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Rethinking Opioid Dose Tapering, Prescription Opioid Dependence, and Indications for Buprenorphine

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The expanded use of opioids for chronic pain has created a population of patients prescribed long-term opioid therapy lasting years or decades. Doses are often above the thresholds suggested in the 2016 Centers for Disease Control and Prevention (CDC) guideline (morphine-equivalent dose >50 or >90 mg/d) (1). Long-term opioid therapy is associated with adverse effects, morbidity, and overdose death; some risks are dose-dependent (2). At the same time, evidence indicates that long-term opioid therapy confers little benefit versus nonopioid therapy, particularly for function (3). Opioid use disorder (OUD) occurs in a subset of patients, and quality of life may be adversely affected despite perceived pain benefits (2, 4).

Therefore, many patients may benefit from tapering to lower, safer opioid doses. We argue that achieving effective, safe, and compassionate tapers requires implementing and incentivizing tapering protocols, recognizing prescription opioid dependence as a distinct clinical condition necessitating treatment, and expanding the indication for buprenorphine formulations approved for OUD to include prescription opioid dependence.

Implementing and Incentivizing Tapering Protocols

Tapering long-term opioid therapy is challenging, starting with determining whose dose to taper. The CDC guideline recommends continuing opioid therapy only in patients with improved function and pain relief, given the risks (1). Therefore, every patient receiving long-term opioid therapy should be assessed for a taper on the basis of pain; function; and adverse consequences, including risk for addiction (1). Assessments should incorporate information provided by the patient as well as from prescription drug use monitoring data, urine drug screens, and collateral sources (such as family members). In stable patients with minimal risks, continued opioid therapy may be warranted. In other cases, a thorough assessment will reveal that benefits do not outweigh harms, and tapering is indicated.

Emerging strategies for addressing challenging tapers include slowing down the taper, providing support, and reframing "success" (5). The CDC guideline suggested that tapering opioid doses by 10% of the initial dose each week (10 weeks to discontinuation) was reasonable to avoid withdrawal symptoms (1). However, this was based almost entirely on studies of opioids for addiction treatment. Newer data indicate that successful tapers in patients with chronic pain may require smaller dose reductions over longer periods, potentially extending to years (6, 7). Taper speed should be informed by patient response to dose reductions, and tapering should be provided in the context of psychological support and pain management with nonopioid treatments (5).

Limited data suggest that patients who successfully taper off opioids may experience improved mood, cognition, social functioning, and coping skills (7). Of note, success should not be defined solely by whether patients reach target doses, which are arbitrary by nature. Overdose risk is reduced when doses are decreased, even if they remain above target thresholds (2). Thus, taper success should be based on multiple factors, including the degree of dose reduction, effects on quality of life, function, adverse effects, and misuse behaviors.

Support and incentives are required for prescribers to assess patients and taper doses at the scale needed to reduce morbidity and mortality. These include implementation of opioid tapering protocols (**Figure**) (8); taper billing codes; time and resources to educate patients and providers; and access to an interdisciplinary team to provide psychological support, alternative pain treatments, and treatment of OUD when indicated. Educational courses on discussing tapers with patients are available, such as the Stanford University "BRAVO" course (9).

Recognizing Prescription Opioid Dependence as a Distinct Condition

As tapering experience accrues, clinicians have observed that many patients with chronic pain receiving long-term opioid therapy struggle to reduce doses. Why are tapers a challenge in some patients? An important reason is dependence, characterized by withdrawal symptoms when opioid doses are decreased or discontinued. In addition to somatic symptoms, withdrawal may manifest as psychological symptoms. Even with stable doses, patients can experience continuous subthreshold withdrawal between doses, dysphoria, and hyperalgesia, all of which can be exacerbated by tapering (10).

Some patients with difficulty tapering may have developed OUD, but many do not neatly fit the OUD criteria in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5). The DSM-5 eliminated opioid dependence as a separate diagnosis; excluded withdrawal and tolerance as OUD criteria when opioids are taken as prescribed; and requires that patients meet at least 1 criterion other than difficulty tapering, including craving, compulsive use, or harmful use. We argue that some patients who have persistent difficulty in tapering and withdrawal but do not meet other DSM-5 criteria have a complex form of prescription opi-

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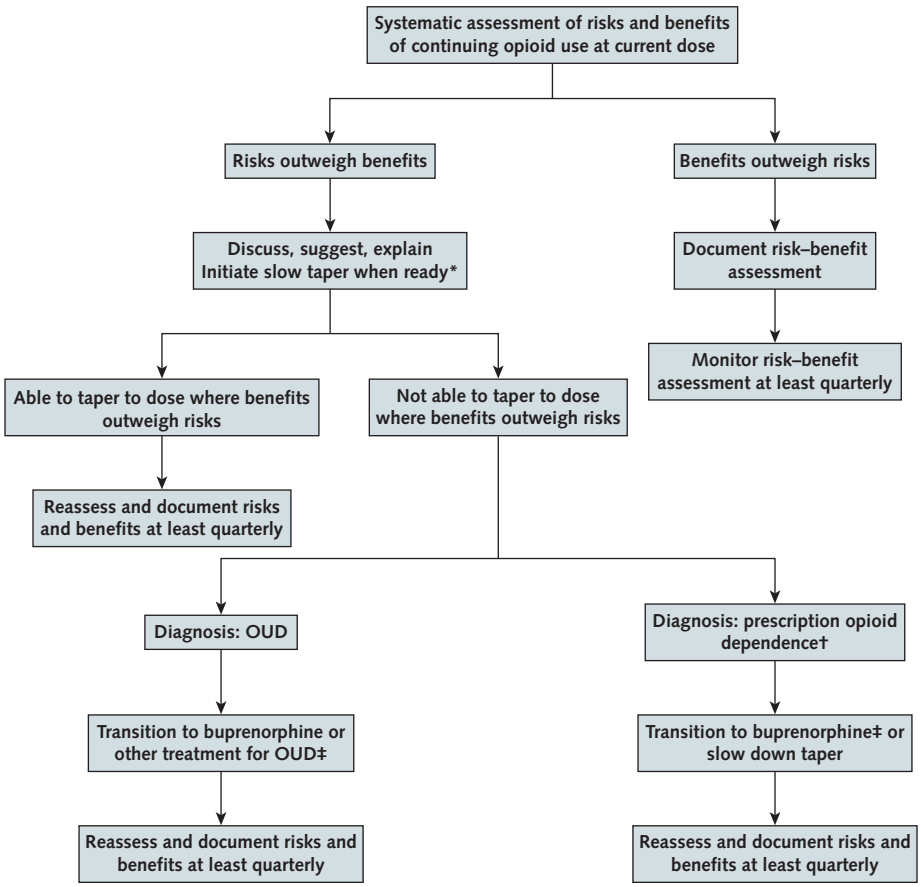
Figure. Clinical pathway for consideration of tapering in patients using opioids for >90 d.



Patients with improved function, adequate pain relief, and low risk for opioid-related harms may continue their current dose (*right side of diagram*), but with regular risk–benefit assessments. Patients in whom risks outweigh benefits (*left side of diagram*) should initiate a dose taper. Those who are unable to taper successfully may meet criteria for OUD or prescription opioid dependence. Those with OUD should receive evidence-based treatment, and those with prescription opioid dependence should receive additional taper support (e.g., BRAVO) or be transitioned to buprenorphine. DSM-5 = *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; OUD = opioid use disorder. (Adapted from reference 8, with permission.)

* Recommendations for successful tapers using the BRAVO framework (9): Broach the subject with empathy (acknowledge anxiety and be clear that tapering is not punitive), Risk–benefit assessment (address effects on pain and function, risk for overdose and addiction, and other adverse events), Addiction assessment (normalize addiction and initiate appropriate management if OUD emerges), Velocity and Validate (do not taper too quickly, slow down if needed, and validate the pain of withdrawal), Other strategies for coping with pain (implement nonopioid alternatives for pain treatment).

† Characterized by persistent difficulty with tapering and meeting ≤1 DSM-5 criterion, excluding withdrawal and tolerance. Other features include negative affect, reward deficiency, and social isolation.

‡ Maintenance therapy with an opioid agonist, partial agonist, or antagonist is considered standard of treatment for OUD because of improved outcomes compared with tapering and withdrawal. Clinicians must undergo training and obtain a waiver from the Drug Enforcement Administration to prescribe sublingual and buccal formulations of the partial opioid agonist buprenorphine (with or without naloxone) for treatment of OUD. Use of these buprenorphine formulations for chronic pain or prescription opioid dependence without OUD is currently off-label.

oid dependence (Figure). Other features include negative affect, reward deficiency, and social isolation. Failure to recognize this as a distinct clinical entity requiring management leaves these patients in diagnostic limbo and at risk for morbidity, including potential escalation to frank OUD.

Expanding the Indication for Buprenorphine to Include Prescription Opioid Dependence

We propose consideration of sublingual or buccal buprenorphine as a treatment option for patients with prescription opioid dependence. Buprenorphine is a partial opioid agonist that carries lower risk for respiratory compromise than pure opioid agonists while providing analgesic benefits. Higher-dose sublingual and buccal formulations are approved by the U.S. Food and Drug Administration for OUD treatment in office-based settings by clinicians who undergo training and obtain a Drug Enforcement Administration waiver. Patients with prescription opioid dependence should also have access to higher-dose buprenorphine formulations for maintenance therapy or to facilitate tapering.

Recognizing prescription opioid dependence as a potential comorbid condition and expanding use of

buprenorphine could save lives, improve quality of life, and reduce incidence of nonlethal unintentional overdose. Although research is needed to evaluate the effects of expanding indications for buprenorphine use, risks are likely to be low due to safety advantages over the opioids already being prescribed. Research is also needed to determine whether a diagnosis of prescription opioid dependence results in fewer negative legal, work, and social consequences; is perceived as less stigmatizing than an OUD diagnosis; or increases acceptance of buprenorphine use compared with no diagnosis. Making such buprenorphine use on-label could also reduce provider liability and increase the likelihood of insurance coverage, which are important considerations for successful clinical implementation.

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