

Public Comments to the
Identifying Risky Opioid Prescribing Practices Report and the
Memorandum on Evaluation of Opioid Prescribing Guidelines Using
AGREE II and the Author's replies¹

1. Comments on RAND Evaluation of Opioid Prescribing Guidelines, received from Work Loss Data Institute (WLDI)
2. Comments on RAND Evaluation of Opioid Prescribing Guidelines, received from Suzanne Novak, Ph.D., University of Texas
3. Comments on Identifying Risky Opioid Practices, received from Christopher J. Wolfkiel, Ph.D., the American College of Occupational and Environmental Medicine (ACOEM)
4. Comments on Memorandum on Evaluation of Opioid Prescribing Guidelines Using AGREE II, received from Christopher J. Wolfkiel, Ph.D., the American College of Occupational and Environmental Medicine (ACOEM)
5. Author's replies, received from Teryl K. Nuckols, MD, MSHS

¹ Deadline for public comment and feedback was January 31, 2013.

To: DIR CHSWC [CHSWC@dir.ca.gov]

Comments on Rand Evaluation of Opioid Prescribing Guidelines

**From: Work Loss Data Institute (WLDI), 169 Saxony Rd, #101,
Encinitas, CA 92024, 760-753-9992, phil@worklossdata.com**

Date: January 7, 2013

OVERALL:

The glaring oversight by Rand was that they did not evaluate ODG itself (which WLDI would have been happy to provide on a complimentary reviewer basis), but instead used the shorthand abstracts of ODG available at the National Guideline Clearinghouse written by content aggregators under AHRQ's contractor, ECRI Institute. These are not authored by ODG, and are not intended to be a complete representation of guideline development methodology or content. NGC explicitly states, "Readers with questions regarding guideline content are directed to contact the guideline developer." ECRI writes those summaries based on looking at ODG. They are missing the functionality, details, evidence links, evidence ranking and discussion in ODG, which is why ODG gets bad ratings on those topics. An organization should not purport to study guidelines without securing the necessary time and resources to actually look at the guidelines.

Furthermore, shortcuts in the evaluation of guidelines could exacerbate the opioid problem, since the ultimate guideline recommended by the Rand study is authored by pain doctors, who are most likely to overstate benefits and underestimate risks of opioids.

Page 14 of the study states that "The guidelines are generally available through the National Guidelines Clearinghouse website." However, this is not an accurate statement. NGC posts only standardized abstracts as extracted by ECRI. NGC abstracts are not intended to be a replacement for ODG or other guidelines. It would not be accurate to state that this study compared ODG with the other guidelines, but instead the more accurate statement would be that abstracts from ODG as written by ECRI were evaluated and compared with full-text versions of other guidelines, which is not an apples-to-apples comparison.

Dr. Nichols and Rand have had full access to the paid guidelines for their first California guideline evaluation study in 2004, including the guidelines they ranked in the top 4, ODG, McKesson, Intracorp and ACOEM, but this time they assumed ODG was not available, without any justification for assuming that. It is the policy of Work Loss Data Institute to make complimentary access to ODG available in full to any organizations or researchers conducting a guideline review or evaluation.

COMMENTS ON THE AUGUST 30, 2012 MEMO:

Page 3: "Of the eight remaining guidelines, we were unable to evaluate the development methods and related aspects of the ODG guideline developed by the Work Loss Data Institute (WLDI) because the content of the guideline was not available. An earlier version of this guideline is currently used in California." This is incorrect. The AGREE information for ODG is available at no cost here: http://www.odg-disability.com/ODG_AGREE.htm. If they could not find it, all they had to do is contact the publisher, as they are directed to do by the National Guideline Clearinghouse

Page 7: Table 2. Results: AGREE II Standardized Domain Scores

This is incorrect: Item #4. Clarity of Presentation: The language, structure, and format of the guideline. ODG received N/A*, with the footnote: * The guideline is proprietary and text was unavailable so raters could not assess clarity of presentation or decide whether to recommend use.

Page 8: Table 3. Results: Updated AMSTAR Quality Scores (with multiple reviewers):

The ratings do not make sense. ODG (WLDI) only received 8/22. For example, when they ask if ODG listed its studies (question #5), ODG received 0/2, but when asked if ODG assessed the studies (question #7), ODG got 2/2. How can you assess studies if they are not there? ODG not only lists studies but links to them from each guideline statement. And question #7 gave ODG 0/2 for assessing study quality. In fact, ODG assesses the quality of every study referenced in ODG. In question #9, "Were the methods used to combine the findings of studies appropriate?" ODG received 0/2 but ACOEM was n/a. Why is this different? In question #11, "Was the conflict of interest stated?" ODG received 0/2. In fact, this is explained in ODG.

Page 9: Table 4: Key Elements of Opioid Treatment:

ODG addresses all of these items, but there is no column for ODG

COMMENTS ON THE MAY 24, 2012 REPORT:

Appendix 3. Quality of Guideline Literature Searches:

In the Table: AMSTAR Ratings for Guidelines Included in Review, why is this different from Page 8 in the August 30, 2012 Memo: Table 3. Results: Updated AMSTAR Quality Scores?

COMMENTS ON THE RECOMMENDED GUIDELINE:

The guidelines recommended by the Rand study could exacerbate the opioid problem, since they were authored by the pain doctors who are most likely to overstate benefits and underestimate risks of opioids. Just as for any medical specialty, these guidelines tend to favor treatments their members prescribe, in this case opioids, with the AAPM/APS guidelines concluding that chronic opioid therapy can be an effective therapy for patients with chronic noncancer pain. Over half of the authors of the AAPM/APS guidelines are identified as receiving money from opioid manufacturers.

Plus these guidelines do not provide specific details needed to improve outcomes in workers' comp. For example, there is little specific guidance about the use of Urine Drug Testing, which is becoming a new area of abuse for pain doctors.

In general, they also do not appear to have any real value for UR (i.e., without clear guidance on what opioids to use, how much, for how long, patient selection, contraindications, etc). They do not have a Drug Formulary. Nor do they provide access to reimbursement codes, i.e., ICD9 diagnosis codes and NDC drug codes.

There is major concern with discussion of 200 MED as high dose. There is clear evidence of increased OD risk > 120 MED from Dunn 2010, Braden 2010, Bonhert 2011, and significant risk even lower per Paulozzi 2012.

This guideline is weak on opioid agreements, it does not provide sufficient risk warnings on fentanyl for benign pain, and it has deficits in recommendations for concerns in sleep apnea.

The guideline is limited in identifying what tools are recommended to assist with screening and monitoring.

There is also a major conflict of interest due to joint authorship of the Rand evaluation study and the guidelines that the evaluation concludes are highest quality. Dr. Chou is Dr. Nichol's co-author, and he is also lead author of the guideline their study recommends, the guidelines from the pain doctors, the AAPM-APS guidelines.

This guideline is not current. It has not been updated in over four years, since it was published in early 2009, and written and first made available in 2008. And the search for published studies occurred through November, 2007 (over 5 years ago)¹. According to a review by the International Association of the Study of Pain: “At face value, the recommendations make practical clinical sense; however, panel members acknowledge numerous research gaps. In fact, they did not rate any of their recommendations as supported by high-quality evidence, and only 4 recommendations were viewed as supported by even moderate-quality evidence.” Another major concern is unclear dates to update the guide in the future based upon expanding medical evidence.

Over half of the authors of the AAPM/APS guidelines (15 out of 21) have disclosed receiving financial payments from opioid manufacturers, including Gilbert J. Fanciullo, Perry G. Fine, Jeremy A. Adler, Jane C. Ballantyne, Pamela Davies, Marilee I. Donovan, Jeffrey Fudin, Aaron M. Gilson, Steven D. Passik, Gavril W. Pasternak, Russell K. Portenoy, Ben A. Rich, Richard G. Roberts, Knox H. Todd, and Christine Miaskowski. Opioid manufacturers have no interest in seeing reduced sales of their products for patients with chronic noncancer pain.

¹ <http://www.iasp-pain.org/AM/Template.cfm?Section=Home&CONTENTID=8924&TEMPLATE=/CM/ContentDisplay.cfm&SECTION=HOME>

Lastly, and perhaps most compelling, is that since the release of the APS/AAPM Guidelines in 2009, opioid use has continued to spiral. Yet, with the implementation of ODG's pharmacy closed formulary adopted by Texas Workers' Compensation Commissioner Rod Bordelon in 2011, substantive, quantifiable results have been obtained: Fewer opioids, narcotics and other "not recommended" drugs are being prescribed in the Texas workers' compensation system according to a recent study of medical billing and payment data collected by the Texas Department of Insurance, Division of Workers' Compensation (TDI-DWC) and the Workers' Compensation Research and Evaluation Group (REG).

The study compared injuries that occurred between September and November 2011 with injuries that occurred during the same timeframe in 2010. To ensure comparability, both sets of claims were analyzed at six months post-injury to account for differences in claim maturity. The study found that under the formulary:

- prescription drug costs specifically attributed to not-recommended ("N") drugs for 2011 claims were reduced by 75 percent (approximately \$841,000) when compared to 2010;
- claims receiving "N" drugs were reduced by 54 percent between 2010 and 2011; the frequency of "N" drug prescriptions being dispensed to injured employees was reduced by 65 percent;
- total prescription drug costs for 2011 claims were reduced by 26 percent (approximately \$1.4 million) when compared to 2010 claims; and
- the frequency of opioid prescriptions dispensed to injured employees decreased by 10 percent and the costs associated with opioid prescriptions decreased by 17 percent.²

² D:\data\TDI\Fewer Texas Workers' Compensation Claims Include Opioids and Not-Recommended Prescriptions.mht

To: DIR CHSWC [CHSWC@dir.ca.gov]

Comments on Rand Evaluation of Opioid Prescribing Guidelines

From: Suzanne Novak, MD, PhD, Clinical Assistant Professor, University of Texas, Chapter Lead, ODG Pain, 1600 Flint Ridge Road, Austin, TX 78746, 512-327-7940, snovak@austinator.com

Date: January 7, 2013

Comments on Memorandum

- This is going to be submitted to peer-reviewed journals.

It could be that Roger Chou did influence the outcome of this study to promote his work, but I'd like to think this was not for monetary gain (except to have even more publications in an academic setting).

- Exclusions included those limited to specific conditions, populations, types of pain or settings.

An argument could be made that ODG was omitted as it is primarily aimed at a workers' compensation population.

- Grading of included material.

ODG does not use AMSTAR.

- ODG was not included as the content was not available.

How did they get ACOEM's guidelines. You have to buy them. Here is what is available in Guidelines.gov

- Opioid use in the setting of chronic, non-malignant, or neuropathic pain is controversial. Opioids used in higher doses tend to have a greater adverse effect profile. A potential for abuse or addiction does exist, especially with inappropriate use; systemic effects also are apparent over time in many patients for whom opioids are prescribed. Patients on opioids should be routinely monitored for signs of impairment, particularly those who are working in safety sensitive positions (including those who have to drive to and from work). However, while there is population-based evidence of approximately doubled crash risk continuing at 2 weeks into opioid treatment, there is also literature that suggests there may not be elevated accident risk among those who are accustomed to opioid use and are on stable doses of medication.
- Use of opioids in patients with chronic pain should be reserved for those with improved functional outcomes attributable to their use, in the context of an overall approach to pain management that also includes non-opioid analgesics, adjuvant therapies, psychological support, and active treatments (e.g., exercise).

Here is what is included under "chronic persistent pain" and "chronic low back pain."

Opioids may be used for select patients (**I**)

Screening patients prior to initiation of opioids (**I**)

Use of an opioid treatment agreement (**I**)

Routine urine drug screening for patients on chronic opioids (C)

- How can they review the WLDI guideline if they don't have it.

I think this is the issue for not only WLDI but ACOEM. You really can't make this kind of analysis based on what is documented in AHRQ summaries.

- Table 2: Agree II

How did ASIPP get a 64% for editorial independence?

How were any of these numbers derived?

- Table 3: AMSTAR

They can't analyze this based on AHRQ.

Why is APS-AAPM so high? I think one of the issues is this guideline specifically addresses opioids.

Why did ODG get a 0/2 for characteristics of included studies provided?

Why did ACOEM have a N/A for question #9 (this allowed for a higher percentage rating).

I don't think you can compare a specific opioid guideline to a chronic pain guideline, especially based on AHRQ summaries.

- Table 4

We basically include most of these topics and many that are not outlined. At the minimum they should make sure they are all addressed.

They have to have examined the actual guidelines to get these sort of details because this information is not in the AHRQ summary.

Comments of actual article

Risks in General Populations: Page 23

They obviously did not look at the ODG

The body of this includes guidelines that were not evaluated as per the memo including Colorado.



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Jan 31, 2013

Commission on Health and Safety and Workers' Compensation (CHSWC)
1515 Clay Street, 17th Floor
Oakland, CA 94612
Via email

Re: Identifying Risky Opioid Prescribing Practices

Dear Commission on Health and Safety and Workers' Compensation,

The American College of Occupational and Environmental Medicine (ACOEM) wishes to thank you for allowing us to comment on "Identifying Risky Opioid Prescribing Practices". As a guideline developer and specifically as developers of the majority of California's Medical Treatment Utilization Schedule (MTUS), with the exception of chronic pain, we take very active interest in how our guidelines are interpreted. It is worth noting that the ACOEM Opioid Guidelines cited were developed under a more rigorous methodology than the Guidelines version published in 2004.

There are multiple errors in the document regarding quality of guidelines literature searches. ACOEM has a clear methodology document that is on-line and has been published in a peer reviewed journal (J Occup Environ Med, 2008; 50:282-295). It specifies status of literature, source inclusion and exclusion, article inclusion and exclusion based upon quantitative analysis, methods which are used to combine studies and methods for the inclusion of studies to formulate recommendations. Furthermore, it appears that the authors fail to take into account that many guidelines are not routinely published with details from the supporting systematic review – this is the case with our posted ACOEM Opioid Guidelines(http://www.acoem.org/uploadedFiles/Knowledge_Centers/Practice_Guidelines/Chronic%20Pain%20Opioid%202011.pdf) which are freely available while SR details are detailed in book form and via online subscription. When reviewed with complete information, the AMSTAR criteria for ACOEM should be:

#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	Score	%
N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	9/11	82

More generally, the authors attempt to use insights from higher quality guidelines developed for patient care decisions as potential criteria for identifying higher risk prescribers in the very limited context of pharmaceutical claims. None of the guidelines reviewed include recommendations on prescribing patterns and the authors attempt to apply quality assessments to the guidelines to select potential criteria is misleading in this regard. Guidelines rarely delve into the specific data elements that pharmaceutical claims impart; indication appropriateness cannot be inferred from claims although fundamental to guidelines and guidelines generally assume that dosage determinations are consistent with approved labeling.



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Conceptually “*Prescriber Risk*” may be a logical continuation of treatment variability identified by the Dartmouth Atlas group which demonstrated that utilization could be extremely variable and due to as much availability of services as the demand for them. And, as to be expected, specialties associated with painful conditions (surgical specialists, oncologists and pain specialists) are more likely to be associated with opioid prescriptions. Certainly one would expect that some portion of a pain specialists practice would include extreme cases that would not be expected to align with guidelines. What that proportion might be has not been evaluated and published and certainly hasn’t made its way into guidelines.

Unfortunately we suggest that guidelines, irrespective of quality, are unlikely to provide much input on “*Prescriber Risk*” and that the authors remove their quality assessment findings and as an alternative approach use an analytics/expert review. This could be accomplished by identifying specialist specific prescribing patterns via analytics, then convening panels of like specialists to assess appropriateness.

Best regards,

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cc Kurt Hegmann, MD, MPH
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Jan 31, 2013

Commission on Health and Safety and Workers' Compensation (CHSWC)
1515 Clay Street, 17th Floor
Oakland, CA 94612
Via email

Re: Memorandum on Evaluation of Opioid Prescribing Guidelines Using AGREE II

Dear Commission on Health and Safety and Workers' Compensation,

The American College of Occupational and Environmental Medicine thanks you for allowing us to comment on "Evaluation of Opioid Prescribing Guidelines Using AGREE II". As a guideline developer and specifically as developers of the majority of California's Medical Treatment Utilization Schedule (MTUS), with the exception of chronic pain we take very active interest in how our guidelines are interpreted. It is worth noting that the ACOEM Opioid Guidelines cited were developed under a more rigorous methodology than the version published in 2004.

There are serious limitations to this study that the Commission should be aware of including an incomplete application of the AGREE II instrument, qualifications of the appraisers and an apparent unfamiliarity with some of the key guidelines.

First and foremost is the application of the AGREE II instrument which the authors note correctly is preferable to have 4 appraisers but utilize 3 with the vast majority of appraisals having 2. Recognizing that 2 were MDs with public health experience and 1 a master's degree student, there is an obvious mismatch in training but with the data supplied it is impossible to assess whether this is a confounding variable. It also should be noted that none were occupationally trained specialists and questions the Commission's requirements for the design of the project.

It should also be noted that recent Institute of Medicine reports on systematic reviews and trustworthy guidelines deeply question the underlying assumption of this study that "more rigorous development methods should produce higher quality guidelines". In fact the IOM authors felt that AGREE "inadequately reflect the full range of quality CPG development". Examples of this inadequacy can be seen in some of the Editorial Independence ratings for the Work Loss Data Institute, ASSIP and the APS-AAPM guidelines.

The potential for bias in Work Loss Data Institute guidelines is overwhelming, the Editor in Chief, Phil Denniston is the owner of the guidelines – he receives financial benefit based upon the acceptance of his guidelines. Furthermore, it has been documented that the Work Loss Data Institute worked with Medtronic as those guidelines were introduced into Texas (see attached). (It is also confusing as to why the authors felt they did not have access to these guidelines for assessing clarity of presentation when they are clearly available on MTUS's website:

http://www.dir.ca.gov/dwc/DWCPPropRegs/MTUS_Regulations/MTUS_ChronicPainMedicalTreatmentGuidelines.pdf)



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The rating of ASSIP editorial independence is noteworthy in that it is exactly the single specialty guideline that the IOM is highlighting “The committee believes potential for conflicts of interest are great when funding for CPG development or for the supporting organization comes from stakeholders, particularly the pharmaceutical and device industries or specialty societies, which might benefit or whose members might gain from guideline recommendations.”

Finally the exceedingly high editorial independence rating of APS-AAPM, almost an outlier, gives the reader pause when one considers that the APS and AAPM are under investigation by the Senate Finance Committee for potential funding biases by pharmaceutical companies - <http://www.finance.senate.gov/newsroom/chairman/release/?id=021c94cd-b93e-4e4e-bcf4-7f4b9fae0047> . Close attention to the disclosures by the co-chairs reveals significant potential bias that would be unacceptable by IOM standards.

These issues severely limit the acceptability of this manuscript and the Commission is advised to ask that the work be redone with more appropriate use of modern standards.

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Texas Pain Society Legislative and Regulatory Update

By Richard Evans

DWC Set to Adopt Non-Network Treatment Guidelines

After much debate, the Texas Department of Insurance/Division of Workers' Compensation is poised to adopt disability management guidelines, including return to work and treatment guidelines. These guidelines apply to health care services that are provided in a non-network setting. The proposed rules, which will become final later this year and unless significantly changed will adopt *The Medical Disability Advisor, Workplace Guidelines for Disability Duration* as return to work guidelines and the Work Loss Data Institute's *Official Disability Guidelines* as treatment guidelines.

DWC held a public hearing in Austin on October 5 to hear testimony from insurance carriers, employers, medical providers and vendors regarding the proposed rule which brought to an end a 30-day public comment period. Representatives from the American College of Occupational and Environmental Medicine (ACOEM) strongly protested the adoption of rival ODG guidelines, however it would be very unlikely that DWC would change course at this point in the process and adopt ACOEM as the treatment guideline. The agency is in the process of reviewing the written comments and testimony from the hearing to determine whether to make any changes to the proposed rule.

The rule would establish that treatment provided within the parameters of the ODG guidelines would be presumed correct. Insurance carriers would still be allowed to challenge the medical necessity of the health care provided within the guidelines, but would have to present evidence-based medical literature that would demonstrate that the treatment was not medically necessary.



Treatment that exceeds or is not covered in the guidelines would be subject to treatment planning and would require preauthorization by the insurance carrier.

For physicians that treat injured workers' with chronic pain, the guidelines do support the use of neurostimulation and intrathecal drug delivery in appropriate circumstances. Medtronic has worked extensively with the Work Loss Data Institute (WLDI) to provide strong medical evidence supporting the efficacy of these treatments, and the Official Disability Guidelines have been greatly improved to reflect this clinical and cost effective evidence. Specifically, it is important to note that the updates now state that the "supporting evidence is significantly supplemented and enhanced when

combined with the individually based observational evidence gained through an individual trial prior to implant. This individually based observational evidence should be used to demonstrate effectiveness and to determine appropriate subsequent treatment." This statement should significantly aid in gaining appropriate patient coverage. Separately, it is important to note that the guideline still is problematic for things such as spinal fusion and Medtronic Spinal is working with WLDI to attempt to update and appropriately improve this section.

The treatment guidelines will likely go into effect in Spring 2007 and providers will need to access the on-line version to review the most up to date version. Medtronic has negotiated a global subscription for the Official Disability Guidelines to allow providers to easily access the guidelines. To obtain access to this one-year complimentary electronic subscription per pain physician, email Phil LeFevre with the Work Loss Data Institute at lefevre@worklossdata.com to request a Medtronic sponsored subscription. Once you have obtained your subscription you are then allowed to cut and paste up to 3 pages of text from the guideline and submit that information directly to payors of all sorts during prior authorization. Whether or not DWC officially adopts ODG this should prove to be a valuable tool in gaining appropriate prior authorizations for these therapies.

Teryl K. Nuckols, MD, MSHS responds to WLDI and Suzanne Novak, Ph.D.:

- 1) Roger Chou did not participate in scoring the guidelines. He provided content and methodological recommendations; other individuals scored the guidelines.
- 2) This project did not have the ability to contact all of the guideline developers to obtain supplemental materials that were not available in the public domain. For example, we did not obtain information on development methods from Washington State so we did not rate the AGREE Instrument for that guideline. When we lacked sufficient information to rate a domain of the AGREE Instrument for an individual guideline, we wrote “not applicable” in the table rather than rating the domain. For example, we did not rate “clarity of presentation” for the proprietary WLDI guideline because we did not have access to the clinical content.
- 3) ACOEM has made the 2011 pain guideline available to the public for free. The link is below:
http://www.acoem.org/uploadedFiles/Knowledge_Centers/Practice_Guidelines/Chronic%20Pain%20Opioid%202011.pdf
- 4) The reason ACOEM didn't score higher wasn't for lack of information on how they develop ACOEM in general, it was for lack of information on how they developed the opioid chapter in particular.
- 5) Some may complain that this evaluation was less comprehensive, as did WLDI, because we didn't contact every developer to obtain all possible information on their guidelines. However, I think by now everyone knows the standards by which guidelines are judged, particularly if they are in the business of developing them. They should be putting the information in the public domain without being asked at this point.

Teryl K. Nuckols, MD, MSHS responds to ACOEM regarding Identifying Risky Opioid Prescribing Practices:

- “ACOEM Opioid Guidelines cited were developed under a more rigorous methodology than the Guidelines version published in 2004.”
 - We have observed the effort that ACOEM has put into improving the rigor of their guideline development process. We obtained from the ACOEM website a document that explains how the ACOEM development methods satisfy the original version of the AGREE criteria.
- Thank you for referring us to the citation in J Occup Environ Med, 2008; 50:282-295.
 - We will review the document and compare it to other available information on the ACOEM development methods and take it into consideration for any future publications resulting from this project.
 - However, we did not find a shortage of information on how ACOEM chapters are developed in general. There is ample information available on the ACOEM website, for example. Rather, the issue, in this case, was the lack of specificity to the chapter being reviewed. We needed to evaluate the *actual* methods used to develop the opioid guideline. How reasonable is it to assume the methods used to develop a guideline published in 2011 were exactly the same as those laid out in a publication from 2008? The execution of most scientific endeavors diverges from their original plans, for a variety of reasons.

- Further, the AGREE II (updated version) and AMSTAR instruments specify that search terms, and inclusion and exclusion criteria should be listed for the specific clinical questions within the guideline. A generic document that describes how guidelines are developed cannot provide such criteria. For example, what types of search terms were used for the concept, opioid? We did not have access to the proprietary documents that you suggest might have contained this information (see below).
- We agree that many guidelines do not make information available from their systematic reviews.
 - This makes it harder to evaluate the quality of the systematic reviews performed. However, it does not mean that evaluators should change the criteria by which they judge the quality of guidelines' systematic reviews.
- The current evaluation differed substantially from the 2004 evaluation. The 2004 evaluation was more comprehensive in two respects.
 - First, due to the larger scope and longer timeline, we were able to contact all of the developers of the guidelines we selected for study in 2004. The current project, in contrast, relied upon publicly available information due to timeline and scope. We did not contact any guideline developers or purchase any proprietary documents.
 - In 2004, the use of guidelines by the State of California was new, and developers might not have expected to have their methods publicly scrutinized. At that time, we were able to contact developers and obtain any additional information they wished to provide.
 - In the current project, developers of proprietary guidelines have expressed concern that they would score better if they gave us complete access to all guideline information. Nevertheless, we believe that basing an evaluation on publicly available information is a fair and balanced approach. A potential user of a guideline should be able to evaluate quality using information in the public domain, particularly if the guideline itself is in the public domain. The criteria by which guidelines are evaluated are well known to guideline developers. The evaluation instruments are in the public domain, including the AGREE II, the AMSTAR, and a recent Institute of Medicine report (which we did not use). Some quality guidelines do make very detailed information on development methods publicly available, including search strategies for specific clinical questions; it seems reasonable for such guidelines to receive somewhat higher ratings than guidelines that do not. When the content of proprietary guidelines is not available, we wrote "N/A" for not applicable for AGREE II domains pertaining to guideline clarity and organization, which avoids unduly penalizing the guideline.
 - Second, unlike 2004, we did not perform an evaluation by clinicians. This evaluation was entirely limited to ratings using the AGREE II and the AMSTAR.
- We would like to make a subtle but important clarification about the objectives of the report. It was not to identify high-risk *providers* but rather high-risk prescribing *practices*.
 - Methodologically and practically speaking, there are many differences between these objectives. In seeking to identify high-risk prescribing practices, we focused on prescribing issues that were simple and concrete. For example, the specific medication is associated with a high rate of adverse events. The dose prescribed is associated with a high rate of adverse events. The patient is receiving multiple medications that together pose a risk for adverse events. Identifying *practices* that are associated with higher degrees of risk raises questions of sensitivity and specificity (some patients will

be able to tolerate the risks better than others); therefore, our suggested criteria for identifying higher-risk practices would need to be tested and refined. Provider profiling is far more complex, raising issues of sample size and the reliability of classifying the providers, potential harm to providers' reputations that may or may not be deserved, and many more concerns. That is not a topic addressed by this report.

Teryl K. Nuckols, MD, MSHS responds to ACOEM regarding Memorandum on Evaluation of Opioid Prescribing Guidelines USING AGREE II:

1. Qualifications of Appraisers:
 - a. Lack of Occupational Medicine Experience among Reviewers
 - i. The AGREE II guideline evaluation process does not require specialty-specific knowledge. The domains within the AGREE II instrument do not refer to clinical content, but rather primarily to methodological issues.
 - ii. The one domain where some clinical knowledge could possibly be relevant is Clarity of Presentation. However, substantial clinical expertise should not be required to assess Clarity of Presentation because the objective of a guideline is to educate providers about a subject. The guideline should seem clear and easy to understand to the providers being educated, who will not, by definition, be content experts.
 - iii. The physicians on the team do have relevant clinical and research expertise. Opioid therapy is an issue that arises frequently in Internal Medicine, the specialty of the two physician reviewers. The Principal Investigator for this project led the 2004 evaluation of medical treatment guidelines for the State of California, and is quite familiar with evaluating guidelines focused on issues related to occupational health topics. In addition, she is currently leading a large research endeavor related to work-associated carpal tunnel syndrome. Dr. Roger Chou, a consultant with substantial expertise in opioids, was available for any clinical-content related questions, yet we did not ask him a single clinical question related to the rating process.
 - b. Use of Masters' Degree Student, among other reviewers
 - i. Previous analyses have used Masters' degree level individuals. In fact, an individual with no more than a Masters' degree wrote an important early article on guideline quality. (Hasenfeld, R., and P. G. Shekelle, "Is the Methodological Quality of Guidelines Declining in the U.S.? Comparison of the Quality of U.S. Agency for Health Care Policy and Research Guidelines with Those Published Subsequently," *Qual Safety Health Care*, 12(6), December 2003, pp. 428–434.)

- ii. In the current project, the reviewer in question project used the training materials available on the AGREE website. Because ratings for practice guidelines were consistent with standardized reviews posted on the website, we felt this individual was qualified. For the opioid guidelines, this reviewer's ratings were as internally consistent, thoughtful, and high quality as those of the physicians on the team.
- 2. Institute of Medicine Report
 - a. The Institute of Medicine report recommends new Standards for Trustworthiness. While it says that the AGREE instrument and other guideline appraisal methods fall short, in fact, just about every aspect of the "Standards for Trustworthiness" that the IOM articulates are encompassed by the domains in the AGREE Instrument.
 - i. The AGREE II addresses some limitations to the AGREE and was released in 2010. A citation referring to the AGREE II is: Brouwers M, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, Fervers B, Graham ID, Grimshaw J, Hanna S, Littlejohns P, Makarski J, Zitzelsberger L for the AGREE Next Steps Consortium. AGREE II: Advancing guideline development, reporting and evaluation in healthcare. Can Med Assoc J. 2010. Available online July 5, 2010. doi:10.1503/cmaj.090449
 - b. The Institute of Medicine report is not a tool for evaluating guidelines. The Standards for Trustworthiness have not been operationalized, for example, nor have they been tested on actual guidelines.
- 3. Rating MTUS version of WLDI guideline
 - a. We are well aware that the California MTUS guideline for the management of opioids is based on the WLDI guideline. However, we did not use the MTUS available on the internet in lieu of the WLDI guideline chapter on opioids. We did not confirm that the version of the MTUS available on the internet meets either of the following two criteria:
 - i. The MTUS is the most up to date version of the WLDI guideline.
 - ii. The version of the MTUS on line reflects the organization and presentation of the actual WLDI guideline. (We suspect it does not, since the WLDI guideline, if we recall correctly, includes multiple different web pages per chapter.)
- 4. Potential for Bias
 - a. We fully agree that potential for bias is an issue. We do take it very seriously. Indeed, in our 2004 evaluation, we observed that a guideline with low ratings for editorial independence was judged invalid by our panelists. However, we do not systematically downgrade a guideline merely for having been developed by a

specialty society. Nor do we systematically downgrade guidelines developed by organizations that sell their guideline materials to the public for a fee. Any organization sponsoring guideline development, including a governmental entity, can create the potential for bias. Yet the potential for bias does not equate with bias. Two key issues for the development materials to disclose are how conflicts of interest were handled, and whether the development group had full editorial independence from the funder.

- b. We used the information available with the guidelines and supporting materials to rate Editorial Independence, as is the standard for performing these analyses. We did not conduct an investigation into potential Congressional investigations, etc.
- c. The APS-AAPM guideline received a high score for Editorial Independence because it disclosed more relevant details. The development of this guideline was led by the individual who leads the Evidence-Based Practice Center at the Oregon Health Sciences University; AHRQ holds the Evidence-Based Practice Center staff to very high standards for editorial independence. This may be why the guideline provides more detail.