

What is responsible antibiotic use? Towards a global definition

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Introduction

- While there is strong agreement that antibiotic overuse is a critical driver of antimicrobial resistance, the definition of its opposite, 'responsible' antibiotic use, remains imprecise and protean.
- Consensus is essential, especially in the face of the rapid global spread of antimicrobial resistance.

Objective:

To develop a global definition of 'responsible' antibiotic use taking into account different perspectives including the medical community, public health, patients, antibiotic R&D, regulators and governments.

Methods

- Systematic literature review (1700 references) and website search were performed.
- Extracted definitions were divided into elements.
- Four groups of stakeholders from 17 countries across all continents (Table 1) appraised the relevance of each element for defining responsible antibiotic use (Figure 1).

Table 1: International and multidisciplinary stakeholders.

Stakeholder groups	Total n=50
Medical Community (e.g. professional societies, hospital pharmacists, ID, clinical microbiologists, nurse)	n =13
Public Health & Patients (e.g. WHO, MSF, national public health institutes, ethicists)	n =12
Antibiotic R&D (e.g. SMEs, large pharmaceutical companies, economist)	n =13
Payers, Policy makers, Government, Regulators (e.g. ECDC, CDC, FDA, EMA, governments, national health insurance advisor)	n =12

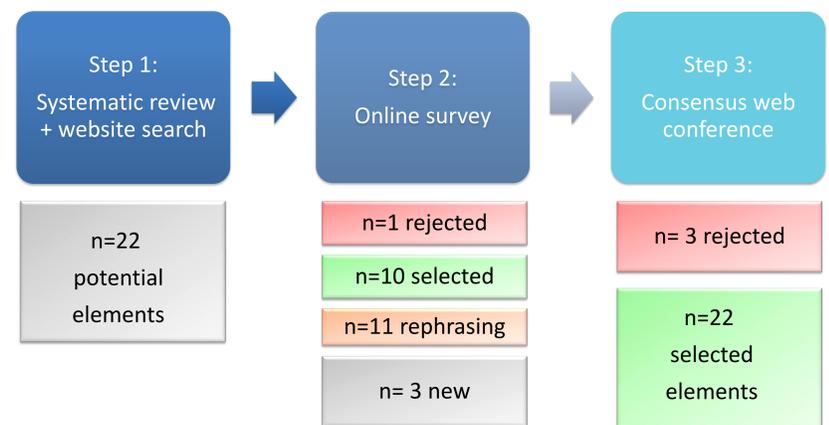


Figure 1: The number of elements of the definition of responsible use resulting from each step of the RAND-modified Delphi method

Results

- 17 synonyms of responsible antibiotic use were identified.
- The stakeholders selected 22 elements of responsible antibiotic use (Figure 2 & Table 2).

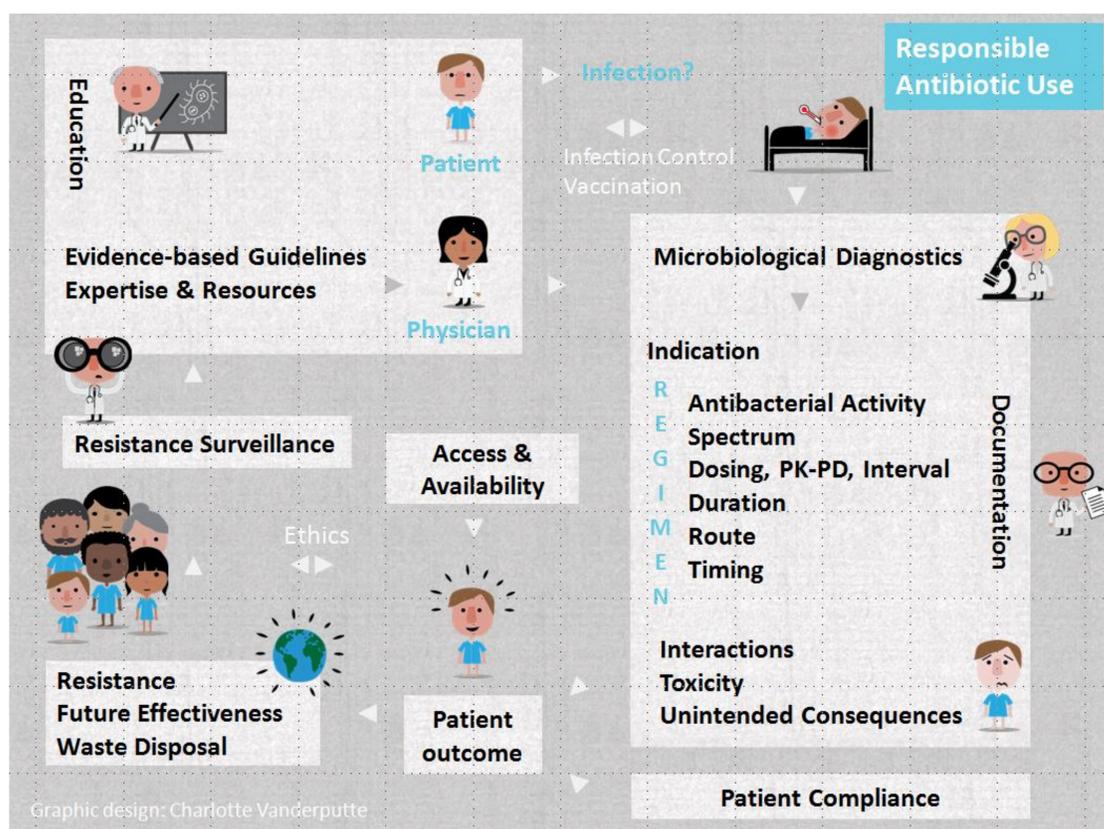


Figure 2: The twenty-two elements of responsible antibiotic use. The elements of responsible antibiotic use are shown in black characters on a white background. On the right: patient-level elements; on the left: societal elements.

Table 2: The phrasing of the twenty-two elements of responsible antibiotic use.

Elements	Phrasing
Microbiological Diagnostics	Using microbiology diagnostic tools to provide diagnostic testing.
Indication	Using antibiotics only to prevent or cure infections for which antibiotic treatment provides a proven benefit.
Antibacterial Activity	Selecting antibiotics based on their antibacterial activity.
Antibacterial Spectrum	Selecting antibiotics based on their antibacterial spectrum (as narrow as possible).
Dosing, PK/PD, Interval	Dose and dosing frequency of the antibiotic regimen based on available knowledge on PK/PD (ensuring sufficient free concentrations of antibiotic at the site of infection).
Duration	Using the shortest possible evidence-based duration of the antibiotic regimen.
Route	Selecting the proper route (e.g. parenteral or oral) based on antibiotic, severity or type of infection and patient characteristics.
Timing	Administering antibiotics in a timely manner.
Interactions	Selecting antibiotics taking into account possible interactions with other medication(s).
Toxicity	Selecting the antibiotic with the least toxicity possible.
Unintended Consequences	Selecting the antibiotic with the lowest risk of secondary infections such as <i>C. difficile</i> diarrhea.
Documentation	Fully documenting the antibiotic regimen including indication in the medical record.
Patient Compliance	Ensuring patient compliance with the antibiotic prescription.
Patient Outcome	Optimising patient outcome (reduced morbidity, mortality and length of hospital stay) by treating or preventing bacterial infections.
Access-Availability	Ensuring access and routine availability of quality antibiotics.
Antibiotic Resistance	Limiting the emergence of antibiotic resistance.
Future Effectiveness	Conserving the effectiveness of antibiotics for the future.
Resistance Surveillance	Using local antibiotic resistance surveillance data for guidelines on empiric antibiotic prescribing.
Evidence-based Guidelines	Ensuring the availability and use of local (or national) evidence-based treatment guidelines.
Expertise and Resources	Using available infectious disease expertise and resources.
Education	Ensuring educational programs on antibiotic use from an early stage for the public and all relevant professionals, including trainees in healthcare curricula.
Waste Disposal	Safely disposing of unused antibiotics and waste products containing antibiotics to prevent selection in the environment.

Conclusion

- This systematic and stepwise method combining both concepts from literature and stakeholder opinions led to an international and multidisciplinary consensus on a global definition of responsible antibiotic use comprising 22 elements.
- This definition will contribute to a standard for responsible antibiotic use that should be considered as the first building block of any model attempting to reconcile incentives for novel antibiotic development with their long-term conservation through appropriate consumption.