



Veteran engagement in opioid tapering research: a mission to optimize pain management

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More than 50 million Americans suffer from chronic pain, and approximately 20 million individuals have severe chronic pain that interferes with life or work activities.¹⁵ This is a particular concern for the Veterans Health Administration (VHA) as chronic pain has been found to be more common, severe, and complex in Veterans.^{32,40} In addition to chronic pain, military Veterans often suffer from other complex medical and mental health issues.³³

Opioid analgesics are often used to treat chronic noncancer pain (CNCP); however, there is insufficient evidence that long-term use improves chronic pain or functioning.^{9,24} Furthermore, long-term opioid use is associated with increased mood disorders prevalence¹ and several potential harms including overdose (OD), the development of opioid use disorder (OUD), and possibly death. Nearly 10 million Americans misuse or abuse opioids, which may elevate the risk for developing OUD. An estimated 2 million individuals have OUD, and to date, approximately 450,000 people have died by OD from prescription or illicit opioids. Approximately 81,230 drug OD deaths occurred in the United States in the 12 month ending in May 2020.³⁶ One study showed that Veterans were twice as likely to die from accidental OD compared with non-Veterans, indicating a strong correlation to dose and to mental health comorbidities.⁶

The 2017 Veterans Health Administration /Department of Defense (DoD) Clinical Practice Guideline for Opioid Therapy recommends against initiating long-term opioid therapy for chronic pain.^{19,39} Similarly, the Centers for Disease Control and Prevention recommends additional caution for prescribing >50 mg morphine equivalent daily dose (MEDD) and recommends against >90 mg MEDD.¹⁶ In general, the recommendation is to keep opioid therapy at the lowest dosage and shortest duration possible, in conjunction with the implementation of opioid risk mitigation strategies²⁶ and consideration of issues related to telehealth, care coordination, stepped care model implementation,¹⁹ and suicide prevention.³⁴

Unfortunately, there are no generally accepted clinical guidelines for opioid tapering that are evidence based. Furthermore, there is no clear scientific evidence regarding the optimal speed of tapering or consistent/scheduled taper vs individualized tapers with frequent adjustments. Moreover, fears surrounding opioid tapering often lead to high dropout rates in these studies making this a challenging area to research.²⁵

The dearth of published comparative effectiveness studies of tapering in patients on long-term opioids for CNCP represents a major clinical dilemma.⁴ The CDC guidelines suggest 10% to 20% reduction per week as “reasonable” but also noted that for many patients a much slower taper would be appropriate.^{16,20} In 2019, the Department of Health and Human Services issued an opioid tapering guide, warning against opioids tapered rapidly or discontinued suddenly, and stated that slower tapers (eg, ≤10% per month) are often better tolerated than more rapid tapers.^{2,38} The VHA/DoD Clinical Practice Guidelines mentions a reduction by 5% to 20% per month as most common, with the formal recommendation to evaluate patients for tapering individually.³⁹ A systematic review by Frank et al. stated that there is overall only “very low-quality evidence” regarding interventions that may be effective to reduce or discontinue long-term opioid therapy.¹⁸ However, pain, function, and quality of life could improve with opioid dosage reduction, with best evidence derived from a small number of studies using behavioral therapies in support of opioid tapering.¹⁸ Murphy et al.³¹ demonstrated that patients with CNCP could be successfully tapered off of opioids within an interdisciplinary treatment program by use of a concealed taper with blinded dosage of hydromorphone. A recent RCT from Sullivan et al. also showed that an outpatient opioid tapering support intervention resulted in improvements in pain interferences, self-efficacy, and perceived opioid-related problems

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compared with usual care.⁴³ Few studies have explored the patient's perspectives on opioid tapering emphasizing a need to bolster patient-centered engagement strategies for these critical stakeholders.²⁸

There are different and biased beliefs about barriers influencing opioid tapering outcomes that exist among both patients¹⁷ and healthcare providers,⁴⁴ making it difficult to implement novel strategies to reduce opioids for pain management. Importantly, providers and patients' expectancies greatly impact pain outcomes when opioids are used.¹¹ The power of treatment expectancy in improving pain-related outcomes is most clearly demonstrated in experiments comparing open vs hidden administration of morphine in patients who underwent thoracotomy to remove lung cancer.¹¹ The patients' knowledge about a therapy seems to be fundamental to induce optimal therapeutic effects.¹¹ These observations have been extended and corroborated by brain imaging studies showing that the mere awareness of receiving a treatment potentiates the pharmacological analgesic effect in both healthy subjects⁵ and patients with neuropathic pain.³⁵

The literature demonstrates that an individual's expectation of a drug's effect critically influences its therapeutic efficacy, with regulatory brain mechanisms differing as a function of expectancy. Therefore, in a novel methodological twist, we anticipate that patients who are not aware of the exact time of tapering will experience better outcomes for pain perception, interference, and mood-related outcomes. Based on this overall dearth of literature, and on the recent literature providing evidence that pain, function, and quality of life may improve with opioid reduction¹⁸ and that sham opioids may help reduce pain,²³ we believe that Veterans suffering from CNCP can benefit from concealed tapering. However, ethical concerns may arise whenever use of tapering is concealed as misleading patients violates autonomy, diminishes provider integrity, and potential erodes societal trust in the health care.^{7,8,29} For these reasons, an ethically permissible approach to reduce opioids could use an explicit preauthorization request that is incorporated in the informed consent form.⁴⁵ A statement such as the following:

"If you agree to this arrangement, then you will be given pre-packaged pills with full-dose opioid pain medication combined with pills with reduced doses of pain medication. At some point during the course of treatment, the amount of pain medication your pills will gradually be reduced, but you won't know exactly when this will happen. You will have the opportunity to contact your provider any time and receive explanations and, if needed, rescue therapies." (page 8,³).

Such a statement could be complemented with an educational video created to provide information about learning-based mechanisms in the context of an appropriately full and unpressured informed consent discussion. Studies show that patients with CNCP are open to expectancy-based interventions, especially when they understand the mechanisms underlying the effects.^{21,22} After the course of treatment, patients can be offered the option of being debriefed about the timing of the taper. The taper schedule does involve nondisclosure of the fact that the reduction is being performed at that time, but the patient would have earlier provided valid consent to this arrangement; thus, the administration meets ethical standards and is not misleading.^{10,13,46} Certain patients may not be appropriate for this tapering approach. This may include those on low MEDDs who are not appropriate for rescue (ie, "breakthrough") medications and patients with comorbid complex opioid dependence who

may be more appropriate for other OUD treatments (eg, buprenorphine).²⁶

Such a tapering approach could benefit from the 10-step patient engagement framework.³⁰ In accordance with the Patient-Centered Outcome Research Institute principles,^{41,42} the 10-step patient engagement framework³⁰ is a vehicle to implement novel opioid tapering informed by consensus recommendations¹⁴ to improve the lives of CNCP Veterans. The engagement should follow these principles.

1. Reciprocal relationships and shared decision-making

Patients and stakeholders ("stakeholder partners") would need to be involved in discussions that resulted in decisions about the study design and plans for study implementation and dissemination. During the study, and as dissemination activities occur, stakeholders should have a vote in the decision-making processes. A stakeholder advisory board of patients and partners should be created to encourage discussion about what is important to patients throughout the life of the study and to promote a culture within study governance that values all perspectives; vetting all members' ideas in the same manner as ideas from our researchers. Patient-centered shared decision-making will bolster Veterans' confidence in the study aims and promote greater trust in VHA services.

2. Colearning

Stakeholder partners would guide—and, in some cases, lead—the interpretation and/or dissemination of findings and the development of engagement strategies. As data emerge, stakeholder partners would be actively involved in its assessment. For example, patients may serve as representatives on the study's data safety monitoring board. Conference calls would allow dialogue and real-time discussions among stakeholder partners and researchers to promote bidirectional learning. Researchers should be given opportunities to hear from stakeholder partners to enhance researchers' understanding of the significance and potential impact of evidence and lessons learned. Importantly, all parties will be educated about principles of human subjects' protection, historical lessons learned from failures to prioritize patient stakeholders,³⁷ and existing opioids tapering guidelines and empirical evidence.¹² Patient stakeholders will be involved in the dissemination of the results, including article feedback and conference presentations.

3. Partnership

The team's researchers should form a strong partnership with their stakeholders. Input from all parties will help to establish a reasonable time commitment and set of activities for stakeholder partners. All parties should partner to assist with designing the study, implementing, and disseminating what is learned in a manner that will be easy to understand for patients and caregivers and stakeholders.

In summary, novel-tapering approaches have the potential to improve pain and functioning for CNCP Veterans on opioid analgesics. However, the success of this line of scientific inquiry is completely dependent on the partnership of all VHA stakeholders—patients, caregivers, clinicians, and researchers. The feasibility, acceptability, and efficacy of concealed tapering studies are contingent on VHA stakeholder shared decision-making, colearning, and collaboration at every stage of the

research strategic plan—from pilot testing to large scale controlled trials. The authors hope that this perspective piece will provide guidance for investigators committed to advancing the science of opioid risk mitigation and pain management.

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