Today’s healthcare practitioners are grappling with how to properly assess, care for, communicate with, and monitor patients with persistent pain, and who may be at risk for substance use disorders, while being mindful of public safety efforts related to inappropriate or excessive prescribing. This document is the first in a series to examine the US Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain¹ (CDC guideline), and its effect on a variety of important clinical practice issues and to help practitioners better understand how the CDC guideline recommendations compare or conflict with state policy. Topics in this series will include opioid dosage and morphine equivalency; naloxone; and non-pharmacological options for managing pain. It is important to emphasize here that, although the CDC guideline provides only recommendations that are NOT binding on any state or individual practitioner, there are practical implications that every practitioner should be aware of while caring for people with chronic pain. Furthermore, despite CDC’s stated intent of producing voluntary recommendations, the guideline could be adopted into law and become a codified standard of care by which non-compliance decisions could be made.

The topics of regulating opioid dosage and determining morphine equivalency are presented together because they are linked in both the CDC guideline and in state-specific policies. The aim of this brief is to highlight the interplay of inconsistent policies between states and the CDC guideline, illustrating how these discrepancies can present a barrier, or at least create ambiguity, to optimal opioid prescribing. To show this interplay, we have compared recommendations from the CDC guideline pertaining to opioid dosage and morphine equivalency to related state standards, describing how a patient could receive care in each scenario.

While the CDC has only made recommendations rather than binding requirements, we believe it is important to consider how these recommendations may affect patient care decisions differently than current state standards. First, the CDC guideline has received a disproportionate amount of attention from policymakers and media in comparison to any other related guidelines that have been recently released by other organizations (e.g., American Academy of Pain Medicine², American Pain Society³, and Federation of State Medical Boards⁴). Second, policymakers, including medical boards, tend to hold CDC recommendations in high regard. The weight that policymakers give these recommendations can influence their own efforts to develop additional policy, especially statutes and rules. In fact, since release of the CDC guideline, state legislators have introduced numerous pieces of legislation that, if passed, would codify portions of those “recommendations” into state legal “requirements.” Finally, there may be other unanticipated ways in which these CDC recommendations become de facto requirements; for instance, there are anecdotal reports of insurers using the thresholds identified in the CDC guideline as new standards for prior authorization, thus creating barriers to allowing prescribers to use their clinical judgment in treating their patients.

The use of dosage thresholds in prescribing policies, and the even more novel use of dosage ceilings, is relatively new. In 2012, Washington was the first state to introduce the use of a dosage level to trigger a required action (referral from general practitioner to pain specialist) on the part of the prescriber who is treating chronic pain with opioid therapy. Since that time, several other states have adopted their own policies tied to dosage (with a number of others considering similar measures; see Appendix). To date, all dosage-related policies require calculation of a patient’s total daily opioid dosage and conversion of that dosage to a morphine equivalent daily dose (MME/day), which itself is an error-prone process.\(^5\),\(^6\),\(^7\),\(^8\).

Two CDC guideline recommendations relate to a daily dosage.

**CDC Recommendation #5:**

> When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day (recommendation category: A, evidence type: 3).\(^9\)

Although the treatment parameters outlined in Recommendation #5 may seem clear, there is ambiguity about how they could be implemented in clinical practice. For example, how is the “lowest effective dosage” determined? Does this standard refer to any particular patient outcome (e.g., pain relief, quality of life, functioning, etc.), and what other factors are considered? In practice, it is not possible to know the “lowest effective dose” until a particular dose is selected, tried, and evaluated for outcomes, meaning that knowing this dose a priori is not possible. The same issue applies to meeting and exceeding the dosage thresholds – what features would satisfy the procedure to “carefully reassess evidence of individual benefits and risks”? Finally, when there comes a need to “carefully justify a decision” to go beyond 90 MME/day, how is this accomplished? The CDC guideline provides no specific guidance for practitioners concerning the manner in which they can satisfactorily achieve these standards to avoid a determination of non-compliance from whatever agency or institution may come to enforce the recommendations.

Further, the CDC also relies upon MME dosing when discussing how to identify and mitigate risk during ongoing treatment of pain with opioid therapy:

**CDC Recommendation #8:**

> Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present (recommendation category: A, evidence type: 4).\(^10\)

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\(^9\) Ibid., 26.

While these recommendations may, at first glance, appear to restrict opioid dosages to below a certain level, a careful reading of the CDC guideline reveals this is not the case. The CDC’s intent not to limit opioid dosing to a specific MME/day level or below is reflected in the CDC’s own comments within its recent guideline:

- The CDC guideline only contains recommendations, meaning that they are not legally binding on anyone. They should help to guide a practitioner’s decision-making, but they do not override the provider’s clinical judgment, nor do they override state law. CDC has made it clear in its own materials that the “recommendations in the guideline are voluntary, rather than prescriptive standards.” ¹¹
- No dosage levels are prohibited by the CDC guideline; rather, the CDC guideline points to certain dosage levels that should trigger caution, further evaluation, and adequate documentation.
- Both recommendations were based on studies with notable or “several major limitations.” ²¹

Moreover, a comparison of the CDC recommendations and the policies of three different states display significant inconsistencies on critical guidance points, highlighting the need to fully understand the interplay between the various policies in order for a healthcare provider to meet the standard of care within their own state.

## VARIABILITY IN PRACTICE GUIDANCE

As of August 22, 2016, nine states have created prescribing policies containing dosage thresholds related to opioids. The following case example will focus on only three states—California, Maine, and Washington—because of their variability in terms of dosage level, and whether their prescribing policies are statutes/rules (mandatory) or guidelines (recommendations). Also, it is important to note that rules can also be recommendations when states use “should” rather than “shall” in the language of the rule. The figure below demonstrates how these nine states and the CDC recommendations vary in their guidance regarding opioid dosage and morphine equivalency when treating patients with chronic non-cancer pain.

### See Appendix for detailed information about each of the recommendations and requirements listed above.

¹¹Ibid., 2.
²¹Ibid., 17.
In order to understand how these differing guidelines can create both confusion and varying standards of care, it is useful to consider a patient example. Consider the case of Jane Doe: how her care would play out differently under the California, Maine, and Washington standards, and how the CDC guideline also would come into play in those various scenarios.

**The Case:**

Jane Doe is a 52-year-old woman with Ehlers-Danlos Syndrome. She was diagnosed approximately 45 years ago, at the age of 7. She has been treated for this condition by a series of primary care physicians, most recently by Dr. Jones, a physician she has seen during the past four years. Over the course of her illness, Jane has undergone multiple courses of physical therapy, acupuncture, and psychological counseling. She routinely uses braces on her hypermobile joints, and uses short courses of acetaminophen if she experiences a joint dislocation. Jane’s blood pressure is chronically elevated, and her renal function is marginal, eliminating NSAIDs as a treatment option for her.

Approximately ten years ago, Jane’s pain worsened to the point where she became unable to work on an assembly line in the local automobile plant. She received a favorable disability determination, and now spends her time doing very limited volunteer work for her church. Jane’s 26-year-old daughter works part-time, and she tries to help out by babysitting her one-year-old grandchild. However, Jane has now reached the point where she thinks that she may no longer be able to do so because of the pain produced by the physical demands of childcare for a toddler.

When she began seeing Dr. Jones, Jane asked whether there are other medications that could help minimize her chronic pain and enable her to continue volunteering and working in her gardens. Dr. Jones discussed carefully with Jane the expected benefits and risks of a variety of therapies used for chronic pain, and shared the most current evidence and his clinical experience with these. Together, they decided that combining non-pharmacological therapies with a course of opioid therapy would be reasonable.

Over the years, Dr. Jones has gradually increased Jane’s oxycodone dose with careful consideration and monitoring, and with evidence of positive results for pain and function from each increase. At this time, Jane takes controlled-release oxycodone, 35 mg twice a day.

At her regular appointment with Dr. Jones today, Jane indicates that the combination of oxycodone with her meditation practice and tai chi is helping, and she has only minor tolerable side effects (slight constipation and dry mouth), which are being effectively treated with over-the-counter products. She believes that a further dose increase would help, and might enable her to continue babysitting her grandchild for a while longer, which would address her daughter’s difficulty with affording childcare. Given her history of improvement with each incremental dose increase, Dr. Jones is inclined to increase her oxycodone dose to 40 mg twice a day with continued close monitoring.

**Consideration of Jane’s Treatment Plan Using Available Guidance**

In addition to the CDC guideline, Jane’s care would be subject to additional recommendations or requirements, based on state guidelines, regulations, and laws. On the opposite page, you can walk through the findings of Dr. Jones after consulting the CDC guideline and differing policies from three states.
While considering Jane’s request, Dr. Jones turns to the recently-issued CDC opioid prescribing guideline for its advice. He finds that, in accordance with Recommendation #5, he should “carefully justify a decision to titrate dosage to >90 MME/day.” He consults a standard equianalgesic dosing table, and discovers that it considers 1 mg of oxycodone to be equianalgesic to 1.5 mg of morphine; for Jane, this means she is currently taking 105 MME/day. Further, Recommendation #8 suggests that, given Jane’s daily opioid requirement of >50 MME/day, Dr. Jones should consider offering her a prescription for naloxone.

If Dr. Jones practices in California, the Medical Board of California’s Guidelines for Prescribing Controlled Substances for Pain recommend that, when Jane’s daily opioid dose exceeded 80 MME/day, Dr. Jones should have considered referring her to a pain management specialist for a consultation. However, because this is a guideline, and not a rule or statute, this consultation was not required, and Dr. Jones had discretion to increase Jane’s opioid dose to its current level. In fact, these guidelines make clear that Dr. Jones can increase Jane’s dose further, if he documents “a sound clinical reason” for doing so. While California has no official policy that recommends or requires Dr. Jones to consider prescribing, or to discuss with Jane the availability of, naloxone, California’s Guidelines for Prescribing Controlled Substances for Pain do contain suggested language on naloxone for use in the pain management agreement.

Under rules established by the Washington Medical Quality Assurance Commission, Dr. Jones would be required to seek a consultation with a pain management specialist before increasing Jane’s oxycodone dose to 40 mg twice a day. The Washington rules require consultation with a pain specialist when a patient’s dose reaches or exceeds a level of 120 MME/day. Jane’s proposed dose of 80 mg of oxycodone per day equals 120 MME/day according to the aforementioned equianalgesic dosing table, triggering the consultation requirement under the Washington rules. Further, neither Jane nor Dr. Jones meets any of the exceptions to the rule, so a consultation must be pursued before Dr. Jones increases Jane’s dose. The State of Washington has no official policy that recommends or requires Dr. Jones to consider prescribing, or to discuss with Jane the availability of, naloxone.

In its 2016 session, Maine passed a law setting an opioid dosing ceiling at 100 MME/day for new prescriptions. Under this new law, effectively immediately, patients may not exceed 300 MME/day, and any patient currently taking more than 100 MME/day of any opioid must be tapered to a dose not exceeding 100 MME/day by July 1, 2017. Given this new law, it would be unlawful for Dr. Jones to further increase Jane’s opioid dose, regardless of his clinical judgment that such an increase is indicated and would likely benefit Jane through improved function, which is one of the most important outcome measures of long-term opioid therapy. Furthermore, before July 1, 2017, Dr. Jones must work with Jane to decrease her oxycodone dose below its current level. Maine law requires Dr. Jones to make this reduction regardless of whether he is able to demonstrate and document Jane’s improved pain control and function on an opioid dose over 100 MME/day, and regardless of his careful patient monitoring and specific documentation of evidence that the benefits to Jane outweigh any harms posed to her by a higher opioid dose. The State of Maine has no official policy that recommends or requires Dr. Jones to consider prescribing, or to discuss with Ms. Doe the availability of, naloxone.

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17 32 MRSA § 2210 (2016).
Federal and state governments display unprecedented agreement about implementing policies that seek to curb prescription medication abuse, misuse, addiction and overdose. With this increased interest and momentum, new opioid-related policies are being created at a faster pace than has been experienced in recent memory. While these laudable efforts are needed, it is important for all stakeholders to understand and consider their potential impact, both intended and unintended.

Clinicians also need to understand the relationships among binding and non-binding policies, at both the federal and state levels. In some cases, one clinician, in treating one patient, could encounter policies that fall into all four of these categories. In these cases, the strictest standards, regardless of their original source, would apply, and the clinician would be responsible for applying those standards correctly. When policies are in conflict, even those enforcing them can become confused and apply them incorrectly. Concerns about regulatory scrutiny resulting from poor understanding of policies, as well as barriers created by the actual policies, may cause clinicians to deliver sub-optimal pain care, thereby creating the potential for other significant health issues, such as worsening chronic pain with decreased function; substance misuse, abuse, and addiction; and even accidental overdose.

High-quality pain care relies on the clinician’s ability to exercise good judgment in applying a combination of available scientific evidence and extensive clinical experience. It should be recognized, however, that the available scientific evidence for virtually any type of pain care is extremely limited, leaving the clinician with little concrete guidance. This results in a situation neatly summed up by the panel of independent experts who participated in an NIH Pathways to Prevention workshop evaluating evidence for the use of opioids in treating chronic pain:

“What was particularly striking to the panel was the realization that there is insufficient evidence for every clinical decision that a provider needs to make regarding the use of opioids for chronic pain, leaving the provider to rely on his or her own clinical experience.”

It can be challenging when all of this comes together to produce an effective treatment plan that policies then arbitrarily force to be adapted in ways that are unintended and not to the patient’s benefit. For example, the CDC guideline is intended to help primary care clinicians decide when to initiate or continue opioids in caring for most adults with chronic pain in outpatient settings. However, the CDC guideline and other states’ policies primarily address the escalation of dosing in the opioid naïve patient or the patient moving from low-dose to “high-dose opioid therapy. These policies do little to help prescribers who are caring for patients on doses that already exceed all recommendations and thresholds, especially those who appear to be benefitting from those doses without significant harms.

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CONCLUSION

As a prescriber or provider of pain care, it’s important to understand the differences between guidelines and statutes/rules when determining the treatment you provide. Prior to April 2016, there were no mandatory policies throughout the nation that placed a ceiling on per-day dosages of opioid analgesics. Maine’s new law, however, does set mandatory limits—a ceiling—for daily opioid doses. As we monitor other state legislative activity, pain care providers should focus on:

1. Understanding the integrative, or integrated, model of pain care which includes consideration of all available therapies (non-pharmacological and pharmacological) to determine the best plan of care for each patient;
2. Working with patients to determine the lowest effective dose (if an opioid is determined to be necessary); and
3. Thoroughly documenting for each patient an individualized treatment plan containing the rationale for using opioids, including the reasons for the patient’s legitimate medical need for higher doses, along with a careful analysis of the benefits and potential risks of each patient’s use of chronic opioid therapy.

Again, although the CDC guideline contains only recommendations that are not binding, there are practical implications that every practitioner should be aware of while caring for people with chronic pain. Because the CDC guideline could be adopted into law and become a codified standard of care, it’s essential to understand what this means to you. And it also is important to realize that this landscape is changing rapidly. For instance, the president recently signed into law a comprehensive bill, S.524, the Comprehensive Addiction and Recovery Act of 2016\(^{20}\), which had unprecedented support from Congress. Among many things, it mandates creation of a task force to develop best practices for pain management and opioid prescribing, an effort that should permit active involvement of all stakeholders concerned about the intersection between pain management and prescription opioid misuse, abuse, and addiction.

This Appendix includes additional details about prescribing policies from CDC and the nine states, as of August 22, 2016, highlighting language regarding opioid dosage thresholds. For a graphic representation, see the chart on page 3, demonstrating the variance in threshold doses.

**CDC** – When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.²¹

Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.²²

**California** – When the treatment plan is being initiated and the opioid dose adjusted, the patient should be seen more frequently.

When doses reach 80 MME/day: It is recommended that physicians proceed cautiously (yellow flag warning). Referral to an appropriate specialist should be considered when higher doses are contemplated. There is no absolute safe ceiling dose of opioids, and caution and monitoring are appropriate for applications of these medications.²¹

**Colorado** – For doses greater than 120 MME/day: Prescribers should use clinical judgement, put in place additional safeguards for the treatment plan (such as utilizing a treatment agreement), and consult a specialist or refer the patient.²⁴

**Indiana** – When doses reach 60 MME/day: A face-to-face review of the treatment plan and patient evaluation must be scheduled, including consideration of referral to a specialist. Physician must develop a revised assessment and treatment plan for ongoing treatment, which must be documented in the patient’s chart, including an assessment of increased risk for adverse outcomes.²⁵

When doses exceed 15 MME/day for more than 3 consecutive months: A face-to-face review of the treatment plan and patient evaluation must be scheduled, including consideration of referral to a specialist. Physician must develop a revised assessment and treatment plan for ongoing treatment, which must be documented in the patient’s chart, including an assessment of increased risk for adverse outcomes.²⁶

**Maine** – Unless an exception applies, >100 MME/day cannot be exceeded. Exceptions exist for pain associated with: active and aftercare cancer treatment; palliative care; end-of-life and hospice care; medication-assisted treatment for substance use disorder; or, other circumstances as determined by the Department of Health and Human Services.

Established patients already exceeding the 100 MME/day limit can be prescribed up to 300 MME/day, but must be tapered to 100 MME/day by July 1, 2017.²⁷
New Hampshire – When a patient receives 100 MME/day for longer than 90 days, the prescriber shall document the consideration of a consultation with an appropriate specialist.\textsuperscript{28}

Ohio – When doses reach 80 MME/day or greater: Strongly consider: reestablishing informed consent, including providing patient with written information about potential adverse effects; reviewing the patient’s functional status and documentation; review progress toward treatment objectives; establishing a treatment agreement; having the patient evaluated by one or more specialists.\textsuperscript{29}

Rhode Island – When doses reach 120 MME/day: Consideration of consultation with a Pain Medicine Physician is required and must be documented in the medical record\textsuperscript{30}

South Carolina – When doses reach 80 MME/day: Strongly consider: reestablishing informed consent; reviewing treatment objectives and current status; reviewing SCRIPTS; consultations with a specialist; offering naloxone.\textsuperscript{31}

Vermont – Prior to exceeding 120 MME/day: Prescriber shall record in the medical record: a reevaluation of the safety and effectiveness of the treatment plan, including an assessment of the patient’s adherence; the potential for the use of non-opioid and non-pharmacological alternatives; a functional status examination; a review of informed consent; an assessment of co-morbid conditions (may be best conducted by a mental health or addictions professional); and any other related actions that may reasonably lead a prescriber to modify the treatment plan.

Washington – Prior to exceeding 120 MME/day: Prescriber shall consult with a pain management specialist unless the consultation is exempted.

Exemptions exist when: the patient is following a tapering schedule; acute pain requires a temporary escalation in opioid dosage; the physician is a pain management specialist; the physician has completed a minimum of 12 continuing education hours on chronic pain management (at least two of which pertained to long-acting opioids) in the past two years; or, the physician is a pain management practitioner working in a multidisciplinary chronic pain treatment center.\textsuperscript{32}

\textsuperscript{21} Ibid., 22.
\textsuperscript{22} Ibid., 26.
\textsuperscript{23} Medical Board of California. Guidelines for Prescribing Controlled Substances for Pain. 2014. Page 14
\textsuperscript{24} Colorado Department of Regulatory Agencies. Policy for Prescribing and Dispensing Opioids. 2014. Page 3.
\textsuperscript{25} Indiana Code § 844-5-6-3; 2015.
\textsuperscript{26} Indiana Code § 844-5-6-9; 2015.
\textsuperscript{27} 32 MRSA §2210 (2016).
\textsuperscript{30} Rhode Island Gen. Laws Ann. § 31-2-6:3.9.