

Health Policy Review

A Critical Appraisal of 2007 American College of Occupational and Environmental Medicine (ACOEM) Practice Guidelines for Interventional Pain Management: An Independent Review Utilizing AGREE, AMA, IOM, and Other Criteria

Laxmaiah Manchikanti, MD¹, Vijay Singh, MD², Standiford Helm II, MD³,
Andrea M. Trescot, MD⁴, and Joshua A. Hirsch, MD⁵

From: ¹Pain Management Center of Paducah, Paducah, KY; ²Pain Diagnostics Associates, Niagara, WI; ³Pacific Coast Pain Management Center, Laguna Hills, CA; ⁴University of Florida, Gainesville, FL; and ⁵Massachusetts General Hospital, Harvard Medical School, Boston, MA

Dr. Manchikanti is Medical Director of the Pain Management Center of Paducah, Paducah, KY, and Associate Clinical Professor of Anesthesiology and Perioperative Medicine University of Louisville, KY
Dr. Singh, is Medical Director, Pain Diagnostic Associates, Niagara, WI
Dr. Helm is Medical Director, Pacific Coast Pain Management Center, Laguna Hills, CA
Dr. Trescot is the Director of the Pain Program at the University of Florida and the Malcolm Randall VA Medical Center, Gainesville, FL
Dr. Hirsch is the Chief of Minimally Invasive Spine Surgery at the Massachusetts General Hospital where he has appointments in the Departments of Radiology and Neurosurgery and is an Assistant Professor of Radiology at Harvard Medical School, Boston, MA.

Address correspondence:
Laxmaiah Manchikanti, MD
2831 Lone Oak Road
Paducah, Kentucky 42003
E-mail: drlm@thepainmd.com

Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of Interest: None.

Manuscript Received: 04/11/2008
Accepted For
Publication: 05/01/2008

Free full manuscript:
www.painphysicianjournal.com

Background: Today, with the growing interest of the medical community and others in practice guidelines, there is greater emphasis on formal procedures and methods for arriving at a widely scrutinized and endorsed consensus than ever before. Conflicts in terminology and technique are notable for the confusion that guidelines create and for what they reflect about differences in values, experiences, and interests among different parties. While public and private development activities continue to multiply, the means for coordinating these efforts to resolve inconsistencies, fill in gaps, track applications and results, and assess the soundness of particular guidelines continue to be limited.

In this era of widespread guideline development by private organizations, the American College of Occupational and Environment Medicine (ACOEM) has developed guidelines that evaluate areas of clinical practice well beyond the scope of occupational medicine and yet fail to properly involve physicians expert in these, especially those in the field of interventional pain management. As the field of guidelines suffers from imperfect and incomplete scientific knowledge as well as imperfect and uneven means of applying that knowledge without a single or correct way to develop guidelines, ACOEM guidelines have been alleged to hinder patient care, reduce access to interventional pain management procedures, and transfer patients into a system of disability, Medicare, and Medicaid.

Objective: To critically appraise occupational medicine practice guidelines for interventional pain management by an independent review utilizing the Appraisal of Guidelines for Research and Evaluation (AGREE), American Medical Association (AMA), Institute of Medicine (IOM), and other commonly utilized criteria.

Methods: Revised chapters of ACOEM guidelines, low back pain and chronic pain, developed in 2007 and 2008 are evaluated, utilizing AGREE, AMA, IOM instruments, and Shaneyfelt et al's criteria, were independently reviewed by 4 appraisers.

Results: Critical appraisal utilizing the AGREE instrument found that both chapters scored less than 10% in 3 of the 6 domains, less than 20% in one domain, over 30% in one domain, and over 70% in one domain. Global assessment also scored below 30% with a recommendation from AGREE, "not recommended or suitable for use in practice."

Based on AMA key attributes, both chapters of ACOEM guidelines met only one of the 6 key attributes, only 3 of the 8 attributes were met by IOM criteria, and based on the criteria described by Shaneyfelt et al, overall only 28% of criteria were met.

Conclusion: Both the low back pain and chronic pain chapters of the ACOEM guidelines may not be ideal for clinical use based on the assessment by the AGREE instrument, AMA attributes, and criteria established by Shaneyfelt et al. They also scored low on IOM criteria (37.5%). These guidelines may not be applicable for clinical use.

Key words: Evidence-based medicine, systematic reviews, guideline development, AHCP, AHRQ, IOM, AMA, AGREE, workers' compensation, guidelines, ACOEM, ASIPP, interventional pain management, interventional techniques, chronic pain guidelines, low back pain guidelines

Pain Physician 2008; 11:3:291-310

Field and Lohr (1) provided the medical community of the United States with a treatise of directions for the preparation of clinical practice guidelines. *Clinical Practice Guidelines: Directions for a New Program*, published by the National Academy of Sciences, was based on a congressional mandate of November 1989, with the creation of the Agency for Health Care Policy and Research (AHCPR-Public Law 101-239), under the broad responsibility for supporting research, data development, and other activities that will "enhance the quality, appropriateness, and effectiveness of healthcare services . . ." and AHCPR's request for advice from the Institute of Medicine (IOM) on how it might approach practice guidelines (1). This comprehensive report (1) encourages standardization and consistency in guidelines development, whether such development is undertaken independently by medical societies, other organizations, or governmental agencies.

Practice guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances. Thus, based on this broad definition, guidelines for clinical practice are not new. The processes of organized clinical education requires various sorts of guidelines, as do the processes of professional licensure, board certification, quality assurance, utilization review, and other aspects of health services administration (1). However, the interest of the medical community and others in practice guidelines has grown exponentially in recent years. Further, today there is a growing emphasis on formal procedures and methods for arriving at a widely scrutinized and endorsed consensus.

The guideline development efforts of private organizations are widespread. Among the medical groups involved with the development of guidelines are the American Academy of Family Physicians, American College of Cardiology, American College of Physicians, American Society of Anesthesiologists, American College of Surgeons, American Society of Interventional Pain Physicians (ASIPP), and many other clinically oriented organizations. These organizations commonly provide guidelines related to expertise demonstrated by the members of the organization, that is, guidelines within the scope of expertise of that specific society. However, the American College of Occupational and Environment Medicine (ACOEM) has developed guidelines that evaluate areas of clinical practice well beyond the scope of occupational medicine and yet

fail to properly involve physicians expert in these, especially those in the field of interventional pain management (2-12).

Field and Lohr (1) concluded that conflicts in terminology and technique characterized the field of guidelines. They are notable for the confusion they create and for what they reflect about differences in values, experiences, and interests among different parties. While public and private development activities continue to multiply, the means for coordinating these efforts to resolve inconsistencies, fill in gaps, track applications and results, and assess the soundness of particular guidelines continues to be limited. The Clinical Practice Guidelines Committee concluded that more and disproportionate attention is paid to developing guidelines than to implementing or evaluating them, a finding which continues to be true as of today. The manual on clinical practice guidelines (1) provided clear, definitions consistent with customary, professional, and legislative usage and acceptable to important interests.

At present there is significant diversity in clinical practice guidelines. While practice variation based on scientific uncertainty or difference in values may be acceptable, both science and values are open to change. However, adherence to unacceptable standards and unwillingness to change based on conflicts of interests is unwarranted. Inconsistency among guidelines can also arise from variations in values, tolerance for risks, preferences, and expertise. Consequently, professionals may simply differ in how they perceive different health outcomes and how they judge when benefits outweigh harms enough to make a service worth providing. Further, inconsistencies may arise from biased or inept development processes (1). While some may result from reasonable differences in the interpretation of scientific evidence or in the application of patient, practitioner, or social values, other inconsistencies may essentially disappear when rationales for specific recommendations are closely examined.

The field of guidelines development is a complex and confusing arena with high expectations, competing organizations, conflicting philosophies, and ill-defined or incompatible objectives (1,13-27). Further, the field of guidelines suffers from imperfect and incomplete scientific knowledge as well as imperfect and uneven means of applying that knowledge. Generally, despite the good intentions of many involved organizations and parties, guideline development continues to lack clearly articulated goals, coherent

structures, and credible mechanisms for evaluating, improving, and coordinating guidelines development to meet social needs for good quality, affordable health care. Thus, there is no single or correct way to develop guidelines, but there is significant guidance to develop guidelines to possess validity, reliability/reproducibility, clinical applicability, clinical flexibility, clarity, multidisciplinary process, and provide scheduled review and documentation. Consequently, all types of conflict must be avoided at all levels of the process including development, implementation, and interpretation.

Guidance for the critical appraisal of evidence has been provided by multiple authors (14,28-30). West et al (14) reviewed different instruments for critical appraisal of systematic reviews and found 20 systems concerned with the appraisal of systematic reviews or meta-analysis. Oxman et al (28-30) also provided guidance for critical appraisal of the evidence. The American Medical Association (AMA), the Institute of Medicine (IOM), Canadian Medical Association (CMA), and Agency for Healthcare Research and Quality (AHRQ) have all formulated methodology for developing scientifically sound guidelines. Standardized approaches have also been developed to evaluate the development and validity of guidelines (24,25,31-41). In fact, the results of evaluation of various guidelines have been less than optimal.

ACOEM first published its guidelines regarding common health complaints of workers in 1997 (2), followed by a second edition in 2004 (8), with updates to the second edition in 2007 to the chapter on low back disorders (3) and an update of the chronic pain chapter not yet published (4). These guidelines (2-4,8) have been alleged to prevent injured workers from receiving the majority of the medically necessary and appropriate interventional pain management services (5-7,10,26,27). Cates et al (26) utilizing Appraisal of Guidelines for Research and Evaluation (AGREE) evaluation concluded that ACOEM guidelines scored low in stakeholder involvement, rigor of development, application, and editorial Independence. Staal et al (41) using the AGREE instrument, reviewed the first edition of ACOEM guidelines and identified similar problems. Harris (42) described the development, use, and evaluation of clinical practice guidelines, the recommendations of which were not documented in the second edition of ACOEM guidelines (2).

Helm (27) evaluated *Occupational Medicine Practice Guidelines* utilizing Shaneyfelt et al's criteria (31). He concluded that ACOEM complied with only 12 out of 25 criteria.

The Institute for Civil Justice and Research and Development (RAND) Health (40) also evaluated ACOEM guidelines and concluded that the evidence base for treatment recommendations for non-surgical conditions were of uncertain validity and comprehensiveness (43). Even then, the ACOEM guidelines were implemented in California on an interim basis in March 2004. Since that time, RAND reports that payors appear to be interpreting and applying the ACOEM guidelines inconsistently, suggesting that this allows cost savings, not quality of care, to be the primary results of its adoption (43).

Thus, it is clear that the guidelines developed by ACOEM have been adopted by several compensation systems as a standard for evaluation and management of work injuries. Consequently, these guidelines impact the manner in which patient care is assessed by peer review and often serve as a basis for payor decision-making regarding the delivery of interventional pain management care along with other care to patients. In California, the ACOEM guidelines are legislatively mandated as "presumptively correct" for evaluation and management of all musculoskeletal injuries in the workers' compensation system (26).

In addition to the criteria described by the AGREE instrument (35), Shaneyfelt et al (31), National Health and Medical Research Council (NHMRC) (44), World Health Organization (WHO) (45), IOM (46), AMA (47), CMA (48), and AHCPR (49) have all carefully formulated the methodology for developing scientifically sound guidelines and rating of the strength of evidence.

A critical appraisal of the 2007 ACOEM guidelines and revisions to the chapters, on low back pain and chronic pain, was undertaken to evaluate the guidelines based on the AGREE instrument (35,39), AMA's key attributes of guidelines (47), IOM's key attributes of guidelines (1), and criteria utilized by Shaneyfelt et al (31).

METHODS

The revised chapters of ACOEM guidelines, i.e., low back pain and chronic pain, developed in 2007 and 2008 (3,4) are evaluated utilizing the AGREE (35,39), AMA (47), and IOM (1) instruments, as well as Shaneyfelt et al's criteria (31).

Study Instruments

- I. The Appraisal of Guidelines for Research and Evaluation (AGREE) guideline evaluation instrument has been assessed as reliable and valid for the purpose of guideline evaluation (24,35,39,40). The AGREE instrument is a generic tool developed by the AGREE Collaboration in 1998. The AGREE instrument has been subjected to extensive evaluation. AGREE evaluation assesses each guideline in 6 domains namely, domain 1 – scope and purpose, domain 2 – stakeholder involvement, domain 3 – rigor of development, domain 4 – clarity and presentation, domain 5 – application, and domain 6 – editorial independence.
- II. Key attributes were described by AMA's Office of Quality Assurance to guide development and evaluation of practice parameters (47). Key attributes include 1) development by a physician organization, 2) utilization of reliable methods that integrate relevant research findings, 3) appropriate clinical expertise, 4) guidelines must be as comprehensive and specific as possible, 5) should provide current information, and 6) should be widely disseminated.
- III. The Institute of Medicine (IOM) (1) has described key attributes of guidelines, these include: 1) validity, 2) reliability/reproducibility, 3) clinical applicability, 4) clinical flexibility, 5) clarity, 6) multidisciplinary process, 7) scheduled review, and 8) documentation.
- IV. Shaneyfelt et al (31) developed an instrument to assess the methodological quality of clinical practice guidelines in the peer-reviewed medical literature. The instrument was developed using the principles formulated by the major medical organizations, a group of experts in guidelines and evidence-based medicine. Based on the careful, comprehensive, and inclusive development process used they felt that the developed criteria were a valid representation of current standards for guidelines. They developed a 25-item instrument, using a yes or no format, to measure adherence to these elements, broadly grouped into standards on guideline format and development (10 items), identification and summary of evidence (10 items), and formulation of recommendations (5 items).

Table 1 illustrates essential components and key attributes to guideline development derived from multiple evaluation instruments used for this study.

Quality Criteria Assessment

Both chapters of ACOEM guidelines were reviewed independently by 4 appraisers using the AGREE instrument (35,39), AMA key attributes (47), IOM key attributes (1), and criteria described by Shaneyfelt et al (31).

The AGREE instrument and its training manual (35,39) provided instructions on proper evaluation of guidelines. The AGREE instrument instructions recommend that guidelines be assessed by at least 2 appraisers and preferably 4 as this will increase the reliability of the assessment (35,39). All 4 reviewers were familiarized with the instrument, its procedures and criteria. Both of the chapters here assessed individually across 6 domains. For the individual domains, each item of each domain was graded on a 4-point Likert scale which ranged from 4 —“strongly agree” to 1—“strongly disagree” with 2 mid points: 3 —“agree” and 2 – “disagree.” As per the guidelines, the scale measured the extent to which the assessor was convinced that a criterion (item) had been fulfilled. Criteria for item scores are presented in the AGREE instrument's manual. Standardized guideline domain scores are calculated by summing up all the scores of individual items in a domain. The standardized total is then presented as a percentage of the maximum possible score for that domain.

A global assessment is also rendered as a summary conclusion for each chapter. The 4 global assessment choices included “strongly recommended for use in practice,” “recommended for use with some modification or proviso,” “not recommended or suitable for use in practice,” or “unsure.” Scores of 60% or over in a majority of domains indicates a high overall quality and are eligible for the conclusion of a strong recommendation. Scores between 30% and 60% on the majority of domains generally fall into “recommend with proviso” indicating a moderate overall quality. The guidelines in the category could still be considered for use in practice when no other guidelines on the same clinical topic are available so long as provisos or alterations are made to account for the inherent weakness, and sufficient information is provided on the guideline development methodology. Others with scores of 30% or less in the majority of domains indicate that the guideline has a low overall quality and possesses serious shortcomings and is not recommended for use in practice.

AMA guidelines (47), IOM guidelines (1), Shaneyfelt et al's (31) criteria have not provided training manuals. Guidelines were reviewed applying described cri-

Table 1. Illustration of the essential components required for guidelines derived from multiple evaluation instruments.

AGREE (35)	AMA (47)	IOM (1)	SHANEYFELT ET AL (31)
I. Scope And Purpose	I. Organization	I. Validity	I. Standards Of Guidelines Development And Format
<ol style="list-style-type: none"> 1. The overall objective(s) of the guideline is(are) specifically described. 2. The clinical question(s) covered by the guideline is (are) specifically described. 3. The patients to whom the guideline is meant to apply are specifically described. 	Practice guidelines should be developed by or in conjunction with physician organizations	Practice guidelines are valid if, when followed, they lead to the health and cost outcomes projected for them, other things being equal.	<ol style="list-style-type: none"> 1. Purpose of the guideline is specified. 2. Rationale and importance of the guideline are explained. 3. The participants in the guideline development process and their areas of expertise are specified. 4. Targeted health problem or technology is clearly defined. 5. Targeted patient population is specified. 6. Intended audience or users of the guideline are specified. 7. The principal preventive, diagnostic, or therapeutic options available to clinicians and patients are specified 8. The health outcomes are specified. 9. The method by which the guideline underwent external review is specified. 10. An expiration date or date of scheduled review is specified.
II. Stakeholder Involvement	II. Methodology	II. Reliability/ Reproducibility	II. Standards Of Evidence Identification And Summary
<ol style="list-style-type: none"> 4. The guideline development group includes individuals from all the relevant professional groups. 5. The patients' view and preferences have been sought. 6. The target users of the guideline are clearly defined. 7. The guideline has been piloted among target users. 	Reliable methods that integrate relevant research findings should be used to develop practice guidelines.	Practice guidelines are reliable and reproducible (1) if—given the same evidence and methods for guidelines development—another set of experts would produce essentially the same statements and (2) if—given the same clinical circumstances—the guidelines are interpreted and applied consistently by practitioners or other appropriate parties.	<ol style="list-style-type: none"> 11. Method of identifying scientific evidence is specified. 12. Time period from which evidence is reviewed is specified. 13. The evidence used is identified by citation and referenced. 14. Method of data extraction is specified. 15. Method for grading or classifying the scientific evidence is specified. 16. Formal methods of combining evidence or expert opinion are used and described. 17. Benefits and harms of specific health practices are specified. 18. Benefits and harms are quantified. 19. The effect on health care costs from specific health practices is specified. 20. Costs are quantified.
III. Rigor Of Development	III. Clinical Expertise	III. Clinical Applicability	III. Standards on the Formulation of Recommendations
<ol style="list-style-type: none"> 8. Systematic methods were used to search for evidence. 9. The criteria for selecting the evidence are clearly described. 10. The methods used for formulating the recommendations are clearly described. 11. The health benefits, side effects, and risks have been considered in formulating the recommendations. 12. There is an explicit link between the recommendations and the supporting evidence. 13. The guideline has been externally reviewed by experts prior to its publication. 14. A procedure for updating the guideline is provided. 	Appropriate clinical expertise should be used to develop practice guidelines.	Practice guidelines should be as inclusive of appropriately defined patient populations as scientific and clinical evidence and expert judgment permit, and they should explicitly state the populations to which statements apply.	<ol style="list-style-type: none"> 21. The role of value judgments used by the guideline developers in making recommendations is discussed. 22. The role of patient preferences is discussed. 23. Recommendations are specific and apply to the stated goals of the guideline. 24. Recommendations are graded according to the strength of the evidence. 25. Flexibility in the recommendations is specified.

Table 1 (cont.). *Illustration of the essential components required for guidelines derived from multiple evaluation instruments.*

AGREE (35)	AMA (47)	IOM (1)	SHANEYFELT ET AL (31)
<p>IV. Clarity And Presentation</p> <p>15. The recommendations are specific and unambiguous. 16. The different options for management of the condition are clearly presented. 17. Key recommendations are easily identifiable. 18. The guideline is supported with tools for application.</p>	<p>IV. Comprehensiveness</p> <p>Practice guidelines should be as comprehensive and specific as possible.</p>	<p>IV. Clinical Flexibility</p> <p>Practice guidelines should identify the specifically known or generally expected exceptions to their recommendations.</p>	
<p>V. Applicability</p> <p>19. The potential organizational barriers in applying the recommendations have been discussed. 20. The potential cost implications of applying the recommendations have been considered. 21. The guideline presents key review criteria for monitoring and/or purposes. 22. The guideline is editorially independent from the funding body.</p>	<p>V. Current Information</p> <p>Practice guidelines should be based on current information.</p>	<p>V. Clarity</p> <p>Practice guidelines should use unambiguous language, define terms precisely, and use logical, easy-to-follow modes of presentation.</p>	
<p>VI. Editorial Independence</p> <p>23. Conflicts of interest of guideline development members have been reported.</p>	<p>VI. Dissemination</p> <p>Practice guidelines should be widely disseminated.</p>	<p>VI. Multidisciplinary Process</p> <p>Practice guidelines should be developed by a process that includes participation by representatives of key affected groups. Participation may include serving on panels that develop guidelines, providing evidence and viewpoints to the panels, and reviewing draft guidelines.</p>	
		<p>VII. Scheduled Review</p>	
		<p>Practice guidelines should include statements about when they should be reviewed to determine whether revisions are warranted, given new clinical evidence or changing professional consensus.</p>	
		<p>VIII. Documentation</p> <p>The procedures followed in developing guidelines, the participants involved, the evidence used, the assumptions and rationales accepted, and the analytic methods employed should be meticulously documented and described.</p>	

Adapted and modified from AGREE (35), AMA (47), IOM (1), and Shaneyfelt et al (31).

teria in these articles by the 4 authors. These 4 authors also utilized the AGREE instrument in evaluating the ACOEM guidelines.

The appraisers included were the first 4 of the 5 authors all with experience in the development of evidence-based guidelines. Any disagreements were resolved by the fifth author.

RESULTS

The low back pain and chronic pain chapters of ACOEM guidelines (3,4) were reviewed by, the AGREE instrument (35), AMA criteria (47), IOM criteria (1), and the criteria described by Shaneyfelt et al (31).

There were no major disagreements. Interexaminer agreement for items scores was very high. Disagreements in the form of different item scores were minor and these were resolved by discussion.

Appraisal by AGREE Instrument

Results of assessment by the AGREE instrument are illustrated in Table 2.

For domain 1, scope and purpose, the ACOEM guidelines chronic pain chapter (4) received a total score of 69.44%, whereas it was 77.78% for the low back pain chapter (3) with an average score of 73.61%. These scores were similar to Cates et al (24) with a mean domain score of 79.63%. All the appraisers agreed that the overall objectives of the guidelines, clinical questions covered by the guidelines, and to whom the guidelines were meant to apply, were described, with some ambiguity.

For domain 2, Stakeholder Involvement, both chapters obtained a low score of 6.25% compared to the 46.06% for Cates et al (24). However, Cates et al (24) considered only the statement from the group but did not investigate further conflicts of interest. Contrary to this, the present appraisers were all aware of the full information. All of the appraisers strongly agreed that the guideline development team failed

to include individuals from all relevant professional groups. Further, the appraisers unanimously reported that there was no indication that either patients' views or preferences had been sought or that the guidelines had been tested or piloted.

Domain 3, rigor of development, evaluated the integrity of the development process, including the reporting of the search methodology, the evidence selection criteria, the methods used to formulate recommendations, the risks and benefits assessment, and the links between evidence and recommendations, external review, and updating mechanisms. All chapters of ACOEM guidelines performed poorly in this domain, receiving a mean chapter score of 26.59%, the lowest of all the domain rating scores in the evaluation performed by Cates et al (24). Similarly, in the present evaluation, all the appraisers provided overall low total scores of 15.48% and 21.43%, with an average mean score of 18.45%, lower than Cates et al (24), but higher than scores of Domains 2, 5, and 6.

All the appraisers strongly agreed that the guidelines failed to document any systematic methods used to search for evidence. Further, there was strong agreement that the guidelines used variable methodology clearly described the criteria for selecting evidence, and have not clearly documented the method used for formulating the recommendations. The reviewers strongly agreed that the health benefits have not been considered in formulating the recommendations, while overtly emphasizing side effects and risks. Further, the appraisers found no explicit linkage between the recommendations and the supporting evidence. Finally, there was agreement among all the appraisers that there was no external peer review by experts prior to its publication.

Domain 4, clarity and presentation, obtained a higher average score of 34.37%, with 39.58% for the chronic pain chapter, and 29.17% for the low back pain chapter, higher than the scores in domains 2, 3, 5, and 6. In the previous study (24), the average scores

Table 2. Averaged AGREE domain scores by chapter for all appraisers.

Chapter	Domain 1 Scope and Purpose	Domain 2 Stakeholder Involvement	Domain 3 Rigor of Development	Domain 4 Clarity and Presentation	Domain 5 Application	Domain 6 Editorial Independence	Global Assessment
Chronic Pain	69.44%	6.25%	15.48%	39.58%	8.33%	4.17%	23.27%
Low Back Pain	77.78%	6.25%	21.43%	29.17%	8.33%	4.17%	24.36%
Average	73.61%	6.25%	18.45%	34.37%	8.33%	4.17%	23.81%

across all chapters for this domain was 86.81% with the low back pain chapter receiving the highest score of 91.67%. In the present analysis, all the appraisers agreed that the recommendations were ambiguous at times and were not easily identifiable.

Domain 5, applicability, involved potential organizational barriers in applying the recommendations, potential cost implications, and key review criteria for monitoring. The ACOEM guidelines scored one of the lowest in this category with 8.33% in both chapters, whereas it scored an average of 31.48% in the evaluation by Cates et al (24). All the appraisers unanimously agreed that none of the criteria were met in this category. There were multiple organizational barriers, cost implications, and lack of review criteria.

Domain 6, editorial independence, is the final criteria, also scored extremely low with a 4.17% in both categories. This domain reviewed editorial independence and freedom from external control or influence over the development team as reported by the document. In Cates et al's (24) appraisal, this category scored 29.17% across all chapters, describing it as the guidelines' second lowest scored domain. However, in the present evaluation, this was the lowest of all the

domains. All the appraisers in this present study felt that biases of the authors of the ACOEM guidelines prevailed extensively.

The rating of both chapters of ACOEM guidelines was uniform on the global assessment, and all appraisers provided essentially the same global assessment suggesting "not recommended for use in practice." Global assessment scores were 23.27% for chronic pain chapter, 24.36% for low back pain chapter, with an average of 23.81%.

Thus, ACOEM guidelines scored high in only one AGREE domain, scope and purpose with a score of 73.61%. All other categories scored low with 34.37% in domain 4 — clarity and presentation, 6.25% in domain 2 — stakeholder involvement, 8.33% in domain 5 — application, 4.17% in domain 6 — editorial independence, 18.45% in domain 3 — rigor of development, and 23.81% on global assessment. Overall, the AGREE scores were low even compared to the previous evaluations (Table 2).

Comparative evaluation as presented by Cates et al (24) is illustrated in Figure 1. Figure 2 compares present assessment with Cates et al (24).

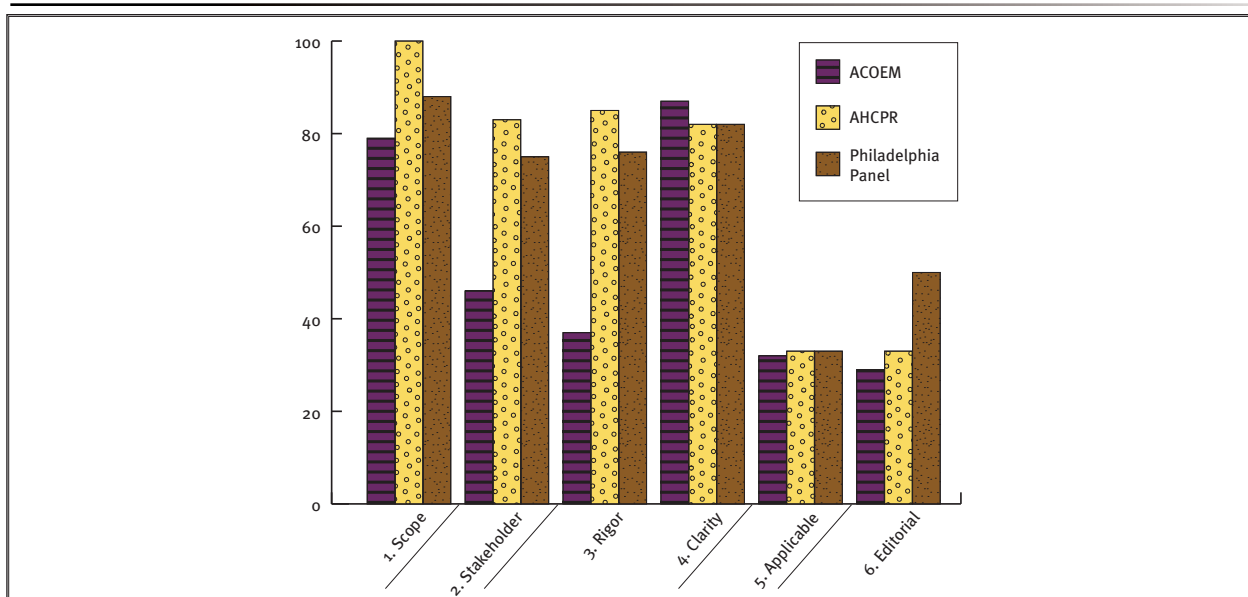
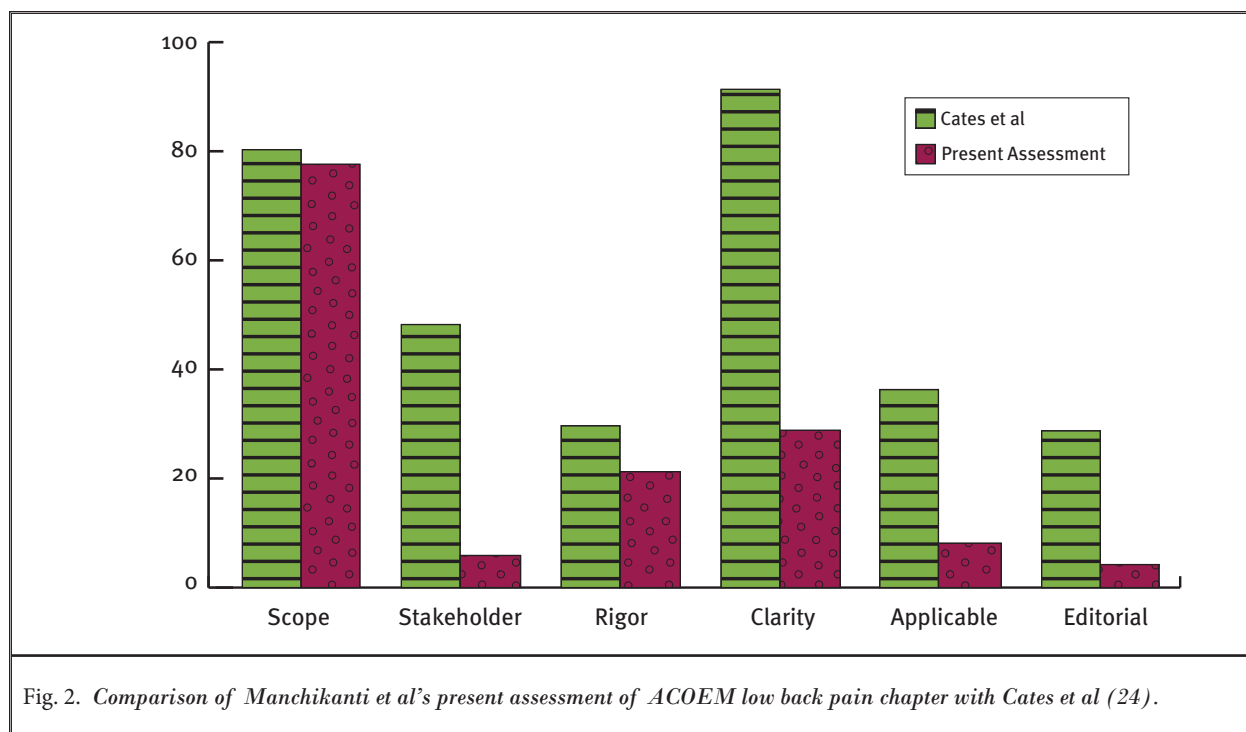


Fig. 1. Comparison of a guideline's AGREE (Appraisal of Guidelines Research and Evaluation) dimension scores provides valuable insight into the strengths and weaknesses of a guideline.

This graph depicts AGREE scores: (A) American College of Occupational and Environmental Medicine (ACOEM) Guidelines, 2nd Ed. Mean domain scores as reported in this study (3). (B) Agency for Health Care Policy and Research (AH CPR). Acute Low Back Problems in Adults (1994) (23), AGREE scores as reported by van Tulder et al (25). (C) Philadelphia Panel. Philadelphia Panel evidence-based clinical practice guidelines on selected rehabilitation interventions (2001), AGREE scores as reported by van Tulder MW, Tuut M, Pennick V, Bombardier C, Assendelft W. Quality of primary care guidelines for acute low back pain. *Spine* 2004; 29:E357–362 (Ref. 25).

Reproduced with permission from Elsevier and Cates JR et al. An independent AGREE evaluation of the Occupational Medicine Practice Guidelines. *Spine J* 2006; 6:72-77 (ref. 26)



Assessment by AMA's Key Attributes

The AMA has described key attributes of guidelines (47). These include the development by a physician organization, utilization of reliable methods that integrate relevant research findings, appropriate clinical expertise, guidelines must be as comprehensive and specific as possible, they should provide current information, and they should be widely disseminated (Table 1).

Attribute 1 relates to the development by a physician organization. Though made up of physicians, ACOEM was described in 2007 as "a professional association in service to industry" (43). Thus, it does not represent a true physician organization except in name.

Attribute 2 describes reliable methods that integrate relevant research findings. The ACOEM guidelines have shown a lack of utilization of reliable methods and integration of relevant research findings in preparation of their guidelines (3-6,50).

Attribute 3 relates to appropriate clinical expertise. Occupational medicine physicians have no expertise in interventional pain management or in any other modalities in managing chronic pain. Occupational diseases represented 8% of workers' compensation

claims and 29% of the costs (51). ACOEM members may be experts in evaluating work place injuries, but not the management of pain. In general, experts must be drawn from multiple specialties involving all types of stakeholders. The majority of the ACOEM panel members do not have expertise in managing low back pain or chronic pain, specifically interventional pain techniques. The major contributors to both sets of the guidelines, including the editor-in-chief, lead chairs, associate chairs, panel members, panel consultants, and methodology committee consultants included a total of 39 members. Based on the correspondence, or lack thereof, with only one designated pain specialist responding affirmatively, it appears that specialists included in pain medicine and interventional pain management were 5, with 4 of 39, from interventional pain management for development of the low back pain and chronic pain chapters (10%). Among these, one appears to be a corporate medical director with no clinical practice and a second one with major research interest rather than a clinical practice. Consequently, only 2 interventional pain physicians remained in active clinical practice. Thus, only 2 members (5%) from interventional pain management appear to have participated in the guideline development rather than

being assessed by experienced practitioners for clinical relevance (52). Further, it is questionable how much involvement, if any, of these panel members had in the development process of the guidelines.

The methodology committee consultants are different for both chapters. However, both chapters provide the same descriptions of multiple interventions (Table 3). There were no endorsements from any society for chronic pain. In fact, many chronic pain organizations have criticized the ACOEM guidelines (5,7,53).

Attribute 4 relates to the comprehensiveness and specificity of guidelines. A superficial evaluation may convince a reviewer that these are comprehensive and specific, but intricacies dictate otherwise. Without proper scientific methodology, apparent comprehensiveness and specificity are not achievable.

Attribute 5 relates to the current information, which has been grossly deficient in the ACOEM guidelines. In preparation of guidelines, it is essential to evaluate the search strategy and assessment of study quality. One of the most powerful arguments used by the supporters of systematic review and authors of guidelines is that they overcome most of the limitations of narrative reviews by being the product of a scientific process to reduce bias and impression and by providing detailed information to allow replication by others (18,54-59). Any systematic review or a guideline with widespread impact on the healthcare system of the United States is expected to include all the relevant trials available (57). Thus, identification of all the relevant trials for guideline preparation is a crucial element and poses a fundamental challenge to the authors (55). Even though, it is well understood that searching the literature can be onerous, resource consuming task, ACOEM with its available resources has not performed this task in identifying trials effectively. Providing current information also reduces bias and facilitates the maximum possible number of relevant, individual trials and provides a detailed description of their strengths and limitations, while publication bias has been described as the publication of positive trials and non-inclusion of unpublished studies (59). However, in recent years it appears that only manuscripts published in society journals are positive trials of their own specialty and negative trials of other specialties. Thus, systematic reviews that fail to identify and include all trials and those who failed to identify or include unpublished trials and those who failed to identify all journals and databases beyond their own specialty, are at the risk of overestimating the effect

of interventions they are interested in and underestimating the interventions oppose (18). Further, there has been significant reviewer bias with lack of identification of published trials and non-identification of unpublished trials and the articles from other journals based on the preference of reviewers. Surprisingly, the ACOEM guideline preparers have missed the studies registered on clinical trials registry and many studies published in journals listed on EMBASE and PubMed. On a pragmatic basis, admittedly without empirical evidence supporting appropriate search for unpublished trials, a guideline preparation in interventional pain management at minimum must have a comprehensive review using at least 3 sources and provide a description of efforts to identify all databases and journals. An effective combination of comprehensive search includes a minimum of 3 bibliographic databases (Medline, EMBASE, Cochrane library), a hand search of references of eligible trials, and direct contact with the corresponding authors of eligible trials asking for additional published or unpublished trials (18). The authors of the ACOEM guidelines have included only selective trials and made a selective search.

Finally, attribute 6 relates to wide dissemination, which is absent with these guidelines. They are not listed on sites such as PubMed, Index Medicus, Medline, EMBASE, and are inadequately listed on the National Guideline Clearinghouse and AHRQ website. They are also expensive to purchase; thus dissemination is seriously lacking. This is in stark contradistinction to guidelines such as ASIPP's with free full manuscript.

In summary, both chapters of ACOEM guidelines met only 1 of the 6 key attributes described by AMA (47). These guidelines have not met attribute 2 – for utilization of reliable methods that integrate relevant research findings, attribute 3 – appropriate clinical expertise, attribute 4 – guidelines must be as comprehensive and specific as possible, attribute 5 – they should provide current information, and attribute 6 – they should be widely disseminated.

Assessment by IOM Criteria

The IOM (1) has described 8 key attributes of guidelines (Table 1). These include 1) validity, 2) reliability/reproducibility, 3) clinical applicability, 4) clinical flexibility, 5) clarity, 6) multidisciplinary process, 7) scheduled review, and 8) documentation.

The number one IOM attribute for good practice guidelines is validity. As shown in Table 1, guidelines are valid, if, when followed, they lead to the health

Table 3. Comparison of low back pain chapter with chronic pain chapter revisions – bolded text showing exact same language.

	Low Back Pain Chapter (3)	Chronic Pain Chapter (4)
Facet Joint Interventions		
Diagnostic Facet Joint Injections	<p><i>1. Recommendation: Diagnostic Facet Joint Injection for Chronic Low Back Pain</i></p> <p>One diagnostic facet joint injection may be recommended for patients with chronic LBP that is significantly exacerbated by extension and rotation or associated with lumbar rigidity, and not alleviated with other conservative treatments (e.g., NSAIDs, aerobic exercise, other exercise, manipulation) in order to determine whether specific interventions targeting the facet joint are recommended. Repeated diagnostic injections in the same location(s) are not recommended.</p> <p><i>Strength of Evidence – No Recommendation, Insufficient Evidence (I)</i></p> <p><i>2. Recommendation: Diagnostic Facet Joint Injections for Acute or Subacute Low Back Pain or Radicular Pain Syndromes</i></p> <p>Diagnostic facet joint injections are not recommended for acute or subacute LBP or radicular pain syndromes.</p> <p><i>Strength of Evidence – Not Recommended, Insufficient Evidence (I)</i></p>	<p><i>1. Recommendation</i></p> <p>One diagnostic facet joint injection may be recommended for patients with chronic LBP that is: 1) significantly exacerbated by extension and rotation or associated with lumbar rigidity, and 2) not alleviated with other conservative treatments (e.g., NSAIDs, aerobic exercise, other exercise, manipulation) in order to determine whether specific interventions targeting the facet joint are recommended. Repeated diagnostic injections in the same location(s) are not recommended.</p> <p><i>Strength of Evidence – No Recommendation, Insufficient Evidence (I)</i></p> <p><i>2. Recommendation</i></p> <p>Diagnostic facet joint injections are not recommended for neck pain or radicular pain syndromes.</p> <p><i>Strength of Evidence – Not Recommended, Insufficient Evidence (I)</i></p>
Therapeutic Facet Joint Injections	<p><i>Recommendation: Therapeutic Facet Joint Injections for Acute, Subacute or Chronic Low Back Pain or Radicular Pain Syndromes</i></p> <p>Therapeutic facet joint injections are not recommended for acute, subacute, or chronic LBP or for any radicular pain syndrome.</p> <p><i>Strength of Evidence – Moderately Not Recommended, Evidence (B)</i></p>	<p><i>Recommendation: Therapeutic Facet Joint Injections –Low Back Pain</i></p> <p>Therapeutic facet joint injections are not recommended for chronic low back pain or for any radicular pain syndrome.</p> <p><i>Strength of Evidence – Not Recommended, Insufficient Evidence (I)</i></p>
Rhizotomy and Facet Rhizotomy	<p><i>Recommendation: Radiofrequency Neurotomy, Neurotomy, and Facet Rhizotomy for Spinal Conditions</i></p> <p>Radiofrequency neurotomy, neurotomy, and facet rhizotomy are not recommended for the treatment of any spinal condition.</p> <p><i>Strength of Evidence – Not Recommended, Evidence (C)</i></p>	<p><i>Recommendation</i></p> <p>Radiofrequency neurotomy, neurotomy, and facet rhizotomy are not recommended for the treatment of cervicogenic headaches or any spinal condition.</p> <p><i>Strength of Evidence – Not Recommended, Evidence (C)</i></p>

Table 3 cont. Comparison of low back pain chapter with chronic pain chapter revisions – bolded text showing exact same language.

	Low Back Pain Chapter (3)	Chronic Pain Chapter (4)
Epidural Injections	<p><i>1. Recommendation: Epidural Glucocorticosteroid Injections for Acute or Subacute Radicular Pain</i></p> <p>An epidural glucocorticosteroid injection is an option for acute or subacute radicular pain syndromes. Its purpose is to provide a few weeks of partial pain relief while hopefully awaiting spontaneous improvement. An epidural steroid injection may cause short-term improvement, which may assist in successfully accruing sufficient time to ascertain whether conservative care will succeed. An “option” means there should be no requirement that a patient receive and fail treatment with epidural glucocorticosteroid, especially repeated injections, prior to discectomy.</p> <p><i>Strength of Evidence – Recommended, Insufficient Evidence (I)</i></p> <p><i>2. Recommendation: Epidural Glucocorticosteroid Injections for Acute Flare-ups of Spinal Stenosis</i></p> <p>Epidural glucocorticosteroid injections are an option as a second-line treatment for acute flare-ups of spinal stenosis, although the evidence is less robust than it is for herniated discs.</p> <p><i>Strength of Evidence – Recommended, Insufficient Evidence (I)</i></p> <p><i>3. Recommendation: Epidural Glucocorticosteroid Injections for Acute, Subacute, or Chronic Low Back Pain without Radicular Symptoms</i></p> <p>Epidural glucocorticosteroid injections are not recommended for acute, subacute, or chronic LBP in the absence of significant radicular symptoms. They are also not recommended as first- or second-line treatment in individuals with LBP symptoms that predominate over leg pain. They are not recommended as treatment for any chronic problem.</p> <p><i>Strength of Evidence – Not Recommended, Evidence (C)</i></p>	<p><i>1. Recommendation: Epidural Injections for Acute or Subacute Lumbar Radicular Pain</i></p> <p>An epidural glucocorticosteroid injection is an option for subacute radicular pain syndromes. This includes their use in patients with chronic lumbar pain who experience an exacerbation of their disease. Its purpose is a few weeks of partial pain relief while hopefully awaiting spontaneous improvement.</p> <p><i>Strength of Evidence – Recommended, Insufficient Evidence (I)</i></p> <p><i>2. Recommendation: Epidural Injections for Spinal Stenosis</i></p> <p>Epidural glucocorticosteroid injections are an option for second line treatment for acute flare ups of spinal stenosis, although the evidence is less robust than it is for herniated discs.</p> <p><i>Strength of Evidence – Recommended, Insufficient Evidence (I)</i></p> <p><i>3. Recommendation: Epidural Injections for Chronic LBP without Radicular Symptoms</i></p> <p>Epidural glucocorticosteroid injections are not recommended for chronic LBP in the absence of significant radicular symptoms. They are also not recommended as first or second line treatment in individuals with LBP symptoms that predominate over leg pain.</p> <p><i>Strength of Evidence – Not Recommended, Evidence (C)</i></p>

and cost outcomes projected for them, other things being equal. A prospective assessment of validity considers the projected health outcomes and costs of alternative courses of action, the relationship between the evidence and recommendations, the substance and quality of the scientific and clinical evidence cited, and the means used to evaluate the evidence. After considering all these requirements, the inevitable conclusion is reached that ACOEM guidelines do not meet validity criteria.

Attribute 2 relates to reliability and reproducibility judged by the emergence of the same statements if reviewed by another set of experts in the same clinical circumstances. However, no such prospective assessment of reliability has been performed and no independent external reviews or pretests of the guidelines were utilized. Thus, reliability and reproducibility is not an attribute of the ACOEM guidelines.

Attribute 3 relates to clinical applicability, specifically that guidelines should be as inclusive of appropriately defined patient populations as scientific and clinical evidence and expert judgment permit, and they should explicitly state the populations to which the statements apply. ACOEM guidelines do meet these criteria as it is narrowly defined for workers' compensation.

Attribute 4 describes clinical flexibility which identifies specifically known or generally expected exceptions to their recommendations. The ACOEM guidelines meet these criteria.

Attribute 5 relates to clarity, with unambiguous language, precisely defined terms, and logical, easy-to-follow modes of presentation. The ACOEM guidelines may appear to use clarity; however, clarity is actually one of the major deficiencies of the chapters reviewed (3,4). These guidelines are too cumbersome, too difficult to understand, and too confusing. Thus, clarity of these guidelines is not preserved.

Attribute 6 relates to multidisciplinary process. On the surface, ACOEM guidelines appear to have utilized a multidisciplinary process. However, there was no external peer review process or representation from diverse groups, specifically from organizations representing interventional pain physicians. Thus, the multidisciplinary process was not appropriately applied.

The seventh attribute relates to scheduled review, which is the easiest one to meet and ACOEM guidelines have met this criteria.

Finally, Attribute 8 relates to documentation. While the different chapters show different coordina-

tors, consultants, panel members, etc., both are virtually the same (Table 3). Thus, documentation is not appropriate.

In summary, the attributes of good practice guidelines as described by the IOM (1), which were based on the congressional mandate, were followed in only 3 of the 8 instances.

Assessment by Shaneyfelt et al's Criteria

Based on the criteria utilized by Shaneyfelt et al (31), both chapters of ACOEM guidelines meet the criteria in a few categories as shown in Table 4. Under the section on Standards of Guidelines Development and Format, ACOEM guidelines met only 40% of the criteria; on Standards on Evidence Identification and Summary, ACOEM guidelines met only 20% of the criteria; and for the Standards on the Formulation of Recommendations, ACOEM guidelines met only 20% of the criteria; with 28% of the overall criteria being met.

DISCUSSION

This independent critical evaluation utilizing multiple instruments to assess guidelines, illustrates that the low back pain and chronic pain chapters of ACOEM guidelines fall considerably short of the well-established standards and much more attention and openness is needed by those involved in both the guideline creation and in the guideline review, publication, and dissemination. Based on the evaluation using the AGREE instrument, this assessment showed extremely low scores with less than 30 in 5 of the 6 domains and global assessment. The highest score was present in domain 1 for scope and purpose with 73.61% whereas domain 4 for clarity and presentation followed it with a 34.37% score. The global assessment score was 23.81% indicating lack of utility for these guidelines in patient care.

According to AMA attributes (47), ACOEM guidelines met only one of the 6, an easy and a low priority, attribute. Further, the guideline evaluation met only 3 of the 8 key attributes described by IOM in the categories of clinical applicability, clinical flexibility, and scheduled review, whereas, the key attributes of validity, reliability/reproducibility, clinical flexibility, multidisciplinary process, and documentation were not met.

Based on evaluation using the criteria described by Shaneyfelt et al (31), the overall guidelines met only 7 of 25 key elements which is also less than 30%

Table 4. Assessment of ACOEM guidelines utilizing criteria by Shaneyfelt et al (31).

Key Element	Chronic Pain	Low Back Pain
STANDARDS OF GUIDELINES DEVELOPMENT AND FORMAT		
1. Purpose of the guideline is specified.	Yes	Yes
2. Rationale and importance of the guideline are explained.	Yes	Yes
3. The participants in the guideline development process and their areas of expertise are specified.	No	No
4. Targeted health problem or technology is clearly defined.	Yes	Yes
5. Targeted patient population is specified.	Yes	Yes
6. Intended audience of users of the guideline are specified.	No	No
7. The principal preventive, diagnostic, or therapeutic options available to clinicians and patients are specified.	No	No
8. The health outcomes are specified.	No	No
9. The method by which the guideline underwent external review is specified.	No	No
10. An expiration date or date of scheduled review is specified.	No	No
TOTAL "YES" Responses	4/10	4/10
STANDARDS OF EVIDENCE IDENTIFICATION AND SUMMARY		
11. Method of identifying scientific evidence is specified.	No	No
12. Time period from which evidence is reviewed is specified.	No	No
13. The evidence used is identified by citation and referenced.	Yes	Yes
14. Method of data extraction is specified.	No	No
15. Method for grading or classifying the scientific evidence is specified.	No	No
16. Formal methods of combining evidence of expert opinion are used and described.	Yes	Yes
17. Benefits and harms of specific health practices are specified.	No	No
18. Benefits and harms are quantified.	No	No
19. The effect on health care costs from specific health practices is specified.	No	No
20. Costs are quantified.	No	No
TOTAL "YES" Responses	2/10	2/10
STANDARDS ON THE FORMULATION OF RECOMMENDATIONS		
21. The role of value judgments used by the guideline developers in making recommendations is discussed.	No	No
22. The role of patient preference is discussed.	No	No
23. Recommendations are specific and apply to the stated goals of the guideline.	Yes	Yes
24. Recommendations are graded according to the strength of the evidence.	No	No
25. Flexibility in the recommendations is specified.	No	No
TOTAL "YES" Responses	1/5	1/5
OVERALL TOTAL	7/25	7/25

indicating a lack of utility in patient care.

The evaluation of ACOEM guidelines by AGREE evaluation (35,39), AMA (47), IOM (1) and Shaneyfelt et al's (31) criteria resulted in guidelines meeting only 1 of the 6 attributes of AGREE (35,39) and AMA (47), 2 of the 8 attributes of IOM (1), and only 28% of Shaneyfelt et al's criteria (31). Thus, a simple revision of these guidelines appears to be insurmountable, consequently improvement appears to be impossible.

Since the guidelines are not ideal for clinical practice, they will invariably reduce patient access and increase costs for injured workers, third party payors, and the government by transferring the injured worker into a non-productive disability system.

Clinical practice guidelines must be based on the practice of evidence-based medicine which is based on 4 basic contingencies (60). These include recognition of the patient's problem and the construction of a structured clinical question, thorough search of medical literature to retrieve the best available evidence to answer the question, critical appraisal of all available evidence, and integration of the evidence with all aspects and context of the clinical circumstances to facilitate the decisional process that determines the best clinical care of each patient. The NHMRC (44) described 9 basic principles in the development of the guidelines: outcomes (survival rates to quality-of-life attributes), best available evidence (according to its quality, relevance, and strength), appropriate systems to synthesize the available evidence (judgment, experience, and good sense), multidisciplinary process of development, flexibility and adaptability, cost-effectiveness of treatments, appropriate dissemination, evaluation of implementation and impact of guidelines, and appropriate revision of the guidelines on a regular basis.

The recommended 25 criteria of Shaneyfelt et al (31), 6 domains described in the AGREE evaluation, the AMA's 6 attributes, and IOM's 8 key attributes are all illustrated in Table 1. This clearly illustrates that the guideline development process should be precise and rigorous to ensure that the results are reproducible and not vague (42,61,62). The medical and research community generally expects that peer review and testing of practice guidelines should be performed prior to their acceptance as being valid and their subsequent utilization in the wide arena of clinical practice (24,32). Consequently, guidelines must be developed by systematically acquiring, analyzing, and transferring research findings into clinical, management, and

policy arenas (63).

Guidelines for Guidelines (45) identified 19 components starting from priority setting to evaluation of the impact of the guideline. Further, the authors of any guidelines must realize that grading the strength of recommendations and quality of evidence in clinical guidelines has been changing rapidly (64). The GRADE process (an acronym for Grading of Recommendations, Assessment, Development, and Evaluation), recommended grading quality and strength of evidence (65). The steps in this approach were to make sequential judgments about the quality of evidence across studies for each important outcome, which outcomes were critical to a decision, the overall quality of evidence across those critical outcomes, the balance between benefits and harms, and the strength of recommendations (6,45-49,61-82).

The complexity of guideline preparation is illustrated by the creation of AHCPR and its rather public and quick demise with the establishment of AHRQ (23,83), the advance guidance created by WHO to prepare guidelines (29,45,67-81), National Institute for Clinical Excellence (NICE) in the United Kingdom (82), U.S. Preventive Services Task Force (83), and Canadian Medical Association (48).

Apart from scientific issues, issues of conflict of interest in guidelines development must be addressed as an essential ingredient. A conflict of interest exists when an individual's secondary interest (e.g. personal, financial) interferes with or influences judgments regarding the individual's primary interest (i.e. patient welfare, education, and research integrity) (70). There is widespread evidence demonstrating the association of financial ties with a breakdown in research integrity. It has been shown that industry funding for research is associated with favorable outcomes for the sponsor (81,84-87), and financial ties of investigators with their sponsors, consulting income, etc., are also associated with favorable research outcomes for the sponsor (87-89). Biased research may be intentional or unintentional (90), and may result from loss of objectivity at multiple stages in the research process, including conceptualization of the question, design, or conduct of research; interpretation of the results; and publication or lack thereof of the research (91,92). In essence, the bias associated with financial and other conflicts of interest may damage both the public's and other researchers' trust in science regardless of its source (93), whereas the type of conflict most likely to affect the public trust is financial conflict where the

scientist tends to gain financially from a particular research outcome (93-98).

In an evaluation of 279 guidelines, published from 1985 to June 1997, produced by 69 different developers, Shaneyfelt et al (31) concluded that 1) there was no difference in the mean number of standards satisfied by guidelines produced by subspecialty medical societies, general medical societies, or governmental agencies; 2) guideline length was positively correlated with adherence to methodological standards; 3) mean overall adherence to standards by each guideline was 43.1%, mean adherence to methodological standards on guideline development and format was 51.1%, mean adherence for identification and summary of evidence was 33.6%, and adherence for formulation of recommendations was 46%; 4) with overall mean adherence to standard by each guideline improving from 36.9% in 1985 to 50.4% in 1997.

Cates et al (26) in a previous evaluation concluded that while ACOEM guideline preparation was very strong in describing objectives of the guidelines, they have not followed other aspects of the guidelines except for clarity and presentation. However, Cates et al (26) reported that there was no indication that either patients' views or preferences had been sought or that guidelines had been tested or piloted. In addition, reviewers of the study by Cates et al (26) unanimously provided a strong assessment that the guidelines failed to document any systematic methods used to search for evidence in the category of rigor of development. The reviewers were also unable to find any explicit linkages between the recommendations and the supporting evidence, as there was no external review by experts before publication and no procedure was offered for updating the guidelines. Cates et al (26) also gave low scores for application of guidelines with no documentation that the potential organization barriers to applying recommendations had been discussed. Finally, editorial independence and the freedom from control or influence over the development team were not confirmed and the reviewers unanimously agreed that the guidelines did not address possible conflicts of interest. Authors of the manuscript by Cates et al (26) unanimously agreed that the second edition of ACOEM guidelines (8) lacked transparency that would allow readers to link citations and data to specific opinions and recommendations contained in the development, with a

poorly described literature review and grading of evidence, making it impossible for the reader to follow a recommendation to the source data, or assess the amount and quality of research supporting any given recommendation. Similar problems were also identified by Staal et al (41) with the first edition of ACOEM guidelines. Thus, the present evaluation while agreeing with the previous evaluations (26,41) has shown a multitude of deficiencies along with much lower scores, leading to the conclusion that these guidelines are not recommended for use in clinical practice. The study conducted by RAND Health also concluded that the evidence base for treatment recommendations for non-surgical conditions were of uncertain validity and comprehensiveness (43). Further, since the guidelines were implemented in California on an interim basis in March 2004, RAND reports inconsistent interpretation of ACOEM guidelines by payors (43). The present evaluation agrees with the conclusions by RAND that the evidence base for treatment recommendations for non-surgical conditions was of uncertain validity and comprehensiveness (43).

Assessment utilizing AMA's key attributes also showed criteria being met in only one of the 6 categories. It is also important to note the similarities in methodology and the use of identical descriptions that are present in both the low back pain chapter and the chronic pain chapter even though they each had distinctly different panels. However, the guidelines have not been evaluated in the past utilizing AMA key attributes, thus there were no comparisons available.

Similar to the assessment by AMA criteria, when utilizing the IOM criteria both of the guideline chapters met only 3 of the 8 key attributes, higher than critical criteria necessity, but still below 40%.

Helm (27) in his evaluation compared ACOEM guidelines with the evidence-based practice guidelines of ASIPP (20), however, ASIPP has, since then, updated their guidelines (13,21). Even then, utilizing the Shaneyfelt et al (31) criteria, ASIPP guidelines complied with 23 out of 25 elements of guideline creation, whereas, ACOEM complied with only 12 out of 25 in the Helm study (27). However, the present critical evaluation showed agreement in only 28% of the criteria or 7 of 25, once again falling below the 30% mark and making both of the chapters of ACOEM guidelines non-applicable in clinical settings.

CONCLUSION

Both the low back pain and chronic pain chapters (3,4) of ACOEM guidelines are not ideal for clinical use based on the current assessment using the AGREE instrument (35), AMA attributes (47), IOM key attributes (1), and criteria established by Shaneyfelt et al (31). This evaluation elicited numerous deficiencies with these guidelines including lack of expertise by the developing organization, lack of utilization of appropriate and current evidence-based principles, the lack of involvement of experts, which ultimately may result in the restriction of the independent practice of medicine and increased cost for injured workers, third party payors, and the government by transferring the injured worker into a non-productive disability system.

ACKNOWLEDGMENTS

The authors wish to thank David S. Kloth, MD, Board Member and Past President of the American Society of Interventional Pain Physicians (ASIPP) and Eric Hauth, MA, MS, Executive Director of Neuro-modulation Therapy Access Coalition (NTAC) for their constructive criticisms, reviews, support, and suggestions in preparation of this manuscript; ASIPP Board of Directors for their support; the Editorial Board of *Pain Physician*, for review and criticism in improving the manuscript; and Vidyasagar Pampati, MSc, Statistician, and Tonie M. Hatton and Diane E. Neihoff, Transcriptionists, for their assistance in preparation of this manuscript.

REFERENCES

- Field MJ, Lohr KN, eds. *Clinical Practice Guidelines: Directions for a New Program*. Institute of Medicine, National Academy Press, Washington, DC, 1990.
- Harris JS, Blais BR; American College of Occupational and Environmental Medicine (ACOEM). *Occupational Medicine Practice Guidelines: Evaluation and Management of Common Health Problems and Functional Recovery in Workers, First Edition*. OEM Press, Beverly Farms, 1997.
- American College of Occupational and Environmental Medicine (ACOEM) Low Back Disorders. In *Occupational Medicine Practice Guidelines: Evaluation and Management of Common Health Problems and Functional Recovery of Workers, Second Edition*. OEM Press, Beverly Farms, 2007.
- American College of Occupational and Environmental Medicine (ACOEM) Chronic Pain. In *Occupational Medicine Practice Guidelines: Evaluation and Management of Common Health Problems and Functional Recovery of Workers, Second Edition*. OEM Press, Beverly Farms; 2008.
- Official comments on the ACOEM Guidelines process provided by ASIPP CEO, Laxmaiah Manchikanti, MD, November 26, 2007, Personal Communication.
- Manchikanti L, Singh V, Derby R, Helm S, Trescot AM, Staats PS, Prager JP, Hirsch JA. Review of occupational medicine practice guidelines for interventional pain management and potential implications. *Pain Physician* 2008; 271-290.
- Letter to Robert K. McLellan, MD, President of the American College of Occupational & Environmental Medicine (ACOEM) from the American Academy of Pain Medicine, American Society of Interventional Pain Physicians, International Spine Intervention Society, and North American Neuromodulation Society. January 22, 2008.
- Glass LS, Harris JS; American College of Occupational and Environmental Medicine (ACOEM). *Occupational Medicine Practice Guidelines: Evaluation and Management of Common Health Problems and Functional Recovery of Workers, Second Edition*. OEM Press, Beverly Farms, 2004.
- Genovese E. "Evidence" versus "science" in practice guidelines. *APG Insights* 2007; 3:1-12.
- Letter to Robert K. McLellan, MD, President of the American College of Occupational & Environmental Medicine (ACOEM) from the Honorable Bart Stupak and Ed Whitfield, US House of Representatives, January 25, 2008.
- Response Letter from Robert K. McLellan, MD, President of the American College of Occupational & Environmental Medicine (ACOEM) to the Honorable Bart Stupak and Ed Whitfield, US House of Representatives, February 5, 2008.
- Response Letter from Robert K. McLellan, MD, President of the American College of Occupational & Environmental Medicine (ACOEM) to Todd Sitzman, MD, MPH, President, American Academy of Pain Medicine; Andrea Trescot, MD, President, American Society of Interventional Pain Physicians; Milton Landers, DO, PHD, President, International Spine Intervention Society; Jamie Henderson, MD, President, North American Neuromodulation Society; and Joshua Prager, MD, Past President, North American Neuromodulation Society. February 19, 2008.
- Boswell MV, Trescot AM, Datta S, Schultz DM, Hansen HC, Abdi S, Sehgal N, Shah RV, Singh V, Benyamin RM, Patel VB, Buenaventura RM, Colson JD, Corder HJ, Epter RS, Jasper JF, Dunbar EE, Atluri SL, Bowman RC, Deer TR, Swicegood JR, Staats PS, Smith HS, Burton AW, Kloth DS, Giordano J, Manchikanti L. Interventional techniques: Evidence-based practice guidelines in the management of chronic spinal pain. *Pain Physician* 2007; 10:7-111.
- West S, King V, Carey TS, Lohr KN, McKay N, Sutton SF, Lux L. *Systems to Rate the Strength of Scientific Evidence*, Evidence Report, Technology Assessment No. 47. AHRQ Publication No. 02-E016. Rockville, MD: Agency for Health-

- care Research and Quality, 2002. www.thecre.com/pdf/ahrq-system-strength.pdf
15. Manchikanti L. Evidence-based interventional pain medicine: Is there any evidence? *Pain Physician* 2002; 5:1-7.
 16. Manchikanti L, Abdi S, Lucas LF. Evidence synthesis and development of guidelines in interventional pain management. *Pain Physician* 2005; 8:73-86.
 17. Manchikanti L, Heavner J, Racz GB, Mekhail NA, Schultz DM, Hansen HC, Singh V. Methods for evidence synthesis in interventional pain management. *Pain Physician* 2003; 6:89-111.
 18. Manchikanti L. Evidence-based medicine, systematic reviews, and guidelines in interventional pain management: Part I: Introduction and general considerations. *Pain Physician* 2008; 11:161-186.
 19. Trescot AM, Helm S, Hansen H, Benjamin R, Adlaka R, Patel S, Manchikanti L. Opioids in the management of chronic non-cancer pain: An update of American Society of Interventional Pain Physicians' (ASIPP) Guidelines. *Pain Physician* 2008; 11:S5-S62.
 20. Manchikanti L, Staats PS, Singh V, Schultz DM, Vilims BD, Jasper JF, Kloth DS, Trescot AM, Hansen HC, Falasca TD, Racz GB, Deer T, Burton AW, Helm S, Lou L, Bakhit CE, Dunbar EE, Atluri SL, Calodney AK, Hassenbusch S, Feler CA. Evidence-based practice guidelines for interventional techniques in the management of chronic spinal pain. *Pain Physician* 2003; 6:3-80.
 21. Boswell MV, Shah RV, Everett CR, Sehgal N, McKenzie-Brown AM, Abdi S, Bowman RC, Deer TR, Datta S, Colson JD, Spillane WF, Smith HS, Lucas-Levin LF, Burton AW, Chopra P, Staats PS, Wasserman RA, Manchikanti L. Interventional techniques in the management of chronic spinal pain: Evidence-based practice guidelines. *Pain Physician* 2005; 8:1-47.
 22. Trescot AT, Boswell MV, Alturi SL, Hansen HC, Deer TR, Abdi S, Jasper JF, Singh V, Jordan AE, Johnson BW, Cicala RS, Dunbar EE, Helm S, Varley KG, Suchdev PK, Swicegood JR, Calodney AK, Ogoke BA, Minore WS, Manchikanti L. Opioid guidelines in the management of chronic non-cancer pain. *Pain Physician* 2006; 9:1-40.
 23. Bigos SJ, Boyer OR, Braen GR, Brown K, Deyo R, Haldeman S, Hart JL, Johnson EW, Keller R, Kido D, Liang MH, Nelson RM, Nordin M, Owen BD, Pope MH, Schwartz RK, Stewart DH, Susman J, Triano JJ, Tripp LC, Turk DC, Watts C, Weinstein JN. Acute low back problems in adults. Clinical Practice Guideline No. 14, AHCPR Publication No. 95-0642. Rockville, Maryland. U.S.A., Agency for Health Care Policy and Research, Public Health Service, U.S., Department of Health and Human Services, December, 1994; pp 1-60.
 24. Cates JR, Young DN, Guerriero DJ, Jahn WT, Armine JP, Korbett AB, Bowerman DS, Porter RC, Sandman TD, King RA. Evaluating the quality of clinical practice guidelines. *J Manipulative Physiol Ther* 2001; 24:170-176.
 25. van Tulder MW, Tuut M, Pennick V, Bombardier C, Assendelft W. Quality of primary care guidelines for acute low back pain. *Spine* 2004; 29:E357-E362.
 26. Cates JR, Young DN, Bowerman DS, Porter RC. An independent AGREE evaluation of the *Occupational Medicine Practice Guidelines*. *Spine J* 2006; 6:72-77.
 27. Helm S. California workers' compensation system: Are occupational medicine practice guidelines sufficient for the treatment of chronic spinal pain or do they require supplementation by guidelines for interventional techniques? *Pain Physician* 2004; 7:229-238.
 28. Oxman AD, Cook DJ, Guyatt GH. Users' guide to the medical literature. VI. How to use an overview. Evidence Based Medicine Working Group. *JAMA* 1994; 272:1367-1371.
 29. Oxman AD, Schünemann HJ, Fretheim A. Improving the use of research evidence in guideline development: 8. Synthesis and presentation of evidence. *Health Res Policy Syst* 2006; 4:20.
 30. Oxman AD. Systematic reviews: Checklists for review articles. *BMJ* 1994; 309:648-651.
 31. Shaneyfelt TM, Mayo-Smith MF, Rothwangl J. Are guidelines following guidelines? The methodological quality of clinical practice guidelines in the peer reviewed medical literature. *JAMA* 1999; 281:1900-1905.
 32. Hayward R, Wilson M, Tunis S, Bass E, Guyatt G. Users' guides to the medical literature. VIII. How to use clinical practice guidelines. *JAMA* 1995; 274:570-574.
 33. Cluzeau FA, Burgers JS, Brouwers M, Grol R, Makela M, Littlejohns P, Grimshaw J, Hunt C, Asua J, Bataillard A, Browman G, Burnand B, Durieux P, Fervers B, Grilli R, Hanna S, Have P, Jovell A, Klazinga N, Kristensen F, Madsen PB, Miller J, Ollenschlaeger G, Qureshi S, Rico-Iturroz R, Vader J-P, Zaat J. 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.
 34. Thomason M, Cluzeau F, Littlejohns P, Ollenschlaeger G, Grilli R, Rico-Iturroz R, Grol R, Burgers J, Kristensen FB, Palmhoj-Nielsen C, Fervers B, Jovell A, Moran S, Grimshaw J, Burnand B, Klazinga N, Ten Have P, Durieux P, Miller J, Feder G, Makela M. Guideline development in Europe: An international comparison. *Int J Technol Assess Health Care* 2000; 16:1039-1049.
 35. AGREE Collaboration (Appraisal of Guidelines, Research, and Evaluation in Europe [AGREE] Collaborative Group). Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument, September 2001.
 36. Hasenfeld R, Shekelle PG. Is the methodological quality of guidelines declining in the US? Comparison of the quality of US Agency for Health Care Policy and research (AHCPR) guidelines with those published subsequently. *Qual Saf Health Care* 2003; 12:428-434.
 37. Grol R, Cluzeau FA, Burgers JS. Clinical practice guidelines: Towards better quality guidelines and increased international collaboration. *Br J Cancer* 2003; 89:S4-S8.
 38. Burgers JS, Fervers B, Haugh M, Brouwers M, Browman G, Philip T, Cluzea FA. International assessment of the quality of clinical practice guidelines in oncology using the Appraisal of Guidelines and Research and Evaluation Instrument. *J Clin Oncol* 2004; 22:2000-2007.
 39. AGREE Collaboration (Appraisal of Guidelines, Research, and Evaluation in Europe [AGREE] Collaborative Group). Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument Training Manual. January 2003.
 40. Nuckols TK, Winn BO, Lim Y-W, Shaw RN, Mattke S, Wickizer T, Harber P, Wallace P, Asch SM, MacLean C, Garland RH. Evaluating medical treatment

- guideline sets for injured workers in California. RAND Corporation. Institute for Civil Justice and RAND Health. www.rand.org/pubs/monographs/2005/RAND_MG400.pdf
41. Staal JB, Hlobil H, van Tulder MW, Waddell G, Burton AK, Koes BW, van Mechelen W. Occupational health guidelines for the management of low back pain: An international comparison. *Occup Environ Med* 2003; 60:618-626.
 42. Harris JS. Development, use, and evaluation of clinical practice guidelines. *J Occupa Environ Med/Am College Occupa Environ Med* 1997; 39:23-34.
 43. Ladou J, Teitelbaum DT, Egilman DS, Frank AL, Kramer SN, Huff J. American College of Occupational and Environmental Medicine (ACOEM): A professional association in service to industry. *Int J Occup Environ Health* 2007; 13:404-426.
 44. A guide to the development, implementation and evaluation of clinical practice guidelines. National Health and Medical Research Council, Canberra, Commonwealth of Australia, 1998, pp 1-79.
 45. Schünemann HJ, Fretheim A, Oxman AD, WHO Advisory Committee on Health Research. Improving the use of research evidence in guideline development: 1. Guidelines for guidelines. *Health Res Policy Syst* 2006; 4:13.
 46. Institute of Medicine, Committee on Quality of Health Care in America. Crossing the Quality Chasm: A New Health System for the 21st Century. National Academy Press, Washington, DC, 2001.
 47. American Medical Association, Office of Quality Assurance. *Attributes to Guide the Development and Evaluation of Practice Parameters*. American Medical Association, Chicago, 1990.
 48. Canadian Medical Association. *Quality of Care Program: The Guidelines for Canadian Clinical Practice Guidelines*. Canadian Medical Association, Ottawa, Ontario, 1993.
 49. Woolf SH. *Manual for Clinical Practice Guideline Development*. Rockville, MD. Agency for Health Care Policy and Research, AHCPR publication 91-0007, 1991.
 50. Manchikanti L, Singh V, Derby R, Staats PS, Hirsch JA. Reassessment of evidence synthesis of occupational medicine practice guidelines for interventional pain management. *Pain Physician* 2008; in press.
 51. Rautiainen RH, Ohsfeldt R, Sprince NL, Donham KJ, Burmeister LF, Reynolds SJ, Saarimaki P, Zweling C. Cost of compensated injuries and occupational diseases in agriculture in Finland. *J Agromedicine* 2005; 10:21-29.
 52. Haynes RB. What kind of evidence is it that evidence-based medicine advocates want health care providers and consumers to pay attention to? *BMC Health Serv Res* 2002; 2:3.
 53. Joint Position Statement: Updated ACOEM Chronic Pain and Low Back Guidelines from American Academy of Pain Medicine (AAPM), American Society of Interventional Pain Physicians (ASIPP), International Spine Intervention Society (ISIS), Neuromodulation Therapy Access Coalition (NTAC), and the North American Neuromodulation Society (NAMS). January 29, 2008.
 54. Jadad AR, Moher D, Klassen TP. Guides for reading and interpreting systematic reviews: II. How do the authors find the studies and assess their quality? *Arch Pediatr Adolesc Med* 1998; 152:812-817.
 55. Chalmers I, Dickersin K, Chalmers TC. Getting to grips with Archie Cochrane's agenda. *BMJ* 1992; 305:786-788.
 56. Haynes RB. Clinical review articles: Should be as scientific as the articles they review. *BMJ* 1992; 304:330-331.
 57. Peto R. Why do we need systematic overviews of randomized trials? *Stat Med* 1987; 6:233-240.
 58. Jadad AR, McQuay HJ. Searching the literature: Be systematic in your searching. *BMJ* 1993; 307:66.
 59. Dickersin K. The existence of publication bias and risk factors of its occurrence. *JAMA* 1990; 263:1385-1389.
 60. Hatala R, Guyatt G. Evaluating the teaching of evidence-based medicine. *JAMA* 2002; 288:1110-1112.
 61. Burgers JS, Cluzeau FA, Hanna SE, Hunt C, Grol R. Characteristics of high-quality guidelines: Evaluation of 86 clinical guidelines developed in ten European countries and Canada. *Int J Technol Assess Health Care* 2003; 19:148-157.
 62. Vergnenegre A. Clinical practice guidelines: A reader's guide. *Revue Des Maladies Respiratoires* 2003; 20:920-927.
 63. Lohr KN. Rating the evidence of scientific evidence: Relevance for quality improvement programs. *Int J Qual Health Care* 2004; 16:9-18.
 64. Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, Raskob G, Lewis SZ, Schünemann H. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians task force. *Chest* 2006; 129:174-181.
 65. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D, Hill S, Jaeschke R, Leng G, Liberati A, Magrini N, Mason J, Middleton P, Mrukowicz J, O'Connell D, Oxman AD, Phillips B, Schünemann HJ, Edejer TT, Varonen H, Vist GE, Williams JW Jr, Zaza S; GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ* 2004; 328:1490.
 66. www.guideline.gov/resources/guideline_resources.aspx
 67. The Agency for Healthcare Research and Quality, U.S. Preventive Services Task Force Guide to Clinical Preventive Services, Vol. 1, AHRQ Pub. No. 02-500.
 68. Oxman AD, Schünemann HJ, Fretheim A. Improving the use of research evidence in guideline development: 2. Priority setting. *Health Res Policy Syst* 2006; 4:14.
 69. Fretheim A, Schünemann HJ, Oxman AD. Improving the use of research evidence in guideline development: 3. Group composition and consultation process. *Health Res Policy Syst* 2006; 4:15.
 70. Boyd EA, Bero LA. Improving the use of research evidence in guideline development: 4. Managing conflicts of interest. *Health Res Policy Syst* 2006; 4:16.
 71. Fretheim A, Schünemann HJ, Oxman AD. Improving the use of research evidence in guideline development: 5. Group processes. *Health Res Policy Syst* 2006; 4:17.
 72. Schünemann HJ, Oxman AD, Fretheim A. Improving the use of research evidence in guideline development: 6. Determining which outcomes are important. *Health Res Policy Syst* 2006; 4:18.
 73. Oxman AD, Schünemann HJ, Fretheim A. Improving the use of research evidence in guideline development: 7. Deciding what evidence to include. *Health*

- Res Policy Syst* 2006; 4:19.
74. Schünemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 9. Grading evidence and recommendations. *Health Res Policy Syst* 2006; 4:21.
 75. Schünemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 10. Integrating values and consumer involvement. *Health Res Policy Syst* 2006; 4:22.
 76. Edejer TT. Improving the use of research evidence in guideline development: 11. Incorporating considerations of cost-effectiveness, affordability and resource implications. *Health Res Policy Syst* 2006; 4:23.
 77. Oxman AD, Schünemann HJ, Fretheim A. Improving the use of research evidence in guideline development: 12. Incorporating considerations of equity. *Health Res Policy Syst* 2006; 4:24.
 78. Schünemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 13. Applicability, transferability and adaptation. *Health Res Policy Syst* 2006; 4:25.
 79. Oxman AD, Schünemann HJ, Fretheim A. Improving the use of research evidence in guideline development: 14. Reporting guidelines. *Health Res Policy Syst* 2006; 4:26.
 80. Fretheim A, Schünemann HJ, Oxman AD. Improving the use of research evidence in guideline development: 15. Disseminating and implementing guidelines. *Health Res Policy Syst* 2006; 4:27.
 81. Oxman AD, Schünemann HJ, Fretheim A. Improving the use of research evidence in guideline development: 16. Evaluation. *Health Res Policy Syst* 2006; 4:28.
 82. Royle P, Waugh N. Literature searching for clinical and cost effectiveness studies used in health technology assessment reports carried out for the National Institute for Clinical Excellence appraisal system. *Health Technology Assessment* 2003, 7(34): www.ncchta.org/execsumm/summ734.htm.
 83. Gonzalez EG, Materson RS. The guidelines, the controversy, the book. In Gonzalez ER, Materson RS (eds). *The Nonsurgical Management of Acute Low Back Pain*. Demos Vermande, New York, 1997, pp 1-4.
 84. Barnes DE, Bero LA. Scientific quality of original research articles on environmental tobacco smoke. *Tob Control* 1997; 6:19-26.
 85. Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: A systematic review. *JAMA* 2003; 289:454-465.
 86. Cho MK, Bero LA. The quality of drug studies published in symposium proceedings. *Ann Intern Med* 1996; 124:485-489.
 87. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: Systematic review. *BMJ* 2003; 326:1167-1170.
 88. Wilson D, Heath D. He saw the tests as a violation of 'trusting desperate human beings.' In *The Seattle Times Seattle*; 2001.
 89. Wilson D, Heath D. Uninformed consent: They call the place Mother Hutch. In *The Seattle Times Seattle*; 2001.
 90. Dana J. Harm avoidance and financial conflict of interest. *J Med Ethics* 2003; Online Electronic Version: 1-18.
 91. Bero LA. Tobacco industry manipulation of research. *Public Health Rep* 2005; 120:200-208.
 92. Montori VM, Jaeschke R, Schunemann HJ, Bhandari M, Brozek JL, Devereaux PJ, Guyatt GH. Users' guide to detecting misleading claims in clinical research reports. *BMJ* 2004; 329:1093-1096.
 93. Friedman PJ. The impact of conflict of interest on trust in science. *Sci Eng Ethics* 2002; 8:413-420.
 94. Drazen JM, Koski G. To protect those who serve. *N Engl J Med* 2000, 343:1643-1645.
 95. Baltimore D. The worsening climate for biological research: Is the public losing faith in science? *Technol Review* 1989; 92:22.
 96. Haerlin B, Parr D. How to restore public trust in science. *Nature* 1999; 400:499.
 97. Cohen JJ. Trust us to make a difference: Ensuring public confidence in the integrity of clinical research. *Acad Med* 2001; 76:209-214.
 98. DeAngelis CD. Conflict of interest and the public interest. *JAMA* 2000; 284:2237-2238.