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Explicit definitions of potentially inappropriate prescriptions of antibiotics in hospitalized older patients

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1 Introduction

The development of antibiotic-resistant bacteria is a major public health issue. According to recent estimates, infections by these microorganisms will constitute the leading cause of mortality by 2050 [1]. One of the main sources of bacterial resistance is the inappropriate use of antibiotics [2,3]. Several national and international action plans have thus been developed, with the goal of reducing inappropriate antibiotic prescriptions and combating antibiotic resistance [4–6]. In these action plans, the evaluation of the appropriateness or inappropriateness of an antibiotic prescription is usually based on an expert's opinion, relative to general guidelines on antimicrobial use and the patient's individual situation. This type of expert opinion corresponds to a so-called implicit approach. Older people are particularly exposed to both bacterial infections and inappropriate drug prescriptions [7–9]. A complementary approach in older populations is the explicit definition of potentially inappropriate drug prescriptions (PIPs) [10–12]. This is based on explicit criteria that (i) provide training tools for prescribers, (ii) enable the development of computerized tools for automated PIP detection, and (iii) provide epidemiological data on these prescriptions [13–15].

A systematic review of the recent literature showed that validated, explicit criteria for potentially inappropriate prescriptions of antibiotics (antibiotic PIPs) in older patients are currently lacking [16].

Hence, the objective of the present study was to collate expert definitions of antibiotic PIPs in hospitalized older patients to address the rise in antibiotic resistance.

2 Method

2.1 Study design

We performed a qualitative, multicenter, focus-group-based study of expert geriatricians and infectious disease specialists in France, in order to collate their proposals for explicit definitions of antibiotic-PIPs in hospitalized older patients. The study comprised three steps: (i) exploratory focus group sessions, (ii) analysis of the focus group data, and formulation of explicit definitions, and (iii) validation of the explicit definitions thus formulated. The study procedures are schematically described in Figure 1. A steering committee was set up to validate the methodology and to monitor the study progress. The study complied with the Consolidated Criteria for Reporting Qualitative Research (COREQ) [17].

2.2 Study objective

The objective of the focus groups was to formulate explicit definitions of antibiotic-PIPs in hospitalized older patients to fight against antibiotic resistance. These aspects are detailed below.

2.2.1 Explicit definitions

The inappropriateness of drug prescriptions can be evaluated in clinical pharmacology using two approaches: the first is based on a so-called “implicit” expert judgement, and the second uses explicit criteria [18,19]. An implicit judgement is based on an expert’s evaluation of the quality of care with regard to the patient’s situation and guidelines on the use of antimicrobial drugs. Several implicit evaluation methods have been developed, such as the Medication Appropriateness Index [20]. In contrast, explicit criteria are based on predefined rules for the analysis of drug prescriptions, and do not require

intervention by an expert. For example, Beers criteria explicitly state that the prescription of hydroxyzine is inappropriate in patients over the age of 75 [10].

2.2.2 Potentially inappropriate prescriptions

Explicit definitions cover situations considered by experts to be generally inappropriate, as defined in the literature or by expert consensus. However, when an explicit definition is applied to a given prescription, the absence of expert opinion means that the prescription inappropriateness cannot be confirmed. Hence, explicit definitions correspond to *potentially* inappropriate prescriptions.

2.2.3 Definitions in hospitalized older patients

Explicit definitions concerned older patients (aged 75 or over) hospitalized in acute care units.

2.2.4 Perspectives: the fight against antibiotic resistance

Explicit definitions of PIPs are usually intended to limit adverse events on the individual patient level [10–12]. In the present study, explicit definitions were deliberately conceived to combat antibiotic resistance at the population level.

2.3 Exploratory focus groups (Figure 1, part 1)

2.3.1 Recruitment of participants

We sought to organize four focus groups with 6 to 10 participants each [21]. Participants had to be hospital-based physicians (infectious disease specialists, geriatricians, and other specialists) with antimicrobial stewardship responsibilities. Study investigators and focus group members had no contact prior to the study commencement. Participants' characteristics (age, gender, year of qualification, medical specialty/specialties, involvement in training on antibiotic stewardship, and type of hospital [general or university]) were recorded.

Participants were recruited by e-mailing all members of the French Infectious Diseases Society (French acronym SPILF), with the help of the joint SPILF-Gerontology and Geriatrics Society interest group.

2.3.2 Focus groups

Focus groups respectively met in four French cities (Saint-Malo, Nimes, Chambery, and Bordeaux) between June 2017 and January 2018. Each focus group met for two hours. Two investigators were present: a facilitator and an observer. All participants had given their consent for the focus groups to be videoed and audiotaped.

At the start of the meeting, participants viewed a presentation of the investigating research group and the study objectives relevant to the focus group (as detailed in section 2.2). The discussion was initiated by asking each participant to list the antibiotics that they thought were worth considering. PIPs were discussed for each antibiotic, so as not to restrict the depth and range of topics covered by the focus groups.

After each session, the steering committee met to adjust the focus group procedure and guide (if necessary).

2.4 Analysis and formulation of explicit definitions (Figure 1, part 2)

2.4.1 Transcription and analysis

The audio recording of each focus group was transcribed verbatim. A discourse analysis of the verbatim was performed independently by two investigators, using NVivo® software (version 11, QSR International, Melbourne, Australia). The objective was to identify all verbatim elements that referred to explicit definitions of antibiotic-PIPs. Any disparities between the two analyses were discussed by the two researchers, resolved by consensus, and then systematically validated by the steering committee.

2.4.2 Transformation of the verbatim into explicit definitions

Each verbatim element referring to an explicit definition was reread independently by two investigators. The objective was to group together verbatim elements that referred to the same definition. For each definition, each researcher suggested a formulation that was as close as possible to the verbatim. Any differences in formulation were discussed by the two researchers, resolved by consensus, and then systematically validated by the steering committee.

2.4.3 Classification

Each explicit definition thus identified was classified by the two researchers as a function of *(i)* the infectious disease domain concerned (infection site, use, type of pathogen, etc.), and then *(ii)* the type of inappropriateness (underuse, overuse, or misuse). Any disagreements were discussed and resolved by consensus. The opinion of a third researcher was sought when required.

2.5 Validation of formulations (Figure 1, part 3)

The objective of this step was to validate the explicit definitions formulated by the two investigators and the steering committee.

2.5.1 External validation

We contacted local networks of expert infectious disease specialists and geriatricians in the North of France. Participants were not linked to our research group and had not participated in the focus groups. Each explicit definition was reviewed by two pairs of experts, in two phases. In the first phase, each expert reviewed the definitions independently. In the second phase, the three pairs of experts compared their respective reviews of each definition in a meeting facilitated by two investigators. Any divergence were discussed and resolved by consensus.

2.5.2 Internal validation

The list of explicit definitions validated by the group of experts from the North of France was then submitted to all focus group participants for final validation.

3 Results

3.1 Focus groups and characteristics of study participants

A total of 28 participants (seven per focus group) were recruited. The participants' median (range) age was 40 (28–61). Most participants were geriatricians (n=12; 42.8%) or infectious disease specialists (n=11; 39.3%). All participants were involved in antibiotic stewardship in their respective institutions, and 22 participants (78.6%) had training responsibilities. Participants' characteristics are summarized in Table 1.

3.2 Classification of antibiotic-PIP explicit definitions

The analysis of focus groups lead to the identification of 65 explicit definitions of antibiotic-PIPs applicable to hospitalized older patients, classified into 18 domains (Table 2). Experts emphasized that these definitions should only be used in two medical situations: in the absence of severe presentation and in the absence of known drug allergies.

For half of suggested definitions, inappropriateness was determined by the infectious context, *i.e.* infection site (n=28; 43%) or specific pathogen (n=4; 6%). For the remaining definitions, inappropriateness was related to general principles of antibiotic use (n=18; 28%) or prescription modes (n=15; 23%), rather than the infectious context.

3.3 Explicit definitions suggested by the experts

All 65 explicit definitions of antibiotic-PIPs suggested by the experts (classified by domains and subdomains) are listed in Table 3. Antibiotics considered in the explicit definitions were mainly fluoroquinolones (n=11; 17%), amoxicillin-clavulanic acid (n=8; 12%),

cephalosporins (n=8; 12%), aminoglycosides (n=7; 11%), and carbapenems (n=5; 8%). Definitions for which inappropriateness was related to the infection site mainly concerned the urinary tract (urinary tract colonization, cystitis, and upper urinary tract infection; n=10; 15%) and the lower respiratory tract (n=7; 11%). Overall, 56 definitions (86%) were new proposals that had not been identified in a recent systematic review of the literature [16].

Table 4 presents a simplified classification of the definitions according to inappropriateness. Forty-seven explicit definitions (73%) concerned misuse, 15 (23%) concerned overuse and three (5%) concerned underuse.

4 Discussion

4.1 Main findings

The present study led to drawing up a list of 65 explicit definitions of antibiotic-PIPs in hospitalized older patients (Table 3); 56 definitions had not been mentioned previously [16]. Given that the methods used here were exploratory and qualitative in nature, these definitions are currently only proposals; they must be validated by expert consensus before being used in routine clinical practice. Moreover, these definitions should only be used in two medical situations: in the absence of severe presentation and in the absence of known drug allergies.

4.2 Definitions with potential value in the fight against antibiotic resistance

Antibiotics most frequently cited in the definitions were fluoroquinolones, amoxicillin-clavulanic acid, cephalosporins, aminoglycosides, and carbapenems. These classes of antibiotics are known to promote the development of bacterial resistance, and have been qualified as critical by the World Health Organization [22]. Furthermore, shorter courses of treatment help to decrease antibiotic consumption and reduce the selective

pressure on multidrug-resistant bacteria. Several guidelines have recently recommended shorter courses of antibiotic therapy [23–25]. The definitions developed in the present study fit well with this perspective, since several definitions relate to treatment duration. Lastly, experts of the focus groups suggested definitions that fell into a new category – “general principles of antibiotic use”. These definitions covered the choice of antibiotics for community-acquired infections or undocumented infections, with a view to sparing the use of broad-spectrum antibiotics.

Some of the explicit definitions proposed are not specific to older people in hospital setting (*e.g.* "to prescribe vancomycin without a loading dose”). Indeed, all definitions were intended to be relevant and applicable to older people, but not limited to older people. Therefore, some definitions could be applied to other patients, such as younger adults or in other care settings (*e.g.* outpatients, rehabilitation).

4.3 The need for validation by expert consensus

Explicit definitions of antibiotic-PIPs generated here were based on the verbatim transcription of the focus group discussions; hence, they do not represent an expert consensus, and must now be validated. Some of the proposals in this work may be questionable or appear to deviate from guidelines. Several versions of proposals may also be redundant or contradictory (*e.g.* definitions 52 and 53, table 3). The aim of this work was to perform a rigorous study that lists explicit definitions that can be conceived or proposed in a particular context (older hospitalized patients, excluding severe presentations). The methodology of the qualitative study does not allow us to modify the content obtained. This also applies to the definitions identified in the recent literature review, since most were cited in a single article only [16]. These observations suggest that the list of definitions in the literature review and the list generated by the present study should be merged, submitted

to a panel of experts, assessed for relevance, and then agreed by consensus. These procedures are regularly used to draw up lists of explicit definitions of PIPs in older patients [26].

4.4 Perspectives for applying explicit definitions of antibiotic-PIPs

After validation by expert consensus, a list of explicit definitions of antibiotic-PIPs would constitute a useful tool in the fight against antibiotic resistance. Explicit definitions may be of value to *(i)* provide training messages to prescribers; *(ii)* develop tools that detect antibiotic-PIPs by analyzing healthcare databases, and *(iii)* generate epidemiological data on antibiotic-PIPs.

Most antimicrobial stewardship strategies are based on the implicit approach, which takes account of the complexity of factors that must be considered when prescribing antibiotics (patient's medical history, clinical/laboratory/microbiological data, etc.). A validated reference set of explicit antibiotic-PIPs would be a useful complement for these training resources.

The explicit definitions of antibiotic-PIPs can be used to screen *potentially* inappropriate situations that must then be re-evaluated by an expert. In geriatric medicine, several randomized trials have shown that the use of these criteria improved the quality of prescriptions in older people [27]. With a view to combating antibiotic resistance, the re-evaluation of a course of antibiotics 48 to 72 hours post-initiation is part of antimicrobial stewardship, and helps to decrease the incidence of inappropriate prescriptions [28,29]. The explicit criteria described above could be integrated into decision-support computer systems that screen patients for antibiotic-PIPs [30,31]. This screening would provide additional assistance with the re-evaluation of antibiotic treatments – notably for multidisciplinary teams involved in antimicrobial stewardship. Hence, the explicit approach might thus

usefully complement the implicit approach, which remains essential to take into account all pieces of information required for the overall patient management.

4.5 Study strengths and limitations

Our qualitative study complied with the COREQ criteria. The exhaustive, verbatim transcription of the whole discussion was analyzed independently by two investigators. The study phases were validated by the project's steering committee. Obtained results were validated by an independent working group and then by all focus group participants.

However, our study also had limitations. First, we only consulted experts based in France. Given that the method used here was exploratory, the final list of explicit definitions is probably not exhaustive. The levels of bacterial resistance and the antibiotics marketed in France differ from those in other countries in Europe or around the world. Hence, the scope of some of the definitions suggested here might be limited. Our chosen methodology was descriptive; thus, our reporting of definitions did not depend on the number of times they were mentioned in the focus groups or by other study participants. Definitions reported in this study are thus novel proposals that must be validated by expert consensus prior to use in clinical practice. Lastly, the applicability of explicit definitions and potential for implementation in computer systems will need to be addressed in further research.

5 Conclusion

Our qualitative, multicenter study generated 65 explicit definitions of antibiotic-PIPs in hospitalized older patients, classified into 18 domains of infectious diseases. Fifty-six definitions (86%) were new, and had not been identified in a recently published systematic review of the literature. The most relevant and useful definitions for clinical practice must

now be selected by expert consensus, to provide a new tool for use in the fight against antibiotic resistance.

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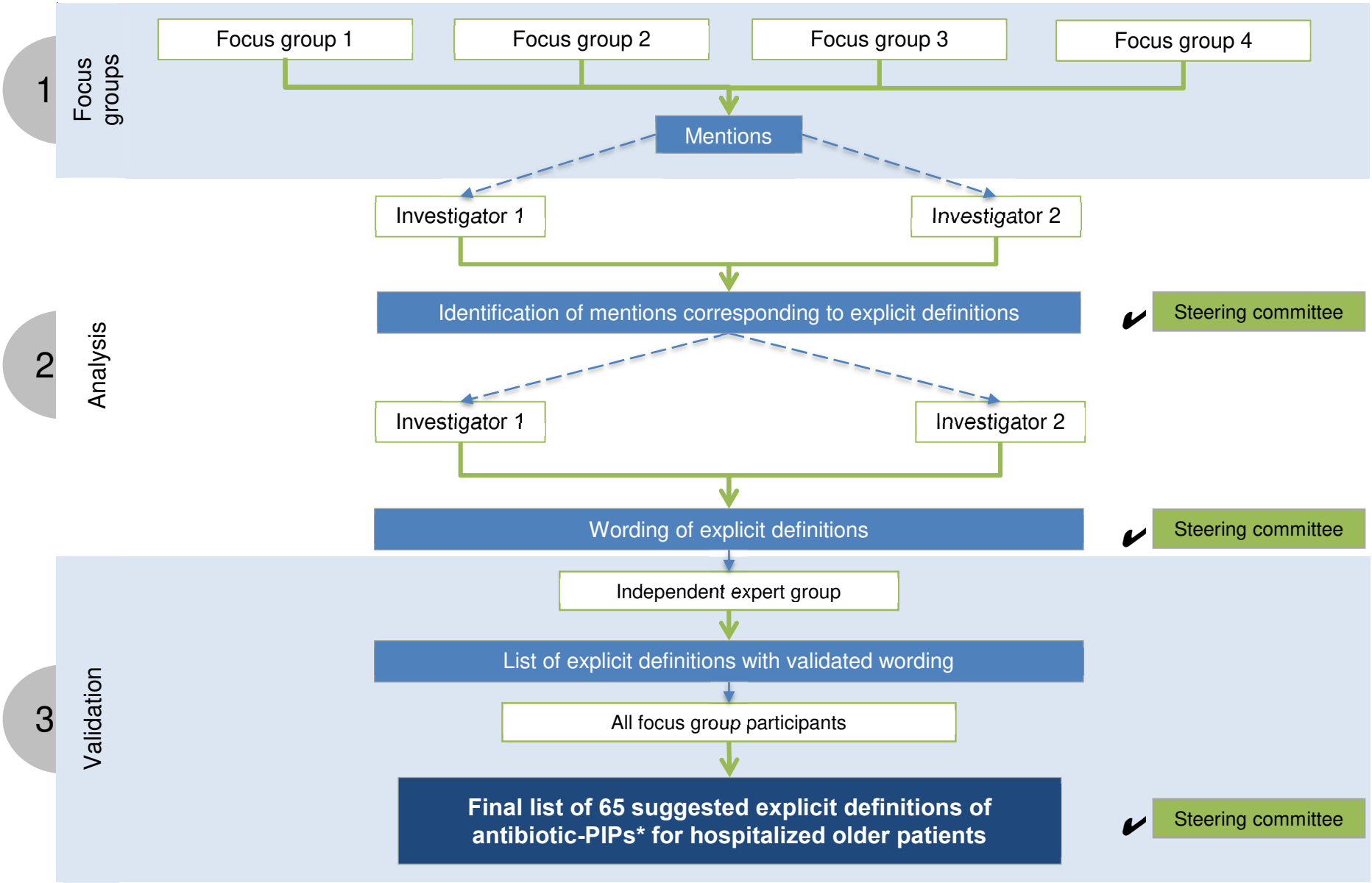
Figure 1. Study flow diagram



* Potentially inappropriate prescriptions of antibiotics

Table 1. Characteristics of focus group participants

Characteristics	**Participants n=28**
Age (median [min ; max])	40 [28 ; 61]
Year of MD thesis (median [min ; max])	2006 [1986 ; 2016]
Female gender	10 (35.7%)
Antimicrobial stewardship activity	22 (78.6%)
Type of hospital	
University hospital	19 (67.8%)
General hospital	9 (32.2%)
Medical specialty	
Geriatrician	12 (42.8%)
Infectious diseases specialist	11 (39.3%)
Geriatrician and Infectious diseases specialist	2 (7.2%)
Other (family physician, dermatologist, hospital pharmacist)	3 (10.7%)

Table 2. Numbers of explicit definitions of antibiotic-PIPs in hospitalized older patients according to domain or usage

Class/domain	Number of definitions (n=65)	
	n	%
Organ systems	**28**	**43%**
Urinary tract	10	15%
Lower respiratory tract	7	11%
Upper respiratory tract	4	6%
Skin and soft tissues	3	5%
Gastrointestinal tract	3	5%
Bones and joints	1	2%
General principles of antibiotic use	**18**	**28%**
All organ systems	9	14%
Undocumented infections	5	8%
Community-acquired infections	4	6%
Types of use	**15**	**23%**
Dosage	5	8%
Duration of treatment	4	6%
Combinations of antibiotics	3	5%
Laboratory assays	2	3%
Administration route	1	2%
Organisms	**4**	**6%**
Viruses	1	2%
Clostridium difficile	1	2%
Pseudomonas spp.	1	2%
Salmonella spp.	1	2%

Table 3. Classification of explicit definitions of potentially inappropriate prescriptions of antibiotics in hospitalized older patients (caution: definitions require external validation through a Delphi survey before being used in practice)

These definitions should only be used in two medical situations: in the absence of severe presentation, and in the absence of known drug allergies.

Class	Domain	Subdomain	Explicit definitions corresponding to the verbatim "It is potentially inappropriate to…"	New definition*
Site of infection	Urinary tract	General	1. prescribe nitrofurantoin for urinary tract infections (apart from cystitis)	X
			2. prescribe norfloxacin for urinary tract infections (apart from cystitis)	X
			3. prescribe amoxicillin-clavulanic acid for the empirical therapy of urinary tract infections	X
			4. prescribe fluoroquinolones for the empirical therapy of urinary tract infections	X
		Urinary tract colonization	5. prescribe antibiotics for urinary tract colonization (in the absence of urinary tract surgery, and regardless of the pathogen identified [ESBL, etc.])	SR
		Cystitis	6. prescribe a 3GC in case of cystitis	X
			7. prescribe a 4GC in case of cystitis	X
			8. prescribe fluoroquinolones for the first-line treatment of cystitis	SR
		Male urinary tract infection	9. prescribe amoxicillin for male urinary tract infections (apart from enterococci)	X
			10. prescribe amoxicillin-clavulanic acid for male urinary tract infections	X
	Lower respiratory tract	Pneumonia	11. prescribe ceftriaxone for documented pneumococcal acute community-acquired pneumonia	X
			12. prescribe amoxicillin-clavulanic acid for documented pneumococcal acute community-acquired pneumonia	X
			13. prescribe an injectable 3GC for a non-severe case of community-acquired pneumonia	SR
			14. prescribe fluoroquinolones for the first-line treatment of pneumonia	SR
			15. prescribe a macrolide for community-acquired pneumonia (apart from legionellosis)	X
			16. prescribe a two-antibiotic combination in case of pneumonia	X
			17. prescribe antibiotics in case of viral pneumonia	SR
	Upper respiratory tract	Non-specific URTI	18. prescribe a 3GC for URTI	X
			19. prescribe a fluoroquinolone for the first-line treatment of URTI	X
		Sinusitis	20. prescribe amoxicillin-clavulanic acid in case of maxillary sinusitis	X
		Otitis	21. prescribe amoxicillin-clavulanic acid in case of acute otitis media	X
	Skin and soft tissues		22. prescribe an antibiotic for the treatment of a wound in the absence of cellulitis	SR
			23. prescribe any molecule other than amoxicillin for cellulitis of the lower limb	X
			24. prescribe topical antibiotics (apart from *Staphylococcus aureus* decontamination)	X

	Gastrointestinal tract	25. prescribe antibiotics for the empirical therapy of diarrhea	SR
		26. prescribe amoxicillin-clavulanic acid for nosocomial gastrointestinal infections	X
		27. prescribe amoxicillin-clavulanic acid for the first-line treatment of digestive tract infections	X
	Bones/joints	28. prescribe antibiotics for the empirical therapy of bone or joint infections before collection of reliable microbiological samples	X
General principles of antibiotic use	All sites of infection	29. prescribe ceftriaxone rather than cefotaxime when venous access is available	X
		30. prescribe oral 3GCs (except for documented switch in case of acute pyelonephritis in women)	X
		31. prescribe ertapenem as a first-line treatment	X
		32. prescribe aminoglycosides when severity criteria are not met	X
		33. prescribe fluoroquinolones as a first-line treatment (apart from male urinary tract infections or acute pyelonephritis)	X
		34. prescribe antibiotics for an isolated elevation of CRP	X
		35. prescribe imipenem if meropenem can be used	X
		36. prescribe fluoroquinolones as empirical therapy in patients treated with fluoroquinolones in the previous 6 months	X
		37. prescribe a fluoroquinolone if a 3GC can be used	X
	Undocumented infections	38. prescribe rifampicin as empirical therapy	X
		39. prescribe carbapenems as empirical therapy	X
		40. prescribe ertapenem as empirical therapy	X
		41. prescribe fluoroquinolones as empirical therapy	X
		42. prescribe cotrimoxazole as empirical therapy (except when pneumocystosis is suspected)	X
	Community-acquired infections	43. prescribe piperacillin-tazobactam for community-acquired infections	X
		44. prescribe a 4GC for community-acquired infections	X
		45. prescribe carbapenems for community-acquired infections	X
		46. prescribe antibiotics effective against methicillin-resistant staphylococci (vancomycin, teicoplanin, daptomycin, linezolid, and dalbavancin) as empirical therapy for community-acquired infections	X
Use	Dosage	47. use the Cockcroft-Gault formula to estimate renal function for antibiotic dose adjustments	X
		48. reduce the dosage of aminoglycosides in the event of kidney failure	SR
		49. fail to re-evaluate dosage according to renal function changes	X
		50. prescribe rifampicin at a dosage of 20 mg/kg/day	X
		51. prescribe vancomycin without a loading dose	X
	Duration of treatment	52. prescribe aminoglycosides for more than 3 days	X
		53. prescribe aminoglycosides for more than a day	X
		54. prescribe a course of antibiotics of more than 7 days	X
		55. prescribe a course of antibiotics of more than 7 days for pneumonia	SR
	Combination of antibiotics	56. combine amoxicillin-clavulanic acid with metronidazole	X
		57. combine two aminoglycosides	X

		58. prescribe rifampicin as a single drug	X
	Laboratory assays	59. assay the peak and residual plasma concentrations of aminoglycosides	X
		60. prescribe a glycopeptide without assaying plasma concentrations	X
	Administration route	61. prescribe a subcutaneously administered aminoglycoside	X
Organisms	Viruses	62. prescribe antibiotics for influenza	X
	Clostridium difficile	63. prescribe metronidazole for *Clostridium difficile* infections	X
	Pseudomonas	64. prescribe a fluoroquinolone alone for the first-line treatment of *Pseudomonas aeruginosa* infections	X
	Salmonella	65. prescribe fluoroquinolones for the first-line treatment of salmonellosis	X

* X: definitions not identified in the systematic literature review; SR: definitions identified in the systematic literature review [16].
3GC: third-generation cephalosporin; 4GC: fourth-generation cephalosporin; URTI: upper respiratory tract infection

Table 4. Explicit definitions of potentially inappropriate prescriptions of antibiotics in hospitalized older patients, by type of inappropriateness (caution: definitions require external validation through a Delphi survey before being used in practice).

These definitions should only be used in two medical situations: in the absence of severe presentation and in the absence of known drug allergies.

Domains	Explicit definitions of potentially inappropriate prescriptions of antibiotics "It is potentially inappropriate to …"
Overuse (n=15; 23%)	
Urinary tract	- prescribe antibiotics for urinary tract colonization (in the absence of urinary tract surgery, and regardless of the pathogen identified [ESBL, etc.])
Lower respiratory tract	- prescribe a two-antibiotic combination in case of pneumonia - prescribe antibiotics in case of viral pneumonia
Skin and soft tissues	- prescribe topical antibiotics (apart from *Staphylococcus aureus* decontamination) - prescribe an antibiotic for the treatment of a wound in the absence of cellulitis
Gastrointestinal tract	- prescribe antibiotics for the empirical therapy of diarrhea
All sites of infection	- prescribe antibiotics for an isolated elevation of CRP - prescribe aminoglycosides when severity criteria are not met
Viruses	- prescribe antibiotics for influenza
Dosage	- prescribe rifampicin at a dosage of 20 mg/kg/day
Duration of treatment	- prescribe aminoglycosides for more than 3 days - prescribe aminoglycosides for more than a day - prescribe a course of antibiotics of more than 7 days - prescribe a course of antibiotics of more than 7 days for pneumonia
Combination of antibiotics	- combine two aminoglycosides
Underuse (n=3; 5%)	
Dosage	- use the Cockcroft-Gault formula to estimate renal function for antibiotic dose adjustments - reduce the dosage of aminoglycosides in the event of kidney failure - prescribe vancomycin without a loading dose
Misuse: inappropriate choice (n=40; 62%)	

Urinary tract	- prescribe nitrofurantoin for urinary tract infections (apart from cystitis) - prescribe norfloxacin in urinary tract infections (apart from cystitis) - prescribe amoxicillin for male urinary tract infections (apart from enterococci) - prescribe amoxicillin-clavulanic acid for male urinary tract infections - prescribe amoxicillin-clavulanic acid for the empirical therapy of urinary tract infections - prescribe a 3GC in case of cystitis - prescribe a 4GC in case of cystitis - prescribe fluoroquinolones for the empirical therapy of urinary tract infections - prescribe fluoroquinolones for the first-line treatment of cystitis
Lower respiratory tract	- prescribe ceftriaxone for documented pneumococcal acute community-acquired pneumonia - prescribe amoxicillin-clavulanic acid for documented pneumococcal acute community-acquired pneumonia - prescribe an injectable 3GC in a non-severe case of community-acquired pneumonia - prescribe fluoroquinolones for the first-line treatment of pneumonia - prescribe a macrolide for community-acquired pneumonia (apart from legionellosis)
Upper respiratory tract	- prescribe amoxicillin-clavulanic acid in case of acute otitis media - prescribe amoxicillin-clavulanic acid in case of maxillary sinusitis - prescribe a 3GC for URTI - prescribe a fluoroquinolone for the first-line treatment of URTI
Skin and soft tissues	- prescribe any molecule other than amoxicillin for cellulitis of the lower limb
Gastrointestinal tract	- prescribe amoxicillin-clavulanic acid for nosocomial gastrointestinal infections - prescribe amoxicillin-clavulanic acid for the first-line treatment of digestive tract infections
All sites of infection	- prescribe fluoroquinolones as a first-line treatment (apart from male urinary tract infections or acute pyelonephritis) - prescribe fluoroquinolones for empirical therapy in patients treated with fluoroquinolones in the previous 6 months - prescribe fluoroquinolones as a first-line treatment (apart from male urinary tract infections or acute pyelonephritis) - prescribe ceftriaxone rather than cefotaxime when venous access is available - prescribe a fluoroquinolone if a 3GC can be used - prescribe ertapenem as a first-line treatment - prescribe imipenem if meropenem can be used
	- prescribe carbapenems for empirical therapy

Undocumented infections	- prescribe fluoroquinolones for empirical therapy - prescribe cotrimoxazole for empirical therapy (except when pneumocystosis is suspected) - prescribe rifampicin for empirical therapy - prescribe ertapenem for empirical therapy
Community-acquired infections	- prescribe antibiotics effective against methicillin-resistant staphylococci (vancomycin, teicoplanin, daptomycin, linezolid, and dalbavancin) for empirical therapy of community-acquired infections - prescribe a 4GC for community-acquired infections - prescribe carbapenems for community-acquired infections - prescribe piperacillin-tazobactam for community-acquired infections
Clostridium difficile	- prescribe metronidazole for *Clostridium difficile* infections
Pseudomonas	- prescribe a fluoroquinolone alone for the first-line treatment of *Pseudomonas aeruginosa* infections
Salmonella	- prescribe fluoroquinolones for the first-line treatment of salmonellosis

Misuse: inappropriate use (n=7; 11%)	
Bones/joints	- prescribe antibiotics for the empirical therapy of bone or joint infections before collection of reliable microbiological samples
Dosage	- fail to re-evaluate the dosage according to renal function changes
Combination of antibiotics	- combine amoxicillin-clavulanic acid with metronidazole - prescribe rifampicin as a single drug
Laboratory assays	- assay the peak and residual plasma concentrations of aminoglycosides - prescribe a glycopeptide without assaying plasma concentrations
Administration route	- prescribe a subcutaneously administered aminoglycoside

CRP: C-reactive protein; 3GC: third-generation cephalosporin; 4GC: fourth-generation cephalosporin