ORIGINAL ARTICLE

Use of a Structured Panel Process to Define Quality Metrics for Antimicrobial Stewardship Programs

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INTRODUCTION. Antimicrobial stewardship programs are being implemented in health care to reduce inappropriate antimicrobial use, adverse events, *Clostridium difficile* infection, and antimicrobial resistance. There is no standardized approach to evaluate the impact of these programs.

OBJECTIVE. To use a structured panel process to define quality improvement metrics for evaluating antimicrobial stewardship programs in hospital settings that also have the potential to be used as part of public reporting efforts.

DESIGN. A multiphase modified Delphi technique.

SETTING. Paper-based survey supplemented with a 1-day consensus meeting.

PARTICIPANTS. A 10-member expert panel from Canada and the United States was assembled to evaluate indicators for relevance, effectiveness, and the potential to aid quality improvement efforts.

RESULTS. There were a total of 5 final metrics selected by the panel: (1) days of therapy per 1000 patient-days; (2) number of patients with specific organisms that are drug resistant; (3) mortality related to antimicrobial-resistant organisms; (4) conservable days of therapy among patients with community-acquired pneumonia (CAP), skin and soft-tissue infections (SSTI), or sepsis and bloodstream infections (BSI); and (5) unplanned hospital readmission within 30 days after discharge from the hospital in which the most responsible diagnosis was one of CAP, SSTI, sepsis or BSI. The first and second indicators were also identified as useful for accountability purposes, such as public reporting.

CONCLUSION. We have successfully identified 2 measures for public reporting purposes and 5 measures that can be used internally in healthcare settings as quality indicators. These indicators can be implemented across diverse healthcare systems to enable ongoing evaluation of antimicrobial stewardship programs and complement efforts for improved patient safety.

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Antimicrobials are among the most commonly prescribed medications in acute care medicine.[1] They are prescribed to up to one-third of hospitalized patients, often inappropriately,[2-6] and over two-thirds of critically ill patients are receiving antimicrobials at any one time.[7] Antimicrobial use is closely linked with the selection of drug-resistant pathogens, and so antimicrobial resistance in institutions and in the broader community has moved in step with antimicrobial consumption.[8-14] The increasing prevalence of drug-resistant pathogens poses a major threat to the health of patients, because drug-resistant infections are associated with increased morbidity and mortality.[15-18]

Although it is widely accepted that antimicrobial use accelerates the development of resistance, the challenge with antimicrobial prescribing lies in the need to balance 2 conflicting goals: the provision of therapy that is adequate to treat documented or presumed infection, and the minimization of antimicrobial use to avoid adverse drug events (eg, *Clostridium difficile* infection and allergy) and the emergence of antimicrobial resistance. Antimicrobial stewardship programs (ASPs) are patient safety initiatives that are intended to complement institutional infection control practices.[19,20] Several terms have been used to describe ASPs, such as "antibiotic management programs" or "antibiotic control policies." Overall, these terms refer to an ongoing effort by healthcare providers to optimize antimicrobial use among

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TABLE 1. Initial List of Indicators and References

Indicator	References
Domain I: antimicrobial consumption measures	
Days of therapy	MacDougall et al,[35] Slama[37]
Defined daily dose	Added by research team content experts
Total quantity of antimicrobial treatment	MacDougall et al[35]
Mean daily dose	Fishman[36]
Domain II: antimicrobial resistance measures	
Tailored antimicrobial use	MacDougall et al,[35] Slama[37]
Total number of antimicrobial resistant organisms	Fishman,[36] MacDougall et al,[35] Slama,[37] Patel et al[34]
Total number of multidrug-resistant organisms	MacDougall et al,[35] Slama,[37] Patel et al[34]
Domain III: patient outcome measures	
Antimicrobial-related organism mortality	Fishman,[36] MacDougall et al,[35] Slama[37]
All cause mortality	MacDougall et al,[35] Slama[37]
Rate of infection due to antimicrobial resistant organisms	Fishman[36]
Duration of hospitalization	MacDougall et al,[35] Patel et al[34]
Rate of unplanned hospital readmission	MacDougall et al,[35] Patel et al[34]
Rate of clinical improvement	MacDougall et al[35]
Rate of increased clinical severity	MacDougall et al,[35] Patel et al[34]

hospitalized patients to improve patient outcomes; reduce adverse effects associated with antimicrobial use, including antimicrobial resistance; and ensure cost-effective therapy. A key role of ASPs is helping clinicians optimize therapeutic choices regarding initiation, spectrum of activity, modification, and discontinuation of antimicrobial therapy.

Various policy-making bodies endorse the development of ASPs, which are being rapidly implemented on national and international scales. The Infectious Diseases Society of America (IDSA) and Society for Hospital Epidemiology of America (SHEA) guidelines on antimicrobial stewardship programs recommend that the impact of the programs on antimicrobial use and resistance be evaluated but do not outline specific indicators of performance.[19] A wide range of ASP-related outcomes are described in the literature, including antimicrobial use, microbiologic response rates (including antibiotic resistance), and many clinical and administrative parameters. At this point, identification of metrics that best evaluate ASPs in a healthcare setting remains unresolved.[21-24] Building upon previously published research, we used a structured panel process to define metrics for evaluating antimicrobial stewardship initiatives in healthcare settings. Our focus was to develop indicators that would be useful for accountability purposes as well as ones that had the potential for broader quality improvement efforts.

This study had 3 domains of focus: (1) antimicrobial consumption measures used to define antimicrobial use, (2) antimicrobial resistance measures, and (3) patient outcome measures used to assess clinical effectiveness and safety.

METHODS

Modified Delphi Panel Process Overview

A modified Delphi consensus technique based on the RAND method was used to develop measures of antimicrobial stewardship programs.[25] Our research group developed a survey of important contextual issues and potential measures of antimicrobial stewardship effectiveness that fall under the 3 domains of interest. Through a series of questionnaires, we surveyed the panel using both anonymous responses and round table meeting techniques to allow for optimal unbiased expression of opinions. The participants were encouraged to revise their previous answers in light of the summary of responses and the in-person discussion. This process for developing quality indicator measures in health care has been shown to be successful in both small- and large-scale research teams.[26-33] Consensus was encouraged but not forced. A survey conducted after the meeting found unanimous agreement from the participants that their opinions were valued, that the process was fair, and that no one changed their answers as a result of feeling intimidated.

Assembly of the Expert Panel

The panel consisted of 10 members and comprised national and international representatives (the panel members are listed in the Acknowledgments). There was broad clinical and professional representation, including experts from the fields of infectious diseases, microbiology, infection control, nursing, and pharmacy as well as from policy-making bodies. There were also 2 consulting content experts from large stakeholder groups (Accreditation Canada and the British Columbia Centre for Disease Control). Final panel members were selected as a result of their shared interests in patient safety, quality improvement, clinical experience, and related research initiatives.

Selection of Indicators

A literature review was conducted to determine which measures had previously been used by the research community to evaluate antimicrobial stewardship programs. A final selection of 4 systematic reviews, with a combined total of 278 articles,

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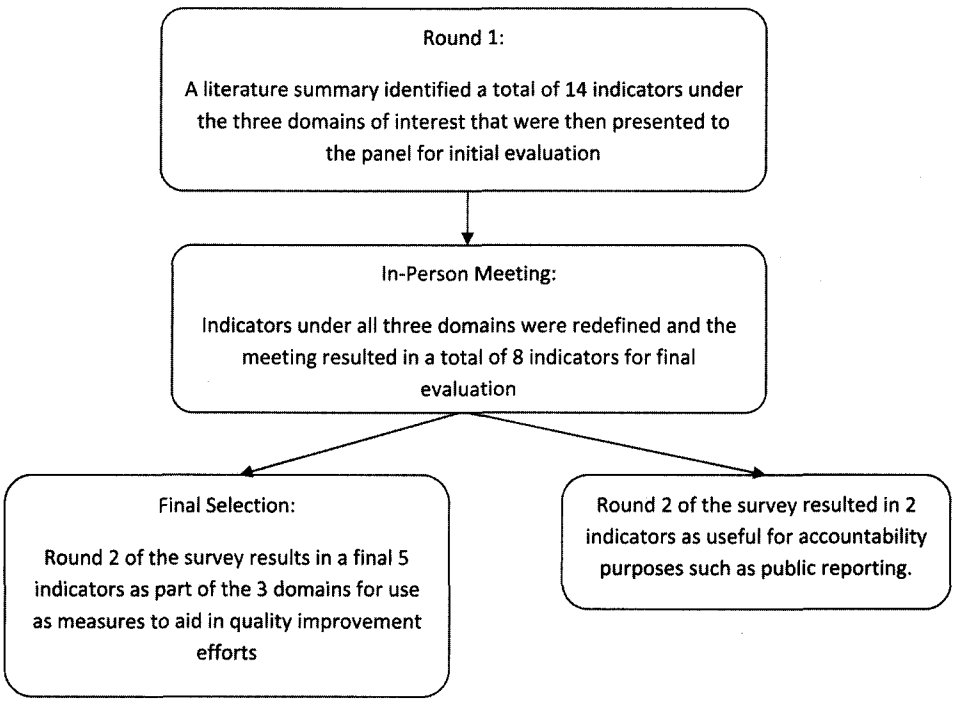


FIGURE 1. Flow chart of indicator development.

were referenced to create the initial list of measures.[34-37] Members of the research team who were not involved in the initial search reviewed the results for clinical relevance and comprehensiveness. Additionally, panel members were provided with the opportunity to amend the presented list of measures before the in-person meeting. Although some metrics proved to be more common and/or easily applied than others, we chose to present all relevant measures to the panel and let the discussion decide the importance of current feasibility versus future potential with respect to each measure. The final list presented to the panel included 14 different indicators (Table 1).

Panel members were also asked to evaluate specific parameters to be applied as inclusion and exclusion criteria to provide an opportunity for feedback regarding criteria (eg, which drugs should be monitored) without interfering with the evaluation of the measures (eg, examining how drugs should be monitored).

Ratings

The panel was provided with a questionnaire and asked to evaluate the proposed measures for both accountability purposes, such as public reporting, and potential usefulness for quality improvement efforts via a 9-point Likert scale. The criteria were designed to capture (1) scientific merit, (2) burden and impact, and (3) accountability. The selected scale considered scores of 1–3 as strong disagreement, 7–9 as strong agreement, and 4–6 as uncertain agreement. Consensus was defined as arriving at 75% agreement.

All panel members met in person for a 1-day facilitated structured discussion of the results compiled from the first round of the questionnaire. At the conclusion of the discussion, members were asked to complete a second round of the questionnaire, and again individual responses remained anonymous to all other panel members. After completion of all discussion and questionnaires, panelists were asked to anonymously comment upon their experience regarding the overall consensus process as a mechanism to ensure that the process was fair and unbiased.

After the final results were tabulated, the panel was contacted one more time and asked to provide a priority ranking among the final selected measures. Panelists were asked for their personal views as to what the priority should be for measure utilization and development, regardless of current data availability and feasibility.

RESULTS

The panel discussion provided an opportunity to redefine some of the metrics and related inclusion and exclusion criteria. As a result of the in-person discussion, 8 of 14 metrics were selected for final evaluation: 2 of 4 antimicrobial consumption measures, 2 of 3 antimicrobial resistance measures, and 4 of 7 patient outcome measures (Figure 1). Some metrics from the initial list were excluded in the final evaluation because the panel felt that they were neither informative nor clinically relevant, whereas others were excluded because the panel felt that there was significant overlap between measures.

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TABLE 2. Round 2 Scores of Measures

Measures presented in final round	Strong agreement,[a] %	Median score
Domain I: antimicrobial consumption measures		
Days of therapy	80	8
Defined daily dose[b]	50	6.5
Domain II: antimicrobial resistance measures		
No. of patients with specific drug-resistant organisms	78	9
Rate of tailored antimicrobial use	70	8
Domain III: patient outcome measures		
Antimicrobial-related organism mortality	78	7
All-cause mortality	70	7.5
Conservable days of therapy among certain patients[c]	80	8
Unplanned hospital readmission within 30 days after hospital discharge[c]	100	9

[a] Measured with use of a 9-point Likert-type scale in which scores 1–3 are strong disagreement, 7–9 are strong agreement, and 4–6 are uncertainty.

[b] World Health Organization defined daily doses.

[c] Among patients who received a diagnosis of community-acquired pneumonia, skin or soft-tissue infection, sepsis, or blood stream infection.

The panel also discussed the possibility of including a fourth domain, cost. It was decided that, over the long term, cost should not be the primary factor on which the effectiveness of an ASP was judged. Cost savings is a commonly used incentive for hospitals to begin an antimicrobial stewardship program, is important in the overall efficiency of care, and is intuitively appealing. However, it was felt that an efficient ASP will eventually reach a minimum sustainable cost for implementation, and thus prospective cost savings should decrease to zero. Costs are also sensitive to patent expiration and drug shortages and therefore are often independent of stewardship efforts. Finally, community-acquired antimicrobial resistance (eg, community-acquired methicillin-resistant *Staphylococcus aureus* infection) may influence antimicrobial prescribing of expensive agents and be beyond the control of an ASP. Final evaluation of all indicators was focused on their usefulness for accountability purposes and their potential to support quality improvement efforts.

With respect to the use of these ASP metrics for accountability purposes, consensus was reached for only 2 of the 8 metrics: (1) days of therapy per 1000 patient-days and (2) number of patients with specific drug-resistant organisms divided by the total number of patients admitted to a ward, service or unit of interest. "Days of therapy" is defined as the aggregate sum of drug days, so each drug (any amount) is counted independently of the patient-days, and combination drugs (eg, trimethoprin-sulfamethoxazole) are counted as 1 drug.

The panel reached consensus for 5 of the 8 metrics with respect to their usefulness in quality improvement efforts, whereas the other 3 measures generated varying levels of uncertainty (Table 2). The panel felt that these 5 metrics were able to provide important support for quality improvement efforts. The final metrics selected for quality improvement efforts were (1) days of antimicrobial therapy per 1000 patient-days; (2) number of patients colonized or infected with organisms with specific resistance profiles of interest (Tables 3 and 4); (3) mortality related to antimicrobial-resistant organisms; (4) conservable days of therapy among patients with community-acquired pneumonia (CAP), skin and soft-tissue infection (SSTI), or sepsis and blood stream infection (BSI); and (5) unplanned hospital readmission within 30 days after discharge from the hospital in cases in which the most responsible diagnosis was one of CAP, SSTI, sepsis, or BSI. It was agreed that the most appropriate denominator for all indicators would be "all hospitalized patients." "Conservable days of therapy" is defined as avoided unnecessary treatment days based on widely accepted targets and benchmarks and was selected by panel members as a more appropriate alternative to length-of-stay metrics, which can be complicated by patient type and regional differences.

There was consensus among the panel that antimicrobial consumption measures should examine patients admitted to intensive care units as a subgroup for analyses. A number of different pathogens and associated antimicrobial resistance profiles obtained consensus for inclusion, but notably, candidemia did not (Table 3). Consensus was also reached on including certain target antimicrobials and specific classes of antimicrobials, but the decision was split regarding the inclusion of antifungals and antivirals (Table 4). There was agreement that the definition of multidrug resistance should be consistent with that of internationally recognized agencies, and so this term was not separately defined by the panel. The panel was split regarding the decision as to whether microbiologic analyses should include 1 isolate per patient, 1 isolate per patient hospitalization, or the first isolate per patient, but there was general agreement that it should not be limited to only the most recent isolate per patient (70% agreement).

When asked to rank the most important final indicators with respect to both quality improvement and public reporting purposes, there were mixed responses regarding exactly what the priority should be. All respondents ranked days

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TABLE 3. Pathogens Evaluated by the Panel

Drug-resistant pathogens	Strong agreement,[a] %
Pseudomonas aeruginosa	90.0
Acinetobacter species	90.0
Klebsiella species	90.0
Staphylococcus aureus	80.0
Enterobacteriaceae	88.9
Candida species	
Overall	10.0
Candida albicans	0.0
Clostridium difficile	90.0

[a] Measured with use of a 9-point Likert-type scale in which scores 1–3 are strong disagreement, 7–9 are strong agreement, and 4–6 are uncertainty.

of therapy and readmission rates among the most important areas on which to focus, irrespective of feasibility.

DISCUSSION

As a result of our modified Delphi panel approach, we have been able to successfully identify 2 measures for public reporting purposes and 5 measures that can be used internally at healthcare facilities as quality indicators. Our inclusion of stakeholders, frontline clinicians, nurses, and pharmacists provides a high likelihood that the selected quality measures have broad applicability and feasibility.[26-33] Our final list of measures includes representation from each of our 3 domains: antimicrobial consumption, antimicrobial resistance, and clinical effectiveness.

To our knowledge, there has been no previous research in the area of quality measures for antimicrobial stewardship that could be applied universally to all institutions with an ASP. The research that has been done in this area has been focused on individual institutional implementation of ASPs, and none of the published studies have included measures across all 3 of the domains that we examined.[21] There is broad applicability in the final quality measures selected, because they use data that are already commonly collected by hospitals and could feasibly be collected and reported on immediately.

The use of days of therapy as a measure of antimicrobial consumption, as opposed to the more broadly used measure of defined daily doses (DDDs), generated considerable discussion. Although DDDs are used by the World Health Organization, the Centers for Disease Control and Prevention National Healthcare Safety Network (formerly the Nosocomial Infection Surveillance) selected days of therapy as a measure for their Antimicrobial Use and Resistance Module. Additionally, many hospitals are currently unable to readily calculate days of therapy. However, because of the obvious limitations of DDDs, the panel chose to endorse days of therapy as the best measure of antimicrobial consumption.[24]

There were limitations to our study. To minimize potential bias in panel representation, our final panel consisted of individuals with broad professional and geographic representation as well as consultants from stakeholder groups. We may have benefited from more interdisciplinary contributions from biostatisticians and microbiologists as well as more representation from rural or smaller community healthcare settings. The second limitation is the potential for selection bias in the quality measures presented for evaluation to the panel. We sought to minimize this possibility through a comprehensive literature summary using key word searches in large databases conducted by a research team member with no perceived or real conflicts of interest in the final choice of quality indicators. In addition, we provided all panel members with the same literature summary and used open-ended questions in the premeeting survey to provide an opportunity for the panel to submit additional measures. A third limitation relates to feasibility, because we did not ask the panel to limit their selection to quality measures that could be applied immediately with commonly available data. The use of administrative data for any quality metric always has the limitation of clinical application, because it is only a part of a patient's clinical story. Additionally, the panel presented concerns for application of quality measures to certain clinical subgroups, such as pediatrics, especially for metrics related to medication dosing quantity. Panel members discussed the potential need for risk adjustments with some of the selected metrics and agreed that such adjustments could be left up to the individuals using the measures. Finally, there is the limitation of the selected methodology. We opted to modify the Delphi method to include an in-person consensus meeting. We followed similar modifications to the Delphi method that have been used successfully in developing quality indicators across a number of different therapeutic areas.[26-33] We ensured that panel members' opinions remained protected by sharing results anonymously and using an unbiased, experienced chair to host the consensus process. The role of this chair was to ensure that all voices were heard and that no single strong personality took over the conversation. The success of this process was reflected in an end-of-day survey in which all panel members stated that they did not feel that their reputations were at stake or that their opinions were overshadowed at any point in the process. Furthermore, upon review of the measures before and after the meeting, it was evident

TABLE 4. Antimicrobial Drugs Evaluated by the Panel

Antimicrobial resistance to monitor	Strong agreement,[a] %
Fluoroquinolones	100.0
Carbapenems	90.0
Cephalosporins (third generation or higher)	75.0
β-lactam and/or β-lactamase inhibitors	88.9
Aminoglycosides	70.0
Vancomycin	77.8

[a] Measured with use of a 9-point Likert-type scale in which scores 1–3 are strong disagreement, 7–9 are strong agreement, and 4–6 are uncertainty.

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that the in-person discussion was a vital component to our process, because indicators and parameters were redefined.

The modified Delphi consensus panel approach enabled us to define quality measures for antimicrobial stewardship programs that encompass aspects of an institutional objective, healthcare provider's goals, and patient experience with nosocomial infections. Our process provided a means by which we could design relevant and useful measures that are important to a broad spectrum of healthcare providers. Our inclusion of international representatives supports our objective of developing indicators that could be adopted by different healthcare systems worldwide. The proposed quality measures from our study will help individual institutions monitor and evaluate ongoing antimicrobial stewardship program efforts and provide healthcare systems with a consistent means to compare program effectiveness across institutions.

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