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Evidence-Based Approaches to Pain Management in 2019

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The evidence for the treatment of non-cancer pain among adults with acute and chronic pain conditions has evolved rapidly in recent years. Earlier recommendations, which have become increasingly acknowledged as being driven by misleading information from opioid manufacturers, resulted in more routine use of opioid analgesics. As a result, it has been estimated that almost 40% of U.S. civilian, non-institutionalized adults used prescription opioids in 2015.[1] In this same study, almost 30% of those using prescription opioids reported opioid misuse or opioid use disorder, and among those with misuse, almost 60% reported using prescription opioids without a prescription.[1] Coinciding with increased opioid prescribing has been a resurgence in illicit heroin use and, more recently, the appearance of highly toxic illicitly manufactured fentanyl in the street drug supply. Through these combined effects, it has been estimated that between 2016 and 2025, more than 700,000 individuals in the United States will die from opioid overdose.[2]

Beyond the health risks and harms associated with prescription opioid use, recent research has clearly demonstrated that the promotion of more routine use of prescription opioids was not evidence-based. For instance, a 2015 systematic review concluded that the "evidence is insufficient to determine the effectiveness of long-term opioid therapy" and instead concluded that "evidence supports a dose-dependent risk for serious harms."[3] A subsequent meta-analysis of 96 randomized controlled trials involving more than 26,000 patients further demonstrated the limited clinical utility of prescription opioids.[4] Among patients receiving opioids for at least a month, benefits

were insignificant in comparison to placebo (weighted mean difference, −0.69 cm [95%CI, −0.82 to −0.56 cm] on a 10-cm visual analog scale for pain with a minimally important difference of 1 cm). Interestingly, while a wide range of oral opioid doses, from 7.5 mg to 242.7 mg daily morphine equivalents, was considered, the analyses demonstrated no difference in outcomes based on opioid dose. Importantly, since modern pain care includes an array of alternatives to opioid-based analgesics, the most clinically relevant part of this meta-analysis was the comparison of opioid and non-opioid analgesics. Here, no differences in pain relief were observed between opioids and opioid-sparing approaches.[4]

Since the evidence suggests that any acute benefit of opioid therapy on chronic pain may diminish within weeks,[4] a limitation of most research in this area is that most opioid trials are very short (e.g., 6 weeks or less).[3] To address this, the Strategies for Prescribing Analgesics Comparative Effectiveness (SPACE) trial was a recent 12-month pragmatic randomized trial of 240 patients that compared opioid analgesic therapy to non-opioid medications for moderate to severe chronic back, hip or knee osteoarthritis pain.[5] Here, the trial demonstrated that treatment with opioids was not superior to opioid alternatives for improving pain-related function. The authors concluded that the results do not support the initiation of opioid therapy for moderate to severe osteoarthritis pain.[5]

In response, recent pain guidelines, such as the U.S. Centers for Disease Control and Prevention opioid prescribing guideline, highlight the importance of carefully screening patients to identify those that are at high risk of opioid use disorder. Further,

a host of screening instruments have been developed with a view to identifying patients among whom opioid analgesics can safely be prescribed. However, until recently, these recommendations and screening instruments have not been scrutinized for diagnostic accuracy. To address this, we recently conducted a rigorous quality assessment and critical appraisal of studies examining risk factors and risk screening instruments and calculated sensitivity, specificity and likelihood ratios to assess the performance of different measures.[6] While the review indicated that a history of substance use disorder, opioid prescriptions ≧ 30 days (and peak doses > 120 milligrams morphine equivalents per day), certain mental health diagnoses and prescription of certain concomitant psychiatric medications appeared useful for identifying higher-risk patients, no symptoms, signs or screening tools appeared useful for identifying those at lower risk. Additionally, the review demonstrated that commonly used screening instruments, such as the Opioid Risk Tool, provide no diagnostic value for clinicians. Collectively, while the meaningful positive likelihood ratios for certain risk factors, such as having a history of substance use disorder, suggest employing caution when prescribing opioid-based medications in those with these risk factors, the absence of any identified useful negative likelihood ratios suggests that the absence of identified risk factors does not imply opioids can be safely prescribed.[6]

These findings coincide with increasing concerns that new prescribing guidelines have resulted in harms from the withholding of opioid medications to those already on opioid therapy for chronic pain.[2] Most importantly, since in some cases these patients

may turn to a street heroin market increasingly contaminated by toxic fentanyl analogs, great caution must be employed in this context as well.

Based on recent literature and the rapidly evolving nature of the opioid overdose epidemic due to the emergence of fentanyl analogs in the illicit drug supply, there are clearly three main clinical scenarios being confronted by clinicians where evidence-based recommendations can be made (Figure). The first clinical scenario is the approach to consider for chronic pain patients (excluding cancer, palliative or other special circumstances) not on opioid therapy. Here, the literature suggests that opioid therapy should be avoided given the limited likelihood of benefit and the major evidence of opioid-related harms,[3] and that efforts to use the clinical examination or screening tools to identify low-risk patients are likely of little value.[6] The second clinical scenario is the approach to consider with chronic pain patients already on opioid therapy. Here, an approach involving individualized care is clearly warranted.[2] Specifically, while the literature suggests potential for improved pain and functioning with opioid tapering, this must be balanced with the risks of exacerbating pain, opioid withdrawal syndrome and the fact that withholding opioid therapies can potentially result in transition to street opioid use.[2] At the same time, given the prevalence and risks associated with prescription opioid diversion and misuse,[1] the proven benefits of opioid agonist therapy in the prescription opioid addiction context, as well as the evidence that buprenorphine/naloxone may provide similar analgesia as full opioid agonists,[7] opioid agonist therapy should be increasingly considered in this context. This will require that efforts to overcome barriers to opioid agonist therapy be redoubled.[2] The third clinical

scenario is the approach to consider in acute pain contexts. Here, given that most chronic pain initially presents as acute pain and the benefits of opioids on acute pain may diminish rather quickly,[4] and given the known risks of prolonged opioid prescription and dose on risk of subsequent opioid addiction,[6] opioid therapy should be avoided in those with minor to moderate acute pain, and when opioids are used in severe acute pain, the dose and duration limited to short (e.g., < 1 week), renewable (if necessary) courses.[3]

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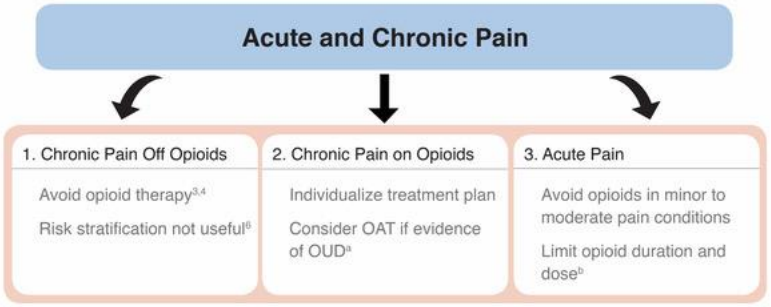
Figure. Evidence-based opioid sparing pain management strategy.



Abbreviations: OAT, Opioid Agonist Therapy; OUD, Opioid Use Disorder.
[a] Buprenorphine/naloxone or methadone should be considered for patients with opioid use disorder
[b] Opioid medications after major surgery or serious injury can be limited to short renewable courses

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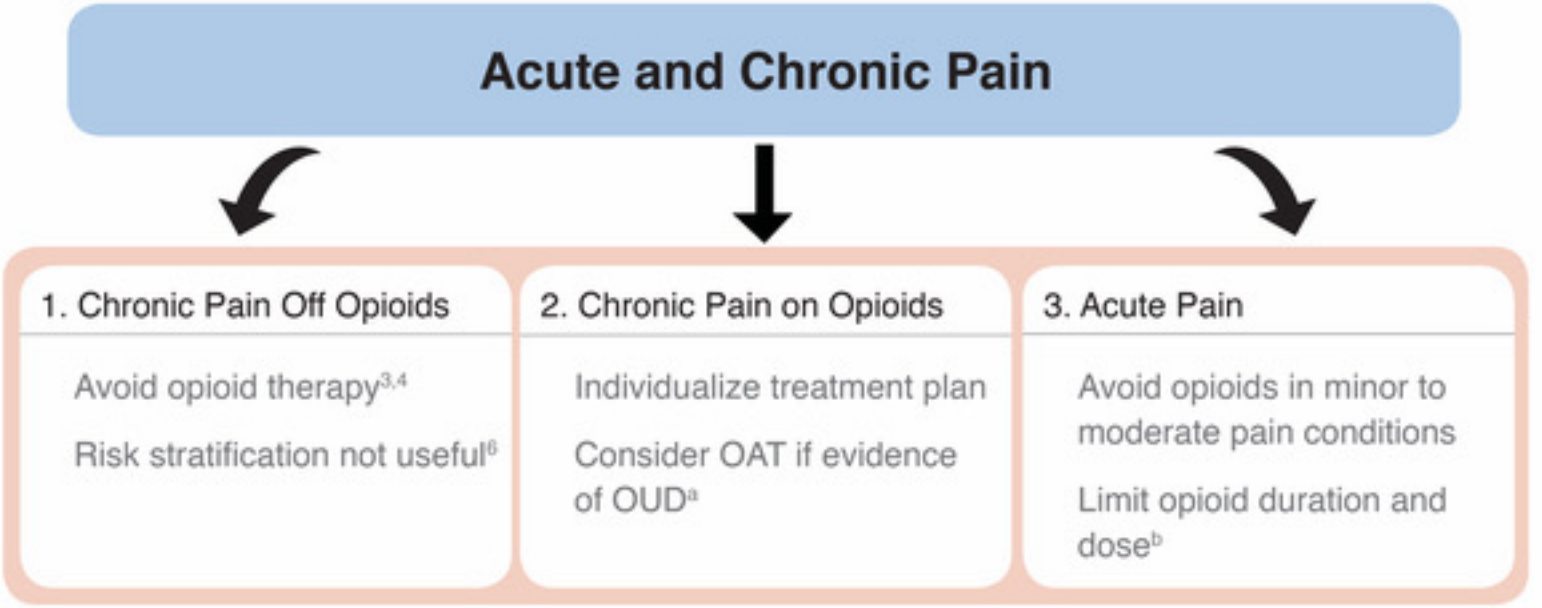
Figure. Evidence-based opioid sparing pain management strategy.



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