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State of the Science Review

Clinical practice guidelines for creating an acute care hospital-based antimicrobial stewardship program: A systematic review

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Quality improvement

Background: Antimicrobial stewardship programs (ASPs) are dedicated to improving antimicrobial use. Although clinical practice guidelines (CPGs) are available for the development of ASPs, it is unclear what the quality of these guidelines are. We therefore systematically reviewed published CPGs for the development of acute care hospital-based ASPs.

Methods: Primary literature, CPG and health technology assessment databases, and infectious diseases society websites were searched. Abstract and full-text review of the search results for inclusion were performed independently by 2 assessors. Overall quality of included CPGs was assessed using the Appraisal of Guidelines for Research and Evaluation II instrument.

Results: We identified 1,064 unique publications; 18 warranted full-text review. Five publications were included in the final review. The National Institute for Care and Excellence from the United Kingdom, the Dutch Working Party on Antibiotic Policy, and the Infectious Diseases Society of America/Society for Healthcare Epidemiology of America from the United States all had high quality guidelines on the Appraisal of Guidelines for Research and Evaluation II scale.

Discussion: We identified 5 CPGs for creating a hospital-based ASP. Prior authorization and/or restriction policies that appeared in all 5 guidelines should be considered essential for the development of an effective hospital-based ASP.

Conclusions: High quality CPGs are available for implementation of ASPs in acute care hospitals.

Since 2013, all acute care facilities in Canada are required to have an antimicrobial stewardship program (ASP) to meet Accreditation Canada's Required Organizational Practices.[1] Accreditation Canada states that the primary focus of the ASP for acute care facilities is "to optimize the use of antimicrobials to achieve the best patient outcomes, reduce the risk of infections, reduce or stabilize levels of antibiotic resistance, and promote patient safety."[1] Although Accreditation Canada provides supporting references for the creation of ASPs, the quality of listed recommendations is not provided.[1] In addition to Accreditation Canada's Required Organizational Practices, the antimicrobial stewardship standard from the Joint Commission in the United States became effective January 1, 2017, for accreditation in critical access hospitals, hospitals, and nursing care centers,[2] and the Centers for Disease Control and Prevention has suggested that ASPs should be present in all health care settings and have provided core elements for hospital ASPs.[3] However, none of these are clinical practice guidelines (CPGs) and they do not provide an assessment of the quality of evidence that they used. In addition, it is unclear whether the recommendations

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are consistent between different ASP CPGs, and what the level of evidence is for each guideline recommendation.

CPGs have been defined by the Institute of Medicine as "statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and the assessment of the benefits and harms of alternative care options."[4] There are a number of reasons for the development and implementation of CPGs, including summarizing the best available evidence to aid in clinical decision making, improving quality of care while decreasing practice variation, maximizing efficient use of resources, and highlighting areas in which more research is needed.[5]

We are not aware of any current literature that has systematically examined the quality of published CPGs in ASP development for acute care facilities. Therefore, we sought to systematically review and summarize published CPGs relating to the development of acute care hospital-based ASPs in terms of methodological quality. In addition to evaluating the overall CPGs, the secondary objectives of this review were to evaluate the level of evidence for each of the specific recommendations contained within the guidelines, and if multiple guidelines existed, to determine the concordant recommendations for an ASP between the CPGs.

METHODS

This study was completed using applicable elements from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist to create a framework[6] (available on request). The PRISMA checklist was designed to be used as a framework for systematic reviews focusing on randomized controlled trials, however, it can be used as a framework for reporting other types of systematic reviews including those of CPGs.[6]

Protocol and registration

The protocol for this systematic review was registered on PROSPERO (registration number CRD42014010015.)

Eligibility criteria

We considered CPGs published from the year 2000 until October 27, 2018. We only considered publications that applied to acute care adult (≥18 years of age) hospitals and that originated from very high human development countries, defined by the United Nations Human Development Index with a score >0.800,[7] given the differences in resource availability between these and lower human development countries.[8,9] All interventions (ie, recommendations) included in the CPGs are of interest, including comparisons in the recommendations between CPGs. There were no language barriers for the search, but only publications available in English were considered for inclusion. Publications that were originally not in English but were available with an English translation were included. Any publication aimed toward hospital and health care workers and administrators was included, and the CPGs did not have to incorporate certain recommendations to be included.

Information sources and search strategy

A comprehensive search strategy was used for this study. We searched a number of primary literature databases including Medline, EMBASE and the Cochrane Database, CPG databases, infectious diseases organizations, and health technology assessment programs (Table 1). In addition, reference lists of identified articles were searched for relevance. The search was conducted in October 2018. We limited the time frame to anything published during or after the year 2000 and for the Cochrane Database, 2005 onwards. Although antimicrobial stewardship has been a formalized concept in Canada since the 1990s,[10] clinical structure and programs are always rapidly changing in medicine, and so the search was completed to only include more recent publications to ensure that only relevant evidence was considered.

Table 1
Information sources searched

Name of information source
Primary literature databases
Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily, and Ovid MEDLINE
Embase
Cochrane Database of Systematic Reviews
Guideline databases
National Guidelines Clearinghouse
Canadian Medical Association Infobase: Clinical Practice Guidelines Database
New Zealand Guidelines Group
Australian National Health and Medical Research Council: Clinical Practice Guidelines
National Institute for Health and Care Excellence Guidance
World Health Organization digital library
Guidelines International Network
Infectious diseases organizations
Association of Medical Microbiology and Infectious Diseases Canada
Infectious Diseases Society of America
Society for Healthcare Epidemiology of America
European Society of Medical Microbiology and Infectious Diseases
European Centre for Disease Control and Prevention
International Society for Infectious Diseases
Centers for Disease Control and Prevention
Public Health Agency of Canada
Laboratory Centre for Disease Control
Health technology assessment programs/health organizations
Canadian Agency for Drugs and Technologies in Health
Health Technology Assessment International
Institute of Health Economics
Joanna Briggs Institute
National Health Service

We used the search terms "antimicrobial stewardship program" and variations of "clinical practice guideline" in our literature search, except in the search of the guideline databases where we searched for "antimicrobial stewardship" only. The search terms and results are available on request.

Study selection and data collection process

Screening of titles and abstracts for potentially relevant guidelines was conducted by 2 independent reviewers (E.R. and D.C.). Full text copies of potentially relevant guidelines were assessed for inclusion by the same 2 reviewers (E.R. and D.C.) using an inclusion assessment form designed for this systematic review (available on request). Disagreements were resolved by consensus. For any disagreements unable to be resolved by consensus, a third reviewer (L.B.) was available. At each stage, Cohen's kappa was calculated as the measure of agreement.[11]

Data items

Variables gathered from the CPGs included year of publication, organizations involved with developing the CPG, country of origin, and funding sources for the development of the guidelines.

Summary measures

The primary outcome of the systematic review was the quality of the encompassed CPGs. The quality was evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument.[12]

We reported each item in the AGREE II instrument for each included CPG. For the AGREE II instrument, the domain scores are calculated from the scoring of 23 individual items of the AGREE II.[13] Each item is rated on a 7-point scale (ie, 1-strongly disagree to 7-strongly agree). The domain score is the sum of the scores for each individual item within a domain, scaled as a total percentage of the maximum score for each domain. A percentage >70% is considered high quality within a given domain.

Our secondary outcome was the level of evidence for each of the recommendations within each guideline, and this was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system.[14] GRADE classifies evidence as very low quality (defined as "any estimate of effect is very uncertain"), low quality (defined as "further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate"), moderate quality (defined as "further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate"), and high quality (defined as "further research is very unlikely to change our confidence in the estimate of effect").[14]

Data extraction were standardized as required by the structure of the AGREE II instrument and GRADE assessment (ie, only specific elements must be extracted and included) and completed independently by 2 authors (E.R. and D.C.). There was no process for unexpected data extraction as the current study only used AGREE II and GRADE. Concordant recommendations between all available CPGs were examined.

Synthesis of results

We conducted a narrative synthesis to report the results of our review.

There were no funding sources for this current study.

RESULTS

Study selection

In total, 1,077 articles were discovered through the searches of the databases, the various national Infectious Diseases Society website searches, searches of health technology assessment programs, and reference lists. Among these, 12 articles were duplicates and 1 was retired and therefore excluded. A total of 1,064 titles and abstracts were examined for relevance, with 18 articles being identified for full text review (kappa: 0.75). After full text review, 5 CPGs were included in this review (kappa: 1.00). Of the 13 excluded, 1 article was excluded as it was specifically stated that it was not a guideline but rather suggestions for how an ASP can be designed.[15] Another was excluded because it did not meet the rigorous criteria for CPGs mentioned earlier that require a systematic review of the literature and the associated references.[16] Two articles were focused on antimicrobial resistance rather than CPGs for ASPs.[17,18] One article was excluded as it was created as a complement to guidelines rather than a guideline itself.[19] Two articles were not focused on acute care hospitals.[20,21] Five articles were consensus statements (which are generally of lower methodological quality compared to CPGs[22]) or opinions rather than CPGs.[23-27] Finally, 1 article did not have an English translation available.[28] Figure 1 provides the PRISMA diagram of the search and screen results.

Included CPGs

The following describes the 5 CPGs included in this review: 1 guideline from 2009 originated from Ireland and was produced by the Strategy for the control of Antimicrobial Resistance in Ireland (SARI) hospital antimicrobial stewardship working group[29]; a guideline from 2015 was from the United Kingdom and was compiled by the National Institute for Health and Care Excellence (NICE)[30]; a guideline from 2016 originated from the United States and was produced by the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA)[31]; a guideline from 2016 originated from the Netherlands from the Dutch Working Party on Antibiotic Policy (SWAB)[32]; and the last guideline was also from 2016 from Germany and authored by the German Society for Infectious Diseases (GSID).[33]

Results of individual studies

Primary outcome: Results of the AGREE II instrument assessment

Figure 2 illustrates the scaled scoring of the 5 guidelines on all domains of the AGREE II instrument. In general, the IDSA/SHEA guideline, the SWAB guideline, and the NICE guideline performed higher than the SARI and GSID guidelines. On 5 of the 6 domains, the NICE guideline was either the top performer or was tied for the highest score. The overall guideline assessment score (on the 7-point scale) was rated as a 7 for the NICE guideline, a 6 for the IDSA/SHEA guideline, a 6 for the SWAB guideline, a 5 for the GSID guideline, and a 4 for the SARI guideline.

We found that the scope and purpose of the guidelines were well described in the NICE, IDSA/SHEA, SWAB, and SARI guidelines. Stakeholder involvement was clearly explained in the NICE guideline and reasonably well in the IDSA/SHEA guidelines, with a domain score of 100% and 75%, respectively, but less so in the other 3 CPGs. The rigor of development domain scored highly for the NICE guideline (95%); the only item within the domain in which they did not achieve the highest score was regarding a direct link between recommendations and evidence. Although they did provide an appendix that explained which evidence was used for which recommendation, this linkage was not explicitly included in the guideline. Additionally, some of the recommendations were made through discussion of the evidence rather than a direct link to the evidence itself. The clarity of presentation scored very highly in all 5 included guidelines (domain scores of 97%-100%).

The applicability of the guidelines did not score highly for the IDSA/SHEA, GSID, or SWAB CPGs (38%, 29%, and 54% respectively), but scored well in the SARI and NICE guidelines (77% and 71%, respectively). Most of the guidelines did not thoroughly discuss the issues with implementing the recommendations, or advice for how these recommendations can be put into place. Although the SARI guidelines did comment on difficulties with implementing guideline recommendations due to resource issues, and that these barriers should be presented to senior management. The CPGs also generally did not clearly explain resource implications of applying the guidelines or how the actual implementation of the guidelines would be monitored. The SWAB guidelines had a recommendation that stated they could not suggest that specific stewardship strategies should be used to achieve the stewardship objectives as a consideration of barriers to implementation should be contemplated first.

Finally, for editorial independence, the NICE, IDSA/SHEA, and SWAB guidelines scored very well (100%, 100%, and 96% respectively), but the guidelines from SARI and GSID did not discuss editorial independence.

Secondary outcome: Results of the GRADE assessment

The GRADE assessment was completed for each recommendation's evidence with the exception of the SARI and the NICE guidelines, as there was no direct linkage of evidence to the recommendations within the guidelines, and therefore GRADE was not applied.

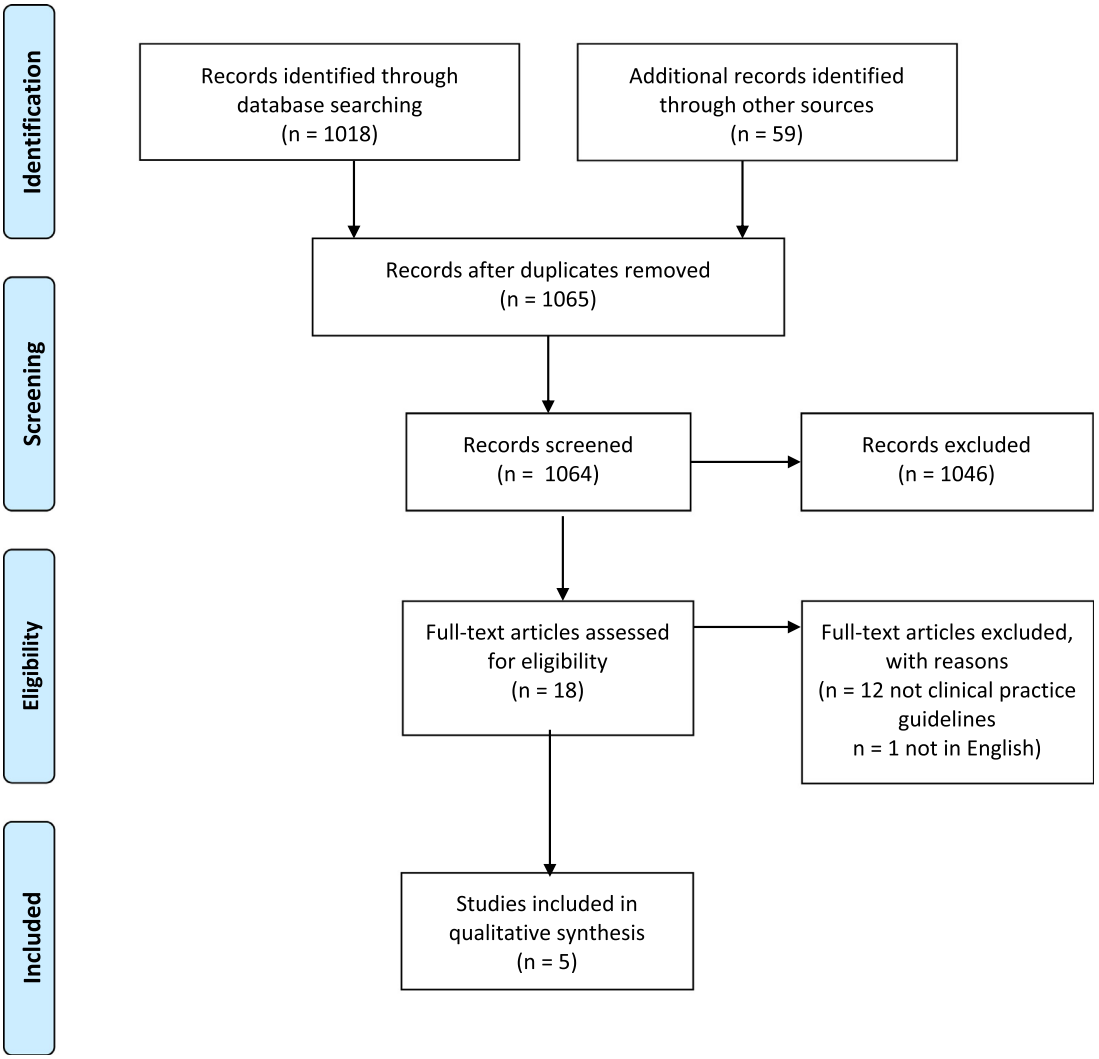

Fig 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Based on the GRADE evaluation of the level of evidence, we found that of the 28 IDSA/SHEA guideline recommendations, 8 were determined to be based on moderate quality evidence, 14 were based on low quality evidence, and 6 were based on very low quality evidence. Of note, IDSA/SHEA completed this exercise themselves, rating each of the recommendations according to GRADE. Our findings were generally consistent with what they found. The SWAB guidelines had 19 recommendations, 6 were based on no evidence, 8 were based on very low quality evidence, 3 were based on low quality evidence, and 2 were high quality evidence. The recommendations were rated by SWAB using GRADE and their findings corroborated with our own. The GSID guidelines had 15 recommendations of which 7 were based on moderate quality evidence, 4 were based on low quality evidence, and 4 were based on very low quality evidence.

The recommendations based on high quality evidence from the SWAB guidelines pertained to the use of procalcitonin in intensive care settings and in treatment guidance for respiratory tract infections and were based on randomized controlled trials and systematic reviews. Generally, recommendations of moderate quality evidence (eg, the use of authorization and prospective audit and feedback, the use of interventions designed to reduce the use of antibiotics associated with a high risk of *Clostridium difficile* infections compared to no such interventions, and the use of computerized clinical decision support systems) had some evidence that stemmed from small randomized controlled trials, or systematic reviews. Those suggestions with low quality were generally retrospective studies and very low quality evidence was frequently based on expert consensus.

Secondary outcome: Concordance of recommendations between guidelines

All guidelines, except for SWAB, emphasized the need for prospective audit and feedback. All of the CPGs discussed restriction of antimicrobials or prior authorization policies. In addition, all guidelines except for SWAB recommended education as part of stewardship interventions (although the IDSA/SHEA guideline did state this should not be a sole component of ASPs) and a team-based approach to antimicrobial stewardship. Although not every specific recommendation was identical throughout the 5 guidelines, and the IDSA/SHEA and NICE guidelines had substantially more recommendations, there were no contradictory recommendations between the 5 guidelines. All recommendations from the 5 guidelines can be found in Table 2. To determine domains of overlap between the different guidelines, the recommendations are grouped into the following categories: recommendations regarding the ASP structure at the organizational/institutional level; antimicrobial stewardship teams and roles; recommendations related

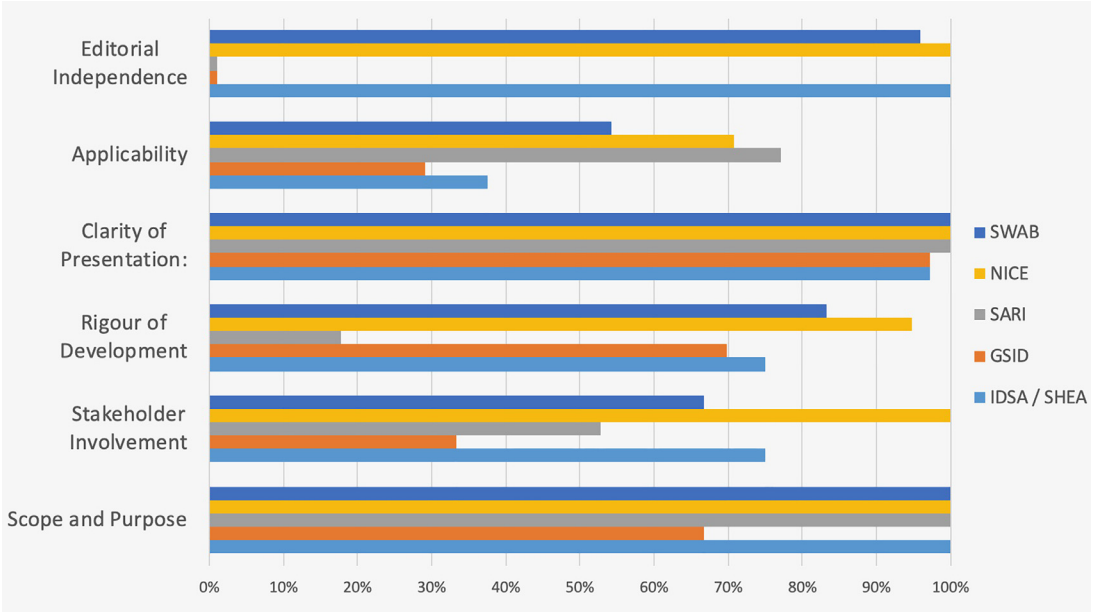

Fig 2. Appraisal of Guidelines for Research and Evaluation (AGREE) II domain scores. *GSID*, German Society for Infectious Diseases; *IDSA*, Infectious Diseases Society of America; *NICE*, National Institute for Health and Care Excellence; *SARI*, Strategy for the control of Antimicrobial Resistance in Ireland; *SHEA*, Society for Healthcare Epidemiology of America; *SWAB*, Dutch Working Party on Antibiotic Policy.

to behavior change in antimicrobial prescribing; communication; recommendations related to antimicrobial prescribing and monitoring; adoption of new antimicrobials; economic stewardship, microbiology and laboratory diagnostics; recommendations related to ASP quality indicators; special populations; and recommendations of local-decision groups.

DISCUSSION

In this systematic review, we found 5 CPGs that focused on the development and management of ASPs in the acute care hospital setting. Of these, the NICE, SWAB, and IDSA/SHEA guidelines were high quality on the AGREE II scale. The GSID and SARI guidelines were moderate quality on the AGREE II scale. Only 3 of the 5 guidelines, the GSID, SWAB, and IDSA/SHEA guidelines, were assessed using GRADE. The only recommendations based on high quality evidence were in the SWAB guidelines and related to procalcitonin. Generally, recommendations were split among moderate, low, and very low quality evidence. However, SWAB did include suggestions based on no evidence in the literature. In all 5 guidelines there were concordant recommendations for preauthorization and/or restriction of certain antimicrobials.

One issue that was consistent across all 5 guidelines was applicability. The AGREE II scale includes 3 different concepts within the applicability domain.[13] These concepts include the following: "the guideline provides advice and/or tools on how the recommendations can be put into practice; the potential resource implications of applying the recommendations have been considered" and; "the guideline presents monitoring and/or auditing criteria."[13] Despite not being able to tie GRADE levels of evidence into these guidelines, SARI and NICE CPGs did still have reasonable AGREE II score within this domain. However, these CPGs had a tendency to make suggestions without in-depth consideration for the difficulty in practically implementing them, which in many cases can include a lack of funding for a dedicated ASP team.[34] Funding can be a major issue in many centers and a barrier to implementation of ASPs.[34] The SWAB guideline recommendation that barriers to implementation must be assessed each time a stewardship strategy is considered is an important and realistic point, given that all hospitals have a unique culture that may impact what strategies and methods would be effective.[32] Additionally, as each of these CPGs came from a different country there would be different barriers to implementation specific to each country because of variations in health care systems.

Another potential issue with implementation is apathy toward the increasing threat of antimicrobial resistance.[35] Although ASPs can help combat the global threat of antimicrobial resistance, many jurisdictions still consider this a hypothetical threat and do not prioritize minimizing antimicrobial resistance when there are many other health care demands requiring resources.[35] It should be noted that in response to the challenges encountered when implementing ASPs, "playbooks" or "toolkits" are emerging that outline strategies for overcoming barriers to implementation.[36,37] Identifying obstacles and methods of implementing ASPs have recently been recognized as a priority area for antimicrobial stewardship research.[38]

Another issue that was found in the SARI and GSID guidelines using the AGREE II scale was a lack of editorial independence. Although the importance of disclosing funding sources and industry relationships is recognized as an important component of developing CPGs,[39] we were unable to assess the editorial independence of the SARI or GSID guidelines as the authors disclosures were not available. Therefore, we could not assess for potential conflicts of interest. The SARI guidelines were not published in a journal but rather available through a webpage, so they may not have faced the rigorous peer-review process that many academic journals require.

On examining the quality of evidence using GRADE when possible in the SWAB, IDSA/SHEA, and GSID guidelines there was a lack of high quality evidence (Table 2). This potentially is reflective of the fact that although ASPs are recognized as a key factor in the management of antimicrobial use, there is a lack of robust research regarding the use of the different ASP techniques and their effect on clinical outcomes to date.

When considering each of the CPGs included in the current study there were no recommendations between CPGs that directly contradicted each other, and all guidelines suggested antimicrobial restriction and/or preauthorization (Table 2). All guidelines except for SWAB suggested prospective audit and feedback. These similarities in

Table 2
Individual clinical practice guideline recommendations grouped by domain to highlight consistencies and discrepancies between individual recommendations across clinical practice guidelines. GRADE level of evidence is included in italics beside each recommendation for the guidelines in which this was applicable.

DOMAIN	IDSA	NICE	SARI	SWAB	GSID

Recommendations regarding the ASP structure at the Organisational/ institutional level	No recommendation	• Commissioners should ensure that antimicrobial stewardship operates across all care settings as part of an antimicrobial stewardship programme.
		• Establish an antimicrobial stewardship programme, taking account of the resources needed to support antimicrobial stewardship across all care settings.
		• Consider including the following in an antimicrobial stewardship programme:
		  • monitoring and evaluating antimicrobial prescribing and how this relates to local resistance patterns
		  • providing regular feedback to individual prescribers in all care settings about:
		  • their antimicrobial prescribing, for example, by using professional regulatory
		  • numbers for prescribing as well as prescriber (cost centre) codes
		  • patient safety incidents related to antimicrobial use, including hospital admissions for potentially avoidable life-threatening infections, infections with *Clostridium difficile* or adverse drug reactions such as anaphylaxis
		  • providing education and training to health and social care practitioners about antimicrobial stewardship and antimicrobial resistance
		  • integrating audit into existing quality improvement programmes.
		• Ensure that roles, responsibilities and accountabilities are clearly defined within an antimicrobial stewardship programme.
		• Involve lead health and social care practitioners in establishing processes for developing, reviewing, updating and implementing local antimicrobial guidelines in line with national guidance and informed by local prescribing data and resistance patterns.
		•Consider developing systems and processes for providing regular updates (at least every year) to individual prescribers and prescribing leads on:
		  • individual prescribing benchmarked against local and national antimicrobial prescribing rates and trends
		  • local and national antimicrobial resistance rates and trends
		  • patient safety incidents related to antimicrobial use, including hospital admissions for potentially avoidable life-threatening infections, infections with *C difficile* or adverse drug reactions such as anaphylaxis.
		• Consider developing systems and processes for identifying and reviewing whether hospital admissions are linked to previous prescribing decisions in patients with potentially avoidable infections (for example, *Escherichia coli* bacteraemias, mastoiditis, pyelonephritis, empyema, quinsy or brain abscess).
			• Development of hospital antimicrobial stewardship programmes, along with provision of appropriate resources, should be a priority for the Health Services Executive (HSE).
			• All acute hospitals should have an annually-assessed antimicrobial stewardship programme.
			• National treatment guidelines for common infections in hospital should be developed, for adaptation at local level.
			• All hospitals should have appropriate administrative and information technology support for antimicrobial stewardship, including an appropriate pharmacy information technology system.
			• The hospital chief executive/manager must ensure promotion of rational antimicrobial use is a strategic goal for the hospital.
			• All acute hospitals should have a multi-disciplinary Drugs and Therapeutics Committee.
				• It is recommended to have a local antibiotic guide present in the hospital (*very low*).
				• The Guideline committee also recommends that the local antibiotic guide corresponds to the national antibiotic guidelines (*no evidence*).
					• Computerized information technology (*low quality*).

Antimicrobial stewardship teams and roles	No recommendation	• Organisations establishing antimicrobial stewardship teams should ensure that the team has core members (including an antimicrobial pharmacist and a medical microbiologist) and can co-opt additional members depending on the care setting and the antimicrobial issue being considered. • Support antimicrobial stewardship teams, by developing processes that promote antimicrobial stewardship or by allocating resources, to: • review prescribing and resistance data and identify ways of feeding this information back to prescribers in	• All acute hospitals must have on-site presence of a medical microbiologist or infectious diseases physician, with responsibility for leading the antimicrobial stewardship programme, and 24-hour access to expert advice for management of infections. • All acute hospitals must have one or more clinical pharmacists with responsibility for antimicrobial stewardship. • All pharmacists with responsibility for antimicrobial stewardship should have access	No recommendation	• Availability of a team of ABS experts (*moderate quality*).

(*continued on next page*)

Table 2 (*Continued*)

DOMAIN	IDSA	NICE	SARI	SWAB	GSID
		all care settings • promote education for prescribers in all care settings • assist the local formulary decision-making group with recommendations about new antimicrobials • update local formulary and prescribing guidance • work with prescribers to explore the reasons for very high, increasing or very low volumes of antimicrobial prescribing, or use of antimicrobials not recommended in local (where available) or national guidelines • provide feedback and advice to prescribers who prescribe antimicrobials outside of local guidelines when it is not justified.	to a structured training programme delivered at a national level.		
Recommendations related to Behaviour change in antimicrobial prescribing	• We recommend preauthorization and/or prospective audit and feedback over no such interventions (*moderate quality*). • We suggest against relying solely on didactic educational materials for stewardship (*low quality*). • We suggest ASPs develop facility-specific clinical practice guidelines coupled with a dissemination and implementation strategy (*low quality*). • We suggest the use of strategies (eg, antibiotic time-outs, stop orders) to encourage prescribers to perform routine review of antibiotic regimens to improve antibiotic prescribing (*low quality*). • We suggest incorporation of computerized clinical decision support at the time of prescribing into ASPs (*moderate quality*). • We suggest ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes (*low quality*).	• Consider using the following antimicrobial stewardship interventions: • review of prescribing by antimicrobial stewardship teams to explore the reasons for increasing, very high or very low volumes of antimicrobial prescribing, or use of antimicrobials not recommended in local (where available) or national guidelines • promotion of antimicrobials recommended in local (where available) or national guidelines • IT or decision support systems • education-based programmes for health and social care practitioners, (for example, academic detailing, clinical education or educational outreach). • Consider providing IT or decision support systems that prescribers can use to decide: (a) whether to prescribe an antimicrobial or not, particularly when antimicrobials are frequently prescribed for a condition but may not be the best option, (b) whether alternatives to immediate antimicrobial prescribing may be appropriate (for example, back-up [delayed] prescribing or early review if concerns arise). • Consider developing systems and processes to ensure that the following information is provided when a patient's care is transferred to another care setting: • information about current or recent antimicrobial use • information about when a current antimicrobial course should be reviewed • information about who a patient should contact, and when, if they have concerns about infection. • Consider prioritising the monitoring of antimicrobial resistance, to support antimicrobial stewardship across all care settings, taking into account the resources and programmes needed. • Consider supplying antimicrobials in pack sizes that correspond to local (where available) and national guidelines on course lengths. • Consider evaluating the effectiveness of antimicrobial stewardship interventions by reviewing rates and trends of antimicrobial prescribing and resistance.	• The recommended core, high impact interventions to promote prudent antimicrobial use are: • clinical review of patients receiving antimicrobials by an antimicrobial stewardship team (microbiologist/infectious diseases physician/pharmacist), with direct advice and feedback to prescribers • regular surveillance/audit of antimicrobial use, with interactive feedback of results to prescribers • limiting the use of specific antimicrobial agents through restricting availability, restricting use to specified clinical settings, or requiring pre-authorisation by a member of the antimicrobial stewardship team prior to prescribing. • The recommended therapeutic interventions to improve the quality of antimicrobial use are: • ensuring antimicrobial therapy is optimised to the individual patient including, where necessary, therapeutic drug monitoring • ensuring empiric antimicrobial therapy is streamlined as soon as possible, to ensure therapy is directed against the causative pathogen(s) • having an effective programme for timely conversion of parenteral antimicrobial therapy to oral therapy. • Antimicrobial stewardship teams should promote the management of patients in Outpatient Parenteral Antimicrobial Therapy (OPAT) programmes, for selected clinical situations. • Undergraduate and postgraduate education of health professionals should include principles of prudent antimicrobial prescribing. • The recommended educational interventions and prescribing aids to improve the quality of antimicrobial use are: • all hospitals should have a programme of ongoing education for prescribers • all hospitals should have local/regional antimicrobial prescribing guidelines, which are regularly updated and are based, whenever possible, on local antimicrobial resistance data • all hospitals should consider using specific order forms, or designate a section of the prescription chart for prescribing of antimicrobials. • Consideration should be given to using	• The Guideline committee cannot make recommendations which Stewardship strategy should be used to achieve the Stewardship objectives (*low*). • It is recommended to use a list of restricted antibiotics. The A-teams should update their hospital antimicrobial restriction list regularly (*very low*).	• Conducting proactive audits of antiinfective use (*low quality*). • Design and implementation of education, training and information (*moderate quality*).

(*continued on next page*)

Table 2 (*Continued*)

DOMAIN	IDSA	NICE	SARI	SWAB	GSID
			prescribing aids, such as standardised documentation of treatment decisions and information technology-based prescribing supports. • Commercial promotion of antimicrobials should follow the Code of Marketing Practice, produced by the Irish Pharmaceutical Healthcare Association, and local guidelines approved by the hospital's Drugs and Therapeutics Committee.		
Communication	No recommendation	• Encourage and support prescribers only to prescribe antimicrobials when this is clinically appropriate. • Encourage health and social care practitioners across all care settings to work together to support antimicrobial stewardship by: • communicating and sharing consistent messages about antimicrobial use • sharing learning and experiences about antimicrobial resistance and stewardship • referring appropriately between services without raising expectations that antimicrobials will subsequently be prescribed. • Consider developing local networks across all care settings to communicate information and share learning on: (a) antimicrobial prescribing, (b) antimicrobial resistance, (c) patient safety incidents. • Consider developing local systems and processes for peer review of prescribing. Encourage an open and transparent culture that allows health professionals to question antimicrobial prescribing practices of colleagues when these are not in line with local (where available) or national guidelines and no reason is documented. • Encourage senior health professionals to promote antimicrobial stewardship within their teams, recognising the influence that senior prescribers can have on prescribing practices of colleagues. • Raise awareness of current local guidelines on antimicrobial prescribing among all prescribers, providing updates if the guidelines change. • Health and social care practitioners should support the implementation of local antimicrobial guidelines and recognise their importance for antimicrobial stewardship.	No recommendation	No recommendation	No recommendation
Recommendations related to antimicrobial prescribing and monitoring	• We recommend antibiotic stewardship interventions designed to reduce the use of antibiotics associated with a high risk of CDI compared with no such intervention (*moderate quality*). • We suggest against the use of antibiotic cycling as a stewardship strategy (*low quality*). • We recommend that hospitals implement pharmacokinetic monitoring and adjustment programs for aminoglycosides (*moderate quality*). • We suggest that hospitals implement pharmacokinetic monitoring and adjustment programs for vancomycin (*low quality*). • We recommend ASPs implement programs to increase both	• When prescribing antimicrobials, prescribers should follow local (where available) or national guidelines on: • prescribing the shortest effective course • the most appropriate dose • route of administration. • When deciding whether or not to prescribe an antimicrobial, take into account the risk of antimicrobial resistance for individual patients and the population as a whole. • When prescribing any antimicrobial, undertake a clinical assessment and document the clinical diagnosis (including symptoms) in the patient's record and clinical management plan. • For patients in hospital who have suspected infections, take microbiological samples before prescribing an antimicrobial and review the prescription when the results are available. • For patients in primary care who have recurrent or persistent infections, consider taking microbiological samples when prescribing an antimicrobial and review the prescription when the results are available. • For patients who have non-severe infections, consider taking microbiological samples before making a decision about prescribing an antimicrobial, providing it is safe to withhold	• All prescribing of antimicrobials, either for treatment or prophylaxis, should follow the principles of prudent antimicrobial prescribing. • Antimicrobials should be used after a treatable infection has been recognised or there is a high degree of suspicion of infection. In general, colonisation or contamination should not be treated. Antimicrobials should be used for the prevention of infection where research has demonstrated that the potential benefits outweigh the risks. Long-term prophylaxis should be avoided unless there is a clear clinical indication (for example, rheumatic fever and post-splenectomy). • The choice of antimicrobial should be determined by the sensitivity of the identified causative organism when this is known. Empiric therapy, for the likely causative organism (s) should be governed by local guidelines that have been informed by recent information about trends in	• The Guideline committee recommends to prescribe empirical antibiotic therapy for community acquired pneumonia according to the guidelines (*low quality*). • The Guideline committee recommends to prescribe empirical antibiotic therapy according to the guideline also for other infections (*low quality*). • It is recommended to take blood cultures and cultures from the site of infection before starting systemic antibiotic therapy (*no evidence*). • It is recommended to change empirical antibiotics to pathogen-directed therapy as soon as culture results become available (*very low*). • It is recommended to adapt the dose and dosing interval of antibiotics to renal function (*very low*). • It is recommended to switch systemic antibiotic therapy from intravenous to oral antibiotic therapy after 48-72 hours on the basis of the clinical condition and when oral treatment is adequate (*very low*).	• Application of local treatment guidelines/pathways, hospital antiinfective formulary, formulary restriction and approval requirements. • Parenteral to Oral Conversion: If sufficient bioavailability is assured, and if the patient's condition allows, therapy should be switched from parenteral to oral antibiotic application (*moderate quality*). • Dose optimization (*very low quality*). • Scheduled switch of antimicrobials: so called "cycling" programmes [are not suitable]. (*very low quality*). • De-escalation of therapy (*moderate quality*). • Duration of Treatment: It is possible to shorten the duration of antiinfective treatment for many indications (eg, perioperative antibiotic prophylaxis) and this is recommended wherever

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Table 2 (*Continued*)

DOMAIN	IDSA	NICE	SARI	SWAB	GSID
	appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics (*moderate quality*). • In patients with a history of β-lactam allergy, we suggest that ASPs promote allergy assessments and penicillin (PCN) skin testing when appropriate (*low quality*). • We recommend that ASPs implement guidelines and strategies to reduce antibiotic therapy to the shortest effective duration (*moderate quality*).	treatment until the results are available. • Prescribers should take time to discuss with the patient and/or their family members or carers (as appropriate): • the likely nature of the condition • why prescribing an antimicrobial may not be the best option • alternative options to prescribing an antimicrobial • their views on antimicrobials, taking into account their priorities or concerns for their current illness and whether they want or expect an antimicrobial • the benefits and harms of immediate antimicrobial prescribing • what they should do if their condition deteriorates (safety netting advice) or they have problems as a result of treatment • whether they need any written information about their medicines and any possible outcomes. • When an antimicrobial is a treatment option, document in the patient's records (electronically wherever possible): • the reason for prescribing, or not prescribing, an antimicrobial • the plan of care as discussed with the patient, their family member or carer (as • appropriate), including the planned duration of any treatment. • Do not issue an immediate prescription for an antimicrobial to a patient who is likely to have a self-limiting condition. • If immediate antimicrobial prescribing is not the most appropriate option, discuss with the patient and/or their family members or carers (as appropriate) other options such as: • self-care with over-the-counter preparations • back-up (delayed) prescribing • other non-pharmacological interventions, for example, draining the site of infection. • When a decision to prescribe an antimicrobial has been made, take into account the benefits and harms for an individual patient associated with the particular antimicrobial, including: • possible interactions with other medicines or any food and drink • the patient's other illnesses, for example, the need for dose adjustment in a patient with renal impairment • any drug allergies (these should be documented in the patient's record) • the risk of selection for organisms causing healthcare-associated infections, for example, *C difficile*. • When prescribing is outside local (where available) or national guidelines, document in the patient's records the reasons for the decision. • Do not issue repeat prescriptions for antimicrobials unless needed for a particular clinical condition or indication. Avoid issuing repeat prescriptions for longer than 6 months without review and ensure adequate monitoring for individual patients to reduce adverse drug reactions and to check whether continuing an antimicrobial is really needed. • Use an intravenous antimicrobial from the agreed local formulary and in line with local (where available) or national guidelines for a patient who needs an empirical intravenous antimicrobial for a suspected infection but has no confirmed diagnosis.	antimicrobial sensitivities. • Targeted therapy should be used in preference to broad-spectrum antimicrobials unless there is a clear clinical reason (for example, mixed infections or life-threatening sepsis). The prescription of broad- spectrum antimicrobials should be reviewed as soon as possible and promptly switched to narrow- spectrum agents when sensitivity results become available. Mechanisms should be in place to control the prescribing of all new broad-spectrum antimicrobials. • The timing, regimen, dose, route of administration and duration of antimicrobial therapy should be optimised and documented. The indication for which the patient is being prescribed the antimicrobials should be documented in the drug chart and case notes by the prescriber. • Wherever possible, antimicrobials should be given orally rather than intravenously. Clear criteria should be defined for when intravenous therapy is appropriate. As soon as possible the prescription should be switched to an oral equivalent. The intravenous prescription should be reviewed after 48 hours as a minimum. • Antimicrobial treatment should be stopped as soon as possible. A stop date or review date should be recorded by the prescriber on the drug chart. In general, antimicrobial courses should be reviewed within five days. • To ensure rapid treatment and infection control, mechanisms should be in place to ensure that patients receive antimicrobial drugs in a timely manner. • Rational antimicrobial prescribing should be included in clinical governance requirements for all clinicians. • Patients, or their legal guardians, should be informed of the rationale for prescribing antimicrobials, and • informed of any associated risks or adverse effects.	• It is recommended to document an antibiotic plan in the case notes at the start of systemic antibiotic treatment (*no evidence*). • It should be considered to discontinue empirical antibiotic therapy for presumed bacterial infection based on the lack of clinical or microbiological evidence of infection (*very low*).	backed by good studies and evidence (*moderate quality*).

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Table 2 (*Continued*)

DOMAIN	IDSA	NICE	SARI	SWAB	GSID
		• Consider reviewing intravenous antimicrobial prescriptions at 48-72 hours in all health and care settings (including community and outpatient services). Include response to treatment and microbiological results in any review, to determine if the antimicrobial needs to be continued and, if so, whether it can be switched to an oral antimicrobial.			
Adoption of new antimicrobials	No recommendation	• Consider establishing processes for reviewing national horizon scanning to plan for the release of new antimicrobials. • Consider using an existing local decision-making group (for example, a drug and therapeutics committee, area prescribing committee or local formulary decision- making group) to consider the introduction of new antimicrobials locally. The group should include representatives from different care settings and other local organisations to minimise the time to approval. • Consider using multiple approaches to support the introduction of a new antimicrobial, including: • electronic alerts to notify prescribers about the antimicrobial • prescribing guidance about when and where to use the antimicrobial in practice • issuing new or updated formulary guidelines and antimicrobial prescribing guidelines • peer advocacy and advice from other prescribers • providing education or informal teaching on ward rounds • shared risk management strategies for antimicrobials that are potentially useful but may be associated with patient safety incidents. • Once a new antimicrobial has been approved for local use, organisations should consider ongoing monitoring by: • conducting an antimicrobial use review (reviewing whether prescribing is appropriate and in line with the diagnosis and local [where available] and national guidelines) • costing the use of the new antimicrobial • reviewing the use of non-formulary antimicrobial prescribing • evaluating local prescribing and resistance patterns • reviewing clinical outcomes such as response to treatment, treatment rates, emerging safety issues, tolerability and length of hospital stay.	No recommendation	No recommendation	No recommendation
Economic stewardship	• In hospitalized patients, we suggest ASPs advocate for the use of alternative dosing strategies versus standard dosing for broad-spectrum β-lactams to decrease costs (*low quality*).	No recommendation	No recommendation	No recommendation	No recommendation
Microbiology and laboratory diagnostics	• We suggest development of stratified antibiograms over solely relying on nonstratified antibiograms to assist ASPs in developing guidelines for empiric therapy (*low quality*). • We suggest selective and cascade reporting of antibiotics over reporting of all tested antibiotics (*low quality*). • We suggest the use of rapid viral	• Ensure that laboratory testing and the order in which the susceptibility of organisms to antimicrobials is reported is in line with: • national and local treatment guidelines • the choice of antimicrobial in the local formulary • the priorities of medicines management and antimicrobial stewardship teams. • Consider point-of-care testing in primary care for patients with suspected lower respiratory tract infections, as described in the NICE guideline on pneumonia.	• The recommended laboratory interventions to improve the quality of antimicrobial use are: • all acute hospitals should have 24-hour access to an accredited microbiology laboratory • laboratories should carry out local surveillance of antimicrobial resistance, including annual review of antibiograms where appropriate • laboratories should report antimicrobial susceptibilities in a restrictive manner, and	• It is recommended to perform therapeutic drug monitoring (TDM) in patients treated with aminoglycosides, glycopeptides, posaconazole or voriconazole (*very low*). • Procalcitonin-guided antibiotic treatment discontinuation should be considered in the ICU setting (*high quality*). • The Guideline committee does not recommend the use of procalcitonin for guiding treatment duration of respiratory tract infections (*high quality*).	• Pathogens and Resistance: Antimicrobial susceptibility data on major pathogens should be available and accessible at least yearly on a hospital-wide level and separately for general and intensive care units, or department-specific, as the case may be. Data on primary isolates should be shown by pathogen and type of specimen, eg, blood, urine, miscellaneous samples. Culture results from

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Table 2 (*Continued*)

DOMAIN	IDSA	NICE	SARI	SWAB	GSID
	testing for respiratory pathogens to reduce the use of inappropriate antibiotics (*low quality*). • We suggest rapid diagnostic testing in addition to conventional culture and routine reporting on blood specimens if combined with active ASP support and interpretation (*moderate quality*). • In adults in ICUs with suspected infection, we suggest the use of serial procalcitonin measurements as an ASP intervention to decrease antibiotic use (*moderate quality*). • In patients with hematologic malignancy at risk of contracting invasive fungal disease (IFD), we suggest incorporating nonculture-based fungal markers in ASP interventions to optimize antifungal use (*low quality*).		reports should include interpretative comments to guide prescribers • laboratories should develop, or provide access to, rapid diagnostic methods and key inflammatory markers.		screening tests should be shown separately. Susceptibility rates should indicate the number of isolates tested. Infection rates should relate consistently to a single denominator (eg, patient-days/number of cases). Participation in an established surveillance system is recommended (*very low quality*). • Special rules for communication of microbiology results: The quality of microbiology diagnostics depends crucially on compliance with guidelines on procedures in the preanalytical phase. Expert consensus recommends that any deviations from protocol ought to be reported and the reasons for rejecting the samples stated. Technical progress and up-to-date molecular diagnostic methods for rapid pathogen detection should be used if they improve the quality of care and/or substantially improve identification and epidemiologic investigation of local outbreaks. Positive blood culture findings, interim microscopic findings, results of rapid testing and rapid susceptibility testing should be delivered promptly to the attending physician. Antibiograms ought to adhere to local guidelines with respect to antimicrobial use and diagnostic findings, be presented selectively in agreement with the ABS team, and, if need be, include relevant interpretative comments. This procedure aids selection of a targeted, guideline-based antibiotic therapy. The microbiology laboratory is responsible for the timely identification of trends in antimicrobial resistance and prompt communication of observations to the ABS team and the physicians responsible for infection control. This way, the clinical and epidemiological significance of the observations can be defined at an early stage (*low quality*).

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Table 2 (*Continued*)

DOMAIN	IDSA	NICE	SARI	SWAB	GSID
Recommendations related to ASP quality indicators	• We suggest monitoring antibiotic use as measured by days of therapy (DOTs) in preference to defined daily dose (DDD) (*low quality*). • We recommend measuring antibiotic costs based on prescriptions or administrations instead of purchasing data (*very low quality*). • Measures that consider the goals and size of the syndrome-specific intervention should be used (*very low quality*).	No recommendation	No recommendation	• The Guideline committee cannot make any recommendation for assessing the patient's compliance with the antibiotic prescription in the hospital setting (*no evidence*).	• Antimicrobial Consumption: Data on antimicrobial consumption, expressed as use density (daily doses per 100 patient-days) should be collected at least annually or preferably quarterly and are generally reported by the pharmacist. Data are reported institution-wide, at the ward level as well as for individual (specialty) departments. On demand, data should be broken down to the agent level and should be provided to the ABS team. Participation in an established surveillance system is recommended (*low quality*). • Quality Indicators: ABS programmes should be integrated within the hospital's quality management. Content overlaps with the Therapeutics and Drugs Committee (drug safety) and Hospital Infection Control Committee (prevention of nosocomial infection) is useful and desired. Appropriate quality indicators to measure prescription practice (process measure), emergence of resistance or trend in consumption (outcome measure) and structure ought to be set and applied in every ABS programme. At least three indicators measuring structural quality and at least three indicators measuring process quality should be set regularly (*low quality*).
Special populations	• We suggest ASPs develop facility-specific guidelines for F&N management in hematology-oncology patients over no such approach (*low quality*). • We suggest implementation of ASP interventions to improve the appropriate prescribing of antifungal treatment in immunocompromised patients (*low quality*). • In nursing homes and skilled nursing facilities, we suggest implementation of antibiotic stewardship strategies to decrease unnecessary use of antibiotics (*very low quality*). • We suggest implementation of antibiotic stewardship interventions to reduce inappropriate antibiotic use and/or resistance in the NICU (*very low quality*). • In terminally ill patients, we suggest ASPs provide support to clinical care providers in decisions related to antibiotic treatment (*very low quality*).	No recommendation	No recommendation	• It is recommended to perform a bedside consultation in patients with *Staphylococcus aureus* bacteremia (*very low*). • The guideline committee recommends to perform a bedside consultation in patients with bacterial endocarditis or (intra)vascular infections (*no evidence*). • The guideline committee is of the opinion that a multidisciplinary consultation for patients with prosthetic joint infections is acceptable and that a bedside consult will not always be necessary for this particular group (*no evidence*). • The guideline committee is of the opinion that tailored application of guideline recommendations for the hospital setting may be considered in the long-term care facility setting (*no evidence*).	• Special rules for management of patients with multidrug–resistant microorganisms and *C difficile* ABS strategies should be used to prevent infection with *C difficile*. Restricting use of certain antimicrobial drugs or substitution of antimicrobial drug classes (eg, penicillin for cephalosporins or fluoroquinolones) can considerably reduce the incidence of *C difficile* infection. Infection prevention and control strategies are frequently also applied at the same time; however, they have less impact on the *C difficile* incidence than in the epidemiology of MRSA or VRE. Targeted ABS strategies are to varying degrees also effective in reducing multidrug resistant Gram-negative bacteria, particularly ESBL-producing microorganisms, MRSA and VRE, and ought to be specifically applied here too. In case of high prevalence of multidrug resistant microorganisms, recommendations on diagnostic tests, evaluation of findings and treatment, as well as infection control management should be coordinated immediately and

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DOMAIN	IDSA	NICE	SARI	SWAB	GSID
					disseminated locally. Routine surveillance of antimicrobial consumption and antimicrobial susceptibility data should be performed to avoid indiscriminate compensatory use of other antimicrobial drug classes, since this can promote the unintentional and uncontrolled emergence of resistance (*moderate quality*).
Recommendations of local-decision groups	No recommendation	• Consider co-opting members with appropriate expertise in antimicrobial stewardship when considering whether to approve the introduction of a new antimicrobial locally; this may include those involved in the antimicrobial stewardship team. • Ensure that local formularies, prescribing guidelines and care pathways are updated when new antimicrobials are approved for use. • When evaluating a new antimicrobial for local use and for inclusion in the local formulary, take into account: • the need for the new antimicrobial • its clinical effectiveness • the population in which it will be used • the specific organisms or conditions for which it will be used • dose, dose frequency, formulation and route of administration • likely tolerability and adherence • any drug interactions, contraindications or cautions • local rates and trends of resistance • whether use should be restricted and, if so, how use will be monitored • any additional monitoring needed • any urgent clinical need for the new antimicrobial • any plans for introducing the new antimicrobial. • Local decision-making groups should assess the benefits and risks of restricting access to a new antimicrobial. • If access to a new antimicrobial is restricted: • document the rationale for and the nature of the restriction, and ensure that this information is publicly available • review the restriction regularly to determine that it is still appropriate. • Ensure that there is a plan for the timely introduction, adoption and diffusion of a • new antimicrobial when this has been recommended for use. • Discuss with commissioners early in the approval process if funding concerns for a new antimicrobial are likely to cause delay in its introduction, adoption and diffusion. • Indicate where prescribers can find accurate, evidence-based and up-to-date information about the new antimicrobial.	No recommendation	No recommendation	No recommendation

ASP, antimicrobial stewardship program; F&N, febrile and neutropenic; *GRADE*, Grading of Recommendations, Assessment, Development and Evaluation; *GSID*, German Society for Infectious Diseases; *IDSA*, Infectious Diseases Society of America; IT, information technology; *NICE*, National Institute for Health and Care Excellence; NICU, neonatal intensive care unit; *SARI*, Strategy for the control of Antimicrobial Resistance in Ireland; *SHEA*, Society for Healthcare Epidemiology of America; *SWAB*, Dutch Working Party on Antibiotic Policy.

recommendations likely reflect the areas of antimicrobial stewardship where there are the most studies and evidence. The heterogeneity between the studies and their recommendations is potentially owing to differences in the data collection process used to inform recommendations. Each group that created a CPG may have had differences in their specific question formulation, search strategy, and differing processes and criteria to determine their recommendations and conclusions. There may be some variability related to process and this inconsistency is recognized as a limitation. However, CPG recommendations reflect clinical queries; each recommendation and its associated evidence is based on that question and its specific search results, and it is likely the clinical queries would have been similar. Additionally, the groups did use an element of discussion and consensus to create their final suggestions that would lead to some subjectivity and differences between the groups that created the guidelines.

A systematic review and meta-analysis from 2016 examined if antimicrobial stewardship objectives had any long-term effects in hospitals and long-term care facilities examining 4 domains of clinical outcomes, adverse events, costs, and bacterial resistance rates.[40] The authors classified 14 unique stewardship objectives and completed a systematic review on each, finding 145 studies that only addressed 9 of the 14 objectives.[40] Of the studies examined, most were found to be of low quality.[40] Although some of the studies did show the benefit of certain stewardship objectives (ie, empirical antibiotic therapy according to guidelines, de-escalation of therapy, switch from intravenous to oral treatment, therapeutic drug monitoring, use of a list of restricted antibiotics, and bedside consultation) in impacting at least 1 of the 4 domains listed earlier, this review demonstrates there is still a lack of high quality evidence to guide antimicrobial stewardship recommendations.[40]

As outlined earlier, 3 of the 5 CPGs did not score well on applicability, and none of the guidelines fully addressed the difficulties with implementation of an acute care hospital ASP. This may be partly owing to the fact that the cost-effectiveness of ASPs is still unclear, and so it is difficult to describe ways in which to use costs to help cross barriers to implementation. A structured review on the cost effectiveness of ASPs was recently completed and found that there was a failure to include complete costs rendering it difficult to know whether or not the interventions were cost-effective.[41]

This is the first systematic review to our knowledge on the evaluation of CPGs for ASPs in acute care hospitals. This is an area of importance given that ASPs are now required in many acute care centers and are becoming mandated in numerous jurisdictions. We thoroughly examined the identified guidelines to assess for quality using both the AGREE II tool and the GRADE scale for each individual recommendation where possible. Our methodology was consistent with a recent publication outlining the methodological guide for systematic reviews of CPGs, including the use of a validated appraisal tool to assess the CPG quality.[42] This systematic review also allows for a connection between ASP CPGs and recommendations from Accreditation Canada, which institutions can use when planning their ASPs. As mentioned previously, Accreditation Canada states that ASPs need "to optimize the use of antimicrobials to achieve the best patient outcomes, reduce the risk of infections, reduce or stabilize levels of antibiotic resistance, and promote patient safety." There is, of course, some overlap between the different areas, but suggestions in Table 2 that fall under the domains of recommendations related to behavior change in antimicrobial prescribing and recommendations related to antimicrobial prescribing and monitoring would also tie into optimizing the use of antimicrobials to achieve the best patient outcomes and reducing the risk of infections. Domains of recommendations related to antimicrobial prescribing and monitoring and microbiology and laboratory diagnostics would connect to reducing or stabilizing the levels of antimicrobial resistance. Also, the recommendations within the domain of the ASP structure at the organizational/institutional level would promote patient safety.

The study was limited in that it only included literature from 2000 onwards. There may have been some earlier guidelines that were missed, however, given that stewardship did not become a part of accreditation for hospitals until recently, it is unlikely that this was the case. Additionally, guidelines in development were not explicitly searched, although, as individual websites were searched, often guidelines in development will be listed there and so may have been found if present. In addition, our systematic review only looked at guidelines for acute care hospitals, and the results are therefore not necessarily applicable to ASPs in long-term care/continuing care or outpatient facilities. As mentioned earlier, the included CPGs were generally not comprised of high quality evidence. Although this reflects the available studies and evidence that currently exist for ASPs, it does decrease the reliability of the CPGs when they are applied to clinical practice. Also, 1 article was excluded on the basis of no English language translation available. Although it is uncertain whether or not this article would have met the inclusion criteria, as only 5 CPGs were included in the current study the exclusion of 1 study could potentially be significant. Another limitation in comparing and contrasting the CPGs is that they each originated from different countries. Because of differing health care systems and variable clinical demands, each guideline suggestion may not be applicable to every country. Table 2 provides an outline of all recommendations that enables readers to review and compare the suggestions and their associated evidence level and determine which are most applicable to their jurisdiction.

CONCLUSIONS

Based on the results of our systematic review, we would recommend the use of the NICE guideline or the IDSA/SHEA guideline for the development and implementation of a hospital-based ASP. Although the NICE guidelines were not assessed using GRADE in the current study, the authors were extremely thorough in their systematic search for evidence and assessed the quality of all the recommendations they included. The SWAB guidelines did rate highly on the AGREE II scale, however, many of their recommendations were based on no evidence.

Additionally, the findings from this review and the lack of high quality evidence to inform recommendations suggests a need for ongoing rigorous research in the area of ASPs, to ensure the desired clinical outcomes are being achieved and guarantee that evidence-based practices are being put in place. Levels of evidence identified with associated recommendations in Table 2 suggest specific areas with low quality evidence necessary for further research within the realm of antimicrobial stewardship. Higher quality evidence and studies may influence the recommendations of the CPGs. This highlights the importance of CPGs having strategies in place to update their recommendations based on new evidence. Finally, future updates to CPGs should strive to address the barriers in implementation and strategies for overcoming these challenges.

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