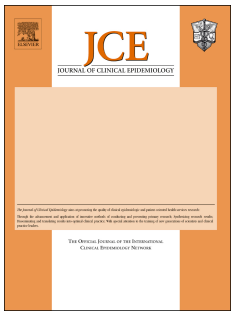

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Methodological Quality in Guidelines for Enhanced Recovery After Surgery was Suboptimal

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Abstract

Objective: We aimed to appraise the methodological quality of existing guidelines for Enhanced Recovery After Surgery (ERAS) using the Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument and to identify the concordance of different recommendations.

Study Design and Setting: PubMed, Embase, Google Scholar, Web of Science, and clinical practice guideline websites were systematically searched. Four reviewers independently assessed the guidelines using the AGREE II instrument. The mean score of each AGREE II item, number of recommendations, strength of recommendation, and level of evidence were calculated. Agreement among reviewers was assessed using the intra-class correlation coefficient (ICC).

Results: We identified 23 guidelines from 7127 records. The overall agreement among reviewers was considered good (ICC, 0.92; 95% CI, 0.86–0.96). The mean scores of the six AGREE domains were: scope and purpose, 60.1% (95% CI, 55.9–64.1); stakeholder involvement, 40.7% (95% CI, 35.4–46.0); rigor of development, 44.7% (95% CI, 42.2–47.2); clarity and presentation, 69.8% (95% CI, 65.3–74.3); applicability, 37.2% (95% CI, 31.8–42.6); and editorial independence, 47.8% (95% CI, 39.0–56.7). Only 2/23 ERAS guidelines were considered applicable without modifications.

Conclusions: The methodological quality of the ERAS management guidelines varied and was generally low. Future guideline development should adhere to the use of the AGREE II instrument and the GRADE system to better guide clinical practice and improve

individualized treatment strategies.

Keywords: AGREE II instrument; ERAS; Clinical Practice Guidelines; Methodological quality;

Running title: Evaluation of the quality of current guidelines for enhanced recovery after surgery

Word count: 3467

1. Introduction

Enhanced Recovery After Surgery (ERAS) is an evidence-based multimodal perioperative pathway focused on reducing stress and promoting early functional recovery in patients undergoing major surgery[1]. The concept of ERAS was initiated by Henrik Kehlet[2] in 1997 and has developed rapidly in the following 20 years. ERAS has expanded exponentially with further development by the ERAS Society and has influenced changes in surgical and anesthesia protocols in many disciplines[3]. Compared to traditional care, ERAS is comprehensive in scope, covering all areas of a patient's surgical process, and it offer standardized patient care based on the best evidence[4]. ERAS represents a fundamental shift in perioperative care. Previous studies have confirmed that ERAS has great potential to reduce patient recovery time, complication rates, and improve the quality of care[5-9]. Despite the increasing prevalence of ERAS, a recent survey[10] revealed significant disciplinary differences in the use of ERAS, with specific implementation varying by institution, disease type, patient, physician, and disease stage, and the problem of heterogeneity is prominent.

Clinical practice guidelines (CPGs) are systematically developed statements that include recommendations designed to optimize patient care, which help practitioners and patients make decisions about appropriate healthcare for specific clinical situations[11]. CPGs use more objective evidence and a more robust methodology in their development and are considered superior to other guidance documents, including expert consensus statements and expert opinions[12]. CPGs play an important role, not only in serving professionals and healthcare organizations to help them make decisions, but also to be accepted by patients and stakeholders. Several studies have indicated that the quality of existing guidelines can be extremely variable[13-15]. The potential benefits of a guideline can only be maximized when the quality of the guideline is sufficient. Therefore, appropriate methodologies and rigorous strategies in the guideline development process are important for successful implementation of the resulting recommendations.

The Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument[16]

is an internationally developed tool to appraise CPGs that, focuses on assessing the methodological rigor and transparency of the guideline. The AGREE II instrument has been extensively applied in many groups that have developed guidelines[17] and is considered the gold standard for the evaluation of guidelines[16, 18]. To our knowledge, a growing number of ERAS guidelines have been published in recent years and the number and scope of ERAS guidelines are increasing[19-25]. It is worth noting that the ERAS guidelines developed by different countries and academic organizations vary and mainly provide principle-based guidance. Implementation of complete ERAS guidelines for a given surgical procedure is a very challenging process[26], and postoperative benefits may be less pronounced if the guidelines are applied inconsistently[27]. In addition, the ERAS guidelines contain information that is complex and sometimes confusing. Hence, healthcare providers still have some degree of apprehension in applying ERAS.

The validity of the recommendations of various published CPGs depends on the quality of the methodology used to create them. However, the quality of ERAS evidence-based clinical guidelines has not yet been assessed using a guideline appraisal tool and not much is known about their quality. Thus, it is necessary to conduct a thorough assessment to understand the current status of the ERAS guidelines. The objective of the present study focused on the methodological analysis, aimed to evaluate the quality of currently available ERAS guidelines using the AGREE II instrument. These results may offer a new perspective on the scientifically sound use of ERAS.

What is new?

Key findings

The methodological quality of the ERAS guidelines evaluated with the Appraisal of Guidelines for Research & Evaluation (AGREE II) instrument was varied and generally low.

There are some CPGs based on higher-quality evidence that can form the framework and assist healthcare professionals to advise their practice and identifying shortfalls that should be addressed to improve future versions of CPGs.

What does this add to what was known?

This study is the first to provide oversight of the methodological quality of ERAS guidelines.

What is the implication and what should change now?

The overall methodological quality of ERAS guidelines is suboptimal. Barriers to methodological reporting should be identified to overcome the deficiencies.

2. Methods and materials

2.1 Search strategy

We searched the PubMed, Embase, Google Scholar, and Web of Science databases from inception until April 2022, to identify the potential ERAS guidelines. Additionally, to ensure comprehensive data collection, we also searched the Clinical Practice Guideline websites, including the Guidelines International Network website (GIN), National Institute for Health and Care Excellence website (NICE), National Guideline Clearinghouse (NGC), and New Zealand Guidelines Group website. The references of the retrieved articles were manually searched for further guidelines. The search terms were as follows: ("enhanced recovery after surgery" OR "Enhanced Recovery Pathway" OR "fast track surgery" OR "enhanced recovery strategy" OR ERAS OR "perioperative protocol") AND ("guideline*" OR "Practice Guideline"). The detailed search strategies for PubMed are presented in Appendix 1.

2.2 Inclusion and exclusion criteria

2.2.1 Study selection and data review extraction

Two researchers (WD and YZ) independently screened titles and abstracts for relevance, and guideline articles describing the implementation of enhanced recovery programs in any surgery setting were included. We excluded guidelines based on the following criteria: systematic reviews, editorials and letters, translation of guidelines, short summaries, guidelines for patients, and guidelines mentioning ERAS as a part. In addition, if the guidelines had more than one version, only the most recent version was assessed. Any disagreements regarding study eligibility were resolved by discussing or consulting a third review author (YL). We documented the selection process using the PRISMA flow chart.

After selecting studies based on the inclusion and exclusion criteria, two review authors (HWB and HLY) independently conducted data extraction using a self-developed form. The

following data were extracted: country of origin, publication year, development and/or revision organization, evaluation measures (guideline developing methods), focus of the guideline, and funding sources.

2.2.2 Appraisal of the quality of the guidelines

We used the AGREE II instrument to evaluate the methodological quality of ERAS guidelines[28, 29]. It includes 23 items divided into six domains: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence. Each ERAS guideline was independently assessed by four appraisers using AGREE II to guarantee appraisal reliability. Before the formal evaluation, they undertook online training (www.agreetrust.org) and conducted pre-piloting using three guidelines to ensure standardization of the assessment. The items explored in each domain are listed in Table S1. Domain scores were calculated using the following formula:

$$\frac{(Obtained\ score - Minimum\ possible\ score)}{(Maximum\ possible\ score - Minimum\ possible\ score)} \times 100\%$$

The overall quality of the guideline evaluation must consider all domain items. Based on the mean score of the six domains, guidelines with a score greater than 60% upon overall appraisal were considered as "strongly recommended" without modifications, between 30%–60% were considered as "recommended with modifications," and "not recommended" for scores less than 30%[30, 31].

2.3 Data synthesis

We calculated the overall average score for each guideline across all the six domains. Based on the AGREE II tool, the results were shown as a percentage of the maximum possible score for each domain. The consistency of evaluations of the AGREE II domain was calculated using intraclass correlation coefficients (ICCs) with 95% CI for each domain across all guidelines. The degree of agreement between 0.01 and 0.20 was deemed minor, 0.21 to 0.40 fair, 0.41 to 0.60 moderate, 0.61 to 0.80 substantial, and 0.81 to 1.00 very good. Statistical significance was set at $P < 0.05$ [32]. Categorical data were presented as frequency counts and percentages. All analyses were performed using SPSS Statistics 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp).

3. Results

3.1 Literature selection

Based on the search strategy, 7,127 studies were selected from the initial database search. Of these, 1,554 studies were excluded because of duplication; therefore, 5,573 studies were selected for further analysis. After screening the titles and abstracts, 5,520 studies were excluded. The remaining 53 articles were retrieved for full-text assessment, and 30 articles were then excluded for the following reasons: 21 were consensus reviews/statements, one was a checklist tool, one was a framework for the development of guidelines, and seven were not the latest versions. Finally, 23 guidelines were included in this study. The detailed flowchart showing the screening process is displayed in Figure 1.

3.2 Characteristics of selected guidelines

The general characteristics of the included studies are summarized in Table 1. The publication date of the included guidelines ranged from 2013 to 2022 by the following organizations: Enhanced Recovery After Surgery (ERAS) Society, International Association for Surgical Metabolism and Nutrition (IASMEN), The European Society for Clinical Nutrition and Metabolism (ESPEN), The French Society of Digestive Surgery (SFCD), The French Associations of Anesthesia and Intensive Care (SFAD), The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), The American Society of Colon and Rectal Surgeons (ASCRS), and The European Society of Thoracic Surgeons (ESTS). Of the included guidelines, most were from the following countries: American[21, 33-37] (26.1%, 6/23), Switzerland[19, 38-41] (21.7%, 5/23), Sweden[25, 42-44] (17.4%, 4/23), Canada[23, 45-47] (17.4%, 4/23), France[20, 24] (8.7%, 2/23), Norway[48] (4.3%, 1/23) and the UK[22] (4.3%, 1/23). Four[20, 24, 39, 40] of the 23 guidelines were based on expert consensus and provided experience-based recommendations. Five studies[36-38, 41, 46] were developed through a literature review and expert consensus. The others were developed through literature analysis and provided data-supported recommendations.

The included ERAS guidelines focus on different diseases/procedures and, mainly included elective colonic surgery, elective rectal/pelvic surgery, gastrectomy, liver surgery,

cesarean delivery, lung surgery, cardiac surgery, elective colorectal surgery, esophagectomy, gynecologic/oncology, vulvar and vaginal surgery, neonatal intestinal surgery, cytoreductive surgery, pancreatoduodenectomy, and bariatric surgery.

3.3 Quality assessment of guidelines with AGREE II instrument

Table 2 shows the AGREE II standardized domain scores for each ERAS guideline and the overall assessment of the included guidelines. The overall quality of the eligible guidelines was highly variable; most guidelines had average scores below 50% in 2–4 domains, whereas only one received an average of > 50% in all six domains (Fig. 2). Among all the evaluated guidelines, only 2/23 (8.7%) [33, 46] were strongly recommended by the appraisers for use without any modifications. 19/23 (82.6%) guidelines were rated as "recommended with modifications". The median score across the domains ranged from 37.2% to 69.8%. The highest domain scores were for the Clarity of Presentation (69.8%) and Score and Purpose (60.1%), while the scores of the other four domains (stakeholder involvement, rigor of development, applicability, and editorial independence) were less than 50%. The domain with the lowest score was applicability (37.2%).

The mean score for the scope and purpose domain was 60.1% (95% CI, 55.9–64.1). 19/23 (82.6%) guidelines scored >50%, with a minimum score of 40.3% and a maximum score of 73.6%. The mean score for the rigor of development domain was 44.7% (95% CI, 42.2–47.2), and no guidelines clearly described their procedures for updating guidelines. The editorial independence domain had a mean score of 47.8% (95% CI, 39.0–56.7), with one guideline scoring 8.3% and eight guidelines (34.8%) scoring > 60%. The clarity and presentation domains achieved the highest mean scores of 69.8% (95% CI, 65.3–74.3), with only one guideline scoring < 30%. Applicability and stakeholder involvement domains yielded low mean scores of 37.2% and 40.7% (95% CI, 31.8–42.6, and 35.4–46.0, respectively) (Table 3).

Table 3. Summary of appraisal of guidelines with AGREE II

Domain	Median score	Minimum score	Maximum score
Domain I: Scope & Purpose	60.1%	40.3%	73.6%

Domain II: Stakeholder Involvement	40.7%	19.4%	75.0%
Domain III: Rigor of Development	44.7%	34.9%	56.8%
Domain IV: Clarity of Presentation	69.8%	29.2%	81.9%
Domain V: Applicability	37.2%	15.6%	58.3%
Domain VI: Editorial Independence	47.8%	8.3%	81.3%

3.4 Level of evidence and strength of recommendation

Of the 23 included guidelines, the GRADE system for grading evidence was used in most (22/23, 95.7%) of the clinical practice guidelines. Only one study[46] used the Society of Thoracic Surgeons/American Association for Thoracic Surgery 2017 updated document "Classification of Recommendations and Level of Evidence," and the American College of Cardiology/American Heart Association clinical practice guidelines to grade the strength of recommendation and level of evidence. All guidelines reported the level of evidence and strength of the recommendations. The level of evidence and strength of the recommendations in the different grading systems varied substantially.

In total, 707 recommendations were extracted from the 23 included guidelines. Among 605 recommendations with the guidelines had the assigned levels of evidence, there was a significant variability regarding the levels of evidence, which accounted for approximately 70% of recommendations based on levels of moderate and low evidence (37.4% and 31.4%, respectively), 28.1% of the recommendations were based on high-quality evidence. Among the 661 recommendations with guidelines having an assigned strength of recommendations, the evidence grades were categorized into two groups: strong and weak. The proportion of strong recommendations was 74.5%, 23.4% were weak, and 2.1% were moderate (Table 4).

Table 4. Distribution of the strength of recommendation and level of evidence among ERAS guidelines

Guidelines	Number of recommendations	Strength of Recommendation, No. (%)		Level of Evidence, No. (%)			
		Strong	Weak	High	Moderate	Low	Very low
Cerantola, Y.	22	20 (90.9)	2 (9.1)	8 (36.4)	7 (31.8)	7 (31.8)	-
Gustafsson, U. O.	25	22 (88.0)	3 (12.0)	11 (44.0)	4 (16.0)	9 (36.0)	1 (4.0)
Nygren, J.	38	26 (68.4)	11 (28.9)	8 (21.2)	13 (34.2)	16 (42.1)	1 (2.6)

Alfonsi, P.	35	28 (80.0)	7 (20.0)	-	-	-	-
Mortensen, K.	30	19 (63.3)	11 (36.7)	11 (36.7)	9 (30.0)	8 (26.7)	2 (6.7)
Melloul, E.	29	20 (69.0)	9 (31.0)	5 (17.2)	17 (58.6)	7 (24.1)	-
Carmichael, J. C.	24	19 (79.2)	5 (20.8)	3 (12.5)	17 (70.8)	-	-
Wilson, R. D.	13	12 (92.3)	1 (7.7)	7 (53.8)	1 (7.7)	3 (23.1)	2 (15.4)
Caughey, A. B.	18	12 (66.7)	6 (33.3)	3 (16.7)	5 (27.8)	6 (33.3)	4 (22.2)
Batchelor, T. J. P.	45	40 (88.9)	5 (11.1)	15 (33.3)	16 (35.6)	14 (31.1)	-
Engelman, D. T.*	22	-	-	-	-	-	-
Gustafsson, U. O.	58	45 (77.6)	13 (22.4)	24 (41.4)	16 (27.6)	18 (31.0)	-
Low, D. E.	57	36 (63.2)	7 (12.3)	10 (17.5)	32 (56.1)	15 (26.3)	-
Macones, G. A.	11	7 (63.6)	4 (36.4)	1 (9.1)	3 (27.3)	6 (54.5)	1 (9.1)
Nelson, G.	26	22 (84.6)	4 (15.4)	14 (53.8)	5 (19.2)	7 (26.9)	-
Altman, A. D.	28	17 (60.7)	3 (10.7)	5 (17.9)	7 (25.0)	7 (25.0)	-
Brindle, M.	17	8 (47.1)	9 (52.9)	6 (35.3)	4 (23.5)	6 (35.3)	1 (5.9)
Hübner, M.	40	20 (50.0)	19 (47.5)	10 (25.0)	18 (45.0)	12 (30.0)	-
Hübner, M.	28	14 (50.0)	14 (50.0)	2 (7.1)	8 (28.6)	16 (57.1)	2 (7.1)
Melloul, E.	40	29 (72.5)	11 (27.5)	8 (20.0)	24 (60.0)	5 (12.5)	3 (7.5)
Berna, P.	32	31 (96.9)	1 (3.1)	-	-	-	-
Peden, C. J.	24	21 (87.5)	3 (12.5)	14 (58.3)	6 (25.0)	4 (16.7)	-
Stenberg, E.	45	35 (77.8)	10 (22.2)	5 (11.1)	14 (31.1)	24 (53.3)	2 (4.4)

*: adopted the Society of Thoracic Surgeons/American Association for Thoracic Surgery 2017 Updated document and American College of Cardiology/American Heart Association clinical practice guidelines:

Level of evidence：A (A-level evidence), B-R (B-level evidence, randomized studies), B-NR (B-level evidence, non-randomized studies), C-LD (C-level evidence, limited Data),

Strength of recommendation：I (strong)，II a (moderate), II b (weak), III: no benefit (moderate), III: harm (strong)

All other included studies used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system.

Level of evidence: High, moderate, low, very low

Strength of recommendation: Strong, weak

3.5 Consistency

Inter-rater reliability was assessed using ICCs. Overall agreement among reviewers was fairly consistent (ICC: 0.92, 95% CI: 0.86–0.96). The ICC values ranged from 0.87 to 0.97. The ICCs were highest in the "Applicability" and "Editorial independence" domain (0.97) and lowest in "Rigor of development," with all ICC values ＞0.75, which indicated that the intra-reviewer inter-rater reliability of the AGREE II domain ratings was good.

Table 5 Intra-class Correlation Coefficient (ICC) in each domain

Domains	ICC value	(95% CI)	P value
Scope and purpose	0.92	(0.86–0.97)	<0.001
Stakeholder involvement	0.95	(0.91–0.98)	<0.001
Rigor of development	0.87	(0.76–0.94)	<0.001
Clarity and presentation	0.95	(0.90–0.98)	<0.001
Applicability	0.97	(0.94–0.99)	<0.001
Editorial independence	0.97	(0.95–0.99)	<0.001

4. Discussion

4.1 Summary of findings

To the authors' knowledge, the present study is the first systematic appraisal of the current ERAS CPGs methodology, using the validated AGREE II instrument. Most of these studies were based on evidence-based literature or consensus among engagement experts. The recommendations and basis for the different guidelines, were not completely consistent. Overall, the scores across all the guidelines had great variability and the quality was mediocre. Only two guidelines were considered applicable without modification. These findings suggest that further work is required to ensure that clinical practice is guided by a robust evidence base in the ERAS field.

In the present study, the highest scores were achieved in domains 1 (scope and purpose) and 4 (clarity of presentation). This is unsurprising and in agreement with numerous previous studies on CPGs for the management of other diseases[14, 30, 49-51]. Most guidelines described special and relevant clinical questions as well as target groups, reflecting the strengths of CPGs in these fields. Another perspective is that criteria within these domains are arguably easier to fulfill and develop, which may offer an explanation.

Domains 2 (stakeholder involvement) and 5 (applicability) had the lowest scores. These two domains have consistently underperformed in the guideline assessment process[49, 51, 52]. Despite the recommendation to increase awareness and facilitate adherence of patients and public involvement in the recommended treatment strategy, most included guidelines do not consider the views of the target population and clearly explain how the various clinicians were involved in making the guidelines. In the current era of patient-centered outcomes, medical decisions must consider patient preferences and views. As key stakeholders, patient

involvement in CPG development and recommendations for healthcare management are more likely to address patient preferences, improve patient compliance, and further improve clinical outcomes[53, 54]. Even though patient biases regarding costs, expectations and cultural background may be introduced, the benefits cannot be ignored. Furthermore, meaningful patient and public involvement in guideline development is also an ethical imperative for developing trustworthy guidance[55]. It appears that bridging the gap in this domain requires adherence to the spirit of holistic and multidisciplinary care with full consideration of all stakeholders. Several educational programs should be implemented, and training and support should be provided to patient representatives as needed. Poor performance in domain 5 is of particular concern because it involves translating recommendations into clinical practice. Recommendations and their applications to clinical practice are completely different processes[49, 56, 57]. The ultimate goal of the guidelines is to be accepted and used by clinical decision makers or patients. Regardless of how good evidence-based recommendations are, they are virtually useless if they are not applied to the target population. Further analysis of the reasons for this may be because most included CPGs did not address how the recommendations can be put into practice with the advice and/or supporting tools provided. Researchers should pay greater attention to these issues in the future. Future clinical guideline practitioners and health systems should improve adherence to the recommendations, especially regarding potential organizational barriers, resource implications, and the clinical context. The resource and practice barriers of hospitals at different levels or regions should be fully considered, and Internet technology should be used for guideline promotion, publicity, and education.

Domain 3 (rigor of development) is considered one of the most critical and influential domains in evaluating guideline development because, in addition to assessing the review and update process, it also reviews the strength of the evidence on which the guideline recommendations are based[57]. It reflects potential bias and greatly affects the credibility of the guideline[51, 58, 59]. A high score in this domain indicates minimum bias and evidence-based guideline development[60]. In this study, the overall domain 3 score recorded

was low (median 43.8, mean 44.7) with only two guidelines identified as high quality, so this should be interpreted with an appropriate amount of caution. It is worth noting that the majority of guidelines in this study disregarded the process of updating recommendations in this field. More specifically, none of them described the detailed updating process of the guidelines, such as whether they were updated, the frequency and periodicity of the updates, or the update methods. As a general rule, guidelines should be reassessed for validity every 3 years[61], as new evidence might cause a considerable change in the recommendations. Procedures for updating the clinical guidelines should be clearly stated in the future. Furthermore, a lack of external review by experts may lead to low scores on the rigor of the development domain.

4.2 Level of evidence and strength of recommendations

In addition to increasing transparency and methodological rigor, ERAS guidelines should rely more on the growing body of high-quality evidence. In this study, we found that most recommendations were based on moderate- or low-quality evidence, and the distribution of the level of evidence varied significantly among different disease guidelines. To expand, the high-quality evidence in the ERAS guidelines for colonic resection patients, which may be related to the earliest implementation of the ERAS model in colorectal patients[62], it has accumulated a lot of clinical experience and research. The quality of evidence regarding bariatric surgery is relatively low. Supporting literature and data from studies evaluating the effects of ERAS pathways in patients undergoing bariatric surgery is sparse[63]. We believe that both these aspects may explain this finding. Generally, a higher quality of evidence requires additional confirmation from randomized controlled trials (RCTs) or large registries. RCTs represent the highest level of evidence in the GRADE system. However, programs attempting to deliver population-based interventions that determine the overall effect face many challenges. Surgical RCTs are notoriously difficult because each patient has a specific pathology and different surgical skills result in different outcomes. ERAS is a process management tool for creating standardized care processes, emphasizing the need of an individual patient with a specific disease needing an individualized therapy.

Thus, it prioritizes an individual over a sick population. The lack of randomized studies (due to the difficulty of design or even their futility) is the reason for this gap. Therefore, well-conducted, high-quality research is needed to improve the evidence base and translate into stronger recommendations. The use of low-quality evidence is a major barrier to guideline development, increasing the gaps between clinical practice evidence and current medical research.

Yet it is still worth noting that recommendations are based not only on the quality of evidence, but also on the balance between desirable and undesirable effects. Although some studies may not improve the quality of evidence in support of specific items, they may increase knowledge and provide a more complete understanding of the impact of specific interventions, as well as clinical protocols. In some cases, strong recommendations may come from low-quality data and vice versa. Overall, guidelines still lack consolidated evidence to provide high-quality recommendations for clinical practice. Hence, it must be based on the best scientific evidence and be developed using the most rigorous methodology. The AGREE system itself has certain weaknesses, including the AGREE checklist, which gives equal importance to all of its domains and lacks detailed information on how to perform the overall assessments. Further collaboration between AGREE and GRADE should be encouraged to develop harmonized standards for guideline development and quality appraisal.

4.3 Strengths and limitations

There are several strengths to our study. First, we performed a comprehensive search (major medical publication repositories, guideline library websites, and individual guideline development group websites) and systematically evaluated the methodological quality of the ERAS guidelines, which is of practical value to policymakers, clinicians, and researchers. Second, four trained appraisers evaluated the quality of the included guidelines, thereby increasing the reliability of the appraisals. Third, our team consisted of people from different academic backgrounds, clinical experts, statisticians, and methodologists who have extensive experience in evaluating clinical guidelines.

However, our study has some limitations. First, we included only the guidelines written in English or Chinese, so potentially relevant guidelines written in other languages may be missed, which may have been led to language bias. Second, the AGREE II instrument focused on methods of guideline development and the transparency of reporting; it does not directly measure the level of evidence base used in the development of each guideline and the impacts of recommendations on patient outcomes. Therefore, this, may lead to appraisal results not being objective. Although limited by the methodology of the reviewed sources, this study serves as an extensive compilation of recommendations for ERAS guidelines management and improvement.

5. Conclusion

The methodology of the clinical practice guidelines for ERAS evaluated using the AGREE II instrument is generally poor. There is still plenty of room for improvement in the overall integrity of guidelines, especially in stakeholder involvement and applicability domains.

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Legends:

Figure.1 Flow graph of the literature selection process

Figure.2 The reporting quality in Chinese SRs/MAs for each item of PRISMA

Table1. Characteristics of 23 available ERAS Guidelines

Guideline	Year	Country/Region	Developing organization	Targets of the guideline	Evidence based	Quality of evidence	Patient population	Number of recommendations	Version	Funding
Cerantola, Y.	2013	Switzerland	ERAS Society	Treatment management	literature review	GRADE	Radical cystectomy for bladder cancer	22	Original	Yes (No fund support)
Gustafsson, U. O.	2013	Sweden	ERAS Society, IASMEN, ESPEN	Treatment management	literature review	GRADE	Elective Colonic Surgery	25	Updated	Yes
Nygren, J.	2013	Sweden	ERAS Society, IASMEN, ESPEN	Treatment management	literature review	GRADE	elective rectal/pelvic surgery	38	Updated	Yes
Alfonsi, P.	2014	French	SFAR, SFCD	Management	Expert Panel (Delphi method)	GRADE	elective colorectal surgery	35	Original	Not reported
Mortensen, K.	2014	Norway	ERAS Society	Treatment management	literature review	GRADE	gastrectomy	30	Original	Not reported
Melloul, E.	2016	Switzerland	ERAS Society	Treatment management	literature review, expert consensus (Delphi method)	GRADE	Liver Surgery	29	Original	Not reported
Carmichael, J. C.	2017	American	ASCRS and SAGES	Treatment management	literature review	Modified GRADE	Colon and Rectal Surgery	24	Original	Yes

Wilson, R. D.	2018	Canada	ERAS Society	Treatment management (Preoperative care)	literature review	GRADE	Cesarean Delivery	13	Original	No
Caughey, A. B.	2018	American	ERAS Society	Treatment management (intraoperative care)	literature review	GRADE	Cesarean Delivery	18	Original	No
Batchelor, T. J. P.	2019	UK	ERAS Society, ESTS	Treatment management	literature review	GRADE	lung surgery	45	Original	No
Engelman, D. T.	2019	Canada	ERAS Cardiac Society	Treatment management	literature review，expert consensus	STS/AATS2017 and Updated document of “CRLE”	Cardiac Surgery	22	Original	No
Gustafsson, U. O.	2019	Sweden	ERAS Society	Treatment management	literature review	GRADE	Elective Colorectal Surgery	58	Updated	No
Low, D. E.	2019	American	ERAS Society	Treatment management	literature review	GRADE	Esophagectomy	57	Original	No
Macones, G. A.	2019	American	ERAS Society	Treatment management (postoperative care)	literature review	GRADE	Cesarean delivery	11	Original	Not reported
Nelson, G.	2019	Canada	ERAS Society	Treatment management	literature review	GRADE	gynecologic/oncology	26	Updated	Yes (No fund

										support)
Altman, A. D.	2019	Canada	ERAS Society Gynecology Chapter	Treatment management	literature review	GRADE	vulvar and vaginal surgery	28	Original	Not reported
Brindle, M.	2020	American	ERAS Society	Treatment management	literature review, A modified Delphi method	GRADE	Neonatal Intestinal Surgery	17	Original	Yes
Hübner, M.	2020a	Switzerland	ERAS Society	Treatment management (Preoperative and intraoperative)	Expert consensus (Delphi rounds)	GRADE	Cytoreductive Surgery (CRS) ±HIPEC	40	Original	Not reported
Hübner, M.	2020b	Switzerland	ERAS Society	Treatment management (Postoperative)	Expert consensus (Delphi rounds)	GRADE	Cytoreductive Surgery (CRS) ±HIPEC	28	Original	Not reported
Melloul, E.	2020	Switzerland	ERAS Society	Treatment management	literature review, Experts consensus, (Delphi method)	GRADE	Pancreatoduodenectomy	40	Updated	Not reported
Berna, P.	2021	France	SFAR, SFCTCV	Treatment management	Experts consensus	GRADE	pulmonary lobectomy	32	Original	Not reported
Peden, C. J.	2021	American	ERAS Society	Diagnosis, Treatment management (Preoperative	literature review, Delphi process	GRADE	Emergency Laparotomy	24	Original	Yes (No fund support)

				Care)						
Stenberg, E.	2022	Sweden	ERAS Society	Treatment management	literature review	GRADE	Bariatric Surgery	45	Updated	Yes

IASMEN: International Association for Surgical Metabolism and Nutrition

ESPEN: The European Society for Clinical Nutrition and Metabolism

SFCD: The French Society of Digestive Surgery (Société Franc ¸aise de Chirurgie Digestive)

SFAD: The French Associations of Anesthesia and Intensive Care (Société Franc ¸aise d'Anesthésie-Réanimation)

SAGES: The Society of American Gastrointestinal and Endoscopic Surgeons

ASCRS: The American Society of Colon and Rectal Surgeons

ESTS: The European Society of Thoracic Surgeons

HIPEC: Hyperthermic intraperitoneal chemotherapy

SFAR: The French Society of Anaesthesia and Intensive Care Medicine (Socie´te´ franc¸aise d'anesthe´sie et de re´animation)

SFCTCV: The French Society of Thoracic and Cardiovascular Surgery (Socie´te´ franc¸aise de chirurgie thoracique et cardiovasculaire)

STS/AATS 2017: The Society of Thoracic Surgeons/American Association for Thoracic Surgery 2017

CRLE: Classification of Recommendations and Level of Evidence

Table 2. AGREE II domain scores for TDM guidelines by 4 appraisers

Author	Scope and Purpose (%)	Stakeholder Involvement (%)	Rigor of Development (%)	Clarity and Presentation (%)	Applicability (%)	Editorial Independence (%)	Overall Assessment
Cerantola, Y.	55.6%	19.4%	34.9%	29.2%	27.1%	70.8%	Not recommended
Gustafsson, U. O.	51.4%	27.8%	46.4%	73.6%	51.0%	77.1%	Recommended with modifications
Nygren, J.	58.3%	36.1%	42.7%	76.4%	43.8%	75.0%	Recommended with modifications
Alfonsi, P.	73.6%	51.4%	49.0%	77.8%	50.0%	8.3%	Recommended with Modifications
Mortensen, K.	52.8%	47.2%	35.9%	70.8%	43.8%	35.4%	Recommended with Modifications
Melloul, E.	66.7%	37.5%	55.2%	72.2%	37.5%	45.8%	Recommended with Modifications
Carmichael, J. C.	70.8%	50.0%	52.1%	75.0%	15.6%	79.2%	Recommended with Modifications
Wilson, R. D.	66.7%	54.2%	47.9%	77.8%	39.6%	43.8%	Recommended with Modifications
Caughey, A. B.	61.1%	45.8%	51.6%	77.8%	57.3%	39.6%	Strongly Recommended
Batchelor, T. J. P.	43.1%	22.2%	38.5%	58.3%	22.9%	62.5%	Recommended with Modifications
Engelman, D. T.	65.3%	75.0%	56.8%	81.9%	58.3%	52.1%	Strongly Recommended
Gustafsson, U. O.	40.3%	31.9%	42.7%	70.8%	51.0%	50.0%	Recommended with Modifications
Low, D. E.	51.4%	36.1%	35.4%	68.1%	20.8%	52.1%	Recommended with Modifications
Macones, G. A.	69.4%	29.2%	44.3%	79.2%	27.1%	25.0%	Recommended with Modifications
Nelson, G.	45.8%	31.9%	43.8%	61.1%	30.2%	81.3%	Recommended with Modifications
Altman, A. D.	48.6%	38.9%	49.5%	73.6%	33.3%	31.3%	Recommended with Modifications
Brindle, M.	69.4%	59.7%	49.0%	68.1%	26.0%	35.4%	Recommended with Modifications
Hübner, M.	72.2%	40.3%	43.2%	76.4%	53.1%	20.8%	Recommended with Modifications
Hübner, M.	72.2%	40.3%	43.2%	76.4%	53.1%	20.8%	Recommended with Modifications
Melloul, E.	56.9%	37.5%	42.2%	72.2%	37.5%	14.6%	Recommended with Modifications
Berna, P.	65.3%	52.8%	37.0%	62.5%	18.8%	52.1%	Recommended with Modifications

Peden, C. J.	69.4%	45.8%	41.7%	65.3%	26.0%	62.5%	Recommended with Modifications
Stenberg, E.	55.6%	25.0%	44.3%	61.1%	32.3%	64.6%	Recommended with Modifications
Mean scores (95% CI)	60.1 (55.9–64.1)	40.7 (35.4–46.0)	44.7 (42.2–47.2)	69.8 (65.3–74.3)	37.2 (31.8–42.6)	47.8 (39.0–56.7)	-

PRISMA 2009 Flow Diagram

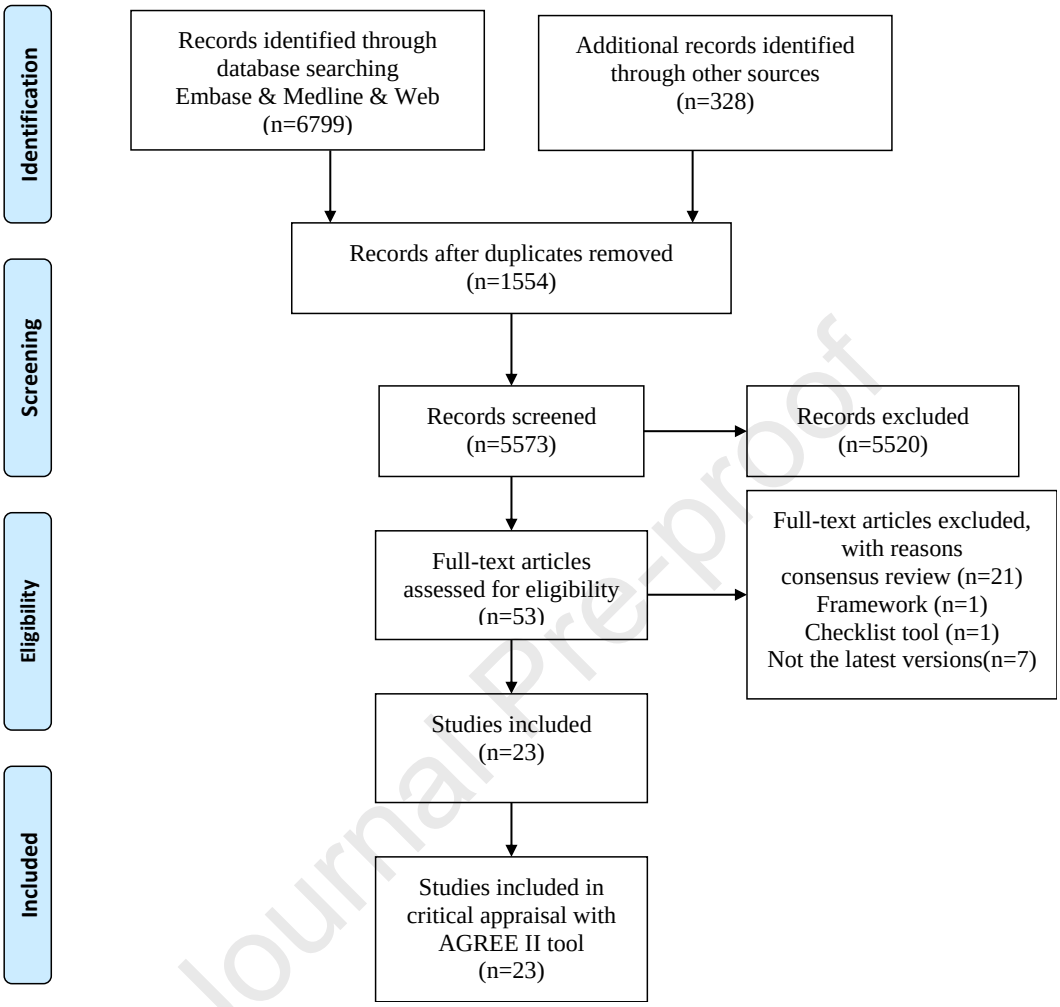

Fig.1 Flow graph of the literature selection process

Fig.2 Domains of included guidelines appraisal with AGREE II

What is new?

Key findings

- The methodological quality of the ERAS guidelines evaluated with the Appraisal of Guidelines for Research & Evaluation (AGREE II) instrument was varied and generally low.
- There are some CPGs based on higher-quality evidence that can form the framework and assist healthcare professionals to advise their practice and identifying shortfalls that should be addressed to improve future versions of CPGs.

What does this add to what was known?

- This study is the first to provide oversight of the methodological quality of ERAS guidelines.

What is the implication and what should change now?

- The overall methodological quality of ERAS guidelines is suboptimal. Barriers to methodological reporting should be identified to overcome the deficiencies.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Liujiao Cao: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Writing - Original Draft.

Liang Yao: Project development, data collection, analysis and interpretation, manuscript writing, article revised.

Wenbo He and Liangying Hou: Validation, Formal analysis, Investigation.

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