

JAMA Clinical Guidelines Synopsis

Clinical Management of Opioid Use Disorder

Beth Dunlap, MD; Adam S. Cifu, MD

GUIDELINE TITLE Guideline for the Clinical Management of Opioid Addiction

DEVELOPER Vancouver Coastal Health, Providence Health Care, and Ministry of Health, British Columbia, Canada

RELEASE DATE November 2015

FUNDING SOURCE Funded publicly through governmental grants

TARGET POPULATION Nonpregnant adult patients with opioid use disorder

MAJOR RECOMMENDATIONS

- Opioid withdrawal alone is not recommended for treatment of opioid use disorder in most patients because of increased risks of overdose death and infectious disease, particularly HIV through intravenous drug use, following detoxification (moderate-quality evidence; strong recommendation).
- In the absence of contraindications, medically supervised opioid agonist treatment should be offered to patients. Buprenorphine/naloxone is the preferred first-line treatment. Methadone is an alternative in certain patient populations (high-quality evidence; strong recommendation).
- Psychosocial supports tailored to patient needs may be offered as an adjunct to medical treatment (moderate-quality evidence; conditional recommendation).

Summary of the Clinical Problem

Death caused by drug overdose is a major problem in the United States. In 2014, nearly 29 000 people died of opiate overdose.¹ Underlying this trend is a parallel increase in opioid use disorder, defined as a problematic pattern of opioid use leading to clinically significant impairment or distress. Opioid use disorder contributes to significant mortality, primarily from overdose, as well as morbidity.

Guidelines for treatment of patients addicted to opiates potentially can improve both patient and public health outcomes. Of the estimated 2.5 million people in the United States with opioid addiction,² fewer than half are able to access medication-assisted treatment (MAT), 53.4% of US counties do not have a single prescriber of medications to treat opioid use disorder, and, as of 2014, only 2.2% of US physicians had obtained the necessary waiver to prescribe buprenorphine.³ MAT is an evidence-based approach that combines medical therapy with an opioid agonist or antagonist with counseling and recovery support. MAT using agonist therapy with methadone or buprenorphine has been shown to be superior to withdrawal (“detox”) for important patient-centered outcomes such as overdose death, rates of communicable disease, retention in treatment, and relapse.^{4,5}

Characteristics of the Guideline Source

The Vancouver Coastal Health (VCH) and Providence Health Care Opioid Use Disorder Treatment Guideline Committee developed the guideline.⁶ This committee was composed primarily of addiction and primary care specialists within VCH, Providence Health Care, and the British Columbia Ministry of Health. Peer review of the guideline was undertaken by a multidisciplinary group that included patients and families, policy managers with the Ministry of Health, generalist physicians, and physicians with training and expertise in treating patients with addiction. A systematic review was performed as part of the development process. The committee was free of conflicts of interest (Table).

Evidence Base

A systematic literature review was the basis of the guideline.⁶ Evidence was summarized using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria. Strong recommendations were given to use of agonist therapy as first-line treatment on the basis of 7 Cochrane reviews published between 2003 and 2014 with high- to moderate-quality evidence. Study heterogeneity and limited outcome information precluded supporting a single approach to psychosocial interventions and support structures. There have been no meta-analyses of residential treatment programs, many of which provide intensive behavioral therapy along with withdrawal or agonist management while removing the patient from prior environmental triggers for opioid use.

Benefits and Harms

MAT is superior to withdrawal alone. Multiple studies of withdrawal demonstrate that the majority of patients relapse with withdrawal management alone, even with tapering with opioid agonist medications to alleviate withdrawal symptoms. One 2010 prospective cohort study of 109 patients discharged from residential detoxification treatment showed that 91% of patients relapsed, with 59%

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Table. Guideline Rating

Rating Standard	Rating
Establishing transparency	Good
Management of conflict of interest in the guideline development group	Good
Guideline development group composition	Good
Clinical practice guideline-systematic review intersection	Fair
Establishing evidence foundations and rating strength for each of the guideline recommendations	Good
Articulation of recommendations	Good
External review	Fair
Updating	Poor
Implementation issues	Fair

relapsing in the first week.⁷ The addition of methadone treatment decreases the rate of relapse. A 2009 Cochrane analysis demonstrated that MAT using methadone was more effective than placebo in treatment retention and suppression of illicit opioid use (6 randomized trials; relative risk, 0.66; 95% CI, 0.56-0.78; absolute risk reduction, 20.8%; number needed to treat = 5).⁸ In this analysis, there was no difference in mortality or criminal behavior between the groups.

MAT decreases rates of infectious disease. A 2012 meta-analysis cited by the guideline authors showed an association between methadone treatment and HIV infection, with a 54% (rate ratio, 0.46; 95% CI, 0.32-0.67) reduction in risk of HIV infection among intravenous drug users who were stabilized with methadone vs no treatment.⁵

Comparing MAT agonist therapies, a 2014 Cochrane review of moderate- to high-quality studies showed no difference in retention in treatment (relative risk, 0.87; 95% CI, 0.69-1.10) or suppression of illicit opioid use (standardized mean difference, 0.25; 95% CI, -0.08 to 0.58) between moderate-dose methadone and buprenorphine.⁴

There were no meta-analyses reviewed by the guideline authors that compared buprenorphine/naloxone combination therapy with buprenorphine alone or methadone. Buprenorphine/naloxone therapy is preferred in this guideline over methadone, in appropriate patients, because of several potential advantages, including lower risk of overdose, more flexible at-home dosing, and lower risk of diversion. Combination buprenorphine/naloxone therapy also may be superior to methadone as it allows for induction, stabilization, and maintenance to be performed in the primary care setting.⁶ Methadone may be considered first-line treatment in some patients, such as in severely addicted patients with high daily doses of opioids, or when a challenging induction is anticipated because of prior treatment failures, history of severe withdrawal symptoms, or an expected need for high maintenance treatment doses.

As prescribing of buprenorphine has increased, concerns about the potential for misuse and diversion also have increased. Much of the diverted buprenorphine/naloxone is likely used to manage withdrawal symptoms. A study of prescription opioid users found that lack of access to MAT was associated with use of diverted buprenorphine/naloxone and that expansion of access may limit diversion.⁹

Discussion

Although implementation of this guideline could lead to improvements to the treatment of opioid use disorder in the United States, there are many important barriers to safe and effective expansion of MAT. In the United States, more than half of buprenorphine prescribers are primary care clinicians who, under the terms of their licensure, must have access to comprehensive services and specialist consultation if indicated. Organizational support within health systems and appropriate reimbursement in the primary care setting must be addressed for successful integration of agonist therapy.

Optimal initial and ongoing training of buprenorphine prescribers is also essential. There is a risk of precipitated withdrawal if buprenorphine/naloxone induction is done incorrectly, and adequate dosing during all phases of treatment with buprenorphine/naloxone is required to prevent relapse.

Areas in Need of Future Study or Ongoing Research

The role and effectiveness of residential treatment in the context of opioid use disorder treatment are uncertain. A better understanding of appropriate patient selection and characteristics of effective programs are particularly important because of the risk of overdose for patients who relapse during and following residential treatment when an approach of withdrawal management only is used. For patients who have achieved long-term abstinence with agonist therapy, there is limited evidence to guide tapering of the maintenance medication. If the population receiving long-term MAT increases, this will become an increasingly important gap in the evidence available to patients and physicians. Additional guidance to prevent, identify, and respond to misuse and diversion of agonist therapies will also be essential.

Related Guidelines and Other Resources

US Department of Health and Human Services Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction
 Providers' Clinical Support System for Medication Assisted Treatment

ARTICLE INFORMATION

Author Affiliations: Northwestern University, Chicago, Illinois (Dunlap); University of Chicago, Chicago, Illinois (Cifu).

Corresponding Author: Adam S. Cifu, MD, University of Chicago, 5841 S Maryland Ave, MC 3051, Chicago, IL 60637 (adamcifu@uchicago.edu).

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