

Assessing the methodologic heterogeneity of Canadian Urological Association guidelines

Adoption of the GRADE approach (2018–2023)

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ABSTRACT

INTRODUCTION: The Canadian Urological Association (CUA) has a longstanding tradition of developing evidence-based guidelines. We conducted this study to assess the heterogeneity of the CUA's guideline methodology for developing recommendations from 2018-2023.

METHODS: We included guidelines from the CUA website from 2018-2023. Two reviewers working independently and in duplicate abstracted all data points and categorized the reported methodologic approaches for formulating recommendations and rating the evidence. We performed descriptive statistics only.

RESULTS: We included 23 guideline documents with a total of 654 recommendations. The median number of recommendations per guideline was 25 (interquartile range 17, 35). Seven guidelines (187 recommendations) used a modified Oxford Center for Evidence-Based Medicine approach for both the strength of recommendations and the levels of evidence, and eight guidelines (177 recommendations) reported the use of GRADE both for the strength of recommendations and the certainty of evidence. Of the remaining eight guidelines, four (154 recommendations) blended the GRADE approach for the strength of recommendations with modified Oxford levels of evidence, and the remaining four combined the American Urological Association's approach to recommendations with Oxford levels of evidence (n=1), GRADE certainty of evidence (n=2), or used GRADE but made no recommendations (n=1).

CONCLUSIONS: CUA guidelines have been marked by considerable methodologic heterogeneity that may confuse end users. Continued advancement in the CUA's approach to guideline development will facilitate greater collaboration and resource sharing, thereby supporting the CUA's mission of promoting high-quality, evidence-based care.

INTRODUCTION

Clinical practice guidelines (CPGs) aim to make transparent, evidence-based recommendations about the most appropriate medical care for individuals and populations. They are widely accepted as standards of care for payers of healthcare services and, therefore, play an influential role in shaping medical practice.

In Canada, the Canadian Urological Association (CUA) has a longstanding tradition of developing guidelines for its members and its guidance documents are among its most accessed resources.¹ These documents serve a pivotal role in supporting the CUA's vision "to promote the highest standard of urologic care for Canadians" and find explicit mention in its mission statement by referring to "leading evidence-based clinical practice through the development of practice standards and guidelines."²

As the science of creating methodologically rigorous and transparent guidelines has evolved over the past decades, the CUA has remained committed to staying in step with the latest developments. Widely accepted standards for guideline development include their foundation in high-quality systematic reviews, a formal process for determining the certainty of evidence, and a transparent approach for developing recommendations.³

Previously, many organizations, including the CUA, have used a "levels of evidence" approach developed by the Center for Evidence-Based

KEY MESSAGES

- There is marked methodologic heterogeneity of CUA guidelines published between 2018 and 2023.
- Many guidelines provided little information as to how the panel determined the quality of evidence or arrived at the strength of recommendation.
- An increasing proportion of CUA guidelines have been applying GRADE.
- A more widespread use of GRADE should enable the CUA to share evidence syntheses and better collaborate with other organizations.
- The continued advancement in the CUA's approach to guideline development supports the CUA's mission of promoting high-quality, evidence-based care.

Medicine in Oxford.⁴ This approach rates individual studies and focuses very much on study design. The resulting “grades of recommendation” (A, B, C, and D) mirror these levels of evidence without identifying any other domains that may impact the strengths of recommendations.

In 2018, the CUA hosted a workshop on how to develop trustworthy guidelines using the GRADE approach,⁵ and subsequently committed to adopting this approach for future guidelines.⁶ GRADE focuses on people-important outcomes. GRADE categorizes the certainty of evidence based on a body of evidence summarized through a systematic review, while recognizing five domains that may reduce our confidence in randomized controlled trials and three domains that may increase our confidence in non-randomized studies.⁷ It also identifies several other factors (aside from the certainty of evidence) that impact the strengths of recommendations, namely people's values and preferences and the relationship of benefits to harms, as well as resource utilization. In addition, considerations of acceptability, feasibility, and equity may affect the strength of a recommendation. Lastly, GRADE has developed a formal framework, referred to as “evidence-to-decision” framework, for a structured and transparent approach to making recommendations.^{8,9}

In recognition of the considerable challenges that the adoption of an entirely new approach to guideline development represents to all professional organizations, but especially smaller ones with limited resources, we conducted this study to evaluate to what extent the CUA has successfully adopted GRADE.¹⁰

METHODS

We identified all documents from the CUA website categorized as guidelines published between January 2018 and June 2023. January 2018 was selected as the cutoff, as that was the year the CUA made their commitment to start adopting GRADE.⁶ We excluded guidance documents labeled best practice statements and consensus statements, as well as guidelines that were secondarily endorsed by the CUA. We included guidelines that were jointly developed by the CUA and other organizations.

Two independent reviewers abstracted data points that included the year of publication, the first author's name, the title, the reported methodologic approach to rating the level of evidence (or quality/certainty of evidence), and the strength of recommendation. We abstracted the actual recommendations, as well as the reported levels of evidence and strength of recommendation associated with each recommendation. We also retrieved any supplemental materials that were related to the process of rating the evidence and that of arriving at a particular recommendation. Subsequently, we categorized guidelines based on the approach used to rate the certainty of the evidence, the strength of the recommendation, the congruence of the reported approaches, and the availability of detailed information as to how the panel arrived at a specific recommendation.

We categorized guidelines using the Oxford level of evidence if they referenced this approach and classified the evidence by levels I, II, III, IV, and V, and recommendations as levels A, B, C, and D.^{4,11} We classified them as having used GRADE if they rated the certainty of evidence as high, moderate, low/very low (or referring to them as levels A, B, C, and D), and recommendations were labeled as strong or weak/conditional, while also allowing some to use the categories of clinical principle and/or expert opinion.⁷ Lastly, we classified them as using the AUA approach for rating the strength of recommendations if they categorized the recommendations by five categories: strong, moderate, weak, clinical principle, and expert opinion.¹² We also distinguished between actionable recommendations that clearly expressed that a certain action should or should not be undertaken vs. non-actionable recommenda-

tions, usually statements of fact. Lastly, we determined whether guidelines provided information as to how panels moved from the summarized evidence to its recommendations and what (if any) other domains it considered.

We used descriptive statistics only in SPSS version 27 for reporting measures of central tendency and distribution for continuous variables, as well as proportions and percentages for dichotomous variables. We did not perform statistical hypothesis testing.

RESULTS

We identified 46 CUA guidance documents, of which 23 met the inclusion criteria for guidelines and were investigated further (Table 1). We excluded 13 best practice reports, nine consensus statements, and one external guideline that the CUA had secondarily endorsed. Most guidelines focused on adults ($n=20$, 87.0%); nearly half ($n=10$, 43.5%) were oncology-related. These guidelines issued a total of 654 recommendations; the median number of recommendations per guideline was 25 (interquartile range [IQR] 17, 35). The range of number of recommendations spanned from five (urethral strictures and erectile dysfunction) to 66 (non-muscle-invasive bladder cancer) recommendations. Of these 654 recommendations, approximately three-quarters ($n=488$, 74.6%) were categorized as actionable, whereas the others were non-actionable ($n=166$, 25.4%). Of the actionable recommendations, most ($n=430$, 86.9%) were recommendations for a certain management approach, whereas the remainder were recommendations against ($n=64$, 13.1%).

Seven guidelines with 187 recommendations reported the use of a modified Oxford Center for Evidence-Based Medicine approach for both the strength of recommendations and the levels of evidence (Table 2). The most common strength of recommendation was a level C ($n=85$, 45.5%); for 33 recommendations (17.6%), no strength was assigned. Eight guidelines with 177 recommendations reported the use of GRADE both for the strength of recommendations and the certainty of evidence (Table 3). The most common recommendation was weak or conditional ($n=99$, 55.9%) and approximately one-fourth ($n=48$, 27.1%) were labeled as strong. Twenty-nine guideline statements were reported as clinical principles ($n=15$, 8.5%) or expert opinion ($n=14$, 7.9%), although these are not standard GRADE strength of recommendation categories.

Four guidelines with 154 recommendations used GRADE for the strength of recommendations but reported the use of a modified Oxford levels of evi-

dence (Table 4). Approximately one-third of these recommendations were either labeled as strong ($n=59$, 38.3%) or weak/conditional ($n=54$, 35.1%). Lastly, four additional guidelines used a different methodology: three guidelines used the AUA's five-tiered system for the strength of recommendations and rated the certainty of evidence either using a modified Oxford approach ($n=1$) or a GRADE approach that categorized the certainty of evidence using the letters A, B, C, and D, or using the standard terms high, moderate, low, and very low certainty. One guideline reported the use of GRADE to rate the certainty of evidence but did not make graded recommendations.

We further assessed what guidelines provided additional information as to how the panelists arrived at recommendations of a given strength. We identified two guidelines that provided the details on judgments made by the panel using a formal evidence-to-decision framework.^{13,14} In addition, the guideline on perioperative thromboprophylaxis used a modified ADAPTE approach to adapt an EAU guideline on this topic (which has since been discontinued), which itself used explicit and transparent methods for developing its recommendations.^{15,16}

DISCUSSION

Principal findings

The most striking finding of our study is the methodologic heterogeneity of CUA guidelines published over a six-year period. These methods range from using a modified Oxford approach for both recommendations and levels of evidence to the use of GRADE for both the recommendations and the certainty of evidence; however, it also includes a blending of both approaches, most commonly in the form of framing the strength of recommendations using GRADE nomenclature but rating the evidence using modified Oxford levels of evidence.

Second, approximately a quarter of recommendations were not actionable, meaning it was not clear how the guideline user would translate them into a healthcare decision.

Third, we found that most guidelines provided little information as to how the panel determined the quality of evidence and perhaps more importantly, how the panel arrived at a given strength of recommendation. We worry that the observed inconsistency and limited transparency may mislead guideline users, undermine their perceived trustworthiness, and ultimately stand in the way of broad-based guideline implementation and the delivery of high-quality evidence-based care.

Table 1. Overview of included CUA guideline documents (n=23)

Guideline title	Year	Certainty of evidence	Strength of recommendation	Recommendations
Followup of patients after treatment of non-metastatic renal cell carcinoma ²⁸	2018	Oxford – modified (Level 1, 2, 3, 4)	Oxford – modified (A, B, C, D)	25
Peyronie's disease and congenital penile curvature ²⁹	2018	Oxford – modified (Level 1, 2, 3, 4)	Oxford – modified (A, B, C, D)	22
Investigation and management of antenatally detected hydronephrosis ^{30†}	2018	Oxford – modified (Level 1, 2, 3, 4)	Oxford – modified (A, B, C, D)	6
Care of the normal foreskin and neonatal circumcision in Canadian infants ³¹	2018	Oxford – modified (Level 1, 2, 3, 4)	Oxford – modified (A, B, C, D)	34
Muscle-invasive bladder cancer ³²	2019	Oxford – modified (Level 1, 2, 3, 4)	AUA terminology	58
Perioperative thromboprophylaxis and management of anticoagulation ¹⁵	2019	GRADE	GRADE (strong, weak)	47
Diagnosis, management, and surveillance of neurogenic lower urinary tract dysfunction ³³	2019	Oxford – modified (Level 1, 2, 3, 4, expert opinion)	Oxford – modified (A, B, C, D)	44
Recurrent uncomplicated urinary tract infections in women ^{34#}	2019	GRADE (A, B, C)	AUA terminology	16
Male urethral stricture ¹³	2020	GRADE	GRADE (strong, weak)	5
Treatment of bladder dysfunction in children ³⁵	2021	GRADE	None	13
Testosterone deficiency in men: Evidence-based Q&A ³⁶	2021	GRADE	GRADE (strong, weak)	21
Management of non-muscle invasive bladder cancer ³⁷	2021	Oxford – modified (Level 1, 2, 3, 4)	GRADE-like wording	66
Erectile dysfunction ¹⁴	2021	GRADE	GRADE (strong, weak)	5
Management of ureteral calculi ³⁸	2021	Oxford – modified (Level 1, 2, 3, 4, 5)	AUA terminology	49
Androgen deprivation therapy: Adverse events and management strategies ³⁹	2021	Oxford – modified (Level 1, 2, 3, 4)	GRADE-like wording (strong, weak, expert opinion)	34
Management of castration-resistant prostate cancer ^{40†}	2022	Oxford (modified)	GRADE-like wording	35
Metastatic castration-naïve and castration-sensitive prostate cancer ^{41†}	2022	Oxford (modified)	GRADE-like wording	19
Male lower urinary tract symptoms/ benign prostatic hyperplasia ⁴²	2022	GRADE (using terms A, B, C and D)	GRADE	32
Management of small renal masses ⁴³	2022	GRADE	GRADE (strong, weak; also: expert opinion, clinical principle)	24
Evaluation and medical management of kidney stones ⁴⁴	2022	Oxford – modified (Level 1, 2, 3, 4)	Oxford – modified (A, B, C, D)	29
Recommendations on prostate cancer screening and early diagnosis ⁴⁵	2022	Oxford – modified (Level 1, 2, 3, 4)	Oxford – modified (A, B, C, D; expert opinion)	27
Diagnosis, management, and follow-up of the incidentally discovered adrenal mass ¹⁷	2023	GRADE	GRADE	25
Management of cystic renal lesions ¹⁸	2023	GRADE	GRADE	17

Developed jointly with †the Society of Pediatric Urologists of Canada; #the AUA and the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU); ‡the Canadian Urologic Oncology Group. GRADE: Grading of Recommendations Assessment, Development and Evaluation; Q&A: Questions and answers.

We also found that an increasing proportion of CUA guidelines have been applying GRADE, including the two most recent on the diagnosis, management, and followup of the incidentally discovered adrenal mass and the one on the management of cystic renal lesions, as the two latest documents we included.^{17,18}

Strengths and weakness of the study

Our study is the first to report a formal assessment of the CUA's guideline methodology. Strengths include the use of a written, a priori protocol, as well as the performance of the data abstraction independently and in duplicate by two members of the research team. Our study includes the most recent guidelines of the CUA and was authored by investigators with considerable expertise in guideline methodology and publication track record in this field.

Limitations include the focus on guidelines only; we excluded other CUA guidance documents, such as best practice statements, which may present similar issues that we are unable to comment on. We recognize that the CUA guidelines published in 2018 and 2019 may have been underway by the time the CUA made its commitment to adopting GRADE in their guideline development process. This may explain the significant number of early guidelines that used the Oxford approach for rating certainty of evidence.

Our study also did not include guidelines by other urological associations, which would have permitted more direct comparisons. We further acknowledge that this study was mainly focused on the CUA's adoption of GRADE and did not include a broader assessment of methodologic quality, for example, by using the Appraisal of Guidelines for Research and Evaluation (AGREE) II or the National Guideline Clearinghouse Extent of Adherence to Trustworthy Standards (NEATS) instruments.^{19,20} We nevertheless believe that the findings of this study provide valuable insight to Canadian guideline developers and may provide the impetus for further movement toward a more unified and consistent approach.

Strengths and weaknesses in relation to other studies

A recent study assessed the guidelines of the EAU, as an organization that has endorsed the use of GRADE.²¹ This study found that EAU guidelines were consistent in framing their recommendations as strong and weak/conditional and using GRADE-recommended terminology, but otherwise did not use GRADE when it comes to rating the certainty of evidence, for which they used

Table 2. CUA guidelines using the modified Oxford approach

Strengths of recommendation	Levels of evidence					
	I	II	III	IV	V	None
A (n=23)	11 (47.8%)	4 (17.4%)	7 (30.4%)	0 (0%)	0 (0%)	1 (4.3%)
B (n=29)	11 (37.9%)	11 (37.9%)	3 (10.3%)	1 (3.4%)	0 (0%)	3 (10.3%)
C (n=85)	0 (0%)	8 (9.4%)	35 (41.2%)	41 (48.2%)	0 (0%)	1 (1.2%)
D (n=15)	0 (0%)	0 (0%)	2 (13.3%)	3 (20.0%)	9 (60.0%)	1 (6.7%)
Expert opinion (n=2)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (100%)
None (n=33)	4 (12.1%)	7 (21.2%)	1 (3.0%)	2 (6.1%)	0 (0%)	19 (57.6%)

Seven CUA guidelines with a total of 187 recommendations used the modified Oxford approach to rate both the strength of recommendations and level of evidence.

Table 3. CUA guidelines using GRADE

Strengths of recommendation	Certainty of evidence				
	High	Moderate	Low	Very Low	None
Strong (n=48)	13 (27.1%)	33 (68.85)	1 (2.1%)	0 (0%)	1 (2.1%)
Weak/conditional (n=99)	0 (0%)	27 (27.3%)	59 (59.6%)	10 (10.1%)	3 (3.0%)
Clinical principle (n=15)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	15 (100%)
Expert opinion (n=14)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	14 (100%)
None (n=1)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)

Eight CUA guidelines with a total of 177 recommendations used GRADE to rate both the strength of recommendations and certainty of evidence. GRADE: Grading of Recommendations Assessment, Development and Evaluation.

Table 4. CUA guidelines using GRADE and the modified Oxford approach

Strengths of recommendation	Levels of evidence					
	I	II	III	IV	V	None
Strong (n=59)	33 (55.9%)	15 (25.4%)	10 (16.9%)	0 (0%)	0 (0%)	1 (1.7%)
Weak/conditional (n=54)	2 (3.7%)	2 (3.7%)	8 (14.8%)	2 (3.7%)	0 (0%)	2 (3.7%)
Expert opinion (n=23)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	23 (100)
None (n=18)	0 (0%)	2 (11.1%)	2 (11.1%)	0 (0%)	0 (0%)	14 (77.8%)

Four CUA guidelines with a total of 154 recommendations used a combination of GRADE to rate both the strength of recommendations and a modified Oxford approach for the level of evidence. GRADE: Grading of Recommendations Assessment, Development and Evaluation.

a modified Oxford approach. Similarly, in these EAU guidelines, it was unclear how the panels arrived at certain recommendations. For most guidelines, it was

not discernible which domains (such as relationship to benefit and harms, patients' values and preferences, and resource utilization) were formally considered and how they impacted the ultimate recommendation. Notably, a large proportion of EAU recommendations were strong recommendations, which is unusual and may signal an issue as to whether GRADE was used appropriately. GRADE suggests against the use of strong recommendations in the absence of high-certainty of evidence because it implies substantial confidence in the benefits and minimal harms.

Another recent study assessed the approach used by the AUA to develop its guidelines, with special emphasis on the wording of its recommendations.²² The main finding of this study was that guideline statements of different strengths used the same wording, making it difficult to interpret the underlying intent of the panel. We did not replicate this type of analysis here, as there was major heterogeneity across CUA guidelines in how recommendations were formulated and worded.

In addition, AUA guidelines were not explicit in clarifying how patient decision-making and clinical action should differ when a recommendation is qualified as strong vs. moderate or conditional. This is in contrast to guidelines using GRADE to rate the strength of recommendations (including those of the CUA); GRADE has clearly operationalized how patients, healthcare providers, and policymakers should interpret different strengths of recommendations.⁷ For example, GRADE dictates that strong recommendations are interventions that are appropriate for most (but not all) people. Conditional/weak recommendations are those that appear appropriate for most people, but the likely net benefit may hinge on their values and preferences, making shared decision-making important.²³

Meaning of the study: Implications for clinicians and policymakers

We believe this study has important implications for the future direction of the CUA guideline effort, which plays a critical role in informing evidence-based practice in Canada, as well as other English- and French-speaking countries, since they are oftentimes pioneering in nature.

For example, the recently updated CUA guideline on renal cystic lesions that used GRADE is the first dedicated urologic guideline of its kind.¹⁸ It is also noteworthy that the CUA guideline on the diagnosis, management, and followup of incidental adrenal masses, which also used GRADE, was formally endorsed by the AUA, which further speaks to the major impact CUA guidelines can have on patient care beyond its borders.^{17,24}

A consistent and coherent approach to rating the certainty of evidence, moving from evidence to recommendations, and framing the recommendations should improve trust in the guidelines and support uptake and implementation. A more widespread use of GRADE in systematic reviews should also allow the CUA to build on existing high-quality systematic reviews and share evidence syntheses with other organizations, such as the AUA, which commits major resources on an annual basis to develop its evidence reports.^{3,25} Given many fundamental differences in healthcare delivery in the various Canadian provinces and the U.S., it is all the more important for Canada to develop its own guidelines; however, the time- and cost-intensive process of developing systematic reviews could be shared with other guideline developers across the globe. The GRADE approach is fast becoming the "lingua franca" of guideline communities and appears the natural first choice for adoption by the CUA.²⁶

As the CUA strives to adopt GRADE, it is important to recognize relevant barriers. In contrast, for example, to the AUA as a much larger organization with the resources to commission comprehensive and customized evidence reports, the CUA relies heavily on busy, practicing urologists with limited methodologic expertise who volunteer their time on behalf of the organization to perform the necessary work. Addressing these issues will require the CUA to find its own path, which may include some greater allocation of resources towards guidelines, as well as a concerted effort to train the next generation of Canada-based methodologists in systematic review and guideline methods.

Unanswered questions and future research

An important issue for the future relates to how guideline developers can better work together on a global scale by sharing scarce resources (for example, as it relates to systematic review development and periodic updates) while continuing to best serve their own communities. A logical partner for the CUA would be the AUA, with which the Canadian urological community already has ample tie-ins that may facilitate future closer collaboration as it relates to guidelines.

In addition, an area that may deserve greater emphasis in the future is CUA guideline implementation. It is well-recognized that the development and publication of a guideline is only the beginning and needs to be paired with efforts to promote awareness of these recommendations. For example, selecting strong recommendations that may be suitable for use as quality

of care and/or performance metrics may require health-care organizations and clinicians to provide documentation as to why they chose to deviate from what is widely considered evidence-based practice. One published example from the Canadian healthcare system relates to the disparate way ureteral colic patients are treated in different parts of the country, specifically the high rates of primary ureteroscopy in Calgary for small ureteral stones compared to a more guideline-concordant clinical practice in Vancouver, with high rates of observation and medical expulsive therapy.²⁷ Performance measures footed in methodologically rigorous and transparent care may not only improve the quality of care but also assure high-value care.

CONCLUSIONS

Evidence-based guidelines by the CUA are marked by considerable heterogeneity in their methods. Overall, few guidelines were fully transparent about how the panels arrived at a certain recommendation. Continued advancement in the CUA's approach to guideline development, including the adoption of GRADE, will enhance transparency and methodologic rigor, as well as facilitate greater collaboration and resource-sharing with other organizations, thereby supporting the CUA's mission of promoting high-quality, evidence-based care.

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