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January 13, 2016

Arlene I. Greenspan, DrPH, MS, MPH
Associate Director of Science, Office of the Associate Director of Science
National Center for Injury Prevention and Control
Centers for Disease Control and Prevention
4770 Buford Highway NE, Mailstop F-63
Atlanta, GA 30341

Re: Comments on Proposed 2016 Guideline for Prescribing Opioids for Chronic Pain

Dear Dr. Greenspan,

On behalf of the more than 8,000 physiatrists of the American Academy of Physical Medicine and Rehabilitation (AAMP&R), we appreciate the opportunity to submit comments on the Center for Disease Control's (CDC) *Proposed 2016 Guideline for Prescribing Opioids for Chronic Pain*. Physiatrists are specialists in the field of physical medicine and rehabilitation (physiatry) and treat adults and children with acute and chronic pain, persons who have experienced catastrophic events resulting in paraplegia, quadriplegia, traumatic brain injury, spinal cord injury, limb amputations, rheumatologic conditions, musculoskeletal injuries, and persons with neurologic disorders or any other disease process that results in impairment and/or disability. Below are the AAPM&R comments on the proposed prescribing guidelines.

General Comments on the CDC Draft Guidance

The CDC guidelines focus on societal risk mitigation in response to the opioid misuse, abuse, and heroin epidemic. There are noted methodological flaws in how the evidence, and in particular, the clinical trial evidence, was interpreted, and in many cases excluded. This flaw may throw into question the applicability of this document as a "true" evidence-based clinical practice guideline. The overall document does support closer monitoring and assessment of patients considered for and maintained on opioids, and highlights the importance of integrating monitoring techniques into primary care practice. We recommend that the consensus panel consider some monitoring and/or auditing criteria (i.e., performance measures). Question 5: See Public Engagement, Guideline Summary p. 6. See Provider and Patient Values and Preferences, Guideline Summary, pp. 12-13.



The Guideline is confusing in terms of who they are specifically meant for. They state PCP and internists but they include pain specialists in stakeholder group. It should be noted there were no pain specialists in the guideline Core Expert Group.

A broad range of professionals treat patients with chronic pain which is nonterminal, and only a subset of "medical professionals" were included in the development of the guidelines. However, a professional group performed the literature review and their background might have been expansive and inclusive.

It's not clear whether the health side effects and risks are included in the literature reviewed. Often just the benefit is addressed and measured.

There was no description of how and when to update the Guidelines.

It is really important in this particular guide to include the views of the populations effected and the cost for implementation. Tracking the outcomes would be very advisable and recording barriers to implementation extremely helpful for moving forward. The CDC and its mission could be able to move such weight since the magnitude of this particular health/medical/wellness condition cost not only individual lives, but society billions of dollars.

Comments on Recommendation 1

Agree with recommendation for nonpharmacologic therapy and nonopioid therapy for chronic pain but concern is that primary care doctors have little experience integrating these successfully into practice. For the primary care world, there is little knowledge or experience with this. Also, reimbursement is poor and limited.

The discussion regarding non-pharmacologic treatments is very brief and incomplete. The key issue here is glossed over – “will there be adequate programs to do the non-pharmacologic treatment and will insurances be required to cover such!” Will need significant education and resources.

The issue of relationship to mental health treatments must be addressed as we know that a moderate segment of patients requesting opioids are being treated psychotropically with these because they do not have access to mental health treatments otherwise.

There are current limitations in both pharmacologic and non-pharmacologic treatment outcomes for specific subpopulations which need to be explored

A big concern at present would be how to address the population of patients already on doses of meds above the 90 MEq level that is proposed later in guidelines.

Interventional procedures common to chronic pain population includes interventional spine procedures. This document does not touch upon how those procedures can be integrated.

Pharmacologic evidence for recommendations for acetaminophen and NSAIDs did not use level of evidence placed on opioids. There is poor to no evidence NSAIDs have efficacy beyond acute period of MSK, joint pain, and even less for other chronic pain conditions. In addition, the chronic and continuous use of these meds have health risks also.

This recommendation states that “given uncertain benefits and substantial risk, experts agreed that opioids should not be considered first-line or routine therapy for chronic pain . . . outside of active cancer, palliative, and end-of-life care.” Given the estimate of over 200 million prescriptions per year for opioids in the US, and possibly 17,000 deaths per year, (related to opioids) the actual percentage is close to 0, which raises a question as to whether this constitutes “substantial” risk. Efforts should be focused on curbing opioid misuse, not to limiting appropriate use for patients that benefit from the opioid. The general discussion of this guideline fails to make a connection between substance abusers, persons with drug addiction history and patients with pain. Although there is an epidemic of deaths related to “opioids,” there is a concern that legitimate pain patients will not be offered opioids when appropriate.

Comments on Recommendation 2

We currently do not have uniform measurement tools to monitor pain/function that are accepted throughout the country. Therefore the implementation of this recommendation without the correct guidance/structure is still very haphazard and subjective.

Currently all measures of pain/function remain self-reported and can therefore be potentially manipulated by a person who has possible substance use disorder. Although there are some proposals in the document regarding which measures to use, if these are to become standards, the structure of monitoring must be more clearly defined.

Disagree with “clinically meaningful improvement in pain and function”. Clearly, any provider that treats patients with pain, understands the challenge to show improved function, and the difficulties with measuring this. Some patients may have improved pain (even modest) that helps their quality of life and decreases suffering, yet not show any objective change in function. The recommendation should be changed to clinically meaningful reduction in pain OR function.

What are physicians to do if a patient is stable on a dose/regimen, and function is stable?

There may also be problems with disease progression with chronic pain, underlying psychosocial factors, and other things which may never change or improve, yet those patients still need the best possible therapy.

Clinically, if one is disagreeing/debating with a patient about continuing or starting opioids, the physician needs to re-assess what it is that is really going on with the patient.

For this recommendation, “strong” recommendations are being made with very low quality evidence.

Comments on Recommendation 3

We Agree with the premise of providing education and guidance to patients and, when needed, family members. Most of what is stated is part of FDA ER/LA Opioid REMS education for practice management of opioids. This should be mandated education for all providers, not voluntary. It remains a challenge to get this educational content to primary care providers. Many of the recommendations on proper education, goal setting, and patient monitoring practices mentioned in this document are core strategies, most can agree on, yet they have not caught on with PCPs. REMS requires education of primary care providers although it is uncertain what percentage of PCPs have undergone this training.

Comments on Recommendation 4

While we agree with the stated premise that “When starting opioid therapy for chronic pain, providers should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids,” however the discussion wanders to whether ER/LA opioids should be used at all and if ER/LA opioids provide any better response or safety that SA opioids. This would be a major shift in clinical practice guidelines if the proposal is really to eliminate ER/LA opioids.

Another statement in the Guidelines is more problematic and we do not agree with it. That statement is: “in general, avoiding the use of immediate-release opioids in combination with ER/LA opioids is preferable, given potentially increased risk and diminishing returns of such an approach for chronic pain.” This statement is not practical or based on any scientific data. It is common practice for patients to be on long-acting opioid and given short-acting breakthrough medicine. Many times, patients take excessive short-acting with long-acting meds, and this is not appropriate. Stating

that short-acting and long-acting should not be used together is a dangerous recommendation. This statement may create unintended risk for providers. Much more evidence needs to be provided to support this recommendation.

Similarly, there was a statement that “Experts indicated that there was not enough evidence to determine the safety of using immediate-release opioids for breakthrough pain when ER/LA opioids are used for chronic pain outside active cancer pain, palliative care, or end-of-life care . . .” This statement is biased and misleading. All FDA trials for short-acting and long-acting opioids are single- drug trials that rarely use active controls let alone combination long-acting and short-acting drugs. The Pharma trials use some short acting medications for breakthrough pain and demonstrated safety because they follow strict criteria. That being said, the AHRQ Opioid Review in 2014, which was the main evidence used for the CDC document, excluded any trial published by pharmaceutical companies less than 1 year in duration. Most FDA approved Phase III, and IV trials are mandated by the FDA (negotiated by FDA in collaboration with the individual companies) and paid for by pharmaceutical companies. Excluding all of short term, long-term efficacy and safety data from pharma-sponsored trials limits any clarification of these complex questions (using short-acting with long-acting opioids). Many of the long-acting studies used very small amounts of “breakthrough” medicine in placebo arms and long-term safety studies. This data would be valuable to include.

Tapentadol and Buprenorphine were left off the list of ER/LA opioids in the first paragraph.

There are also hidden recommendations within the text regarding limiting methadone and fentanyl due to safety issues. However, most insurance carriers require the use of these drugs before approving other ER/LA opioids that are not in generic forms yet. The fact that insurance carriers can require a patient to try the less safe meds before other ER/LA is a concern. Even in the REMS info, it recommends that methadone and fentanyl not be used as first line meds, but insurance carriers continue to require this due to cost issues. Currently the cost/expense issues are being allowed to outweigh the clinical expertise and safety of the recommendations from clinicians. This is especially true with most Medicaid coverage which is part of the government agencies that are proposing these changes, and associated REMS guidelines. Government funding agencies will need to be required to follow these guidelines also!

Comments on Recommendation 5

This recommendation tends to overlap with guideline #1. To be able to accomplish the recommended options, there certainly needs to be funding for the alternative treatments, especially behavioral health interventions (i.e. psychological evaluations,

cognitive behavioral therapy, counseling, multidisciplinary care, physical and occupational therapies) . The most appropriate clinical pathway for evaluating and monitoring risk stratification is with a clinical psychologist, and will need funding to be required/available. Behavioral health intervention (psychological treatment and counseling) in conjunction with the provider working on tapering would most likely be of strong benefit.

These are very difficult tapering patterns and likely may need to move from PCP to specialists. The availability and funding of these specialists/programs must be part of the requirements in this guideline.

The biggest dilemma clinically at present is the group of patients that started opioids many years ago and remain on moderate to high doses but are functional.

In the text under the guideline, the term high dose opioids is used but there is no definition of this. There should be a listed number here for all to measure against.

We also have significant concerns that 50 MME and 90 MME are at best arbitrary and not specifically supported by scientific evidence. Although we agree that one should keep doses as low as possible and avoid dose escalation, there is a false sense of security with lower doses. The CDC limitation on MME fails to consider receptor variability, genetic differences, and problems with equi-analgesic tables and dosing. This same conclusion was reached by the Food and Drug Administration (FDA) in the 2013 response to the Citizen’s Petition requesting limits on routine opioid daily dose and duration of treatment, and led to a significant change in the FDA indication of extended release (ER), long-acting (LA) opioids and updated box warning for these formulations . Most pain societies have moved away from supporting specific equianalgesic tables due to similar recognized physiologic differences. Use of these tables have led to overdoses and other adverse events. Most of this verbiage on MME limits has come from the Washington State Guidelines. I have seen firsthand how arbitrary focus solely on “MMEs” and use of equianalgesic tables and aps (State sponsored and published) has caused many providers to be more focused on an “MME number” vs assessing the patient in a more comprehensive manner.

Recommendation includes removing last sentence “Providers should implement additional monitoring precautions when increasing dosage to > 50 MME/day and should generally avoid increasing dosage to > 90 MME/day.”

Recommendation should be amended to include:

When opioids are started, providers should prescribe the lowest effective dosage. Providers should use caution when prescribing opioids at any dosage, and should implement additional precautions and monitoring when considering dose increases.

The nonbolded text following this specific recommendation could remain, but expand on examples of dosage thresholds as explaining lower from higher doses in this context.

The later recommendations on how to approach a patient transitioned in care on high doses and the need to be non-judgmental, as well as steps to help taper doses down along with assessing for unmasking of depression and anxiety, and the potential need to refer the patient to a pain specialist is well written.

Not sure it is appropriate or practical to provide a patient with a naloxone script if they are on ≥ 50 MMEs. Many questions arise. Are patients and family members able to be properly educated? Can they actually accurately assess overdose? IM naloxone by trained professionals, firefighters, police officers, medics, seems more appropriate until this intervention can be better studied. Use of naloxone in lower dose patients vs. high-risk patients (methadone, high MMEs) may be two very different subtypes of patients. This recommendation fails to address that.

Note – This recommendation will receive the most attention from the press and general public.

Comments on Recommendation 6

This is a very major topic but very incomplete discussion. It does note that there is no data regarding how long or how much opioid is really necessary for any specific diagnoses. It does not discuss the variability of different diagnoses with probability of different levels of pain management required. In addition, this starts to develop recommendation for non-traumatic and non-surgical issues. However, a large proportion of opioids prescribed but not utilized are from post-op and other post-hospitalization prescriptions. Even a large percentage of patients being discharged from hospitals without a surgical admission are given a prescription for pain medications. Many times, a considerable number of pills prescribed are never taken by the patient and “leftover” medications are stored away in medicine cabinets. This relatively large number of unprotected pills have been thought to be a significant contributor to increase recreational abuse, misuse, and potential overdose and harm to the community, by other persons with pain, recreational users, and those with substance abuse problems.

A valuable discussion within this section would be to separate the amount of prescriptions/meds that are prescribed for acute vs chronic pain and then link this back to which group experiences the higher percentage of overdoses and substance use disorders. This is still not clear in the literature and the transition for many people from

the use of pain meds as a substance of abuse to other things such as heroin occurs in people who have access to other people's meds but are not patients themselves!

There are inappropriate statements within this section including:

1. "The lowest effective dose can be determined using product labeling as a starting point ..." There is nothing in product labeling for any of the opioids to indicate proper prescribing or dosing. Labeling will only address what dosing options are available. Obviously the lowest dose possible is zero and anything increasing from there is possible based on side effect profile or not. This has nothing to do with labeling as short acting meds can even be cut in half for lower doses, or liquid forms can be considered.; and
2. "...calibration as needed based on the severity of pain..." is entirely incorrect. The higher pain levels begin to demonstrate the emotional response to having pain and titrating based on these numbers is utilizing more opioids for emotional/psychological issues related to pain. This is often the group of patients that we do not want to get started on opioids or higher doses, and responding just to higher numbers of pain rating is not correct! Unfortunately this demonstrates to me that the persons highly involved with putting together these guidelines still do not truly understand what pain is about and how it is generated or changed in the nervous system!

There is also significant concern regarding the statement that "three or fewer days will be sufficient" for non-traumatic pain conditions. This was based mostly on ER data, one study on paracetamol, not inpatient data. This ignores severe pain related to pancreatitis, other GI problems, sickle cell disease, etc.

Agree that we need to limit overprescribing to patients after discharge from the hospital and need to limit unused opioids that many times remain in medicine cabinets (after elective surgery or acute pain problems). Recommendations should be on closer monitoring of pain and more frequent follow ups. Limiting medication supply to 3 or fewer days may lead to patient undertreatment of pain. May also lead to more ER visits. We recommend removing the last sentence from the recommendation that states "three or fewer days usually will be sufficient for most nontraumatic pain not related to major surgery" until more evidence is available and keep focus of recommendation on prescribing at lowest possible dose, and only for expected duration, and need for close follow up. Consider inserting . . ."The duration of severe pain varies depending on the individual's medical conditions but the need for opioids for acute pain rarely exceeds one to two weeks for most nontraumatic or nonsurgical pain.

Comments on Recommendation 7

We agree with this recommendation but have some suggestions on improving it. This guideline does demonstrate the need for more frequent follow-up/monitoring of

patients during times of change in medications or doses. Increased structure and framework for patient visits as the dose changes, and at variable levels would be helpful for the clinicians. It may be helpful to stratify these issues in relation to the levels of MEq that are discussed in guideline #5.

This is an area that needs much more discussion than the current text, and there should be examples of a timeline framework for how often and when to see persons following changes. This should include guidelines for follow-up from ED visits, surgical or non-surgical hospitalizations, etc., as was proposed in guideline #6. In these situations, the patients are not scheduled for routine follow-ups with the assumption that the PCP or other pain provider will see them and continue a regimen of meds that these providers did not start. This creates a very difficult and undefined management pathway.

All of these requirements for future monitoring, smaller prescriptions and frequency of follow-up must be incorporated into insurance company pathways as currently many will only allow 30 day prescriptions and if a smaller number is filled, there cannot be additional prescriptions filled in the same month (more likely with Medicaid and/or Medicare carriers) and for most carriers, there will be multiple co-pays if a person has to fill a new prescription every 3-5-7 days. These insurance requirements/payments ultimately determine a lot of how prescriptions are written at the present time and must change for patients/providers to act differently!

More framework in this area would also allow better tracking through pharmacy computers and with the use of the Prescription Drug Monitoring Programs, as certain MEq levels would trigger what could and could not be filled at certain times in a pharmacy. This would allow for assistance for the PCPs in tracking these issues instead of placing all of the responsibility on the PCP office for monitoring and compliance.

This section does contain some recommendations for which measurement tools to follow for pain and function levels, which is needed and currently absent in most national guidelines. However, the currently proposed 3 item “PEG”, although validated in the literature, is not commonly utilized in pain practices or pain studies. Many of the functional measures are more validated and utilized but not in a primary care setting and will add significant time and effort in the PCP offices.

As noted under guideline #2, in the clinical setting, if the provider is disagreeing/debating with a patient about the frequency of visits or effects of changing opioids, the physician needs to re-assess what it is that is really going on with the patient as this is a demonstration of the psychological desire for opioids as opposed to the possible need for analgesia.

Note - The recommendations on the amount of days are largely based upon consensus, not based upon strong evidence. More structure for kinds of dosing changes and

fluctuations on the best way to approach this so that all are in agreement – education for physicians, patients, and insurance companies is necessary to do this. A framework for how to set up one's practice is needed in these guidelines.

Comments on Recommendation 8

Managing higher risk patients (including those with substance abuse problems or histories of psychiatric disorders and/or ongoing depression, anxiety) can be very problematic for specialists (PM&R, pain medicine), let alone for primary care physicians. The recommendation should include mention of referring these patients on higher dose or with greater risks earlier to pain medicine specialists, addictions specialist, or behavioral medicine. Much of this recommendation focuses on offering naloxone, although this remains a controversial approach, and the practicality of education and use remains to be proven especially in primary care setting.

General AGREEMENT – There is definite need for ongoing monitoring of risk vs benefit and, as noted under guideline #5, this should include regular and easy access to clinical psychology as needed. The most effect evaluations regarding opioid use disorders comes from this specialty group as opposed to the screening tools currently utilized.

The definitive need for dispensing naloxone with opioid prescriptions is still highly in debate. The success of public utilization is not established and whether this has a positive impact on patients receiving opioids for physician-provided pain management or might be of overall societal benefit for people misusing opioids or other controlled substances is questionable. In either case, there would have to be a massive distribution and educational process performed, and this massive educational need would be better served in teaching the general population about pain, pain pathways in the nervous system, and proper pain management that is not biased by whoever is funding the ads, such as at present.

Clinically, it seems part of the support for the use of naloxone is based on prescriptions given to persons who previously had a history of abuse or overdose. It is highly debatable whether this patient group should be receiving opioids at all for their pain (with the limited evidence of successful treatment with the opioids) and if so, should certainly not be receiving them from their PCP, but should likely only be receiving them from a specialist in substance abuse treatment. This would further decrease the incidence of need for PCPs to be prescribing naloxone with the regular use of opioids.

Comments on Recommendation 9

We generally agree with this recommendation. However, the guideline lists this for “high opioid dosages”, which is not defined, once again. This guideline is necessary/beneficial for all persons receiving chronic opioid management regardless of

the size of the dose. There could be consideration for stratification for how often it is required based on the size of the doses. It is appropriate that this guideline and #11 address the complex safety issues regarding the interactions with benzodiazepines. They did acknowledge the limitations/gaps in the reporting structure at present.

Within the text it discusses the need for completing the review of PDMP, but then notes that patients should not be discharged from the practice if there are variances on the review. This is really placing the primary care physician in very unmanageable situations, as patients will continue to demand prescriptions even though there are concerns by the provider. I would agree that discharge may not be the first step to take with a patient, but to not discharge, it should be noted that a patient would have to agree to substance abuse treatment by a specialist and remain compliant with the treatment. This will require all insurance carriers to provide coverage for this type of treatment.

PDMP data is still too state specific. Societies need to push for more comprehensive sharing of data between state PDMPs.

The recommendation discusses weaning benzodiazepines when on opioids. Should consider adding more specific recommendation including a need to additionally change patient to less hazardous or dependency producing anxiolytics, referring to behavioral health professional for more comprehensive evaluation of anxiety, etc.

Comments on Recommendation 10

Recommending “at least annually” is too weak. At least 2-3 times per year for all patients and/or left to discretion of provider.

This is a standard that became more prominent with the REMS for ER/LA opioid management. For example, some PM&R physicians have followed the same pathway for all patients who are receiving routine/continuous opioid management regardless of the dose and type of med. This guideline would further emphasize the continuation of this philosophy and if everyone is being tested it does remove the stigmatization of this as the text discusses.

As in guideline #9 though, the recommendation to do the testing and then not discharge the patient if abnormal is very controversial and difficult to manage in a PCP office. Some framework for repeating the testing if abnormal, and discussion of levels of concern with different abnormalities would likely be helpful and necessary to enhance the intent of this guideline. As noted above, with many abnormalities, the patient would need specialist evaluation and treatment, and continued management alone in the PCP office may not be indicated

There is concern with the listing of heroin in paragraph #2 as one of the substances to look for in urine drug testing, since heroin is a rarity to find based on rapid

metabolism, and if heroin identification is one of the key points for this guideline, then there needs to be more discussion of how to interpret UDS to see the downstream metabolites of heroin in the system.

Comments on Recommendation 11

Good recommendation. This provides very clear structure to the clinician to be able to discuss and implement tapering, whether opioids or benzos with the patient. It should be emphasized if a patient is receiving both, that since the opioid is likely providing some anti-anxiety management, there should be inclusion of psychology management for these patients as they are tapered. Once again, the need/requirement for insurance coverage of these issues is essential.

Should also include mention of pitfalls of prescribing soma (carisoprodil) and related benzodiazepine metabolite issue. Soma should not be prescribed, and patients transitioned to practice on it should be tapered off and evaluated appropriately

Comments on Recommendation 12

The type of treatment described in this recommendation must be accessible and covered as noted. As in the issues with Guidelines #9 and #10, the patient must agree to participate in this treatment to remain in the management of a particular provider. The inclusion of these medications in the PDMP allows clinicians to see that treatment has occurred for this person within a program. This should alert any clinician to not prescribe opioids to this patient, but in general as a medical community we will have to decide what to do with the patients who do not maintain compliance with their program.

The recommendation should more specifically mention referral to substance abuse specialist, and/or pain medicine specialists. Patients with substance abuse histories (active or stable) are complex and recommendations to PCPs should highlight need to include specialists earlier, and in many instances, as part of the treatment team.

AAPM&R appreciates the opportunity to offer these comments and looks forward to working with the CDC as these guidelines becoming finalized. Should you or your staff have questions regarding these comments, please do not hesitate to contact Kate Stinneford, RN, JD AAPM&R Manager of Health Policy, at kstinneford@aapmr.org for more information.

Sincerely,

Richard Zorowitz, MD
Chair, Clinical Practice Guidelines Committee
American Academy of Physical Medicine and Rehabilitation