

© 2016 EDIZIONI MINERVA MEDICA

The online version of this article is located at <http://www.minervamedica.it>

Minerva Anestesiologica 2016 February;82 (2):230-5

## EXPERT OPINION

# A critical appraisal of the quality of analgosedation guidelines in critically ill patients

Massimo GIRARDIS <sup>1\*</sup>, Cosetta CANTARONI <sup>1</sup>, Gennaro SAVOIA <sup>2</sup>  
Rita MELOTTI <sup>3</sup>, Giorgio CONTI <sup>4</sup>

<sup>1</sup>Anesthesia and Intensive Care Department, University of Modena and Reggio Emilia, Modena, Italy; <sup>2</sup>Anesthesia Intensive Care Department, Hospital Cardarelli, Naples, Italy; <sup>3</sup>Anesthesia and Intensive Care Department, University of Bologna, Bologna, Italy; <sup>4</sup>Anesthesia and Intensive Care Department, Catholic University of Rome, Rome, Italy

\*Corresponding author: Massimo Girardis, Azienda Ospedaliera Universitaria di Modena, L. go del Pozzo, 71, 41100 Modena, Italy. E-mail: [girardis.massimo@unimo.it](mailto:girardis.massimo@unimo.it)

## ABSTRACT

**BACKGROUND:** The management of analgesia and sedation in critically ill patients is still a challenge due to the shortage of evidence-based treatments. The main objectives of the present study were to critically evaluate the quality of current clinical practice guidelines (CPGL) published on this matter and to identify the contrasting positions and unsolved questions.

**METHODS:** Four members of the Italian Society of Anesthesia and Intensive Care (SIAARTI) council, with an extensive background in the management of critically ill patients and practice guidelines, evaluated CPGL on sedation and analgesia in critically ill patients published from January 2006 to December 2013. Evaluation was performed in accordance with the appraisal of guidelines for research and evaluation tool (AGREE II).

**RESULTS:** Five documents proposed by European and American scientific societies of critical care medicine were identified and evaluated. The CPGL published in 2013 by the American Society of Critical Care Medicine showed the highest scores in all domains of the AGREE II tool, whereas scores for CPGL published in 2006 by SIAARTI showed the lowest scores. In all documents, most recommendations on the use of drugs or non-pharmacological strategies for analgesia, sedation and delirium treatment had low evidence.

**CONCLUSIONS:** This quality evaluation indicated that CPGLs published by the German Association of Scientific Medical Societies, the American College of Critical Care Medicine and the PanAmerican and Iberica Federation of the Critical Care Medicine Societies should be recommended for use. Even in guidelines with a high quality rating, numerous recommendations have moderate or low levels of evidence.

*(Cite this article as: Girardis M, Cantaroni C, Savoia G, Melotti R, Conti G. A critical appraisal of the quality of analgosedation guidelines in critically ill patients. Minerva Anestesiologica 2016;82:230-5)*

**Key words:** Analgesia - Delirium - Intensive Care Units - Guidelines as Topic.

The management of pain, agitation and delirium (PAD) is still a challenge in critically ill patients. Clinical studies have demonstrated that a protocolized and evidence based approach to PAD is cost-effective and can significantly improve patient outcomes.<sup>1</sup> Nevertheless, factors related to pre-existing patients' conditions, type and degree of organ dysfunc-

tion and intensive care unit (ICU) organization processes often make this approach difficult to adopt. In recent years, many tools for bedside assessment of pain, sedation and delirium have been proposed, and their systematic application in clinical practice seems to offer a relevant benefit.<sup>2-4</sup> By contrast, few high level clinical trials have evaluated the efficacy of pharmacological and non-pharmacological strategies for PAD treatment. For instance, although current-

Comment in p. 157.

ly recommended by recent guidelines,<sup>1, 5</sup> the use of quetiapine and of re-orientation strategies for the prevention and management of delirium is based on low-quality studies.<sup>6</sup>

Due to these aforementioned considerations, the use of clinical practice guidelines (CPGL) based on the best available evidence is essential for supporting the decision-making process in PAD management. In the last decade, numerous CPGL documents on this issue have been published worldwide by several scientific societies of critical care medicine. As for other publications, a CPGL ought to be critically appraised prior to endorsing its use, because poor quality guidelines may contribute to inappropriate recommendations and low adherence.<sup>7-9</sup> The appraisal of guidelines, research and evaluation (AGREE) tool has been developed and validated as a useful instrument to assess the methodological rigour and transparency with which a guideline has been developed.<sup>10, 11</sup> The aim of our study, supported by the Italian Society of Anaesthesia and Intensive Care Medicine (SIAARTI), was to assess the quality of the published guidelines on PAD management using the AGREE II tool.

### Materials and methods

Four members of the SIAARTI council, with an extensive background in the management of critically ill patients and CPGL methodology, were involved in the quality assessment. CPGL documents were selected by searching the Medline (PubMed), Scopus and Intercollegiate Studies Institute Web of Knowledge databases from 2006 to 2013. Relevant databases of guidelines including the National Guideline Clearing House, National Institute for Healthcare Excellence, Scottish Intercollegiate Guidelines Network and the National Guideline System were also searched. We restricted our search to the adult population.

For the quality assessment of CPGL, the appraisal of guidelines, research and evaluation (AGREE) tool has been developed and validated.<sup>10</sup> AGREE II evaluation includes 23 items subdivided within 6 domains: scope and purpose, stakeholder involvement, rigor

of development, clarity and presentation, applicability and editorial independence. Each of the AGREE II items are rated on a 7-point scale (1–strongly disagree; 7–strongly agree). Domain scores are calculated by adding together all the scores of the individual items in a domain, and by scaling the total as a percentage of the maximum possible score for that domain.<sup>10</sup> In addition, the AGREE II tool also includes an overall assessment of the guideline and whether it should be strongly recommended, recommended with provisos, or not recommended.

Assessments were performed independently by the four members using a specific electronic database with accompanying explanatory notes. To determine whether errors may have occurred during item scoring, one investigator (GM) examined all final item scores across the 4 appraisals. Discrepancies were defined as inter-rater score differences of three points on any domain item. All appraisers were then asked to perform another AGREE II assessment on the discordant item in question. For each selected CPGL, the median scores for the various domains were calculated and compared among the CPGLs using the Kruskal-Wallis Test. Analysis was performed using SPSS version 20 (SPSS Inc., Chicago, IL, USA) and  $P < 0.05$  was considered statistically significant.

### Results

#### *Clinical practice guideline selection and characteristics*

The databases analysis provided 5 CPGL on PAD management in critically ill adult patients published from January 2006 to December 2013. Throughout the years, the methodologies for developing CPGL have changed from the Delphi method to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) method.<sup>12, 13</sup> The topics included were quite similar, except for delirium identification and management that were discussed extensively only in the more recent CPGLs. Specific indications for particular populations (e.g. elderly, trauma and burns) were



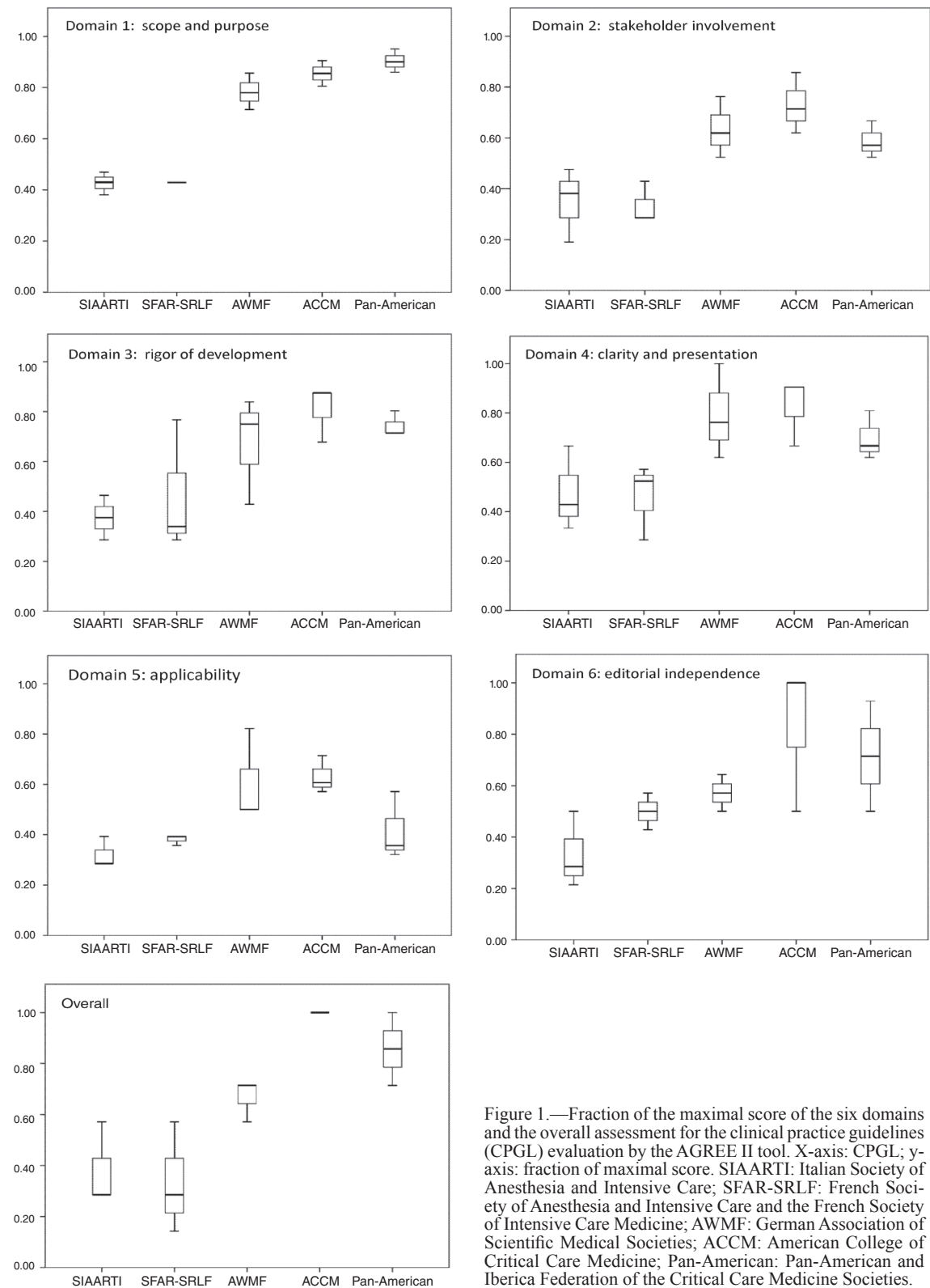


Figure 1.—Fraction of the maximal score of the six domains and the overall assessment for the clinical practice guidelines (CPGL) evaluation by the AGREE II tool. X-axis: CPGL; y-axis: fraction of maximal score. SIAARTI: Italian Society of Anesthesia and Intensive Care; SFAR-SRLF: French Society of Anesthesia and Intensive Care and the French Society of Intensive Care Medicine; AWMF: German Association of Scientific Medical Societies; ACCM: American College of Critical Care Medicine; Pan-American: Pan-American and Iberica Federation of the Critical Care Medicine Societies.

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The production of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

of Critical Care Medicine and the Pan-American and Iberica Federation of the Critical Care Medicine Societies revealed high overall assessment scores and, thereby, are recommended for use.<sup>1, 5, 14</sup> To our knowledge, this is the first systematic evaluation of the quality of CPGLs for the management of PAD.

The highly scored CPGLs adequately coped with the majority of domains included in the AGREE II tool. Indeed, applicability and stakeholder involvement were the domains that performed most poorly. Compliance in clinical practice to the recommendations of a CPGL is still difficult and the reasons are wide-ranging. Among these, difficulty in CPGL dissemination and implementation play a pivotal role. Therefore, a CPGL should include a clear description of facilitators and barriers to its application, tools on how recommendations can be put into practice, and the potential resource implications. Unfortunately, as reported in other CPGL quality evaluations,<sup>7, 17</sup> these items were not or only partially included in the CPGLs on PAD management.

The scarce involvement of stakeholders in the development of a CPGL may further hinder its implementation in clinical practice. In the AGREE II tool, the domain on the stakeholders' involvement explores whether the CPGL represents the views of its intended users. Involving stakeholders is recognized as an important part of producing credible, rigorous, and transparent CPGLs.<sup>18</sup> A review of the NICE guideline program by the World Health Organization stated that "collaboration with stakeholders in the development of the guidelines through the consultation and feedback mechanisms available was in general very effective".<sup>19</sup>

It is important to note that the AGREE II tool has been developed to assess the methodological quality of a guideline, but it does not evaluate the clinical content and the quality of the evidence supporting the recommendations.<sup>11</sup> In fact, our CPGLs appraisal outlined common criticisms related to the low level of evidence for the majority of the strong recommendations, particularly on analgesia and delirium management.<sup>1, 5, 14</sup> For instance, in

contrast with the others, the CPGL by the Pan-American and the Iberica Federation of the Critical Care Medicine Societies strongly recommend the use of low dose remifentanyl continuous infusion for analgesia and sedation in patients undergoing weaning from mechanical ventilation despite the low level of evidence.<sup>5</sup> Moreover, although the evidence from literature was the same, the recommendations for the use of antipsychotic drugs in the management of delirium are clearly different between the CPGLs by the ACCM and the Pan-American and Iberica Federation of the Critical Care Medicine Societies.<sup>1, 5</sup> The shortage of high level studies for many of the items included in the CPGLs poses questions on the reliability of these recommendations, and their effects remain uncertain and may vary in different patients, contexts and organizations.

## Conclusions

Our quality evaluation provides useful indications for the appropriate use of available CPGLs on PAD management. Considering the possible legal implications of guidelines produced by national professional bodies and accepted as "the standard to be achieved", old and low-quality level documents should be discarded in favor of the more recent and high-quality level ones. Unfortunately, the adoption of CPGLs developed in different regions may be difficult due to possible differences in availability of resources and in clinical behavior. Therefore, an urgent revision and updating of the SIAARTI and SFAR-SRLF documents<sup>15, 16</sup> is highly recommended. Moreover, our study advises different CPGL developers to integrate the GRADE approach, used for grading the quality of evidence and strength of recommendations, with the suggestions by the AGREE II Collaboration when preparing future guidelines on PAD, with particular focus on stakeholder involvement and methods for its implementation in clinical practice. Last but not least, as for many other issues in critically ill patients, there is an urgent need for large and appropriate clinical studies on analgo-sedation and delirium treatment.

### Key messages

— A protocolized and evidence based approach to pain, analgesia and delirium management is cost-effective and can significantly improve the patient outcomes.

— The use of clinical practice guidelines is essential for supporting the decision-making process, and numerous documents on pain, analgesia and delirium management have been published in the last decade.

— The recent guidelines by the German Association of Scientific Medical Societies, the American College of Critical Care Medicine and the Pan-American and Iberica Federation of the Critical Care Medicine Societies are recommended for use.

— The shortage of high level studies poses some questions on the true effects of guideline recommendations on pain, analgesia and delirium management. High quality clinical trials on this issue are urgently needed.

### References

- Barr J, Fraser GL, Puntillo K, Ely EW, Gélinas C, Dasta JF, *et al.* American College of Critical Care Medicine: Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* 2013; 41:263-306.
- Chanques G, Jaber S, Barbotte E, Violet S, Sebbane M, Perrigault PF, *et al.* Impact of systematic evaluation of pain and agitation in an intensive care unit. *Crit Care Med* 2006; 34:1691-9.
- Payen JF, Bosson JL, Chanques G, Mantz J, Labarere J, DOLOREA Investigators. Pain assessment is associated with decreased duration of mechanical ventilation in the intensive care unit: a post Hoc analysis of the DOLOREA study. *Anesthesiology* 2009; 111:1308-16.
- Devlin JW, Fong JJ, Fraser GL, Riker RR. Delirium assessment in the critically ill. *Intensive Care Med* 2007; 33:929-40.
- Celis-Rodríguez E, Birchenall C, de la Cal MÁ, Castorena Arellano G, Hernández A, Ceraso D, *et al.* Clinical practice guidelines for evidence-based management of sedoan-

algnesia in critically ill adult patients. *Med Intensiva* 2013; 37:519-74.

- Reade MC, Finfer S. Sedation and delirium in the intensive care unit. *N Engl J Med* 2014;370:444-54.
- Sinuff T, Patel RV, Adhikari NK, Meade MO, Schünemann HJ, Cook DJ. Quality of professional society guidelines and consensus conference statements in critical care. *Crit Care Med* 2008;36:1049-58.
- Eldh AC, Vogel G, Söderberg A, Blomqvist H, Wengström Y. Use of evidence in clinical guidelines and everyday practice for mechanical ventilation in Swedish intensive care units. *Worldviews Evid Based Nurs* 2013;10:198-207.
- Pun BT, Balas MC, Davidson J. Implementing the 2013 PAD guidelines: top ten points to consider. *Semin Respir Crit Care Med* 2013;34:223-35.
- Brouwers MC, Kho ME, Brouman GP, Burgers JS, Cluzeau F, Feder G, *et al.* AGREE II: advancing guideline development, reporting, and evaluation in health care. *Prev Med* 2010;51:421-4.
- AGREE Collaboration. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. *Qual Saf Health Care* 2003;12:18-23.
- Schünemann HJ, Jaeschke R, Cook DJ, Bria WF, El-Solh AA, Ernst A, *et al.* An official ATS statement: grading the quality of evidence and strength of recommendations in ATS guidelines and recommendations. *Am J Respir Crit Care Med* 2006;174:605-14.
- Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, *et al.* Grading strength of recommendations and quality of evidence in clinical guidelines: report from an american college of chest physicians task force. *Chest* 2006;129:174-81.
- Martin J, Heymann A, Bäseler K, Baron R, Biniek R, Bürkle H, *et al.* Evidence and consensus-based German guidelines for the management of analgesia, sedation and delirium in intensive care--short version. *Ger Med Sci* 2010;8: Doc02.
- Mattia C, Savoia G, Paoletti F, Piazza O, Albanese D, Amantea B, *et al.* SIAARTI recommendations for analgo-sedation in intensive care unit. *Minerva Anestesiologica* 2006;72:769-805.
- Sauder P, Andreoletti M, Cambonie G, Capellier G, Feissel M, Gall O, Goldran-Toledano D, *et al.* Sedation and analgesia in intensive care (with the exception of newborn babies). French Society of Anesthesia and Resuscitation. French speaking Resuscitation Society. *Ann Fr Anesth Reanim* 2008;27:541-51.
- Gorman SK, Chung MH, Slavik RS, Zed PJ, Wilbur K, Dhingra VK. A critical appraisal of the quality of critical care pharmacotherapy clinical practice guidelines and their strength of recommendations. *Intensive Care Med* 2010;36:1636-43.
- Kastner M, Bhattacharyya O, Hayden L, Makarski J, Estey E, Durocher L, *et al.* Guideline uptake is influenced by six implementability domains for creating and communicating guidelines: a realist review. *J Clin Epidemiol* 2015;10: S0895-4356.
- National Institute for Health and Clinical Excellence The guideline development process: an overview for stakeholders, the public and the NHS. Third edition; 2007.

*Conflicts of interest.*—G. Conti received honoraria for consulting and lecturing from GSK and Orion Pharma. The Catholic University received research grants from Orion Pharma.

Article first publication online: October 16, 2015. - Manuscript accepted: October 14, 2015. - Manuscript revised: September 9, 2015. - Manuscript received on May 5, 2015.