



Consensus statement

Quality indicators for appropriate antimicrobial therapy in the emergency department: a pragmatic Delphi procedure

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ABSTRACT

Objectives: Antimicrobial stewardship (AMS) has established its importance for inpatient care. AMS is, however, also urgently needed in emergency departments (ED), where many antimicrobial prescriptions are initiated. It is currently unclear what metrics stewardship teams can use to measure and improve the appropriateness of antimicrobial prescription in the ED. In this study we develop quality indicators (QIs) for antimicrobial use in the ED.

Methods: A RAND-modified Delphi procedure was used to develop a set of QIs applicable to adult patients who present at the ED with a potential infection. First, pragmatically using two recent papers of the international expert-group DRIVE-AB, potential ED-specific QIs for appropriate antimicrobial use were retrieved. Thereafter, an international multidisciplinary expert panel appraised these QIs during two questionnaire rounds with a meeting in between.

Results: Thirty-three potential QIs were extracted from the DRIVE-AB papers. After appraisal by 13 experts, 22 QIs describing appropriate antimicrobial use in the ED were selected. These indicators provide recommendations within five domains: stewardship prerequisites (six QIs); diagnostics (one QI); empirical treatment (ten QIs); documentation of information (four QIs); and patient discharge (one QI). **Conclusions:** We pragmatically developed a set of 22 QIs that can be used by stewardship teams to measure the appropriateness of antimicrobial prescription in the ED. There is probably room for additional QI development to cover all key aspects of AMS in the ED. Measuring QIs can be a first step for stewardship teams to, in collaboration with ED professionals, choose targets for improvement and optimize antimicrobial use. **Teske Schoffelen, Clin Microbiol Infect 2021;27:210**

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Introduction

In recent years, the importance of antimicrobial stewardship (AMS) has been well established [1,2]. Since the term was first introduced, it has been described in a variety of ways. Recently, Dyar et al. defined stewardship as ‘a coherent set of actions which

promote using antimicrobials in ways that ensure sustainable access to effective therapy for all who need them’ [3]. This points to the persistent efforts a health-care institution must make to measure and improve the appropriate use of antimicrobial agents, with the ultimate aim to improve patients’ clinical outcomes, while reducing adverse events and costs, and slowing down the development of antimicrobial resistance [4]. Measurement is essential to stewardship as it is key to assess the quality of current antimicrobial use, identify targets for improvement and determine the impact of improvement efforts. Measurement may involve the evaluation of quality indicators (QIs). Many QIs for appropriate

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antimicrobial use in hospitalized adult patients have been published [5].

The majority of research and activities of hospital AMS programmes focuses on inpatient care [6]. Surprisingly, the emergency department (ED), where many of the antimicrobial prescriptions for both inpatients and outpatients are initiated, has been relatively neglected [7]. QIs that define appropriate antimicrobial use in the ED have not systematically been developed. It is, therefore, currently unclear what metrics stewardship teams can use to measure and improve the appropriateness of antimicrobial prescription in the ED.

In this paper, we present a set of QIs for appropriate antimicrobial use in the ED that followed from a systematic, pragmatic procedure.

Methods

Potential ED-specific quality indicators for appropriate antimicrobial use

To pragmatically arrive at a list of ED-specific quality indicators for AMS, we extracted QIs from two recent papers of an international expert-group (DRIVE-AB) [8]. DRIVE-AB published generic QIs for responsible antibiotic use in the inpatient and outpatient settings, i.e. generic QIs applicable to large groups of patients, non-specific to a particular infectious disease, patient group or treatment location [9,10]. Combining evidence from literature and stakeholder opinion led to multidisciplinary international consensus on 51 inpatient and 32 outpatient QIs. We (TS, JAS, JJH, JtO and MEJLH) merged both sets and rephrased the extracted QIs to match the ED setting, which led to 33 ED-specific indicators applicable to the large group of adult patients who present at the ED with a potential infection (see Supplementary material, [Table S1](#)).

RAND-modified Delphi procedure

A RAND-modified Delphi procedure was then performed to achieve expert consensus on these potentially relevant QIs for AMS in the ED. This method is well established and is one of the preferred methods for the development of QIs [11,12]. In short, this expert consensus procedure comprises two online questionnaire rounds and a face-to-face meeting between rounds. The procedure took place between November 2019 and February 2020. Purposeful sampling was performed to build a multidisciplinary panel of 16 international experts comprising infectious disease specialists, clinical microbiologists, pharmacists and ED specialists (four of each). They were selected based on their involvement in AMS and in the treatment of patients with infectious diseases in the ED. All experts were invited by email to participate. They received no financial incentive for participation.

First questionnaire round

The 33 QIs from the literature were put into a written questionnaire that was sent by email (Limesurvey) to the expert panel. The panel was asked to appraise the relevance of the various indicators assessing appropriateness of antimicrobial use in the ED using a nine-point Likert scale (with 1 denoting 'highly irrelevant' and 9 denoting 'highly relevant'), including the option 'cannot assess'. Some of the QIs were followed by defining questions to clarify specific aspects. For example, following the appraisal question on the relevance of documentation of an antibiotic plan, experts were asked to indicate the various topics that should (yes/no) be included in the plan. The experts could provide comments for each potential QI and provide suggestions for rephrasing. In

addition, they were given the opportunity to add QIs at the end of the questionnaire.

Rating procedure

Analysis of the results from the first questionnaire round was performed by standardized methodology. QIs were accepted if the median score was ≥ 8 and $\geq 70\%$ of the scores were in the top tertile (score 7, 8 or 9). QIs were to be discussed at the consensus meeting if $\geq 70\%$ of the scores were in the top tertile but the median score was between 7 and 8 or if they had a median score ≥ 8 but $<70\%$ of the scores were in the top tertile.

Expert meeting

Next, an expert panel meeting by means of a conference call was organized in December 2019. All experts who completed the first-round questionnaire were invited to this meeting. Before the meeting, all experts received a personal feedback report that described per QI the group score and the individual score. By using colour codes, the report also clearly described whether the QI was accepted (green), up for discussion (yellow) or was rejected (red). During the consensus meeting the results and comments expressed in the questionnaire round were presented and the QIs labeled 'for discussion' were discussed. In addition, accepted QIs with comments from the experts were rephrased in consensus where applicable and newly suggested potential QIs were discussed.

Second questionnaire round

After the consensus meeting, in January 2020, a second questionnaire was sent to the consensus panel for final appraisal with the accepted, rephrased and newly suggested QIs in an extensive summary. The experts were asked to express their agreement (yes/no) on rephrased QIs, and were asked to rate newly suggested QIs (using a nine-point Likert scale).

Results

First questionnaire round

Thirteen of 16 invited experts (response rate 81%) returned the first questionnaire (see Supplementary material, [Table S2](#)). The expert panel accepted 21 QIs, rejected 8 QIs and 3 QIs were labelled 'for discussion'. One QI had a 31% response proportion of 'cannot assess', which led to its re-appraisal in the second questionnaire round.

Expert meeting

Five experts from four countries (the Netherlands, Belgium, Italy and the USA) attended the expert panel meeting in addition to three of the team members (TS, JJH, JAS). During the consensus meeting, three QIs labelled 'for discussion' were discussed, of which one was rejected and two were rephrased. In addition, seven accepted QIs with comments from experts were rephrased in consensus, three QIs were merged into a single QI, and newly suggested indicators were discussed that led to the formulation of two new potential QIs.

Second questionnaire round

The second questionnaire that was sent for final appraisal to the consensus panel had a response rate of 77% (10/13). All seven rephrased QIs were accepted (agreement $\geq 70\%$). The two newly suggested QIs were rated on a nine-point Likert scale and one was accepted. The QI with 31% of responses of 'cannot assess' in the first round was rated again and rejected.

The procedure as described above resulted in a final set of 22 QIs for AMS in the ED. We (TS, JAS, JJH, JtO and MEJLH) thematically grouped the resulting QIs into five domains (a) stewardship prerequisites (i.e. appropriate structural or system preconditions that should be met when embarking on stewardship [13]) (six QIs); (b) diagnostics (one QI); (c) empirical treatment (ten QIs); (d) documentation of information (four QIs); (e) discharge (one QI) (Table 1).

Discussion

Our pragmatic RAND-modified Delphi procedure provided a set of 22 QIs that can be used by stewardship teams to measure the appropriateness of antimicrobial prescription in the large group of adult patients who present at the ED with a potential infection. These indicators provide recommendations within five domains: stewardship prerequisites, diagnostics, empirical treatment, documentation of information and discharge. Although these 22 QIs all apply to the ED, only three of them apply to the ED exclusively: two QIs on the initiation of antibiotics in the ED—of which one of them was added by the expert panel—and one QI on discharge.

From the work by May et al. [22], it can be deduced that stewardship metrics should at least encompass the four key processes typically performed by front-line health-care professionals in the ED: (a) making a (tentative) clinical diagnosis, (b) starting empirical therapy based on that diagnosis, (c) performing microbiological

tests before starting that therapy and (d) following up patients who are discharged from the ED. These are critical processes as they impact appropriate use further downstream. When critically comparing our five QI domains with these four key processes, several things stand out. First, indicators are lacking to measure the appropriateness of the first key process ‘making a (tentative) clinical diagnosis’. Such metrics would be valuable as they strongly relate to the rationale for starting antibiotics in the first place: not starting when an antibiotic is not indicated may importantly influence antimicrobial use and related stewardship end points. It should be acknowledged that guidelines (and thus QIs) related to AMS rarely discuss the clinical reasoning process of the prescribing professional (‘does this patient have an infection or not?’) but focus on what to do if a (tentative) infection is present or not (‘should I treat the infection and if so how should I treat it?’). In infectious-disease-specific guidelines however, this is often meticulously described [14,15]. It might be innovative to develop ED stewardship indicators that focus on the quality of the process to come to a tentative diagnosis in patients presenting at the ED with a potential infection. Hansen et al. [16], for example, developed QIs for respiratory tract infections in general practice with a special focus on the diagnostic process. None of the indicators focusing on the diagnostic process, however, achieved consensus. The authors suggested that the heterogeneous availability of, for example, rapid *Streptococcus A* antigen detection test and C-reactive protein rapid test might have influenced the uneven assessment of the diagnostic indicators.

Table 1
Quality indicators for antimicrobial stewardship in the emergency department

Stewardship prerequisites

1. An antibiotic stewardship programme that comprises measuring and improving antibiotic use should also cover the ED (QI 1)
2. A local antibiotic guideline should be present in the ED of the health-care facility (QI 2)
 - The local guideline should correspond to the national guideline but should be adapted based on local resistance patterns (QI 3)
3. Essential antibiotics as defined by local antibiotic guidelines should be stocked in the ED (QI 4)
4. Antibiotics in stock in the ED should not be beyond the expiration date (QI 5)
5. Antibiotics should be adequately conserved and handled in the ED (QI 6)

Diagnostics

6. Diagnostic microbiological tests relevant for the site of infection should be collected in the ED preferably before antibiotic administration (QI 7)

Empirical treatment

7. Antibiotics should be prescribed in the ED according to local antibiotic guidelines or according to national guidelines when no local guidelines are available (QI 8)
 - Dosing and dosing interval of antibiotics should be prescribed in the ED according to guidelines (QI 9)
 - The route of administration of antibiotics given in the ED should be compliant with guidelines (QI 10)
 - Timeliness of administration of antibiotic therapy and prophylaxis in the ED should be compliant with guidelines (QI 11)
8. When prescribing antibiotics in the ED, the following should be taken into account:
 - Relevant* results of previous cultures and susceptibilities (QI 12) *as defined by the local or national guidelines
 - Previous antibiotic use (QI 13)
 - Allergy status (QI 14)
 - Contraindications (QI 15)
9. Antibiotics prescribed by an ED provider for an admitted patient should be initiated while the patient is in the ED (QI 16):
 - In patients with sepsis or septic shock, administration of antibiotics should be initiated promptly in the ED aiming to reduce that time to as short a duration as feasible (QI 17)

Documentation of information

10. Antibiotic prescriptions in the ED that deviate from guidelines should be justified (QI 18)
11. An antibiotic plan should be documented in the ED medical record at the start of the antibiotic treatment (QI 19). The antibiotic plan should include:
 - Indication
 - Name
 - Dose
 - Route
 - Interval of administration
 - Duration (for patients discharged from the ED)
12. When prescribing antibiotics in the ED, the following should be documented in the medical record:
 - Allergy status (including nature and severity and date the reaction occurred) (QI 20)
 - Previous antibiotic use (including date and duration) (QI 21)

Discharge

13. Patients in the ED who are discharged with an antibiotic prescription should be educated (QI 22) on:
 - How to take it
 - The dosage
 - The expected side effects and potential interaction with other therapies
 - Duration of treatment

Second, ten QIs for ‘starting empirical therapy based on a (tentative) clinical diagnosis’—the second key process—were selected, describing several aspects of empirical treatment at the ED. Each aspect (choice of the agent, timeliness, dose) should, as stipulated by our QIs, be in accordance with the local guideline. To fit the ED, this guideline should cover both inpatient and outpatient management initiated in the ED. It might be important for stewardship teams to check whether this is actually the case. In addition, it might be important—again with the stewardship objective to only start antibiotics when indicated—to check whether the guideline also explicitly states what not to do in ED populations. In this manner stewardship would explicitly connect to the Choosing Wisely Campaign, a worldwide initiative to advance a national dialogue on avoiding unnecessary medical tests, treatments and procedures. A good example is provided by Schuur et al. [17] who describe 17 ‘low value’ clinical actions that are within the control of ED health-care providers. Seven actions actually address AMS topics of which two address empirical treatment, for example, ‘Do not give IV antibiotics to non-critically ill patients who can tolerate oral antibiotics’.

Third, only one QI was developed for ‘performing microbiological tests before starting that therapy’, the third ED key process. Similar to the discussion above, it is striking that this recommendation only focuses on what to do. In diagnostics ‘what not to do’ may be even more relevant than in empirical therapy, as unnecessary diagnostic tests importantly add to the patient burden and the financial burden of health-care systems. Schuur et al. [17] suggest four ‘what not to do’ stewardship actions in this section, among which ‘Do not order blood cultures for patients with a skin infection (eg, cellulitis, abscess) without sepsis’.

Fourth, only one QI was developed for ‘following up patients who are discharged from the ED’, clarifying what topics should be included in the education of patients who receive an antibiotic, which constitutes only one aspect of the discharge process. No follow-up indicators were suggested for patients who were discharged with or without antimicrobials or culture taking, for example on the monitoring of clinical response or culture results. Schuur et al. [17] suggested in this domain to ‘Do not mandate follow-up wound checks in the ED for patients discharged with uncomplicated abscesses or cellulitis’.

Overall, 12 of our QIs relate to three out of the four suggested key processes. Our remaining ten QIs describe structural preconditions that, in line with Donabedian’s quality model [18], might lead to improvements in clinical processes: six stewardship prerequisite QIs and four documentation QIs.

Our study has several strengths and limitations. This set of QIs was specifically developed for stewardship in the ED. The study set out to develop and appraise QIs for appropriate antimicrobial use in the ED using a systematic, pragmatic procedure including a well-established Delphi procedure. To come to a list of ED-specific QIs, we merged and adapted two multidisciplinary international consensus-based generic indicator sets for the inpatient and outpatient settings to fit the ED context. These were appraised by an international expert panel and indicators were selected applying strict criteria. Using the two published consensus-based indicator sets may, at the same time, constitute a potential limitation of our study. Although experts were explicitly asked to add missing ED-specific QIs, this choice may have created a possible tunnel vision, as a result of which we have overlooked certain aspects that are essential and unique for stewardship in the ED. Our critical comparison of our QIs with the four key processes typically performed by front-line ED health-care professionals indicates that indeed three out of the four key processes give room for additional QI development. Also, we may have missed important aspects of ED empirical therapy (e.g. regarding when not to treat and different

recommendations for inpatient versus outpatient settings) by combining all possible recommendations in one QI [8]: ‘Antibiotics should be prescribed in the ED according to local antibiotic guidelines’. This generalization may have obscured potentially relevant aspects of AMS in the ED. A last limitation may be that only five of thirteen first-round responding experts attended the consensus meeting. An extensive summary of the consensus meeting accompanied, however, the second questionnaire and the response rate to this questionnaire was high. We therefore assume that the low attendance rate does not undermine the results of the procedure.

Despite the signalled room for future development of additional QIs, the current set provides 22 important metrics for stewardship teams and serves as a framework to find targets for improvement. Continuously measuring 22 QIs will be a huge task, so it may be important to focus on the QIs with the greatest potential for benefit in a specific ED. In daily practice, stewardship teams can for example use this overview for discussion to select, in consensus with ED professionals, a small set of three to five indicators. The results of the measurement of these indicators should be reported back to the ED for discussion. If the measurement shows suboptimal antimicrobial use for certain QIs, improvement strategies should specifically target these aspects of care in the ED. When selecting an improvement strategy, the unique ED workflow and health-care system context, and other ED-specific drivers of appropriate antibiotic use, should be taken into account [19–21].

Authors’ contribution

TS, JAS, JJH, JtO and MEJLH conceived and designed the study. TS performed the study and analysed the data. TS, JAS, JtO and MEJLH interpreted the data and drafted the manuscript. JJH, AMQ and LSM critically revised the manuscript. All authors approved the final version of the manuscript.

Transparency declaration

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cmi.2020.10.027>.

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