WHO AWaRe antibiotic book survey results

Table of contents

List of figures

World Health Organization

1. Executive summary

The 2022 WHO AWaRe antibiotic book (1) is used to support antibiotic stewardship efforts globally. An online survey was used to obtain feedback on its content, format and suggestions for future updates. The survey was available in English, Spanish and French and open between 15 July to 15 September 2024.

A total of 301 responses were received, of which 81% (n=244) were from low- and middle-income countries (LMICs). The majority (n=282, 94%) of responses were recorded in English and approximately half (157/301, 52%) were health-care workers. Respondents indicated a reliance on multiple resources and guidelines for clinical decision support.

Clarity and format were generally well received with no major issues identified. Respondents expressed interest in making the book available in different formats and employing various methods such as colour coding and indexing to improve useability.

According to respondents, the most important topics to consider for addition to the book include targeted therapy for infections caused by *Staphylococcus aureus* (97%, 273/281), *Escherichia coli* (97%, 269/278) and *Klebsiella pneumoniae* (96%, 268/278), clinical management of surgical site infections (96%, 286/297) and healthcare-associated infections such as catheter-related bloodstream infections (95%, 265/279) and catheter-associated urinary tract infections (95%, 267/282).

The high ranking of most suggested additional content complicates the prioritization of new topics; however, this also indicates that these updates would be well-received. Updates to the book will be prioritised and completed based on the availability of resources.

2. Key findings

2.1 Background

Antibiotic stewardship optimises antibiotic use, improves patient outcomes and preserves the effectiveness of antibiotics. The 2022 World Health Organization (WHO) AWaRe (Access, Watch, Reserve) antibiotic book provides guidance on empiric antibiotic use for common clinical bacterial infections in children and adults in primary care and hospital settings and is used to support antibiotic stewardship efforts globally. Feedback about its content and format is important to inform and prioritise updates and future versions.

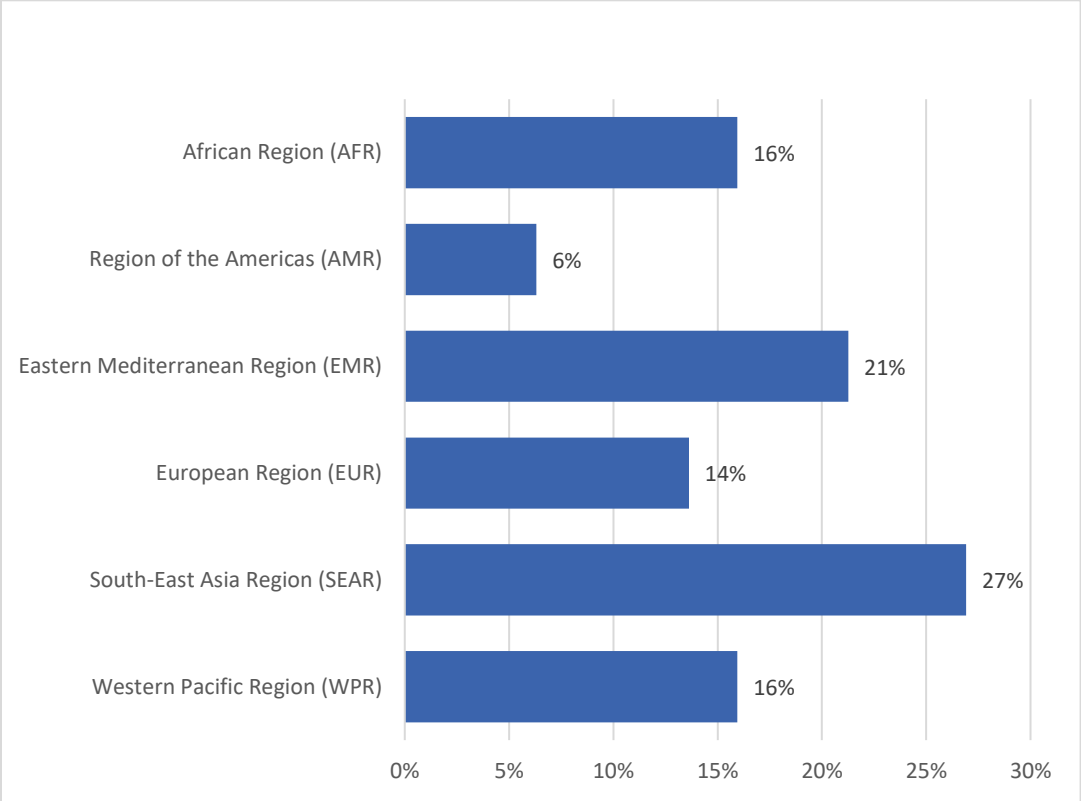
A 26-question Microsoft Forms (2) online survey (Annex 1) was disseminated to end users and experts in antibiotic stewardship in English, French and Spanish between 15 July to 15 September 2024 for voluntary and anonymous completion. A 4-point Likert scale was used for half of the questions and the rest were open-ended and allowed for free-text input from the respondents. A snowball sampling method was implemented through WHO regional offices, government and non-government partners, WHO collaborating centres and advisory

groups, contacts involved in developing the AWaRe system and LinkedIn (3); and a survey link was integrated within the WHO AWaRe book app.

The survey aimed to obtain end-user feedback on (i) modifications to the existing material, including format and content; and (ii) additional content considered to be useful. It also collected demographic and contextual information about the respondents such as country, profession and type of antimicrobial guidelines used.

A total of 301 responses from all six WHO regions (Figure 1) were recorded in English (n=282), Spanish (n=12) and French (n=7). Based on the World Bank income classification, almost 53% of respondents (n=159) were from lower-middle income countries, 22% (n=66) from upper middle-income countries, 19% (n=57) from high income countries, and 6% (n=19) from low-income countries. (Question 25)

Figure 1: Distribution of respondents of the WHO AWaRe book survey by WHO region, 2024



Approximately half the respondents were health-care workers (52%, 157/301), followed by academics (20%, 61/301), government policy or programme staff (14%, 43/301), WHO workforce (5%, 15/301), non-government organization (NGO) staff (2%, 6/301) and others (6%, 19/301), with each respondent allowed to select only one option. (Question 24)

Of those who responded to the question about guidelines, national (61%, 180/296) or local (39%, 116/296) guidelines were most commonly used. Many also reported using the AWaRe antibiotic book (44%, 129/296) while some used professional society (37%, 110/296), subnational (15%, 44/296), NGO (3%, 9/296), and Sanford (1.5%, 4/296) guidelines, indicating a reliance on multiple resources to inform antibiotic use. (Question 26)

Within the 26 questions, 36 topics (Figure 2) explicitly explored the need for additional indications, targeted therapy for specific organisms, and support material by asking the respondents to rank the importance of addition of guidance on those specific topics. Opportunities to add other suggestions through free text were available through open-ended questions and summaries of these suggestions are included below.

All original responses are reported in Annex 2.

2.2 Feedback on format

Respondents had limited feedback about the format of the book with only 9 of 51 comments having specific actionable recommendations. In general, the clarity and format of the book were appreciated, with no significant concerns noted. Respondents suggested making the book accessible through audio (n=1), video (n=1), pocketbooks (n=3), and pocketbooks of infographics (n=1). One respondent wanted easier access to the printed version of the complete book, which for now is available through the WHO headquarters bookstore or WHO country offices. One respondent shared concern about the translated infographics as they do not contain all the text and lack some useful content contained in the full English version. There was only one comment about the format of the app, which was to improve indexing to facilitate quickly locating relevant information. (Questions 20, 21, 22, and 23, and one outlier response in question 16 on format).

2.3 - Feedback on content

2.3.1 - Feedback on current content of the book and the app

Several comments identified through the survey may be addressed by referring to chapters 1 and 2 of the book as well as the peer-reviewed publication (4) that describes the method in which the AWaRe book was developed. Specific feedback relating to content, some of which are from a single respondent, are described below.

Choice of antibiotic

Recommendations for the choice of antibiotic for some indications were perceived to be too narrow. One example included a comment about the use of narrow spectrum penicillins such as phenoxymethylpenicilin (penicillin V) in community-acquired pneumonia (CAP). In general, the book recommends the narrowest spectrum agent for the most likely causative pathogen which can be applied globally based on available evidence. The justification for the recommendation of phenoxymethylpenicillin in CAP is based on the most likely causative pathogen, *Streptococcus pneumoniae*, which remains susceptible to this antibiotic in most settings. This is well evidenced and has been explicitly described in the methods publication (4). (Question 16)

One respondent commented on the exclusion of some antibiotics recommended in other international guidelines. This is because of an intentional alignment between the AWaRe book and the WHO Model List of Essential Medicines (EML) (5), meaning that all antibiotics recommended in the AWaRe book are in the EML. As such, some antibiotics, such as fidoxamicin, which is not on the EML, are not included in the AWaRe book. Refer to the EML for more information on the characteristics needed for a medicine to be included.

On the other hand, some feedback highlighted that fixed-dose combinations classified as "Not Recommended" by the AWaRe classification are still being used in countries. WHO acknowledges the current list of Not Recommended antibiotics contains both inappropriate fixed-dose combinations of multiple antimicrobials, as well as some beta-lactam/beta-lactamase inhibitor (BL/BLI) combinations (in which the beta-lactamase inhibitor is not a separate antimicrobial but serves to extend the spectrum of the beta-lactam) and which may not necessarily be inappropriate. It is in the process of reviewing and updating the definitions of Not Recommended antibiotics so that the same general principles are applied to the list. As the AWaRe book promotes best practice (for which Not Recommended antibiotics are not indicated), it is important for each national EML and hospital formulary to review the use of these combinations. (Question 16)

One respondent identified the lack of ranking of antibiotic choices in some indications. An order of preference to antibiotic recommendations (i.e. defining first and second choice) is used in several indications where appropriate, such as otitis media, as there is epidemiological information identifying the most likely causative organism in different geographic and patient settings. However, in many other indications, there is not enough evidence to support such wide prioritised recommendations for all settings and as the WHO AWaRe book aims to suggest treatment regimens that can work in many settings, definitively specifying first and second choice becomes challenging. Additionally, the book acknowledges variable local availability of medicines, including shortages and stock-outs of essential antibiotics, and seeks not to be too prescriptive on appropriate treatment options. Furthermore, the WHO EML aims to balance parsimony (i.e. not listing too many medicines for the same indication) while offering some alternatives, recognizing that not all medicines are equally available in all settings. Therefore, tailoring the recommendations to local contexts based on the available medicines and local epidemiology, if sufficient, and generating robust local data to help advise this decision at a local level (if possible) are useful next steps, and can be guided by sections entitled "Using microbiology surveillance data" in each chapter of the AWaRe book. (Question 16)

Specific guidance, such as the equal recommendation for amoxicillin+clavulanic acid and amoxicillin for sinusitis, was highlighted. The key messages section of the acute sinusitis chapter states that "if antibiotic treatment is required, amoxicillin has good activity against *S. pneumoniae*, the most common bacterial cause of acute bacterial sinusitis" but does not explicitly suggest that amoxicillin is first line in the antibiotic treatment section. The rationale for not prioritizing amoxicillin over amoxicillin+clavulanic acid in the AWaRe book is due to the possibility of infections caused by *Haemophilus influenzae*, as described in pages 79-80 of The Selection and Use of Essential Medicines Report of the WHO Expert Committee, 2017 (6). (Question 16)

Feedback about specific phrases in the book were also provided. For example, the use of amoxicillin+clavulanic acid for lower urinary tract infections has a footnote stating "active against some extended-spectrum beta-lactamase (ESBL)-producing isolates". We clarify that this sentence does not suggest using this antibiotic for ESBLs. Nitrofurantoin is recommended as the preferred option, but amoxicillin+clavulanic acid may be effective for some ESBL-producing organisms, and this depends on local susceptibility patterns. (Question 16)

Dose and frequency

Addressing dose ranges and clarifying maximum doses per dose and per day was suggested. Further dosing guidance was requested for pharmacokinetic/pharmacodynamic (PK/PD) optimization and therapeutic drug monitoring, particularly for vancomycin dosing. (Question 17)

Duration of therapy

Requests for more guidance were popular, including how to determine sufficient and optimal duration, and a summary table of common optimal durations by indication. Feedback about specific treatment durations in the book was also shared. Specific considerations for shortening treatment duration to 3 to 5 days were suggested for pneumonia (different types) and cystitis. For bacteremia caused by coagulase negative staphylococci, a suggestion was shared to ensure that recommendations clarify that treatment is only warranted in case a culture is positive from at least 2 blood culture samples from different sites, and that treatment duration should be limited to 7 days of vancomycin in most cases. The review of updated evidence relating to recommended durations was also suggested. (Question 18)

Availability

Some respondents expressed concerns about the lack of availability of certain antibiotics in various settings, such as cloxacillin, penicillin G, oxacillin (Access antibiotics), clindamycin, clarithromycin, piperacillin+tazobactam, meropenem (Watch antibiotics), cefiderocol, fosfomycin, linezolid and plazomicin (Reserve antibiotics). It is important for national antimicrobial resistance (AMR) committees to identify the reasons for non-availability of antibiotics. A common consideration includes misalignment of guidelines with national EMLs. Refer to the selection of essential medicines at country level (5). (Question 19)

Additional indications

Some infectious diseases were identified as not being covered in the AWaRe book. Some suggestions, such as invasive fungal infections, were out of scope because they are not bacterial infections. Such infections may be considered for addition in the future. Other suggestions, such as malaria (7) and visceral leishmaniasis in HIV (8), are covered in existing WHO guidelines, and the AWaRe book links to these where appropriate. (Question 2)

Implementation

One respondent recommended supporting implementation of the AWaRe book through the development of an implementation protocol. Another recommendation suggested to elaborate on how to adapt empiric therapy to severity, host vulnerability and local AMR. The development of relevant guidance is in progress. (Question 22)

Other

Another comment suggested that there could be better explanation of the roles and differences of the WHO List of Medically Important Antimicrobials 2024 (MIA) (9), the WHO model EML (5), and the AWaRe book (1). The MIA identifies antimicrobial classes and subclasses that should not be used in animals in order to safeguard their use for human health. The model EML contains medicines that countries should have access to in order to address the priority health needs of the population, and does not include all antimicrobials used globally. There are currently 41 antibiotics on the WHO model EML while 167 different substances were reported as being used globally through the Global Antimicrobial Resistance and Use Surveillance System (GLASS) in 2022 (10). The AWaRe book helps to optimize the use of antibiotics in humans and recommends antibiotics on the model EML. An antibiotic could be on one of the MIA lists as “authorized for use in humans” but not on the model EML and not recommended in the AWaRe book. This means the antibiotic exists and is marketed for use in humans, but it does not have a key role in managing common infections in accordance with stewardship principles and is therefore not considered essential for countries to have on national EMLs. (Question 16)

Feedback about specific content was shared such as to adjust the prevention section in oral and dental infections to include tobacco use and not only smoking cessation. Another specific request was made to include the potential adverse effects of quinolones every time these antibiotics are recommended. (Question 20)

2.3.2 - Suggestions for additional content to be added

Respondents agreed that guidelines on the management of healthcare-associated infections (HAIs) (92%, 273/296) and targeted therapy (92%, 273/297) are important, and identified the need for other new content. The below section highlights the content considered in descending order of perceived importance.

Healthcare-associated infections

Other than hospital-acquired pneumonia which is already covered in the book, 92% of respondents (n=273/296) deemed it important to include recommendations for catheter-related bloodstream infections (95%, 265/279), catheter-associated urinary tract infections (95%, 267/282), ventilator-associated pneumonia (90%, 250/277), intra-abdominal infections (90%, 248/275), skin and soft tissue infections (87%, 244/282) and central nervous system infections (84%, 237/281). (Questions 8 and 9)

Other HAI guidelines suggested to be included (N=91) include surgical site infections and more detailed surgical antibiotic prophylaxis recommendations (n=15), *Clostridiodes difficile* associated diarrhea (n=9), bone and joint infections (n=4), and implantable device related infections (n=5). (Question 10)

The inclusion of more HAIs was discussed when the AWaRe book was initially developed. The marked differences in the local epidemiology of pathogens and AMR makes it, however, very difficult to issue evidence-based global guidance for these infections.

Targeted therapy

Nearly 92% (n=273/297) of respondents felt that recommendations for targeted antibiotic treatment based on microbial identification and antimicrobial susceptibility testing (AST) are crucial. Respondents prioritized including guidance for targeted treatment of *S. aureus* (97%, 273/281), *K. pneumoniae* (97%, 269/278), *E. coli* (96%, 268/278), *P. aeruginosa* (94%, 263/279), *S. pneumoniae* (90%, 245/273), *Acinetobacter baumannii* (89%, 246/276), *Salmonella enterica* serotype Typhi (88%, 244/276), *Enterobacter* spp. (88%, 239/273), *Enterococcus* spp. (87%, 238/273) and Group B *Streptococcus* (79%, 216/274). (Questions 4 and 5)

When asked about targeted therapy for specific pathogen/infection combinations, respondents suggested adding guidance for treatment of infections caused by *K. pneumoniae* (n=14) and *E. coli* (n=10), with urinary tract infections highest for *E. coli* (n=7/10) and bacteremia highest for *K. pneumoniae* (n=3/14). (Question 7)

Additional pathogens suggested for targeted therapy recommendations in free text responses (N=31) included *Candida* spp. and other invasive fungal infections (n=9), *Haemophilus influenzae* (n=3), *Stenotrophomonas maltophilia* (n=2), *Brucella* spp. (n=2), and carbapenemase-producing *Enterobacterales* (n=2). In addition, two respondents suggested more treatment guidance on infections caused by methicillin-resistant *S. aureus* (MRSA) and multi-drug-resistant *Acinetobacter* spp. (Question 6)

The WHO AWaRe antibiotic book already has recommendations for targeted therapy of sexually transmitted infections and certain gastrointestinal infections (e.g. cholera).

Additional indications

Over 60% of respondents (N=293 to 298) indicated that it is important to include the suggested additional indications: surgical site infections (96%, 286/297), diabetic foot infections (92%, 273/298), cardiac infections (89%, 265/298), antibiotic prophylaxis post-injury (86%, 254/296), fungal infections (84%, 250/297), prosthetic joint infections (82%, 244/298), antibiotic prophylaxis for dental procedures (79%, 236/298), severe traumatic wound infections (76%, 225/295), COVID-19 (62%, 185/298) and melioidosis (60%, 177/293). (Question 1)

Other indications suggested by respondents included empiric treatment for suspected antibiotic resistance, skin and soft tissue infections related to aesthetic procedures, catheter-related infections, brucellosis, malaria, bloodstream infections, viral infections, emerging infections, conditions associated with immunocompromised patients like HIV, tuberculosis, and hepatitis, and other infections such as visceral leishmaniasis, and those caused by *P. aeruginosa.* (Question 2)

Additional supporting guidance

All five additional content areas proposed in the survey were considered important by over 85% of respondents, including summary tables for antibiotic classes and spectra of activity (94%, 275/293), antibiotic stewardship in hospitals (94%, 272/290), common antibiotic interactions/side effects (92%, 269/292), antibiotic stewardship in primary care (89%, 261/293) and guidance on interpreting antibiograms (85%, 247/290). (Question 14)

From the 42 free text responses, common suggestions for additional content included information on antimicrobial-related adverse events (n=4), pharmacological properties such as bioavailability and intra- and inter- class differences (n=3) and treatment duration (n=3). Single response recommendations included a myth-busting section, diagnostic stewardship, allergy de-labeling, PK/PD optimization, method for dilution of antibiotics, and guidance on combination therapy (synergy, additive effect, or antagonism). (Question 15)

Some of the additional supporting content suggested overlap with that already included the WHO AMS practical toolkit (11) which is undergoing an update, as well as the development of other implementation guidance for the book.

Antibiotic dosing, allergies, and algorithms

Around 90% of respondents (n=263/291) agreed that detailed antibiotic dosing guidance for patients with altered renal or hepatic function is important. Additionally, approximately 83% of respondents (n=247/298) consider it is important to offer alternative treatment options for patients with allergies to first or second choice antibiotics. When the AWaRe antibiotic book was developed, a conscious decision was made not to include options in case of allergy as allergy is overreported, true severe allergy is rare and prescribers may have a tendency to opt for potentially less effective and safe alternatives, which may also disproportionately contribute to AMR since these alternatives are often Watch antibiotics. (Questions 11 and 3 respectively)

Almost 76% (n=223/294) supported the inclusion of algorithms for symptom associations to guide differential diagnoses and management strategies. Lower respiratory tract infections (n=10), urinary tract infections (n=9), upper respiratory tract infections (n=3), sepsis (n=3), gastrointestinal (n=3), and skin and soft tissue infections (n=3) were all among the most cited infections. (Questions 12 & 13)

3. Conclusion

The survey responses represented a variety of perspectives from different geographical and professional backgrounds. Responses indicated that the book has been generally well received and that there is interest in having more content developed to support patient care and antimicrobial stewardship. Almost all content suggested by the survey was rated as very important or important by the majority of respondents, making it difficult to prioritize the topics. However, the survey provides an important starting point for the newly established WHO Technical Advisory Group on AWaRe (12), which will discuss and provide input on next steps and further improvement of the AWaRe system, including the AWaRe antibiotic book.

The need to update the AWaRe antibiotic book, including to provide guidance on a broader range of infections, is acknowledged. While there is a particular and justified demand for guidance on the treatment of HAIs given the complexity and severity of these infections, providing definitive recommendations is challenging given differences in epidemiology. Other updates may take into consideration the inclusion of additional useful information (such as principles of antibiotic prescribing) in infographics, and development of implementation guidance.

Figure 2: Dot plot of potential additional content from the closed ended survey questions

4. References

1. The WHO AWaRe (Access, Watch, Reserve) antibiotic book [Internet]. [cited 2025 Jan 27]. Available from: https://www.who.int/publications/i/item/9789240062382

2. Surveys, Polls, and Quizzes | Microsoft Forms [Internet]. [cited 2025 Jan 27]. Available from: https://www.microsoft.com/en-us/microsoft-365/online-surveys-polls-quizzes

3. Tong D. Survey posted on LinkedIn [Internet]. 2024 [cited 2025 Feb 2]. Available from: https://www.linkedin.com/feed/update/urn:li:activity:7223991750976028672/

4. Moja L, Zanichelli V, Mertz D, Gandra S, Cappello B, Cooke GS, et al. WHO's essential medicines and AWaRe: recommendations on first- and second-choice antibiotics for empiric treatment of clinical infections. Clinical Microbiology and Infection. 2024 Apr;30:S1–51.

5. World Health Organization. WHO Model Lists of Essential Medicines [Internet]. [cited 2024 Jul 27]. Available from: https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists

6. World Health Organization. The selection and use of essential medicines: report of the WHO Expert Committee, 2017 (including the 20th WHO model list of essential medicines and the 6th model list of essential medicines for children) [Internet]. Geneva: World Health Organization; 2017 [cited 2025 Jan 27]. (WHO technical report series;1006). Available from: https://iris.who.int/handle/10665/259481

7. Global Malaria Programme [Internet]. [cited 2025 Jan 28]. Available from: https://www.who.int/teams/global-malaria-programme/guidelines-for-malaria

8. WHO guideline for the treatment of visceral leishmaniasis in HIV co-infected patients in East Africa and South-East Asia [Internet]. [cited 2025 Jan 28]. Available from: https://www.who.int/publications/i/item/9789240048294

9. WHO. WHO Medically Important Antimicrobials List for Human Medicine [Internet]. 2024 [cited 2025 Jan 27]. Available from: https://cdn.who.int/media/docs/default-source/gcp/who-mia-list-2024-lv.pdf?sfvrsn=3320dd3d_2

10. Global Antimicrobial Resistance and Use Surveillance System (GLASS) report: antibiotic use data for 2022 [Internet]. [cited 2025 May 12]. Available from: https://www.who.int/publications/i/item/9789240108127

11. Antimicrobial stewardship programmes in health-care facilities in low - and middle -income countries [Internet]. [cited 2025 Mar 14]. Available from: https://www.who.int/publications/i/item/9789241515481

12. WHO announces proposed members of its Technical Advisory Group on AWaRe (TAG-AWaRe) [Internet]. [cited 2025 Jan 27]. Available from: https://www.who.int/news-room/articles-detail/who-announces-proposed-members-of-its-technical-advisory-group-on-aware-(tag-aware)