Opioid Prescribing: A Systematic Review and Critical Appraisal of Guidelines for Chronic Pain

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Background: Deaths due to prescription opioid overdoses have increased dramatically. High-quality guidelines could help clinicians mitigate risks associated with opioid therapy.

Purpose: To evaluate the quality and content of guidelines on the use of opioids for chronic pain.

Data Sources: MEDLINE, National Guideline Clearinghouse, specialty society Web sites, and international guideline clearinghouses (searched in July 2013).

Study Selection: Guidelines published between January 2007 and July 2013 addressing the use of opioids for chronic pain in adults were selected. Guidelines on specific settings, populations, and conditions were excluded.

Data Extraction: Guidelines and associated systematic reviews were evaluated using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument and A Measurement Tool to Assess Systematic Reviews (AMSTAR), respectively, and recommendations for mitigating opioid-related risks were compared.

Data Synthesis: Thirteen guidelines met selection criteria. Overall AGREE II scores were 3.00 to 6.20 (on a scale of 1 to 7). The AMSTAR ratings were poor to fair for 10 guidelines. Two received high AGREE II and AMSTAR scores. Most guidelines recommend that clinicians avoid doses greater than 90 to 200 mg of morphine equivalents per day, have additional knowledge to prescribe methadone, recognize risks of fentanyl patches, titrate cautiously, and reduce doses by at least 25% to 50% when switching opioids. Guidelines also agree that opioid risk assessment tools, written treatment agreements, and urine drug testing can mitigate risks. Most recommendations are supported by observational data or expert consensus.

Limitation: Exclusion of non-English-language guidelines and reliance on published information.

Conclusion: Despite limited evidence and variable development methods, recent guidelines on chronic pain agree on several opioid risk mitigation strategies, including upper dosing thresholds; caution with certain medications; attention to drug–drug and drug–disease interactions; and use of risk assessment tools, treatment agreements, and urine drug testing. Future research should directly examine the effectiveness of opioid risk mitigation strategies.

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A cross the United States, opioid-related overdoses have been implicated in increasing numbers of emergency department visits, hospitalizations, and deaths. Annual fatalities associated with prescription opioids increased from 4000 in 1999 to nearly 14 000 by 2006 (1). Several factors may explain these trends. First, over the past several decades, the number of patients receiving opioids and the number of doses prescribed have increased dramatically (2–4). Treating chronic pain with opioids went from being largely discouraged to being included in standards of care (2, 5, 6), and titrating doses until patients self-report adequate control has become common practice (5, 7). Today, 8% to 30% of patients with chronic noncancer pain receive opioids, with average doses typically ranging from 13 to 128 mg of morphine equivalents daily; some receive much higher doses (8). Second, the public seems to consider prescription opioids safer to abuse than illicit drugs, influencing patterns of overdose deaths (9, 10). Third, common drug–drug and drug–disease interactions contribute to overdoses. Half of fatal opioid overdoses involve the concomitant use of sedative-hypnotics, particularly benzodiazepines (1).

Given current rates of opioid overdose, policymakers are seeking solutions and standards of care are again evolving. The White House has issued action items, and an Institute of Medicine (IOM) report provides recommendations for policy audiences (11, 12). High-quality clinical practice guidelines would assist clinicians in making informed prescribing decisions and would mitigate the risks associated with using opioids. The objective of the current study was to systematically search for and evaluate the quality of guidelines addressing the use of opioids for chronic pain. A secondary objective was to compare guidelines’ recommendations related to mitigating the risk for accidental overdose and misuse, including considering the quality of the evidence that guidelines provide in support of their recommendations.

Methods

Study steps included searching for guidelines, applying selection criteria, assessing guideline quality, and extracting relevant content.
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**RESULTS**

**Search and Selection of Guidelines**

Of 1270 documents identified, 1132 unique records were eligible for screening, 19 full-text guidelines were considered for evaluation, and 13 were eligible (Appendix Figure). An online report includes a previous version of the search (39). Of 6 guidelines considered but found ineligible, 1 was derived from another guideline (18) and 5 lacked details on development methods (17, 40–43).
### Table. Selected Guideline Recommendations Related to Mitigating the Risks of Opioid Therapy During Long-Term Use for Chronic Noncancer Pain

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Guideline Development Group (Reference)*</th>
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</thead>
<tbody>
<tr>
<td><strong>Dose that warrants scrutiny, mg of morphine equivalents per day</strong></td>
<td></td>
</tr>
<tr>
<td>Most patients successfully treated with lower doses; higher doses associated with adverse effects and overdose</td>
<td></td>
</tr>
<tr>
<td>Medications and formulations</td>
<td></td>
</tr>
<tr>
<td>Methadone: risks for QTc prolongation and bioaccumulation; only experienced providers should prescribe methadone</td>
<td>√</td>
</tr>
<tr>
<td>Fentanyl patch: limit to opioid-tolerant patients; variable absorption, exercise, and heat increase risk for overdose</td>
<td>√</td>
</tr>
<tr>
<td>Immediate-release fentanyl: limit to opioid-tolerant patients; safety unknown for CNCP; risk for overdose and misuse</td>
<td>√</td>
</tr>
<tr>
<td>Meperidine: do not use for CNCP because of bioaccumulation and central nervous system toxicity</td>
<td>√</td>
</tr>
<tr>
<td>Codeine: ability to convert to morphine varies greatly</td>
<td></td>
</tr>
<tr>
<td><strong>Initiation and titration of dose</strong></td>
<td></td>
</tr>
<tr>
<td>Strategies to minimize risk for overdose</td>
<td></td>
</tr>
<tr>
<td>Start low-dose, short-acting opioid as needed; visit in 2–3 d</td>
<td></td>
</tr>
<tr>
<td>Switching between opioids</td>
<td></td>
</tr>
<tr>
<td>Dose reduction: equianalgesic dosing tables omit variability</td>
<td></td>
</tr>
<tr>
<td>Switching to methadone: conversion ratios vary with dose</td>
<td></td>
</tr>
<tr>
<td>Drug–drug interactions</td>
<td></td>
</tr>
<tr>
<td>Sedative-hypnotics: risk for sedation, cognitive impairment, motor vehicle accidents, and overdose</td>
<td></td>
</tr>
<tr>
<td>Pharmacokinetic interactions: other medications affect the metabolism of specific opioids</td>
<td></td>
</tr>
<tr>
<td>Drug–disease interactions</td>
<td></td>
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<tr>
<td>Preexisting substance abuse disorders: increased risk for overdose and misuse</td>
<td></td>
</tr>
<tr>
<td>Mood, personality, and cognitive disorders: increased risk for overdose and misuse</td>
<td></td>
</tr>
<tr>
<td>Sleep and obstructive pulmonary disorders: opioids exacerbate</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td></td>
</tr>
<tr>
<td>Active metabolites of morphine accumulate</td>
<td></td>
</tr>
<tr>
<td>Screening tools for assessing risk for misuse (used in addition to patient history)</td>
<td></td>
</tr>
<tr>
<td>Recommends use</td>
<td></td>
</tr>
<tr>
<td>Provides examples</td>
<td></td>
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<tr>
<td>Written treatment agreements (used in addition to informed consent)</td>
<td></td>
</tr>
<tr>
<td>Recommends use</td>
<td></td>
</tr>
<tr>
<td>Provides example</td>
<td></td>
</tr>
<tr>
<td>Urine drug testing</td>
<td></td>
</tr>
<tr>
<td>Recommends use</td>
<td></td>
</tr>
</tbody>
</table>

ACAEM = American College of Occupational and Environmental Medicine; AGS = American Geriatrics Society; APS = American Pain Society; ASIPP = American Society of Interventional Pain Physicians; BZD = benzodiazepine; CNCP = chronic noncancer pain; DoD = Department of Defense; DWC = Division of Workers’ Compensation; ICSI = Institute for Clinical Systems Improvement; NOUGG = National Opioid Use Guideline Group; UDOH = Utah Department of Health; UMHS = University of Michigan Health System; VA = Veterans Affairs.

* Guidelines by the American Society of Anesthesiologists (53), Fine and colleagues (54), and the Work Loss Data Institute (56) are omitted. The American Society of Anesthesiologists guideline did not address topics in the table. The guideline by Fine and colleagues addressed switching from one opioid to another but not the other topics. The Work Loss Data Institute guideline content is proprietary.

† Evidence from randomized, controlled trial.
‡ Evidence from observational study.
§ Evidence from expert consensus.
|| Evidence from another guideline.

AAPM = American Academy of Pain Medicine; ACOEM = American College of Occupational and Environmental Medicine; AGS = American Geriatrics Society; APS = American Pain Society; ASIPP = American Society of Interventional Pain Physicians; BZD = benzodiazepine; CNCP = chronic noncancer pain; DoD = Department of Defense; DWC = Division of Workers’ Compensation; ICSI = Institute for Clinical Systems Improvement; NOUGG = National Opioid Use Guideline Group; UDOH = Utah Department of Health; UMHS = University of Michigan Health System; VA = Veterans Affairs.

* Guidelines by the American Society of Anesthesiologists (53), Fine and colleagues (54), and the Work Loss Data Institute (56) are omitted. The American Society of Anesthesiologists guideline did not address topics in the table. The guideline by Fine and colleagues addressed switching from one opioid to another but not the other topics. The Work Loss Data Institute guideline content is proprietary.

† Evidence from randomized, controlled trial.
‡ Evidence from observational study.
§ Evidence from expert consensus.
|| Evidence from another guideline.
**Table—Continued**

<table>
<thead>
<tr>
<th>Guideline Development Group (Reference)*</th>
<th>NOUGG (46, 60–62)</th>
<th>Colorado DWC (19)</th>
<th>ICSI (47)</th>
<th>UMHS (44)</th>
<th>UDOH (48, 50)</th>
<th>VA/DoD (45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009 (adverse effects)</td>
<td>120 (adverse effects)</td>
<td>200 (adverse effects)</td>
<td>100</td>
<td>120–200]</td>
<td>2006 (trials used ≥300†)</td>
<td></td>
</tr>
<tr>
<td>Start low-dose opioid; increase gradually; monitor§</td>
<td>Trial; visits every 2–4 wk; multidisciplinary pain management</td>
<td>Titrato to maximize benefits and minimize risks]</td>
<td>Visits weekly to monthly§</td>
<td>Trial; visits every 2–4 wk</td>
<td>Titrato up no more than every 5 half-lives§</td>
<td></td>
</tr>
<tr>
<td>Decrease dose by 25%-50%</td>
<td>–</td>
<td>Decrease dose by 30%</td>
<td></td>
<td></td>
<td>Decrease dose by 25%-50%</td>
<td>Decrease dose by 30%-50%</td>
</tr>
<tr>
<td>Try to taper BZDs†</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>List for tramadol</td>
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<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Comanage with addiction specialist</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Consider screening</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Morphine, codeine</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Decrease oxymorphone</td>
</tr>
</tbody>
</table>

Consider†

| May be helpful, particularly if risk is high§ | | | Strongly consider, particularly if risk is high§ | Agree on plan; signature is optional | Request that patient sign‡ |
| If using, consider pros and cons§ | Mandatory | Baseline and at least yearly thereafter§ | Consider| Baseline and at random thereafter§ |
Selected Guidelines

Appendix Table 1 (available at www.annals.org) lists the 13 eligible guidelines; all were published in 2009 or later. Systematic reviews were conducted in 2008 or later (among guidelines that reported this).

Seven guidelines apply broadly to adults with chronic pain (13, 44–50). Six have slightly narrower scopes: The American Geriatrics Society guideline addresses adults older than 65 years (51, 52); the American Society of Anesthesiologists guideline emphasizes procedures (53); a guideline by Fine and colleagues addresses opioid rotation (54); and guidelines from the American College of Occupational and Environmental Medicine, the Work Loss Data Institute, and the Colorado Division of Workers’ Compensation consider individuals with pain due to work-related conditions (19, 55, 56).

Guideline Quality Assessment

AGREE II

Overall guideline assessment scores were 3.00 to 6.20 (Appendix Table 2, available at www.annals.org). Rigor-of-development scores were 20% to 84%, clarity-of-presentation scores ranged from 37% to 93%, applicability scores were 13% to 56%, and editorial independence scores ranged from 0% to 88%.

Ratings were highest for a guideline by the American Pain Society and the American Academy of Pain Medicine (APS-AAPM) (13) and one by the Canadian National Opioid Use Guideline Group (46), the only guidelines that more than 50% of appraisers voted to use without modification. Most appraisers recommended against using 4 other guidelines because of limited confidence in development methods, lack of evidence summaries, or concerns about readability (19, 44, 53, 54).

Among the low- to intermediate-quality guidelines (19, 44, 45, 47–56), shortcomings included limited or no descriptions of input from guideline end users or patients; criteria for selecting evidence, strengths and limitations of evidence, and methods for formulating recommendations; external reviews before publication; plans for updating; barriers to implementation, resource implications, and how to implement guideline recommendations; monitoring and auditing criteria; and measures taken to ensure editorial independence.

AMSTAR

Systematic reviews within 10 guidelines were of poor or fair quality (19, 44, 47–56). The APS-AAPM review was of excellent to outstanding quality, the review by the Canadian National Opioid Use Guideline Group was of good to excellent quality, and the review by the Department of Veterans Affairs and Department of Defense (VA/DoD) was of good quality (Appendix Table 3, available at www.annals.org) (13, 45, 46).

Reasons for lower scores included limited information about whether inclusion criteria were selected beforehand, whether at least 2 reviewers participated in study selection and data extraction, whether more than 1 database was searched, search terms used, inclusion criteria, lists of included studies, whether the scientific quality of the studies was assessed, how information from different studies was combined, and whether publication bias was considered.

Guideline Synthesis and Analysis

The Table compares recommendations from 10 guidelines about mitigating risks when prescribing opioids (3 guidelines had little relevant content). The APS-AAPM, Canadian National Opioid Use Guideline Group, American Society of Interventional Pain Physicians, and VA/DoD guidelines make explicit links between each recommendation and original research evidence more frequently than the other guidelines do (13, 45, 46). Among recommendations in the Table, only upper dosing thresholds are reported to be supported by evidence from randomized, controlled trials; others are supported by lower-quality evidence or expert opinion. Even the higher-quality guidelines typically relied on modest numbers of lower-quality observational studies for many recommendations (13, 45, 47, 57, 60). Nonetheless, many recommendations are concordant across the guidelines.

Eight guidelines concur that higher doses require caution (19, 44, 45, 47, 50, 57, 59, 60). Four consider higher doses to be 200 mg of morphine equivalents per day, on the basis of randomized, controlled trials showing that most patients achieve pain control with lower doses and observational data showing that the prevalence of adverse effects increases at higher doses (45, 47, 57, 60). Because recent observational studies detected more overdoses with doses greater than 100 mg, the American Society of Interventional Pain Physicians guideline (2012) recommends staying below 90 mg unless pain is intractable (49, 59). The University of Michigan Health System guideline (2012) advises that patients receiving more than 100 mg be treated by pain specialists (44).

Ten guidelines—6 of which cite observational data—agree that methadone poses risks for dose-related QTc prolongation and respiratory suppression due to a long half-life and unique pharmacokinetics (13, 19, 44–47, 49, 50, 52, 55, 57, 60). These guidelines generally recommend that only knowledgeable providers prescribe methadone. Eight guidelines recommend caution with the fentanyl patch, including limiting use to opioid-tolerant patients and being aware that unpredictable absorption can occur with fever, exercise, or exposure to heat (19, 44, 45, 47, 49, 50, 55, 60, 61). Cited evidence includes an observational study investigating fentanyl overdoses in Ontario, Canada, as well as case reports submitted to the U.S. Food and Drug Administration (47, 49, 60, 63).

Ten guidelines make variable consensus-based statements about initiating and titrating opioids, such as using a trial period, individualizing therapy, engaging multidisciplinary pain management teams, increasing doses slowly,
and scheduling regular follow-up visits (13, 19, 44–48, 50, 52, 55, 59).

Regarding switching from one opioid to another, 7 guidelines agree that reducing doses by at least 25% to 50% is necessary to avoid inadvertent overdose; the guideline by Fine and colleagues provides nuanced recommendations (13, 45, 47, 48, 50, 54, 55, 59, 60). Two guidelines cite a systematic review of observational studies, which found that patients respond variably to different drugs (13, 54). Five guidelines mention that many persons of Cauca-
sian or Chinese ancestry cannot metabolize codeine to morphine and are therefore less responsive to its analgesic effects and cannot develop tolerance (19, 45, 47–61). Conversely, 5 guidelines note that some patients metabo-
lize codeine to morphine ultra-rapidly, potentially resulting in overdose (19, 47, 49, 59, 60); certain ethnicities are at greater risk, particularly persons from North Africa and the Middle East (45).

Ten guidelines concur, on the basis of observational data, that benzodiazepines and opioids are a high-risk combi-
nation, particularly in elderly adults (13, 19, 44, 45, 47, 48, 50, 52, 55, 59–61). Five recommend against prescrib-
ing both together unless clearly indicated (19, 44, 49, 52, 60, 61). Six guidelines describe pharmacokinetic interac-
tions between other medications and opioids, particularly methadone, fentanyl, oxycodone, and tramadol (19, 45, 47–49, 55). Six guidelines mention the accumulation of active, toxic metabolites of morphine among patients with kidney disease (19, 45, 47, 49, 50, 60). Ten guidelines consider the leading risk factors for overdose or misuse as having a personal or family history of substance abuse and having psychiatric issues (13, 44, 45, 47–49, 52, 55, 59–61); 3 cite observational studies (13, 52, 60, 61). Seven guidelines identify obstructive respiratory disorders as risk factors for overdose, also on the basis of observational data (13, 19, 44, 45, 48, 50, 59–61).

In terms of mitigating risks, the evidence for opioid risk assessment tools, treatment agreements (“contracts”), and urine drug testing is weak, but recommendations vary in strength from “may consider” to “must.” Nine guidelines recommend considering or using opioid risk assessment tools and treatment agreements on the basis of observa-
tional studies and expert consensus (13, 44, 45, 47, 48, 50, 52, 55, 59–61). Eight guidelines mention or pro-
vide specific risk assessment instruments for use when ini-
tiating therapy with long-term opioids, such as the Screener and Opioid Assessment for Patients with Pain (SOAPP), version 1 (64); the revised SOAPP (65); and the Opioid Risk Tool, or monitoring tools for use during follow-up, including the Pain Assessment and Documen-
tation Tool (66, 67) and the Current Opioid Misuse Mea-
sure (44, 45, 47–50, 55, 57, 60, 68). For detecting aber-
rant drug-related behaviors, the self-administered SOAPP, version 1, and the Current Opioid Misuse Measure per-
formed well in higher-quality observational studies (57). Treatment agreements may improve adherence and provid-
ers’ willingness to prescribe opioids, on the basis of a few small, observational studies (49, 57, 60).

Nine guidelines find urine drug testing to be helpful, but recommendations vary (13, 19, 44, 45, 47, 48, 55, 59, 60). Two recommend mandatory testing for all patients (19, 49), another advises testing for patients at higher risk for substance abuse disorders (13), and 2 comment that screening low-risk populations increases false-positive results and is less cost-effective (13, 60, 61). False-negative results can occur because a common test, the enzyme-linked immunoassay, does not consistently detect hydro-
codone, fentanyl, hydromorphone, oxycodone, metha-
done, or certain benzodiazepines; gas chromatography or mass spectrometry will identify specific substances when requested (44, 46, 50, 60–62). Nonadherence, diversion, tampering, and lactic acidosis can also cause unexpected negative results. The differential for unexpected positive results includes abuse, consulting multiple physicians, self-
treatment of uncontrolled pain, interference by other med-
ications, eating poppy seeds, and laboratory error (13, 44, 46, 49, 59–62).

**DISCUSSION**

Increasing overdoses on prescription opioids have prompted efforts to redefine standards of care, particularly for patients with chronic pain, who may be prescribed opio-
oids for long-term use. We evaluated the quality of 13 guidelines on using opioids to treat chronic pain and com-
pared recommendations related to mitigating risks for overdose and misuse. Two guidelines received high ratings: one by APS-AAPM (13) and another by the Canadian National Opioid Use Guideline Group (46). Both apply to a broad range of adults, were developed using comprehensive systematic reviews and rigorous methods for formulat-
ing recommendations, and frequently link recommenda-
tions to evidence. Our appraisers found 7 other guidelines to be of intermediate quality and recommended against using the remaining 4. Systematic reviews supporting 10 guidelines were judged, on the basis of publicly available information, to be of poor to fair quality.

Although the guidelines involve varied development methods and clinical emphases, a consensus has emerged across them on several issues. They generally agree about the need for caution in prescribing doses greater than 90 to 200 mg of morphine equivalents per day, having knowl-
edgable clinicians manage methadone, recognizing risks associated with fentanyl patches, titrating with caution, and reducing doses by at least 25% to 50% when switching from one opioid to another. They also agree that opioid risk assessment tools, written treatment agreements, and urine drug testing can be helpful when opioids are pre-
scribed for long-term use. Recommendations from earlier guidelines are generally similar to those published recently. Most of these recommendations are based on epidemi-
ologic and observational studies showing associations be-
Among 3 migraine guidelines, AGREE II rigor-of-epidemic (69), developers seem to agree on forging recommendations based on relatively weak or indirect evidence now rather than waiting for more rigorous studies.

It may be unusual for multiple guidelines to make such similar recommendations, but the variability in guideline quality that we observed is not. For example, among 19 breast cancer guidelines, AGREE II rigor-of-development scores were 16.7% to 89.6%, clarity-of-presentation scores ranged from 52.8% to 94.4%, applicability scores were 6.3% to 83.6%, and editorial independence scores ranged from 12.5% to 79.2% (70).

Among 3 migraine guidelines, AGREE II rigor-of-development scores were 35% to 93%, clarity-of-presentation scores ranged from 6% to 92%, applicability scores were 20% to 88%, and editorial independence scores ranged from 29% to 86%; overall scores were 2 to 6, and appraisers recommended against using 1 guideline (71). Among 11 mammography guidelines evaluated using the original AGREE instrument and AMSTAR, appraisers recommended against implementing 5 guidelines, and 5 systematic reviews performed poorly (72).

Compared with these previous guidelines, the current opioid guidelines received lower scores on “applicability”: None scored higher than 56%. Applicability includes consideration of potential barriers to and facilitators of implementation, strategies to improve uptake by providers, and resource implications of applying the guideline. Barriers to implementation are a major reason that physicians are often slow to incorporate clinical guidelines into their decision making (73). To identify such barriers, guideline developers and implementers are starting to use the GuideLine Implementability Appraisal (GLIA) tool (74–76), which assesses “executability” (know what to do), “decidability” (can tell when to do it), validity, flexibility, effect on process of care, measurability, novelty or innovation, and “computability” (can be operationalized in an electronic health record system) (77). Although GLIA is labor-intensive (76), it probably requires fewer resources than pilot testing and is preferable to issuing a guideline that is not used. Developers of opioid guidelines could incorporate GLIA into the next updating process, thereby improving applicability.

Although we selected guidelines that had been updated within the past 6 years, some evidence has already started to change, particularly regarding the risk for overdose. Five guidelines published before 2012 consider doses greater than 200 mg of morphine equivalents per day to confer higher risk. Three observational studies from 2010 increased 1.9- to 3.1-fold with doses of 50 to 100 mg and increases dramatically with doses greater than 100 to 200 mg (78–80). Guidelines published in 2012 use thresholds of 90 to 100 mg. In 2007, the state of Washington implemented workers’ compensation guidelines recommending evaluation by a pain management expert for patients receiving more than 120 mg/d as well as other risk mitigation strategies that are similar to or, in some areas, more restrictive than those of the guidelines reviewed here. Although pain control has not been described, the number of patients receiving opioids and the doses prescribed started decreasing in 2007 and fatal overdoses decreased in 2010 (4).

Given that overdoses occur even at lower doses, some may wonder about the overall risks and benefits of using opioids for chronic pain. According to previous systematic reviews of randomized, controlled trials, oral opioids are substantially more effective than placebo or nonsteroidal agents, with 30% to 50% decreases in pain severity and significant improvements in functional status (14, 81–83). However, study quality has not been high, and the duration of follow-up has often been limited (14, 84). At least one third of patients stop opioid use because of adverse effects (46, 81, 82, 85). Abuse occurs in 0.43% to 3.27% of patients and addiction affects 0.042%, but 11.5% engage in aberrant drug-related behaviors or illicit use (14, 85, 86). This evidence has generally been incorporated into the guidelines and is reflected in the supportive but cautious approach that they take toward long-term opioid therapy.

Our evaluation has several limitations. First, we relied on publicly available information, so we were unable to evaluate several guidelines (17, 40–43, 87) or the clarity of the proprietary Work Loss Data Institute guideline. Although AGREE scores can improve when developers provide supplemental information (88), the IOM recently outlined guideline development standards stating, “The processes by which a [clinical practice guideline] is developed and funded should be detailed explicitly and publicly accessible” (32). Second, neither the IOM nor AGREE stipulate how guidelines should select topics. To be useful, guidelines should address the challenges that clinicians face in practice, but developers may exclude clinically important topics when available evidence does not meet minimum standards.

In conclusion, rigorous clinical practice guidelines could help providers to attenuate the increasing rates of opioid misuse and overdose among patients with chronic pain. Recent guidelines make similar recommendations about strategies for reducing these risks despite variability in development methods, suggesting a clinical consensus for practices that could be adopted until more evidence becomes available. They agree on using upper dosing thresholds; cautions with certain medications; attention to drug–drug and drug–disease interactions; and risk assessment tools, treatment agreements, and urine drug testing. Although such recommendations can guide practice now,
future research should directly examine the effectiveness of opioid risk mitigation strategies, including effects on pain control and overdose rates.

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