

## Health Policy Review

## Guidelines Warfare Over Interventional Techniques: Is There a Lack of Discourse or Straw Man?

Laxmaiah Manchikanti, MD<sup>1</sup>, Ramsin M. Benyamin, MD<sup>2</sup>, Frank J.E. Falco, MD<sup>3</sup>,  
David L. Caraway, MD<sup>4</sup>, Sukdeb Datta, MD<sup>5</sup>, and Joshua A. Hirsch, MD<sup>6</sup>

From: <sup>1</sup>Pain Management Center of Paducah, Paducah, KY, and University of Louisville, Louisville, KY; <sup>2</sup>Millennium Pain Center, Bloomington, IL; <sup>3</sup>Mid Atlantic Spine & Pain Physicians of Newark, Newark, DE; and Temple University Hospital, Philadelphia, PA; <sup>4</sup>St. Mary's Pain Relief Center, Huntington, WV; <sup>5</sup>Laser Spine & Pain Institute, New York, NY; and <sup>6</sup>Massachusetts General Hospital and Harvard Medical School, Boston, MA.

Dr. Manchikanti is Medical Director of the Pain Management Center of Paducah, Paducah, KY, and Associate Clinical Professor, Anesthesiology and Perioperative Medicine, University of Louisville, Louisville, KY.

Dr. Benyamin is the Medical Director, Millennium Pain Center, Bloomington, IL, Clinical Assistant Professor of Surgery, College of Medicine, University of Illinois, Urbana-Champaign, IL. Dr. Falco is Medical Director of the Mid Atlantic Spine & Pain Physicians of Newark, DE, Director, Pain Medicine Fellowship, Temple University Hospital, Philadelphia, PA, and Associate Professor, Department of PM&R, Temple University Medical School, Philadelphia, PA. Dr. Caraway, St. Mary's Pain Relief Center, Huntington, WV. Dr. Datta is Medical Director, Laser Spine & Pain Institute, New York, NY. Dr. Hirsch is Chief of Minimally Invasive Spine Surgery, Depts. of Radiology and Neurosurgery, Massachusetts General Hospital and Associate Professor of Radiology, Harvard Medical School, Boston, MA.

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

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Guideline development seems to have lost some of its grounding as a medical science. At their best, guidelines should be a constructive response to assist practicing physicians in applying the exponentially expanding body of medical knowledge. In fact, guideline development seems to be evolving into a cottage industry with multiple, frequently discordant guidance on the same subject. Evidence Based Medicine does not always provide for conclusive opinions. With competing interests of payers, practitioners, health policy makers, and third parties benefiting from development of the guidelines as cost saving measures, guideline preparation has been described as based on pre-possession, vagary, rationalization, or congeniality of conclusion.

Beyond legitimate differences in opinions regarding the evidence that could yield different guidelines there are potentials for conflicts of interest and various other issues play a major role in guideline development. As is always the case, conflicts of interest in guideline preparation must be evaluated and considered.

Following the development of American Pain Society (APS) guidelines there has been an uproar in interventional pain management communities on various issues related to not only the evidence synthesis, but conflicts of interest. A recent manuscript published by Chou et al, in addition to previous publications appear to have limited clinician involvement in the development of APS guidelines, demonstrates some of these challenges clearly.

This manuscript illustrates the deficiencies of Chou et al's criticisms, and demonstrates their significant conflicts of interest, and use a lack of appropriate evaluations in interventional pain management as a straw man to support their argument. Further, this review will attempt to demonstrate that excessive focus on this straw man has inhibited critique of what we believe to be flaws in the approach.

**Key words:** Guidelines, interventional pain management, professionalism, discourse, disclosure, conflicts of interest, evidence-based medicine, comparative effectiveness research, Patient-Centered Outcomes Research Institute

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**T**he critical review of American Pain Society (APS) clinical practice guidelines for interventional techniques (1,2) was published in response to APS guidelines by Chou and Huffman (3). The initial manuscript by Chou and Huffman (3) was followed by multiple publications (4-6) with the addition of multiple other authors in addition to Chou, but without Huffman. However, the critical review (1,2) of this manuscript (3) resulted in a barrage of criticism of the process of development of guidelines by the American Society of Interventional Pain Physicians (ASIPP) (7-13). Using this as an example, one could argue that evidence-based medicine (EBM), comparative effectiveness research (CER), and guideline development have become political science rather than medical science evolving into out of control cottage industries (14-38). The unfortunate result is that guideline development may no longer be a constructive response to assist practicing physicians into assimilating and applying the exponentially expanding, often contradicting, body of medical knowledge (14-61). Clinical practice guidelines attempt to define practices that meet the needs of most patients under most circumstances without supplanting the independent judgement of clinicians in responding to particular situations (15). Ideally, the specific clinical recommendations that are contained within the practice guidelines have been systematically developed by panels of experts who have access to the available evidence, have an understanding of the clinical problem, have clinical experience with a subject procedure, disclose any financial conflicts of interest, and have the relevant research methods to make considered judgements. These panels should consist of clinicians and methodologists. While the viewpoint of these 2 groups are potentially disparate they are not irreconcilable. Methodologists attempt to focus on the methodology more than the clinical problem or intervention itself. Methodologists appear to enjoy the perception of having limited opportunity for conflicts of interest. Clinicians, focus primarily on the diagnosis and treatment of problems. Because the clinicians may perform the intervention, there may be a perception of greater possibility of conflict of interest. Both groups must be objective and produce recommendations that are unbiased, up-to-date, and free from conflicts of interest. When these principles are followed guidelines are widely perceived as evidence-based, rather than authority-based, and therefore unbiased and valid (16).

This manuscript has been developed in response to so-called guideline warfare over interventional tech-

niques in low back pain. Chou et al (13) claimed that discourse needs to be raised. Indeed, we agree. However, we perceive the continued badgering on these issues is not based on either professionalism or EBM. It seems clear that Chou et al are using the lack of appropriate evaluations in interventional pain management as a straw man to support their arguments. Essentially authors try to promote their own view of inaccurate assessment in an effort to change the focus from legitimate critiques of seeming deficiencies in their evaluation. This review will attempt to demonstrate that excessive focus on this straw man has inhibited critique of the flawed approach and hazards associated with EBM. EBM and methodologists would be best served removing the straw man and modifying their perspective to meet the clinical criteria.

We don't use the term straw man casually or accidentally. We believe it to be a relevant concept in understanding the challenges that are associated with the critical analysis of guidelines. The straw man fallacy occurs by various means. One of them being presenting a best representation of the opponent's position or quoting an opponents word's out of context – i.e., choosing quotations that misrepresent the opponent's actual interventions or ignoring the information provided by the opponent or oversimplifying an opponent's argument, then attacking this oversimplified version. This reasoning is considered fallacious, because attacking a distorted version of a position fails to constitute an attack on the actual position. By the same token, attacking the facts which have been already admitted is also fallacious.

This manuscript will focus on not only Chou et al's criticism with regards to professionalism, but also the hazards of evolving concepts of EBM in interventional pain management. Edward Bulwer-Lytton, a British philosopher, who stated that "art and science have their meeting point in method," thus, methodology can bring art and science together, or can destroy both of them.

## **1.0 EVIDENCE-BASED MEDICINE AND COMPARATIVE EFFECTIVENESS RESEARCH**

EBM, CER, and clinical guidelines are experiencing an exponential growth, not only in terms of publications, but also in terms of funding. (1-61). With disagreements in the evidentiary bases of certain treatment, with competing interests of payers, practitioners, health policy makers, and third parties benefiting from development of the guidelines as cost saving measures,

guideline preparation has been described as based on pre-possession, vagary, rationalization, or congeniality of conclusion. Yamey and Feachem (57) described evidence-based policy making in global health with a quote that, “the good news is that evidence can matter. The bad news is that it often does not.”

A pre-possession is defined as the mental phenomenon whereby, when we seek the evidence of our pre-conceptions, we find it. In contrast, vagary is defined as the obsessive pursuit of a particular conclusion, decided upon early, whatever the contrary evidence. Rationalization is the intellectual art of piecing together valid evidence in such a way as to produce an invalid conclusion. Finally, congeniality of conclusion is whereby we reach the conclusion we like rather than the one dictated by evidence and logic.

EBM and CER, the cornerstones of guideline development, have taken center stage with enactment of the Affordable Care Act (ACA) in press, but not in practice (14,17,22,39,62). In fact, the supporters of the Patient-Centered Outcomes Research Institute (PCORI) tout its advantages and components including the methodologic committee (14,22-24,44-46). The supporters of PCORI, which may be translated to EBM and guidelines, believe that the research could educate patients and help them make better medical decisions. While it is true that PCORI could foster patient education and benefit patients and doctors, in a 2008 Congressional Budget Office (CBO) report, it was stated that CER would gradually generate modest changes in medical practices, the net effect of which would be to reduce the total spending on health care in the United States, by an estimated \$8 billion from 2010 to 2019 or essentially by less than one-tenth of 1% (63). However, this estimation is without taking into account the majority of the regulatory costs and bureaucratic oversight on the practice of medicine, which will translate into a negative result (14,17-20,39,62,64-66). Further, President Obama has promised CER won't lead to rationing. In contrast, Donald Berwick, MD, the outgoing Administrator of the Centers for Medicare and Medicaid Services (CMS), has expressed lavish praise for the National Institute for Health and Clinical Excellence (NICE) and its restrictions on care (67).

While the proponents of EBM state that every intervention must be based on EBM and CER, it is not just applied to either federal regulations or synthesis of evidence itself (14,22-25,44-48). In the modern environment the potential harm from EBM and CER depends on how the research is used, which could easily quell medical innovation by centralizing care (30,49,50,53,56-59).

It is always feared that officials seeking to control costs would use this research to restrict access to more costly medical interventions as done by NICE extensively supported by EBM methodologists (31-38,49,68-72).

It is well-known that clinicians can be overwhelmed by the quantity of reported evidence, and often need to rely on aggregated experience to guide decision-making. However, it is also essential to understand how this evidence has been synthesized and what guidance has been provided. After spending millions of dollars, the Institute of Medicine (IOM) recommended 21 standards for systematic reviews and 8 for guidelines(22,73). In fact, many of the same investigators and agencies have provided the same or similar guidelines with previous failures such as the Agency for Health Care Policy and Research (AHCPR) and the Agency for Healthcare Research and Quality (AHRQ) (27-29,74). These factors have led to numerous publications, regulations, and organizations with ever-evolving concepts increasing the costs of implementation in an ad-hoc manner, essentially creating ideal conditions for a perfect storm in health care with exploding costs, declining reimbursements, and increasing regulations leading to a reduction in quality and access (1,2,14,17,21,41,64-66,75-77).

## **2.0 EVIDENCE-BASED MEDICINE VERSUS EXPERIENCE-BASED MEDICINE**

In an editorial in *Spine*, Croft et al (78) described that in a debate “Evidence-Based Medicine: Savior or Pariah,” “evidence-based medicine made it as savior but it was close.” EBM conveys the idea that up-to-date evidence can be applied consistently in clinical practice, in combination with the clinician's individual expertise and the patient's own preferences and expectations to achieve the best possible outcomes. EBM has become widely disseminated among medical practitioners since the 1990s, which by some is regarded as a major advance in medico-scientific thinking (79,80). However, as scientists expect, even though 20 years have elapsed, the benefits of EBM have not materialized for numerous conditions including spinal pain. For many common ailments, the benefits are only clear for a small proportion of patients. For example, with myocardial infarction and beta-blockers (81), a large proportion of patients remain in poor control despite excellent evidence guiding management and treatment. For two-thirds of Americans with diabetes and half of those with hypertension – conditions with strong evidence-based guidelines – these conditions are inadequately controlled (82,83).

Clinical proponents of EBM have emphasized the range of evidence that can be used in clinical decision-making (84,85). However, since evidence can apply to any observation, proponents could argue that there is always evidence, even if it is clinical experience without research data (86). Consequently, EBM may essentially mean experience-based medicine.

EBM has focused on randomized controlled trials (RCTs) dogmatically refusing to acknowledge other sources of valid data about outcome interventions (87). Evidence on effectiveness from non-randomized observational studies may be utilized if RCT evidence is unavailable. Grading of Recommendations Assessment, Development and Evaluation (GRADE) (88,89) has been recommended by the Cochrane Collaboration (90). Even though this evidence starts as high quality evidence it may be lowered even to very low quality evidence if there are deficiencies in validity or precision, inconsistencies in outcomes, indirectness of evidence, or publication bias. In contrast, observational evidence starts as low quality evidence, but may rise to the highest level if there are factors strengthening the evidence (strong association dose-response effect, or confounding that underestimates effectiveness) and no factors diluting or reducing it (91). However, methodologists or clinicians who are not aware of clinical aspects and biased clinicians with their own interjections have changed this concept.

Some of the major interventions accepted without RCT evidence include insulin for diabetes, suturing for large wounds, and defibrillation for ventricular fibrillation (92). Consequently, strong observational alternatives are needed to counter the impossibility of experimentally randomizing every component of interventions and translating the results into every day practice. Active control trials are a good example. Even though these represent clear alternatives, there are those that continue to ignore these essential elements (1-3,13,65-67,93-121). Consequently, in the field of interventional pain management a straw man has been created which points to the deficiencies of existing non-RCT evidence.

While all clinicians accept that EBM is useful and that practice should be supported by adequate research evidence, its assessment and finally implementation in clinical practice is a major challenge. It has been illustrated that implementation of any guidelines is difficult (122). By way of example, general practitioners in the Netherlands have more than 90 clinical guidelines; many neither read nor use them (78). Simi-

larly, German general practitioners know about and agree with the content of back pain guidelines, but view an excessive number of information sources as a barrier to engagement with guidelines in practice (123). The guidelines may be improved if appropriate representation for clinical practitioners is provided in the guideline preparation and methodologists are willing to accept the input from clinicians with elimination of bias from both sides.

Croft et al (78) described the complexity of clinical practice which is not limited to implementation, but lies in the very nature of clinical practice. As an example, if a patient visits a physician for chronic low back pain complicated with work absence, depression, and opioid dependence, there are no guidelines to manage such a patient. Cochrane Collaboration reviews and numerous other guidelines evaluate only single interventions and provide specific care patterns (3,97-101,124,125). Consequently, the physician needs to be familiar with the results of all relevant reviews and treatments for low back pain and depression in any type of setting, considering that multitude of these guidelines may not be applicable clinically and there may be substantial contradictions and bias based on the developer(s). Further, in practice, a patient will often be offered multiple interventions within the multimodal treatment program. Patients with multiple comorbid conditions might be thought to be less likely to receive quality care of the basis of multiple guidelines, evidence contradicts this assumption and suggests that in practice they might receive better care (126).

Further, research mainly tends to focus on treatment rather than diagnosis, thus, most evidence used to support recommendations in clinical guidelines concerns therapeutic interventions (101), and evidence for recommendations about prognosis and diagnosis is often weak (1-3,97-101,127). Single diagnostic tests are evaluated whereas in a clinical practice multiple tests are utilized. As an EBM trend, experts in this field are utilizing improperly evaluated diagnostic tests to discredit any therapeutic intervention.

In general, it has been stated that there is evidence from a range of countries and settings that use of EBM by practicing clinicians is restricted more by perceived lack of time, skills, and knowledge to apply in practice than by skepticism about concept itself (128,129). However, in practice, these issues may not be as important as the diversity of the guidelines, conflicts of interest, and the bias interjected into these reviews.

Most trials in managing low back pain, specifically in primary care, including systematic reviews, often conclude that the trials are not good enough or that effect sizes in those of reasonable quality are too small to be of much help. The same applies for interventional techniques. Thus, clinicians may feel that guidelines do not help in their decision-making when they are developed by parties with substantial bias (14,65,66,97-101), whereas the guidelines developed by practitioners, though sometimes contradictory, are not accepted by policy makers.

By contrived means guideline developers may interject their own bias, perform inappropriate evaluations, and conclude that the studies are of poor quality or the effect size is too small. However, the small effect sizes are fractional extra effects or overall improvements. They are alleged to reflect the favorable natural course of the condition, explained in part by the placebo effect of talking with the clinician or confident optimistic therapist, or more precisely the context effect, which is highly valued by patients. But, these positive effects are ignored by methodologists along with nocebo effects of randomized trials, the nocebo effects in practice with failure to recognize the true placebo versus theoretical placebo (130-137).

Major criticism continues to be generalizability of the results. While uniformity in clinical practice is encouraged on the basis of average results taken from populations included in randomized trials and systematic reviews, it is ignored that these randomized trials were conducted in highly specialized settings and systematic reviews tend to include only randomized trials. Consequently, populations in clinical practice are heterogeneous and individual treatments are a necessity. Thus, practical clinical research may fit this criteria to a certain extent, however, these are treated as low quality evidence, misevaluated by methodologists and others with self-interest (1-3,13,65-67,97-121). While EBM emphasizes the need to evaluate the generalizability of research evidence for application to individuals, there is very little evidence to that effect in practice.

It has been stated that evidence alone is never sufficient to make a clinical decision (78). Further, even if the evidence is clear, individuals vary in how they weigh benefits and risks. The final decision is influenced by clinicians' and patients' values, preferences, and expectations and the inconvenience, availability, and costs of the treatment.

### **3.0 HAZARDS OF EVIDENCE-BASED MEDICINE**

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Based on the above descriptions, there is substantial conflict in the development of EBM. Thus, EBM may be hazardous to medicine equally as it is beneficial, unless proper methodologies are developed and bias and conflicts of interest are eliminated.

In an editorial Livingston and McNutt (30) described the hazards of EBM. They describe shortfalls in assessment of variations in care utilizing quality of care, using measures of process of care, such as Medicare's 25 quality metrics (138). It has been long thought that adherence to these processes lead to improved outcomes. One of the examples is the Surgical Care Improvement Project which was introduced in 2006, with a goal of reducing surgical complications by 25% by 2010 (139). Based on observational studies demonstrating associations between process and outcomes, experts concluded that adherence to this series of process measures would result in better care. Consequently, Medicare adopted these and published them on its Hospital Compare Website (138) as measures of hospital quality. However, for some process measures, studies have shown that adherence to these measures is not necessarily associated with improved outcomes, which has been the case for perioperative antibiotic use and post-operative wound infection (140), and for acute myocardial infarction, heart failure, and pneumonia (141). However, more worrisome is that in some cases, adherence to the prescribed process measures may be associated with considerable harm, such as with tight glucose control in critically ill patients (142). Thus, quality of care as determined by process measures penalized some systems for their alleged poor performance and rewarded others for alleged better performance, is flawed (143,144). Thus, Livingston and McNutt (30) concluded that without an assessment of hard, irrefutable measures of clinical decision-making that include individual preferences for treatment, decisions about the appropriateness of clinical treatment and variations of care cannot be made.

Numerous examples of hazards include effects of care coordination on hospitalization, quality of care, and health care expenditures among Medicare beneficiaries. In an evaluation of 15 randomized trials, Peikes et al (145) concluded that viable care coordination programs without a strong transitional care component are unlikely to yield net Medicare savings. Programs with substantial in-person contact that target moderate to severe patients can be cost neutral and may im-

prove some aspects of care, which is in contrast to the estimations that care coordination will reduce health care expenditures and improve care, patient adherence, and communication. Rauh et al (146) discussed various issues related to the savings illusion and why clinical quality improvement fails to deliver bottom-line results. While it has become a core brief in U.S. health care that improving clinical quality will reduce health care costs, true bottom-line savings from improved clinical quality rarely materialize, and costs continue to climb.

Many health advocacy organizations in a recent IOM survey contended that EBM should serve merely as an aid in medical decision-making, not as the basis for it (147). Thus, it is not only an issue for health care spending, but leads to doctors' dilemmas in deciding what is "appropriate" care. Fuchs (148) describes that most physicians want to deliver appropriate and ethical care, but the transformation of a small-scale professional service into a technologically complex sector makes it increasingly difficult to know what is "appropriate" and what is "ethical." The quest for eliminating unnecessary care and controlling health care costs, and empowerment of insurers is resulting in denial of access to appropriate ethical and necessary care.

Well publicized outrage following mammography guidelines is an example of unintended consequences of guidelines (149-158). Review of risk prediction models for hospital readmission (159), illustrated that most current readmission risk prediction models that were designed for either comparative or clinical purposes performed poorly. The significant increase in the risk of prostate cancer among healthy men with Vitamin E and guidelines issued by AHRQ recommending against prostate-specific antigen (PSA) screening have been a focus of discussions and at times outrage (160-168).

A study sponsored by the National Heart, Lung, and Blood Institute (NHLBI) (169) showed that in 2 behavioral interventions, one delivered with in-person support and the other delivered remotely, without face-to-face contact between participants and weight loss coaches, obese patients achieved and sustained clinically significant weight loss over a period of 24 months. In another 2-year randomized trial funded by NHLBI of obesity treatment in primary care practice (170), results illustrated that enhanced weight loss counseling helps about only one-third of obese patients achieve long-term. Unfortunately, several components of the new guidelines (171) lack scientific foundation. In fact, the 35% limit on calories from fat may inadver-

tently undermine the quality of federally funded nutrition programs. Further, the new focus on reducing solid fats and added sugar could be confusing to many consumers. Even though adulthood obesity has been established as a risk factor for cardiovascular disorders (172,173), unexpectedly, the NHLBI recommended cholesterol testing for kids (174).

As illustrated above, interventional pain management is not alone in facing guideline challenges. There are substantial controversies in cardiology. The joint cardiovascular practice guidelines of the American College of Cardiology (ACC) and American Heart Association (AHA) have become important documents for guiding cardiology practice and establishing benchmarks for quality of care (175,176). However, evaluation of the scientific evidence underlying their clinical practice guidelines showed that the recommendations they issued are largely developed from lower levels of evidence or expert opinion. Further, the proportion of recommendations for which there is no conclusive evidence also seems to be growing. It was noted that these findings highlight the need to improve the process of writing guidelines and to expand the evidence base from which clinical practice guidelines are derived (176). In addition, in a summary of systematic reviews conducted for the United States Preventive Services Task Force (USPSTF) on emerging risk factors for coronary artery disease (177), authors concluded that the evidence does not support the routine use of any of the 9 risk factors for further risk stratification.

Mandatory human papilloma virus (HPV) vaccination and political as well as scientific debate continues, even though vaccinations are among the most cost-effective and widely used public health interventions (178,179).

While mammography has been restricted, the new literature shows the relationship between alcohol and the risk of breast cancer even in healthy persons with moderate drinking patterns (180,181). This is in contrast to the numerous advantages described with moderate alcohol consumption to benefit cardiovascular health (182-186).

In the Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer randomized trial (187), it was illustrated that the annual screening with chest radiograph did not reduce lung cancer mortality compared with the usual care. However, in another study, the National Lung Screening Trial (NLST) (188) found that the annual low-dose computed tomography (CT) reduced lung cancer mortality by 20% relative to annual chest

radiography. Thus, clinicians may be confused that screening with low-dose CT reduces lung cancer mortality by 20% relative to no screening, whereas chest radiographs do not reduce mortality. Even though, the evaluation by CT convincingly showed that the earlier detection lowers the risk of death from lung cancer, no one knows how that evidence will translate into policy and practice, as CT scanning would be expensive and associated with more significant radiation exposure than chest radiography, potentially resulting in 29,000 cases of cancer with estimated 15,000 deaths annually (189-193).

There are also questions with regards to restriction of salt intake, a subject which has been considered to be non-controversial (194-200) with continued debate and controversial recommendations from one group compared to the other. A 2011 urinary sodium and potassium excretion and risk of cardiovascular events study (194) alluded to the World Health Organization's (WHO) recommendations of a sodium intake of < 2 gm per day, a level that is largely based on projections made from relatively small and short-term clinical trials evaluating the effects of sodium restriction on blood pressure in primary prevention populations. However, findings from prospective cohort studies, evaluating the association between sodium intake and cardiovascular events, have been rather conflicting. Some studies have reported a positive association between sodium intake and cardiovascular mortality (201-203), others have not (204-206), and some have reported an inverse association (207,208). The study by O'Donnell et al (194) concluded that the association between estimated sodium excretion and cardiovascular events was J-shaped. They showed that compared with baseline sodium excretion of 4 to 5.9 gm per day, sodium excretion of > 7 gm per day was associated with an increased risk of all cardiovascular events, and a sodium excretion of < 3 gm per day was associated with increased risk of cardiovascular mortality and hospitalization for congestive heart failure (CHF). Thus, it is important that a safe range for sodium intake be established by means of RCTs. A simple issue of salt intake clearly illustrates the known and unknown hazards of so-called guidelines based on EBM, but with limitations in evidence.

Simple issues such as infection control during surgical procedures, preoperative fasting, and discontinuation of antithrombotics prior to interventions continue to be debated based on inadequate evidence (21,209,210). In addition, illustrating the practice pat-

terns, it was shown the Cleveland Clinic's "top tests for 2012" clashed with many guidelines (211). Thus, for regulators and insurers, numerous regulations and regulatory bodies have been enacted in the arena of the practice of medicine which include PCORI (14), patient effectiveness research programs, Independent Payment Advisory Board (IPAB) (40), infection control measures (14,21,75), and impending implementation of ICD-10 and regulations related to electronic medical record (EMR) systems (20,64).

Further, it is not only the question of hazards of EBM based on the lack of irrefutable evidence and final regulations, but also conflicts of interest and various other issues that play a major role in guideline development (1-3,14-16,27-33,36-38,49,65-67). However, the agencies, organizations, and individuals monitoring and describing the conflicts and controversies may themselves have issues. Further, in the development of regulations, it is not a common practice to look at the benefits derived by the recommending organizations and their industry relationships, the relationships among the agencies which failed to look at the actual evidence such as the Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), and CMS, and finally the cottage industry of organizations of evidence medicine development, whose revenues depend on contributions from one or the other type of industry. As a fundamental example it bears pointing out that, the advantages of multiple regulations and their impact on medicine, utilizing either the principles of EBM or CER, as established by the IOM (29) and AHRQ have not been proven (1,2,14,26-38,65,66,74,212).

#### **4.0 APS GUIDELINES AND CRITICAL ANALYSIS**

The APS developed and published guidelines in managing low back pain resulting in multiple publications (3-6,213-216). The American College of Occupational and Environmental Medicine (ACOEM) (98) and the Official Disability Guidelines (ODG) (99) also have published their own guidelines. There are numerous other guidelines available, including those from ASIPP (100), and American Society of Anesthesiologist (ASA) and American Society of Regional Anesthesia and Pain Medicine (ASRA) (101). However, all the guidelines come to different conclusions. ASIPP guidelines were developed based on an extensive search and review of the literature, including development of systematic reviews and quality assessment of individual articles (100).

However, APS guidelines were based on 2 documents prepared by 2 individuals, with one physician (non-pain and non-interventional pain physician) and a marriage and family therapist (3,125). There were no published systematic reviews associated with the ASA and ASRA guidelines (101). The ACOEM and ODG guidelines claim that the entire guideline development is based on the principles of EBM and were developed with strict adherence to principles of EBM including the newly published IOM guidelines.

Following the development of ACOEM and APS guidelines, there was substantial uproar in interventional pain management communities related to not only the evidence synthesis, but potential conflicts of interest. Our group published a critical analysis of the ACOEM and APS guidelines. (1,2,102). Following the analysis, extensive criticism has been carried out with multiple letters (9,10,103,217-220) and a recent manuscript published by Chou et al (13). Our group submitted a letter for publication to Journal of Pain of APS which was rejected (220). In critical evaluation it seems that Chou's letter (8) failed to meet the criteria of the journal for letters to the editor based on for example length, was published. Thus, Chou et al (8,13) and Spectrum Research (11) continue to seemingly battle a straw man working on misinformation that has ultimately been provided by those same groups. We continue to question the seeming conflict of interest that has thus far not been acknowledged.

Critical review of APS guidelines (3) by Manchikanti et al (1,2) concerned significant methodologic issues which, in turn, raised concerns about transparency, accountability, consistency, and independence. Following this, Chou et al published extensive letters to the editor (8,103) which was also accompanied by a long response (9,10). Insurers, as well as the professional evidence-based guideline makers (11) have embraced Chou's response and ignored the critical analysis performed (12,220). The full manuscript published by Chou et al (13), which continues to ignore the questions raised with reverse criticism. They state that they show that the ASIPP critiques contain numerous errors and fail to adhere to scientific standards for reviewing evidence, and provide suggestions on how future disputes regarding guidelines might be addressed in a more constructive manner. The first paragraph of this manuscript states that APS found insufficient evidence to make recommendations for most interventional procedures (3). However, with similar levels of evidence, APS makes recommendations to use opioids (125). Further, Chou et al

(13) contend that ASIPP has published guidelines (100) recommending most interventional therapies. Finally, they state that they illustrate that ASIPP critiques fall short of providing accurate information and adhering to rigorous scientific standards. We posit that a solution to resolving differences might be to answer the appropriate questions by providing accurate information.

It is essential to develop clinical guidelines, defined as a body of evidence regarding safety, effectiveness, appropriate indications, cost-effectiveness, and other attributes of medical care (65,66). Further, researchers, clinicians, professional organizations, and governments should recognize that the value of evidence is only as good as the type of evidence reviewed, the methodology utilized, the knowledge and experience of the reviews, and many other factors, including bias, self-interest, and economics (1). A formal set of rules must complement medical training and common sense for clinicians to interpret the results of clinical research effectively (85,221,222). , knowing the tools of evidence-based practice methodology is necessary, but not sufficient, for delivering the highest quality patient care. The clinical guidelines panel must incorporate not only the methodologists, but also the clinicians who actually practice medicine and are experts in the technique being reviewed.

In addition, conflicts of interest in guideline development and inappropriate methodologies have been questioned (1-17,21,27-38,65,66,97-103,125). The controversial issues surrounding practice guidelines development and the evidence utilized in those guidelines are not limited to interventional pain management. (1-3,14,30,65,66,75,138-200,223-230).

Croft et al (78) described conflicts of interest, in essence EBM as an industry. Examples quoted include that there are more reviews than original RCTs on manipulation for low back pain and neck pain (231,232). Many are claimed to have been conducted by professional groups who may have an interest, explicitly stated or not, conscious or unconscious, in showing that spinal manipulation is effective. However, evidence about behavior treatment for chronic low back pain shows a small difference over wait list controls, but none compared with other interventions (233), yet, this weak finding was used to promote behavioral treatment in a majority of the guidelines. Many guidelines, including the subject of this manuscript (3), however, when the evidence is synthesized for interventional techniques, multiple biases from policy makers, insurers, and even the industry among opposing forces (controlled sub-

stance versus interventional techniques) and competing societies have provided evidence which is not favorable for interventional techniques based on bias and inappropriate methodology. For example, Chou and Huffman (3) and Spectrum Research (11,12) have utilized the same philosophy and the same evidence. One of the major flaws of this evidence synthesis is that they will only compare the change between the 2 groups, but not baseline to the treatment. It is illogical to attempt to compare the effect size in 2 different active groups. This type of analysis always results in a status that neither treatment is effective. Consequently, for interventional techniques utilizing active control trials there is significant evidence of effectiveness, however, once the local anesthetic injection is considered as a placebo, the evidence is equivalent to other modalities. Thus, methodologists tend to consider them as equivalent, consequently no treatment is recommended. They also apply the same logic with diagnostic techniques that there is no diagnostic technique with a gold standard of biopsy, thus, with any therapeutic modality based on the particular diagnosis (i.e., facet joint pain, sacroiliac joint pain, or discogenic pain) the treatments are ineffective, even if they are effective (1,234-249). Further, they also utilize therapeutic modalities which have proven to be ineffective to justify discreditation of a diagnostic modality (1,234,237,249).

Methodologists and clinicians also ignore the fact that active control trials provide generalizability rather than randomized trials. Further, in addition to the above, clinical practice guidelines are seen as a method for cost control by health insurance companies or by the government in some countries. Thus, lack of evidence may be used as an argument to exclude an intervention from coverage policies, public health insurance, or public funding (65,66,69-72,250). However, it has been stated that this can only be justified if there is evidence of no effect (78). Further, it has been shown that purchasing on the basis of best evidence does not inevitably reduce costs of health care (251).

Conflicts of interest invariably are generated from industries involved in pharmaceuticals as well as equipment and other supplies. All health care professionals involved in research or guideline development, insurance companies, health care policy makers, and finally the independent labeled organizations which base their income on providing the guidelines perceived to be favorable by payers should acknowledge their need to provide complete disclosure of potential conflicts of interest.

## 5.0 CRITICISM OF ASIPP CRITIQUE

Chou et al (13) alleged that ASIPP critiques include a number of erroneous statements regarding the employment status and clinical expertise of the members of the APS guidelines panel, various aspects of the guideline development process, and discussed specific studies illustrating these issues as Table 1 and 2 of the original manuscript (13). They further state that such misleading statements distract from the important methodological and scientific issues.

Chou and Huffman (3) quote that the misunderstanding (pages E161 [1] and E247 [2]) that other undisclosed professional societies may have cosponsored the APS guidelines was due in part to an error in the header of the evidence review on the APS Website (3). Subsequently, APS has corrected those mistakes. The corrections came as APS guideline critical analysis of diagnostic interventions was published. After the ASIPP Annual Meeting with corrections from Chou, these issues were corrected. However, Chou et al (8,11,13) continued to hammer the same issue even though it has been corrected and it is of their own doing and their mistake – a straw man concept. In the first manuscript, it was stated that Chou is an employee of the United States Government as the Scientific Director of Oregon Evidence-Based Practice Center, which is funded by the AHRQ, and is also the lead investigator for Center Support for the USPSTF. The creative presentation and technical differences of an employee or an independent contractor appears to therefore make a substantial difference for some. With regards to other societies involved, the original document prior to the correction (3) illustrated the American Academy of Pain Medicine (AAPM) as the sponsor and there was no wording that APS was the sole sponsor. In the press release, the American College of Physicians (ACP) was also involved, which has no explanation. Surprisingly, the text on page E247 (2) does not state that the lead author of the APS guidelines, Dr. Chou, is a federal employee and did not provide the information. The manuscript accurately states that no other disclosures were provided as to the nature of the financial support from the government, as well as from APS to all or some authors.

The professionalism and raising the level of discourse comes from honesty and ability to admit the mistakes when they are mistakes.

The next issue relates to Table 1 of the manuscript (13) assertion that Chou and other members of the guideline development group are methodologists

and not clinicians. The APS response states that most panel members are active clinicians and only one panel member is a non-clinician researcher. Further, they acknowledge that a list of panel members and clinical background was inadvertently omitted from the guidelines, but has been submitted for publication in a letter to the editor to *Spine* (103). This was published in *Spine* in 2011, 2 years after the publication of the criticism. The assertion that Chou and Huffman are not interventional pain management clinicians is accurate. Most of the work would appear to have been performed by these 2 authors. This is affirmed by the lack of any difference between the original guidelines authored by Chou and Huffman (3) and multiple subsequent publications. The third issue relates to Table 1 of the manuscript (13) is that conflict of interest policies and external peer review were not described. They illustrate on pages E161 (1) and E248 (2) to explain the conflict of interest policies and the external peer review process. They referred to yet another manuscript (6) published in 2009 after submission of critiqued manuscripts. Further, they state that they have inadvertently omitted from the guideline the conflicts of interest but have submitted for publication (103). Another issue relates to members of the APS guideline panel withdrawing their support (13). Chou et al (13) state that on pages E160 (1), E247 and E248 (2), that ASIPP instructed one expert whom they had nominated to work with APS on the guidelines to not be listed as an author (a violation of editorial independence), but he did not withdraw from the panel, and agreed to be listed as a full participant of the guideline working group. To date we are unable to find any such lists of participants and appropriate disclosures of the conflicts of interest including \$1.17 million received from APS (based on APS tax returns due to lack of information from authors and APS) in preparation of these guidelines and the nature of the distribution of these funds (how do we know this number. Further, commenting on the conflicts of interest of University of Wisconsin Pain Policy Group, in reference to academic profits by making the case for opioid painkillers (36), Chou stated that the University of Wisconsin Pain Group clearly has taken a position that narcotic painkillers are appropriate for chronic pain. He added that how much of that is influenced by Pharma or that they believe it, he can't really say, but he commented that there was a legitimate argument that they should not be taking money from the companies that make the drugs. However, it appears that, the same companies

may have provided funding used for APS guidelines by Chou et al. In addition, prominent authors Joranson and Gilson essentially published misleading opinions by omitting certain important data (252).

While none of the assertions are true with regards to instructing the expert to withdraw, there were also other experts who withdrew, and their names were not listed at all. Further, an ASIPP member did withdraw from the panel even though he agreed to be listed as a participant of the guideline working group which was never done. Finally, the assertion that this violated the editorial independence is accurate in that these editors had no independence at all.

The final example of erroneous statements alleged by Chou et al (13) states that the APS review based its conclusions regarding the efficacy of interventional procedures on previously published systematic reviews or guidelines and they refer to page E244 (2). They go on replying that as described in their methods (3,5), all placebo and sham-controlled randomized trials of interventional therapies were independently abstracted and were the primary source of evidence. They continued elaborating on this that previously published systematic reviews were a secondary source of information and merely described to provide context and to help identify and explore potential areas of discordance between our review and others. While multiple deficiencies were described in their reviews, there were no such statements made (2). Instead, Manchikanti et al (2) critically assessed multiple systematic reviews as included by Chou and Huffman (3).

## **6.0 INCORRECT APPLICATION OF SYSTEMATIC REVIEW METHODS**

While Chou et al (13) allege that the ASIPP critique methods was inaccurate, we acknowledge that minor differences in quality ratings are expected, since applying quality criteria requires some subjective judgment, and methods for operationalizing criteria vary (253,254). Chou et al (13) also support their view that there was no reason to assume that the ASIPP findings were correct, since the APS review followed standards for reducing subjectivity by predefining each of the quality criteria, implementing dual independent review, and dissolving discrepancies between reviewers through discussion and consensus (255). However, Chou et al (13) ignore the fact that ASIPP had done the same and they should acknowledge that there will be minor differences in quality ratings when different authors evaluate the evidence.

In addition, Chou et al (13) also support their reviews by quoting an independent review of 10 low back pain guidelines, which included APS guidelines, which was the only one to receive perfect scores for all items related to rigor of development (61). Unfortunately, this review was also filled with significant bias and authors appear to have significant conflicts with consultation with multiple industries and are also employees of Palladian Health, a company that manages specialty health benefits on behalf of other health insurers. Very conveniently, these authors have chosen 2 guidelines from the United States and both were from Chou et al (13), including the guidelines in question.

The second issue relates to discrepancies between quality ratings in the APS review and the ASIPP critiques which are considered as a major concern for APS. They reexamined the quality ratings and found major inconsistencies between how the APS quality criteria were defined and how they were applied in the ASIPP critiques. They quote as an example the randomized trial by Mathews et al (256) and expressed concern about the substantial disagreement between the APS quality score of 4 out of 11, and ASIPP criteria of 8 of 11. They further described various aspects which related to the randomization criterion, the dropout rate, and the time of outcome assessment criterion as inaccurate in ASIPP's ratings. The study by Mathews et al (256) was published in 1987, some 14 years prior to the publication of Consolidated Standards of Reporting Trials (CONSORT) guidelines (257-260). In fact, Koes et al (104,105) and Nellemans et al (106) in their well-established, respected, gold standard Cochrane reviews provided the second highest score of 67 of 100 to this study. Watts and Silagy (107), in a meta-analysis, also provided the highest score of 9 from evaluation of 13 studies. Further, Cochrane reviews and guidelines (108) illustrate that the dropout rate of 20% is considered as not acceptable for short-term follow-up and 30% is considered as unacceptable for long-term follow-up. Thus, Chou et al (3,13) are willing to use a dropout rate of 15% which would appear to be their own opinions. In addition, Mathews et al also received full score in the above esteemed reviews for intention-to-treat analysis (104-106).

The third issue with regards to discrepancies includes the criticism of a non-issue about a caudal epidural study (261). Chou et al (13) accused Manchikanti et al (2) of stating that the APS document described the study excluded because of 24 weeks of follow-up, but APS had no such criteria. Consequently, the ASIPP critique utilized the study in the analysis mentioning

only the facts why the study was excluded in systematic reviews (2,262-264). Even though, this study was with inadequate description, variable amounts of injectate, and overall utilized poor methodology, it was rated as high by Chou and Huffman (3). Our evaluation also showed methodological quality to be high, illustrating the fact that the study could be poorly performed, yet may achieve high scores which is repeatedly illustrated in the evaluations performed by Chou and Huffman (3). They also state that the ASIPP critique includes other trials of 24 weeks or less, suggesting arbitrary application of this criterion without showing the evidence. What Chou et al (13) do not recognize is that ASIPP attempted to emulate the same principles of APS guidelines to avoid differences in the inclusion criteria, etc. ASIPP essentially excluded these in the systematic reviews and guidelines in 2009. They also make a statement with regards to exclusion of foreign language articles and active control trials as erroneous despite specific exclusions for them (265-267). However, there is no such criticism in either of the documents (1,2) with regards to foreign language publications and active-control trials. The simple statement made was that these were 3 randomized trials which were not assessed by APS-AAPM evidence synthesis.

Next, they criticized the grading of the systematic reviews as ASIPP critiques incorrectly applied the Oxman and Guyatt instrument (89) on pages E150 (1) and E226 (2), which allegedly resulted in discrepancies with the APS review. Once again, they described technical and convenient measures to discard the studies that do not seem to be in keeping with their thesis.

## **7.0 DEFICIENCIES IN THE UNDERSTANDING OF UNDERLYING SCIENTIFIC PRINCIPLES**

Chou et al (13) claim that they are unique experts, whereas authors of ASIPP critique (1,2) would not meet standards for synthesizing evidence (89,268,269) and the ASIPP method for grading evidence is based almost entirely on a study design hierarchy, and largely ignores or downplays the presence of inconsistency or sparse data. Further, they bolster their argument stating that being able to independently duplicate research results is a core principle of the scientific method, particularly since early studies are often overturned in subsequent studies (270,271). However, what Chou et al (3,8-11,13) are ignoring is the simplicity and invite the complexities so that they can interject their own views and use preformed decisions rather than evaluating the actual evidence and basing conclusions on such evidence.

As an example, they provide the radiofrequency denervation of presumed facet joint pain. ASIPP guidelines and reviews have eliminated 4 studies because of technical or methodological flaws (272-275). Consequently, Chou et al (13) claim that this leaves only 2 trials with a total of 100 patients (276,277). However, ASIPP guidelines (100) and systematic review (278) also excluded Tekin et al (277). They (100,278) included only one study by Nath et al (276). In this criticism, Chou et al (3,8-11,13) ignore the methodological flaws which were not only described by authors of ASIPP critiques, but multiple others, including the authors of the manuscript who admitted that their methodology was flawed (279-282). Essentially, in reference to radiofrequency neurotomy, it appears to be clear that Chou et al (13) do not understand clinical significance, as they do not think that there is any value for properly positioning a radiofrequency cannula. Even though Tekin et al's manuscript (277) failed to meet inclusion criteria by ASIPP, by comparing 3 active control techniques, the authors showed significant decrease from baseline in all 3 groups, including local anesthetic injection or control, pulsed radiofrequency, and conventional radiofrequency neurotomy. However, the differences were higher in the conventional radiofrequency group with baseline VAS of 6.5 1.5, declining at one year to 2.4 ± 1.1. With reference to Nath et al (276) Chou et al (3,8-11,13) continued to refuse to admit the errors in their evaluation, now resorting to criticizing the randomization method, even though it was appropriate. Neither Bogduk (283), Nath et al (10,276), Datta et al (278), nor us, feel that has made any significant difference. Chou and Huffman (3) originally reported the final outcome scores in both groups were identical and there was no change in low back pain. This is in contrast to the manuscript which showed clear and distinct differences between both groups in all aspects of pain and quality of life variables. Chou and Huffman (3) also missed the fundamental and basic fact that it was an active control study with needle placement, as well as local anesthetic injection over the nerve. The recent criticism from Chou et al (13) has been that "the sham control group (which had higher baseline scores) had greater potential to experience improvement from baseline." This criticism is not justified due to lack of a placebo group. Nath et al (10) also defended the study Chou et al (13) misunderstood, as it was the active treatment group that had higher baseline scores of pain, not the sham group as was stated by Chou et al (13). They considered the criticism by Chou et al (13) unsubstantiated. Of the mul-

iple other studies, Chou and Huffman (3) have included, Van Wijk et al (275), and multiple other studies did not meet inclusion criteria by others due to deficiencies (272-275,277,284). Chou and others (8-11,13) continues to deny the fact that these procedures were not performed appropriately. Of most interest is Leclaire et al (273) which invited criticism because it failed to define the study population and had inappropriate diagnostic criteria with a single intraarticular injection with inappropriate evaluation of response (50% relief for one day any time during the week) to identify patients for radiofrequency neurotomy. Finally, there was no placebo control. Interestingly enough, in response to Gauci's (279) request, Leclaire et al (280) acknowledged multiple deficiencies. They described that their study used an invalidated and dated approach (278-285), and acknowledged the value of controlled local anesthetic blocks, false-positive results, and technical aspects – which were all lacking (280). It is very interesting that Leclaire is the second author of the manuscript published by Carette et al (286), which is considered as a standard for negative response to treatment and also for positive response with sodium chloride solution injected into a closed space. Other studies including Van Wijk (275) also provided contradictory opinions of their own results (287).

In addition, APS interjects their own evidence rather than that based on the grading defined by their own guidelines and that the study has to be at least 100 patients. In fact, the guidance reads that the good evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly affects health outcomes (at least 2 consistent, higher quality RCTs or studies of diagnostic accuracy). Nowhere does this document state that it has to be 100 patients. Further, fair quality describes that evidence is sufficient to determine effects on health outcomes, but the strength of evidence is limited by the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (at least one higher quality trial or study of diagnostic test accuracy of sufficient sample size; 2 or more higher quality trials or studies of diagnostic test accuracy with some inconsistency; at least 2 consistent, lower quality trials or studies of diagnostic test accuracy, or multiple consistent observational studies with no significant methodological flaws). Once again, this does not include 100 patients.

The second issue is related to active-control trials, which they consider as inappropriate if we use base-

line to follow-up period outcomes. We all understand that they are designed to compare one treatment to another, but it does not dictate that only the difference between 2 treatments must be utilized as in placebos. This is an untenable argument for active-control trials. The authors try to emulate so that they can refuse and reject any and all types of evidence. Their philosophy of placebo is also erroneous based on previous studies performed improperly (285,288-290), misconceptions of local anesthetic as placebo (3,290), and lack of understanding of true placebo (132-137) however, there has been only one true placebo study with appropriate methodology published in 2011 (291).

The lack of understanding of clinical effects, of active-controls is also confirmed by Chou et al's (13) criticism about local anesthetic injection being a placebo. Local anesthetics have been proven to be providing long-term effect without steroids (109-121,292-300). Even then, Chou et al (13) continued to argue that there is no justification for performing the actual procedure in question if local anesthetics are equivalent to another treatment. Again, this brings the issue of not understanding the clinical aspects and focusing only on methodology.

The next issue relates to the weighted scoring. The weighted scoring was recommended by Cochrane review group in the past, even though they have changed their opinion over time (104-106). Thus, there is continued debate on this issue with legitimate differences of opinions (301). Quality appraisal tools often use numeric scoring systems to rank individual studies with an overall quality score (302-305). However, opinions differ over the weighting of the scores for individual items on the appraisal tool (254,306,307). Further, it has been recommended that each item on a quality appraisal tool be considered separately for its impact on the quality of the study rather than relying on an overall quality score (306,308,309). Consequently, some of the new developments do not include an overall numeric scoring system. This does not mean that one system is superior to the other, and, further, these approaches do not make any significant difference in actual evaluation of the evidence. Another issue is with regards to West et al (212) where they continue to state that these are not developed to be utilized as criteria; however, these are only to be showcased with government expense. Subsequently, they also state that studies with short duration of follow-up, lack of placebo-control, or use of high volume injections were described as poor quality, even though none of the issues were associated with risk of

bias per se. Once again, this illustrates that they can be clinically irrelevant, but if there is no bias and even if they are methodologically flawed, they are appropriate as long as it meets the criteria or needs of the authors.

With regards to the invasive diagnostic studies, they inaccurately quote that ASIPP critique does not seem to dispute that there is little evidence showing that provocative discography or facet joint blocks improve clinical outcomes. This actually presents the conclusions opposite of what were reached in the manuscript. On the diagnostic accuracy of invasive diagnostic techniques, multiple manuscripts (1,2,100,234,235,246,278) have provided in detail various criterion standards including long-term follow-up, which is utilized in diagnostic facet joint nerve blocks. Further, Chou et al (13) misquote us when they say that we do not dispute that there is little evidence showing that provocative discography or facet joint blocks improve clinical outcomes. They also added a very poorly performed study (310) which presents issues with regard to scientific methodology and the practice of interventional pain management. In fact, a reader would assume that double blocks are specific, cost-effective, and recommended (310). Cohen et al (310) started with an inadequate sample and provided statements implying that repeat blocks continue to increase false-positives. This has not been shown to be true in multiple studies using the criterion standard of 80% pain relief with dual comparative blocks and the ability to perform previously painful movements, with a sustained diagnosis of facet joint pain after 2 years in 90% of the patients (235,246).

In Cohen et al's manuscript (310), the first issue relates to references that do not accurately represent the current state of the art. The authors failed to take into consideration the multiple systematic reviews and other references involving studies which have been performed in the U.S. with large populations, which essentially reflect the contemporary practice and the actual prevalence in the United States (278,311,312). The second issue is related to the sample size. It appears inadequate to compare 50 patients to 14 patients. The third issue is related to the statements implying that repeat blocks continue to increase false-positives. This has not been shown to be true in multiple studies using the criterion standard of 80% pain relief with dual comparative blocks and the ability to perform painful movements, with sustained diagnosis of facet joint pain after 2 years in 90% of the patients (235,246). Based on the authors' statements, one would theorize that as more blocks are performed, they would result in more

and more false-positive blocks. In fact, the studies have shown that if the diagnosis is based on 80% relief with double blocks, the diagnosis of facet joint pain is sustained after 2 years in 90% of patients. The fourth issue is related to false-negatives, which could be accurate or inaccurate. However, in reality, false-negatives might reduce some needed treatments, but it is the false-positives or treating without a diagnostic algorithm that increases both fraud and abuse, a major issue in the United States (313-319). The references the authors quoted regarding discography are not applicable to facet joint pain. Further, Cohen et al (310) recognize that discography has been compared to unproven fusion techniques (236-248). However, patients who are proven to be false-negatives will go on to some other treatment such as epidural injections and will respond to a great extent (112,117,118). In fact, this has been shown to be true with discogenic pain, after ruling out facet joint pain, with a similar response to epidural injections as there is with disc herniation (113,116,119). If they fail to respond to epidural injections, a re-evaluation might be in order. Instead, if clinicians proceed on Cohen et al's (310) proposition, the issue is again related to over-utilization, but not under-utilization and impediment to access. In this era of cost containment, we believe that it is better to miss 10% to 15% of patients rather than treat 65% to 85% of patients unnecessarily with an inappropriate treatment. Further, facet joint interventions are not as innocuous or as safe as the authors describe. The fifth issue is related to cost-effectiveness versus cost-analysis. The authors never performed a cost-effectiveness evaluation in this study. Cost-effectiveness is performed based on improvement and quality-of-life years gained. That does not appear to be the case here. However, if a patient is not treated, that would be the least costly, because the cost would be \$0 instead of over \$6,000. The sixth issue is related to cost estimations. Even \$1,000 to \$1,200 is too low considering that many of these patients have bilateral problems. If the authors claim that radiofrequency neurotomy costs \$1,000 and diagnostic facet joint nerve blocks cost \$500 per patient, the math is difficult to understand. Based on these numbers, Group "0" should cost \$60,000; Group I, with a single block paradigm of 49 patients who underwent single blocks, translates into \$24,500, plus 20 patients who underwent radiofrequency neurotomy at a cost of \$1,000 per patient, or \$20,000; together they total \$44,500. In Group II, the double-block paradigm, there were 49 patients at \$500 for the first block (\$24,500) followed by 29 patients who

underwent a second block (\$14,500), plus 14 patients who underwent radiofrequency neurotomy (\$14,000). These 3 total \$53,000.

Based on these figures, quality-of-life improvement appears to be approximately 13 weeks per patient and the cost would be \$25,144 per year, which is not particularly great for Group 0. Further, the authors exclude all the relief patients obtained with diagnostic blocks, but they include the cost. The final issue is related to follow-up. We believe that the 3-month follow-up is insufficient. If the authors had continued with a 6-month or even a one-year follow-up, the results would likely have been much different. The gold standard they applied is based on relying on chart reviews and interviews with 15 patients and 5 pain physicians to devise this 3-month duration. In conclusion, Cohen et al (310) inadvertently appear to prove the importance of diagnostic blocks, and Chou et al (13) seems to embrace it.

Chou and Huffman (3) also inappropriately included Birkenmaier et al's study (320) while excluding Rubinstein and van Tulder's best evidence review (321). The Birkenmaier et al study (320) is not only of poor quality, but has not met any inclusion criteria for a diagnostic accuracy study. It essentially compared 2 uncontrolled procedures. They utilized high concentrations of bupivacaine, 0.5%, and volumes higher than 1 mL. Even so, Birkenmaier et al (320) showed that patients who had been selected by medial branch blocks had better pain relief than did patients who had been diagnosed using pericapsular block with statistical significance noted at 6 weeks and 3 months. They also concluded that if serial controlled blocks cannot be used, lumbar facet joint pain remains a diagnostic dilemma.

The misunderstandings or lack of understanding of placebo continues to be a major issue. There are numerous difficulties related to placebo groups and interventional techniques. An active control study utilizing local anesthetic is not a placebo, even though Chou and Huffman (3), Nelemans et al (106) and Staal et al (322) converted it into a placebo.

By definition, the placebo effect is a physiological and/or psychological reaction to an inactive substance or an inactive procedure. Consequently, placebo effect represents a key interphase between physiology, psychology, and patient care (132,133,323,324). It has been shown that the magnitude of placebo analgesia is highly variable (325). Consequently, understanding predictors of placebo analgesia is important, as treatment for chronic pain can benefit from clinically meaningful placebo effects. Similarly, it is essential for clinicians and

methodologists to understand nocebo effects.

In contrast to placebo, nocebo represents a phenomenon opposite that of placebo analgesia, characteristically considered to be a worsening or consistent lack of change of symptoms after the administration of some agent known to be effective – hyperalgesia (132,133,324). However, nocebo effects in interventional pain management have not been carefully distinguished from drug-induced hyperalgesia, tachyphylaxis, tolerance, and/or progression of the underlying organic pathology causing increased pain and diminished sensitivity to a particular pharmacologic agent or procedure.

Chou et al (13) also erroneously desired to include Manchikanti et al's study (326) utilizing the control group after they failed epidural injection to show that it is a failure, but failing to appropriately evaluate the manuscript in reference to placebo effect. Yet they ignored Dashfield et al (120) showing successful outcomes in non-surgical patients with explanation which does not correlate with the actual descriptions in the guidelines.

## **8.0 IMPROVING THE DISCOURSE**

The discourse can be improved only when parties are honest, not only to the science but to themselves. As the authors have stated, conflicts of interest come in numerous ways, one of them being funding. The authors may want to look into numerous publications, their interests, and conflicting opinions in different publications and not only the industry sponsorship in the United States, but from abroad. Further, the close relationship of authors with various guideline making organizations and lack of disclosures of funding from them raises multiple questions.

As described, professional societies often are involved in and are passionate about the development of guidelines for the care provided by their members. It is well understood that this responsibility requires understanding and adhering to scientific standards and acknowledging conflicts of interest in a vigorous and transparent manner. Interventions must not be justified based on erroneous statements, utilizing inadequate scientific methods and ignoring important deficiencies in the evidence undermine clinical credibility in patient care.

However, the same applies to physicians who function as methodologists or physicians who depend on the income from guidelines, which in turn is dependent on the industry sponsorship. Their responsibility

requires understanding and adhering to the scientific nature of clinical practice, technique, and acknowledging conflicts of interest in a vigorous and transparent manner, which seems to be lacking among methodologists, while it is improving among academicians and clinicians.

Finally, instead of erroneously presenting the same evidence over and over again, the parties must behave professionally and improve the discourse by providing updated evidence. To that effect, ASIPP is revising the guidelines and waiting for similar action from APS. The authors (13) never addressed the issues raised about their search criteria missing multiple published manuscripts.

## **9.0 CONCLUSION**

In this manuscript, we have described various misconceptions and hazards of evolving concepts of development of guidelines in interventional pain management. We also looked at various aspects of these guidelines if they were based on professionalism and evidence-based medicine. We believe that any guideline panel should consist of clinicians and methodologists and the goals of these 2 groups, though disparate can be reconciled. Thus, all professionals must remember that the ultimate value of any clinical guideline is in helping the patients we serve. As Yudkin et al (327) noted in the Lancet: "The most entrenched conflict of interest in medicine is a disinclination to reverse a previous opinion." Let us come together; the development of medicine is dependent on proving this statement wrong.

Croft et al (78) in their editorial, "Pro's and Con's of Evidence-Based Medicine," state that commitment only to things with an evidence base gives a limited view of what is needed in clinical practice. It may promote interventions that are easier to study such as pharmaceuticals and may ignore interventions for which trial funding is difficult to obtain such as interventional techniques. Unnecessary bias, misconceived strict adherence, and ability to refuse all types of evidence by industry specialists of EBM hampers new interventions as if implementation of these interventions is justified only if sufficient evidence is available, the process of which may take decades. Further, the issue becomes especially relevant if one RCT is considered insufficient evidence for implementation (78). Generally the first trial of an intervention may be positive, and later trials less positive. As an example, the first trial comparing lumbar fusion surgery to conservative care found surgery

more effective, but later trials failed to confirm this (328-330). In contrast, later interventional pain management trials, though not placebo controlled, have been shown to be more effective than earlier ones and also more effective than observational studies.

Criticism should be taken seriously and addressed (78). EBM proponents need to better explain the principles of EBM and include room for clinical expertise and other types and sources of information on which to base decision-making in practice (78). The common concept that a serious problem exists and is difficult to tackle is related to the hampering of innovation of EBM, and is strictly applied to new interventions.

EBM experts, users, and followers, must focus not only and strictly on the evidence derived from RCTs, but acknowledge that “true” EBM acknowledges that evidence is important, but that other aspects play a role as well in making final clinical or policy decisions – patients’ and clinicians’ preference, availability of treatments, comorbidities, and financial, ethical, and legal issues.

Finally there are useful arguments both for and against EBM. In our opinion, the problem is not so much that the principles of EBM are flawed, but application of EBM with unrecognized conflicts of interest do not lend EBM to be applied appropriately in clinical or policy practice settings. Creating a straw man and destroying him will improve either discourse or professionalism.

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