LETTER TO THE EDITOR

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The conundrum of guidelines, recommendations, and strength of recommendation

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To the Editor,

Clinicians often get perplexed by the ever-updating evidence, recommendations, and guidelines in their respective specialties and subspecialties. The United States Department of Health and Human Services Agency for Health Care Policy and Research drafted the "Statements of Evidence and Grades of Recommendations" which is shown in Tables 1 and 2 (United States Department of Health and Human Services Agency for Health Care Policy and Research 1993). Practice guidelines released by experts provide recommendations for managing a particular disease or justification for a particular intervention and treatment modality. They are either evidence-based, i.e., based on systematic reviews or meta-analysis or are consensus statements, i.e., based on expert opinion made by certain societies based on the currently available evidence (Atkins et al. 2004).

These recommendations are made after a detailed review of the advantages and disadvantages of a particular modality for a given clinical situation or an intervention. Recommendations also depend on the clinical question under evaluation and the most appropriate study suitable for finding an answer to that question. The recommendation is low if the type of study used to find the answer is not appropriate. These recommendations are usually graded based on current evidence along with rating the quality of evidence from which the information is gathered. Level of evidence is described as high (high confidence that the evidence reflects the true effect), moderate (moderate confidence that the evidence reflects the true effect), low (low confidence that the evidence reflects the true effect), insufficient, or very low (evidence either is unavailable or does not permit a conclusion) (Definition of levels of evidence (LoE) and overall strength of evidence (SoE) 2015).

The recommendations should be easy to understand, generated from unbiased, robust evidence, and practical to use and implement. Confounding factors, publication bias, and inappropriate study designs all lead to misinterpretation of pooled data, thereby leading to the formulation of practical guidelines which are not only based on low-quality evidence but also lead to the implementation of scientifically incorrect guidelines.

The grading system usually used to have several flaws like the confusion between the strength of recommendations and quality of evidence leading to misinterpretation, lack of transparent judgments, and difficulty to implement on occasions. To overcome these issues and to have a comprehensive, unbiased evidence-based recommendation, GRADE (Grading of Recommendations, Assessment, Development and Evaluations) system was introduced. GRADE system is used to derive recommendations for systematic reviews and guidelines. GRADE differs from other tools because it separates the quality of evidence and strength of recommendation, quality of evidence is assessed for each outcome, observational studies can be upgraded if they meet certain criteria, and language used is simple and not confusing to clinicians implementing guidelines (Goldet and Howick 2013).

The GRADE approach rates the quality of evidence by analyzing the study design, i.e., randomized trials, case-control studies, cohort studies, and observational studies. Based on the study design, GRADE either rates down the quality of evidence (by analyzing 5 reasons: limitations in study design, inconsistent results, indirect evidence, imprecision, and publication bias) or rates up the quality of evidence (by analyzing 3 reasons: large magnitude of effect, dose-response gradient, and less confounding factors (Zhang et al. 2018).

Four factors determine the direction and strength of recommendation. They are balance between desirable and undesirable outcomes, confidence in values

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Table 1 Showing statements of evidence

Statements of evidence	
Ia	Evidence obtained from meta-analysis of RCTs
Ib	Evidence obtained from at least 1 RCT
IIa	Evidence obtained from at least 1 well-designed controlled study without randomization
IIb	Evidence obtained from at least 1 other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case reports
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

and preferences, quality of evidence, and costs of the intervention. GRADE describes two categories of the strength of a recommendation: strong and weak. The strength of a recommendation implies the extent to which a guideline is confident about the desirable effects of an intervention or treatment outweighing undesirable effects. GRADE ranking of recommendation is shown in Table 3.

GRADE system is used by many societies to draft guidelines and recommendations; the recent one is that of Missair et al.'s "Impact of perioperative pain management on cancer recurrence: an ASRA/ESRA (American Society of Regional Anesthesia/European Society of Regional Anesthesia) special article" in *Regional Anesthesia and Pain Medicine Journal* (Missair et al. 2019).

To conclude, clinicians should know and understand the methodology used for drafting guidelines and recommendations. GRADE system is used by many researchers and guideline makers which describe the quality and strength of recommendation. The ease of using the GRADE system and the simple language used in describing the details are possibly the reasons why the system is preferred.

Table 2 Showing statement of evidence and grade of recommendations

Grades of recommendations	
A	Requires at least 1 prospective RCT as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence levels Ia and Ib)
B	Requires the availability of well conducted clinical studies, but no prospective, randomized clinical trials on the topic of recommendation (evidence levels IIa, IIb, III)
C	Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (evidence level IV)

Table 3 Showing GRADE ranking

Recommendation	What it implies?
High	Confident that the effect in the study reflects the actual effect.
Moderate	Quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	True effect may differ significantly from the estimate.
Very low	True effect is likely to be substantially different from the estimated effect.

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