Antimicrobials in serious illness and end-of-life care: lifting the veil of silence

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Global rates of antimicrobial consumption increased by 65% between 2000 and 2015, by 16% between 2016 and 2023, and are estimated to increase by an additional 52% by 2030. Antimicrobial use and misuse remains high among people with serious illness and at end of life, despite scarce evidence of benefit. In addition, the overuse and misuse of antimicrobials at end of life further exacerbate antimicrobial resistance, which is a substantial public and global health concern. This Personal View synthesises global interprofessional and multidisciplinary perspectives on antimicrobial use, stewardship, and resistance at end of life and implications at patient and population levels. Guidelines have been summarised from multiple countries, some of which offer guidance for antimicrobial use at end of life. Countries at different income levels are included (ie, Chile, Colombia, Germany, India, Malaysia, Nigeria, Rwanda, and Sudan) to show how practice norms and standards vary internationally. These examples are combined with a case of non-beneficial end-of-life antimicrobial use and clinical guidance for patient and family communication regarding antimicrobial treatment. This Personal View also provides recommendations to improve antimicrobial stewardship with the goal of engaging multidisciplinary stakeholders and decreasing inappropriate antimicrobial use at end of life.

Introduction

Global rates of antimicrobial consumption increased by 65% between 2000 and 2015, primarily in high-income countries (HICs) but with similar trends in low-income and middle-income countries (LMICs).[1] Across 67 countries, antimicrobial consumption increased from 29·5 to 34·3 billion defined daily doses from 2016 to 2023, and is expected to increase to 75·1 billion defined daily doses by 2030.[2] The COVID-19 pandemic confounded antimicrobial use in the context of a global public health emergency response. According to WHO, an estimated 8% of patients who had been hospitalised with COVID-19 were positive for bacterial co-infections that required antibiotics, but around 75% received precautionary antimicrobial therapy.[3] Antimicrobial use is also common in patients who have serious illnesses (eg, critical illness, advanced dementia, end-organ diseases, advanced cancer).[4] A 12-year retrospective study in South Korea found that people who have serious illnesses are more likely to receive antimicrobials in the last month of life, with high exposure to broad-spectrum antimicrobials.[5] Antimicrobials continue to be prescribed in the last 1–2 weeks of life, ranging from 90% to 96% in patients with terminal illness who have been hospitalised[6] and patients with cancer.[7]

End-of-life antimicrobial use is common in both acute care contexts and outpatient settings, with an estimated 18–52% of patients in hospice and palliative care settings receiving antimicrobials.[8–10] In a retrospective national report from the USA of over 66 000 patients, 9% of patients admitted to hospice had been prescribed at least one antimicrobial (fluoroquinolones were the most common).[11] Another US report (a representative random sample of 892 nursing homes) found that 52·8% of surveyed nursing home residents receiving palliative care were given antimicrobials.[12]

Broad patterns in antimicrobial prescribing can be challenging to characterise in advanced serious illness and end of life due to heterogeneous populations, varying study designs, and inconsistent endpoints.[13] Antimicrobial decision making is further complicated by long-standing challenges with prognostic ambiguity[14–17] across several conditions and diverse definitions of which timeframes and factors could constitute transitional, palliative, or end-of-life care.[18–23] Prescribing decisions are informed by both the high treatability of infectious diseases and variability of infection risk across medical conditions at end of life, and also by clinician knowledge and attitudes, patient signs and symptoms, and health system factors (eg, policies, guidelines, time constraints).[24,25] Moreover, antimicrobial prescription and use is informed by patient and clinician factors, such as cultural or societal norms, mistrust, self-medication, attitudes and fears, traditional or alternative medicine use, inconsistent health-care access, and financial situation.[26–37]

The conditions most commonly treated with antimicrobials at end of life are urinary tract and pulmonary tract infections, which are frequently treated with penicillin derivatives and vancomycin (in hospital), fluoroquinolones (outpatient), and cephalosporins.[38] Antimicrobials are often used at end of life with clincians' assumptions that they will delay the progression of refractory infections, relieve distressing symptoms, prolong life, or are desired by the patient or their caregivers.[4,7,39–43] Although antimicrobials could relieve dysuria from urinary tract infections,[4,44] little evidence supports the role of antimicrobials in alleviating other

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common symptoms.[4–7,11,12,39,42,45–51] Latuga and colleagues reported no difference in the management of terminal delirium when antimicrobials were given for suspected urinary tract infection.[39] Some researchers have suggested that for patients with cancer who transitioned to comfort-focused care from curative care, prescribed antimicrobials could prolong their length of hospital stay.[46]

Antimicrobial use in end-of-life settings can have adverse effects, which range from allergic reactions, mental status changes, gastrointestinal issues, drug–drug interactions, and *Clostridioides difficile* infection to end-organ dysfunction.[4,5,7,11,39–43,50,51] Thompson and colleagues found that of patients with advanced cancer who died in a hospital, 7 of 126 patients (5·6%) who received antimicrobials developed *C difficile* infection.[51] Other potential harms of antimicrobials at end of life include discomfort from evaluative procedures and treatments (ie, blood draws, cultures, catheterisation, intravenous lines); volume overload; protraction of the dying process; and prolonged, frequent, or terminal hospitalisation.[4,7,11,40–43,46,50,51] Unfortunately, patients who receive intravenous antimicrobial treatment at end of life could experience barriers to accessing community-based or hospice services, often due to costs or logistics (eg, patient transport, timely administration, and effective management of adverse effects).[42,50] Overuse or inappropriate selection of antimicrobials at end of life is associated with the development and spread of multidrug-resistant organisms and contributes to rising health-care costs globally.[4,5,7,11,39–43,45,46,49,51] Describing and studying the financial implications of antimicrobial use at end of life is challenging due to limitations in isolating cost and analysis. However, a 2020 report from Türkiye found that antimicrobial use at end of life was associated with increased costs that were related to prolonged hospitalisation.[6] Notably, antimicrobials might be beneficial for symptom control or provision of comfort in selected patients, but should be used only when necessary.

Multiple clinical challenges in prescribing and de-prescribing antimicrobials at end of life exist, including poor evidence-based guidance on antimicrobial stewardship at end of life, inadequate prognostication skills for end of life by health-care professionals, high emotional stakes of patients and families in the end-of-life setting, poor integration of patient and family goals of care in care planning, absence of antimicrobials from end-of-life discussions, lack of generalist clinician (ie, non-infectious disease specialist) knowledge on indications of antimicrobials, and time constraints to effectively individualise antimicrobial use.[7,40,43,45,50,51] Generalist clinicians often rely on infectious disease colleagues to provide expert recommendations on appropriateness of antimicrobial use at the end of life. Infectious disease consultants are often asked to evaluate patients with multiple comorbidities or those with a terminal admission,[48] associated with high emotional exhaustion and burnout among infectious disease specialists.[52] However, these specialists are not available in all settings; for example, in the USA, where infectious disease is an established specialty, over 60% of US counties do not have an infectious disease specialist.[53] Palliative care specialists also frequently prescribe or maintain antimicrobials during end-of-life care,[13] which is a reminder that cross-team collaboration and involvement of all clinical partners is key to promoting person-centred care without unnecessary antimicrobial use.

Given the challenges of conducting rigorous research in terminally ill patients on perceived symptom benefits or the direct and short-term harms of antimicrobial use at end of life,[51] we urge the international infectious disease community to actively integrate discussion on antimicrobial use into clinicians' communications with patients and their family throughout the serious illness trajectory across practice settings. By synthesising evidence on how antimicrobial use at end of life contributes to antimicrobial resistance (AMR) and offering a global, interprofessional, and multidisciplinary perspective of current guidelines and clinical practice norms from a range of countries, we identify key gaps that deserve urgent attention. We subsequently provide a case study of non-beneficial and potentially harmful antimicrobial use in a patient requiring complex acute care at end of life, revisit the case through the lens of missed communication opportunities, and offer communication strategies to navigate goals of care conversations and difficult scenarios for infectious disease specialists and other collaborating clinicians to use independently and in collaboration with primary teams and palliative specialists.

Antimicrobial stewardship and resistance

According to the UN Food and Agriculture Organization, effective antimicrobial stewardship is dependent on four pillars: (1) awareness of all stakeholders; (2) local and global governance; (3) clinical and production practices; and (4) surveillance.[54] Globally, antimicrobial stewardship has numerous benefits on clinical, performance, and economic measures including appropriateness of antibiotic prescribing and reductions in antimicrobial consumption, length of hospital stay, mortality, and overall antimicrobial-related costs.[55–58] Various approaches to stewardship have proven effective at improving outcomes, such as pharmacist-led and telehealth-delivered models.[59–62] The implementation of antimicrobial stewardship programmes (ASPs) in LMICs is hindered by human resource shortages and insufficient microbiology laboratories, leadership, and government support.[56,63] Conversely, ASP implementation in LMICs can be facilitated by readily available antibiotic guidelines, ASP protocols, dedicated multidisciplinary ASP staff, and timely laboratory support.[56] Although there are clear

benefits to ASP, a focus on standardised infection control and antimicrobial monitoring protocols for patients at the end of life could prevent clinicians from individualising care needs and optimally providing comfort-focused care, which is a common goal for patients at end of life.

A public and global health concern,[64,65] AMR is the point at which bacteria, fungi, viruses, and parasites no longer respond to some or all antimicrobial medications.[66] Costs from antimicrobial use at the end of life contribute to the estimated US$100–210 trillion global economic burden of AMR.[67] An estimated 4·95 million deaths were associated with bacterial AMR in 2019, with higher incidences in LMICs,[68] and 2024 estimates predict 10·13 million deaths attributable to or associated with AMR in 2050.[69] An estimated 92 million deaths associated with AMR could be avoided cumulatively between 2025 and 2050 by improved antimicrobial stewardship.[69] Despite the global focus on rising AMR in both HICs and LMICs across people's life course and in animals, there is little attention on how the use of antimicrobials in advanced serious illness and at the end of life contributes to AMR.[68]

In 2015, WHO established the Global Antimicrobial Resistance and Use Surveillance System as a standard for AMR assessment and management.[70] Using a One Health model, the programme evolved from monitoring only bacterial infections in humans to full scope surveillance of antimicrobials, and has recruited 127 countries as of 2022. Also in 2015, WHO member states launched the Global Action Plan to tackle AMR with the goal of assuring the long-term, safe, equitable, and effective management of infectious diseases.[71]

WHO and other organisations have collaborated to support countries in implementing their own national action plans to combat AMR. As of 2024, 84% of UN member states have provided annual information on the implementation of their multisectoral AMR national action plans and activities across all relevant sectors.[72] Patel and colleagues conducted a separate analysis of the national action plans of 114 different countries by searching for language on AMR, and found great variability in efforts to address AMR.[71] Norway had the highest governance score and the Federated States of Micronesia had the lowest score.[71] In 2023, WHO published the first global research agenda for AMR in human health, which provides 40 priorities in 11 AMR areas across five themes: (1) prevention; (2) diagnosis; (3) treatment and care; (4) crosscutting; and (5) drug-resistant tuberculosis.[73] Although the themes of the research agenda are universal, different countries and contexts have unique priorities. For instance, self-medication without prescription in LMICs is common, and should be tackled in conjunction with clinical practice changes to effectively reduce AMR.[74] In addition, many vulnerable populations, such as refugees and asylum seekers (particularly those in overcrowded living conditions and lacking access to health services and vaccines), have an increased risk for AMR carriage and infection.[75]

In 2024, *The Lancet* published a Series that highlighted AMR as a key public health threat.[76] The Series papers ranged in scope and address the global impact of AMR,[77] provide evidence-based recommendations for high-yield interventions to reduce preventable AMR-associated deaths in LMICs,[78] examine factors associated with inequitable antimicrobial access,[79] and propose recommendations for the UN General Assembly to achieve globally sustainable access to antimicrobials.[80] Despite acknowledging AMR-associated mortality is higher in sub-Saharan countries than in HICs,[80] the Series did not address antimicrobial stewardship among patients at the end of life, how antimicrobial use in this population contributes to AMR, or how recommended confirmatory testing might be overly burdensome for people with a serious or terminal illness.

Guidelines and practice norms

The global community should set broad clinical practice guidelines on end-of-life antimicrobial use that can be applied across international settings. Although more is known about end-of-life antimicrobial use in HICs, monitoring antimicrobial prescribing is more challenging in LMICs. In many settings, paper medical records are used, and medications can be collected without a prescription.

Collaboration between infectious disease and palliative care specialists, ASPs, primary care clinicians, patients, and their families is necessary when considering prescribing or de-prescribing antimicrobial therapy for patients who are at the end of life.[4,5,40,41,43,46,48,50,51] Yet end-of-life antimicrobial use is rarely addressed in international infectious disease guidelines. We have summarised nine different international guidelines (using the European Centre for Disease Prevention and Control as an example and guide)[81] relating to antimicrobial use, mention of end of life, and opportunities for inclusion of related serious illness and end-of-life language (table).

Antimicrobial use at end of life globally

We present a globally diverse collection of examples to highlight the universality of antimicrobial use and risks at end of life. Interprofessional and multidisciplinary clinicians and researchers in both palliative care and infectious disease have provided examples from Rwanda and Sudan (low-income countries), India and Nigeria (lower-middle-income countries), Colombia and Malaysia (upper-middle-income countries), and Chile and Germany (HICs). Although these examples provide a broad range of perspectives they are limited in scope and are not exhaustive regarding end-of-life antimicrobial use decisions.

There is substantial variation across countries on whether antimicrobials are considered life-sustaining

For more on **Choosing Wisely Australia** see https://www.choosingwisely.org.au/

For more on **Firstline** see https://firstline.org/canada/

For more on **Treatment Guidelines for Antimicrobial Use in Common Syndromes** see https://amrtg.icmr.org.in/

treatments and if withholding or withdrawing them is legally permissible. Clinicians in most of the included countries make joint end-of-life antimicrobial prescribing decisions with their patients. Some countries lack precise legislation, relying on physician expertise or a patient's ability to pay for antimicrobials (ie, Nigeria, Rwanda, and Sudan). In Chile and Colombia, there are no legal restrictions to withholding or withdrawing treatments if misaligned with established clinical goals. In India, antimicrobials are generally not considered life-sustaining and can be legally withdrawn in end-of-life scenarios. In Germany, if the treatment goal is survival then antimicrobials would be considered life-sustaining. Life-sustaining interventions in Germany have to be withheld or withdrawn if the patient (or their surrogate or advanced directive) does not provide informed consent, if the patient withdraws their consent, or if the physician no longer sees a medical indication for the intervention. In

	Mention of end of life	Summary of contributions	Opportunities to inform end-of-life care
Antimicrobial Stewardship (Australia; 2021)[82]	No	Database of various antimicrobial management guidelines and links to prescribing support and resources; the Australian Government has issued guidance on how clinicians can approach antimicrobial stewardship, which includes using best practice standards on drug selection, length of therapy, delayed prescribing when appropriate (eg, respiratory infections), and shared decision making in which the clinician discusses options, harms, and benefits, and helps guide the decision in the context of the patient's values, preferences, and circumstances	Specific recommendations on stewardship at the end of life can be incorporated directly in this guideline, and specific recommendations for end-of-life antimicrobial prescribing can be provided in the nation's Choosing Wisely Australia programme (initiative to improve health-care quality and safety)
Pan Canadian Action Plan on AMR (Canada; 2023–27)[83]	No	5-year plan to combat AMR compiled into 10 priority actions across 5 pillars; pillar 3 plans to accomplish improved antimicrobial stewardship goals via awareness or education campaigns, feedback mechanisms, and policy and regulatory initiatives; Canada uses Firstline (ie, clinical decision support platform for clinicians) to access WHO's AWaRe system and antimicrobial book at the point of care[84]	Efforts to bolster stewardship and combat AMR cannot be achieved without acknowledging all phases of illness, including advanced serious illness and end of life; action plans should make these efforts explicit
EU Guidelines for the Prudent Use of Antimicrobials in Human Health (EU; 2017)[85]	No	Provides an extensive guide on multistakeholder roles in reducing AMR; clinicians should advise the patient on their expected prognosis, the low or absent benefit of antimicrobials, adverse effects, symptom management recommendations, and guidance on action steps if clinical condition worsens and antimicrobials are inappropriate; this recommendation is also paired with the need to counsel patients and caregivers on expectations of therapy; in section 4·7, the guideline mentions that nurses can advocate for patients by reminding the clinician to review antimicrobial prescriptions within 48–72 h of therapy	Although the guidelines do not explicitly mention end of life, there are mentions of counselling on expectations and continuous re-assessment of appropriateness; these recommendations could be useful in conversations on goals of care at the end of life; mention of criteria for cessation of therapy in those who are either not responding or at the end of life could be added
National Strategy for Preventing Infections and Antibiotic Resistance (France; 2022–25)[86]	No	Aims to prevent AMR, elevate infection prevention measures, limit and ration the use of antimicrobials with specific evidence-based interventions, and promote appropriate prescribing for bacterial infections are presented using priority areas; 9 priorities range from public awareness to research; provides details on approaches to meet target data points in 2025	The scope of this guideline makes it ideal to include information on antimicrobial use in end-of-life care, especially in sections about evidenced-based use of antimicrobials, stewardship approaches, and AMR
Guideline from the German Society for Infectious Disease on Strategies to Enhance Rational Use of Antibiotics in Hospital (Germany and Austria; 2016)[87]	No	Provides recommendations and elements of stewardship programmes to promote the well-informed use of antimicrobials and reduce AMR; antimicrobial consumption is mentioned as an important outcome measure despite absence of EOL reference	Recommended education and training could include guidance on end-of-life antimicrobial use; section 2·3 (conducting proactive audits of anti-infective use) could include ASP members providing guidance on antimicrobial use at the end of life; section 2·4 (quality indicators) can include monitoring if antimicrobials are initiated in patients who are receiving end of life care and reasons for use
Treatment Guidelines for Antimicrobial Use in Common Syndromes (India; 2019)	No	Provides evidence-based treatment guidelines for common syndromes in an attempt to reduce AMR; no mention of approach to antimicrobial management at the end of life	There are opportunities in at least 2 sections to include mentions of stewardship approaches at end of life (eg, general guidance and care of immunocompromised individuals)
The Practical Guide to Antimicrobial Stewardship (Netherlands; 2018)[88]	No	Intended for hospital use in setting up an antimicrobial stewardship programme; highlights the need to monitor antimicrobials in hospitalised patients with computerised alerts or interprofessional consultation	Mention of approaches to stewardship at the end of life is key, including how programmes can align with non-infectious disease specialists to reach shared goals
Good Practice Recommendations for Use of Antibiotics Towards the End of Life (Scotland; 2023)[89]	Yes	Emphasises having discussions that clearly outline goals and limits of antimicrobial therapy; highlights that clinicians do not have to treat infection with antimicrobials if symptoms are not present but if they are to be considered there should discussion about risks and adverse effects, such as AMR; if symptoms are present, these can be treated aggressively without antimicrobials and clinicians should consider referral to palliative care;[90] refers to the 2020 Scottish Palliative Care Guidelines	This guideline shares specific end-of-life language and can be a model for other national policies; cites 2 scientific articles used to develop and support recommendations (ie, systematic review and qualitative study)
Guidelines on Implementation of the Antimicrobial Strategy in South Africa: One Health Approach and Governance (South Africa; 2017)[91]	No	Focuses on antimicrobial prescribing to curb AMR using 4 strategic pillars (legislation, education, communication, and research); reviews national and provincial governance structures and their roles in implementing standards to reduce AMR, focusing on organisational and systems processes	Several opportunities to incorporate language on serious illness, palliative care, and end of life in the tables and appendices; appendix D provides recommendations for monitoring antimicrobial consumption in which there is an opportunity to include language on the need to monitor potentially inappropriate antimicrobial use at the end of life

(Table continues on next page)

	Mention of end of life	Summary of contributions	Opportunities to inform end-of-life care
(Continued from previous page)			
National Plan against Antibiotic Resistance: Programmes for optimising the use of antibiotics (Spain; 2017)[92]	No	This document is in Spanish and none of the following terms were found: *final de la vida, enfermedad grave, paliativa,* or *paliativo*	Omitting end-of-life care in AMR programmes omits a key group of patients who benefit from strategic and nationally and institutionally supported antimicrobial stewardship
National Institute for Health and Care Excellence Guideline on Antimicrobial Stewardship: Changing Risk-Related Behaviours in the General Population (UK; 2017)[93]	No	Offers systems-based approaches to reducing inappropriate antimicrobial requests and prescribing; provides recommendations for prescribers, primary care, and community pharmacy teams with an emphasis on community care rather than acute or hospital care	There is ample opportunity to describe stewardship approaches in all phases of illness, especially at the end of life; guideline targets various stakeholders who could benefit from education about antimicrobial use at end of life and interdisciplinary approaches to mitigating inappropriate prescribing
Infectious Diseases Society of America and Society for Healthcare Epidemiology of America Clinical Practice Guidelines for Implementing an Antibiotic Stewardship Program (USA; 2016)[94]	Yes	Recommends that antibiotic stewardship programmes are used to provide clinical decisional support on whether antimicrobials should be used at the end of life (1 of 28 recommendations); comments on the challenges of when to use antimicrobials in patients who are immunocompromised, such as people living with cancer;[94] highlights that antimicrobials should be considered "aggressive care",[94] mostly due to the potential for adverse effects	End-of-life care language could be strengthened to define when antimicrobials should be withheld or withdrawn in the care of patients who are dying; provides an evidence summary for each recommendation, citing 20 articles from the literature review, which includes randomised controlled trials, meta-analyses, qualitative studies, prospective designs, and retrospective reviews

AMR=antimicrobial resistance.

Table: **Summary of international antimicrobial guidelines and opportunities for inclusion of serious illness and end-of-life language**

Malaysia, where much of the population are Muslim, there are no current legal frameworks that explicitly address withholding or discontinuing life-sustaining treatments in adults, including antimicrobials, but several state-level fatwas (legal rulings on points of Islamic law issued by religious authorities) address the issue. Decisions in Malaysia would therefore be based on clinical practice guidelines; discussions between clinicians, patients, and their families; and corresponding fatwas.

Low-income country examples

Rwanda

Despite policies, drug availability, education, and research advancements, palliative care remains a largely new field in Rwandan health care.[95–97] In clinical settings, antimicrobials are widely prescribed for managing infectious diseases,[98] yet no national protocol exists for antimicrobial use in patients who are receiving end-of-life care.

The Rwandan public health system is decentralised and pyramid-structured from teaching hospitals to community levels.[55] Although traditionally, physicians at hospitals handle most prescriptions, the task-shifting programme[99] introduced in the past decade has caused a notable shift, empowering nurses,[100] clinical officers, and community health workers to prescribe antimicrobials.[101]

Antimicrobial use at end of life remains common. Clinicians often regard such treatments (including antimicrobials) as a means to alleviate the psychological distress of families, who might incorrectly perceive discontinuing antimicrobials as stopping life-prolonging treatment. There is an urgent need for research and the development of protocols in Rwanda to prevent the misuse of antimicrobials in end-of-life care.

Sudan

Sudan has several policies and regulations guiding the rationed use of antimicrobials and follows WHO guidelines on AMR.[102] Sudan's health-care system faces many challenges, which results in a high reliance on antimicrobial use for treating common infections in patients with terminal illness, such as an absence of clear practice guidelines, education, and training in the proper use of antimicrobials at end of life, the increased empirical use of antimicrobials due to poor infection control resources, and the low access to palliative care services that could otherwise provide holistic and multimodal symptom management.[102–104] Patients and their families often misunderstand that expensive medications are effective ones; trained clinicians have to frequently educate their colleagues, patients, and the patients' families to understand that this is not the case.

In Sudan, cultural and religious norms, coupled with familial dynamics, contribute to the reluctance to discuss end-of-life issues, leading to the continued use of antimicrobials even when not medically necessary. The belief in divine intervention and the stigma around death can prevent open discussions, and families can pressure clinicians to maintain curative treatments. Additionally, health-care professionals might avoid conversations about treatment futility. This practice contributes to the growing issue of AMR in the country.[102,105]

Lower-middle-income country examples

India

INDICAPS II, a multicentre study of 5222 patients from 141 intensive care units in India (data analysed for 4669 patients age 16 years or older from 132 ICUs), reported no difference in mortality between ICU survivors and non-survivors who received four or more antimicrobials in a critical care setting.[106] Factors such as cancer diagnosis, end-stage organ impairment, multiple dependencies on others to complete activities of daily living, overall poor health status, and advanced age are linked to increased sepsis-associated mortality.[107] In a study of a palliative care setting in India, 19% of patients had been administered antimicrobials in the final 2 weeks of their lives, and the intravenous route was more prevalent than the oral route.[108] Patients at high risk for developing bacterial infections are often immunocompromised, frequently visited hospitals, and had previously received antimicrobials, and were at high risk of being colonised with or having drug-resistant infections.[109] In India, infections with carbapenem-resistant Enterobacteriaceae, carbapenem-resistant *Pseudomonas aeruginosa*, and carbapenem-resistant *Acinetobacter baumannii* are common among patients who have been hospitalised.[110,111] Although the Indian Council of Medical Research has provided guidelines for treating drug-resistant infections using reserved antimicrobials, there are no specific guidelines for antimicrobial prescription at end of life.[112] A retrospective study showed that palliative care consults, regardless of affordability, were associated with fewer antibiotics at the end of life and minimum use of reserve antibiotics.[113] Therefore, weighing the benefits versus harm and making clinically informed choices regarding antimicrobials at end of life is an essential area of inquiry that requires focus in India.[112]

Nigeria

Insufficient knowledge and ineffective health insurance limit the provision of palliative care in Nigeria.[114,115] In 2017, a National Action Plan on AMR was developed,[116] with concerted efforts made to establish antimicrobial stewardship in some tertiary hospitals.[117] However, with gaps in implementation, the core elements of the ASP at the national government level were ranked intermediate by researchers using a WHO antimicrobial stewardship assessment tool.[118,119] There are no national guidelines and policies on the management of individual infectious disease syndromes, including antimicrobial use in patients at end of life, except for the Nigerian Essential Medicines List.[120]

Infections at end of life are managed by the attending physicians or surgeons. Infectious disease specialists are only involved when there is no improvement in the patient's condition. Antimicrobial use is at the doctor's discretion in end-of-life cases and is largely empirical, without referring to microbiological investigations.[121] The decision to initiate or progress with antimicrobial use is based on what the patient can afford. Treatment goals are rarely discussed in end-of-life cases and are often not chosen by most patients and their families when discussed, largely due to religious and cultural beliefs.[114] There are no published data on antimicrobial use in end-of-life care in Nigeria. Antimicrobials are largely overprescribed at all care levels,[121,122] and possibly more in patients at the end of life, despite no evidence of benefit.

Upper-middle-income country examples

Colombia

In Colombia, recent efforts have focused on developing and updating clinical practice guidelines for managing infectious diseases, including urinary tract infections,[123] community-acquired pneumonia,[124] skin and soft tissue infections,[125] and opportunistic infections in patients with HIV.[126,127] These guidelines have progressively been integrated into ASPs across Colombia's six major cities.[128,129] However, there is currently no standardised protocol for antimicrobial use in patients who are nearing the end of life.

In institutions with established ASPs and active monitoring by infectious disease specialists or palliative care physicians, decisions to initiate or continue antimicrobials for patients receiving palliative care are tailored according to therapeutic goals and the potential to alleviate symptoms linked to infection.[130] This approach carefully balances the risks and adverse effects of these treatments, but decision making relies heavily on specialists who are concentrated in major cities, which leads to a shortage of personnel and a lack of technology-assisted solutions to support other clinicians. As a result, in primary care settings, emergency departments, rural hospitals, and the remaining 26 regions of the country, antimicrobials are often overprescribed due to unclear therapeutic goals or poor understanding of the benefits—or lack thereof—for this patient population.[131]

Malaysia

The Malaysian Ministry of Health issues and continuously updates guidelines on the rational use of antimicrobials. These include the National Antibiotic Guidelines, consensus guidelines on the treatment of multidrug-resistant organisms, and infection prevention and control guidance, including guidance on vaccination.[132,133] Health facilities widely adopt these guidelines and, when necessary, make local adaptations based on the practical needs of specific health facilities. Since 2014, the Ministry of Health has developed a national antimicrobial stewardship protocol to promote the implementation of stewardship activities across all health-care facilities.[134] This protocol outlines multiple strategies, including the de-escalation of antimicrobials and the use of multidisciplinary antimicrobial stewardship clinical rounds. Health facilities seeking accreditation from the Malaysian Society for Quality in Health have to show that these strategies have been

Panel: **Composite case and response focused on opportunities to improve care**

Composite case: Mrs B

Mrs B is an Arabic-speaking woman aged 53 years with a medical history of hypertension and allergy-induced asthma, who was recently diagnosed with left sarcomatous diffuse pleural mesothelioma. She has dyspnoea and weight loss that have worsened over the past year, and began seeking medical attention about 6 months ago. She and her son, Sa'id (age 20 years), recently immigrated to the USA from Egypt. She has no other family living locally.

Mrs B is admitted to hospital for the fourth time in 6 months with dyspnoea caused by increased abdominal distension and on exertion. Due to transportation issues, she has not received consistent care and has visited three hospitals. During her last hospital admission, she had a pleural catheter placed. She is accompanied by Sa'id. An Arabic-speaking interpreter is used to communicate with the patient and her son during their first visit, but is unavailable for follow-up conversations.

The emergency room (ER) physician consults the palliative care team. Mrs B tells the palliative care consultant that her short-term goal is to be more physically mobile and have improved breathing. She verbalises an understanding of her multiple acute medical issues and says "Allah will save me." She is a Muslim with a strong faith in Allah, and has a supportive relationship with her son.

A rapid response is called in the ER for tachycardia (>190 beats per minute). Mrs B has a penicillin allergy and was started on broad-spectrum antimicrobials for empyema. Her pleural catheter became dislodged during this hospitalisation, and she has developed a new left hydropneumothorax. Mrs B becomes delirious, is placed on high-flow nasal cannula (HFNC), and is prescribed constant intravenous opioids to treat refractory breathlessness unresponsive to the HFNC. Sa'id, who is at her bedside, does not let the nurse administer this opioid prescription, saying that "she doesn't need those. She doesn't have pain."

Cultures collected from the pleural catheter site grew methicillin-resistant *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Stenotrophomonas maltophilia*, and *Finegoldia magna*. As it is unclear whether the pathogens reflect colonisation of the tube, exit site infection, or pleural space infection—and as Mrs B is unable to make additional goals of care clear at this time—the infectious disease consultants recommend continuing vancomycin, meropenem, and co-trimoxazole. Her condition continues to deteriorate and the settings on the HFNC are increased. Sa'id continues to prevent opioid administration. The ethics team is consulted.

Palliative care consultants meet again with both Mrs B and Sa'id. Her son explains that his mother was always very active and says that "this doesn't seem like her". He also says that opioids are not given in Egypt and are "only for those addicted to drugs". The palliative care consultants communicate that Mrs B is dying and, with Mrs B only intermittently alert, ask Sa'id about his mother's end-of-life wishes. He says that he does not want to "give up" but recognises that intubation and cardiopulmonary resuscitative efforts are more likely to hurt than help his mother.

A chaplain consult is requested, and an Imam is able to meet with Mrs B and Sa'id at the bedside. The patient's son explains that the rest of his family is living abroad. He states his family would want her to be home if she is not going to get better. In her current state, she is now dependent on HFNC and unable to be discharged.

Now in a hospice bed on an inpatient floor, Mrs B becomes weaker over the next few days and is unable to participate in conversations. Several goals of care discussions are facilitated by palliative care. The ethics team assists in educating Sa'id on the intent of the opioids, and he allows them to be administered. Antimicrobials continue unquestioned. Mrs B experiences an acute decline in respiratory status. Her son is alone with her at the bedside when she dies.

Case response

This case shows the importance of addressing goals of care (including antimicrobial use and invasive interventions) with patients and their family as early in the treatment course as possible. When discussing the goals of any therapy, considering the patient's overall prognosis (eg, quantity of time, trajectory of their functioning) and patient and family values are imperative. In cases of short prognoses (ie, weeks), there is little evidence that antimicrobials provide a survival benefit. Antimicrobial use at end of life has not consistently shown improvements in symptoms or overall functioning, with some exceptions. Understanding the patient or family's goals, priorities, and values should be weighed against the evidence of benefit from using an antimicrobial and the risk to both the patient and community, regarding worsening antimicrobial resistance.

In this case, Mrs B's goals and priorities are unclear. The team interprets Sa'id's comment on not giving up with an imperative to use life-sustaining treatments regardless of how likely those treatments will be in improving her condition. A person-centred, shared decision-making model that considered cultural factors would explore Mrs B and her family's priorities (eg, increased mobility, improved respiratory function, opioid avoidance, returning home to Egypt, seeing her family, dying without distress, not being a burden to others).

The impact of an interdisciplinary team approach is evident. Infectious disease consultants (for antimicrobial therapy), palliative specialists (to clarify goals of care with Sa'id and prioritise symptom management), chaplain services (to provide spiritual support and ensure ready access to an Imam), and an ethics team (to promote ethically sound care) could collaborate with primary and inpatient teams to promote safe and

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dignified end-of-life services. Clarifying questions and clear communication with an Arabic interpreter would facilitate understanding of how Mrs B, Sa'id, and their family make decisions. Once their priorities have been set, establishing which of these are achievable with existing medical therapies and care delivery models (hospital *vs* home care) can be addressed. Some of Mrs B's goals would not likely be achieved (eg, returning to Egypt), or would be at odds with each other (eg, not receiving opioids and improving her respiratory distress). Once Mrs B's highest priorities are understood in light of her situation, clinicians could determine which treatment options make sense and provide recommendations. The recommendations should focus on priorities that are compatible with her values and achievable with her prognosis.

In summary, clinicians need to understand their own biases along with the patient's unique goals and priorities by using a shared decision-making model. Clinicians should consider which treatments could provide medical benefit at the end of life and the burdens of each therapy in each situation. In the case of antimicrobials, this consideration should also include the impacts of AMR, which could affect both the patient and future patients in the community. Treatments that are efficacious during the disease trajectory might not have the same benefit at the end of life, especially when considering impact on quality of life, wellbeing, or symptom reduction, which are often the primary goals when meaningful life prolongation (ie, being able to engage fully with people or activities that bring purpose or joy) is no longer achievable.

incorporated into their organisations.[135] As such, patients in palliative care units and end-of-life care pathways in health facilities with ASPs are reviewed for appropriate antimicrobial use.

There are little data regarding antimicrobial use at the end of life in Malaysia. However, a 2022 study by Ng and colleagues conducted in a single tertiary hospital in 2019 reported that 74·5% of patients older than 70 years received antimicrobials during their last 24 h of life.[136] Studies have reported that Malaysian patients did not mind receiving antimicrobials at end of life, despite declining other forms of life-prolonging treatment (cardiopulmonary resuscitation, mechanical ventilation, etc).[137,138] In 2024, the Ministry of Health launched the national Advance Care Planning guide, which recommends exploring patients' choices for therapies (including antimicrobials) at the end of life.[139] A nationwide survey in 2022 reported that 86·6% of Malaysians wanted to discuss the use of antimicrobials in their advance care plans, highlighting an opportunity to reduce the inappropriate use of antimicrobials at the end of life.[140]

HIC examples

Chile

In Chile, technical recommendations and guidelines for outpatient antimicrobial use in community-acquired infections,[141] pneumonia,[142] and neutropenic fever[143] exist. National guidelines on stewardship programmes also require hospitals to develop local protocols for antimicrobial use.[144] Although antimicrobial use at end of life is not addressed in these guidelines, the Chilean Technical Guideline[145] on universal palliative care advises to consider using antimicrobials in case of fever or coughing due to an infection and in cases of infected tumoural wounds. DIPRECE guidelines also recommend considering the withdrawal of antimicrobials in the end-of-life context. In a document on end-of-life care from Universidad Católica de Chile, antimicrobial use is recommended when the aim is to provide symptomatic relief, weighing these benefits against side-effects.[146]

For more on **DIPRECE** see https://diprece.minsal.cl/

Practically, antimicrobial use is not considered a specific topic to address in conversations on goals of care. As a general strategy, palliative care specialists help patients and family members identify the main goals of care (eg, to go home or to focus on comfort), and after these goals have been established, the palliative care team organises the implementation of treatments accordingly. In some cases, antimicrobials are initiated to allow discharge for a patient with an infection when the patient's goal is to go home, but are withheld when they do not contribute to improved comfort in other cases. Therefore, the appropriateness of prescribing an antimicrobial is decided by the palliative care team depending on whether antimicrobials contribute to reaching the patient's predetermined goal of care. The paucity of available palliative care specialists in Chile could challenge the ability to expand this approach at the national level. Most palliative care in Chile is provided by general physicians, which could be associated with overuse of antimicrobials during the end of life.[147]

Germany

In Germany, the Robert Koch Institute offers guidance through several standing committees which regularly issue recommendations (eg, on structural requirements for rational antimicrobial use in hospitals).[148] The German Infection Protection Act passed in 2000,[149] which mandated hygiene plans and dedicated hygiene staff, and the surveillance of antimicrobial use for hospitals. Numerous guidelines on antimicrobial therapy have been developed by the German Association of the Scientific Medical Societies, including guidelines on the rational use of antimicrobials in hospitals,[150] sepsis,[151] or community-acquired pneumonia.[152] Postgraduate courses on antimicrobial stewardship have also been introduced, albeit with a focus on non-palliative settings.[153]

For palliative care, the network of comprehensive cancer centres has published a guideline on the

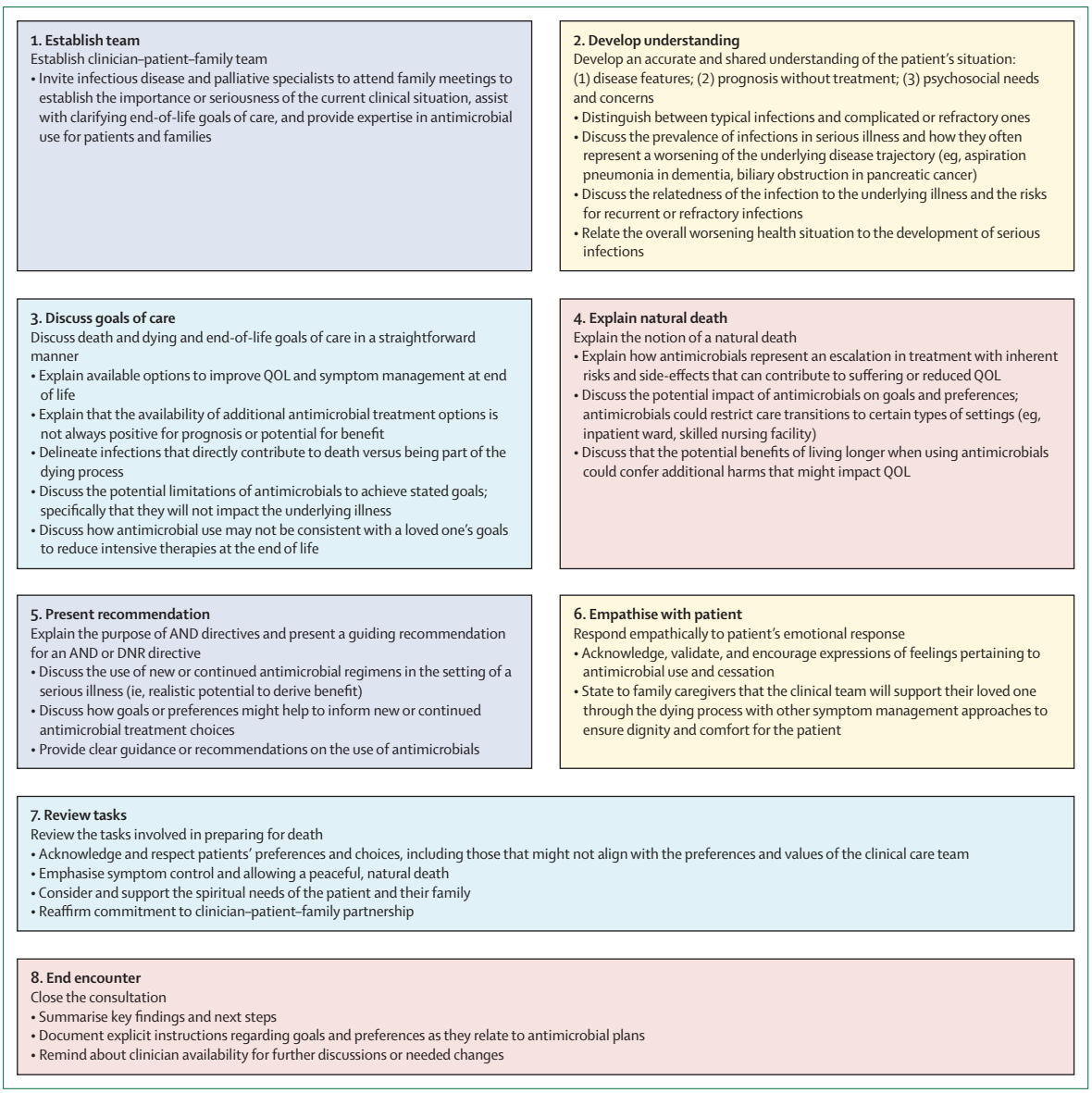

Figure 1: **Communication strategies and skills for antimicrobial treatment discussions at end of life**
QOL=quality of life. AND=allow for natural death. DNR=do not resuscitate. Adapted from Coyle and colleagues.[157]

treatment of multidrug-resistant pathogens in palliative care,[154] focusing on the balance between protective measures and maintenance of social contacts. A nationwide survey on the use of antimicrobials in palliative care found that a third of patients' antimicrobials were withdrawn due to deterioration of general status, inefficiency, or at the patient's explicit request.[155] Physicians sought the involvement of other team members in the decision-making process more often for withholding antimicrobials than for initiating antimicrobials. Recently, some templates for advance care planning have included preferences for antimicrobial therapy, such as those from the Federal Ministry of Justice.[156]

Role of palliative care and goals of care conversations

As the table and global example summaries show, there is an absence of guidance on antimicrobial prescribing at end of life. Educating clinicians, patients, and families on the risks and benefits of antimicrobials at the end of life and setting clear expectations are consistent recommendations for clinicians when considering prescribing antimicrobials at the end of life.[7,12,40,41,45,50] Antimicrobial therapy is often absent from advance care planning conversations, leading to uncertainty among clinicians, patients, and families, but clarifying patient goals in these conversations could be helpful in guiding the appropriate use of antimicrobial therapy.[4,5,11,12,40,42,43,49,50] In

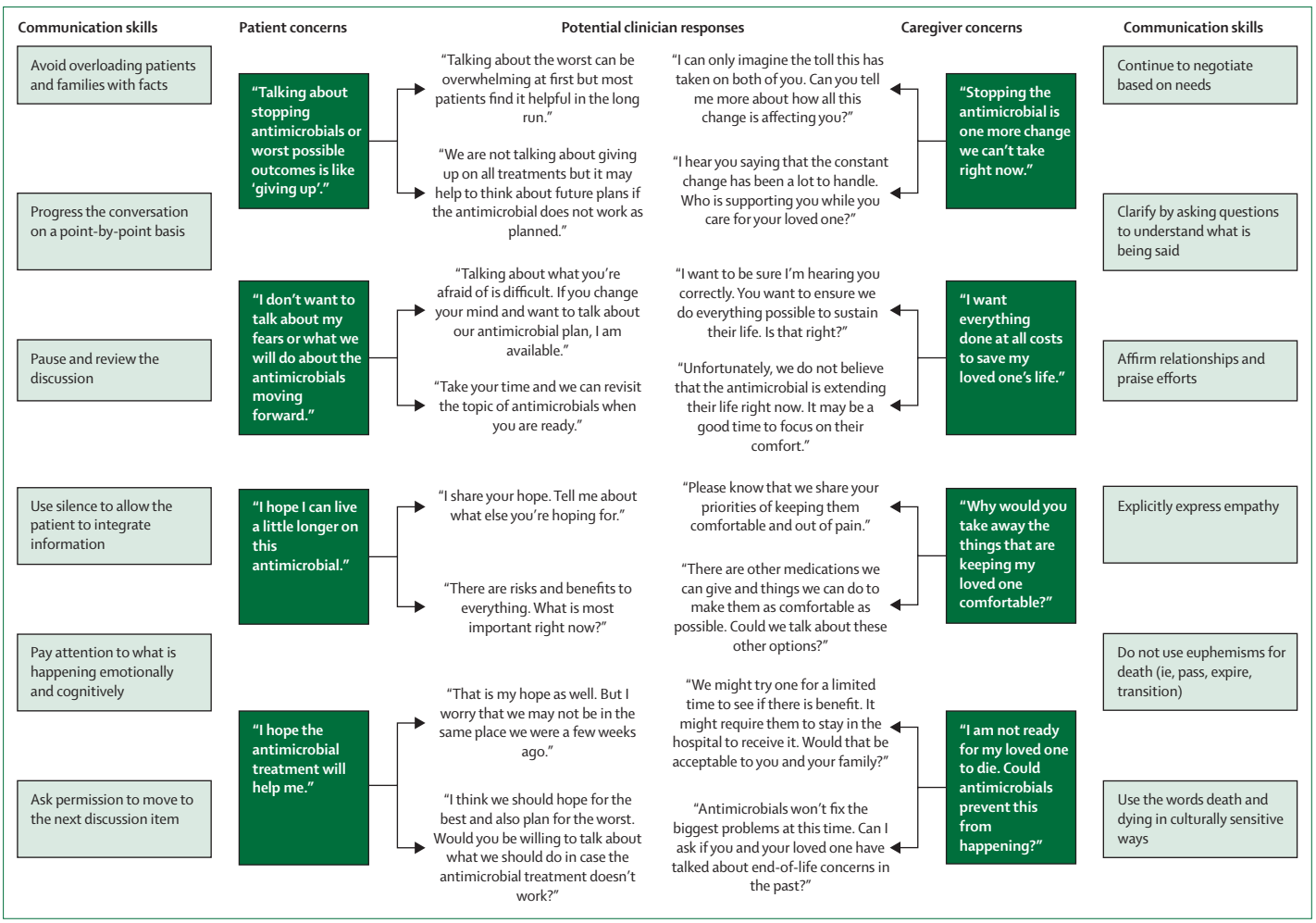

Figure 2: **Patient and caregiver concerns with potential clinician responses and additional communication skills**
Adapted from Brown and Bylund[170] and Arnold and colleagues.[171]

clinically uncertain situations, the use of time-limited trials for short-term antimicrobial therapy could be a useful strategy.[39,50] The primary goal of time-limited trials has to be defined in advance, and in most cases will be alleviation of pain, breathlessness, or other symptoms caused by the infection, or even short-term survival or functional improvement if this is aligned with the personal values of the patient. We provide a composite case of non-beneficial and potentially harmful antimicrobial use at the end of life (panel) with an analysis of missed opportunities to reconsider antimicrobial prescribing, and a summary of communication strategies and skills that can assist clinicians in addressing antimicrobial use in the end-of-life context more effectively.

Communication strategies surrounding antimicrobial treatment at end of life

A key element of serious illness and end-of-life care delivery is communication, which should include discussion on antimicrobial treatment in the end-of-life context. Communication needs to be person-centred, but eliciting and acting upon patients' values at the end of life can be challenging. Therefore, communication on the roles and indications of antimicrobials should be started early in the disease process and ideally in the primary care setting (if available) to ensure shared decision making that reflects the patient's values and goals. Infections are usually curable, and discussions surrounding the withdrawal of antimicrobial treatment can foster confusion or mistrust. In people who are critically ill particularly, source control might not be possible and refractory or recurrent infections are commonplace. We have provided a series of communication strategies and skills to address antimicrobial use at the end of life (figure 1). These strategies are not necessarily linear and should be adapted for the clinician, patient, and context.

Communication and corresponding strategies should be informed by cultural humility,[158,159] and recognise

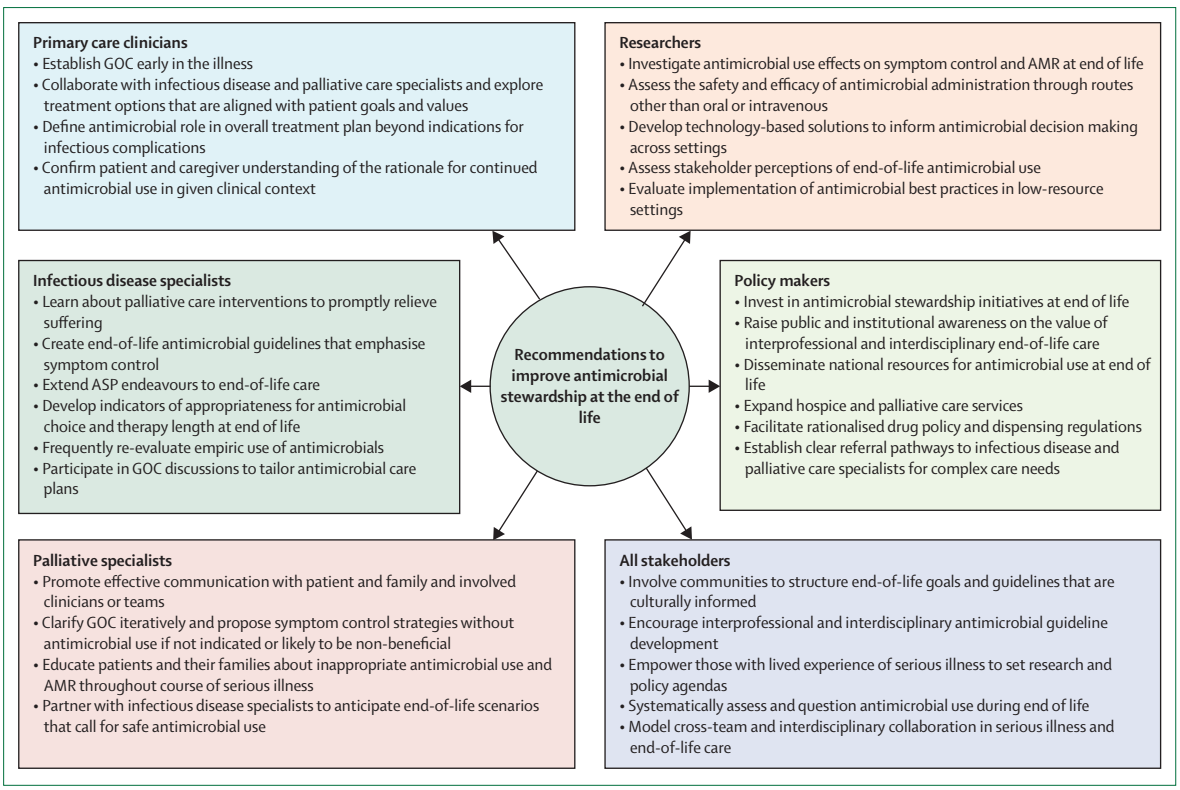

Figure 3: **Diverse stakeholder recommendations to improve antimicrobial stewardship at end of life**
AMR=antimicrobial resistance. ASP=antimicrobial stewardship programme. GOC=goals of care.

differing approaches to end of life, and the patient and their families' wide-ranging goals and values throughout serious illness and near the time of death.[160–166] End-of-life care is characterised by varied human identities, behaviours, societal norms, and countless microcultures among patients, clinicians, health systems, and institutions.[167,168] For example, hierarchies exist within health care across professions and levels of seniority, which can influence antibiotic use and prescribing, despite evidence-based recommendations.[167,168] Clinicians need to understand the thought process and beliefs of prescribers and understand the language of risk that will best resonate with a given target audience when having goals of care conversations. Clinicians should also identify what risks and outcomes matter to their colleagues and the patient and their family, and how the threat of AMR can influence these risks and outcomes.[167,168] Conversations should start with clinicians understanding their own professional and personal bias and seeking to understand, educate, and ally with patients and families to ensure collaborative, person-centred care. The volume of conversations in clinical patient settings about antimicrobial use and de-prescribing at end of life is often low or absent, especially when topics that are perceived to be more important (such as code status and suffering) have yet to be addressed. The Wellcome Trust report on Reframing Resistance identifies five universal principles that could be effective across cultures and countries: (1) frame drug-resistant infections as undermining modern medicine; (2) explain the fundamentals of AMR succinctly; (3) emphasise that this is a universal issue that affects everyone; (4) focus on the present; and (5) encourage immediate action.[169]

Some strategies for clinicians to better integrate person-centred antimicrobial therapy can include discussing how infections can be a common cause of death and often coincide with chronic underlying illness at the end of life (such as pneumonia in chronic obstructive pulmonary disease). Emphasising that infections are a common part of the dying process might help patients to reconcile with the potential futility of further antimicrobial treatment. Perhaps most crucially, focusing on the potential drawbacks of antimicrobials (physical adverse effects [eg, nausea, *C difficile* infection, and diarrhoea], psychological sequelae [eg, delirium], and quality-of-life decrements [eg, permanent intravenous access]) could help to improve patients' and their families' understanding of the potential drawbacks of antimicrobial treatment that could be potentially harmful, futile, or inappropriate. Additionally, antimicrobials administered intravenously could limit care provision to acute care settings, which might not be consistent with patients' goals and preferences.

Throughout serious illness and end of life, patients and their family caregivers often verbalise a wide array of concerns. Some of these concerns are outlined (figure 2), accompanied by potential clinician responses and additional communication skills that can be used during clinical encounters.

Conclusions

Poor antimicrobial stewardship and AMR are urgent and global public health crises that continue to grow. AMR is a substantial concern when treating patients with antimicrobials at end of life, as these treatments frequently prove ineffective. This situation has important implications for both patients' and their families' quality of life, and public health more broadly. Examples, both globally and by income level, illustrate the heterogeneity in antimicrobial use at end of life, and in some cases, the lack of national recommendations and policies regarding this use. These examples underscore the need for interprofessional and multidisciplinary collaboration, resource allocation, and contextualised global research in the context of person-centred communication that is informed by cultural humility.[158,159] Intentionally and consistently integrating palliative care and infectious disease experts in end-of-life care could facilitate individualised services that are supportive of patients' goals and health-related values.

We have summarised further recommendations for diverse and multidisciplinary stakeholders (figure 3). Antimicrobial stewardship is the responsibility of each person at every stage of the care continuum, especially when caring for patients with serious illness and at the end of life. Consistent antimicrobial stewardship efforts could contribute to more dignified deaths for patients and assist in mitigating AMR on a global scale, thereby reducing costs, conserving human and clinical resources, and focusing care on optimising the wellbeing and symptom control of patients with serious illness and at the end of life.

Contributors

WER conceptualised the manuscript. All authors prepared the original draft and reviewed and edited the final manuscript. All authors had responsibility to submit for publication.

Declaration of interests

CB has received royalties from UpToDate for editorial and reviewer contributions and participates on Tuesday Health's clinical advisory board. LR holds a position as the Chair of Board of Directors for the International Association for Hospice and Palliative Care. KS is a Deputy Treasurer for the Clinical Infectious Diseases Society, India and has received malaria rapid diagnostic tests and Haemozoin test equipment for research purposes from Hemex Health. All other authors declare no competing interests.

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References

1 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 USA* 2018; **115:** E3463–70.

2 Klein EY, Impalli I, Poleon S, et al. Global trends in antibiotic consumption during 2016–2023 and future projections through 2030. *Proc Natl Acad Sci USA* 2024; **121:** e2411919121.

3 WHO. WHO reports widespread overuse of antibiotics in patients hospitalized with COVID-19. 2024. https://www.who.int/news/item/26-04-2024-who-reports-widespread-overuse-of-antibiotics-in-patients--hospitalized-with-covid-19 (accessed Oct 11, 2024).

4 Kang M, Wang WS, Chang Z. Antibiotic use at the end of life: current practice and ways to optimize. *Am J Hosp Palliat Care* 2024; published online July 19. https://doi.org/10.1177/10499091241266986.

5 Kim NH, Han K, Ji E, et al. Trends of antibiotic use at the end-of-life of cancer and non-cancer decedents: a nationwide population-based longitudinal study 2006–2018. *Antimicrob Steward Healthc Epidemiol* 2024; **4:** e83.

6 Dagli O, Tasdemir E, Ulutasdemir N. Palliative care infections and antibiotic cost: a vicious circle. *Aging Male* 2020; **23:** 98–105.

7 Kwon MK, Jung KH, Choi S, et al. Antibiotics use patterns in end-of-life cancer patients and medical staff's perception of antimicrobial stewardship programs. *Korean J Intern Med* 2023; **38:** 758–68.

8 Marra AR, Clore GS, Balkenende E, et al. Association of entry into hospice or palliative care consultation during acute care hospitalization with subsequent antibiotic utilization. *Clin Microbiol Infect* 2023; **29:** 107.

9 Albrecht JS, McGregor JC, Fromme EK, Bearden DT, Furuno JP. A nationwide analysis of antibiotic use in hospice care in the final week of life. *J Pain Symptom Manage* 2013; **46:** 483–90.

10 Servid SA, Noble BN, Fromme EK, Furuno JP. Clinical intentions of antibiotics prescribed upon discharge to hospice care. *J Am Geriatr Soc* 2018; **66:** 565–69.

11 Lantz TL, Noble BN, McPherson ML, et al. Frequency and characteristics of patients prescribed antibiotics on admission to hospice care. *J Palliat Med* 2022; **25:** 584–90.

12 Tark A, Estrada LV, Tresgallo ME, Quigley DD, Stone PW, Agarwal M. Palliative care and infection management at end of life in nursing homes: a descriptive survey. *Palliat Med* 2020; **34:** 580–88.

13 Marra AR, Puig-Asensio M, Balkenende E, Livorsi DJ, Goto M, Perencevich EN. Antibiotic use during end-of-life care: a systematic literature review and meta-analysis. *Infect Control Hosp Epidemiol* 2021; **42:** 523–29.

14 Tanneberger KS, Pannuti F, Malavasi I, Mariano P, Strocchi E. New challenges and old problems: end of life care and the dilemma of prognostic accuracy. *Usp Gerontol* 2002; **10:** 131–35.

15 Bouchard S, Iancu AP, Neamt E, et al. Can we make more accurate prognoses during last days of life? *J Palliat Med* 2024; **27:** 895–904.

16 Hiratsuka Y, Hamano J, Mori M, Maeda I, Morita T, Suh SY. Prediction of survival in patients with advanced cancer: a narrative review and future research priorities. *J Hosp Palliat Care* 2023; **26:** 1–6.

17 Bischoff KE, Patel K, Boscardin WJ, O'Riordan DL, Pantilat SZ, Smith AK. Prognoses associated with palliative performance scale scores in modern palliative care practice. *JAMA Netw Open* 2024; **7:** e2420472.

18 Ryan S, Wong J, Chow R, Zimmermann C. Evolving definitions of palliative care: upstream migration or confusion? *Curr Treat Options Oncol* 2020; **21:** 20.

19 Humphrey GB, Inacio MC, Lang C, et al. Estimating potential palliative care needs for residential aged care: a population-based retrospective cohort study. *Australas J Ageing* 2024; **43:** 782–91.

20 Hanna N, Quach B, Scott M, Qureshi D, Tanuseputro P, Webber C. Operationalizing burdensome transitions among adults at the end of life: a scoping review. *J Pain Symptom Manage* 2021; **61:** 1261–77.e10.

21 Froggatt K, Payne S. A survey of end-of-life care in care homes: issues of definition and practice. *Health Soc Care Community* 2006; **14:** 341–48.

22 Huang YL, Alsaba N, Brookes G, Crilly J. End-of-life care for older people in the emergency department: a scoping review. *Emerg Med Australas* 2020; **32:** 7–19.

23 Radbruch L, De Lima L, Knaul F, et al. Redefining palliative care—a new consensus-based definition. *J Pain Symptom Manage* 2020; **60:** 754–64.

24 Teixeira Rodrigues A, Roque F, Falcão A, Figueiras A, Herdeiro MT. Understanding physician antibiotic prescribing behaviour: a systematic review of qualitative studies. *Int J Antimicrob Agents* 2013; **41:** 203–12.

25 Md Rezal RS, Hassali MA, Alrasheedy AA, Saleem F, Md Yusof FA, Godman B. Physicians' knowledge, perceptions and behaviour towards antibiotic prescribing: a systematic review of the literature. *Expert Rev Anti Infect Ther* 2015; **13:** 665–80.

26 Ahmed I, King R, Akter S, Akter R, Aggarwal VR. Determinants of antibiotic self-medication: a systematic review and meta-analysis. *Res Social Adm Pharm* 2023; **19:** 1007–17.

27 Alhomoud F, Aljamea Z, Basalelah L. Antibiotics kill things very quickly—consumers' perspectives on non-prescribed antibiotic use in Saudi Arabia. *BMC Public Health* 2018; **18:** 1177.

28 Chung P, Scandlyn J, Dayan PS, Mistry RD. Working at the intersection of context, culture, and technology: provider perspectives on antimicrobial stewardship in the emergency department using electronic health record clinical decision support. *Am J Infect Control* 2017; **45:** 1198–202.

29 Chan OSK, Lam W, Zhao S, Tun H, Liu P, Wu P. Why prescribe antibiotics? A systematic review of knowledge, tension, and motivation among clinicians in low-, middle- and high-income countries. *Soc Sci Med* 2024; **345:** 116600.

30 Wagner CE, Prentice JA, Saad-Roy CM, et al. Economic and behavioral influencers of vaccination and antimicrobial use. *Front Public Health* 2020; **8:** 614113.

31 Kim JK, Kim KH, Shin YC, Jang BH, Ko SG. Utilization of traditional medicine in primary health care in low- and middle-income countries: a systematic review. *Health Policy Plan* 2020; **35:** 1070–83.

32 Savatagi SB, Srinivas PN, Payyappallimana U. Factors influencing the emergence of self-reliance in primary health care using traditional medicine: a scoping review. *Indian J Public Health* 2022; **66:** 214–22.

33 Kwon KT. Implementation of antimicrobial stewardship programs in end-of-life care. *Infect Chemother* 2019; **51:** 89–97.

34 Lee S, Datta R. Frontiers in antimicrobial stewardship: antimicrobial use during end-of-life care. *Antimicrob Steward Healthc Epidemiol* 2023; **3:** e164.

35 Daneman N, Campitelli MA, Giannakeas V, et al. Influences on the start, selection and duration of treatment with antibiotics in long-term care facilities. *CMAJ* 2017; **189:** E851–60.

36 Daneman N, Gruneir A, Bronskill SE, et al. Prolonged antibiotic treatment in long-term care: role of the prescriber. *JAMA Intern Med* 2013; **173:** 673–82.

37 Gaw CE, Hamilton KW, Gerber JS, Szymczak JE. Physician perceptions regarding antimicrobial use in end-of-life care. *Infect Control Hosp Epidemiol* 2018; **39:** 383–90.

38 Crowley PD, Whalen FX, Siegel LR, Challener DW. Antibiotics at end of life: where are we now and where are we going? A narrative review. *Am J Hosp Palliat Care* 2024; published online Sept 9. https://doi.org/10.1177/10499091241282627.

39 Latuga NM, Grant PC, Levy K, Luczkiewicz DL. Treatment of positive urine cultures at end-of-life and the effect on terminal delirium management. *Am J Hosp Palliat Care* 2022; **39:** 1014–22.

40 Boton N, Larnard J. When should patients at the end of life get antimicrobials? *AMA J Ethics* 2024; **26:** E456–62.

41 Juthani-Mehta M, Allore HG. Design and analysis of longitudinal trials of antimicrobial use at the end of life: to give or not to give? *Ther Adv Drug Saf* 2019; **10:** 2042098618820210.

42 Karlin D, Pham C, Furukawa D, et al. State-of-the-art review: use of antimicrobials at the end of life. *Clin Infect Dis* 2024; **78:** e27–36.

43 Goedken CC, Balkenende E, Livorsi D, et al. Improving shared decision-making around antimicrobial-prescribing during the end-of-life period: a qualitative study of veterans, their support caregivers and their providers. *Antimicrob Steward Healthc Epidemiol* 2024; **4:** e89.

44 Reinbolt RE, Shenk AM, White PH, Navari RM. Symptomatic treatment of infections in patients with advanced cancer receiving hospice care. *J Pain Symptom Manage* 2005; **30:** 175–82.

45 Datta R, Topal J, McManus D, et al. Education needed to improve antimicrobial use during end-of-life care of older adults with advanced cancer: a cross-sectional survey. *Palliat Med* 2021; **35:** 236–41.

46 Datta R, Zhu M, Han L, Allore H, Quagliarello V, Juthani-Mehta M. Increased length of stay associated with antibiotic use in older adults with advanced cancer transitioned to comfort measures. *Am J Hosp Palliat Care* 2020; **37:** 27–33.

47 Ke LS, Cheng HC, Liu CL, et al. Taiwanese older adults prefer to use antibiotics and intravenous infusion at the end of life based on a cartoon version of the life support preferences questionnaire. *Int J Environ Res Public Health* 2023; **20:** 3430.

48 Smith AGC, Yarrington ME, Baker AW, et al. Beyond infection: mortality and end-of-life care associated with infectious disease consultation in an academic health system. *Clin Infect Dis* 2024; **79:** 864–70.

49 Opperman CJ. Withdrawing antibiotics in the terminally ill ICU patient: should it be a road less travelled? *J Intensive Care Soc* 2023; **24:** 234.

50 Pandey S, Wisniewski R, Morjaria S, et al. Factors associated with antimicrobial use at the end-of-life among hospitalized cancer patients. *Am J Hosp Palliat Care* 2024; **41:** 8–15.

51 Thompson AJ, Silveira MJ, Vitale CA, Malani PN. Antimicrobial use at the end of life among hospitalized patients with advanced cancer. *Am J Hosp Palliat Care* 2012; **29:** 599–603.

52 Fedorowsky R, Bachner YG, Borer A, Ciobotaro P, Kushnir T. Use of antibiotics among end-of-life hospitalized patients with advanced directives: status examination and association with infectious disease consultation and physician burnout. *Infect Control Hosp Epidemiol* 2019; **40:** 1222–28.

53 Walensky RP, McQuillen DP, Shahbazi S, Goodson JD. Where is the ID in COVID-19? *Ann Intern Med* 2020; **173:** 587–89.

54 Food and Agriculture Organization of the United Nations. The FAO Action Plan on Antimicrobial Resistance 2021–2025. 2021. https://openknowledge.fao.org/server/api/core/bitstreams/dd6c0ba1-fd85-4a3e-b398-53b610c35318/content (accessed Dec 1, 2024).

55 Binagwaho A, Farmer PE, Nsanzimana S, et al. Rwanda 20 years on: investing in life. *Lancet* 2014; **384:** 371–75.

56 Harun MGD, Sumon SA, Hasan I, Akther FM, Islam MS, Anwar MMU. Barriers, facilitators, perceptions and impact of interventions in implementing antimicrobial stewardship programs in hospitals of low-middle and middle countries: a scoping review. *Antimicrob Resist Infect Control* 2024; **13:** 8.

57 Albahar F, Alhamad H, Abu Assab M, Abu-Farha R, Alawi L, Khaleel S. The impact of antifungal stewardship on clinical and performance measures: a global systematic review. *Trop Med Infect Dis* 2023; **9:** 8.

58 Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneau C. Value of hospital antimicrobial stewardship programs: a systematic review. *Antimicrob Resist Infect Control* 2019; **8:** 35.

59 Dighriri IM, Alnomci BA, Aljahdali MM, et al. The role of clinical pharmacists in antimicrobial stewardship programs: a systematic review. *Cureus* 2023; **15:** e50151.

60 St Louis J, Okere AN. Clinical impact of pharmacist-led antibiotic stewardship programs in outpatient settings in the United States: a scoping review. *Am J Health Syst Pharm* 2021; **78:** 1426–37.

61 Otieno PA, Campbell S, Maley S, Obinju Arunga T, Otieno Okumu M. A systematic review of pharmacist-led antimicrobial stewardship programs in sub-Saharan Africa. *Int J Clin Pract* 2022; **2022:** 3639943.

62 Dirjayanto VJ, Lazarus G, Geraldine P, et al. Efficacy of telemedicine-based antimicrobial stewardship program to combat antimicrobial resistance: a systematic review and meta-analysis. *J Telemed Telecare* 2023; published online Oct 17. https://doi.org/10.1177/1357633X231204919.

63 Setiawan E, Abdul-Aziz MH, Roberts JA, Cotta MO. Hospital-based antimicrobial stewardship programs used in low- and middle-income countries: a scoping review. *Microb Drug Resist* 2022; **28:** 566–84.

64 General Assembly of the United Nations. High-level meetings of the 70th session. 2016. https://www.un.org/en/ga/70/meetings/index.shtml (accessed Dec 1, 2024).

65 UN. Political declaration of the High-Level Meeting of the General Assembly on antimicrobial resistance. 2016. https://digitallibrary.un.org/record/842813 (accessed Dec 1, 2024).

66 WHO. Antimicrobial resistance. 2023. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance (accessed Oct 11, 2024).

67 Nandi A, Pecetta S, Bloom DE. Global antibiotic use during the COVID-19 pandemic: analysis of pharmaceutical sales data from 71 countries, 2020–2022. *EClinicalMedicine* 2023; **57:** 101848.

68 Murray CJL, Ikuta KS, Sharara F, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet* 2022; **399:** 629–55.

69 Naghavi M, Vollset SE, Ikuta KS, et al. Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. *Lancet* 2024; **404:** 1199–226.

70 WHO. Global Antimicrobial Resistance and Use Surveillance System (GLASS) report. 2022. https://www.who.int/publications/i/item/9789240062702 (accessed Oct 11, 2024).

71 Patel J, Harant A, Fernandes G, et al. Measuring the global response to antimicrobial resistance, 2020–21: a systematic governance analysis of 114 countries. *Lancet Infect Dis* 2023; **23:** 706–18.

72 WHO. Implementing the global action plan on antimicrobial resistance: first quadripartite biennial report. 2024. https://www.who.int/publications/i/item/9789240074668 (accessed Oct 11, 2024).

73 WHO. Global research agenda for antimicrobial resistance in human health. 2023. https://www.who.int/publications/m/item/global-research-agenda-for-antimicrobial-resistance-in-human-health (accessed Oct 11, 2024).

74 Cabral C, Zhang T, Oliver I, Little P, Yardley L, Lambert H. Influences on use of antibiotics without prescription by the public in low- and middle-income countries: a systematic review and synthesis of qualitative evidence. *JAC Antimicrob Resist* 2024; **6:** dlae165.

75 Hermsen ED, Amos J, Townsend A, Becker T, Hargreaves S. Antimicrobial resistance among refugees and asylum seekers: a global systematic review and meta-analysis. *Lancet Infect Dis* 2025; **25:** e34–43.

76 The Lancet. Antimicrobial resistance: an agenda for all. *Lancet* 2024; **403:** 2349.

77 Okeke IN, de Kraker MEA, Van Boeckel TP, et al. The scope of the antimicrobial resistance challenge. *Lancet* 2024; **403:** 2426–38.

78 Lewnard JA, Charani E, Gleason A, et al. Burden of bacterial antimicrobial resistance in low-income and middle-income countries avertible by existing interventions: an evidence review and modelling analysis. *Lancet* 2024; **403:** 2439–54.

79 Laxminarayan R, Impalli I, Rangarajan R, et al. Expanding antibiotic, vaccine, and diagnostics development and access to tackle antimicrobial resistance. *Lancet* 2024; **403:** 2534–50.

80 Mendelson M, Lewnard JA, Sharland M, et al. Ensuring progress on sustainable access to effective antibiotics at the 2024 UN General Assembly: a target-based approach. *Lancet* 2024; **403:** 2551–64.

81 European Centre for Disease Prevention and Control. Antimicrobial stewardship. 2017. https://www.ecdc.europa.eu/en/publications-data/directory-guidance-prevention-and-control/prudent-use-antibiotics/antimicrobial (accessed Oct 15, 2024).

82 Australian Government. Antimicrobial stewardship. 2021. https://www.amr.gov.au/what-you-can-do/general-practice/antimicrobial-stewardship (accessed Oct 11, 2024).

83 Government of Canada. Pan-Canadian Action Plan on Antimicrobial Resistance. 2023. https://www.canada.ca/en/public-health/services/publications/drugs-health-products/pan-canadian-action-plan-antimicrobial-resistance.html (accessed Oct 11, 2024).

84 Pan American Health Organization. The WHO AWaRe (Access, Watch, Reserve) antibiotic book–infographics. 2024. https://www.paho.org/en/documents/who-aware-access-watch-reserve-antibiotic-book-infographics (accessed Oct 11, 2024).

85 EU. Commission notice—EU Guidelines for the prudent use of antimicrobials in human health. 2017. https://eur-lex.europa.eu/legal-content/EN/TXT/%20PDF/?uri=CELEX:52017XC0701(01)&from=ET (accessed Feb 12, 2025).

86 WHO. France: a broad vision of infection prevention and control and the importance of local action. 2022. https://www.who.int/news-room/feature-stories/detail/france--a-broad-vision-of-infection-prevention-and-control-and-the-importance-of-local-action (accessed Oct 11, 2024).

87 de With K, Allerberger F, Amann S, et al. Strategies to enhance rational use of antibiotics in hospital: a guideline by the German Society for Infectious Diseases. *Infection* 2016; **44:** 395–439.

88 Stichting Werkgroep Antibioticabeleid. Practice guide–antimicrobial stewardship in the Netherlands. 2024. https://swab.nl/en/practice-guide-antimicrobial-stewardship-in-the-netherlands (accessed Oct 11, 2024).

89 Healthcare Improvement Scotland. Antimicrobial-specific guidance. 2024. https://www.sapg.scot/guidance-qi-tools/antimicrobial-specific-guidance (accessed Oct 11, 2024).

90 Healthcare Improvement Scotland. Good practice recommendations for antimicrobial use in frail older people. 2024. https://www.sapg.scot/guidance-qi-tools/good-practice-recommendations/antimicrobial-use-in-frail-older-people (accessed Oct 11, 2024).

91 KnowledgeHub. Guidelines on implementation of the antimicrobial strategy in South Africa: One Health approach and governance. 2017. https://knowledgehub.health.gov.za/elibrary/guidelines-implementation-antimicrobial-strategy-south-africa-one-health-approach (accessed Oct 11, 2024).

92 Plan Nacional Resistencia Antibióticos. Programas de optimización de uso de los antibióticos. 2024. https://www.resistenciaantibioticos.es/es/lineas-de-accion/control/programas-de-optimizacion-de-uso-de-los-antibioticos-proa (accessed Oct 11, 2024).

93 National Institute for Health and Care Excellence. Antimicrobial stewardship: changing risk-related behaviours in the general population. 2017. https://www.nice.org.uk/guidance/ng63 (accessed Oct 11, 2024).

94 Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016; **62:** e51–77.

95 Ntirenganya C, Manzi O, Muvunyi CM, Ogbuagu O. High prevalence of antimicrobial resistance among common bacterial isolates in a tertiary healthcare facility in Rwanda. *Am J Trop Med Hyg* 2015; **92:** 865–70.

96 Ntizimira CR, Nkurikiyimfura JL, Mukeshimana O, Ngizwenayo S, Mukasahaha D, Clancy C. Palliative care in Africa: a global challenge. *Ecancermedicalscience* 2014; **8:** 493.

97 Ntizimira C, Deo MS, Dunne M, Krakauer E. Decolonizing end-of-life care: lessons and opportunities. *Ecancermedicalscience* 2022; **16:** ed121.

98 Rickard J, Ngarambe C, Ndayizeye L, et al. Antibiotic use and antimicrobial resistance of surgical patients with peritonitis at a tertiary referral hospital in Rwanda. *Surg Infect (Larchmt)* 2018; **19:** 382–87.

99 Shumbusho F, van Griensven J, Lowrance D, et al. Task shifting for scale-up of HIV care: evaluation of nurse-centered antiretroviral treatment at rural health centers in Rwanda. *PLoS Med* 2009; **6:** e1000163.

100 Moreland PJ, Rosa WE, Uwimana P, et al. Palliative and end-of-life care self-perceived educational needs of physicians and nurses in Rwanda. *J Hosp Palliat Nurs* 2021; **23:** 557–63.

101 Chandani Y, Noel M, Pomeroy A, Andersson S, Pahl MK, Williams T. Factors affecting availability of essential medicines among community health workers in Ethiopia, Malawi, and Rwanda: solving the last mile puzzle. *Am J Trop Med Hyg* 2012; **87** (suppl)**:** 120–26.

102 Shouna GO, Omar MA, Mohammed GK, Abdelrahman SH. Optimising the use of antimicrobial medicines in Sudan. *J Pharm Res* 2021; **6:** 1–8.

103 WHO. Antimicrobial resistance in the Eastern Mediterranean region. 2017. https://iris.who.int/handle/10665/259051 (accessed Oct 14, 2024).

104 African Palliative Care Association. APCA atlas of palliative care in Africa. 2017. https://www.africanpalliativecare.org/resource-center/apca-atlas-palliative-care-africa (accessed Oct 11, 2024).

105 Poudel A, Kc B, Shrestha S, Nissen L. Access to palliative care: discrepancy among low-income and high-income countries. *J Glob Health* 2019; **9:** 020309.

106 Divatia JV, Mehta Y, Govil D, et al. Intensive care in India in 2018-2019: the second Indian intensive care case mix and practice patterns study. *Indian J Crit Care Med* 2021; **25:** 1093–107.

107 Courtright KR, Jordan L, Murtaugh CM, et al. Risk factors for long-term mortality and patterns of end-of-life care among Medicare sepsis survivors discharged to home health care. *JAMA Netw Open* 2020; **3:** e200038.

108 Poojary S, Deodhar J, Chodankar A, Damani A, Ghoshal A, Muckaden MA. Antibiotic use during end of life in patients with advanced malignancy: a retrospective analysis. *J Clin Oncol* 2021; **39** (suppl)**:** e24002.

109 Palacios-Baena ZR, Giannella M, Manissero D, et al. Risk factors for carbapenem-resistant gram-negative bacterial infections: a systematic review. *Clin Microbiol Infect* 2021; **27:** 228–35.

110 One Health Trust. Scoping report on antimicrobial resistance in India. 2017. https://onehealthtrust.org/publications/reports/scoping-report-on-amr-india/ (accessed Oct 12, 2024).

111 Verma V, Valsan C, Mishra P, et al. Antimicrobial resistance profile in ICU patients across India: a multicenter, retrospective, observational study. *Cureus* 2024; **16:** e57489.

112 Indian Council of Medical Research. Guidance on diagnosis and management of carbapenem-resistant gram-negative infections. 2022. https://iamrsn-audit.icmr.org.in/index.php/resources/guideline (accessed Feb 12, 2025).

113 Thomas D, Kamalumpundi V, Thampi A, et al. Antibiotic stewardship in Indian palliative care: a single-center retrospective study. *Antimicrob Steward Healthc Epidemiol* 2023; **3:** e196.

114 Ndukwu GU, Olamuyiwa TE, Eke GK. The practice of palliative care medicine in the developing world: a review of the challenges in providing palliative care services in south-South Nigeria. *The Nigerian Health Journal* 2021; **21:** 1–10.

115 Afolabi OA, Nkhoma K, Soyannwo O, et al. Integrated primary palliative care in Nigeria–perspectives of patients, families and providers. *J Pain Symptom Manage* 2022; **64:** 319–29.

116 Food and Agriculture Organization of the United Nations. National Action Plan for Antimicrobial Resistance 2017–2022. 2017. https://www.fao.org/faolex/results/details/en/c/LEX-FAOC188358/ (accessed Oct 14, 2024).

117 Fadare JO, Ogunleye O, Iliyasu G, et al. Status of antimicrobial stewardship programmes in Nigerian tertiary healthcare facilities: findings and implications. *J Glob Antimicrob Resist* 2019; **17:** 132–36.

118 Fuller WL, Aboderin AO, Yahaya A, et al. Gaps in the implementation of national core elements for sustainable antimicrobial use in the WHO-African region. *Front Antibiot* 2022; **1:** 1047565.

119 WHO. WHO policy guidance on integrated antimicrobial stewardship activities. 2021. https://www.who.int/publications/i/item/9789240025530 (accessed Feb 12, 2025).

120 Federal Ministry of Health and Social Welfare. Nigeria essential medicines list 7th edn. 2020. https://www.policyvault.africa/policy/nigeria-essential-medicines-list-seventh-edition/ (accessed Feb 12, 2025).

121 Aboderin AO, Adeyemo AT, Olayinka AA, et al. Antimicrobial use among hospitalized patients: a multi-center, point prevalence survey across public healthcare facilities, Osun State, Nigeria. *Germs* 2021; **11:** 523–35.

122 Manga MM, Mohammed Y, Suleiman S, et al. Antibiotic prescribing habits among primary healthcare workers in northern Nigeria: a concern for patient safety in the era of global antimicrobial resistance. *PAMJ One Health* 2021; **5:** 19.

123 Cortés JA, Arenas NC, Blanco JDC, et al. Guía de práctica clínica para la infección de vías urinarias complicada. *Infectio* 2023; **27:** 52–68.

124 Cortés JA, Cuervo-Maldonado SI, Nocua-Báez LC, et al. Guía de práctica clínica para el manejo de la neumonía adquirida en la comunidad. *Rev Fac Med (Caracas)* 2022; **70:** e93814.

125 Valderrama-Beltrán S, Cortés JA, Caro MA, et al. Guía de práctica clínica para el diagnóstico y manejo de las infecciones de piel y tejidos blandos en Colombia. *Infectio* 2019; **23:** 318–46.

126 Cortés JA, Valderrama-Rios MC, Lizarazo J, et al. Guía de práctica clínica para el diagnóstico y tratamiento de la criptococosis en personas adultas que viven con el VIH. *Infectio* 2024; **28:** 45–67.

127 Cortés JA, Valderrama-Rios MC, Tobón AM, et al. Guía de práctica clínica para el diagnóstico y tratamiento de la histoplasmosis en personas adultas que viven con el VIH – versión corta. *Infectio* 2024; **28:** 118–29.

128 Valderrama-Rios MC, Álvarez-Moreno CA, Cortes JA. Interventions to improve antibiotic use in hospitals with different levels of complexity in Colombia: findings from a before-and-after study and suggestions for the future. *Antibiotics (Basel)* 2023; **12:** 867.

129 Pallares C, Hernández-Gómez C, Appel TM, et al. Impact of antimicrobial stewardship programs on antibiotic consumption and antimicrobial resistance in four Colombian healthcare institutions. *BMC Infect Dis* 2022; **22:** 420.

130 Asociación Colombiana de Infectología. Lineamientos técnicos para la implementación de programas de optimización de antimicrobianos en el escenario hospitalario y ambulatorio. 2019. https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/PP/ET/lineamientos-optimizacion-uso-antimicrobianos.pdf (accessed Feb 12, 2025).

131 Machado-Alba JE, Valladales-Restrepo LF, Gaviria-Mendoza A, Machado-Duque ME, Figueras A. Patterns of antibiotic prescription in Colombia: are there differences between capital cities and municipalities? *Antibiotics (Basel)* 2020; **9:** 389.

132 Ministry of Health Malaysia. National Antimicrobial Guideline (NAG). 2025. https://sites.google.com/moh.gov.my/nag (accessed Feb 12, 2025).

133 Malaysian Society of Infectious Diseases and Chemotherapy. Guidelines for adult immunisation 3rd edn. 2020. https://adultimmunisation.msidc.my/read-book/ (accessed Oct 12, 2024).

134 Ministry of Health Malaysia. Protocol on antimicrobial stewardship (AMS) programme in healthcare facilities, second edition 2022. 2017. https://pharmacy.moh.gov.my/en/documents/protocol-antimicrobial-stewardship-ams-programme-healthcare-facilities-second-edition-2022.html (accessed Oct 12, 2024).

135 Malaysian Society for Quality in Health. 6th edition standards. 2024. https://www.membership.msqh.com.my/accreditation/index.php/6th-edition-standards (accessed Oct 12, 2024).

136 Ng TS, Lam CL, Ong T. Hospital healthcare utilisation among older adults admitted to a university hospital in the last months of life: a retrospective observational study. *Med J Malaysia* 2022; **77:** 585–89.

137 Htut Y, Shahrul K, Poi PJ. The views of older Malaysians on advanced directive and advanced care planning: a qualitative study. *Asia Pac J Public Health* 2007; **19:** 58–67.

138 Azahar A, Ibrahim NA. Differences in attitude towards end-of-life care among haemodialysis patients and their family members in two Malaysian hospitals. *IIUM Med J Malaysia* 2022; **21:** 54–59.

139 Ministry of Health Malaysia. My advance care plan (ACP). 2024. https://hq.moh.gov.my/medicaldev/my-acp/ (accessed Oct 12, 2024).

140 Ilman SSS, Zin ZM, Rahman AB, et al. Understanding the views of Malaysian public towards decision making for end-of-life care: an online study. 2022. https://research.monash.edu/en/publications/understanding-the-views-of-malaysian-public-towards-decision-maki (accessed Oct 12, 2024).

141 Sociedad Chilena de Medicina Familiar. Orientación técnica para el uso de antibióticos en infecciones comunitarias de manejo ambulatorio. 2021. https://www.medicinafamiliar.cl/mf/wordpress/2021/07/12/orientacion-tecnica-para-el-uso-de-antibioticos-en-infecciones-comunitarias-de-manejo-ambulatorio-2021/ (accessed Oct 12, 2024).

142 Superintendencia de Salud. Neumonía adquirida en la comunidad de manejo ambulatorio en personas de 65 años y más. 2024. https://www.superdesalud.gob.cl/difusion/665/w3-article-18808.html (accessed Oct 12, 2024).

143 Álvarez AM, Morales R, Raijmakers M, et al. Consenso de la Sociedad Chilena de Infectología para el manejo de episodios de neutropenia febril en adultos y niños con cáncer. *Rev Chilena Infectol* 2023; **40:** 105–65.

144 Sociedad Chilena de Infectología. Norma general técnica para la racionalización del uso de antimicrobianos en atención Clínica. 2021. https://sochinf.cl/norma-general-tecnica-para-la-racionalizacion-del-uso-de-antimicrobianos-en-atencion-clinica/ (accessed Oct 12, 2024).

145 Ministry of Health of Chile. Technical guidance on universal palliative care. 2024. https://www.minsal.cl/wp-content/uploads/2023/12/Orientacion-Tecnica-Cuidados-Paliativos-Universales-1.pdf (accessed Feb 12, 2025).

146 Pontificia Universidad Católica de Chile. Evaluación y manejo de pacientes en fin de vida. 2023. https://facultadmedicina.uc.cl/noticias/medicina-paliativa-uc-lanzo-el-manual-evaluacion-y-manejo-de-pacientes-en-fin-de-vida/ (accessed Oct 12, 2024).

147 Gallastegui-Brana A, Rodríguez-Nunez A, Palacios J, et al. Development and validation of a tool to assess the structural quality of palliative care services. *J Pain Symptom Manage* 2023; **65:** 490–99.

148 Bundesverband Deutscher Krankenhausapotheker V. Strukturelle und personelle Voraussetzungen für die Sicherung einer rationalen Antiinfektivaverordnung in Krankenhäusern. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2020; **63:** 749–60.

149 Bundesministerium der Justiz. Gesetz zur Verhütung und Bekämpfung von Infektionskrankheiten beim Menschen. 2000. https://www.gesetze-im-internet.de/ifsg/BJNR104510000.html (accessed Oct 12, 2024).

150 Association of the Scientific Medical Societies in Germany. AWMF Leitlinienregister 092-001. https://register.awmf.org/de/leitlinien/detail/092-001 (accessed Oct 12, 2024).

151 Association of the Scientific Medical Societies in Germany. AWMF Leitlinienregister 079-001. https://register.awmf.org/de/leitlinien/detail/079-001 (accessed Oct 12, 2024).

152 Ewig S, Kolditz M, Pletz M, et al. Behandlung von erwachsenen Patienten mit ambulant erworbener Pneumonie–update 2021. *Pneumologie* 2021; **75:** 665–729.

153 Bundesärztekammer. BÄK-Curriculum Antibiotic Stewardship (ABS) Rationale Antiinfektivastrategien. 2024. https://www.bundesaerztekammer.de/fileadmin/user_upload/BAEK/Themen/Aus-Fort-Weiterbildung/Fortbildung/BAEK-Curricula/BAEK-Curriculum_Antibiotic_Stewardship.pdf (accessed Feb 12, 2025).

154 Ostgathe C, Stachura P, Hofmann S, et al. SOP–Umgang mit multiresistenten Erregern auf der Palliativstation. *Onkologe* 2017; **23:** 303–10.

155 Stiel S, Krumm N, Pestinger M, et al. Antibiotics in palliative medicine–results from a prospective epidemiological investigation from the HOPE survey. *Support Care Cancer* 2012; **20:** 325–33.

156 Bundesministerium der Justiz. Die Textbausteine für eine schriftliche Patientenverfügung als PDF. 2024. https://www.bmj.de/SharedDocs/Downloads/DE/Formular/Patientenverfuegung_Textbausteine_pdf.html (accessed Oct 12, 2024).

157 Coyle N, Manna R, Shen M, et al. Discussing death, dying, and end-of-life goals of care: a communication skills training module for oncology nurses. *Clin J Oncol Nurs* 2015; **19:** 697–702.

158 Tervalon M, Murray-García J. Cultural humility versus critical competence: a critical distinction in defining physician training outcomes in multicultural outcomes in multicultural education. *J Health Care Poor Underserved* 1998; **9:** 117–25.

159 Foronda C. A theory of cultural humility. *J Transcult Nurs* 2020; **31:** 7–12.

160 Dee EC. The alleviation of existential suffering as part of a good death. *Lancet Healthy Longev* 2021; **2:** e778.

161 Kohli K, Feliciano EJG, Swami N, et al. Dying with dignity: how can we deliver values-concordant end-of-life care for immigrant patients in the United States? *Lancet Reg Health Am* 2024; **35:** 100776.

162 Butler SS, Winkfield KM, Ahn C, et al. Racial disparities in patient-reported measures of physician cultural competency among cancer survivors in the United States. *JAMA Oncol* 2020; **6:** 152–54.

163 Ho FDV, De Luna DV, Cubarrubias DLPF, et al. Palliative and supportive care in the Philippines: systems, barriers, and steps forward. *J Palliat Care* 2024; **39:** 87–91.

164 Balante J, van den Broek D, White K. Mixed-methods systematic review: cultural attitudes, beliefs and practices of internationally educated nurses towards end-of-life care in the context of cancer. *J Adv Nurs* 2021; **77:** 3618–29.

165 Ohr S, Jeong S, Saul P. Cultural and religious beliefs and values, and their impact on preferences for end-of-life care among four ethnic groups of community-dwelling older persons. *J Clin Nurs* 2017; **26:** 1681–89.

166 Racine L, Fowler-Kerry S, Aiyer H. Integrative review of the needs and challenges of indigenous palliative care in rural and remote settings. *J Adv Nurs* 2022; **78:** 2693–712.

167 Charani E. BSAC Vanguard series: why culture matters to tackle antibiotic resistance. *J Antimicrob Chemother* 2022; **77:** 1506–07.

168 Charani E, McKee M, Ahmad R, et al. Optimising antimicrobial use in humans–review of current evidence and an interdisciplinary consensus on key priorities for research. *Lancet Reg Health Eur* 2021; **7:** 100161.

169 Wellcome. Reframing resistance. 2019. https://wellcome.org/reports/reframing-antimicrobial-resistance-antibiotic-resistance (accessed Dec 1, 2024).

170 Brown RF, Bylund CL. Communication skills training: describing a new conceptual model. *Acad Med* 2008; **83:** 37–44.

171 Arnold RM, Back AL, Carey EC, Tulsky JA, Wood GJ, Yang HB. Navigating communication with seriously ill patients, 2nd edn. Cambridge University Press, 2024.