JAC Antimicrob Resist
https://doi.org/10.1093/jacamr/dlae123

JAC-Antimicrobial Resistance

Antimicrobial prescribing in referral hospitals in Timor-Leste: results of the first two national point prevalence surveys, 2020–21

Guilherme Ximenes[1,2], Sajal K. Saha[1,3,4], Helio Guterres[5], Adriano Vieira[1], Lisa Harris[1], Michelle Mahony[1,6], Agata Dos Santos[2], Lucia Toto[1,5], Elfiana Amaral[1,5], Jessie C. Spargo[6], Sze Yen Tay[1,7], Salvador Amaral[1], Karen Champlin[1], Anthony D. K. Draper[1,8,9], Joshua R. Francis[1,6], Jennifer Yan[1,6] and Sarah A. Lynar[1,7,8]*

[1]Menzies School of Health Research, Charles Darwin University, Dili, Timor-Leste; [2]Pharmacy Department, Hospital Nacional Guido Valadares, Dili, Timor-Leste; [3]Department of Infectious Diseases, Melbourne Medical School, National Centre for Antimicrobial Stewardship (NCAS), University of Melbourne, Melbourne, 3010 Victoria, Australia; [4]Centre for Innovation in Infectious Disease and Immunology Research (CIIDIR), IMPACT, Deakin University, Geelong 3220, VIC, Australia; [5]Department of Internal Medicine, Hospital Nacional Guido Valadares, Dili, Timor-Leste; [6]Department of Paediatrics, Royal Darwin Hospital, Darwin 0810, Northern Territory, Australia; [7]Department of Infectious Diseases, Royal Darwin Hospital, Darwin 0810, Northern Territory, Australia; [8]Northern Territory Centre for Disease Control, Darwin 0810, Northern Territory, Australia; [9]National Centre for Epidemiology and Population Health, College of Health and Medicine, Australian National University, Canberra 0200, Australian Capital Territory, Australia

*Corresponding author. E-mail: sarah.lynar@nt.gov.au

Received 10 April 2024; accepted 8 July 2024

Objectives: To describe antimicrobial use (AMU) in patients admitted to hospitals in Timor-Leste.

Methods: In 2020 and 2021, we undertook antimicrobial prescribing point prevalence surveys across all six hospitals in Timor-Leste (one national and five municipal) to describe AMU and appropriateness in admitted patients.

Results: In 2020, 291/394 (73.9%) surveyed patients had been prescribed antimicrobials, compared with 260/403 (64.5%) in 2021 ($P=0.004$). Most (309/551; 56.1%) were prescribed one antimicrobial, and 179/551 (32.5%) were prescribed two. The most commonly prescribed antibiotics were ceftriaxone (38.5% in 2020, 41.5% in 2021) and ampicillin (35.7% in 2020, 32.3% in 2021), followed by gentamicin, metronidazole and cloxacillin. Reserve antibiotics like meropenem and vancomycin were minimally used. Of all antimicrobial prescriptions, 70.8% were deemed appropriate in 2020 and 69.1% in 2021. Antimicrobial prescriptions for surgical and post-partum prophylaxis were frequently deemed inappropriate [37/50 (74.0%) and 39/44 (88.6%) prescriptions, respectively].

Conclusions: Most patients admitted to hospital in Timor-Leste are prescribed antimicrobials, and approximately one-third of these prescriptions are inappropriate. However, this was in the context of limited local guideline availability at the time of surveys and limited microbiological culture capacity outside of the capital, Dili. Improved microbiological guidance, iterative guideline revisions based on local antimicrobial resistance (AMR) surveillance data, and enhanced stewardship activities including further point prevalence studies, could improve antimicrobial use, optimize patient outcomes and reduce AMR in Timor-Leste.

Introduction

Antimicrobial resistance (AMR), the capacity of microorganisms to evolve and withstand the effectiveness of antimicrobials, is a global health concern with associated morbidity, mortality and economic impact.[1–3] Antimicrobial use (AMU), particularly when inappropriate, is a major contributor to increasing global AMR.[4–8] The use of inappropriate antibiotics is also a risk factor for poor outcomes from infection, particularly in hospitalized inpatients.[9] Inappropriate AMU may be due to inappropriate spectrum (too narrow or too broad), dosing (too frequent or infrequent; too high or low dose per administration), duration (too short or

long), or no indication for antimicrobials based on best evidence. Optimal AMU may also require consideration of other factors such as available microbiology, allergies, patient weight, age, or hepatic or renal function.

Since the WHO Global AMR Action Plan[10] and 71st General Assembly on AMR[11] provided recommendations on collection and reporting of antimicrobial usage data,[12] rising consumption has been observed in many countries.[13–16] Between 2000 and 2010, antibiotic use increased by 36% across 71 countries,[15] and between 2000 and 2015 by 65% across 76 countries (21.1–34.8 billion DDD).[16] Approximately one-third of hospital patients consume an antimicrobial during their admission, with half of those deemed unnecessary.[17–19] However, while consumption information is important, data on antimicrobial appropriateness are essential in assessing antimicrobial misuse, identifying trends and defining targets for intervention and policy measures in future.[20,21]

In Timor-Leste, evidence of high rates of AMR has emerged.[22,23] In the setting of high rates of AMR, inappropriate use of antimicrobials may be suspected, as has been observed in similar low-and middle-income countries (LMICs).[24–26] However, up until now local data have remained scarce.[10] A 2019 study of antibiotic distribution data[27] estimated human consumption of antibiotics at 11.1 DDD/1000 inhabitants/day, similar to other LMICs such as the Philippines, Indonesia and India.[16] Approximately 32% of distributed antimicrobials were restricted according to the WHO 'AWaRe' (Access, Watch and Reserve) classification[28] and were not on Timor-Leste's Essential Medicines List (EML). In 2020, Timor-Leste incorporated a national drugs and medicine policy. The first national AMR action plan was developed in 2017 and revised in 2022.[29]

Regular, standardized point prevalence surveys (PPSs) provide a useful mechanism for assessment of trends in AMU and misuse across both time and geographical regions.[30,31] This study aimed to conduct Timor-Leste's first two nationwide hospital-based PPSs with the goal of establishing capacity for ongoing annual PPSs. Since completion of the surveys, Timor-Leste's first national empirical antimicrobial prescribing guideline has been published[32] and laboratory capacity has begun expanding to the municipal hospitals,[33] paving the way for enhanced antimicrobial stewardship (AMS) programmes and improved patient outcomes.

Materials and methods

Study setting

Timor-Leste is an independent country in Southeast Asia with a population of 1.3 million.[34] It is a low-income country, with approximately 42% of its inhabitants estimated to be living below the poverty line.[35] Public hospital health services are provided through Hospital Nacional Guido Valadares (HNGV), the 250-bed tertiary referral hospital in the capital of Dili, and five municipal referral hospitals across the country: Baucau (75 beds), Maubisse, Maliana, Suai and Oecusse (each 24 beds). All hospitals provide internal medicine, surgical, paediatric and obstetric care; HNGV also houses neonatology and ICUs. Diagnostic microbiology at HNGV is provided by the National Health Laboratory (NHL); regional laboratory services were minimal during the study period. Four oral and written languages (English, Spanish, Tetum and Bahasa Indonesia) are variably used in each hospital.

Study design

We conducted a cross-sectional prospective antimicrobial PPS across the six public hospitals in Timor-Leste between October and December of both 2020 and 2021, utilizing WHO methodology.[36] Inpatients admitted by 8:00am on the census date for each ward were enrolled. All antimicrobial routes (oral, parenteral, rectal, topical and inhalational) and all antimicrobial agents (antibiotic, antifungal, antiparasitic and antiviral) were included.

Survey tools

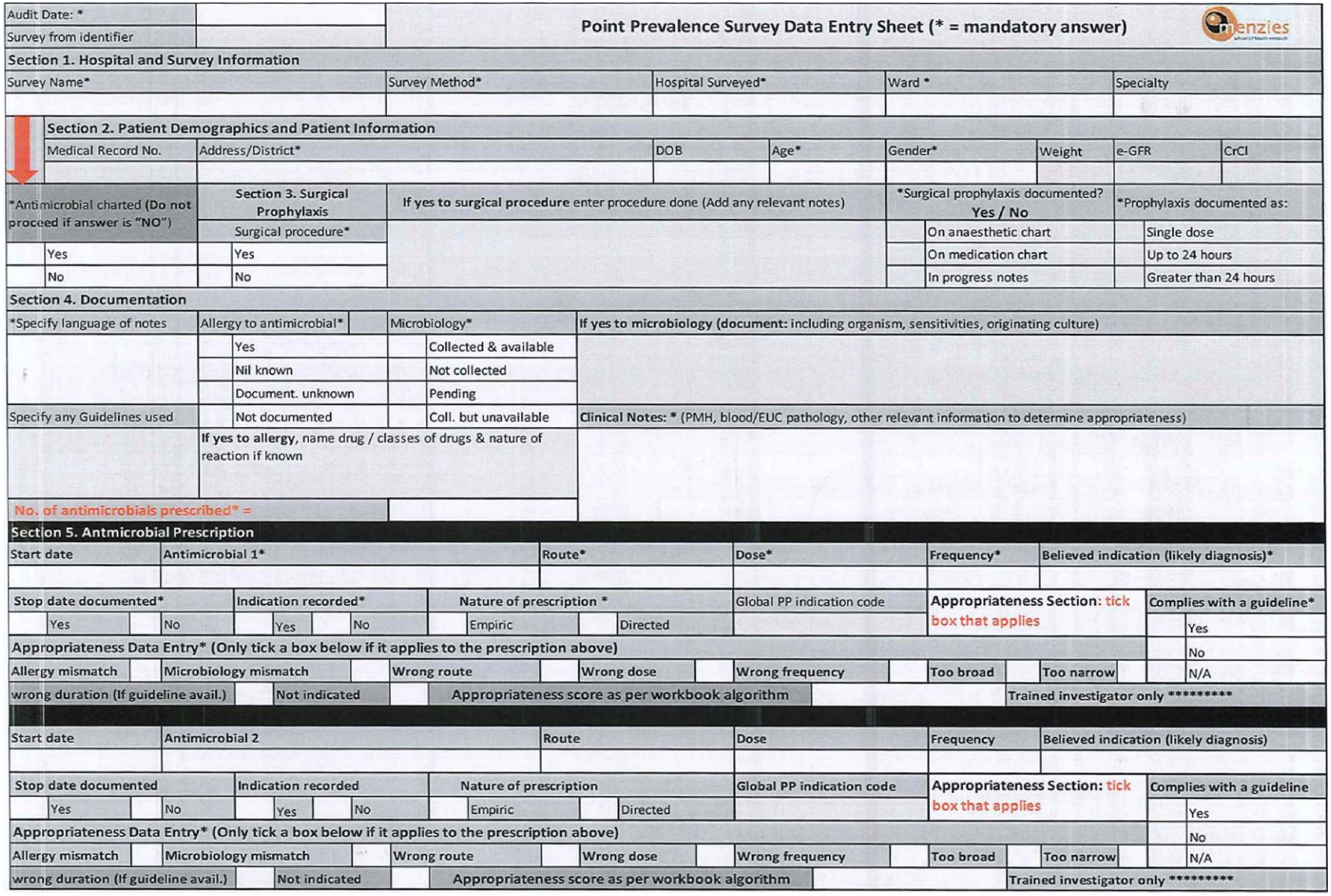
The PPS questionnaire (Figure 1) was adapted in-country using both the WHO Global Point Prevalence Survey methodology[36] and the Australian National Antimicrobial Prescribing Survey (NAPS) tool.[37,38] The NAPS Appropriateness Definitions tool (Figure 2) was used to determine the appropriateness of antimicrobial prescribing,[39] retrospectively in 2020 and prospectively in 2021. The survey tool was tested on a small cohort of patients at the tertiary referral hospital (HNGV) prior to commencement to ensure suitability. Data were collected using paper forms due to logistical challenges in more remote areas, then entered into REDCap™ (Research Electronic Data Capture, Vanderbilt University), an electronic data capture tool hosted at Menzies School of Health Research.

Data collection

Study personnel consisted of pharmacists, physicians and medical officers from Timor-Leste and Australia. De-identified patient data were collected from paper medication charts and progress notes. In the hospitals that were not routinely using medication charts, data were collected from prescriptions documented in patient progress notes. Study teams included multilingual clinicians to account for variable language use. Demographics and antimicrobial prescription details were collected for those patients on at least one antimicrobial. For each antimicrobial agent, data included: dose; frequency; duration; route of administration; indication; whether empirical, directed or prophylactic; any relevant microbiology; and documented antimicrobial allergies. In 2020, antimicrobial appropriateness was determined retrospectively by a team of four Timorese and Australian internal medicine and infectious diseases specialists utilizing clinical data collected by the survey team from medical records. This method was used due to challenges in resourcing each survey team with trained clinicians, and also to create consistency and an opportunity for expert discussion. In 2021, appropriateness was determined prospectively by each survey team led by a medical expert, in line with the standard NAPS strategy of contemporaneous assessment. For analysis, antimicrobials that were rated either as 1 or 2 using the tool were deemed 'appropriate', and those rated as 3 or 4 were determined as 'inappropriate'. At HNGV, an in-hospital antimicrobial guideline[40] was available and guided assessment of appropriateness. For the municipal hospitals, in the absence of a national antimicrobial guideline at the time of the study (published subsequently) the expert team consulted all locally accessible guidelines including the HNGV guideline. Members of the team scored separately then came together for discussion and collaborative guideline evaluation to reach consensus. Opportunistic bedside feedback was provided on antimicrobial choice where appropriate. Formal feedback and teaching sessions on AMU and AMR were also provided for doctors, pharmacists and hospital directors in the Tetum language, in the form of 1–2 day workshops at each hospital. In the second year, data from the first year were collated and presented during these sessions. All sessions were well attended and received.

Statistical analysis

Statistical analysis was performed using Stata/SE 17.0. Categorical variables were compared using Fisher's exact test or Pearson's chi-squared test depending on number. Results were considered significant at the $P < 0.05$ level.



Audit Date: *		Point Prevalence Survey Data Entry Sheet (* = mandatory answer)	Menzies
Survey from identifier			

Section 1. Hospital and Survey Information

Survey Name*	Survey Method*	Hospital Surveyed*	Ward *	Specialty

Section 2. Patient Demographics and Patient Information

Medical Record No.	Address/District*	DOB	Age*	Gender*	Weight	e-GFR	CrCl

*Antimicrobial charted (Do not proceed if answer is "NO")		Section 3. Surgical Prophylaxis		If yes to surgical procedure enter procedure done (Add any relevant notes)	*Surgical prophylaxis documented? Yes / No		*Prophylaxis documented as:	
		Surgical procedure*						
	Yes		Yes			On anaesthetic chart		Single dose
	No		No			On medication chart		Up to 24 hours
						In progress notes		Greater than 24 hours

Section 4. Documentation

*Specify language of notes	Allergy to antimicrobial*		Microbiology*		If yes to microbiology (document: including organism, sensitivities, originating culture)
		Yes		Collected & available	
		Nil known		Not collected	
		Document. unknown		Pending	
Specify any Guidelines used		Not documented		Coll. but unavailable	Clinical Notes: * (PMH, blood/EUC pathology, other relevant information to determine appropriateness)
	If yes to allergy, name drug / classes of drugs & nature of reaction if known				
No. of antimicrobials prescribed* =					

Section 5. Antmicrobial Prescription

Start date	Antimicrobial 1*	Route*	Dose*	Frequency*	Believed indication (likely diagnosis)*

Stop date documented*		Indication recorded*		Nature of prescription *		Global PP indication code	Appropriateness Section: tick box that applies	Complies with a guideline*	
Yes	No	Yes	No	Empiric	Directed			Yes	
								No	
								N/A	

Appropriateness Data Entry* (Only tick a box below if it applies to the prescription above)													
Allergy mismatch		Microbiology mismatch		Wrong route		Wrong dose		Wrong frequency		Too broad		Too narrow	
wrong duration (If guideline avail.)		Not indicated		Appropriateness score as per workbook algorithm				Trained investigator only *********					

Start date	Antimicrobial 2	Route	Dose	Frequency	Believed indication (likely diagnosis)

Stop date documented		Indication recorded		Nature of prescription		Global PP indication code	Appropriateness Section: tick box that applies	Complies with a guideline	
Yes	No	Yes	No	Empiric	Directed			Yes	
								No	
								N/A	

Appropriateness Data Entry* (Only tick a box below if it applies to the prescription above)													
Allergy mismatch		Microbiology mismatch		Wrong route		Wrong dose		Wrong frequency		Too broad		Too narrow	
wrong duration (If guideline avail.)		Not indicated		Appropriateness score as per workbook algorithm				Trained investigator only *********					

Figure 1. Case report form.

Start date	Antimicrobial 3	Route	Dose	Frequency	Believed indication (likely diagnosis)

Stop date documented		Indication recorded		Nature of prescription		Global PP indication code	Appropriateness Section: tick box that applies	Complies with a guideline	
	Yes	No	Yes	No	Empiric	Directed			Yes
Appropriateness Data Entry* (answer all questions)									No
Allergy mismatch		Microbiology mismatch		Wrong route	Wrong dose	Wrong frequency	Too broad	Too narrow	N/A
wrong duration (If guideline avail.)		Not indicated		Appropriateness score as per workbook algorithm			Trained investigator only *********		

Start date	Antimicrobial 4	Route	Dose	Frequency	Believed indication (likely diagnosis)

Stop date documented		Indication recorded		Nature of prescription		Global PP indication code	Appropriateness Section: tick box that applies	Complies with a guideline	
	Yes	No	Yes	No	Empiric	Directed			Yes
Appropriateness Data Entry* (Only tick a box below if it applies to the prescription above)									No
Allergy mismatch		Microbiology mismatch		Wrong route	Wrong dose	Wrong frequency	Too broad	Too narrow	N/A
wrong duration (If guideline avail.)		Not indicated		Appropriateness score as per workbook algorithm			Trained investigator only *********		

Start date	Antimicrobial 5	Route	Dose	Frequency	Believed indication (likely diagnosis)

Stop date documented		Indication recorded		Nature of prescription		Global PP indication code	Appropriateness Section: tick box that applies	Complies with a guideline	
	Yes	No	Yes	No	Empiric	Directed			Yes
Appropriateness Data Entry* (Only tick a box below if it applies to the prescription above)									No
Allergy mismatch		Microbiology mismatch		Wrong route	Wrong dose	Wrong frequency	Too broad	Too narrow	N/A
wrong duration (If guideline avail.)		Not indicated		Appropriateness score as per workbook algorithm			Trained investigator only *********		

Start date	Antimicrobial 6	Route	Dose	Frequency	Believed indication (likely diagnosis)

Stop date documented		Indication recorded		Nature of prescription		Global PP indication code	Appropriateness Section: tick box that applies	Complies with a guideline	
	Yes	No	Yes	No	Empiric	Directed			Yes
Appropriateness Data Entry* (Only tick a box below if it applies to the prescription above)									No
Allergy mismatch		Microbiology mismatch		Wrong route	Wrong dose	Wrong frequency	Too broad	Too narrow	N/A
wrong duration (If guideline avail.)		Not indicated		Appropriateness score as per workbook algorithm			Trained investigator only *********		

Start date	Antimicrobial 7	Route	Dose	Frequency	Believed indication (likely diagnosis)

Stop date documented		Indication recorded		Nature of prescription		Global PP indication code	Appropriateness Section: tick box that applies	Complies with a guideline	
	Yes	No	Yes	No	Empiric	Directed			Yes
Appropriateness Data Entry* (Only tick a box below if it applies to the prescription above)									No
Allergy mismatch		Microbiology mismatch		Wrong route	Wrong dose	Wrong frequency	Too broad	Too narrow	N/A
wrong duration (If guideline avail.)		Not indicated		Appropriateness score as per workbook algorithm			Trained investigator only *********		

Figure 1. (Continued)

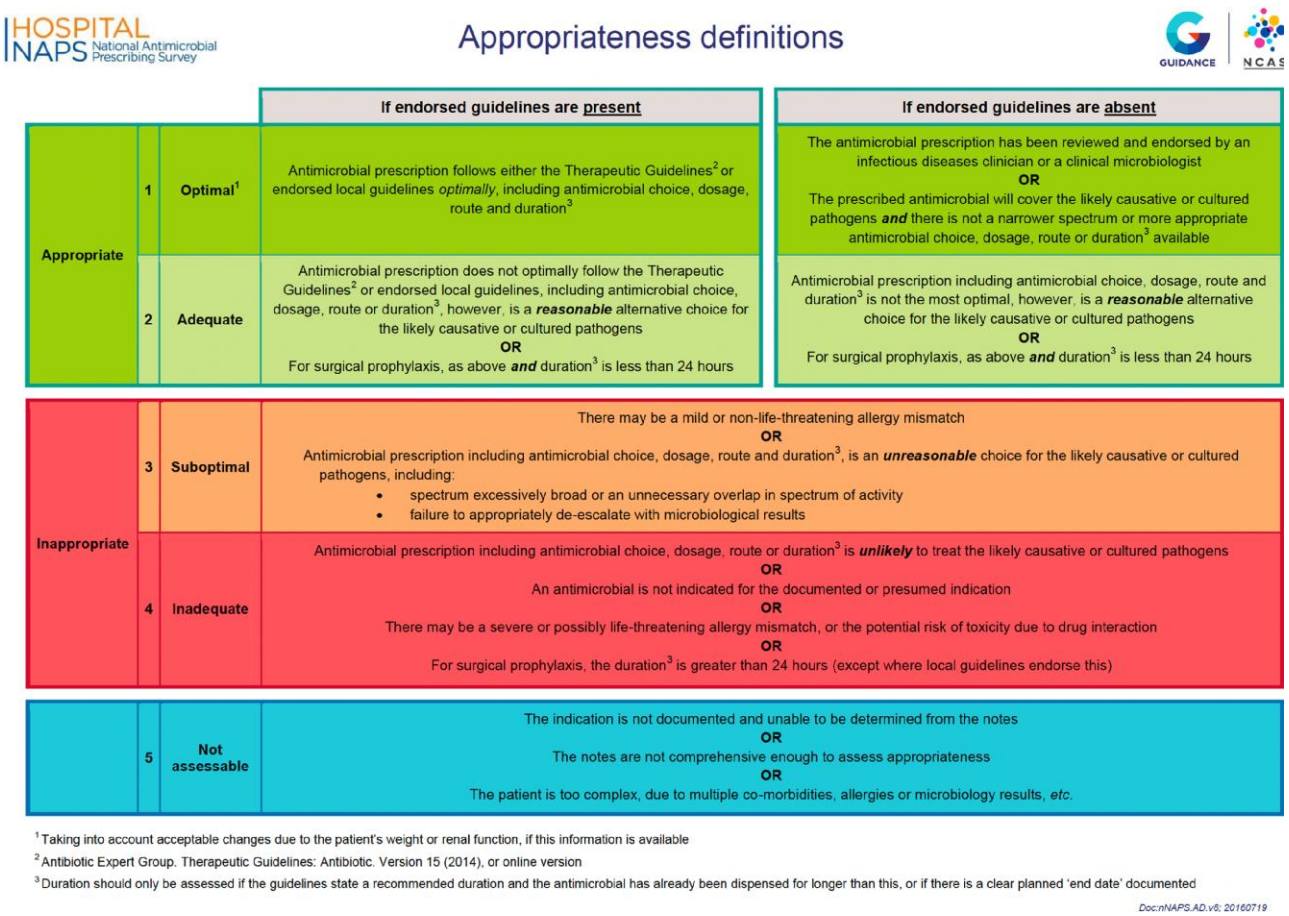


Figure 2. Hospital National Antimicrobial Prescribing Survey – appropriateness definitions. Reprinted from 'National Antimicrobial Prescribing Survey 2022 – Technical Supplement'.[38] Copyright 2024 Melbourne Health. Reprinted with permission.

Table 1. Point prevalence of admitted patients prescribed antimicrobials, by hospital and year

	2020		2021	
	Patients admitted, *n*	Patients on antimicrobials, *n* (%)	Patients admitted, *n*	Patients on antimicrobials, *n* (%)
Total	394	291 (73.9)	403	260 (64.5)
HNGV	262	189 (72.1)	310	197 (63.5)
Baucau	39	28 (73.7)	36	23 (63.9)
Maliana	33	29 (87.9)	15	10 (66.7)
Maubisse	18	16 (88.9)	7	5 (71.4)
Oecusse	22	16 (72.7)	17	14 (82.4)
Suai	20	13 (65.0)	18	11 (61.1)

Ethics

Ethics approval was obtained from the Human Research Ethics Committee of the Instituto Nacional de Saude of the Ministry of Health, Timor-Leste (No. Ref/110MS-INS/GDE/VIII/2020) and the Menzies Human Research Ethics Committee, Charles Darwin University, Australia (HREC 2020-3657).

Results

Across the two surveys, 551/797 (69.1%) were prescribed antimicrobials: 291/394 (73.9%) in 2020 compared with 260/403 (64.5%) in 2021 ($P=0.004$) (Table 1). Most patients who were on antimicrobials were prescribed either one or two different antimicrobials (Table 2). Antimicrobial regimens for all patients on five or more antimicrobials included anti-TB treatment.

Ceftriaxone and ampicillin were the most commonly prescribed antimicrobials across both years (Table 3). Ceftriaxone was prescribed in 38.5% and 41.5% patients on antimicrobials in 2020 and 2021, respectively, and ampicillin in 35.7% and 32.3%, respectively. The use of antimicrobials reserved for more resistant organisms, such as meropenem and vancomycin, was limited across both years (Table 3). Three hospitals were using neither vancomycin nor meropenem at census in either year.

Antimicrobial appropriateness

Overall, 70.8% of antimicrobial prescriptions were deemed appropriate in 2020 compared with 69.1% in 2021 (Table 4). The most common reasons for a classification of suboptimal or inadequate related to incorrect dosing (142/260; 54.6%) or

Table 2. Number of antimicrobials prescribed per patient on antimicrobials, by year

Number of antimicrobials prescribed	2020 (*N* = 291), *n* (%)	2021 (*N* = 260), *n* (%)	Total (*N* = 551), *n* (%)
1	162 (55.7)	147 (56.5)	309 (56.1)
2	95 (32.6)	84 (32.3)	179 (32.5)
3	13 (4.5)	2 (0.8)	15 (2.7)
4	9 (3.1)	16 (6.2)	25 (4.5)
5	7 (2.4)	7 (2.7)	14 (2.5)
≥6	5 (1.7)	4 (1.5)	9 (1.6)

Table 3. Number of antimicrobial prescriptions for specific antimicrobials

	Number of prescriptions (% of total patients)	
Antimicrobial	2020 (*n* = 291)	2021 (*n* = 260)
β-Lactams		
Amoxicillin	16 (5.5)	5 (1.9)
Amoxicillin/clavulanate	2 (0.7)	0
Ampicillin	104 (35.7)	84 (32.3)
Cefazolin	0	3 (1.2)
Cefixime	1 (0.3)	0
Cefotaxime	0	1 (0.4)
Ceftriaxone	112 (38.5)	108 (41.5)
Cloxacillin	29 (10.0)	20 (7.7)
Meropenem	10 (3.4)	16 (6.2)
Other antibiotics		
Amikacin	2 (0.7)	0
Azithromycin	11 (3.8)	5 (1.9)
Chloramphenicol	0	1 (0.4)
Ciprofloxacin	9 (3.1)	14 (5.4)
Clindamycin	0	2 (0.8)
Doxycycline	2 (0.7)	1 (0.4)
Erythromycin	1 (0.3)	0
Gentamicin	53 (18.2)	24 (9.2)
Levofloxacin	2 (0.7)	1 (0.4)
Metronidazole	42 (14.4)	39 (15.0)
Trimethoprim/sulfamethoxazole	2 (0.7)	3 (1.2)
Vancomycin	5 (1.7)	3 (1.2)
Anti-TB		
Ethambutol	20 (6.9)	26 (10.0)
Isoniazid	18 (6.2)	27 (10.4)
Pyrazinamide	18 (6.2)	26 (10.0)
Rifampicin	18 (6.2)	27 (10.4)
Streptomycin	2 (0.7)	0
Antifungal		
Fluconazole	3 (1.0)	2 (0.8)
Nystatin	6 (2.1)	2 (0.8)
Antihelminth		
Albendazole	3 (1.0)	2 (0.8)
Antiviral		
Tenofovir	0	1 (0.4)
Antiretroviral (not specified)	0	2 (0.8)

Table 4. Appropriateness of antimicrobial prescriptions by year

	Number of prescriptions (%)	
Appropriateness classification	2020 (*N* = 493), *n* (%)	2021 (*N* = 447), *n* (%)
1 (Optimal)	222 (45.0)	226 (50.6)
2 (Adequate)	127 (25.7)	83 (18.6)
3 (Suboptimal)	37 (7.5)	27 (6.0)
4 (Inadequate)	85 (17.2)	111 (24.8)
5 (Not assessable)	22 (4.5)	0
Total appropriate	349 (70.8)	309 (69.1)
Total inappropriate	122 (24.7)	138 (30.9)

Table 5. Primary reasons for being labelled inappropriate, by year

Reason	2020[a] (*N* = 471), *n* (%)	2021 (*N* = 447), *n* (%)
Does not comply with available guideline	7/33[b] (21.2)	137[c] (38.4)
Microbiology mismatch	1 (0.2)	5 (1.1)
Wrong route	14 (3.0)	0
Wrong dose	93 (19.7)	49 (11.0)
Wrong frequency	13 (2.8)	44 (9.8)
Too broad	32 (6.8)	37 (8.3)
Too narrow	42 (8.9)	47 (10.5)
Antimicrobial not indicated	80 (17.0)	94 (21.0)

[a]Excluding 22 patients with appropriateness score 5 as insufficient information for assessment.
[b]N/A for 460 as guidelines not widely available.
[c]N/A for 90 as guidelines only available in HNGV and for certain infections.

antimicrobial prescription without a documented indication (174/260; 66.9%) (Table 5).

The most common indications for antimicrobial prescription were community-acquired pneumonia (118 antimicrobials; 90 patients), neonatal sepsis (107; 62), surgical (50; 36) and post-partum (44; 38) prophylaxis, skin and soft tissue infections (76; 57) and TB (180; 45). Most antimicrobials were charted empirically; only 144/551 (26.1%) patients on antimicrobials had specimens collected for microbiological culture and susceptibility testing.

Antimicrobials prescribed for post-partum prophylaxis and surgical prophylaxis were infrequently judged appropriate [5/44 (11.4%) for post-partum prophylaxis and 13/50 (26.0%) for surgical prophylaxis, combining 2020 and 2021].

Antimicrobial prescribing appropriateness varied between different antimicrobials (Figure 3). For both of the most frequently prescribed antimicrobials, ceftriaxone and ampicillin, the most common indication for which these antimicrobials were deemed appropriate was community-acquired pneumonia (46/147 and 37/108 prescriptions, respectively). Ciprofloxacin and amoxicillin were the antimicrobials deemed most likely to be inappropriate when prescribed. Ciprofloxacin was prescribed for a wide range

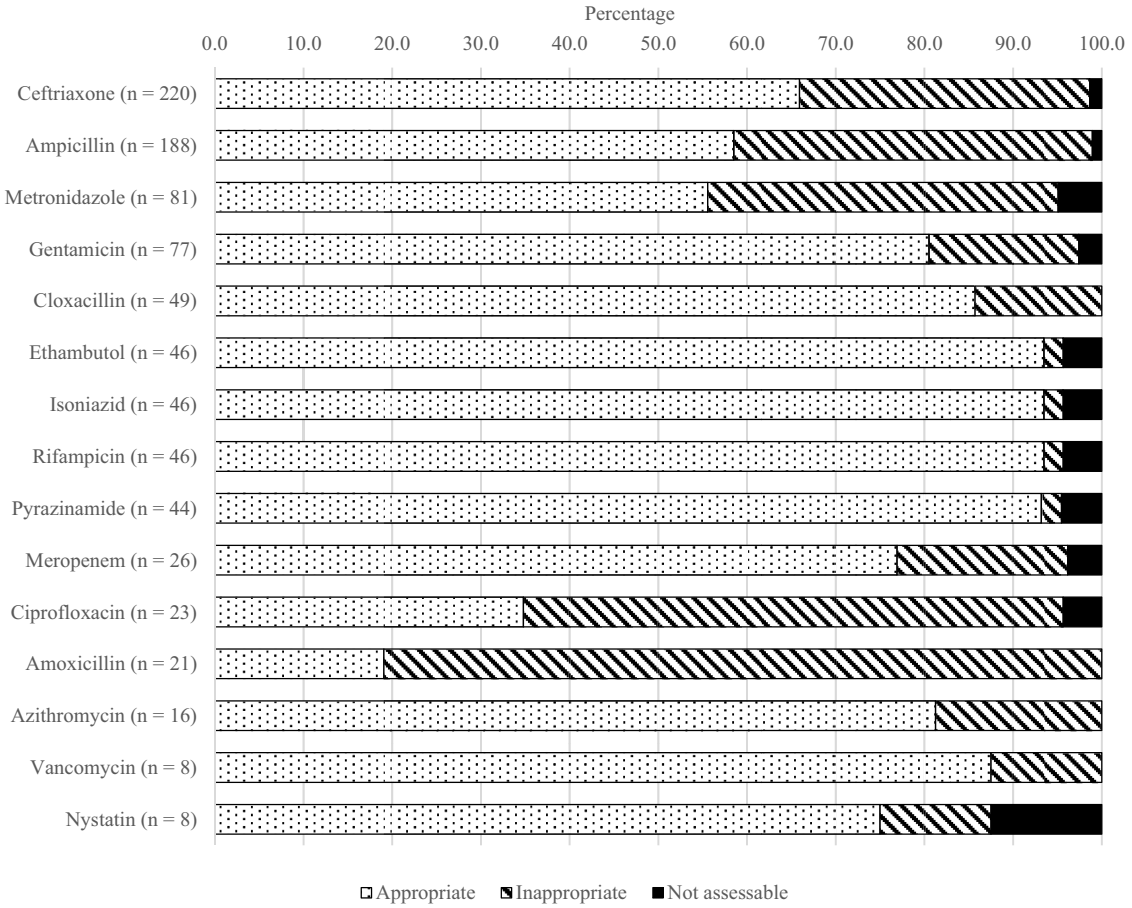


Figure 3. Appropriateness of the 15 most commonly prescribed antimicrobials, 2020–21.

of indications, while 15 of the 21 prescriptions of amoxicillin were for either post-partum or post-surgical prophylaxis.

HNGV had a slightly higher rate of appropriate prescriptions (71.7%) compared with the municipal hospitals combined (64.2%) over the 2 years. All meropenem, vancomycin and ciprofloxacin use was seen in municipal hospitals, with none in use at HNGV at census.

Discussion

These PPSs provide the first national data for Timor-Leste to assess the prevalence and appropriateness of hospital-based antimicrobial prescriptions. Almost 70% of admitted patients were on at least one antimicrobial, which represents a higher prevalence of antimicrobial prescribing in hospital settings compared with the global average of 34% reported in the 2015 Global-PPS study including 53 countries.[41] However, it is similar to rates published from some similar settings such as in a hospital in Eastern India, where antimicrobial prescribing point prevalence rates of 62% and 69% have been reported at different timepoints,[42] and a 2019 survey of six hospitals in Indonesia that reported a 62.0% inpatient antimicrobial point prevalence.[43]

Non-compliance with an available guideline and no indication for antimicrobials were the most frequent reasons for an inappropriate rating (Table 5). The observed high rates of AMU are likely due to many factors. Poverty, poor sanitation, malnutrition and poor health literacy are all known to contribute to high rates of communicable diseases. Respiratory tract infections, diarrhoeal diseases, febrile illnesses and TB account for approximately 80% of all paediatric admissions to the national hospital of Timor-Leste, with high case-fatality rates.[44] AMR is commonly seen[22] and awareness of this may contribute to cautious approaches to empirical antimicrobial prescribing. Availability and awareness of national prescribing guidelines, as well as improved diagnostic microbiological availability and usage, will help to address these issues.

By 2020, the diagnostic microbiology service at the NHL was well established, providing testing across a range of samples submitted from HNGV.[33] While ongoing capacity-building and laboratory-strengthening efforts have resulted in expanded access to blood culture and other diagnostic microbiology testing around the country,[33,45] both of these PPSs were conducted at a time when diagnostic microbiology testing was not possible in any of the referral hospitals outside of the capital city of Dili so no broader antibiogram was available. Empirical antibiotic prescribing guidelines were developed for HNGV in 2016, but these were based on very limited understanding of local epidemiology of AMR and they were not implemented in hospital or clinic

settings outside HNGV. The slightly higher rates of appropriate prescribing in HNGV compared with the other hospitals, as well as their lack of carbapenem, fluoroquinolone and glycopeptide prescriptions, may in part be due to locally developed guideline availability. In 2023, updated national empirical antibiotic prescribing guidelines were finalized, based on local microbiological data showing high rates of AMR in Timor-Leste.[23,46] These guidelines will provide a good basis for future AMS work, including appropriateness analysis for future PPSs. However, they may also lead to higher rates of (appropriate) use of broad-spectrum antimicrobials including fluoroquinolones, aminoglycosides, glycopeptides and carbapenems, if higher rates of resistance are found.

Inappropriate surgical prophylaxis has been identified internationally as a stewardship issue, both in developed countries[39] and LMICs.[47,48] One common theory in LMICs is that higher rates of infection often lead to a reliance on prophylaxis in an attempt to reduce rates, although this was not assessed.[49] Similarly, high rates of inappropriate post-partum prophylaxis have been reported elsewhere.[50] The WHO recommendations on prevention and treatment of maternal peripartum infections[51] were a useful resource in providing education to clinicians following the survey findings. Ongoing engagement regarding surgical and peripartum prophylaxis would be beneficial.

Limitations of this study included small patient numbers in small hospitals, further limited by the effects of the coronavirus disease 2019 (COVID-19) pandemic, which resulted in a reduction in hospital admissions and travel restrictions on the study team during the survey years. Seasonal variations in infection presentations may impact on AMU, but this could not be measured in this study. Comparison between the 2 years was limited by differing data collection methods (retrospective versus prospective) in determination of appropriateness. The potential for inter-rater variability between the 2 years and during the second year of data collection could also not be fully evaluated. Availability of certain antimicrobials regularly impacts on antimicrobial prescription and use in Timor-Leste, and this study did not assess whether this factor may have affected prescriptions during the study period. The range of languages used by medical officers across Timor-Leste, both orally and in medical documentation, proved challenging for the interpretation of clinical records and prescriptions. The lack of electronic medical records, and a range of documentation and transcription templates without standardization, also made data collection challenging. Additionally, the need to adapt already recognized tools for these surveys could potentially affect the generalizability of results and comparisons with other similar regional surveys, although alterations were minor.

Despite these limitations, important information was gathered on areas for improvement as part of local and national AMS activities. These surveys highlighted the relevance of ongoing PPS activities, and some of the future challenges to overcome. While 2 years of data provide useful information, routine and regular ongoing monitoring by local teams and local experts can provide significantly greater data on trends and continue to inform stewardship activities. Antimicrobial prescribing rates are high in Timor-Leste hospitals, with areas identified for improvement in antimicrobial prescribing appropriateness. Since this study, a national antibiotic guideline has been developed, which will assist in standardization of future PPS activities. An AMS Committee has been established within HNGV, although none has yet been formed outside of Dili, with the potential for hub-and-spoke AMS committee development in municipal hospitals. Ongoing microbiological service development, restrictions on reserve antimicrobials, national antimicrobial guideline revisions as antibiograms emerge, and continued educational activities are important for optimizing evidence-based antimicrobial practices across Timor-Leste, in addition to regular monitoring through annual PPSs.

Acknowledgements

We would like to thank the Directors and all staff at the six surveyed hospitals for their generous involvement and support.

Funding

This project was funded by the Fleming Fund from the Department of Health and Social Care using UK Aid. The Fund supports up to 25 countries across Africa and Asia to tackle AMR, a leading contributor to deaths from infectious diseases worldwide. The views expressed in this publication are those of the authors and not necessarily those of the UK Department of Health and Social Care or its Management Agent, Mott MacDonald.

Transparency declarations

The authors declare no conflicts of interest.

References

1 Laxminarayan R, Duse A, Wattal C *et al*. Antibiotic resistance—the need for global solutions. *Lancet Infect Dis* 2013; **13**: 1057–98. https://doi.org/10.1016/S1473-3099(13)70318-9

2 Laxminarayan R, Matsoso P, Pant S *et al*. Access to effective antimicrobials: a worldwide challenge. *Lancet* 2016; **387**: 168–75. https://doi.org/10.1016/S0140-6736(15)00474-2

3 Lim C, Takahashi E, Hongsuwan M *et al*. Epidemiology and burden of multidrug-resistant bacterial infection in a developing country. *Elife* 2016; **5**: e18082. https://doi.org/10.7554/eLife.18082

4 Fridkin SK, Steward CD, Edwards JR *et al*. Surveillance of antimicrobial use and antimicrobial resistance in United States hospitals: project ICARE phase 2. *Clin Infect Dis* 1999; **29**: 245–52. https://doi.org/10.1086/520193

5 Ayukekbong JA, Ntemgwa M, Atabe AN. The threat of antimicrobial resistance in developing countries: causes and control strategies. *Antimicrob Resist Infect Control* 2017; **6**: 47. https://doi.org/10.1186/s13756-017-0208-x

6 Costelloe C, Metcalfe C, Lovering A *et al*. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ* 2010; **340**: c2096. https://doi.org/10.1136/bmj.c2096

7 Steinke D, Davey P. Association between antibiotic resistance and community prescribing: a critical review of bias and confounding in published studies. *Clin Infect Dis* 2001; **33** Suppl 3: S193–205. https://doi.org/10.1086/321848

8 Goossens H, Ferech M, Vander Stichele R *et al*. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 2005; **365**: 579–87. https://doi.org/10.1016/S0140-6736(05)17907-0

9 Cosgrove SE. The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. *Clin Infect Dis* 2006; **42** Suppl 2: S82–89. https://doi.org/10.1086/499406

10 WHO. Global Action Plan on Antimicrobial Resistance. 2015. https://www.who.int/publications/i/item/9789241509763.

11 United Nations. Draft Political Declaration of the High-level Meeting of the General Assembly on Antimicrobial Resistance. 2016. https://www.un.org/pga/71/wp-content/uploads/sites/40/2016/09/DGACM_GAEAD_ESCAB-AMR-Draft-Political-Declaration-1616108E.pdf.

12 WHO. Integrated Surveillance of Antimicrobial Resistance. 2013. https://iris.who.int/bitstream/handle/10665/91778/9789241506311_eng.pdf?sequence=1.

13 Van Boeckel TP, Gandra S, Ashok A *et al*. Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. *Lancet Infect Dis* 2014; **14**: 742–50. https://doi.org/10.1016/S1473-3099(14)70780-7

14 Col NF, O'Connor RW. Estimating worldwide current antibiotic usage: report of Task Force 1. *Rev Infect Dis* 1987; **9** Suppl 3: S232–243. https://doi.org/10.1093/clinids/9.Supplement_3.S232

15 Hogberg LD, Muller A, Zorzet A *et al*. Antibiotic use worldwide. *Lancet Infect Dis* 2014; **14**: 1179–80. https://doi.org/10.1016/S1473-3099(14)70987-9

16 Klein EY, Van Boeckel TP, Martinez EM *et al*. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci U S A* 2018; **115**: E3463–70. https://doi.org/10.1073/pnas.1717295115

17 Ansari F, Erntell M, Goossens H *et al*. The European Surveillance of Antimicrobial Consumption (ESAC) point-prevalence survey of antibacterial use in 20 European hospitals in 2006. *Clin Infect Dis* 2009; **49**: 1496–504. https://doi.org/10.1086/644617

18 Hecker MT, Aron DC, Patel NP *et al*. Unnecessary use of antimicrobials in hospitalized patients: current patterns of misuse with an emphasis on the antianaerobic spectrum of activity. *Arch Intern Med* 2003; **163**: 972–8. https://doi.org/10.1001/archinte.163.8.972

19 Dellit TH, Owens RC, McGowan JE Jr *et al*. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007; **44**: 159–77. https://doi.org/10.1086/510393

20 Collineau L, Belloc C, Stark KD *et al*. Guidance on the selection of appropriate indicators for quantification of antimicrobial usage in humans and animals. *Zoonoses Public Health* 2017; **64**: 165–84. https://doi.org/10.1111/zph.12298

21 Versporten A, Bolokhovets G, Ghazaryan L *et al*. Antibiotic use in eastern Europe: a cross-national database study in coordination with the WHO Regional Office for Europe. *Lancet Infect Dis* 2014; **14**: 381–7. https://doi.org/10.1016/S1473-3099(14)70071-4

22 Francis JR, Sarmento N, Draper ADK *et al*. Antimicrobial resistance and antibiotic use in Timor-Leste: building surveillance capacity with a One Health approach. *Commun Dis Intell (2018)* 2020; **44**: https://doi.org/10.33321/cdi.2020.44.1

23 Marr I, Sarmento N, O'Brien M *et al*. Antimicrobial resistance in urine and skin isolates in Timor-Leste. *J Glob Antimicrob Resist* 2018; **13**: 135–8. https://doi.org/10.1016/j.jgar.2017.12.010

24 Komagamine J, Yabuki T, Hiraiwa T. A trend in prevalence of antimicrobial use and appropriateness of antimicrobial therapy in an acute care hospital from 2018 to 2019: repeated prevalence surveys in Japan. *BMC Res Notes* 2019; **12**: 811. https://doi.org/10.1186/s13104-019-4849-0

25 Cotta MO, Robertson MS, Upjohn LM *et al*. Using periodic point-prevalence surveys to assess appropriateness of antimicrobial prescribing in Australian private hospitals. *Intern Med J* 2014; **44**: 240–6. https://doi.org/10.1111/imj.12353

26 Thu TA, Rahman M, Coffin S *et al*. Antibiotic use in Vietnamese hospitals: a multicenter point-prevalence study. *Am J Infect Control* 2012; **40**: 840–4. https://doi.org/10.1016/j.ajic.2011.10.020

27 Harris L, Bongers A, Yan J *et al*. Estimates of antibacterial consumption in Timor-Leste using distribution data and variation in municipality usage patterns. *Antibiotics (Basel)* 2021; **10**: 1468. https://doi.org/10.3390/antibiotics10121468

28 WHO. 2021 AWaRe Classification. 2021. https://www.who.int/publications/i/item/2021-aware-classification#.

29 Ministry of Health, Timor-Leste. Democratic Republic of Timor-Leste: National Action Plan on Antimicrobial Resistance 2017–2020. 2017. https://www.who.int/publications/m/item/democratic-republic-of-timor-leste-national-action-plan-on-antimicrobial-resistance-2017-2020.

30 Pauwels I, Versporten A, Vermeulen H *et al*. Assessing the impact of the Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS) on hospital antimicrobial stewardship programmes: results of a worldwide survey. *Antimicrob Resist Infect Control* 2021; **10**: 138. https://doi.org/10.1186/s13756-021-01010-w

31 Saleem Z, Godman B, Hassali MA *et al*. Point prevalence surveys of health-care-associated infections: a systematic review. *Pathog Glob Health* 2019; **113**: 191–205. https://doi.org/10.1080/20477724.2019.1632070

32 República Democrática de Timor-Leste Ministério da Saúde. Timor-Leste Antimicrobial Guidelines. 2022. https://ins.gov.tl/wp-content/uploads/2024/01/Timor-Leste-Antimicrobial-Guidelines.pdf.

33 Sarmento N, Oakley T, da Silva ES *et al*. Strong relationships between the Northern Territory of Australia and Timor-Leste. *Microbiology Australia* 2022; **43**: 125–9. https://doi.org/10.1071/MA22039

34 Worldometer. Timor-Leste Demographics. 2020. https://www.worldometers.info/demographics/timor-leste-demographics/.

35 United Nations Development Programme Timor-Leste. Economic Transformation: Limited Income and Livelihood Opportunities. 2024. https://www.undp.org/timor-leste/economic-transformation#:~:text=Limited%20income%20and%20livelihood%20opportunities, below%20the%20national%20poverty%20line.

36 WHO. WHO Methodology for Point Prevalence Survey on Antibiotic Use in Hospitals. 2019. https://www.who.int/publications/i/item/WHO-EMP-IAU-2018.01.

37 James R, Nakamachi Y, Morris A *et al*. The feasibility and generalizability of assessing the appropriateness of antimicrobial prescribing in hospitals: a review of the Australian National Antimicrobial Prescribing Survey. *JAC Antimicrob Resist* 2022; **4**: dlac012. https://doi.org/10.1093/jacamr/dlac012

38 Royal Melbourne Hospital and the National Centre for Antimicrobial Stewardship. *National Antimicrobial Prescribing Survey: Technical Supplement 2022*. NCAS, 2024.

39 Ierano C, Nankervis JM, James R *et al*. Surgical antimicrobial prophylaxis. *Aust Prescr* 2017; **40**: 225–9. https://doi.org/10.18773/austprescr.2017.073

40 WHO. Antibiotic Guidelines: Hospital Nacional Guido Valadares, Timor-Leste 2016, 1st edn. 2016. https://extranet.who.int/uhcpartnership/sites/default/files/reports/Timor-Leste-Antibiotic-Guidelines.pdf.

41 Versporten A, Zarb P, Caniaux I *et al*. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey. *Lancet Glob Health* 2018; **6**: e619–29. https://doi.org/10.1016/S2214-109X(18)30186-4

42 Ravi N, Laha A, Hmar L *et al*. Exploring the prescribing behaviours and the mind of antibiotic prescribers is critical for a successful antibiotic stewardship programme: results of a survey from Eastern India. *Indian J Med Microbiol* 2017; **35**: 299–301. https://doi.org/10.4103/ijmm.IJMM_17_133

43 Limato R, Nelwan EJ, Mudia M *et al*. A multicentre point prevalence survey of patterns and quality of antibiotic prescribing in Indonesian hospitals. *JAC Antimicrob Resist* 2021; **3**: dlab047. https://doi.org/10.1093/jacamr/dlab047

44 Bucens IK, Reid A, Barreto AC *et al*. Three years of paediatric morbidity and mortality at the National Hospital in Dili, East Timor. *J Paediatr Child Health* 2013; **49**: 1004–9. https://doi.org/10.1111/jpc.12305

45 Sarmento N, Soares da Silva E, Barreto I *et al*. The COVID-19 laboratory response in Timor-Leste; a story of collaboration. *Lancet Reg Health Southeast Asia* 2023; **11**: 100150. https://doi.org/10.1016/j.lansea.2023.100150

46 Oakley T, Le B, da Conceicao V *et al*. Gastrointestinal carriage of antimicrobial resistance in school-aged children in three municipalities of Timor-Leste. *Antibiotics (Basel)* 2022; **11**: 1262. https://doi.org/10.3390/antibiotics11091262

47 Joyce J, Langsjoen J, Sharadin C *et al*. Inappropriate use of antibiotics in patients undergoing gynecologic surgery. *Proc (Bayl Univ Med Cent)* 2017; **30**: 30–2. https://doi.org/10.1080/08998280.2017.11929518

48 Kaya S, Aktas S, Senbayrak S *et al*. An evaluation of surgical prophylaxis procedures in Turkey: a multi-center point prevalence study. *Eurasian J Med* 2016; **48**: 24–8. https://doi.org/10.5152/eurasianjmed.2015.15222

49 Rickard J, Beilman G, Forrester J *et al*. Surgical infections in low- and middle-income countries: a global assessment of the burden and management needs. *Surg Infect (Larchmt)* 2020; **21**: 478–94. https://doi.org/10.1089/sur.2019.142

50 Graham WJ, Morrison E, Dancer S *et al*. What are the threats from antimicrobial resistance for maternity units in low- and middle-income countries? *Glob Health Action* 2016; **9**: 33381. https://doi.org/10.3402/gha.v9.33381

51 WHO. WHO Recommendations for Prevention and Treatment of Maternal Peripartum Infections. 2015. https://www.who.int/publications/i/item/9789241549363.