *Serratia* possess inducible AmpC β-lactamase encoded in their chromosomes

*β-lactamase inhibitor

1.6 Carbapenem-resistant Enterobacterales (CRE)

1. Enterobacterales can acquire resistance to carbapenem through production of carbapenemase (Table 1.7), modification of outer membrane permeability and efflux pump. [63]
2. Carbapenemase, KPC-producing *K. pneumoniae* was first discovered from a clinical isolate through the Intensive Care Antimicrobial Resistance Epidemiology (ICARE) surveillance in North Carolina in 1996 [64,65] and followed by a substantial spread in New York, [66] Israel, [67] and Greece. [68] Enterobacterales producing KPC has also been described in South America (Colombia, Brazil and Argentina) [69–71] and China. [72,73] Other than *K. pneumoniae*, the KPC-enzyme has also been described in many other Enterobacterales species. [65] Infections caused by carbapenem-resistant organisms increases the risk of complications and mortality. [74]
3. New Delhi metallo-β-lactamase 1 (NDM-1) was first described in 2009 in a Swedish patient of Indian origin. He was hospitalised in India and acquired urinary tract infection caused by a carbapenem-resistant *K. pneumoniae*. [75] Like other metallo-β-lactamases, the enzyme NDM-1 can hydrolyse all β-lactams except aztreonam. Resistance to aztreonam is usually due to the coexisting ESBL or AmpC β-lactamase. Majority of the NDM-1-producing organisms harbour other resistance mechanisms, rendering them resistant to almost all classes of antibiotics with the possible exception of colistin. [76,77]
4. NDM-1-producing Enterobacterales has spread across Europe. In a survey conducted in 29 European countries, cases were reported in 13 countries. [76] Majority of the cases had a history of travel to the Indian subcontinent. Many countries have developed their own national guidelines to deal with the problem of NDM-1. [76]
5. The first NDM-1-producing *E. coli* in Hong Kong was isolated in October 2009 from a patient with urinary tract infection with travel history to India. [78] Several cases of IMP-4 were found in hospitalised patients since mid-2009 in Hong Kong. [79] The first KPC-2-producing *K. pneumoniae* was described in February 2011. [80]
6. The spread of NDM-1 is probably due to the huge selection pressure created by widespread non-prescription use of antibiotics in India [81] and involvement of promiscuous mobile elements in the gene's dissemination. [82]

7. A local review of the NDM detected from 2009–2014 was performed by the CHP. From 2009–2013, there was a gradual rise of NDM cases detected, ranging from 1 to 19 patients, but there were no local cases of NDM detected during this period. Twelve local cases of NDM were first detected in 2014, where four patients had signs of infection. Majority of the imported NDM cases were from China, followed by India and other South East Asian countries. [83]
8. A local study in 2016 investigated the clonality and mechanism of resistance of 92 strains of CRE isolated between 2010 and 2012. Only 10% were genotypic CPE confirmed by polymerase chain reaction (PCR). Porin loss combined with AmpC and/or CTX-M type ESBL was the major mechanism of resistance of the CRE isolated. [84]
9. Plasmid-mediated colistin resistance by *mcr-1*, a gene that can be transferred horizontally among bacteria has been first described in China in both food animals and human. [85] Hong Kong has also detected CPE with *mcr-1*. [86] The coexistence of MCR-1 with carbapenemase (e.g. NDM, KPC) has been described in China, [87–89] South America, [90] Singapore, [91] and Germany. [92]
10. A local study on epidemiology and risk of CPE carriage in hospital showed an increasing trend from 2011 to 2019, with NDM as the predominant enzyme produced. [93,94] There is a significant rise of number of CPE isolates sent to the Public Health Laboratory Services Branch (PHLSB) for confirmation, from 1,868 in 2019 to 9,896 in 2023, where NDM accounts for 76.4% of all CPE, consistent with previous published findings (Figure 1.4).
11. CPE has been found in various food items, both raw and ready-to-eat, leading to potential silent and widespread dissemination within the community. Based on local surveillance data from the Centre for Food Safety, the detection rates of ESBL-E and CPE in raw chicken, pork, and beef were 74.3% and 29.4%, 71.9% and 32.0%, and 61.8% and 9.6%, respectively. [95] In ready-to-eat foods such as vegetable salad, sashimi, cut fruits, *siu mei*, and *lo mei*, 9% tested positive for ESBL-E, while 0.3% tested positive for CPE. [96]

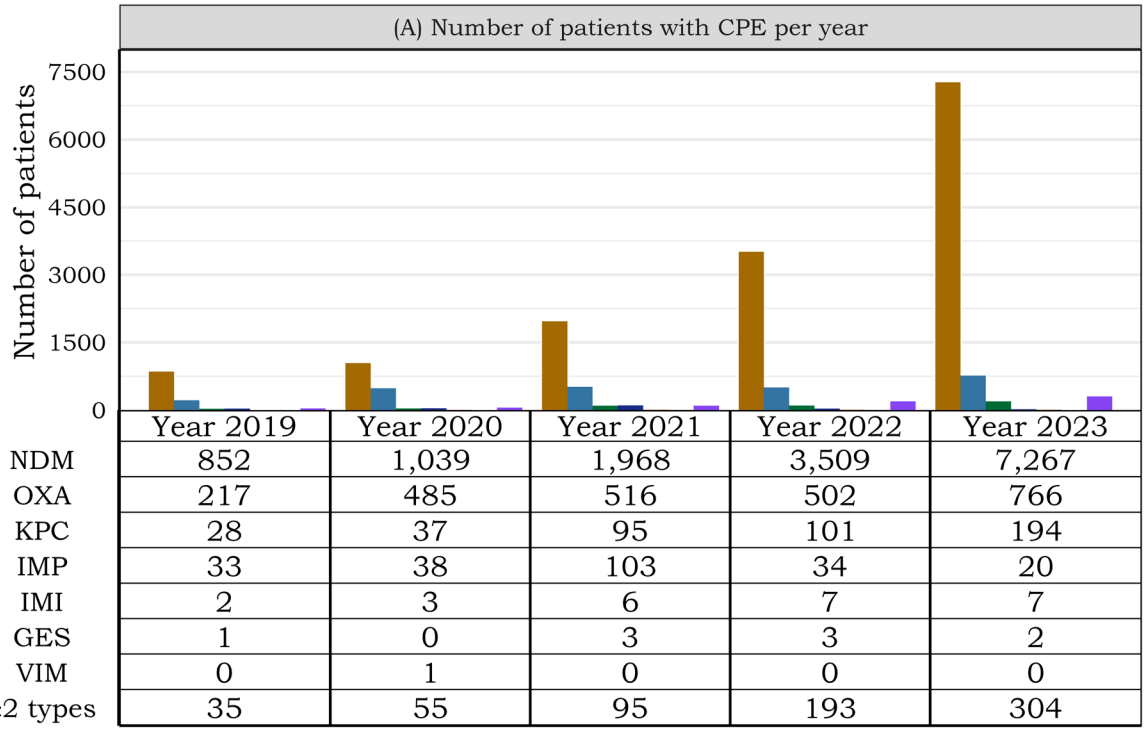
Table 1.7: Different Classes of Carbapenemase

	Class A	Metallo-β-lactamase	OXA carbapenemase
Molecular class	Class A	Class B	Class D
Functional class	2f	3	2d
Gene location	Usually transposon	Usually plasmid	Usually plasmid
Examples	KPC[1] GES SME IMI/NMC-A[1]	IMP[1] VIM[1] NDM[1]	OXA-23, 24, 51, 58 (types in *Acinetobacter* spp.)[2] OXA-48, 181, 232 (types in Enterobacterales)[1]
Found in	Enterobacterales	Non-fermenters and Enterobacterales	Non-fermenters and Enterobacterales
Inhibited by	Clavulanate and tazobactam	EDTA	No effective inhibitor
Active site	Serine	Zinc ion	Serine
Carbapenem	Hydrolysed	Hydrolysed	Hydrolysed
Aztreonam	Hydrolysed	Not hydrolysed	Not hydrolysed
Early β-lactam	Hydrolysed	Hydrolysed	Hydrolysed
Extended spectrum cephalosporin	Hydrolysed (except SME)	Hydrolysed	Hydrolysed poorly

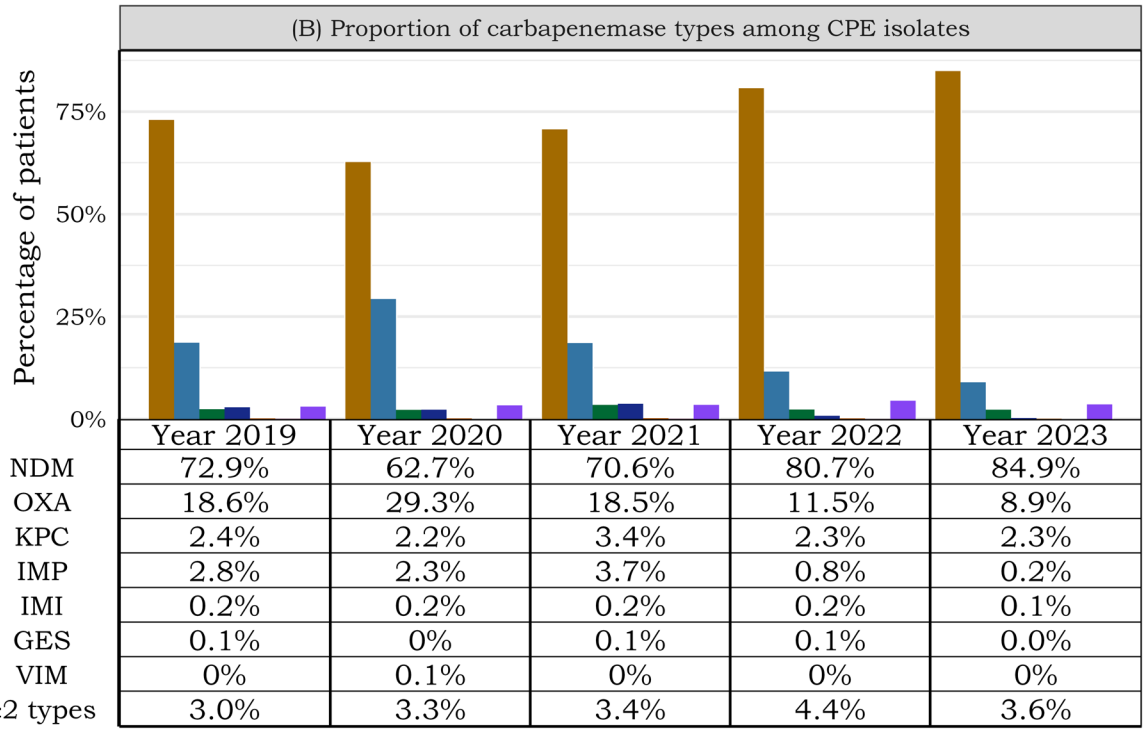
[1] Seen in Hong Kong

[2] Common in Hong Kong

Figure 1.4: Carbapenemase-Producing Enterobacterales (CPE) in Hong Kong, 2019 to 2023. (A) Number of Patients With CPE per Year, (B) Proportion of Carbapenemase Types Among CPE Isolates.



	Year 2019	Year 2020	Year 2021	Year 2022	Year 2023
NDM	852	1,039	1,968	3,509	7,267
OXA	217	485	516	502	766
KPC	28	37	95	101	194
IMP	33	38	103	34	20
IMI	2	3	6	7	7
GES	1	0	3	3	2
VIM	0	1	0	0	0
≥2 types	35	55	95	193	304



	Year 2019	Year 2020	Year 2021	Year 2022	Year 2023
NDM	72.9%	62.7%	70.6%	80.7%	84.9%
OXA	18.6%	29.3%	18.5%	11.5%	8.9%
KPC	2.4%	2.2%	3.4%	2.3%	2.3%
IMP	2.8%	2.3%	3.7%	0.8%	0.2%
IMI	0.2%	0.2%	0.2%	0.2%	0.1%
GES	0.1%	0%	0.1%	0.1%	0.0%
VIM	0%	0.1%	0%	0%	0%
≥2 types	3.0%	3.3%	3.4%	4.4%	3.6%

Note: Only *Escherichia coli* and *Klebsiella* spp. are included.

1.7 Carbapenem-resistant *Acinetobacter baumannii* (CRAB)

1. The term Multidrug-resistant *Acinetobacter baumannii* (MRAB) is commonly used but lacks a standardised and precise definition internationally. [92,97] Resistance to carbapenems, a crucial class of antimicrobials for treating *A. baumannii* infections, is considered a significant event. [98–100] To enhance clarity and comparability of surveillance data across different centres, it is recommended to use the term CRAB (carbapenem-resistant *Acinetobacter baumannii*). The global increase in resistant *A. baumannii* strains is primarily attributed to the spread of strains carrying the Class D OXA type β-lactamase. [101–104] Therefore, for surveillance purposes, CRAB more accurately reflects the current scenario compared to MRAB. In 2024, the World Health Organization designated CRAB as a critical priority pathogen based on specific criteria including virulence, resistance, limited treatment options, and high mortality rates. [105]
    - Carbapenem resistance in *A. baumannii* can arise from enzymatic degradation and efflux pumps. Nonetheless, the prevailing increase in resistant *A. baumannii* strains is primarily attributed to those producing the Class D OXA type β-lactamase. [104,106] Among these enzymes, OXA-23, OXA-24, and OXA-58 are the most prevalent carbapenemases produced by *A. baumannii*, playing a significant role in global carbapenem resistance within this pathogen. [107]
    - Metallo-β-lactamases belong to class B β-lactamases and feature at least one zinc ion within their active sites (refer to Table 1.7). These enzymes are highly effective carbapenemases, capable of hydrolysing all β-lactams except for the monobactam aztreonam. [107] However, metallo-β-lactamases are less frequently observed in *A. baumannii*. The presence of multiple resistance determinants often harboured on integrons contributes to CRAB's concurrent resistance to other antibiotic classes. [22]
    - A local survey conducted in 2010 on CRAB revealed that the majority of strains were attributed to the HKU1 and HKU2 clones. [99] OXA-23 was identified in all HKU1 isolates and was associated with a high level of carbapenem resistance. Additionally, OXA-51 was detected in both the HKU1 and HKU2 clones. The colonisation or infection of CRAB in chronic wounds was found to be linked, potentially serving as a reservoir for CRAB. This study underscored CRAB dissemination driven by two new clones. [101]

- Carbapenem resistance was found to have a significant impact on the mortality of *Acinetobacter* bacteraemia [108] which is mainly accounted by the higher rate of discordant antimicrobial therapy. *Acinetobacter* resistant to carbapenem was also found to have a higher rate of resistance to other classes of antimicrobial agents.
- The endemicity of CRAB is increasing in Hong Kong, with CRAB bacteraemia incidence rising from 0.27 per 100,000 patient-days in 2009 to 1.86 per 100,000 patient-days in 2013. The increase in the absolute number of CRAB bacteraemia better reflects the true burden to the healthcare system caused by CRAB. Risk factors include residing in an elderly home and recent use of carbapenems and β-lactam/β-lactamase inhibitor combinations within 90 days before admission. [109]
- In a recent study conducted within a 3,200-bed healthcare network, 17,760 faecal specimens from 9,469 patients were screened for CRAB over a 7-month period. The results indicated that 2.6% of patients were carriers of CRAB. Use of fluoroquinolones 6 months before admission was the only significant factor associated with high bacterial load in culture swabs. [110]
- An analysis of antibiogram data from private hospitals in Hong Kong revealed that the percentage of meropenem non-susceptibility among *Acinetobacter* ranged from 12% to 15% between 2014 and 2019. [111]

1.8 Macrolide-resistant *Mycoplasma pneumoniae* (MRMP)

1. The proportion of community-acquired bacterial pneumonias caused by *Mycoplasma pneumoniae* varies according to age, with school-age children and adolescents being the most common age groups affected, but this organism can cause infections in persons from infancy up through old age. [112,113]
2. MRMP was first reported in Japan in 2001. [114] Since then, there have been reports in China, [115–118] Taiwan, [118,119] Korea, [120] the United States of America, [120,121] and various European countries, including Scotland, [122] Spain, [123] and Germany. [124]

3. In China, MRMP prevalence is exceptionally high, accounting for over 90% of all *M. pneumoniae* detections, potentially due to selective testing of failure cases. [116] Hong Kong reported its first imported MRMP case in 2009, in an adult returning from Xi'an, [125] followed by its first locally acquired case in 2010. [126]
4. Two local studies have explored MRMP rates among hospitalised patients. The first study assessed various molecular methods for detecting genotypic resistance in *M. pneumoniae* in both adults and children. [127] Pyrosequencing detected the A2063G mutation in 79% of *M. pneumoniae* PCR-positive cases, whereas Sanger sequencing and melting curve analysis identified the mutation in less than 40% of cases. The difference is mainly due to the ability of pyrosequencing to identify low-frequency MRMP quasispecies. In a retrospective review of 48 children hospitalised for *Mycoplasma pneumoniae* infection from March 2010 to March 2013, MRMP accounted for 70% of *M. pneumoniae*-related community-acquired pneumonia cases. Doxycycline was significantly more effective than macrolide for treatment of MRMP-related community-acquired pneumonia in terms of achievement of rapid defervescence within 24 hours. [128]
5. The prevalence of *M. pneumoniae* infection fluctuates over time, with peak disease occurrences observed every 3 to 7 years. While detection rates vary by age groups (Figure 1.5, Figure 1.6), the prevalence of MRMP remains consistently high. [128,129]

Figure 1.5: Prevalence of *Mycoplasma pneumoniae* in Respiratory Specimens According to Patient Age Groups, All HA Hospitals, 2023

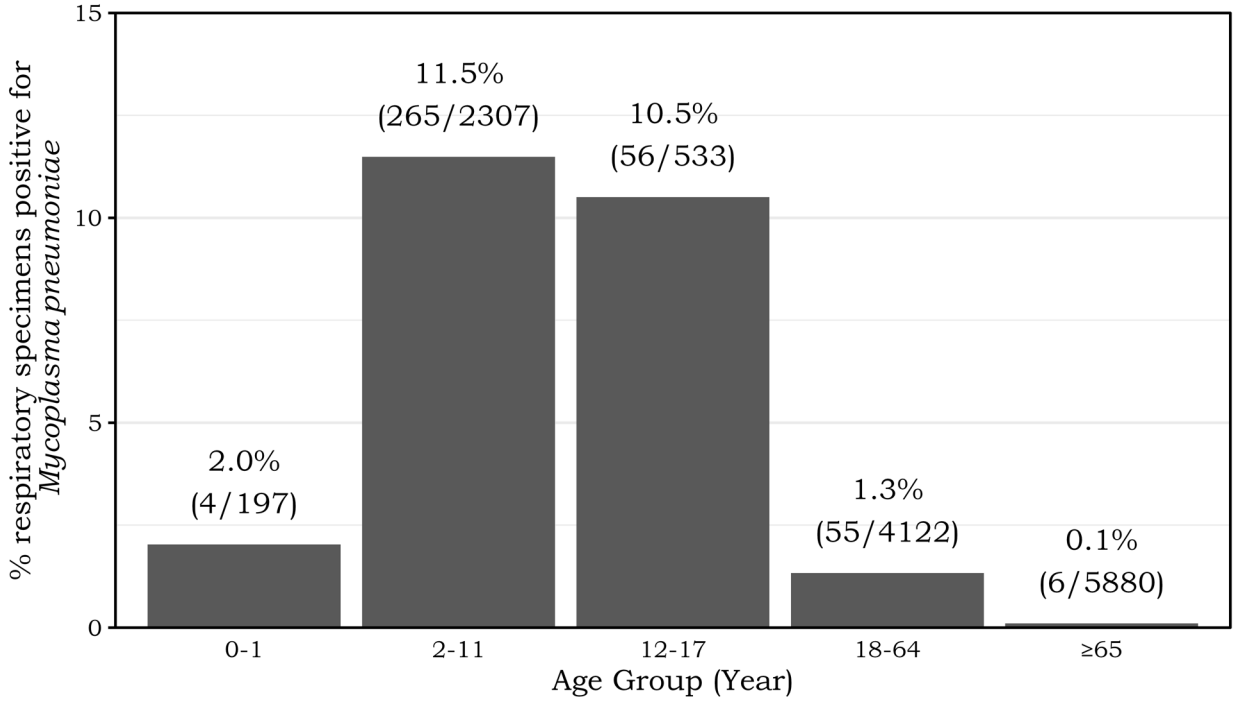
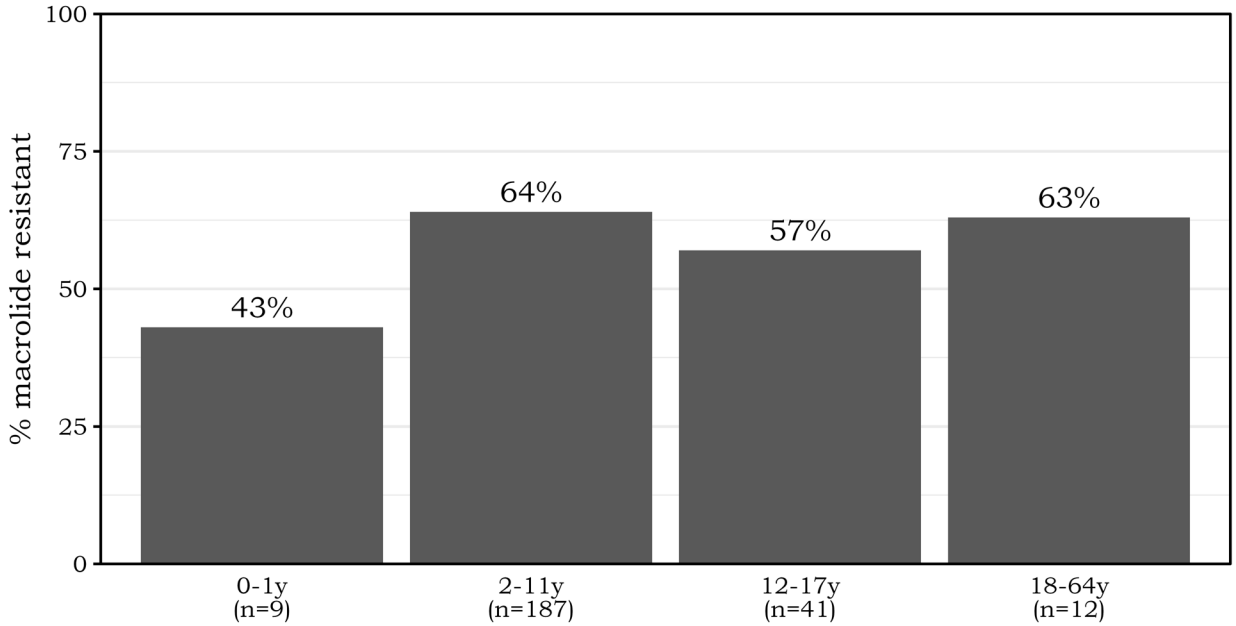
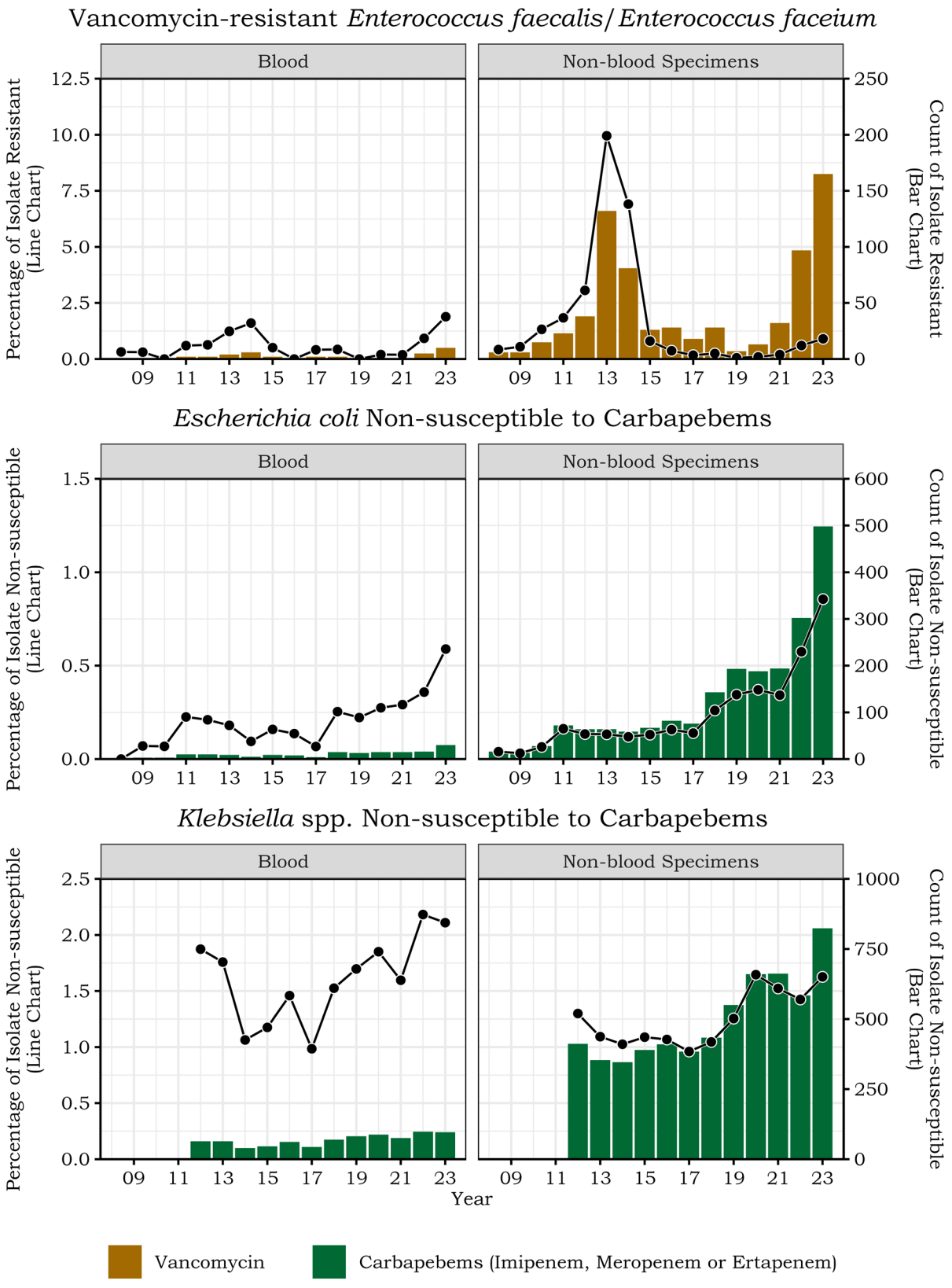


Figure 1.6: Prevalence of Macrolide Resistance Among *Mycoplasma pneumoniae*, QMH.



A total of 3349 respiratory specimens from December 2023 to June 2024 were tested and 249 specimens were positive for *Mycoplasma pneumoniae*. All samples (n=384) from elderly aged ≥65 years were negative for *Mycoplasma pneumoniae*. The proportions of macrolide resistance in the 249 positive samples from patients aged 0–64 years were analysed by molecular methods.

Figure 1.7: Resistance Trends of *Escherichia coli*, *Klebsiella* spp., and *Enterococcus* in Blood and Non-Blood Specimens (2008–2023)



Isolates were de-duplicated using the "first isolate per patient per calendar year" method.
Isolates from screening specimens were excluded.

Part II: Outpatient Parenteral Antimicrobial Therapy

1. The primary goals of the OPAT service are to allow patients to complete antimicrobial treatment safely, comfortably and effectively in the outpatient setting and to avoid inpatient-related inconveniences and complications. [130–132]
2. An OPAT team is a multidisciplinary team consisting of infectious disease (ID) specialists, nurses and pharmacists. Timely communication between nurses, pharmacists, ID specialists and patients is essential in OPAT program. [130–132]

Table 2.1: Roles of OPAT Team Members

Team Members	Roles
ID specialist	Establish clinical diagnosis Determine whether patient is fit for outpatient care Be responsible for clinical care decisions Determine whether OPAT is appropriate Select appropriate antimicrobials Order appropriate tests for monitoring Assess patient at follow-up visits Monitor for potential antimicrobial associated adverse events
ID Nurse	Assess patient and caregiver suitability for parenteral therapy at ambulatory setting Play a lead role in recommendation for the type of vascular access device and in the care of the infusion device Provide education on the care of vascular access device and catheter infusion site, information for common problems, side effects, precautions Assess patient at follow-up visits Monitor for antimicrobial adverse events and catheter related problems Coordinate patient care Ensure rapid and reliable communications about problems and for monitoring of therapy in place between members of OPAT team
ID/Clinical Pharmacist	Recommend on PK/PD and stability of antimicrobials Provide advice on potential drug-drug interactions
Patient and caregiver	Any person (include family members, friends, or caregivers like elderly home aides) with the ability and willingness to assist the transfer of patients between their home and the hospital Involved in planning of the OPAT service and follow-up arrangement

Table 2.2: Main Bundle Components of OPAT

Main Bundle Components	Key Aspects of Component
Patient Identification/ Selection	• Afebrile and stable vital signs
	• Infection should be reasonably stabilised and non-progressive
	• Not likely to abuse a vascular access system (e.g. injection drug user)
	• Fully aware of benefits and risks
	• Appropriate and adequate social support
	• Capable and responsible for the infusion, care of the vascular access device, and the care of the catheter infusion site, and be able to recognise and report new problems such as fever and rash.
	• Willingness to comply with follow-up plan
ID Consultation	• Establishment of clinical diagnosis
	• Selection of appropriate antimicrobials
Selection of Antimicrobials	Factors:
	• the definite or probable infecting organism
	• the pharmacodynamics and pharmacokinetic properties of antimicrobials and drug stability
	• patient's medical condition
Patient/family education	• Vascular access education/sterile technique/teach-back method
	• Emergency contact numbers for patients
	• Side effects of medication
	• Potential Complications
Care transition	• Clear communication between inpatient and outpatient services
	• ID/OPAT plan documented in discharge summary
	• Laboratory tests ordered as part of discharge plan
Outpatient monitoring	• Clinical response
	• Microbiological, laboratory and radiological monitoring
	• Addressing lab abnormalities
	• Vascular access care, and removal at the end of therapy
	• Medications adjustment as needed (choice, dose, duration)
	• Adverse effects of antimicrobial
	• Change in management if needed
	• Good communication between members of OPAT team

Main Bundle Components	Key Aspects of Component
Written policies and protocols	• Outline of responsibilities of OPAT team members
	• Outline of communications between patient and OPAT team
	• Outline of service arrangement during severe weather
	• Patient selection criteria
	• Patient education materials
OPAT program outcomes measures	• Patient satisfaction
	• Readmission rates
	• Clinical outcomes including any complications of disease and adverse effects of antimicrobials
	• Complications of vascular access
	• Program improvements

Part III: Guidelines for Selected Antimicrobial Use

3.1 Vancomycin

1. The first glycopeptide antibiotic against Gram-positive bacteria by inhibiting cell wall synthesis.
2. Vancomycin can be used to treat serious infections caused by β-lactam resistant Gram-positive bacteria, e.g. MRSA, coagulase-negative staphylococci.
3. When administered orally, it can be used for *Clostridioides difficile*-associated diarrhoea or colitis. [133]
4. Intravenous dosing for adult patients weighing 50 kg [134–136]
    - Loading dose: 1 g
    - **Infuse each dose over 2 hours** to minimise the risk of 'vancomycin infusion reaction' (formerly known as 'Red Man syndrome') [137,138]
    - Maintenance dose for adults weighing 50 kg with normal renal function:
        - 1 g every 12 hours administered as an intermittent infusion, assuming a vancomycin MIC of 1 microgram/mL or below
    - Maintenance dose for adults weighing 50 kg with renal impairment:
        - Based on creatinine clearance (CrCl) when it can be accurately measured or estimated (note: NOT applicable for functionally anephric patients, including patients requiring dialysis): [135,139]
            - CrCl >50–100 mL/min: 1 g every 12 hours
            - CrCl 20–49 mL/min: 1 g every 24–48 hours
            - CrCl <20 mL/min: 1 g every 4–5 days
        - Clinical circumstances can differ; please review frequently and adjust as needed. [140]
5. Vancomycin has a narrow therapeutic index with nephrotoxicity risk increases with serum trough level, particularly when exceeding 15 mg/L[1]. [141–150]

[1] The measurement unit mg/L (milligram per liter) is equivalent to microgram/mL (microgram per milliliter).

6. Therapeutic drug monitoring of vancomycin remains a subject of ongoing debate, with controversies surrounding the ideal target exposure and monitoring approach. [134,146,147,151–154]
7. Vancomycin dosing should be customised based on individual clinical circumstances. Key factors to consider include patient-specific factors, site and severity of infection, and vancomycin MIC of the target organism.
8. Adverse reactions (non-exhaustive)
    - Dose-dependent nephrotoxicity
    - Vancomycin infusion reaction
    - Drug fever
    - Neutropaenia and thrombocytopaenia
    - Drug reaction with eosinophilia and systemic symptoms (DRESS) [155]
9. If there is any uncertainty, please consult a clinical microbiologist or infectious disease physician for the use of vancomycin.

3.2 Linezolid

1. Linezolid is an oxazolidinone antibiotic, which inhibits bacterial protein synthesis by binding to a site on 23S ribosomal RNA of the 50S subunit.
2. It is active against antibiotic-resistant Gram-positive bacteria, such as MRSA, VRE, and some mycobacteria. It is not active against aerobic and facultative anaerobic Gram-negative bacteria. Multiple mechanisms of oxazolidinone resistance have been described. [156]
3. It can be used to treat pneumonia, skin and soft tissue infections caused by susceptible Gram-positive bacteria.
4. Dosing [157]
    - Adults with normal kidney function:
        - Nosocomial pneumonia, community-acquired pneumonia, complicated skin and soft tissue infections, vancomycin-resistant *Enterococcus faecium* infections: oral or intravenous, 600 mg every 12 hours
        - Uncomplicated skin and soft tissue infections: oral, 400 mg every 12 hours

- Renal impairment
  - No adjustment is recommended in the manufacturer's labelling. [157] However, caution and frequent monitoring of complete blood count are advised, and the duration of use should be limited whenever possible. Increased risk of thrombocytopaenia associated with linezolid use in patients with kidney impairment has been observed, with the odds increased up to six-fold in end-stage renal disease. [158–161] Some experts advocated standard dose reduction of 50% after 2 days of standard dosing in patients with estimated glomerular filtration of <60 mL/min/1.73m^2. [162]
- Hepatic impairment
  - No dosage adjustment in mild to moderate impairment (Child-Pugh class A or B); there are no dosage adjustment provided in the manufacturer's labelling for severe impairment. [157] However, linezolid concentrations may be increased in patients with cirrhosis leading to increased risk of thrombocytopaenia. [163,164]

5. Adverse reactions (non-exhaustive)
   - Myelosuppression including anaemia, leukopaenia, thrombocytopaenia or pancytopaenia
     - Linezolid-related thrombocytopaenia has been described as dose dependent and generally occurs after two weeks of treatment. [162]
     - Risk factors associated with thrombocytopaenia include renal insufficiency, liver dysfunction, and prolonged duration of therapy. [161,164,165]
   - Lactic acidosis [166]
   - Peripheral neuropathy [167]
   - Optic neuropathy (recovery of visual function may not be complete) [168]
   - Serotonin toxicity
     - Being a weak non-selective monoamine oxidase (MAO) inhibitor, the concomitant administration of linezolid and drugs that increase serotonin concentrations (e.g. fluoxetine, mirtazapine, tramadol) potentially causes the rare but life-threatening serotonin syndrome. [169–171]
   - Hypoglycaemia [172]
   - Hyponatraemia and/or syndrome of inappropriate antidiuretic hormone secretion (SIADH) [173]

6. Please consult a clinical microbiologist or infectious disease physician for the use of linezolid.

3.3 Daptomycin

1. Daptomycin is a lipopeptide antibiotic.
2. It is only active against Gram-positive bacteria with *in vitro* activity includes MSSA and MRSA, VRE, methicillin-resistant *Staphylococcus epidermidis*, *Streptococcus pyogenes* and other streptococci. [174,175]
3. It can be used to treat complicated skin and soft tissue infections (cSSTI), *S. aureus* bloodstream infections, including right-sided infective endocarditis. It should not be used to treat pneumonia since it is inactivated by lung surfactant. [176]
4. Microbiologic failure has been reported in patients with *S. aureus* bacteraemia with or without endocarditis and who received daptomycin monotherapy. [177]
5. The optimal dosage of daptomycin is being updated and should be tailored based on the infecting pathogen, MIC distribution, and type of infection. [178–180] Higher doses (8–12 mg/kg/day) have been used in serious infections like bacteraemia, endocarditis, and osteomyelitis. [19,181–187] Higher doses have been associated with increased rate of elevated serum creatine kinase. [180]
6. Dosing
    - Adults with creatinine clearance (CrCl) greater than or equal to 30 mL/min
        - cSSTI: 4 mg/kg once every 24 hours
        - *S. aureus* bacteraemia: 8–10 mg/kg once every 24 hours [19,181,187]
    - Adults with kidney impairment
        - Reduction in dosing is required in patients with CrCl <30 mL/min, including haemodialysis and continuous ambulatory peritoneal dialysis (CAPD). Please refer to drug package insert and/or drug information database for the latest recommendation.

- Adults with liver impairment
  - The pharmacokinetics of daptomycin in patients with severe hepatic impairment (Child-Pugh Class C) have not been evaluated. [188]

7. Adverse reactions (non-exhaustive)
   - Myopathy and rhabdomyolysis
     - Watch out for muscle pain, weakness
     - Monitor serum creatine kinase
     - More frequent monitoring when higher doses are used
     - HMG-CoA reductase inhibitors (i.e. statins, e.g. atorvastatin, rosuvastatin, and simvastatin) were associated with daptomycin-related myopathy and rhabdomyolysis in meta-analysis. [189] Consider temporarily suspending statin in patients receiving daptomycin. [189]
   - Eosinophilic pneumonia [190]
   - Immune thrombocytopaenia [191]
8. Please consult a clinical microbiologist or infectious disease physician for the use of daptomycin.

3.4 Tigecycline

1. Tigecycline is a tetracycline derivative and belongs to the antibiotic group glycylcycline. [192]
2. Its activity includes MRSA, VRE, *Escherichia coli*, *Klebsiella pneumoniae*, and rapidly growing, nontuberculous mycobacteria. [193]
3. *Morganella morganii*, *Proteus mirabilis*, *Proteus penneri*, *Proteus vulgaris*, *Providencia rettgeri*, *Providencia stuartii*, and *Pseudomonas aeruginosa* are intrinsically resistant to tigecycline. [194]
4. Tigecycline can be used to treat complicated skin and soft tissue infections, complicated intra-abdominal infections, and community-acquired bacterial pneumonia in adults.
5. Limitation of use
   - Warnings and reports have been published on the higher all-cause mortality observed in patients treated with tigecycline than comparator drugs. [195–198]

6. Dosing [135,199]
    - Standard dosing for adults
        - Initial dose of 100 mg followed by 50 mg every 12 hours, administered intravenously over approximately 30–60 minutes.
    - Hepatic impairment
        - Reduce maintenance dose (25 mg every 12 hours) for patients with severe liver impairment (Child-Pugh Class C).
7. Adverse reactions (non-exhaustive)
    - Nausea, vomiting, diarrhoea, headache
    - Increased alanine aminotransferase (ALT); Monitor liver function periodically.
    - Pancreatitis [200–203]
    - Coagulopathy and hypofibrinogenaemia; [204–207] Check coagulation parameters at baseline and during tigecycline therapy.
8. Please consult a clinical microbiologist or infectious disease physician for the use of tigecycline.

3.5 Polymyxin B and Colistin

1. Polymyxin B and colistin (polymyxin E) have resurged as salvage therapy for Gram-negative infections, most notably multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains of *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and Enterobacterales. [208–210]
2. *Burkholderia cepacia*, *Morganella* species, *Proteus* species, *Providencia* species, and *Serratia* species are intrinsically resistant to polymyxin B and colistin.
3. Plasmid-mediated mobile colistin resistance (*mcr*) gene family conferring resistance to polymyxin B and colistin has been described since 2016. The *mcr* genes are geographically widely distributed. [211]
4. Polymyxin B
    - Polymyxin B is preferred over colistin for routine systemic use in invasive infections, due to its superior pharmacokinetic (PK) characteristics in humans and decreased potential to cause nephrotoxicity. [210]

- Dosing [210,212]
  - Adults with normal renal function:
    - Loading dose: 20,000–25,000 units/kg, based on total body weight (equivalent to 2–2.5 mg/kg) over 1 hour [210]
    - Initial daily maintenance dose for patients with severe infections: 12,500–15,000 units/kg (equivalent to 1.25–1.5 mg/kg) every 12 hours, infused over 1 hour. [210]
  - There is limited data on dosing in obese patients. Consider adjusted body weight. For tailored dosing guidance, please consult a clinical microbiologist or infectious disease physician. [213–215]
  - No dosage adjustment for renal insufficiency. [135,210,212] While the manufacturer labelling for polymyxin B recommends dose reduction in patients with renal impairment, clinical data suggests that polymyxin B clearance is not significantly altered in kidney dysfunction. [212,216–218] Reducing the polymyxin B dose in patients with renal impairment may result in suboptimal drug exposure, treatment failure, or development of antibiotic resistance. [210,212,218–220]
- Adverse reactions (non-exhaustive)
  - Nephrotoxicity [212,221,222]
  - Neurotoxicity: neuromuscular blockade; circumoral paresthesias, extremity numbness, blurred vision, drowsy, irritable, ataxia; can manifest as respiratory arrest. [135,223]
  - Skin hyperpigmentation [224]

5. Colistin
   - Appears as colistin sulphate for oral and topical uses, and as colistimethate sodium for parenteral and inhalational uses.
   - Because of its renal clearance with presence of active colistin in the urinary tract, and less favourable PK characteristics for systemic infection, colistin is preferred for the treatment of lower urinary tract infections. [210]
   - Dosing
     - Adults with normal renal function:
       - Loading dose: I.V. ~9 million units, infused over 1 hour, and to administer the first maintenance dose 12–24 hours later. [210]

- Initial daily maintenance dose: I.V. ~4.5 million units, infused over 1 hour, at 12-hour intervals. [210]
- Monitor renal function and adjust the daily dose accordingly. [210]

- There is limited data on dosing in obese patients. Consider ideal body weight and avoid total body weight. For tailored dosing guidance, please consult a clinical microbiologist or infectious disease physician. [215,225–228]

- Adverse reactions (non-exhaustive)
  - Nephrotoxicity: In general, colistin is more nephrotoxic than polymyxin B. [218,229]
  - Neurotoxicity: Vertigo, facial circumoral paresthesias, abnormal vision, confusion, ataxia; neuromuscular blockade results in respiratory failure; may unmask myasthenia gravis. [135]
  - Pseudo-Bartter syndrome including metabolic alkalosis and electrolyte abnormalities. [230]

6. Please closely monitor renal function in patients receiving polymyxin B or colistin.
7. Wherever possible, concomitant nephrotoxic agents should be avoided in patients receiving polymyxin B or colistin. [210]
8. Please consult a clinical microbiologist or infectious disease physician for the use of polymyxin B or colistin.

3.6 Fosfomycin trometamol

1. A low-molecular-weight phosphoric acid derivative antibiotic which inhibits bacterial cell wall synthesis. [231]
2. *In vitro* activity against a variety of Gram-positive and Gram-negative bacteria, including *Escherichia coli* and *Staphylococcus aureus*. [232]
3. *Acinetobacter* species, *Burkholderia cepacia*, *Bacteroides* species, *Morganella morganii*, *Pseudomonas* species, *Stenotrophomonas maltophilia*, *Staphylococcus capitis*, and *Staphylococcus saprophyticus* are intrinsically resistant to fosfomycin. [232,233]

4. Oral fosfomycin trometamol (3 g in a single dose) can be a treatment choice for acute uncomplicated urinary tract infection in premenopausal, non-pregnant women with no known urological abnormalities or co-morbidities, although it appears to have inferior efficacy compared to other standard therapy. [234–237]
5. Adverse reactions (non-exhaustive)
    - Gastrointestinal upsets like diarrhoea are described as common side effects. [238,239]
6. For treatment of infections other than uncomplicated cystitis, please consult a clinical microbiologist or infectious disease physician regarding the use of fosfomycin.

3.7 Ceftaroline

1. Ceftaroline is an extended-spectrum cephalosporin with high affinity binding for penicillin-binding protein 2a (PBP2a) which accounts for its *in vitro* activity against MRSA. It is also active against *Streptococcus pneumoniae*. [240,241]
2. It is not active against ESBL-producing or AmpC-overexpressing Enterobacterales and has limited activity against non-fermenting Gram-negative bacilli such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. [240]
3. Ceftaroline can be used to treat acute bacterial skin and soft tissue infections and community-acquired bacterial pneumonia. [242–245] Retrospective studies reported ceftaroline use in MRSA-related bacteraemia, endocarditis, or pneumonia. [246,247]
4. Dosing
    - Adults with normal renal function:
        - 600 mg q12h or q8h, by intravenous infusion over 1 hour [135,248]
    - Dosage reduction is required in adult patients with creatinine clearance (CrCl) ≤50 mL/min and in end-stage renal disease including dialysis. [135]

5. Adverse reactions (non-exhaustive)
    - Nausea, diarrhoea [249,250]
    - Rash, phlebitis [250]
    - Headache, insomnia, [249,250] encephalopathy [251]
    - Elevated liver enzymes [249]
6. Please consult a clinical microbiologist or infectious disease physician for the use of ceftaroline.

3.8 Ceftazidime-avibactam

1. Avibactam is a non-β-lactam β-lactamase inhibitor that binds covalently and reversibly to β-lactamases. [252]
2. *In vitro* activity against Enterobacterales, including those producing ESBL, Ambler class C (e.g. AmpC), and some of the class D β-lactamases (e.g. OXA-48). [253,254]
3. Ceftazidime-avibactam can be used to treat *Klebsiella pneumoniae* carbapenemase (KPC)-producing bacteria. [255,256] In combination with aztreonam, it can be used to treat New Delhi metallo-β-lactamase (NDM)-producing bacteria. [256,257] However, caution is advised in these cases due to the potential for resistance. [258,259]
4. Clinical data on CRE are limited to observational, mostly retrospective, non-comparative studies. [254]
5. Ceftazidime-avibactam can be used to treat complicated intra-abdominal infections (in combination with metronidazole), complicated urinary tract infections, hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia, caused by susceptible Gram-negative microorganisms.
6. Dosing [135]
    - Adults with creatinine clearance (CrCl) >50 mL/min
        - Ceftazidime-avibactam 2.5 g (ceftazidime 2 g and avibactam 0.5 g), every 8 hours, infusion for 2 hours
    - Dose adjustment is needed in persons with CrCl ≤50 mL/min.
7. Please consult a clinical microbiologist or infectious disease physician for the use of ceftazidime-avibactam.

3.9 Ceftolozane-tazobactam

1. Ceftolozane is a cephalosporin with an enhanced affinity for the penicillin-binding proteins of *Pseudomonas aeruginosa*. [254]
2. Documented activity against many ESBL-producing Enterobacterales, and some multidrug resistant *P. aeruginosa*. [254]
3. It is not generally active against carbapenemase-producing Enterobacterales. [254,260]
4. Ceftolozane-tazobactam can be used to treat complicated intra-abdominal infections (cIAI) (in combination with metronidazole), complicated urinary tract infections (cUTI), hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP).
5. Dosing [135]
    - Adults with creatinine clearance (CrCl) >50 mL/min
        - Ceftolozane-tazobactam 1.5–3 g every 8 hours by intravenous infusion over 1 hour
    - Dose adjustment is needed in persons with CrCl ≤50 mL/min.
6. Please consult a clinical microbiologist or infectious disease physician for the use of ceftolozane-tazobactam.

3.10 Cefiderocol

1. Cefiderocol consists of a cephalosporin and a siderophore which binds iron, allowing it to enter bacteria through iron transporters. After entry, the cephalosporin detaches from iron and binds primarily to PBP3 and inhibits bacterial cell wall synthesis. [256,261]
2. It may be active against some Gram-negative bacteria. [262,263] It has no activity against Gram-positive and anaerobic bacteria. [264]
3. Cefiderocol can be used to treat urinary tract infections, hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia. [262]
4. Dosing
    - Adults with creatinine clearance (CrCl) 60–119 mL/min
        - 2 g every 8 hours, by intravenous infusion over 3 hours [135,265]
    - Dose reduction is needed in those adults with CrCl <60 mL/min. [265]
5. Please consult a clinical microbiologist or infectious disease physician for the use of cefiderocol.

3.11 Sulbactam-durlobactam

1. Sulbactam is a β-lactam with intrinsic activity against *Acinetobacter baumannii*, however, it is hydrolysed by various β-lactamases produced by the bacteria. [254]
2. Durlobactam is a β-lactamase inhibitor with activity against Ambler class A, C, and D β-lactamases. [254] It does not inhibit class B metallo-β-lactamases, for example, NDM. [256]
3. Sulbactam-durlobactam demonstrates *in vitro* activity against *A. baumannii*, including carbapenem-resistant isolates. [266–268] and the majority of CRAB resistant to colistin and cefiderocol. [269]
4. Dosing
    - Adults with creatinine clearance of 45–129 mL/min
        - Sulbactam-durlobactam (1 g of sulbactam, 1 g of durlobactam) every 6 hours by intravenous infusion over 3 hours [256,270]
    - Dosing adjustments are recommended for creatinine clearance (CrCl) <45 mL/min or CrCl greater than or equal to 130 mL/min. [270]
5. Concomitant administration of organic anion transporter 1 (OAT1) inhibitor (e.g. probenecid) is not recommended as co-administration may increase plasma concentrations of sulbactam. [270]
6. At the time of writing, sulbactam-durlobactam is not available in Hong Kong. Please consult a clinical microbiologist or infectious disease physician regarding the use of sulbactam-durlobactam.

3.12 Cefepime-taniborbactam

1. Taniborbactam is a boronic-acid-containing β-lactamase inhibitor that inhibits Ambler class A, C, D, and class B β-lactamases, including VIM, NDM, SPM-1, and GIM-1 [254] but not IMP-type metallo-β-lactamases. [271]
2. Cefepime-taniborbactam is an investigational β-lactam and β-lactamase inhibitor combination which has shown activity against Enterobacterales species and *Pseudomonas aeruginosa* expressing serine- and metallo-β-lactamases. [272]
3. At the time of writing, cefepime-taniborbactam is not available in Hong Kong. Please consult a clinical microbiologist or infectious disease physician regarding the use of cefepime-taniborbactam.

3.13 Once Daily Aminoglycosides

1. Once daily aminoglycoside is an effective and established method to achieve therapeutic efficacy while limiting the risk of toxicity and simplifying the processes of dosing and monitoring. [273]
2. Results from meta-analyses suggested that the β-lactam-aminoglycoside combination did not provide an advantage over β-lactams alone, while the former was associated with nephrotoxicity. [274,275]
3. With a few exceptions, in general, aminoglycosides should not be given for more than two days. [276,277]
4. The most prevalent side effects of aminoglycosides are nephrotoxicity and ototoxicity. Ototoxicity can influence both vestibular and auditory functions. [278]
5. Aminoglycosides were associated with neuromuscular blockade and may worsen myasthenia gravis. [279,280]
6. If there is any uncertainty, please consult a clinical microbiologist or infectious disease physician for the use of aminoglycosides.

3.14 Fluoroquinolones

1. Ciprofloxacin, levofloxacin, and moxifloxacin are some common examples of fluoroquinolones (FQs) for systemic use.
2. A number of health authorities have issued safety updates or warnings regarding the systemic use of FQs. [281–293]
3. The following is a non-exhaustive list of possible serious side effects that have been suggested to be associated with FQs:
    - Neuropsychiatric
        - Psychiatric reactions including depression, psychotic reactions which may potentially lead to suicidal thoughts and attempts. [293]
        - Central nervous system toxicity: gait disturbance, memory impairment, sleep disorders [290,292]
        - Peripheral neuropathy [288]
        - Pseudotumour cerebri [294]
        - Exacerbation of myasthenia gravis [295]
    - Cardiovascular
        - Aortic aneurysm or dissection [281,285,296,297]
        - Prolonged QT interval, arrhythmia or death [298,299]
    - Musculoskeletal
        - Tendinitis, tendon injury or tendon rupture especially in people older than 60 years, people on corticosteroid, people with renal impairment or solid-organ transplants. [290]
    - Blood glucose disturbances [285]
    - Drug-drug interactions
4. Clinicians should weigh risk and benefits when prescribing FQs:
    - For patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections, FQs should be reserved for those who do not have alternative treatment options. [283]
    - Consider past history, such as previous exposure and tolerance. Avoid FQs in patients who have previously had serious adverse reactions with a quinolone antibiotic (for example, nalidixic acid) or a FQ. [290]

- Patients should be advised to stop FQs at the first signs of a serious adverse reaction, e.g. tendinitis or tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling, peripheral neuropathy and central nervous system effects, and to contact their doctor immediately. [286,290,292]

3.15 Macrolides

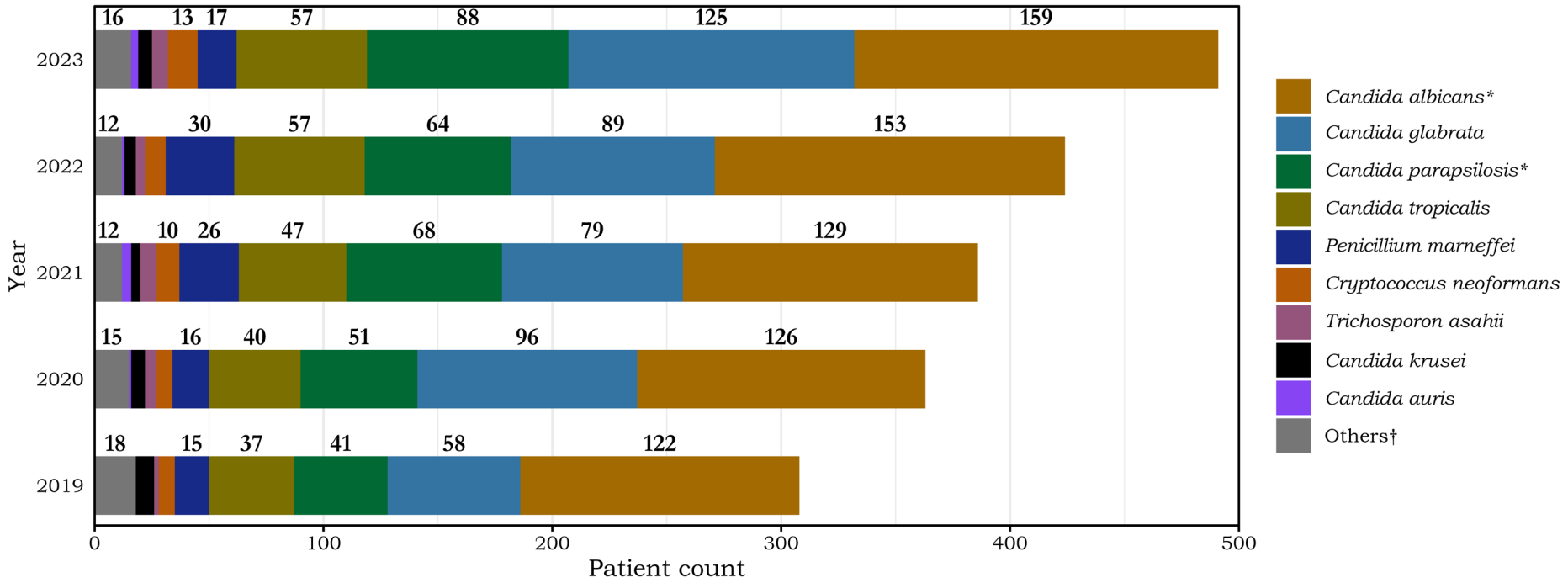
1. Erythromycin, clarithromycin, and azithromycin are some common examples of macrolides for systemic use.
2. A number of health authorities have provided updates or warnings regarding the use of macrolides, especially azithromycin [300–304]
3. The following is a non-exhaustive list of possible serious side effects that have been suggested to be associated with macrolides:
    - Ototoxicity including tinnitus [305,306]
    - Prolonged QT interval, arrhythmia or death [299,300,303,307,308]
        - A meta-analysis reported macrolide treatment is associated with an absolute risk increase of 118.1 additional sudden cardiac deaths or ventricular tachyarrhythmias, and 38.2 additional cardiovascular deaths per one million treatment courses. [309]
        - Macrolides should be avoided in patients with known QT interval prolongation or a history of ventricular arrhythmia; Caution should be exercised in patients with pre-existing cardiac conditions, e.g. coronary artery disease, severe cardiac insufficiency, conduction disturbances, or clinically relevant bradycardia. [301]
        - Carefully consider the benefits and risk before prescribing macrolides to patients taking drugs that can prolong QT interval. For example, co-administration of azithromycin with hydroxychloroquine in patients with rheumatoid arthritis has been associated with an increased risk of cardiovascular events and cardiovascular mortality. [302]
        - Consider screening electrocardiogram in high-risk patients, e.g. those with pre-existing cardiac conditions.
    - Drug-drug interactions

3.16 Antifungal Drugs

1. The taxonomy of pathogenic yeasts is undergoing changes, with several antifungal-resistant yeast species being reclassified into different genera. [310–312] To avoid confusion among clinicians, this document maintains the familiar genus *Candida* for these organisms. Figure 3.1 illustrates the distribution of fungal species associated with fungaemia in the Hospital Authority from 2019 to 2023.
2. Table 3.1 provides a summary of the mechanisms of action for the major antifungal classes. The antifungal spectrum varies significantly within and among classes of antifungal agents, along with different pharmacokinetic properties necessitating dosage adjustments for patients with kidney or liver impairment.
3. Fluconazole demonstrates activity against *Candida albicans* and some non-albicans *Candida*. However, certain strains, particularly *C. glabrata*, may exhibit higher MICs or resistance. *C. krusei* is considered intrinsically resistant to fluconazole. [313]
4. Echinocandins lacks activity or demonstrated limited activity against *Cryptococcus neoformans*, dematiaceous moulds, *Fusarium* species, *Trichosporon* species, *Zygomycetes*, and dimorphic fungi (*Blastomyces*, *Coccidioides*, *Histoplasma*) because these fungi do not have the target necessary for echinocandins to exert their effects.
5. Invasive candidiasis
    - To treat non-neutropenic adults with candidaemia, an echinocandin is the preferred initial antifungal while fluconazole is an acceptable alternative when they are not critically ill and who are considered unlikely to have a fluconazole-resistant *Candida* species. [313–315]
    - To treat neutropenic adults with candidaemia, an echinocandin is the preferred initial antifungal while lipid formulation amphotericin B is an effective but less attractive alternative due to toxicity concerns. [313–315]

6. Invasive aspergillosis
    - For invasive pulmonary aspergillosis, voriconazole is the preferred first-line treatment. [316–318]
    - For invasive aspergillosis in solid-organ transplant recipients, voriconazole is the preferred choice, while isavuconazole or lipid formulation amphotericin B as alternative agents. [319]
7. Please consult a clinical microbiologist or infectious disease physician for invasive fungal infections.

Figure 3.1: Species Distribution of Fungaemia Patients in the Hospital Authority (2019–2023)



Note:
Each fungal species was counted only once per patient. Only patient counts of ten or more were displayed.
* Both the specific species and its associated complex or group are included: *Candida albicans* complex (*Candida albicans*, *Candida dubliniensis*, and *Candida africana*), *Candida parapsilosis* complex (*Candida parapsilosis*, *Candida metapsilosis*, and *Candida orthopsilosis*).
† The following list of other fungi includes conventional names of fungi along with their corresponding new names within brackets, where applicable, that were isolated from blood in the years 2019–2023 under others (total = 73): *Blastobotrys* species (1); *Candida duobushaemulonii* (2); *Candida guilliermondii* (13); *Candida haemulonii* complex (3); *Candida lipolytica* (1); *Candida lusitaniae* [*Clavispora lusitaniae*] (12); *Candida nivariensis* [*Nakaseomyces nivariensis*] (1); *Candida* species (3); *Candida utilis* [*Cyberlindnera jadinii*] (1); *Cryptococcus gattii* (1); *Cryptococcus* species (4); *Exophiala dermatitidis* (1); *Fusarium solani* complex (2); *Fusarium* species (5); *Geotrichum* species (1); *Kluyveromyces marxianus* (3); *Lodderomyces elongisporus* (2); *Magnusiomyces* species (1); *Malassezia furfur* (1); *Meyerozyma* species (1); *Pichia ohmeri* [*Kodamaea ohmeri*] (6); *Rhodotorula rubra* (1); *Rhodotorula* species (1); *Saccharomyces cerevisiae* (1); *Saccharomyces* species (1); *Trichosporon mucoides* (1); and *Trichosporon* species (3).

Table 3.1: Summary of the Mechanisms of Selected Antifungals and Their General Spectrum of Activity

Organism[1,2]	Triazoles	Echinocandins	Amphotericin B	5-flucytosine
Mechanism of action	Inhibit fungal ergosterol synthesis	Inhibit fungal 1,3-beta-D-glucan synthase	Damages fungal cell membrane by binding to ergosterol	Inhibits fungal RNA and DNA synthesis
Yeasts				
Candida albicans	Susceptible	Susceptible	Susceptible	Susceptible
Candida auris	Variable	Variable	Variable	Variable
Candida glabrata	Variable	Susceptible	Susceptible	Susceptible
Candida krusei	Variable	Susceptible	Susceptible	Resistant
Candida parapsilosis	Susceptible	Variable	Susceptible	Susceptible
Candida tropicalis	Susceptible	Susceptible	Susceptible	Susceptible
Cryptococcus neoformans	Susceptible	Resistant	Susceptible	Susceptible
Trichosporon species	Variable	Resistant	Variable	Resistant
Mould				
Aspergillus fumigatus	Variable	Susceptible	Susceptible	Resistant
Fusarium species	Variable	Resistant	Variable	Resistant
Scedosporium species	Variable	Resistant	Resistant	Resistant
Mucorales	Variable	Resistant	Susceptible	Resistant
Dimorphic fungus				
Talaromyces marneffei	Variable	Resistant	Susceptible	Resistant

Footnotes:

1. The following fungi have been assigned new names: *Candida auris* as *Candidozyma auris*, *Candida glabrata* as *Nakaseomyces glabratus*, *Candida krusei* as *Pichia kudriavzevii*, *Candida lusitaniae* as *Clavispora lusitaniae*, *Penicillium marneffei* as *Talaromyces marneffei*. Tests routinely used in clinical laboratories may not be able to differentiate among members of the *Candida albicans* complex (*C. albicans*, *Candida dubliniensis*, and *Candida africana*), *Candida parapsilosis* complex (*Candida parapsilosis*, *Candida metapsilosis*, and *Candida orthopsilosis*).
2. The information provided serves as a general reference based on selected published articles in the literature. [135,314,320–333] Readers should keep in mind that antifungal resistance patterns can vary significantly within a group or genus of fungal pathogens, as well as across different geographical regions and clinical settings. Antifungal resistance can also emerge or evolve over time, making it essential to stay updated on current trends. When available, please refer to the antifungal susceptibility testing results. Beware that breakpoints may not be available for certain organisms. In the event of uncertainty, please consult a clinical microbiologist and infectious disease physician.

Part IV: Recommendation for the Empirical Therapy of Common Infections

4.1 Guidelines for empirical therapy

Musculoskeletal Infections

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Septic arthritis, adult [334–338]	*Staphylococcus aureus*; *Streptococcus agalactiae* (Group B *Streptococcus*); *Neisseria gonorrhoeae*; other streptococci	I.V. cefazolin 2 g q8h or (I.V. cloxacillin + ampicillin)	I.V. ceftriaxone (if *Neisseria gonorrhoeae* or Gram-negative organism is suspected, ceftriaxone is the preferred choice.)	•Urgent diagnostic tapping for Gram stain to guide therapy. •Factors suggest *N. gonorrhoeae* aetiology: sexually active teenager/adult ± rash •Consider Group B *Streptococcus* in patients with a history of handling raw freshwater fish. [339,340] •Consider vancomycin in patients with risk factors for MRSA infection (e.g. known carriers, elderly home residents). [341]
Osteomyelitis, adult [342,343]				•Occasionally *Salmonella* •Often vertebral •Intravenous drug user (IVDU): *Staphylococcus aureus* (vertebral); *Pseudomonas aeruginosa* (ribs, sternoclavicular joint). •Consider vancomycin in patients with risk factors for MRSA infection (e.g. known carriers, elderly home residents). [341]
Vertebral	*Staphylococcus aureus*, streptococci, *Escherichia coli*	I.V. ceftriaxone		

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Non-vertebral	*Staphylococcus aureus*	I.V. cefazolin or I.V. cloxacillin		
Diabetic foot infection [344–350]				
Previously untreated, no osteomyelitis	*Staphylococcus aureus*, β-haemolytic streptococci	I.V./P.O. amoxicillin-clavulanate	I.V./P.O. clindamycin or P.O. cephalexin	
Chronic, recurrent, limb threatening	Polymicrobial: aerobes + anaerobes	I.V./P.O. amoxicillin-clavulanate	If allergic to penicillins: I.V./P.O. levofloxacin/ ciprofloxacin + I.V./P.O. clindamycin For severe infections: piperacillin-tazobactam or meropenem	•Cultures from ulcers unreliable. •Early radical debridement to obtain tissue for culture; to exclude necrotising fasciitis and for cure. •A positive probe-to-bone test involves using a sterile, blunt, stainless instrument to palpate bone in infected pedal ulcers, strongly correlating with underlying osteomyelitis. It is confirmed when a rock-hard, gritty structure is felt at the ulcer base without intervening soft tissue during gentle probing. [351,352]

Skin and Soft Tissue Infections

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Erysipelas or cellulitis [353,354]	*Streptococcus pyogenes*, *Streptococcus agalactiae*, other streptococci, (± *Staphylococcus aureus*)	I.V./P.O. amoxicillin-clavulanate or I.V. cefazolin or P.O. cephalexin	If CA-MRSA concern: P.O. cotrimoxazole or P.O. linezolid or I.V. vancomycin (if severe infection).	•In Hong Kong, 50%–80% *Streptococcus pyogenes* are resistant to clindamycin. [355,356] •Consider CA-MRSA coverage in cases of purulent cellulitis if risk factors present, non-responsive to first-line treatment and/or severe infection (systemic signs of infection, hypotension). [30]
Necrotising fasciitis [353,357,358]				•Immediate radical surgical intervention essential. Urgent consult clinical microbiologist or infectious disease physician.
Following exposure to freshwater; seawater or seafood	*Aeromonas hydrophila*, *Aeromonas caviae*; *Vibrio vulnificus*	I.V. levofloxacin + I.V. amoxicillin-clavulanate		•*Aeromonas* spp., including *A. hydrophila* and *A. caviae* possess the chromosomal carbapenemase, CphA which could cause resistance to meropenem and many other beta-lactams.
Following cuts and abrasion; recent chickenpox; IVDU; healthy adults; following intra-abdominal; gynaecological or perineal surgery [360]	*Streptococcus pyogenes* Polymicrobial: Enterobacterales, streptococci, anaerobes	I.V. meropenem + I.V./P.O. linezolid		•Add high dose intravenous immunoglobulin (IVIG) (1 g/kg on day 1, followed by 0.5 g/kg on days 2 and 3) for streptococcal toxic shock syndrome. [359,361–363] •In Hong Kong, 50%–80% *Streptococcus pyogenes* are resistant to clindamycin. [355,356] •No clinical data exists on the benefit of clindamycin in clindamycin-resistant strains. *In vitro* and mice data are limited and contradictory. [364–367]

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Infection bite wound (animal or human) [353,354,368,369]	*Staphylococcus aureus*, streptococci, anaerobes, *Pasteurella multocida* (cats and dogs), *Capnocytophaga* spp. (dogs), *Eikenella* spp. (human)	I.V./P.O. amoxicillin-clavulanate	(P.O. penicillin V or P.O. ampicillin) + P.O. cloxacillin Penicillin allergy: P.O. fluoroquinolones + P.O. clindamycin	• Up to 18% of dog bites become infected; 28–80% of cat bites become infected. [370] • Monotherapy with penicillin, cloxacillin or first-generation cephalosporin inadequate. • Increasing prevalence of resistance in anaerobes; [371,372] • Consider adding metronidazole empirically if poor response to cover anaerobes resistant to β-lactams or β-lactam/β-lactamase inhibitor combinations. • Preemptive antimicrobial therapy for 3–5 days is recommended for patients who (a) are immunocompromised, (b) are asplenic, (c) have advanced liver disease, (d) have pre-existing or resultant edema of the affected area, (e) have moderate to severe injuries, especially to the hand or face, or (f) have injuries that may have penetrated the periosteum or joint capsule. [353]

Central Nervous System Infections

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Brain abscess [373–375]	Usually polymicrobial with aerobes and anaerobes	I.V. ceftriaxone + I.V. metronidazole	I.V. meropenem	•Urgent consult neurosurgery. •Exclude primary focus in middle ear, mastoid, paranasal sinuses, dental and lung. •Carbapenem use is associated with a small increased risk of seizures compared with non-carbapenem group of antibiotics. [376]
Meningitis [377–381]	*Streptococcus pneumoniae*, *Neisseria meningitidis*, *Streptococcus agalactiae*, *Streptococcus suis*, *Haemophilus influenzae*	I.V. ceftriaxone + I.V. vancomycin [382]	I.V. meropenem + I.V. vancomycin	•If impaired cellular immunity (e.g. high dose steroid) consider adding ampicillin to cover *Listeria* spp. [383] •Promptly review rapid test result (e.g. Gram stain, polymerase chain reaction) and streamline antibiotics accordingly. [384] •An adjuvant regimen of dexamethasone at 0.15 mg/kg I.V. q6h for 4 days is recommended to be administered either 15–20 min before the first dose of antibiotics or simultaneously with the first dose of antibiotics. [384,385] •In adults, adjunctive steroids have demonstrated a reduction in mortality and/or hearing loss specifically in cases of meningitis caused by *Streptococcus pneumoniae* or *Streptococcus suis*. The efficacy of steroids in meningitis caused by other bacteria and whether a 2-day course is as effective as a 4-day course, remains uncertain. [385–388]

Intra-abdominal and Gastrointestinal System Infections (Community-Acquired)

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Secondary peritonitis (perforated peptic ulcer, other bowel perforation, ruptured appendicitis, diverticulitis) [389–392]	Enterobacterales, *Bacteroides fragilis* group, other anaerobes, enterococci	I.V. amoxicillin-clavulanate or I.V. piperacillin-tazobactam	I.V. cefuroxime + I.V. metronidazole Severe infections (e.g. due to ruptured colon): I.V. meropenem + metronidazole	•Surgical intervention essential. •β-lactam/β-lactamase inhibitor combinations or meropenem usually can provide coverage against anaerobes. However, due to increasing prevalence of resistance in anaerobes to β-lactams and β-lactam/β-lactamase inhibitor combinations, consider adding metronidazole empirically in patients with severe infections or suboptimal response. [371,372,393]
Cholangitis, cholecystitis or other biliary sepsis [392,394]	Enterobacterales, enterococci, *Bacteroides fragilis* group	I.V. amoxicillin-clavulanate or I.V. piperacillin-tazobactam	I.V. cefuroxime + I.V. metronidazole Severe infections: I.V. meropenem + metronidazole	•Adequate biliary drainage essential. •Send bile for culture. •β-lactam/β-lactamase inhibitor combinations cover most Enterobacterales, enterococci and anaerobes.

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Liver abscess (community-acquired) [394–396]	*Klebsiella pneumoniae* and other Enterobacterales, *Bacteroides fragilis* group, enterococci, *Entamoeba histolytica*, *Streptococcus anginosus* group	I.V. ceftriaxone + I.V./P.O. metronidazole (for *Entamoeba histolytica*)	I.V. amoxicillin-clavulanate + I.V./P.O. metronidazole (for *Entamoeba histolytica*) Severe infections: I.V. meropenem + I.V./P.O. metronidazole (for *Entamoeba histolytica*)	•The detection of *Entamoeba histolytica* by PCR in liver pus/stool, and serological assay are valuable for diagnosing amoebic liver abscess. [397] •Image-guided or open drainage for large abscess. •For amoebic infection: high dose metronidazole for 10 days then followed by diloxanide. [398,399] •Ophthalmological assessment to rule out endophthalmitis if pus aspirate grew *Klebsiella pneumoniae*. Endogenous endophthalmitis in patients with *Klebsiella* liver abscess occurred in 3% to 10.4%, especially if diabetes mellitus. [400–407] •Ceftriaxone (meningitic dose) is the drug of choice for better central nervous system penetration if concomitant central nervous system involvement is likely to occur. Use of amoxicillin-clavulanate should be reserved for patients with drained abscess, clinical responding and without evidence of endophthalmitis.
Mild gastroenteritis	Mostly viral in origin; Food poisoning (*Bacillus cereus*, *Staphylococcus aureus*, *Clostridium perfringens*), *Salmonella*, *Escherichia coli*, *Campylobacter* spp., *Aeromonas* spp.	Routine antibiotic therapy not recommended.		•Fluid and electrolytes replacement.

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Moderate to severe gastroenteritis (presume bacterial) in persons with immunosuppressive disease [e.g. for human immunodeficiency virus (HIV) +ve; high dose steroid when laboratory results not available] [408–413]	*Campylobacter* spp., *Salmonella*, *Shigella* spp., *Vibrio* spp.	P.O. azithromycin	P.O. ciprofloxacin	•Fluoroquinolone resistance is very high in *Campylobacter* and is also on the rise in *Salmonella*. [414–416] •Consider *Clostridioides difficile* infection in patients recently treated with antibiotics (please refer to known-pathogen therapy Part V for *Clostridioides difficile* infection treatment). •Replace fluid and electrolytes; •Avoid antimotility agents, e.g. loperamide [Imodium], diphenoxylate/atropine [Lomotil]. [417,418]
Traveller's diarrhoea (Incidence 10–40% usually self-limiting) [408,413,419–423]	Enterotoxigenic *Escherichia coli* (ETEC) and Enteroaggregative *Escherichia coli* (EAEC), *Shigella* spp., *Salmonella*, *Campylobacter* spp., rarely *Aeromonas* spp., *Plesiomonas*	P.O. azithromycin	P.O. rifaximin (for non-invasive infections)	•Avoid antimotility agents, e.g. loperamide [Imodium], diphenoxylate/atropine [Lomotil], especially if fever or blood in stool. •Patients from South Asia: concern of *Salmonella* with resistance to ceftriaxone and fluoroquinolones. [424,425]

Cardiovascular Infections

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Subacute infective endocarditis (chronic rheumatic heart disease, degenerative or congenital valvular diseases) [426–432]	*S. viridans*, *S. gallolyticus* group, *Haemophilus* spp., *Aggregatibacter* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella* spp. (HACEK), Enterococci	I.V. ceftriaxone ± I.V. ampicillin		•The choice of empirical therapy should take into account the most likely pathogens. Obtain at least 3 sets of blood cultures, ideally by 3 different venepunctures and spaced over 30–60 minutes (put down 'suspected infective endocarditis' in test request); then start I.V. antibiotics as soon as possible. [433,434]
Acute infective endocarditis (intravenous drug users) [426–432]	*S. aureus*	I.V. cloxacillin 2 g q4h	I.V. cefazolin 2 g q8h	•Usually tricuspid valve infection ± metastatic lung abscesses. •Blood culture for 3 sets (label 'suspected infective endocarditis' in test request); then start I.V. antibiotics immediately. [433,434] •MRSA concern: Local prevalence of CA-MRSA is low and invasive infection is still rare. [28,435] •Consider adding empirical vancomycin if there are risk factors for MRSA infection, or if the patient is critically ill. •Consider adding empirical coverage for Gram-negative and fungal organisms, such as *Pseudomonas aeruginosa* and *Candida* spp. in critically ill patients. [436]

Gynaecological Infections

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Pelvic inflammatory disease (PID) (or upper genital tract infection) [437–440]	*Neisseria gonorrhoeae*, *Chlamydia trachomatis*, Enterobacterales, anaerobes	Inpatient: I.V. ceftriaxone 2 g q24h + P.O. doxycycline ± P.O. metronidazole or (I.V. amoxicillin-clavulanate + P.O. doxycycline)	Inpatient: I.V. clindamycin 600–900 mg q8h + I.V. gentamicin 3 mg/kg q24h × 1 to 2 doses; once stabilised, switch to oral clindamycin plus doxycycline for completion of therapy.	• Gentamicin is an alternative to ceftriaxone in gonococcal infections. [441,442] and can be considered in patients with severe β-lactam allergy. • Coverage of anaerobes important in tubo-ovarian abscess, co-existing bacterial vaginosis, HIV positive. [443] • The following regimen can be considered for outpatient therapy of mild-to-moderately severe acute PID: I.M. ceftriaxone 500 mg single dose + P.O. doxycycline ± P.O. metronidazole. [439] • Due to high prevalence of gonococcal resistance, P.O ceftibuten or fluoroquinolones not suitable for empirical treatment of acute PID. [443–445]
Breast abscess [446–448]	*Staphylococcus aureus* (± anaerobes in non-puerperal abscess)	I.V./P.O. amoxicillin-clavulanate	(I.V. cefazolin or P.O. cephalexin 1 g q.i.d.) (+P.O. metronidazole if anaerobes likely)	• Incision and drainage essential; send pus for Gram smear and culture.

Head and Neck Infections

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Odontogenic or neck infection [449–451]	Oral anaerobes	I.V./P.O. amoxicillin-clavulanate	(P.O. amoxicillin + P.O. metronidazole) or I.V./P.O. clindamycin	

Urinary Tract Infections

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Cystitis [234,452–454]	*Escherichia coli*; *Staphylococcus saprophyticus*, *Streptococcus agalactiae*	P.O. nitrofurantoin or P.O. amoxicillin-clavulanate		•Encourage fluid intake. •Nitrofurantoin should be used with caution in elderly patients; avoid in patients with creatinine clearance <30 mL/min. [455]
Acute pyelonephritis [234,452–454,456,457]	Enterobacterales, *Enterococcus*, (*Pseudomonas* in catheter-related, obstructive uropathy or transplant)	I.V. amoxicillin-clavulanate	(I.V. piperacillin-tazobactam if *P. aeruginosa* suspected) or (I.V. imipenem or I.V. meropenem if ESBL-producing organisms suspected)	•Blood culture and midstream urine (MSU) cultures, need to rule out obstructive uropathy. •I.V. until afebrile 24–48 h, then switch to oral drugs based on susceptibility for completion of therapy. •Carbapenem is recommended for severe or rapidly-deteriorating cases.

Respiratory Tract Infections

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
Acute bacterial exacerbation of chronic bronchitis (ABECB) - Appropriate use of antibiotics in ABECB is imperative to help control the emergence of multidrug resistant organisms. [458–462]	Respiratory viruses, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*	I.V./P.O. amoxicillin-clavulanate [total antibiotic duration of 5–7 days] [463,464]	I.V. ceftriaxone [I.V./P.O. fluoroquinolone may be considered for penicillin allergy, or suspected *Pseudomonas aeruginosa* infection] [total antibiotic duration of 5–7 days] [463,464]	• Antibiotics should be given to patients with: a) Following three cardinal symptoms: increased dyspnoea, increased sputum volume, increased sputum purulence; b) Increased sputum purulence and one other cardinal symptom; c) Requiring mechanical ventilation (invasive or non-invasive) • *Streptococcus pneumoniae* (MIC 1–2 microgram/mL) can be treated by high dose P.O. amoxicillin e.g. at least 1.5 g/day or I.V. penicillin G (high dose amoxicillin-clavulanate e.g. 1 g b.i.d. if co-infection by ampicillin-resistant *H. influenzae*). [459]
Acute bacterial exacerbation or pneumonia in patients with bronchiectasis [465–468]	*Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pneumoniae*	I.V. piperacillin-tazobactam	I.V. ceftazidime [Anti-pseudomonal fluoroquinolones may be used for treatment of susceptible *Pseudomonas aeruginosa*]	• For *Pseudomonas aeruginosa*, ciprofloxacin or levofloxacin should be given at high dose (e.g. P.O. 500 mg b.i.d. or 500–750 mg daily respectively).
Aspiration pneumonia [469,470]	Oral anaerobes: *Bacteroides*, Peptostreptococci, *Fusobacterium*, *Streptococcus milleri* group	I.V./P.O. amoxicillin-clavulanate	(I.V. ceftriaxone + P.O. metronidazole), I.V. ticarcillin-clavulanate or I.V. piperacillin-tazobactam	• Penicillin allergy: levofloxacin plus (clindamycin or metronidazole)

Community-Acquired Pneumonia (CAP)

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
CAP, not hospitalised [471,472]	*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Chlamydia psittaci* (influenza A, *M. tuberculosis*)	P.O. amoxicillin-clavulanate (e.g. 1 g b.i.d.) ± doxycycline or P.O. high dose amoxicillin (at least 1.5 g/day) ± doxycycline	P.O. levofloxacin	•Penicillin allergy: levofloxacin
CAP, hospitalised in general ward [471–476]	As above	I.V./P.O. amoxicillin-clavulanate ± P.O. doxycycline	I.V. ceftriaxone ± P.O. doxycycline	•Modifying factors: bronchiectasis: either (ticarcillin-clavulanate or piperacillin-tazobactam or cefepime) + a macrolide; or fluoroquinolone + an aminoglycoside •Low prevalence of *Mycoplasma pneumoniae* infections in patients aged above 65. •If empirical coverage of atypical pneumonia is necessary for patients aged above 65, consider replacing doxycycline with macrolides or quinolones. •Local prevalence of macrolide-resistant *Mycoplasma pneumoniae* (MRMP) is estimated to be >40%, hence doxycycline is the preferred atypical coverage for younger hospitalised patients in general wards. [113] •With concern for influenza: add oseltamivir 75 mg b.i.d.

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
CAP, hospitalised in ICU or serious pneumonia [471–477]	As above + *Legionella pneumophila* + Enterobacterales	I.V. piperacillin-tazobactam or ceftriaxone + a macrolide [doxycycline is preferred over macrolides for young patients at low risk of *Legionella* pneumonia, to cover macrolide-resistant *Mycoplasma pneumoniae* (MRMP).] [+P.O. oseltamivir 75 mg b.i.d. during influenza season]	I.V. cefepime + a macrolide (or P.O. doxycycline)	•Ticarcillin-clavulanate and ceftazidime are not useful against penicillin-non-susceptible *Streptococcus pneumoniae*. •With concern for CA-MRSA: (e.g. presence of Gram-positive cocci in cluster, history of recurrent boils/abscesses or skin infections or preceding 'flu-like' illness, severe disease), add I.V. linezolid 600 mg q12h (preferred) or I.V. vancomycin 1 g q12h.

Hospital-Acquired Pneumonia (HAP)

	Usual organisms	Preferred regimens	Alternatives	Special considerations/Remarks
HAP, onset <4 days after admission + no previous antibiotics [478–481]	*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*	I.V./P.O. amoxicillin-clavulanate	I.V. ceftriaxone	
HAP, onset ≥4 days after admission + had antibiotics recently, OR onset ≥5 days after admission OR mechanical ventilation [478–481]	MRSA, *Pseudomonas aeruginosa*, *Acinetobacter*, *Klebsiella* spp., *Enterobacter* spp.	I.V. piperacillin-tazobactam	I.V. cefepime or I.V. ceftazidime	•With ESBL-E concern: I.V. imipenem-cilastatin/meropenem •With MRSA concern: Add I.V. vancomycin

4.2 Management of Community-Acquired Pneumonia (CAP)

General Considerations and Principles

1. A number of guidelines on the management of CAP were released or updated recently. While these guidelines were drawn on the basis of the same set of literature, patient stratification and specific suggestions still vary. [472–475]
2. The implementation of rapid, multiplex PCR assays may enhance the management of severe community-acquired pneumonia when non-standard antibiotics are utilised. However, performing multiplex PCR on sputum specimens may result in a large number of false-positive results from the oropharyngeal flora. [475,482,483]
3. *S. pneumoniae* remains one of the most common pathogens identified in CAP [484–487] as stated in the guidelines. Hence, the choice of agents for empirical therapy should consider the regional data on prevalence and risk factors for drug-resistant *S. pneumoniae* (DRSP).
4. Factors to be considered in choosing empirical therapy for CAP:
    - Place of therapy (outpatient, inpatient ward, or ICU).
    - Role of atypical pathogens (e.g. *Chlamydia pneumoniae*, *Mycoplasma pneumoniae* and *Legionella* spp.) is increasingly being recognised. Coverage for atypical pathogens should always be given for hospitalised patients with moderate to severe disease, although it is considered optional for non-hospitalised patients with low-severity CAP. [472,473]
    - Presence of modifying factors including risk factors for DRSP (e.g. age >65 years, β-lactam therapy within past 3 months, alcoholism, multiple medical comorbidities, exposure to a child in a day care centre), enteric Gram-negatives (residence in a nursing home, underlying cardiopulmonary disease, multiple medical comorbidities, recent antibiotic therapy), and *P. aeruginosa* (e.g. bronchiectasis).
    - Emerging resistance patterns among the major pathogens. In Asia, including Hong Kong, high prevalence of macrolide resistance has been reported among *Mycoplasma pneumoniae* strains in recent years. [26,125,126,488–491]

- *Burkholderia pseudomallei* is endemic in Hong Kong. An increase in cases of Melioidosis may be expected during summer, when heavy rainfalls and tropical cyclones can expose the bacteria previously buried in soil to the ground surface. Airborne transmission was postulated to be involved in a local outbreak in 2022. [492–496]

5. Certain antibiotics active against *P. aeruginosa* including cefepime and piperacillin-tazobactam are generally active against DRSP. They can be used for patients having specific risk factors for *P. aeruginosa*.
6. For most patients, appropriately-chosen initial antibiotic therapy should not be changed in the first 72 hours, unless there is marked clinical deterioration.
7. Most patients with CAP will have an adequate clinical response within 72 hours. After the patient has met appropriate criteria, switch from I.V. to P.O. therapy can be made.

Management of Community-Acquired Pneumonia in the Era of Pneumococcal Resistance

1. Comparative studies of adults and children have reported that pneumonia due to penicillin-nonsusceptible pneumococci (most had MIC >0.1–1 microgram/mL) does not influence the outcome of pneumonia treatment. [497,498] At higher level of resistance (penicillin MIC 2–4 microgram/mL), recent evidence suggests that risk of mortality or suppurative complications were increased. [499,500] In one study, [501] the observed increase in mortality was confined to patients with pneumococcal isolates with penicillin MIC of ≥4 microgram/mL.
2. Since 2012, different breakpoints have been used for interpretation of penicillin susceptibility according to the site of infections and route of drug administration. [60,502]

Table 4.1: Interpretation of Penicillin Susceptibility for *Streptococcus pneumoniae*

Syndrome, route of administration and agent	Penicillin or amoxicillin MIC (microgram/mL)		
	Susceptible	Intermediate	Resistant
Meningitis, Parenteral penicillin	≤0.06	-	≥0.12
Non-meningitis, Parenteral penicillin	≤2	4	≥8
Non-meningitis, Oral (high dose) amoxicillin or amoxicillin-clavulanate	≤2	4	≥8
Oral penicillin V	≤0.06	0.12–1	≥2

3. By modifying the breakpoints, it is hoped that there will be decreased use of broad-spectrum antimicrobial therapy in favour of more narrow-spectrum therapy. Patients with pneumococcal pneumonia caused by strains with penicillin MIC ≤1 microgram/mL can be treated appropriately with optimal dosage of I.V. penicillin and several other P.O./I.V. β-lactams. Comparative anti-pneumococcal activities of commonly used β-lactams are shown in Table 4.2.
4. Vancomycin is not routinely indicated for treatment of CAP or for pneumonia caused by DRSP.
5. Newer fluoroquinolones are not recommended as first-line treatment of CAP. [503] The reasons are:
    - Most penicillin-nonsusceptible *S. pneumoniae* pneumonia can be appropriately treated with a β-lactam with good anti-pneumococcal activity at optimal dosage. [504,505]
    - Concerns that resistance among pneumococci will rapidly emerge after widespread use of this class of antibiotics.
    - Their activity against pneumococci with high level penicillin resistance (MIC ≥4 microgram/mL) makes it important that they be reserved for selected patients with CAP.

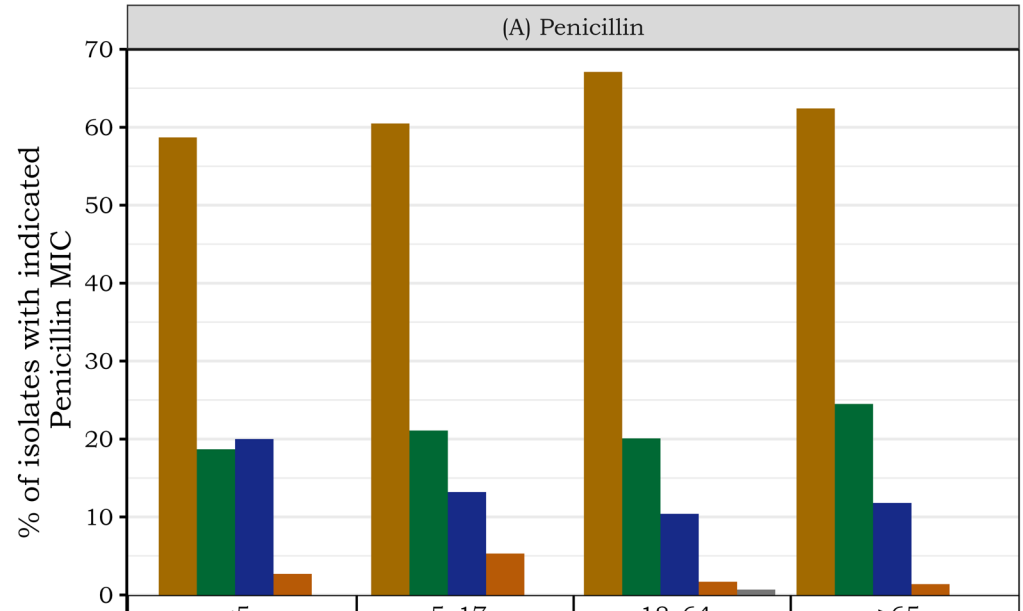
Table 4.2: Comparative Activities of Commonly Used β-Lactams Against *Streptococcus pneumoniae* With Different Levels of Penicillin Susceptibility

Agent	Penicillin MIC			
	≤0.06 microgram/ mL	0.12–1 microgram/ mL	2 microgram/ mL	≥4 microgram/ mL
Penicillin V	+++	+	–	–
Penicillin G	+++	+++	++	±
Ampicillin P.O.	+++	++	±	–
Ampicillin I.V.	+++	+++	++	±
Amoxicillin P.O.	+++	++	+	–
Piperacillin	+++	++	+	–
Ticarcillin	++	+	–	–
Cefotaxime	+++	+++	++	±
Ceftriaxone	+++	+++	++	±
Cefepime	+++	++	+	±
Cefuroxime I.V.	+++	++	+	–
Cefuroxime P.O.	+++	++	±	–
Cefpodoxime	+++	++	–	–
Ceftazidime	+++	+	–	–
Cefaclor	+++	–	–	–
Cefixime/ceftibuten	+++	–	–	–
Imipenem/meropenem	+++	+++	+	–

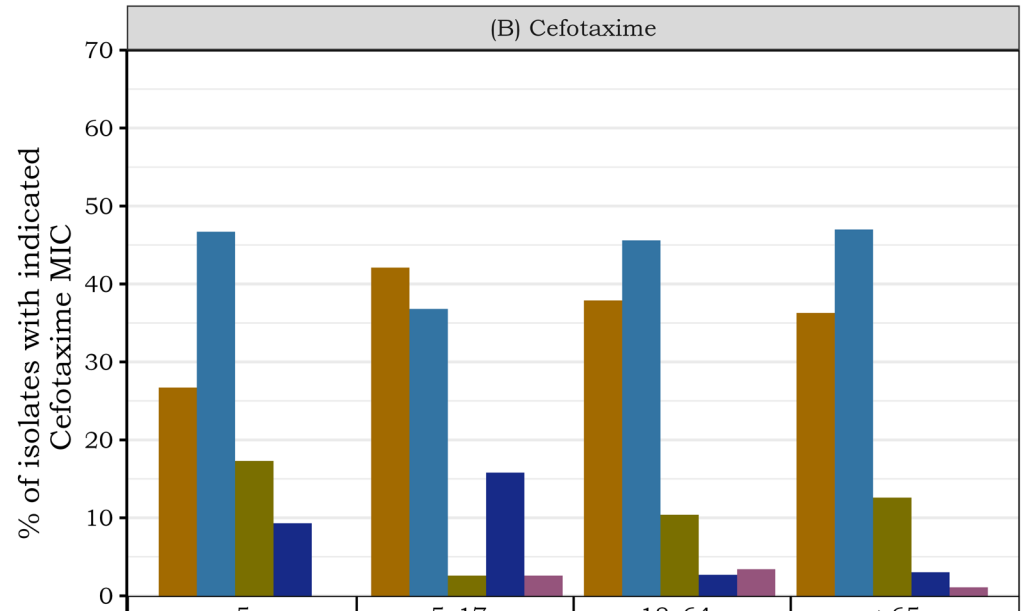
Regional Considerations for *Streptococcus pneumoniae*

1. In Hong Kong, reduced susceptibility to penicillin (Figure 4.1) and resistance to macrolides were high in both hospital [506–510] and community settings. [511–515] Recent evidence suggests an increase in carriage of certain serotypes (such as 15) after introduction of childhood vaccination by pneumococcal conjugate vaccine-13, [507,508,512] although the significance of this phenomenon remains uncertain at this stage. [5,6,506–514,516–519]
2. Erythromycin-resistant isolates are also resistant to the newer macrolides/azalides such as clarithromycin and azithromycin. [520] In 2012–2016, the age group-specific rates of macrolide resistance among 775 invasive pneumococcal isolates were as follows: 76% in <5 years, 92% in 5–17 years, 74% in 18–64 years and 75% in ≥65 years. Accordingly, macrolides should not be used as sole therapy for empirical treatment of presumed pneumococcal infection.
3. In Hong Kong, fluoroquinolone resistance (levofloxacin MIC ≥8 microgram/mL) is emerging among *S. pneumoniae*, especially among respiratory isolates from elderly patients with chronic lung diseases. [507] Other risk factors for fluoroquinolone-resistant *S. pneumoniae* include residence in old age home or nosocomial pneumococcal infections. [519,521]
4. Moreover, tuberculosis (TB) was reported to account for ~10% of CAP in the elderly. [522] Excess use of fluoroquinolones in CAP may lead to: (1) delay in diagnosis of TB; (2) increased fluoroquinolone resistance among *Mycobacterium tuberculosis*. [523–525]
5. Ciprofloxacin and ofloxacin should not be used to treat pneumococcal infection. Use of a suboptimal dose of levofloxacin (e.g. <500 mg daily or in divided dose), which has been shown to be associated with the emergence of fluoroquinolone-resistant *S. pneumoniae*, should be avoided. [477]
6. The following β-lactams are not recommended because of poor intrinsic activities against *S. pneumoniae*: penicillin V, all first-generation cephalosporins, cefaclor, cefixime, ceftibuten, and loracarbef. [503]
7. Penicillins combined with β-lactamase inhibitors (ampicillin-sulbactam, amoxicillin-clavulanate, piperacillin-tazobactam) offer no advantage over penicillin G or amoxicillin for the treatment of pure pneumococcal pneumonia, including penicillin-resistant strains because *S. pneumoniae* does not produce β-lactamase. The MIC of ampicillin, amoxicillin, piperacillin for most local strains were similar to that of penicillin. However, the MIC of ticarcillin is increased disproportionately among penicillin non-susceptible strains.

Figure 4.1: Susceptibility of Invasive Pneumococcal Isolates to Penicillin and Cefotaxime According to Patient Age Groups



	<5y	5–17y	18–64y	≥65y
≤0.06 microgram/mL	58.7%	60.5%	67.1%	62.4%
0.12–1 microgram/mL	18.7%	21.1%	20.1%	24.5%
2 microgram/mL	20.0%	13.2%	10.4%	11.8%
4 microgram/mL	2.7%	5.3%	1.7%	1.4%
8 microgram/mL	0.0%	0.0%	0.7%	0.0%



	<5y	5–17y	18–64y	≥65y
≤0.06 microgram/mL	26.7%	42.1%	37.9%	36.3%
0.12–0.5 microgram/mL	46.7%	36.8%	45.6%	47.0%
1 microgram/mL	17.3%	2.6%	10.4%	12.6%
2 microgram/mL	9.3%	15.8%	2.7%	3.0%
4–8 microgram/mL	0.0%	2.6%	3.4%	1.1%

Part V: Guidelines for Known-pathogen Therapy

	Drug Choice	Alternatives	Remarks
Acinetobacter baumannii-calcoaceticus complex (ACBC)	•I.V. ampicillin-sulbactam ± an aminoglycoside	•Fluoroquinolone ± an aminoglycoside (if allergic to penicillin)	•Sulbactam is highly active against ACBC. •For multidrug-resistant isolates: please consult a clinical microbiologist or infectious disease physician.
Clostridioides difficile	•Initial non-severe episode: P.O. vancomycin or P.O. metronidazole (preferred for patients at low risk of recurrence) [133,529] •First recurrence, non-severe: P.O. vancomycin	•Severe disease, ileus or toxic megacolon: I.V. metronidazole + P.O. vancomycin ± per rectum vancomycin + consult surgeon	•Multiple recurrences: please consult a clinical microbiologist or infectious disease physician regarding options, including vancomycin taper or faecal microbiota transplant. [530]
Enterobacter cloacae complex	•P.O. nitrofurantoin for uncomplicated/lower urinary tract infection •P.O./I.V. levofloxacin for complicated urinary tract infection •I.V. piperacillin-tazobactam for non-severe infection	•For severe infection, I.V. cefepime or I.V. carbapenem (for ESBL-producing strain)	•Cefepime is highly active *in vitro* against almost all *Enterobacter* isolates. •Emergence of AmpC derepressed mutants emerges in 20–40% of infections treated with the second- or third-generation cephalosporins. Use of these agents for serious infections is not recommended. •One study in Hong Kong found high prevalence of ESBL production among *Enterobacter hormaechei* (a member of the *E. cloacae* complex). [531] •Resistance rate in 2023: nitrofurantoin (22%), levofloxacin (8%) •For multidrug-resistant isolates: please consult a clinical microbiologist or infectious disease physician.

	Drug Choice	Alternatives	Remarks
Escherichia coli (ESBL-negative)	•(I.V./P.O. amoxicillin-clavulanate or I.V./P.O. cefuroxime) ± an aminoglycoside if rapid bactericidal action desirable on clinical grounds.	•P.O./I.V. fluoroquinolones (if allergic to penicillin)	
Haemophilus influenzae	•P.O. amoxicillin or P.O./I.V. amoxicillin-clavulanate or I.V. ceftriaxone	•P.O./I.V. fluoroquinolones (if allergic to penicillin)	•Amoxicillin-clavulanate also provides good coverage for *Moraxella catarrhalis* and *Streptococcus pneumoniae*.
Klebsiella pneumoniae (ESBL-negative)	•(I.V./P.O. amoxicillin-clavulanate or I.V./P.O. cefuroxime) ± an aminoglycoside if rapid bactericidal action desirable on clinical grounds.	•P.O./I.V. fluoroquinolones (if allergic to penicillin)	
Escherichia coli (ESBL-positive)	•P.O. nitrofurantoin or P.O. amoxicillin-clavulanate for uncomplicated/lower urinary tract infection •I.V. piperacillin-tazobactam for non-severe infection	•I.V. carbapenem for bacteraemia or other severe infection	•Carbapenem has been shown to be effective clinically and is currently the β-lactam agent of choice for serious infection by ESBL-positive *Escherichia coli*.

	Drug Choice	Alternatives	Remarks
K. pneumoniae (ESBL-positive)	•P.O. nitrofurantoin or P.O. amoxicillin-clavulanate for uncomplicated/lower urinary tract infection •I.V. piperacillin-tazobactam for non-severe infection	•I.V. carbapenem for bacteraemia or other severe infection	•Carbapenem has been shown to be effective clinically and is currently the β-lactam agent of choice for serious infection by ESBL-positive *Klebsiella pneumoniae*.
Pseudomonas aeruginosa	•(I.V. ceftazidime or I.V. cefepime or I.V. piperacillin-tazobactam) ± an aminoglycoside	•I.V./P.O. levofloxacin/ciprofloxacin ± an aminoglycoside (if allergic to penicillin)	•Meta-analysis demonstrated no difference in cure rate and mortality when treated with combination therapy. [532] •For multidrug-resistant isolates: please consult a clinical microbiologist or infectious disease physician.
Methicillin-sensitive *Staphylococcus aureus* (MSSA)	•P.O./I.V. cloxacillin or I.V. cefazolin or P.O. cephalexin	•I.V./P.O. amoxicillin-clavulanate •Clindamycin (if allergic to penicillin)	

	Drug Choice	Alternatives	Remarks
Methicillin-resistant *Staphylococcus aureus* (MRSA)	•I.V. vancomycin (bacteraemia or other invasive infections)	•I.V. ceftaroline or I.V./P.O. linezolid or I.V. daptomycin if (1) vancomycin allergy - extensive rash, other than vancomycin infusion reaction (red man syndrome) develops after vancomycin, or (2) bacteraemia caused by MRSA with vancomycin MIC ≥2 microgram/mL.	•Cotrimoxazole, fusidic acid or rifampicin are useful adjuncts for deep-seated infections (e.g. osteomyelitis) but these agents should not be administered as monotherapy. •Considerations in the choice of agent include site of infection, individual patient's circumstances such as underlying conditions and concurrent medications, risk of side effects and susceptibility profile. •Most abscesses or uncomplicated skin and soft tissue infections caused by CA-MRSA could be treated with drainage and oral antibiotics with *in vitro* activities (e.g. clindamycin or cotrimoxazole).* •Vancomycin intermediate *Staphylococcus aureus*/Vancomycin resistant *Staphylococcus aureus*: please consult a clinical microbiologist or infectious disease physician.
Mycoplasma pneumoniae	•P.O./I.V. doxycycline	•P.O./I.V. levofloxacin or moxifloxacin	•Doxycycline is recommended in view of high incidence of macrolide-resistant *Mycoplasma pneumoniae*. [533]

*For details, please refer to Figure 7.2.

	Drug Choice	Alternatives	Remarks
Stenotrophomonas maltophilia	•P.O./I.V. cotrimoxazole + I.V. ticarcillin-clavulanate	•P.O./I.V. cotrimoxazole + P.O./I.V. (fluoroquinolone or minocycline)	•Cotrimoxazole + ticarcillin-clavulanate is synergistic *in vitro*. Cotrimoxazole is a key component in therapy. [256,534] •Combination therapy recommended for synergy and to prevent resistance.
Streptococcus pneumoniae (for infection outside the central nervous system)	•Penicillin-sensitive (MIC ≤0.06 microgram/mL): I.V. penicillin G (4–8 million units/day, q6h)	•β-lactam/β-lactamase inhibitor combination with the exception of cefoperazone-sulbactam (for mixed infections).	•Most pneumococcal pneumonia can be treated with high dose amoxicillin or high dose amoxicillin-clavulanate.
	•Penicillin-intermediate (MIC 0.12–1 microgram/mL): I.V. penicillin G (high dose, 12–18 million units/day, q4h)*	•P.O./I.V. levofloxacin or P.O./I.V. moxifloxacin (if allergic to penicillin) for non-meningeal infections and penicillin-sensitive strains.	•For pure pneumococcal infection, penicillin G instead of amoxicillin-clavulanate is preferred, switch therefore recommended.
	•Penicillin-resistant (MIC ≥2 microgram/mL): I.V. ceftriaxone		•>70% resistant to erythromycin. Cross-resistance to clindamycin very common. •Resistance to erythromycin = resistance to other newer macrolides (clarithromycin, azithromycin).

*These Clinical and Laboratory Standards Institute (CLSI) breakpoints were decided mainly for the relevance on meningitis. For pneumococcal pneumonia, pharmacokinetic/dynamic data indicates that isolates with penicillin MIC of up to 1–2 microgram/mL should be considered 'sensitive' to appropriate dose of penicillin, ampicillin and amoxicillin.

	Drug Choice	Alternatives	Remarks
Streptococcus pneumoniae (for central nervous system infection)	•Penicillin-sensitive (MIC ≤0.06 microgram/mL): I.V. penicillin G (18–24 million units/day, q4h) or I.V. ampicillin 2 g q4h		•MIC (meningitis) breakpoints for penicillin and ceftriaxone to be used here.
	•Penicillin-resistant (MIC ≥0.12 microgram/mL) and third-generation cephalosporin MIC ≤0.5 microgram/mL: I.V. ceftriaxone 2 g q12h		•In *Streptococcus pneumoniae*, cross resistance between penicillin and ceftriaxone/cefotaxime is common. [507,517] Local data indicates that approximately half of the penicillin-resistant (meningitis) isolates are intermediate/resistant (meningitis) to cefotaxime.
	•Penicillin-resistant (MIC ≥0.12 microgram/mL) and third-generation cephalosporin MIC >0.5 microgram/mL: I.V. vancomycin plus I.V. ceftriaxone 2 g q12h		

Part VI: Guidelines for Surgical Prophylaxis

6.1 General Principles

Background

1. Surgical prophylaxis refers to the administration of antibiotics before surgery to prevent surgical site infections (SSIs). It is recommended for most clean-contaminated and specific clean procedures in which the consequence of infection is severe, such as those involving placement of prostheses or implants. [535]
2. Moreover, patient-specific factors may justify the use of antimicrobial prophylaxis in certain procedures where it might not typically be recommended. Risk factors that may warrant prophylaxis include extremes of age, obesity, diabetes mellitus, and immunosuppression. [536]
3. SSI is commonly classified into 'superficial incisional' (involving only skin and subcutaneous tissue of the incision), 'deep incisional' (involving deep soft tissues of the incision for example fascial and muscle layers), and 'organ-space' (involving any part of the body deeper than the fascial/muscle layers that is opened or manipulated during the operative procedure). [537]
4. The causative organisms of SSI are usually skin commensals or flora that are present at the bodily site of operation (for example, Gram-negative and anaerobic bowel flora for surgeries traversing the colon).
5. The choice, dosing and timing of antimicrobial agent are crucial for the effectiveness of surgical prophylaxis.
6. Surgical prophylaxis is not a replacement of proper infection control practices.
7. In cases of contaminated or infected wounds, such as traumatic or bite injuries, ruptured or suppurative viscus, postoperative antibiotic treatment is recommended instead of prophylaxis.

Choice of Antimicrobial Agent

1. The antimicrobial should target the anticipated pathogens and reach adequate concentration at the site of the incision.
2. Narrow-spectrum agents are preferred because they pose a lower risk of causing *Clostridioides difficile* infection and antimicrobial resistance. [538] Other important considerations include local resistance patterns, prior antibiotic use history, and instances of antibiotic-resistant infections.

Administration Timing

1. For many prophylactic antimicrobial agents, the initial dose should be administered within 30 minutes before incision, coinciding with the induction of anaesthesia, to achieve bactericidal serum and tissue concentrations at the time of the initial incision. This process can be facilitated by having the anaesthesiologist administer the drug in the operating room during induction. The antimicrobial agents should be infused completely prior to the incision. [539,540]
2. When administering surgical prophylaxis for drugs that requires prolonged infusion times (e.g. 2 hours for intravenous 1 g vancomycin, 60 minutes for intravenous 500 mg levofloxacin, 60 minutes for intravenous 400 mg ciprofloxacin), it is important to plan ahead to ensure that the medication is given within the appropriate timeframe before the surgical incision. [535,536]

MRSA

1. Screening and decolonisation is recommended for high-risk surgery such as cardiac, orthopaedic and neurosurgery involving implant. In general, mupirocin without proper screening is not advised as indiscriminate use can contribute to the development of resistance. [541,542]
2. Patients with a history of MRSA colonisation or a recent MRSA infection should receive surgical prophylaxis with MRSA coverage for high-risk surgeries. [535]

Dosing and Redosing Intervals

1. Redose prophylactic antimicrobial agent(s) for lengthy procedures (Table 6.1) and in cases with excessive blood loss during the procedure (i.e. >1500 mL). [535,543–546] For example, redose cefazolin after 4 hours in procedures >4 hours long.

Table 6.1: Dosing and Redosing Intervals for Surgical Prophylaxis

Antimicrobial	Standard I.V. Dose*	Half-life (Hour)*	Recommended Redosing Interval (Hour)
Cefazolin†	1–2 g	1–2	4
Cefuroxime	1.5 g	1–2	4
Clindamycin	600–900 mg	2–4	6
Amoxicillin-clavulanate	1.2 g	1	2
Metronidazole	500 mg	6–8	N/A‡
Vancomycin	1 g infused over 2 hours	4–8	N/A‡
Ceftriaxone	2 g	5–11	N/A‡
Gentamicin	3 mg/kg	2–3	N/A‡
Ciprofloxacin	400 mg infused over 60 min	3–7	N/A‡

*In patients with normal renal function.

†For patients allergic to cefazolin, vancomycin 1 g administered over a 2-hour infusion can serve as an alternative. It is important to note that the rapid intravenous administration of vancomycin may result in hypotension, which poses a particular risk during the induction of anaesthesia.

‡For antimicrobials with a short half-life (e.g. cefazolin) used before long procedures, redosing in the operating room is recommended at an interval of approximately two times the half-life of the agent in patients with normal renal function. Recommended redosing intervals marked as "not applicable" (N/A) are based on typical case length; for unusually long procedures, redosing may be needed.

Dosing in Obese Patients

1. The recommended dosages for cefazolin are as follows: 1 g for adult patients weighing ≤80 kg, 2 g for patients weighing 81–120 kg, and 3 g for patients weighing over 120 kg. [535,547,548]
2. Calculation of dosing for aminoglycosides in obese patients (i.e. actual body weight >20% above the ideal body weight) should be based on patient's adjusted body weight. [535,549]
3. Adjusted body weight = Ideal body weight + 0.4 × (Total body weight–Ideal body weight), where:
    - Ideal body weight (male) is 50 + 2.3 × (height in inches − 60)
    - Ideal body weight (female) is 45.5 + 2.3 × (height in inches − 60)

Patients with β-lactam Allergy

1. Self-reported β-lactam allergy has been linked to a higher risk of SSIs due to use of alternative, non-β-lactam and often inferior antibiotics. [550,551]

2. A β-lactam antibiotic can be used as prophylaxis after thorough consideration and discussion [Please refer to Part VII (Other Issues - Management of Antibiotic Allergy) for more information].

Patients on Antibiotic Treatment for Active Infection at the Time of Operation

1. If the antimicrobial agent used to treat the current infection is deemed appropriate for surgical prophylaxis, an extra dose should be administered within 30 minutes before the surgical incision.
2. If the current antimicrobial agent is insufficient for surgical prophylaxis, additional coverage according to guideline recommendations is required. In the event of uncertainty, please consult a clinical microbiologist or infectious disease physician.

Multi-drug Resistant Organisms Colonisation or Infection

1. Colonisation of multi-drug resistant organisms (MDRO) other than MRSA and consequent SSI caused by these pathogens are controversial issues. Whether prophylaxis should be expanded to cover for these pathogens depends on many factors, including the host, the MDRO and its antimicrobial susceptibility profile, the procedure and the proximity of the pathogen reservoir to the operative site.
2. Please consult a clinical microbiologist or infectious disease physician for the use of surgical prophylaxis. [535,552,553]

Duration of Antimicrobial Prophylaxis

1. There is no evidence to suggest that administering prophylactic antimicrobial agents after incisional closure reduces SSIs, even when drains are inserted during the procedure. [549,554–560] On the contrary, antibiotics given after closure can lead to increased antimicrobial resistance, superinfections by fungi and *Clostridioides difficile*, as well as side effects such as rash and acute kidney injury. [554,561]
2. A review by the WHO indicates that there is low to very low-quality evidence suggesting that a brief postoperative prophylaxis duration may offer some benefits in reducing SSIs in cardiac and jaw (orthognathic) surgery. However, RCTs in these procedures have not shown any advantage in extending prophylaxis beyond 24 hours. In vascular surgery, evidence from a single RCT suggests that extending prophylaxis until the removal of intravenous lines and tubes may be beneficial in reducing SSI. [554]

Recommendations for Surgical Antimicrobial Prophylaxis in Adults

Note: The recommended dosage of antimicrobial agents in the guidelines is tailored for adult patients with normal renal function. It is essential to carefully consider patients with renal impairment, those on renal replacement therapy, and those at risk of drug-drug interactions. In complicated cases, consultation with clinical microbiologists, infectious disease physicians, and clinical pharmacists is necessary.

Cardiac Surgery

Nature of Operation	Recommend Drugs	Remarks
Prosthetic valve Coronary artery bypass Pacemaker implant Open heart surgery	I.V. cefazolin 1 g then redose intraoperatively every 4 hours.	

Gastrointestinal Surgery

Nature of Operation	Recommend Drugs	Remarks
Upper gastrointestinal tract		
Gastroduodenal (high-risk) • Obstruction • Haemorrhage • Gastric ulcer • Malignancy • H_2 blocker • Proton pump inhibitor • Morbid obesity • Gastric bypass • Percutaneous endoscopic gastrostomy	I.V. cefuroxime 1.5 g or I.V. amoxicillin-clavulanate 1.2 g	
• Oesophageal operation with manipulation of pharynx	I.V. cefuroxime 1.5 g or I.V. cefazolin 1 g ± metronidazole 500 mg	

Nature of Operation	Recommend Drugs	Remarks
Hepatobiliary system		
Laparoscopic gall bladder surgery (high-risk) • Age more than 70 years • Acute cholecystitis/pancreatitis • Obstructive jaundice • Common bile duct stones • Morbid obesity • Intraoperative cholangiogram • Bile spillage • Pregnancy • Immunosuppression • Insertion of prosthetic devices • Laparoscopic converted to laparotomy	I.V. amoxicillin-clavulanate 1.2 g or I.V. cefuroxime 1.5 g + I.V. metronidazole 500 mg	
Endoscopic retrograde cholangiopancreatography (ERCP) [563,564]		
Biliary obstruction	P.O. ciprofloxacin 500–750 mg at 2 hours prior to procedure or I.V. piperacillin-tazobactam 4.5 g at 1 hour prior to procedure.	

Nature of Operation	Recommend Drugs	Remarks
Appendectomy	I.V. amoxicillin-clavulanate 1.2 g or I.V. cefuroxime 1.5 g + I.V. metronidazole 500 mg	
Hernia repair†		
• Non mesh hernia repair	Antimicrobial prophylaxis is not indicated.	
• Adult hernia mesh repair	I.V. cefazolin 1 g or I.V. cefuroxime 1.5 g	
Colorectal		
Most procedures require parenteral ± oral prophylaxis [565–568]	Parenteral I.V. amoxicillin-clavulanate 1.2 g or I.V. cefuroxime1.5 g + I.V. metronidazole 500 mg Oral P.O. neomycin and erythromycin base 1 g each tds the day before operation.	

†Amoxicillin-clavulanate may be used if the operation is such that anaerobic coverage is needed, such as in diabetic foot, hernia repair with bowel strangulation or incarcerated/strangulated hernia or mastectomy with implant or foreign body.

Genitourinary Surgery

Nature of Operation	Recommend Drugs	Remarks
Urological procedures • Significant bacteriuria • Transurethral resection of the prostate (TURP) • Transurethral resection of bladder tumour (TURBT) • Stone operations • Nephrectomy • Total cystectomy	Treat according to midstream urine culture results prior to elective procedures.	
Transperineal prostate biopsy (TPPB) [454,569–577]	Prophylaxis is not indicated in general.	Prophylaxis may be considered for immunocompromised patients.
Transrectal prostate biopsy (TRPB) [290,454,572–574,577–590]	Prophylaxis is indicated but no consensus could be reached by the Editorial Board on the choice of agent due to insufficient evidence.	

Gynaecologic and Obstetric Surgery

Nature of Operation	Recommend Drugs	Remarks
Hysterectomy (abdominal/vaginal/laparoscopic) [591–593]	I.V. cefazolin 1 g + I.V. metronidazole 500 mg or I.V. cefuroxime 1.5 g + I.V. metronidazole 500 mg or I.V. amoxicillin-clavulanate 1.2 g	
Caesarean section [594]		
All caesarean sections are indicated for prophylaxis. [595]	I.V. cefazolin 1 g or (When vaginal wound is present) I.V. cefuroxime 1.5 g + I.V. metronidazole 500 mg or I.V. amoxicillin-clavulanate 1.2 g	The initial dose of antimicrobial agents should be given before surgical incision instead of after clamping the umbilical cord. [596]
Operative Vaginal Delivery (delivery of fetal head assisted by vacuum extractors or forceps) [597–601]	I.V. amoxicillin-clavulanate 1.2 g	Give single dose as soon as possible after delivery.
Surgical abortion		Antimicrobial prophylaxis should be based on individual clinical condition and local epidemiology. [602,603]‡

‡ The optimal antibiotic and dosing regimens for abortion are unclear. The antimicrobial prophylaxis for abortion stated in Royal College of Obstetricians and Gynaecologists (United Kingdom) [562] clinical guidelines is Level C recommendations and may be suitable. They include: metronidazole 1 g rectally at the time of abortion plus doxycycline 100 mg orally b.i.d. for 7 days, commencing on the day of abortion; OR metronidazole 1 g rectally at the time of abortion plus azithromycin 1 g orally on the day of abortion.

Head and Neck Surgery

Nature of Operation	Recommend Drugs	Remarks
Thyroid and parathyroid glands		Antimicrobial prophylaxis is not indicated in general.
Oral-pharyngeal/ nasal • Maxillofacial • Rhinoplasty • Turbinate/ septoplasty	I.V. amoxicillin-clavulanate 1.2 g or (If *Pseudomonas aeruginosa* is suspected) I.V. amoxicillin-clavulanate 1.2 g + I.V. gentamicin 3 mg/kg or I.V. amoxicillin-clavulanate 1.2 g + I.V. ceftazidime 1–2 g	Antimicrobial prophylaxis is not indicated for tonsillectomy in general. [604–606]
Ear • Myringotomy • Tympanostomy tube insertion	Quinolone or Sofradex ear drop	

Neurosurgery

Nature of Operation	Recommend Drugs	Remarks
Craniotomy Ventriculoperitoneal shunt Implantation of intrathecal pump [607]	I.V. cefazolin 1 g or I.V. cefuroxime 1.5 g	
Re-exploration or microsurgery	I.V. cefuroxime 1.5 g or I.V. amoxicillin-clavulanate 1.2 g	

Orthopaedic Surgery

Nature of Operation	Recommend Drugs	Remarks
Total joint replacement with prosthesis Internal fixation of closed fractures	I.V. cefazolin 1 g or I.V. cefuroxime 1.5 g	Note: Antimicrobial agents should be completely infused before inflating the tourniquet if applied.
Open fractures	I.V. amoxicillin-clavulanate 1.2 g ± I.V. gentamicin 3 mg/kg or I.V. ceftriaxone 2 g ± I.V. penicillin G or other third generation cephalosporin ± I.V. penicillin G§	Prophylaxis indicated for all open fractures and should be given as soon as possible. Wound cultures and sensitivity testing are useful for informing subsequent choice of antimicrobials. [608–610] For Gustilo type III tibial fractures, prophylaxis given within 1 hour was associated with reduced infection risk. [611] Duration of antimicrobial prophylaxis for open fracture depends on the classification – 24 hours for Gustilo type I and II open fractures and up to 72 hours for Gustilo type III open fractures. Antibiotics should not be given for more than 24 hours after soft tissue coverage of the wound, whichever occurs first.

§ Choice of agent(s) depends on the type of open fractures by the Gustilo classification and the likely organisms contaminating the wound. In general, prophylactic antibiotic should be directed against Gram-positive organisms for Gustilo type I and II open fractures; additional Gram-negative coverage should be added for Gustilo type III open fractures. In the setting of faecal or potential clostridial contamination (e.g. soil exposure), a penicillin should be included in the regimen. [610,614]

Thoracic (Non-cardiac) Surgery

Nature of Operation	Recommend Drugs	Remarks
Pulmonary resection Closed tube thoracostomy for chest trauma	I.V. cefazolin 1 g or I.V. cefuroxime 1.5 g or I.V. amoxicillin-clavulanate 1.2 g	

Vascular Surgery

Nature of Operation	Recommend Drugs	Remarks
Abdominal aortic operations Prosthesis Groin incision Lower extremity amputation for ischaemia	I.V. cefazolin 1 g or I.V. cefuroxime 1.5 g or I.V. amoxicillin-clavulanate 1.2 g	

Breast Surgery

Nature of Operation	Recommend Drugs	Remarks
Breast cancer surgery [612]*	I.V. cefazolin 1 g or I.V. cefuroxime 1.5 g	

*Amoxicillin-clavulanate may be used if the operation is such that anaerobic coverage is needed, such as in diabetic foot, hernia repair with bowel strangulation or incarcerated/strangulated hernia or mastectomy with implant or foreign body.

Additional references on Recommendations for Surgical Antimicrobial Prophylaxis in Adults: [615–644]

Part VII: Other Issues

7.1 Management of Antibiotic Allergy

Background

1. Drug allergy (also known as hypersensitivity reactions) are adverse drug reactions (ADR) resulting from specific immune-mediated responses.
2. Most ADR are not allergy, but are often misdiagnosed and incorrectly labelled.
3. ~7% of the Hong Kong population have reported drug 'allergy' labels in their medical records, of which the majority are to antibiotics (with one-third to β-lactams). [645]
4. However, up to 85% of these β-lactam 'allergy' labels are found to be incorrect after allergist evaluation. [646]
5. This pattern is consistent with different populations, evidenced by inter-population comparisons. [647,648]
6. Most antibiotic and penicillin 'allergy' labels in Hong Kong are created during adulthood, frequently mistaken for other non-allergic adverse drug reactions. [649]
7. *In vivo* tests (such as skin prick tests (SPT), intradermal tests (IDT) and patch tests (PT)) can be helpful in assisting with diagnosis but must be evaluated in the context of the individual's clinical history. *In vivo* tests for certain antibiotics, e.g. piperacillin-tazobactam, have particularly poor predictive values and should be interpreted with caution. [650]
8. A major source of incorrect penicillin allergy mislabelling is due to inappropriate use (and interpretation) of penicillin skin tests still performed in Mainland China (>97% are false positive). [651]
9. *In vitro* tests, such as basophil activation tests, lymphocyte transformation tests, and enzyme-linked immunosorbent spot assays, are not routinely recommended and primarily performed within research institutes.
10. Mislabelled antibiotic allergy labels can lead to a myriad of adverse clinical outcomes: including increased morbidity and mortality, unnecessary use of second-line antibiotics, impaired health-related quality of life and development of MDRO. [652,653] It is, therefore, vital to correct mislabelled drug allergy labels and avoid unnecessary avoidance of mislabelled antibiotics.

11. Prevalence and potential harms of mislabelled antibiotic allergies are further exaggerated among particularly susceptible patient populations, including the elderly and immunocompromised. [654–656]

Assessment of patients with history of suspected antibiotic allergy

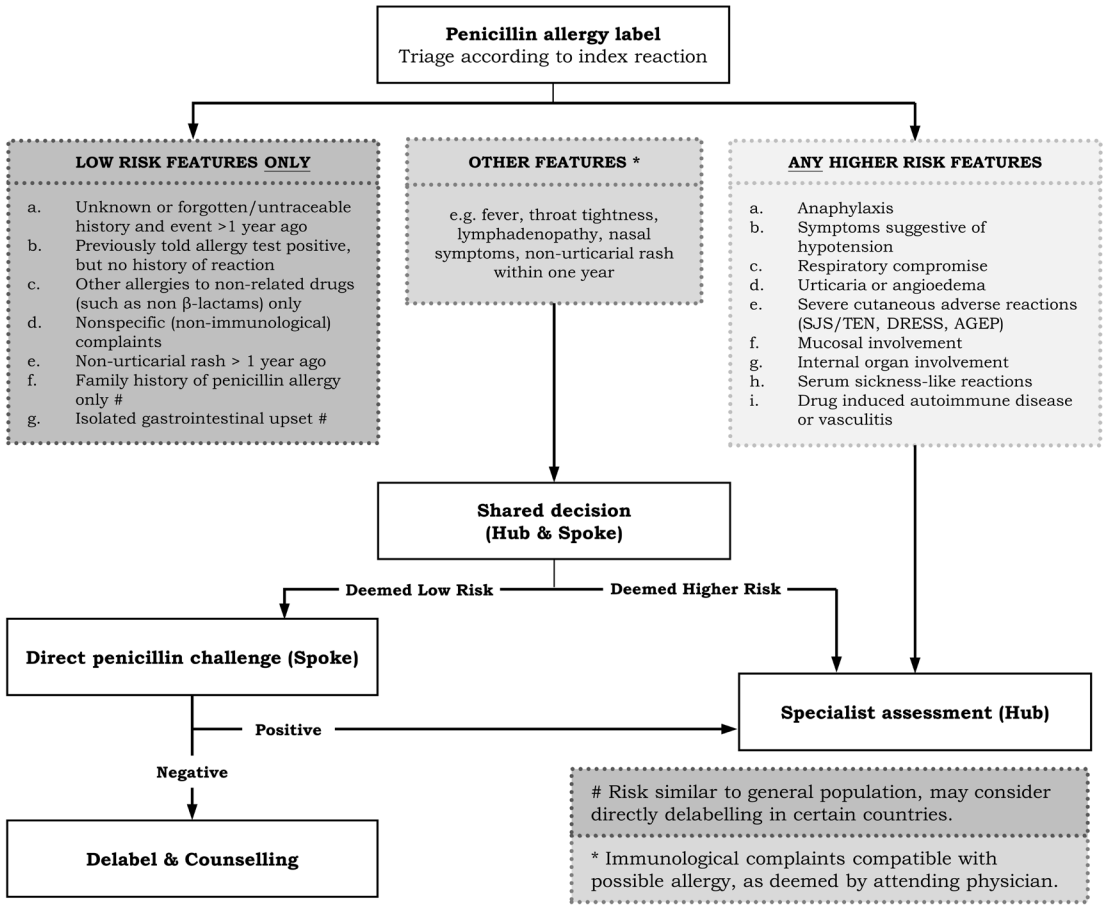
1. Although drug provocation test (DPT, also known as 'drug challenges') remains the gold standard, the most important diagnostic aid to antibiotic/drug allergy is the clinical history.
2. Many patients are mislabelled due to self-fear or incorrect concerns regarding suspected allergy: e.g. family history of allergy, non-immune mediated ADR (such as isolated gastrointestinal symptoms) or previously told skin testing positive (but no history of reaction).
3. A comprehensive history to ascertain all details pertaining the index reaction (i.e. the reaction which lead to the labelling of suspected antibiotic allergy) and subsequent reactions/tolerance of the same culprit drugs must be documented.
4. It is also useful to differentiate into immediate vs non-immediate/delayed (from clinical history) to guide subsequent investigations and management.
5. After history taking, the reaction should be stratified according to individual risk. For patients with suspected penicillin allergy, low- and high-risk features criteria used in the Asia Pacific are listed in Table 7.1. [657]
6. Most patients in Hong Kong with suspected penicillin allergy have 'low-risk' features only.
7. Low-risk patients are at low risk of genuine penicillin allergy and/or severe potential reactions.
8. For adult patients, the Hospital Authority currently employs a 'Hub-and-Spoke' approach [the Hong Kong Drug Allergy Delabelling Initiative (HK-DADI)]. HK-DADI currently accepts all referrals, from the public or private sectors, across the entire territory.
9. Designated 'Spoke' centres have been trained to perform allergy testing for patients with low-risk penicillin allergy (i.e. low-risk features only). The Hong Kong West Cluster ('Hub') provides advice, training and support for Spoke centres (Figure 7.1). [658]
10. All medical professionals (including clinicians, nurses, and pharmacists) need to be properly trained, and undergo periodic audits on practice, systems, and processes. Maintenance of competency through continuing medical education is also essential. [659]

11. If patients have low-risk features only, a direct DPT (without need for prior skin testing or *in vitro* test) may be considered at Spoke centres (Figure 7.1).
12. If patients have any high-risk features, then allergist review is necessary at the Hub.
13. If patients have other features (not specified as Low- or High-Risk), cases should be discussed with the Hub before proceeding.

Table 7.1: Low- and High-Risk Features During the Evaluation of Penicillin Allergy

Low-risk features	High-risk features
• Unknown or forgotten/untraceable history and event more than 1 year ago	• Anaphylaxis
• Previously told allergy test positive, but no history of reaction	• Symptoms suggestive of hypotension
• Other allergies to non-related drugs (such as non-β-lactams) only	• Respiratory compromise
• Non-specific (non-immunological) complaints	• Urticaria or angioedema
• Non-urticarial rash which occurred more than 1 year ago	• Severe cutaneous adverse reactions (Stevens-Johnson syndrome/toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalised exanthematous pustulosis)
• Family history of penicillin allergy only	• Mucosal involvement
• Isolated gastrointestinal upset	• Internal organ involvement
	• Serum sickness-like reactions
	• Drug-induced autoimmune disease or vasculitis

Figure 7.1: Summary of the Asia Pacific Clinical Pathway on Direct DPT for Penicillin Allergy



Drug provocation tests at Spoke centres

1. Negative DPTs can confidently rule out allergy and provide assurance in the process of delabelling.
2. Clinical assessments and DPT conducted by non-specialists have been demonstrated to be equally effective and safe for low-risk patients. [660,661]
3. Patients with the following conditions should not be evaluated for DPT at Spoke centres but instead have their evaluations deferred or be referred to the Hub:
   - Pregnancy;
   - Immunocompromised patient (or on systemic immunosuppression in the past 4 weeks);

- Unable to withhold medications potentially interfering with DPT (e.g. antihistamines, tricyclic antidepressants);
- Uncontrolled asthma, urticaria, or other diseases limiting the use of rescue medications.

4. DPT should be performed in an appropriate setting with resuscitation facilities readily accessible and under the supervision of trained personnel.
5. Medications potentially interfering with DPT (e.g. antihistamines) should be stopped for 7 days before DPT.
6. The index penicillin should be used for DPT (if known).
7. If the index penicillin is unknown, DPT should be performed with amoxicillin.
8. A graded approach to the maximum single dose (e.g. 3-step: 10%, 30%, 60%, or 2-step 10%, 90%) given at 30-minute intervals is recommended.
9. Patient should be observed at least 1 hour after the final dose of DPT, with clear instructions on what to do if symptoms develop after leaving.
10. An immediate-type hypersensitivity to the DPT agent is confidently excluded if there is no reaction after >1 hour after completion of DPT.
11. Patients should be contacted at least 72 hours later to ensure there were no non-immediate type manifestations.
12. A DPT is considered negative if there is no definite reaction after at least 72 hours after the completion of the DPT.
13. Patients with reported reactions after DPT should be called back for review at Spoke centres and treated, if and as necessary.
14. Patients with equivocal reactions can be offered repeat DPT or referred to the Hub.
15. Inaccurate penicillin allergy labels should be delabelled following a negative DPT with proper patient counselling and written documentation (such as a drug allergy notification letter).

Skin testing for suspected penicillin allergy

1. Skin testing should only be performed when there is clinical suspicion of possible drug allergy.
2. SPT and IDT (immediate reading) are useful for suspected immediate-type reactions.
3. PT and IDT (delayed reading) are useful for suspected non-immediate-type reactions.

4. If indicated, skin testing should be performed at least 8 weeks after (and as soon as possible) following history of suspected allergic reaction.
5. Antihistamines and tricyclic antidepressants should be withheld at least 1 week prior to skin testing.
6. Positive (histamine) and negative controls must be used for SPT and IDT.
7. Regarding drug dilutions and reagents for SPT and IDT:
    - SPT followed by IDT at the highest non-irritating concentration should be performed.
    - All SPT should be accompanied by a positive and negative control.
    - All IDT should be accompanied by a negative control.
    - SPT and IDT should be performed using recommended concentrations of benzylpenicilloyl-poly-L-lysine (5×10^{-5} mmol/L), minor determinant mixture (2×10^{-5} mmol/L), benzylpenicillin (10,000 units/mL), amoxicillin (20 mg/mL) and culprit drug (if known).
8. Regarding interpretation of SPT and IDT:
    - SPT is considered positive if a wheal size diameter at least 3 mm larger than negative control, with surrounding erythema.
    - IDT is considered positive if diameter of the wheal is at least 3 mm greater than the initial wheal, with surrounding erythema.
    - Delayed IDT readings at 48–72 hours may be considered if a non-immediate type reaction is suspected.
    - Patients with positive SPT or IDT results should be referred for specialist review.
9. PT can be performed by diluting the drugs with petrolatum or aqueous (10%), prepared and interpreted as per the International Contact Dermatitis Research Group.
10. Following skin testing, DPT is the gold standard for diagnosis and remains necessary to prove tolerance.
11. DPT should generally be performed when there is a low pre-test probability (and following negative skin testing, if performed) as described above.

Managing suspected allergic reactions to antibiotics

1. The first step in identifying allergic reactions is to classify them into immediate (Type I) or non-immediate (Type IV) types.
2. Type II (e.g. drug-induced cytopaenias, hepatitis, nephritis) and Type III (serum sickness, vasculitis, drug fever) reactions are much less common and not amenable to traditional drug allergy testing.

3. Immediate-type reactions are classically IgE-mediated, and typically occur within 1 hour if there has been prior exposure.
4. However, immediate-type reactions can also occur after several days if it is during the first treatment course.
5. Manifestations of immediate-type reactions are typically related to mast-cell degranulation, including urticaria (hives and/or angioedema), bronchospasm, abdominal pain, diarrhoea or anaphylactic shock.
6. Immediate-type reactions should be treated initially according to the local anaphylaxis protocols, and if there are any signs of systemic involvement, intramuscular adrenaline should be administered as soon as possible. Anti-histamines and systemic corticosteroids only serve as an adjunct. After the patient has stabilised, serum should be collected and saved for acute tryptase levels. The sample can be stored as clotted blood at 4°C, and an acute sample should be saved preferably at 30 minutes to 4 hours after the event. In addition, a baseline sample should be taken after >24 hours following the event.
7. If a patient has a confirmed immediate-type hypersensitivity, desensitisation may be an option, but only after consultation with an allergist and if there are no alternative medications available.
8. Non-immediate (delayed)-type reactions are classically T-cell-mediated, and typically occur >1 hour (up to days/weeks) administration and lesions can usually last for days to weeks.
9. Cutaneous manifestations are not urticarial in nature, and can include maculopapular or morbilliform rashes, erythema multiforme, fixed drug eruptions, contact dermatitis.
10. The most severe non-immediate reactions are the Severe Cutaneous Adverse Reactions (SCAR), which Drug reaction with eosinophilia & systemic symptoms (DRESS) syndrome, acute generalised exanthematous pustulosis (AGEP), Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN). Mortality for SCAR can reach up to ~30%.
11. Some SCAR may occur weeks to months (especially DRESS syndrome and SJS/TEN) following drug exposure and may be missed without high index of suspicion.
12. Most reactions resolve after withdrawal of causative agent, but severe cutaneous reactions which may warrant steroids or immunomodulation.
13. SCAR usually contraindicates further re-exposure to suspected culprit drugs.

14. Desensitisation for non-immediate reactions are seldom possible and 'treating through' not routinely recommended.

Documentation of newly suspected drug allergy

1. All documentation should be clearly recorded in medical records and provided to the patient, (either in written form or drug alert bracelet/jewellery), whenever feasible.
2. Drug allergy (immune-mediated) should be clearly differentiated from and documented separately with non-immune mediated ADR, whenever possible.
3. Documentation of all suspected or confirmed drug allergies should include, at a minimum, the names of suspected culprits (preferably with both generic and proprietary names, if known), dates and manifestations of all reactions, and timing of reactions (immediate, within 1 hour, vs. non-immediate, >1 hour).
4. If available, the reason for drug prescription, method of administration, necessity for treatment, or requirement for hospitalisation due to suspected drug reactions should also be included.
5. If the patient has received medications belonging to the same labelled drug class(es) AFTER their index reaction, subsequent reactions or tolerance to these specific agents should also be recorded (including name of drug and date of reaction or tolerance).
6. Relevant drug allergy investigations (especially drug provocation or tolerance tests) with details of drug names and dates should also be documented.

Choosing alternative antibiotics for patients with suspected penicillin allergy

1. Since most penicillin 'allergy' labels are incorrect, the most important step is to confirm the index allergy label, as described above.
2. If there is a dubious allergy history, a graded drug provocation test may be a suitable strategy for low-risk individuals, with the patient's consent.
3. For patients with a confirmed penicillin allergy, there is no contraindication for carbapenem use, although consulting with an allergist to test for suitable alternatives may be considered. [662]
4. Cross-reactivity between penicillin and cephalosporins is generally low, and is usually due to recognition of similar side chains.

5. Therefore, if cephalosporins are the desired treatment (and no other alternatives are available), it is advisable to select a cephalosporin with dissimilar side-chains from that of the index offending penicillin (Table 7.2). After consulting with an allergist, skin testing or *in vitro* testing can be performed to test selected cephalosporins, if possible.
6. If there are no alternative antibiotics available, and penicillins are the desired treatment, desensitisation may be possible for patients with a history of immediate-type reactions.
7. Although the need for desensitisation is low due to the recognition of incorrect antibiotic allergy labels and the availability of more antibiotic alternatives, the decision to proceed with desensitisation should be a shared decision made by allergists and patients, balancing individualised risk versus benefit.

Table 7.2: Cross-Reacting Side Chains Between β-Lactam Antibiotics

	Amoxicillin	Ampicillin	Cefaclor	Cefadroxil	Cefepime	Cefoperazone	Cefotaxime	Cefoxitin	Cefpodoxime	Ceftazidime	Ceftibuten	Ceftriaxone	Cefuroxime	Cephalexin	Cephaloridine	Cephalothin	Cephradine	Penicillin G
Amoxicillin		6	6/7	6/7										6/7			6/7	
Ampicillin	6		6/7	6/7										6/7			6/7	
Cefaclor	6/7	6/7		7										7			7	
Cefadroxil	6/7	6/7	7											3,7			3,7	
Cefepime							7		7			7						
Cefoperazone																		
Cefotaxime					7				7			7				3		
Cefoxitin													3		7	7		6/7
Cefpodoxime					7		7					7						
Ceftazidime																		
Ceftibuten																		
Ceftriaxone					7		7		7									
Cefuroxime								3										
Cephalexin	6/7	6/7	7	3,7													3,7	
Cephaloridine								7								7		6/7
Cephalothin							3	7							7			6/7
Cephradine	6/7	6/7	7	3,7										3,7				
Penicillin G								6/7							6/7	6/7		

Numbers denote position of side chains: 3, similarity at the cephalosporin 3—position side chain; 7, similarity at the cephalosporin 7—position side chain; 6/7, similarity at the penicillin 6-position side chain and the cephalosporin 7-position side chain.
Each number in the matrix indicates side-chain similarity between two drugs. Cross-allergenicity is expected between each similar pair. For example, a patient allergic to amoxicillin would very likely manifest an allergic reaction to ampicillin, cefadroxil, cefaclor, cephalexin and cephradine. However, the patient would not be expected to exhibit an allergic response to cefepime, cefoperazone, cefotaxime, etc., unless he/she was also allergic to another cephalosporin or penicillin with a similar side chain to the reference drug.

Reference: [663]

7.2 Clinical Guideline for Management of Suspected/Confirmed CA-MRSA Infections

Figure 7.2: Flowchart for the Clinical Management of Suspected/Confirmed CA-MRSA Infections

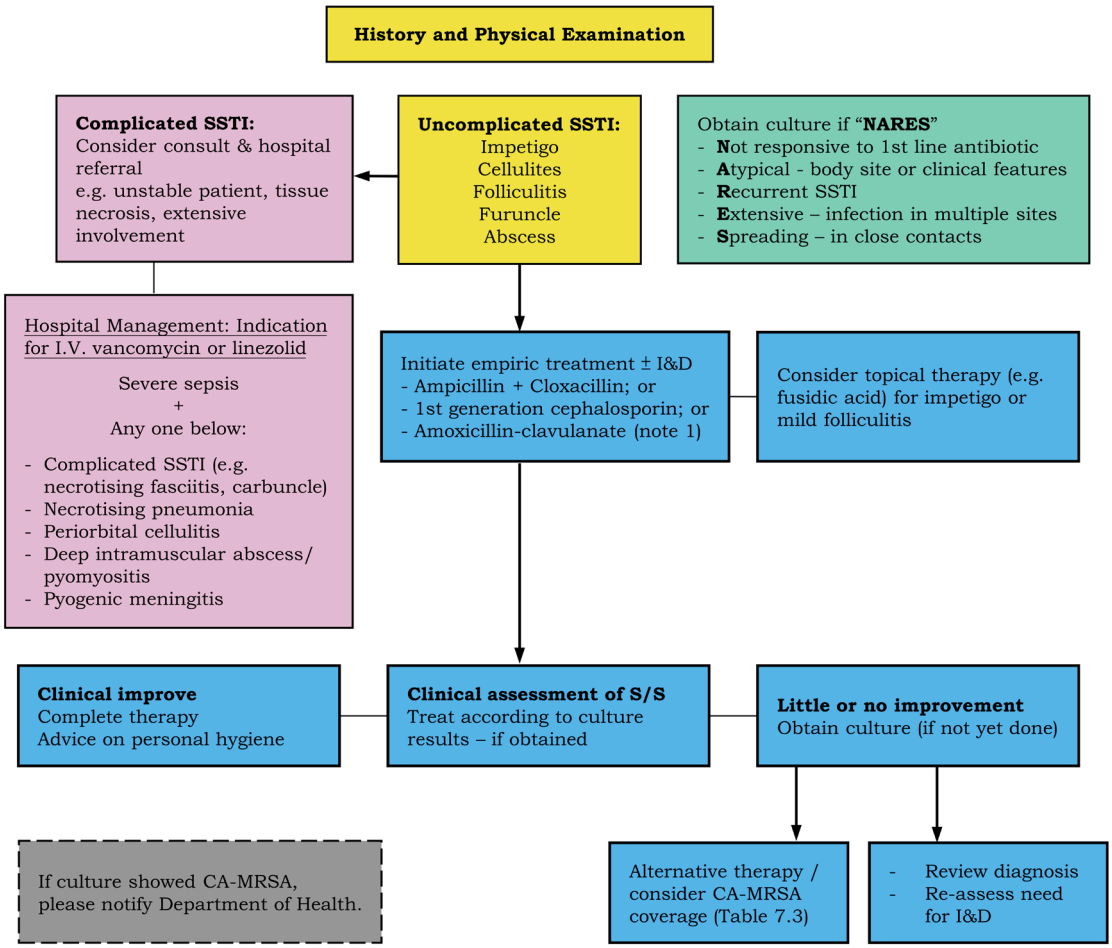


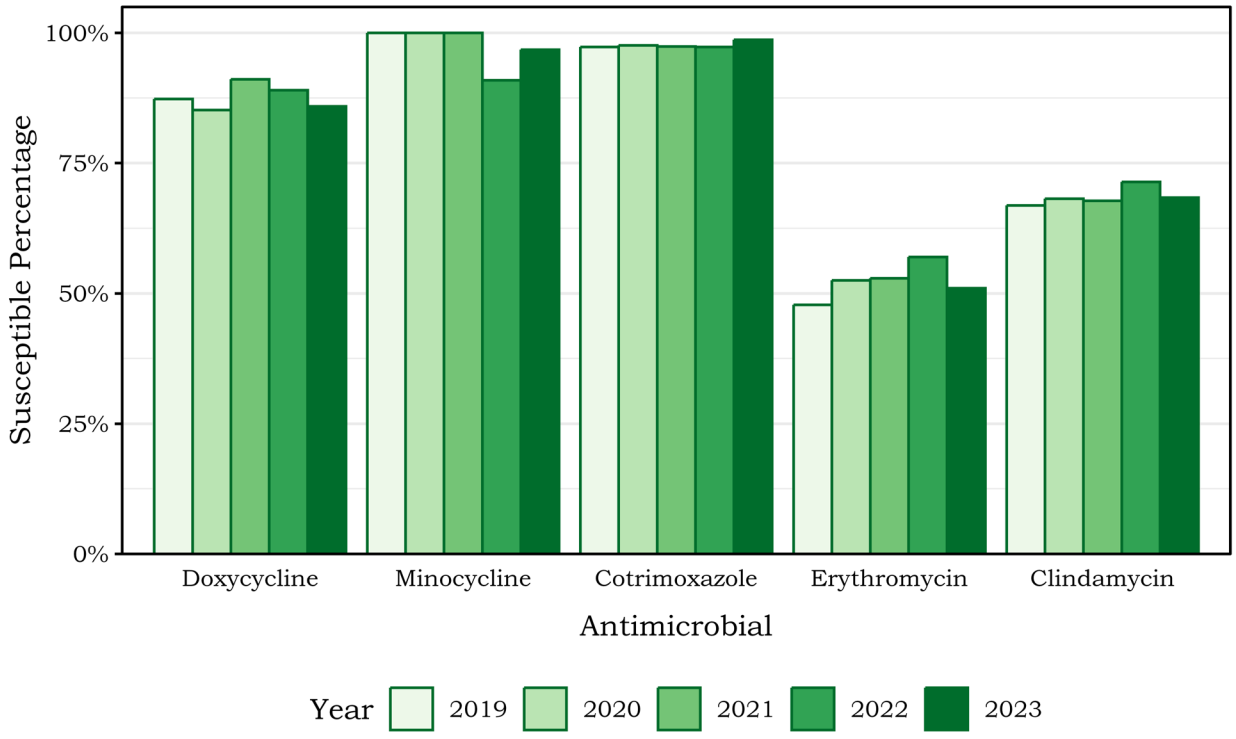
Table 7.3: Antimicrobial Agents for Outpatient Therapy of Uncomplicated CA-MRSA SSTI

Agent[Footnote 1–3]	Potential advantage	Precautions	Usual dose for adult
Cotrimoxazole (Septrin)	Oral	Not for patients with sulphur allergy	P.O. 960 mg b.i.d.
Doxycycline/ minocycline	High skin concentration	Not for children <8y or pregnant women [526]	P.O. 200 mg once, then 100 mg b.i.d.
Clindamycin	Inhibit toxin production	[Footnote 4]	P.O. 300–450 mg tds

Footnotes:

1. Clinicians should consult complete drug prescribing information. Antibiotic therapy should be modified according to results of culture and susceptibility testing. Information available at present showed that most CA-MRSA isolates in HKSAR are susceptible to the above oral antibiotics. The duration of therapy for most SSTI is 5 to 7 days; longer therapy (10 days) is necessary for more severe infection (e.g. if patient is febrile &/or abscess size >5cm).
2. Oral antibiotics are not indicated for MRSA carriage/colonisation.
3. Abscess with size <5cm may resolve with incision & drainage alone. Treatment with antibiotic might have higher cure rate and is important if patient is febrile &/or abscess size >5cm. [176,527,528]
4. If clindamycin is considered, isolate resistant to erythromycin but with apparent "sensitivity" to clindamycin should undergo laboratory testing for inducible clindamycin resistance using the 'D' test (flattening of the clindamycin zone adjacent to the erythromycin disc).

Figure 7.3: Susceptibility of CA-MRSA Isolates to Five Common Antimicrobial Agents



Abbreviations

ABECB	Acute bacterial exacerbation of chronic bronchitis
ACBC	*Acinetobacter baumannii-calcoaceticus* complex
ADR	Adverse drug reactions
AGEP	Acute generalised exanthematous pustulosis
ALT	Alanine aminotransferase
AMR	Antibiotic Resistance
b.i.d.	Twice a day
CA-MRSA	Community-associated methicillin-resistant *Staphylococcus aureus*
CAP	Community-acquired pneumonia
CAPD	Continuous ambulatory peritoneal dialysis
CC17	Clonal complex 17
CDC	Centers for Disease Control and Prevention
CFU	Colony-forming unit
CHP	Centre for Health Protection
CK	Creatine kinase
CLSI	Clinical and Laboratory Standards Institute
COVID-19	Coronavirus Disease 2019
CPE	Carbapenemase-producing Enterobacterales
CRAB	Carbapenem-resistant *Acinetobacter baumannii*
CRE	Carbapenem-resistant Enterobacterales
cIAI	Complicated intra-abdominal infections
cSSTI	Complicated skin and soft tissue infections
cUTI	Complicated urinary tract infections
DH	Department of Health
DNA	Deoxyribonucleic acid
DPT	Drug provocation test
DRESS	Drug reaction with eosinophilia & systemic symptoms
DRSP	Drug-resistant *Streptococcus pneumoniae*
EAEC	Enteroaggregative *Escherichia coli*
EDTA	Ethylenediaminetetraacetic acid

ERCP	Endoscopic retrograde cholangiopancreatography
ESBL	Extended-spectrum β-lactamase
ESBL-E	Extended-spectrum-β-lactamases-producing Enterobacterales
ETEC	Enterotoxigenic *Escherichia coli*
FQ	Fluoroquinolone
GDP	Gross domestic product
GLASS	Global Antimicrobial Resistance and Use Surveillance System
HA	Hospital Authority
HA-MRSA	Hospital-associated methicillin-resistant *Staphylococcus aureus*
HABP	Hospital-acquired bacterial pneumonia
HACEK	*Haemophilus* spp., *Aggregatibacter* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella* spp.
HAP	Hospital-acquired pneumonia
HDU	High dependency unit
HIV	Human immunodeficiency virus
HK-DADI	Hong Kong Drug Allergy Delabelling Initiative
HKSAR	Hong Kong Special Administrative Region
HKWC	Hong Kong West Cluster
I.M.	Intramuscular
I.V.	Intravenous
ICARE	Intensive Care Antimicrobial Resistance Epidemiology
ICU	Intensive care unit
ID	Infectious disease
IDT	Intradermal tests
IVDU	Intravenous drug user
IVIG	Intravenous immunoglobulin
KCC	Kowloon Central Cluster
KEC	Kowloon East Cluster
KPC	*Klebsiella pneumoniae* carbapenemase
MAO	Monoamine oxidase
MDR	Multidrug-resistant
MDRO	Multi-drug resistant organisms

MIC	Minimum inhibitory concentration
MRAB	Multidrug-resistant *Acinetobacter baumannii*
MRMP	Macrolide-resistant *Mycoplasma pneumoniae*
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	Methicillin-susceptible *Staphylococcus aureus*
MSU	Midstream urine
N/A	Not applicable
NDM	New Delhi metallo-β-lactamase
OAT1	Organic anion transporter 1
OPAT	Outpatient Parenteral Antimicrobial Therapy
P.O.	By mouth
PBP	Penicillin-binding protein
PCR	Polymerase chain reaction
PD	Pharmacodynamics
PHLSB	Public Health Laboratory Services Branch
PID	Pelvic inflammatory disease
PK	Pharmacokinetic
PT	Patch tests
PVL	Panton-Valentine leukocidin
QMH	Queen Mary Hospital
q.i.d.	Four times daily
q12h	Every 12 hours
RCT	Randomised controlled trial
RNA	Ribonucleic acid
RTE food	Ready-to-eat food
rRNA	Ribosomal RNA
SCAR	Severe Cutaneous Adverse Reactions
SCC	Staphylococcal Cassette Chromosome
SIADH	Syndrome of inappropriate antidiuretic hormone secretion
SJS	Stevens-Johnson syndrome
SPT	Skin prick tests

SSI	Surgical Site Infection
SSTI	Skin and soft tissue infections
TB	Tuberculosis
TEN	Toxic epidermal necrolysis
TPPB	Transperineal prostate biopsy
TRPB	Transrectal prostate biopsy
TURBT	Transurethral resection of bladder tumour
TURP	Transurethral resection of the prostate
VABP	Ventilator-associated bacterial pneumonia
VRE	Vancomycin-resistant Enterococci
VREfm	Vancomycin-resistant *Enterococcus faecium*
WHO	World Health Organization
XDR	Extensively drug-resistant

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Index

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