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Selection of proxy indicators estimating the appropriateness of antibiotic prescriptions in general practice: a national consensus procedure in France

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Background: GPs are responsible for more than 70% of outpatient antibiotic prescriptions in France. Metrics are important antibiotic stewardship tools that can be used to set targets for improvement and to give feedback to professionals and stakeholders.

Objectives: The primary objective of the present study was to select a set of proxy indicators (PIs) based on 10 previously developed PIs, to estimate the appropriateness of antibiotic prescriptions by GPs. The secondary objective was to evaluate the clinimetric properties of the selected PIs.

Methods: A RAND-modified Delphi consensus procedure was conducted with a multidisciplinary panel of stakeholders. This procedure consisted of two successive online surveys with a consensus meeting in between. Clinimetric properties (measurability, applicability and potential room for improvement) were evaluated for the PIs selected through the consensus procedure, using 2022 Regional Health Insurance data.

Results: Seventeen experts participated in the first-round survey and 14 in the second-round. A final set of 12 PIs was selected. Among the 10 initial PIs, 3 were selected without modification and 7 were modified and selected. Moreover, two newly suggested PIs were selected. Ten of the 12 PIs presented good clinimetric properties.

Conclusions: The 12 selected PIs cover the main situations responsible for inappropriate and unnecessary use of antibiotics in general practice. These PIs, easily calculable using routinely collected health insurance reimbursement data, might be used to give feedback to prescribers and stakeholders and help improve antibiotic prescriptions in primary care.

Introduction

Antimicrobial resistance (AMR) is an increasing threat to global health.[1] Around 1.3 million deaths were attributable to bacterial AMR around the world in 2019.[2] In France, it was estimated that around 100 000 persons are infected by MDR bacteria each year, causing approximately 4500 deaths.[3] In 2021, 78% of antibiotics were prescribed in primary care in France, with approximatively 70% of those by GPs.[4] Inappropriate and/or unnecessary use of antibiotics, which accelerates AMR,[5] represents about half of outpatient antibiotic prescriptions in France.[6]

Antimicrobial stewardship (AMS) has been defined as a 'coherent set of actions which promote a responsible use of antimicrobials'.[7] Metrics are important AMS tools that can be used to set targets for improvement and to give feedback to professionals and stakeholders.[8] Quality indicators generally require clinical data to be calculated. In most European countries, including France, there are no computerized

national systems able to link drug prescriptions to clinical indications.[9]

To overcome this issue, Thilly *et al.*[10] developed 10 proxy indicators (PIs) estimating the appropriateness of antibiotic prescriptions at the GP level and calculable from routine reimbursement databases without requiring clinical data. For each PI, they defined an optimal target (to be reached when practices are 100% compliant with guidelines) and, when relevant, an acceptable target, less restrictive (to take into account that guidelines do not cover the full range of clinical situations). However, the definitions and targets of these PIs are debatable as they were based on the opinion of a limited number of experts.[10] To be used on a large scale, the understanding and relevance of PIs for GPs' routine practice need to be assessed through a structured consensus procedure involving a multidisciplinary group of stakeholders, including GPs. Such a process should result in a set of PIs selected by GPs on their relevance in routine practice. This process might improve GPs' confidence in the accuracy of PIs to describe their clinical performance, and thus their acceptability of feedback interventions displaying these PIs.[11]

The primary objective of the present study was to select a set of PIs based on the 10 developed by Thilly *et al.* to estimate the appropriateness of antibiotic prescriptions by GPs, through a RAND-modified Delphi consensus procedure. The secondary objective was to evaluate the clinimetric properties (measurability, applicability and potential room for improvement) of the selected PIs.

Methods

Study design

This study used a RAND-modified national Delphi consensus procedure,[12,13] conducted between July 2021 and January 2022. Briefly, the study consisted in presenting 10 PIs to relevant stakeholders, and included two successive online surveys (first and second rounds) with a consensus meeting in between. The study involved several groups: (i) The 'research team', with researchers from the APEMAC research unit (specialized in antibiotic stewardship, epidemiology and public health) who previously developed 10 PIs,[10] experts from the regional antibiotic stewardship centre, and members of the Regional Health Insurance. This group supervised every stage of the study (i.e. the questionnaires' conception, data collection and management, data analyses and drafting of the manuscript), moderated the consensus meeting, and provided their expertise on the PIs' rationale and calculation during this meeting. (ii) The 'experts', with GPs and infectious disease physicians (target $n=15$[14]; see details in the section 'Recruitment of the participants'), who assessed the relevance of the PIs through the online surveys and during the consensus meeting. (iii) The 'observers', including experts from the National Health Insurance and the French Public Health agency who participated in the consensus meeting discussions to bring their expertise to the debate, without getting involved in the evaluation process.

Initial proxy indicators

Thilly *et al.*[10] developed 10 PIs estimating the appropriateness of antibiotic prescriptions at the GP level, calculable from routine French health insurance databases, without requiring clinical indications. These indicators were derived from the DRIVE-AB European project list of 32 quality indicators of antibiotic prescriptions in the outpatient setting.[15] Definition (numerator and denominator) and target population were adapted to be calculable using the health insurance databases. Target values were defined to estimate the appropriateness of antibiotic prescriptions, i.e. the compliance with national guidelines. The clinimetric properties (measurability, applicability and potential room for improvement) of the 10 PIs were evaluated using 2017 regional health insurance reimbursement data, and showed satisfying results.[10] Table S1 (available as Supplementary data at *JAC-AMR* Online) presents the 10 initial PIs, with their definition, target population and target value(s).

Recruitment of the participants

The experts involved in the RAND-modified national Delphi consensus procedure were selected through their membership of different relevant French national societies or organizations from different regions, to have a nationwide representative panel of various opinions. We contacted the GPs' Regional Union of Health Professionals (Union Régionale des Professionnels de Santé Grand Est—URPS Médecins), the national College of General Practice (Collège de Médecine Générale—CMG), the national French Society of Infectious Diseases (Société de Pathologie Infectieuse de Langue Française—SPILF), and the regional antimicrobial stewardship centre (AntibioEst). These organizations were invited by e-mail to appoint two to four members to participate in the two rounds of the questionnaire survey and the consensus meeting. Members who consented to participate were e-mailed full details of the study (including the Thilly *et al.* paper) and a link to the first-round online questionnaire.

The RAND-modified Delphi consensus procedure

First-round survey

The list of 10 PIs developed by Thilly *et al.* was presented as an internet-based questionnaire using Google Forms® (Table S2). The questionnaire was e-mailed on 26 July 2021. Experts were asked to complete the questionnaire within 8 weeks. A reminder was sent to the non-responders 2 weeks before the deadline.

PIs were presented with their definition, target population, target value(s), and the rationale and evidence regarding their definition and interpretation. Experts were asked to evaluate the relevance of the PIs and their target(s) to estimate the appropriateness of antibiotic prescriptions at the GP level. For each PI, experts were asked to indicate if (i) the definition, (ii) the target population, and (iii) the target value(s) were appropriate (yes, more or less, or no), and to suggest modifications if they answered more or less, or no. They were also asked to rate the global relevance of the indicator, using a 9-point Likert scale. Experts could also suggest new PIs for further discussion.

At this stage, consensus among respondents was defined on the global relevance criterion, evaluated with a 9-point Likert scale ranging from 1 ('not relevant at all') to 9 ('highly relevant'). PIs rated 7 to 9 by ≥75% of experts and 1 to 3 by ≤15% of experts were selected; PIs rated 7 to 9 by ≤15% of experts and 1 to 3 by ≥75% of experts were excluded; all other combinations reflected a lack of consensus.[16]

Consensus meeting

Experts who participated in the first-round survey were invited to an online consensus meeting organized by the research team and received a detailed summary of the first-round questionnaire results. The 'observers' [professionals from the National Health Insurance, and the French Public Health agency (Santé Publique France)] were also invited to participate in the discussion. The meeting was held on 6 October 2021 virtually on Zoom® and was led by two members of the research team.

The objective of this meeting was to discuss: (i) PIs for which there was a lack of consensus at the first-round survey (see definition above), (ii) PIs selected but for which modifications were suggested, and (iii) suggestions for new PIs. During this meeting, results of the first-round questionnaire were presented for each PI with the global relevance results, the relevance results for each item [definition, target population, target value(s)]

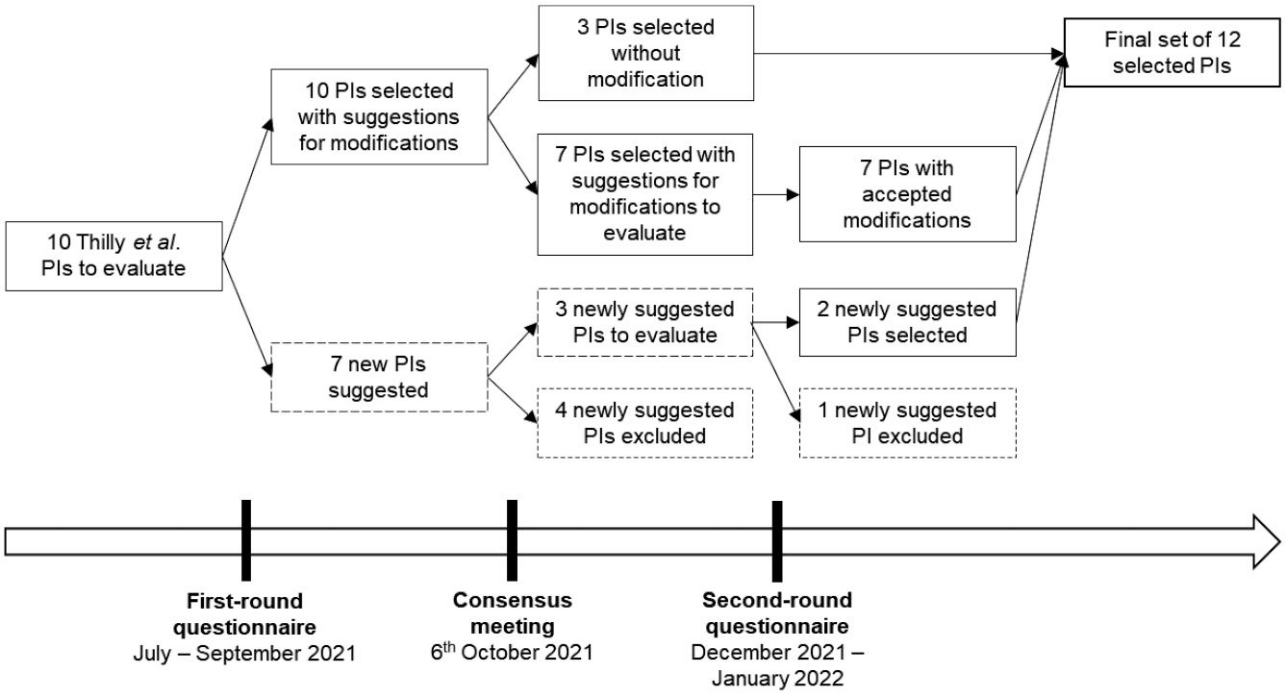

Figure 1. Flowchart of the RAND-modified Delphi consensus procedure. PI, proxy indicator.

Table 1. First-round survey results: rates of the proxy indicators' global relevance and decision ($n=17$)

Proxy indicator (PI)	Global relevance rates,[a] *n* [1–3]	[4–6]	[7–9]	Decision at the end of the first round[b]
PI 1—Antibiotic prescriptions against urinary tract infections in men (ratio)	1	3	13	Selected
PI 2—Antibiotic prescriptions against urinary tract infections in women (ratio)	1	3	13	Selected
PI 3—Repeated prescription of quinolones (%)	0	1	16	Selected
PI 4—Seasonal variation of total antibiotic prescriptions (%)	1	2	14	Selected
PI 5—Seasonal variation of quinolone prescriptions (%)	2	2	13	Selected
PI 6—Amoxicillin/second-line antibiotics prescriptions (ratio)	0	0	17	Selected
PI 7—Prescriptions of not indicated antibiotics (%)	0	1	16	Selected
PI 8—Estimated duration of antibiotic prescriptions >8 days (%)	1	2	14	Selected
PI 9—Co-prescription of antibiotic and systemic non-steroidal anti-inflammatory drugs (%)	0	0	17	Selected
PI 10—Co-prescription of antibiotic and systemic corticosteroids (%)	0	2	15	Selected

[a]Global relevance rates were estimated using a 9-point Likert scale ranging from 1 ('not relevant at all') to 9 ('very relevant').
[b]Consensus was defined as follows: PIs rated 7 to 9 by ≥12/17 experts and 1 to 3 by ≤3/17 experts were selected for the next stage; PIs rated 7 to 9 by ≤12/17 experts and 1 to 3 by ≥3/17 experts were excluded; all other combinations reflected a lack of consensus.

and the main modifications suggested. Newly suggested PIs were also presented and debated.

At this stage, discussions led to the identification of modified and new PIs to be submitted for evaluation during the second-round survey.

Second-round survey

The second-round Google Forms® questionnaire was developed based on the modifications and newly suggested PIs retained during the consensus meeting (Table S3). It was e-mailed on 17 December 2021 to all experts who participated in the first-round survey; they were asked to complete the questionnaire within 5 weeks. A reminder was sent to the non-responders 1 week before the deadline. They were asked to accept or not the modifications suggested during the consensus meeting, and to evaluate the newly suggested PIs using the same methodology as for the first-round survey.

Suggested modifications were accepted if ≥75% of experts agreed. Consensus regarding the newly suggested PIs was defined as for the first-round survey.

Table 2. Modifications suggested during the first-round survey and accepted during the second-round survey

Proxy indicator (PI)	Item	Suggestion of modification	Rationale
PI 1—Antibiotic prescriptions against urinary tract infections in men (ratio)	Definition (numerator)	Removal of lomefloxacin and norfloxacin Addition of pivmecillinam	Lomefloxacin and norfloxacin are no longer reimbursed in France. Pivmecillinam belongs to the recommended antibiotics for female UTIs and is not recommended in male UTIs
PI 2—Antibiotic prescriptions against urinary tract infections in women (ratio)	Target value	New target value of >5	The lack of ambition of the initial target value (>1) was pointed out, considering that quinolones are never recommended as first-line treatment for cystitis, and the cystitis/pyelonephritis ratio of GPs' patients is 10/1
PI 4—Seasonal variation of total antibiotic prescriptions (%)	Definition (numerator and denominator)	Division of both the numerator and the denominator by the number of consultations during the same period	There are important variations in the number of consultations between cold-weather and hot-weather months (around 15% difference)
PI 5—Seasonal variation of quinolone prescriptions (%)	Definition (numerator and denominator)	Division of both the numerator and the denominator by the number of consultations during the same period	There are important variations in the number of consultations between cold-weather and hot-weather months (around 15% difference)
	Target population	Exclusion of patients <16 years old	Quinolones are not recommended for children
PI 6—Amoxicillin/second-line antibiotics prescriptions (ratio)	Target population	Exclusion of patients >65 years old	Amoxicillin is less often recommended as a first-line treatment in patients >65 years old
	Target value	New target value of >3	The lack of ambition of the initial target value (>1) was pointed out, considering that amoxicillin is the first-line treatment for most community-acquired bacterial infections encountered in general practice
PI 7—Prescriptions of not indicated antibiotics (%)	Definition (numerator)	Removal of lomefloxacin and norfloxacin	These molecules are no longer reimbursed in France
PI 8—Estimated duration of antibiotic prescriptions >8 days (%)	Definition (numerator)	Inclusion of estimated duration of antibiotic prescriptions >7 days	The initial duration was set at >8 days, because the data used are reimbursement of dispensed packages of antibiotic (and not antibiotic units), which often contain more units than needed. However, for most community-acquired bacterial infections, the recommended duration is ≤7 days. This new target has moreover pedagogic value, to be more in line with guidelines

Clinimetric properties

Using data from the 2022 Grand Est Regional Health Insurance reimbursement data (5 563 000 inhabitants according to the 2020 national population census[17]), clinimetric properties were evaluated for each PI selected through the RAND-modified Delphi consensus procedure, as previously described[10]:

- Measurability: a PI was measurable if data necessary to calculate the PI were missing for <25% of prescriptions/patients;
- Applicability: a PI was considered not meaningful for a GP if it covered fewer than 10 relevant clinical situations the GP encountered during the evaluation period (year 2022). More precisely, PIs 1, 3, 7, 8, 9, 10 and 11, expressed as percentages, could not be calculated for a GP if <10 antibiotic prescriptions or patients were identified for the denominator; PIs 2, 4, 5, 6 and 12, expressed as ratios, or related to seasonal variation, could not be calculated if fewer than 10 prescriptions were identified for either the numerator or the denominator.
- Potential room for improvement: expressed as (100 – % of GPs who reached the acceptable target); it measured the sensitivity of a PI to detect variability in appropriateness of prescriptions between physicians and over time.

Overall, a PI was considered to have good clinimetric properties if its measurability was ≥75%, its applicability was ≥75%, and its potential room for improvement was ≥15%.[10]

Results are presented as numbers and percentages. All analyses were performed using SAS Enterprise Guide version 8.3 (SAS Institute Inc., Cary, NC, USA).

Ethics

The study participation was voluntary and not compensated. As no information on respondents was collected, the questionnaires were anonymous and ethical approval was not required.

Results

Study participation

Seventeen experts participated in the first-round survey (14 GPs and 3 infectious diseases physicians). Among them, nine (53%) participated in the consensus meeting (seven GPs and two infectious diseases physicians). Fifteen observers also participated in the

Table 3. Second-round survey results: rates of the global relevance and conclusion for the newly suggested proxy indicators ($n=14$)[a]

New proxy indicator (PI)	Suggested definition	Suggested target population	Suggested target value(s)	Global relevance rates[b] *n* [1–3]	[4–6]	[7–9]	Decision at the end of the first round[c]
PI 11—Prescriptions of pristinamycin and macrolides (%)	Number of prescriptions of pristinamycin (J01FG01) + macrolides (J01FA)/Total number of antibiotic prescriptions (J01)	All patients	Optimal: <1% Acceptable: <5%	0	0	14	Selected
PI 12—Amoxicillin/amoxicillin-clavulanate prescriptions (ratio)	Number of prescriptions of amoxicillin (J01CA04)/Number of prescriptions of amoxicillin-clavulanate (J01CR02)	≤65 years old	>3	1	1	12	Selected
PI 13—Prescriptions of pristinamycin (%)	Number of prescriptions of pristinamycin (J01FG01)/Total number of antibiotic prescriptions (J01)	All patients	Optimal: <1% Acceptable: <5%	3	3	8	Non-consensus

[a]Antibiotic molecules/classes are followed by their anatomical, therapeutic, chemical (ATC) classification.
[b]Global relevance rates were estimated using a 9-point Likert scale ranging from 1 ('not relevant at all') to 9 ('very relevant').
[c]Consensus was defined as follow: PIs rated 7 to 9 by ≥10/14 experts and 1 to 3 by ≤2/14 experts were selected; PIs rated 7 to 9 by ≤10/14 experts and 1 to 3 by ≥2/14 experts were excluded; all other combinations reflected a non-consensus.

consensus meeting. Fourteen (82%) experts participated in the second-round survey (11 GPs and 3 infectious diseases physicians).

The RAND-modified Delphi consensus procedure

Figure 1 summarizes all stages of the RAND-modified Delphi consensus procedure.

First-round survey

The first-round questionnaire resulted in the selection of the 10 initial PIs (Table 1). Suggestions of modifications were made for all these PIs. For 6/10 PIs (PIs 1 to 6), modifications were suggested for the definition, the population and the target(s). For 2/10 PIs (PIs 7 and 8), modifications were suggested for the definition and the target(s). For 2/10 PIs (PIs 9 and 10), modifications were suggested for the target(s). Moreover, seven new PIs were suggested.

Consensus meeting

The consensus meeting lasted 2 h 15 min. Discussions during the meeting resulted in the selection of three initial PIs without modification (PIs 3, 9 and 10). For the other seven initial PIs (PIs 1, 2, 4, 5, 6, 7 and 8), Table 2 presents the modifications suggested during the first-round survey and retained for evaluation during the second-round survey. Discussions regarding the newly suggested PIs led to three new PIs being submitted for evaluation during the second-round survey (PIs 11, 12 and 13) (Table 3).

Second-round survey

The second-round survey resulted in the acceptance of all the modifications suggested for the seven initial PIs (PIs 1, 2, 4, 5, 6, 7 and 8). Among the three newly suggested PIs, two were consensually selected (PIs 11 and 12) (Table 3). Consensus was not reached for PI 13 and it was therefore not selected.

The overall procedure resulted in a final set of 12 PIs, which are described in Table 4.

Clinimetric properties

Table 5 presents the clinimetric properties of the 12 final PIs. PIs presented good clinimetric properties, except PI 1 [antibiotic prescriptions against urinary tract infections (UTIs) in men], which had a potential room for improvement ≤15%, and PI 5 (seasonal variation of quinolone prescriptions), which had an applicability ≤75%.

Discussion

Main results

This RAND-modified Delphi consensus procedure, involving a nationwide representative panel of GPs and infectious diseases physicians, resulted in a final set of 12 PIs selected by prescribers on their relevance in routine practice. These PIs estimate the appropriateness of antibiotic prescriptions at the GP level and are easily calculable routinely from the Health Insurance reimbursement databases without clinical indication (not available in those databases). Among the 10 initial PIs, 3 were selected without modification and 7 were modified and selected. Moreover, two newly suggested PIs were selected. Ten of the 12 selected PIs presented good clinimetric properties based on the 2022 Regional Insurance reimbursement data.

Table 4. Final set of 12 selected proxy indicators estimating the appropriateness of antibiotic prescriptions in general practice[a]

Proxy indicator (PI)	Definition	Target population	Target value(s)
PI 1—Antibiotic prescriptions against urinary tract infections in men (ratio)	Number of prescriptions of nitrofurantoin (J01XE01) + urinary quinolones [other quinolones (J01MB)[b] and enoxacin (J01MA04)] + fosfomycin-trometamol (J01XX01) + pivmecillinam (J01CA08)/100 active[c] male patients ≥16 years old	Men ≥16 years old	Optimal: 0 Acceptable: <0.5
PI 2—Antibiotic prescriptions against urinary tract infections in women (ratio)	Number of prescriptions of nitrofurantoin (J01XE01) + pivmecillinam (J01CA08) + fosfomycin-trometamol (J01XX01)/ Number of prescriptions of quinolones (J01 M)	Women ≥16 years old	>5
PI 3—Repeated prescription of quinolones (%)	Number of prescriptions of quinolones (J01 M) among patients having been prescribed a quinolone (J01 M) in the preceding 6 months/Total number of prescriptions of quinolones (J01 M)	≥16 years old	Optimal: 0 Acceptable: <10%
PI 4—Seasonal variation of total antibiotic prescriptions (%)	{[Number of prescriptions of antibiotics (J01) during the cold-weather season (January–March and October–December)]/ [number of consultations during the cold-weather season]}/ {[Number of prescriptions of antibiotics (J01) during the hot-weather season (April–September)]/[number of consultations during the hot-weather season] – 1}×100	All patients	<20%
PI 5—Seasonal variation of quinolone prescriptions (%)	{[Number of prescriptions of quinolones (J01 M) during the cold-weather season (January–March and October–December)]/ [number of consultations during the cold-weather season]}/ {[Number of prescriptions of quinolones (J01 M) during the hot-weather season (April–September)]/[number of consultations during the hot-weather season] – 1}×100	≥16 years old	Optimal: <5% Acceptable: <10%
PI 6—Amoxicillin/second-line antibiotics prescriptions (ratio)	Number of prescriptions of amoxicillin (J01CA04)/Number of prescriptions of: amoxicillin-clavulanate (J01CR02) + quinolones (J01 M) + cephalosporins (J01D) + MLSK[d] (J01F)	≤65 years old	>3
PI 7—Prescriptions of not indicated antibiotics (%)	Number of prescriptions of: moxifloxacin (J01MA14), spiramycin-metronidazole (J01RA04) and cefaclor (J01DC04)/ Total number of antibiotic prescriptions (J01)	All patients	Optimal: 0 Acceptable: <0.5%
PI 8—Estimated duration of antibiotic prescriptions >8 days (%)	Number of prescriptions >7 days for the following antibiotics: amoxicillin (J01CA04), amoxicillin-clavulanate (J01CR02), cefuroxime (J01DC02), cefpodoxime (J01DD13), roxithromycin (J01FA06), clarithromycin (J01FA09), pristinamycin (J01FG01) and nitrofurantoin (J01XE01)/Total number of antibiotic prescriptions for these eight antibiotics	All patients	Optimal: <5% Acceptable: <10%
PI 9—Co-prescription of antibiotic and systemic non-steroidal anti-inflammatory drugs (%)	Number of antibiotic(s) (J01) + systemic non-steroidal anti-inflammatory drugs (M01A) co-prescribed on the same day/ Total number of antibiotic prescriptions (J01)	All patients	Optimal: 0 Acceptable: <5%
PI 10—Co-prescription of antibiotic and systemic corticosteroids (%)	Number of antibiotic(s) (J01) + systemic corticosteroid(s) (H02AB) co-prescribed on the same day/Total number of antibiotic prescriptions (J01)	All patients	Optimal: 0 Acceptable: <5%
PI 11—Prescriptions of pristinamycin and macrolides (%)	Number of prescriptions of pristinamycin (J01FG01) + macrolides (J01FA)/Total number of antibiotic prescriptions (J01)	All patients	Optimal: <5% Acceptable: <10%
PI 12—Amoxicillin/amoxicillin-clavulanate prescriptions (ratio)	Number of prescriptions of amoxicillin (J01CA04)/Number of prescriptions of amoxicillin-clavulanate (J01CR02)	≤65 years old	>3

[a]Antibiotic molecules/classes are followed by their anatomical, therapeutic, chemical (ATC) classification.
[b]J01MB (rosoxacin, nalidixic acid, piromidic acid, pipemidic acid, oxolinic acid, cinoxacin, flumequine, nemonoxacin).
[c]An active patient is a patient seen at least once by the GP during the year.
[d]MLSK: macrolides, lincosamides, streptogramins and ketolides.

Table 5. Clinimetric properties of the 12 selected proxy indicators, calculated using 2022 Regional Health Insurance reimbursement databases ($n = 4300$ GPs)

Proxy indicator (PI)	Measurability[a] %	Applicability[b] % (*n*)	Potential room for improvement[c] % (*n*)
PI 1—Antibiotic prescriptions against urinary tract infections in men (ratio)	100	99.9 (4298)	10.3 (441)
PI 2—Antibiotic prescriptions against urinary tract infections in women (ratio)	100	93.4 (4015)	46.7 (1882)
PI 3—Repeated prescription of quinolones (%)	100	76.1 (3271)	57.7 (2392)
PI 4—Seasonal variation of total antibiotic prescriptions (%)	100	97.8 (4205)	53.4 (2279)
PI 5—Seasonal variation of quinolone prescriptions (%)	100	60.3 (2591)	49.9 (2012)
PI 6—Amoxicillin/second-line antibiotics prescriptions (ratio)	100	97.7 (4200)	98.6 (4238)
PI 7—Prescriptions of not indicated antibiotics (%)	100	99.9 (4298)	45.9 (1969)
PI 8—Estimated duration of antibiotic prescriptions >8 days (%)	100	98.7 (4243)	84.2 (3603)
PI 9—Co-prescription of antibiotic and systemic non-steroidal anti-inflammatory drugs (%)	100	99.6 (4283)	49.5 (2122)
PI 10—Co-prescription of antibiotic and systemic corticosteroids (%)	100	99.7 (4285)	80.6 (3453)
PI 11—Prescriptions of pristinamycin and macrolides (%)	100	99.3 (4271)	98.9 (4239)
PI 12—Amoxicillin/amoxicillin-clavulanate prescriptions (ratio)	100	96.4 (4143)	43.8 (1885)

[a]A PI was measurable if data necessary to calculate the PI were missing for <25% of prescriptions/patients.
[b]A PI was not meaningful for a GP if it covered less than 10 of the clinical situations the GP encountered. Therefore, PIs were not calculated for a given GP if less than 10 prescriptions were identified for the numerator and/or the denominator in 2022.
[c]Expressed as (100 – % of GPs who reached the acceptable target).

Clinical situations addressed by the PIs

The 12 PIs cover the main situations responsible for inappropriate and unnecessary use of antibiotics in general practice, by focusing on three key elements of antibiotic stewardship. First, seven PIs promote the use of first-line antibiotics recommended in the national guidelines. The prescription of antibiotics that are not recommended for male UTIs (PI 1) and for female UTIs (PI 2) might result in an increased risk of treatment failure and adverse events (e.g. side effects and development of bacterial resistance) and should be avoided.[18] Some antibiotics are rarely indicated as first-line treatment (PI 7), notably pristinamycin and macrolides (PI 11).[19,20] Moreover, amoxicillin should be the preferred antibiotic choice in most general practice clinical situations (PI 6 and 12).[21] The repeated prescriptions of quinolones should be avoided as it causes an increased risk of resistance (PI 3).[21] Second, three PIs addressed the unnecessary use of antibiotics, by limiting cold-weather overprescribing as cold-weather infections are mostly viral (PIs 4 and 5), and by complying with recommended treatment durations (PI 8).[22,23] Third, two PIs were related to the co-prescriptions of anti-inflammatory drugs and antibiotics (PIs 9 and 10), not recommended in national guidelines.[24]

Strengths and limitations

We conducted a RAND-modified Delphi consensus procedure to select a set of PIs that are relevant for GPs. These PIs were based on 10 initial PIs developed by experts in antibiotic stewardship and metrics, using international recommendations. This consensus procedure was conducted to ensure that these initial PIs were relevant for GPs in their routine practice. It resulted in lots of discussions, debates and propositions from GPs that were considered relevant by the other involved stakeholders (e.g. infectious diseases physicians, researchers, professionals from the Health Insurance). It also led to the design of two new PIs that cover misuse situations frequently encountered in general practice in France.

However, we acknowledge that our approach has several limitations. First, it requires a significant commitment from experts, and three physicians who participated in the first-round survey did not attend the second-round survey. Second, GPs who agreed to participate might be more concerned about AMR and AMS than those who did not, and therefore might have better than average prescribing practices. This might have influenced their suggestions, notably regarding the target values defining appropriate use. Indeed, we noticed that they were inclined to suggest much more difficult-to-reach targets than those initially defined. Third, although we took care in making this panel of experts as nationally representative as possible, by selecting experts from different disciplines (in particular GPs), various regions and various national societies, we could not exclude that this process would have resulted in a slightly different list of PIs if different experts were included.

Use of PIs

This set of PIs is easily calculable using routine reimbursement databases without clinical data related to drug prescriptions. Several applications of PIs were proposed by Thilly *et al.*,[10] notably as an individual feedback to prescribers or as aggregated data for AMS teams and policy-makers to evaluate interventions or public policy. PIs are now cited in the 2022–2025 French national strategy for preventing infections and antibiotic resistance in human health, coordinated by the Ministry of Health.[25]

Previous studies evaluating the impact of feedback on primary care antibiotic prescription practices reported inconsistent results.[26,27] Feedback including PIs' results might have an improved effectiveness to reduce antibiotic misuse if associated with interventions favouring GPs' behaviour change (e.g. communication about core antibiotic stewardship messages, recommended use of practical tools and resources, and personalized advice).[28,29] Further work is needed to implement and assess antibiotic audit and feedback at GP level using these PIs, both regarding the process (e.g. to evaluate if the intervention was implemented as planned, and the facilitators and barriers to its implementation) and the impact (to evaluate the effectiveness of such an antibiotic stewardship intervention). As an example, the ANTIBIORESIST intervention is currently pilot-tested in northeastern France to help GPs improve their antibiotic prescribing practices. This intervention includes a personalized feedback (displaying the 12 selected PIs), antibiotic stewardship tools, training resources and an-academic detailing with peers. Impact and process evaluation of this intervention is planned.[30]

The use of PIs in other countries for the above-mentioned purposes might follow a similar development and selection method: (i) content development: adaptation of the definition and target(s) to national guidelines and databases (as described by Thilly *et al.*[10]); (ii) clinimetric properties evaluation: measurability, applicability and improvement potential (as described by Thilly *et al.*[10]); and (iii) face validity, i.e. selection of PIs on their relevance and understanding by the targeted healthcare professionals (as described in the present article).

PIs might be used to complement other antibiotic stewardship tools such as the WHO AWaRe initiative, which classified antibiotics into three groups (Access, Watch and Reserve), and also set a target for improvement: at least 60% of all prescribed antibiotics should belong to the Access group at national level.[31] These PIs are of great value due to their ease of calculation at large scale using routine reimbursement databases. They would be usefully complemented by quality indicators based on clinical indications, even though these usually require manual collection of data, and there is a need for the development and validation in parallel of such indicators.

Conclusion

This national RAND-modified Delphi consensus procedure resulted in the selection of 12 relevant PIs to estimate the appropriateness of antibiotic prescriptions at the GP level, among which 10 presented good clinimetric properties. Such indicators might help to improve antibiotic prescribing by GPs and evaluate the impact of antibiotic stewardship interventions. These PIs are now routinely used by the French government to describe and evaluate the evolution of the appropriateness of antibiotic prescriptions by GPs in all regions.[32]

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Supplementary data

Tables S1 to S3 are available as Supplementary data at *JAC-AMR* Online.

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