CLINICAL PRACTICE

Opioid Deprescribing in Patients with Noncancer Pain

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.*

A 62-year-old woman presents with a history of chronic low back pain. She has been taking modified-release oxycodone for more than 3 years and has been taking her current dose of 40 mg twice daily for 3 months. She also takes 5 mg of immediate-release oxycodone up to three times a day on most days for breakthrough pain. The patient's medical history includes hypertension, which is well-controlled with amlodipine, and constipation, for which she had been using laxatives regularly. She rates her pain score as 7 on a scale of 0 to 10 (with 10 indicating the most severe pain) on most days and feels that it has not improved substantially, despite increasing doses of opioids. She reports low mood and feeling increasingly fatigued in the past 2 months, stating that her pain prevents her from engaging in activities she enjoys. She asks whether she should try an increased dose of oxycodone or consider alternative pain relief. How should this case be managed?

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N Engl J Med 2025;393:1833-42.
DOI: 10.1056/NEJMcp2414789

CME

THE CLINICAL PROBLEM

Opioid analgesics are a common treatment for pain. Their global use has more than doubled in recent decades,[1] an outcome that has been driven primarily by Organization for Economic Cooperation and Development member countries, including the United States, Canada, and Australia,[2,3] although opioid consumption declined in these countries between 2015 and 2019.[4] A review of data from 1990 to 2017 indicated that approximately 25% of persons with chronic noncancer pain had used opioids regularly.[5] Furthermore, many people receiving short-term opioid therapy transition to long-term use, with an estimated one in seven who fill a repeat opioid prescription and continue to receive opioid therapy 1 year later.[6] Among persons receiving new opioid prescriptions, the risk of long-term use increases with each additional day of supply, particularly in the first days of therapy, and with the use of higher opioid doses or long-acting opioids.[6] Risk-stratification tools do not allow clinicians to accurately predict whether a patient will transition to long-term use, have an overdose, or have an opioid use disorder, although persons with mood, anxiety, and mental disorders and those who take a sedative–hypnotic drug or have substance use disorder are at higher risk.[6,7]

Despite their frequent use, opioids have limited benefits in managing noncancer pain (Fig. 1). For acute musculoskeletal pain, opioids have a small mean effect in reducing pain (a decrease of <10 points on a scale of 0 to 100, with 0 indicating no pain and 100 worst pain) relative to placebo in the first days, have no effect after the first week, and are probably associated with a small increase in pain

KEY POINTS

OPIOID DEPRESCRIBING IN NONCANCER PAIN

- Opioids are commonly used to treat noncancer pain but have limited effectiveness, as compared with placebo or nonopioid analgesics, and are associated with an increased risk of harm.
- Opioid deprescribing is recommended when the potential harms of opioid therapy outweigh the potential benefits and ideally involves the patient in shared decision making to tailor the plan to the patient's circumstances, goals, and preferences.
- Inflexible application of opioid deprescribing without considering the individual patient can worsen outcomes and lead to serious harm.
- Key strategies for opioid deprescribing include forming an agreed-on and individualized deprescribing plan with the patient that includes tailored and gradual dose reduction with pauses if required, frequent monitoring to assess patient response and progress, and offering treatments to minimize withdrawal symptoms and other negative effects (e.g., provision of naloxone to mitigate the risk of overdose).
- Maximizing the use of nonpharmacologic and noninterventional pain management strategies and providing psychosocial support and multidisciplinary care are also recommended, although trial evidence on their effectiveness is often limited.

after 12 weeks.[11] On the basis of evidence with very low to moderate certainty, opioids have no effect on physical function.[11] For chronic noncancer pain, opioids have a small effect on pain reduction relative to placebo in the short-to-medium term (Fig. 1) and either a small effect or an effect similar to that with placebo on other clinical outcomes (e.g., physical function and quality of life).[12,13] The effects of opioids relative to placebo for chronic pain beyond 6 months are unknown.[13]

Opioids are associated with higher risks of adverse events, such as vomiting, constipation, and somnolence,[11] and serious harm, including hyperalgesia, overdose, and opioid use disorder.[3] Higher opioid doses, as well as coprescription of benzodiazepines and gabapentinoids, further elevate these risks.[8,13] As compared with some nonopioid analgesics, particularly nonsteroidal antiinflammatory drugs, opioids show no clear treatment benefit on chronic pain or certain acute pain conditions but are associated with a higher risk of adverse events.[9,10,12,13]

The lack of evidence on the long-term benefits of opioids, the similar effectiveness of opioids and nonopioids on some pain conditions, and the dose-dependent relationship of opioid-related harm together suggest that avoiding long-term opioid use, reducing the opioid dose, or replacing opioids with nonopioid alternatives may reduce the risk of opioid-related harm. However, large observational studies show that although sustained (≥3 months) opioid cessation is associated with a reduced risk of overdose,[14] opioid cessation or dose reduction is also associated with an increased risk of suicide, overdose, and mental health crises.[14-17] This risk is highest in the first month after opioid cessation[17] but may persist up to 2 years[16] and increases with more rapid opioid tapering,[15] higher baseline opioid doses,[16] higher dose variability,[14] or longer durations of therapy.[17] In addition, as compared with continuation, opioid cessation is significantly associated with termination of care.[18] Observational studies do not provide information on causality, and key factors such as individual patient characteristics, tapering methods, or available supports are often unknown. Nevertheless, the complexity of opioid deprescribing is increased by the risk of negative consequences, and therefore an intentional strategy of closely monitored deprescribing is warranted.

STRATEGIES AND EVIDENCE

PRINCIPLES OF OPIOID DEPRESCRIBING

Deprescribing is a crucial component of rational prescribing and refers to the "withdrawal of an inappropriate medication, supervised by a health care professional with the goal of … improving outcomes."[19] Essential to this process is ensuring that patients are well informed about the possible benefits and harms of continuing and discontinuing opioid use, empowering them to participate in shared decision making, and developing a personalized deprescribing plan tailored to their circumstances, goals, and preferences. To ensure that ethical principles of autonomy and informed consent are upheld and to reduce the risk of unintended harm,[14-17] deprescribing should

ideally be a voluntary process.[20] Some argue that dichotomizing deprescribing as voluntary or involuntary is overly simplistic and that voluntary deprescribing is not always possible,[21] such as when continuing opioid therapy poses an immediate and serious risk of harm. Data comparing voluntary with involuntary opioid deprescribing are limited but have shown no meaningful between-group difference in opioid cessation or pain intensity outcomes.[22,23] Nevertheless, inflexible applications of opioid deprescribing without considering individual circumstances can worsen outcomes.[24]

Guidelines recommend deprescribing opioids when the risks of opioid therapy outweigh the potential benefits or at the patient's request (Table 1) and planning for deprescribing as early as the initiation of therapy.[25] Studies examining the perspectives of patients and clinicians highlight the importance of shared decision making in opioid deprescribing.[30,31] Key enablers include active patient participation, clear patient–provider communication, and support from family, friends, and multidisciplinary teams.[30,31] Conversely, resistance by the patient often stems from poor communication and the fear that deprescribing may worsen pain and function.[30] Clinicians have described difficulties in conducting conversations about opioid deprescribing, expressing fears of jeopardizing the therapeutic relationship. To support patients and clinicians in navigating these complex discussions, conversation guides and shared decision-making models have been developed and are described elsewhere.[32-34]

STRATEGIES FOR OPIOID DEPRESCRIBING

If opioid deprescribing is deemed to be appropriate, guidelines recommend developing an agreed-on and individualized plan with the patient, documenting therapeutic goals, creating a schedule of dose reduction and check-ins, managing potential withdrawal symptoms, and providing nonopioid support (Table 2). Gradual dose reduction is recommended (except if there is risk of impending serious opioid-related harm), because abrupt cessation can cause withdrawal symptoms (e.g., cravings, anxiety, insomnia, and gastrointestinal distress)[35] and lead to serious harm.[14-17] A cohort study involving persons receiving long-term opioid therapy at an oral morphine-equivalent daily dose of 120 mg or higher showed that each additional week of discontinuation was associated with a 7% reduction in the risk of opioid-related emergency department visits or hospitalization.[36] Beyond this, evidence to inform a tapering protocol is limited. One trial compared a 10% reduction in the daily opioid dose every 1 to 2 weeks with no change in the daily opioid dose for 6 months, but the results were inconclusive.[37] A systematic review showed that in 60% of primary studies, the opioid-tapering approach was not defined.[38] Accordingly, guidelines vary, with reductions of 5 to 10% in the oral morphine-milligram-equivalent daily dose scheduled to occur every 2 to 4 weeks or at longer intervals (Table 2),

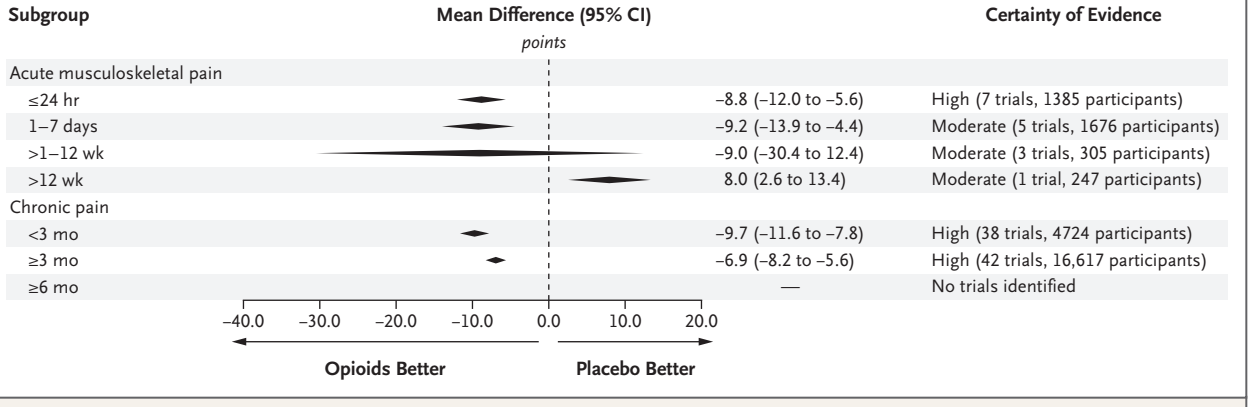

Figure 1. Effects of Opioids, as Compared with Placebo, on Pain Intensity from Meta-Analyses of Randomized, Controlled Trials Involving Adults.

Pain intensity was measured on a scale of 0 to 100, with 0 indicating no pain and 100 worst pain. The certainty of the evidence is presented as reported in the cited systematic reviews of opioids for acute musculoskeletal pain[8] and chronic pain.[9,10]

Table 1. Summary of Key Guideline Recommendations and Practice Points on the Timing of Opioid Deprescription.*

Country	Recommendations and Practice Points
Australia[25]	Develop and implement a deprescribing plan at the point of initiation of opioid therapy (consensus). Deprescribe when there is a lack of improvement or progress toward agreed-on therapeutic goals (weak or conditional). Consider deprescribing if there are coexisting medical conditions that may increase the risk of opioid-related harms, if there is concomitant use of medicines or substances with sedating effects, or when the dose of a prescribed opioid is high (consensus).
Canada[26]	Deprescribe if the patient is receiving an opioid dose of ≥90 morphine milligram equivalents per day (weak or conditional). Consider deprescribing if there is no improvement in pain or function, if a patient does not adhere to the treatment plan, if there are signs of misuse, if there are serious opioid-related adverse events, or at the patient's request (weak or conditional). Regularly evaluate all patients receiving long-term opioid therapy at any dose and counsel them about the benefits and harms of ongoing therapy and the potential benefits of tapering (weak or conditional).
Germany[27]	Deprescribe if the effectiveness of an opioid does not improve, if the patient is not achieving functional goals, or if adverse events arise within the first 12 weeks after therapy initiation (strong). Deprescribe if the same effect can be obtained with other treatments (strong). Deprescribe if a patient abuses or misuses opioid medications (strong). Deprescribe after 6 months of continued opioid therapy (strong).
United Kingdom[28]	Deprescribe if an opioid is no longer beneficial, if there are dependence problems, if the condition has resolved, if harms outweigh benefits, or at the patient's request. If a shared decision cannot be reached regarding opioid use, do not prescribe if it is believed that it is not in the patient's best interests, explain the reasons for the decision to the patient, document all discussions and give a copy to the patient, and offer an opportunity for a second opinion from another clinician. Be aware that opioids should not be stopped abruptly in most cases.
United States[29]	Carefully weigh both the benefits and risks of continuing and tapering opioid therapy (weak or conditional). If the benefits of continued opioid therapy outweigh the risks maximize the use of nonopioid therapies while continuing opioid therapy (weak or conditional). If the benefits of continued opioid therapy do not outweigh the risks, maximize the use of other therapies and gradually taper to lower doses or to discontinuation (weak or conditional).

* Guidelines from select countries with high opioid use were included in the summary. The strength or category of the recommendations (shown in parentheses) was obtained from the cited guideline; the United Kingdom guideline does not report the strength of recommendations. A strong recommendation indicates that most or all persons should receive the recommendation; a weak or conditional recommendation, that not all persons will be best served by the recommendation and that choices may vary according to individual values, preferences, and clinical situations; and a consensus recommendation, that the evidence is insufficient and that the recommendation was formed by expert consensus.

and are typically informed by physiological evidence of neuroadaptations resulting from long-term opioid exposure, pharmacokinetic data, and clinical consensus. Some advocate for further slowing of the dose-reduction schedule in patients who find opioid deprescribing challenging.[39] Tailored approaches with adjustment for the tapering speed and timing and type of support, coupled with regular monitoring to assess patients' response and progress, are proposed strategies to help patients engage in and persist with deprescribing.

Monitoring measures include the recommended outcome domains for pain (e.g., pain intensity and interference), physical function, and quality of life.[40] Another key patient concern and monitoring measure is opioid withdrawal symptoms,[30] the frequency, severity, and duration of which can vary appreciably.[35] Gradual opioid reduction is key to mitigate withdrawal. Other pharmacologic strategies have been described elsewhere.[35] For some, opioid deprescribing may result in substantial withdrawal symptoms or a noticeable decline in function, quality of life, or pain control, necessitating a pause or termination of deprescribing and a plan to recommence later (Table 2). In these instances, the aim is to stop further dose escalations, although the medication may need to be restarted at the previous minimum effective dose. In addition, opioid tolerance decreases with dose reduction. If a person resumes the previous dose, the diminished tolerance heightens the risk of opioid-induced respiratory depression, overdose, or death. Provision of naloxone and overdose education is recommended to mitigate the risk of overdose.[25,29] For others, challenges associated with deprescribing may prompt

Table 2. Strategies for Opioid Deprescribing Based on Key Guidelines from Select Countries with High Opioid Consumption.*

Country	Strategies for Opioid Deprescribing
Australia[25]	Gradually taper the dose — abrupt cessation of opioids without prior dose reduction may increase the risks of harm (strong). Tailor the deprescribing plan on the basis of individual clinical characteristics, goals, and preferences (strong). Conduct regular monitoring and review in relation to therapeutic goals in the deprescribing plan (consensus). Incorporate interdisciplinary or multidisciplinary care, a multimodal approach, or evidence-based cointerventions (weak or conditional).
Canada[26]	Prepare the patient by maximizing the use of nonopioid strategies, setting realistic goals, maximizing the use of psychosocial support, creating a schedule or plan of dose reductions, conducting follow-up visits, and managing withdrawal symptoms and emerging pain (weak or conditional). Gradually reduce the dose by 5 to 10% of the morphine-milligram-equivalent dose every 2 to 4 weeks, with frequent follow-up (weak or conditional). Switching from immediate-release to controlled-release opioids on a fixed-dosing schedule may assist some patients (weak or conditional). Consult a pharmacist to assist with dose reductions (weak or conditional). Rapid dose reduction is best performed in a medically supervised center (weak or conditional). Consider rotating to methadone or buprenorphine–naloxone and then gradually taper (weak or conditional). Pause and reevaluate the patient's clinical status in those struggling with tapering. Coordinate multidisciplinary collaboration (weak or conditional). Consult mental health experts if warranted (weak or conditional). Implement a formal multidisciplinary program (strong).
Germany[27]	Gradually discontinue opioids with long-term use and replace them with other therapies, including options for patients to manage their care (strong). Consider inpatient opioid dose reduction if outpatient programs were unsuccessful (strong). Complete an evaluation of relevant factors before deprescribing and inform the patient and family about deprescribing procedures and withdrawal symptoms (strong). Additional psychotherapeutic support may be useful (strong).
United Kingdom[28]	Shared-decision making: Explain benefits and allow time to explore individual circumstances. Do not stop abruptly unless in exceptional circumstances, such as serious side effects. In these circumstances, consider more frequent reviews or medicines to treat withdrawal symptoms. Consider the urgency of the withdrawal, the initial goal of cessation or dose reduction, which medicine to reduce first if >1 medicine, factors that might increase risks, concurrent medicines, and individual circumstances. Information and support for patients: Give individualized information and sources of support. Discuss withdrawal symptoms and management. Dose reduction: When agreeing on a schedule with the patient, explain the risk of abrupt cessation, balance the risks of adverse events and withdrawal symptoms by a slow taper, ensure that rate of tapering is acceptable, explain that the schedule can be modified, agree on review intervals, and ensure that the patient knows who to contact if problems occur. Suggest a slow, stepwise rate of tapering that is proportionate with the dose, unless a rapid withdrawal is needed. If using a published schedule, apply it flexibly for the individual patient. Offer continued management of the underlying condition. If dose reduction is unsuccessful, aim to stop further dose escalation and make a plan for dose reduction at a later date.
United States[29]	Do not discontinue opioids abruptly or rapidly reduce the dose unless there are indications of a life-threatening issue, such as warning signs of overdose (weak or conditional). Establish goals with the patient — patient agreement and interest is likely to be key to success. Maximize the effectiveness of pain treatment with nonpharmacologic and nonopioid pharmacologic treatments (weak or conditional). Collaborate with the patient on the tapering plan (weak or conditional). Conduct frequent follow-up assessments — at least monthly (weak or conditional). Use a taper slow enough to minimize withdrawal symptoms (weak or conditional). Consider slower tapers for patients receiving long-term therapy, such as for ≥1 year — tapers of 10% per month or slower are likely to be better accepted than more rapid tapers (weak or conditional). Maximize nonopioid treatments and address distress for patients struggling with tapering (weak or conditional). Pausing and restarting a taper might be warranted for some patients (weak or conditional). Screen for anxiety, depression, opioid misuse, or opioid use disorder and treat or refer for management (weak or conditional).

* The strength or category of the recommendations (shown in parentheses) was obtained from the cited guideline; the United Kingdom guideline does not report the strength of recommendations. A strong recommendation indicates that most or all persons should receive the recommendation; a weak or conditional recommendation, that not all persons will be best served by the recommendation and that choices may vary according to individual values, preferences, and clinical situations; and a consensus recommendation, that the evidence is insufficient and that the recommendation was formed by expert consensus.

evaluation, as well as treatment, for an opioid use disorder.[39]

EFFECTIVENESS OF INTERVENTIONS TO SUPPORT OPIOID DEPRESCRIBING

Guidelines recommend the establishment of strategies to support the patient before and during deprescribing. Such strategies include maximizing the use of nonpharmacologic and noninterventional pain management and providing psychosocial support and multidisciplinary care (Table 2). In a systematic review of interventions in adults with chronic pain,[41] pain management programs incorporating education on nonopioid strategies, cognitive behavioral therapy, motivational interviewing, or mindfulness were probably effective in reducing the opioid dose, as compared with usual care, a wait-list control, or participation in a support group, but evidence that these programs led to opioid discontinuation was of very low certainty (Table 3).[41] It was also very uncertain that acupuncture led to a greater reduction in the opioid dose than sham, no acupuncture, or medical management or that the addition of spinal cord stimulators to medical management was more likely to led to opioid discontinuation than medical management alone (Table 3).[41] Opioid replacement therapy (buprenorphine or methadone) may have no effect on opioid use.[41] There was no trial evidence showing that ketamine[41] or cannabinoids[42] have an effect on opioid dose reduction or discontinuation (Table 3).

One cluster-randomized trial showed that a multicomponent intervention that was directed at clinicians in primary care and included nurse care management, an electronic registry, academic detailing, and electronic decision tools, as compared with electronic decision tools alone, was effective in leading to the discontinuation of opioids (adjusted odds ratio, 1.4; 95% confidence interval [CI], 1.02 to 2.1), as well as in reducing the opioid dose, at 12 months (mean [±SE] difference in the morphine-equivalent daily dose, −6.8±1.6 mg) (Table 3).[44] Another trial of a multicomponent intervention directed at patients in primary care also led to a higher likelihood of opioid discontinuation (odds ratio, 5.55; 95% CI, 2.80 to 10.99) and dose reduction (odds ratio for a ≥50% reduction from baseline in the morphine-milligram-equivalent dose, 3.76; 95% CI, 2.47 to 5.71) (Table 3).[45] The intervention consisted of an individualized opioid deprescribing plan, group meetings for education and peer support, and nurse consultations.

Evidence is inconsistent regarding the effects of opioid deprescribing on clinical outcomes (e.g., pain intensity and physical function) in patients with chronic pain, depending on the interventions investigated. At worst, trials indicate that opioid deprescribing may lead to slightly worse pain but no meaningful difference with respect to adverse events.[41,45] Whether opioid deprescribing results in increased use of substances that may be equally or more harmful (e.g., alcohol, illicit pharmaceuticals, or other inappropriate medicines) is uncertain, since existing trials rarely measure these outcomes.[41] Hence, frequent monitoring to evaluate the appropriateness of deprescribing for the individual patient is advised.

Less trial-based evidence is available for persons with acute pain or at transitions of care.[46,47] What evidence is available corroborates observational data[6] showing that reducing the quantity and duration of opioids from the outset is key. For example, after orthopedic surgery, the use of multimodal or nonopioid analgesia led to lower opioid use at 3 months after surgery than opioid analgesia alone (mean difference, −4.34 morphine milligram equivalents; 95% CI, −6.77 to −1.90; low-certainty evidence).[47]

AREAS OF UNCERTAINTY

Existing trials examining opioid deprescribing practices are small and heterogeneous, which limits their ability to provide high-certainty evidence to guide practice across the diverse clinical contexts in which opioid deprescribing might be indicated. The most promising interventions for patients with chronic noncancer pain are multicomponent, but it remains uncertain which or if all components are effective. This uncertainty has implications for implementing these complex, often resource-intensive interventions into practice. Both patients and clinicians identify a lack of knowledge, access to alternative treatments or services, inefficiencies in the health system, and a lack of care continuity as barriers to opioid deprescribing,[30] which suggests that providing patients and clinicians with information and access to alternative treatments and making system changes may be required to facilitate

Table 3. Effectiveness of Interventions on Opioid Dose Reduction or Discontinuation from Randomized, Controlled Trials in Persons with Chronic Noncancer Pain.*

Intervention	Summary of Investigational Treatment vs. Control Interventions	Outcomes
Acupuncture[41]	Electroacupuncture vs. sham electroacupuncture or medical management, or outpatient medication management with vs. without auricular acupuncture	Dose reduction: mean difference in the OME daily dose, −1.56 mg (95% CI, −19.03 to 15.92), favoring investigational treatment (3 studies with 158 participants; very-low-certainty evidence)
Cannabinoids[42]	Cannabinoids vs. placebo, analgesics, or usual care	No trials reported on the effect on opioid use
Ketamine[41]†	Ketamine infusions vs. placebo	No trial evidence
Guideline implementation[43]	Intensive strategy (educational meetings with audit and feedback, plus a clinic-level strategy that targets clinic process and workflows, plus a prescriber-level strategy providing consultation with an experienced physician) vs. less intensive strategy (educational meetings with audit and feedback only)	Dose reduction: no significant difference over a 3-mo period reported for those with long-term (≥3 mo) opioid use (raw data not provided) (1 study with 8978 participants, but the number of participants with long-term opioid use is unclear)
Multicomponent intervention directed at clinicians[44]	Nurse care management, electronic registry, academic detailing, and electronic decision tools vs. electronic decision tools only	Dose reduction: mean (±SE) difference in the morphine-equivalent daily dose at 12 mo, −6.8±1.6 mg, favoring investigational treatment (1 study with 985 participants) Discontinuation: adjusted odds ratio at 12 mo, 1.4 (95% CI, 1.02 to 2.1), favoring investigational treatment (1 study with 985 participants)
Multicomponent intervention directed at patients[45]	Mutually agreeable opioid cessation plan, group meetings led by a nurse and a lay person for education on opioids and pain management by the patient, nurse consultations for individualized tapering, and usual care consisting of a self-help booklet and relaxation compact disk vs. usual care only	Discontinuation: odds ratio at 12 mo, 5.55 (95% CI, 2.80 to 10.99), favoring investigational treatment (1 study with 433 participants) Dose reduction (≥50% reduction in the MME dose from baseline): odds ratio at 12 mo, 3.76 (95% CI, 2.47 to 5.71), favoring investigational treatment (1 study with 433 participants)
Pain management programs[41]	Outpatient or online programs, incorporating interventions such as physician consultations, cognitive behavioral therapy, motivational interviewing or mindfulness vs. usual care, wait-list control, or a support group	Dose reduction: mean difference in the OME daily dose, −14.31 mg (95% CI, −21.57 to −7.05), favoring investigational treatment (5 studies with 428 participants; moderate-certainty evidence) Discontinuation: risk ratio, 2.15 (95% CI, 1.02 to 4.53), favoring investigational treatment (2 studies with 238 participants; very-low-certainty evidence) Trials not included in the meta-analysis mostly showed similar findings, with very-low-certainty to low-certainty evidence
Consumer education[48]	Direct mail-out of an education brochure vs. wait-list control	Dose reduction: at 6 mo, more people reported a dose reduction in the investigational-treatment group than those in the control-intervention group, but the between-group difference in the MME dose per day was not significant (−1.6 mg; 95% CI, −7.3 to 4.1) (1 study with 4225 participants) Discontinuation: 11% in both groups; between-group difference, 0% (95% CI, −1.9 to 1.9) (1 study with 4225 participants)
Spinal cord stimulator[41]	Spinal cord stimulation plus conventional medical management vs. conventional medical management alone	Discontinuation: risk ratio, 6.07 (95% CI, 1.16 to 31.77), favoring investigational treatment (2 studies with 97 participants; very-low-certainty evidence)

* MME denotes morphine milligram equivalent, and OME denotes oral morphine equivalent. The systematic review by Avery et al.[29] identified one trial of ketamine use, which was in fact a retrospective study.

† The systematic review by Avery et al.[29] identified one trial of ketamine use, which was in fact a retrospective study.

successful outcomes. Singular efforts, such as consumer education alone (Table 3),[48] are unlikely to yield satisfactory or sustained results. But coordinating efforts across multiple levels is burdensome on the individual patient and clinician.

Evidence is particularly scarce in vulnerable patient populations in which the risk of opioid-related harm is often higher. These patient populations include those who are required to undergo involuntary opioid deprescribing, are taking concurrent psychotropic medications,[49] are receiving higher-dose opioids, are socioeconomically disadvantaged, are culturally diverse, are older, or have a disability. The challenge of advancing the evidence base in this area and implementing evidence into practice is that one size does not fit all — strategies and interventions need to be tailored on the basis of individual circumstances, clinical contexts, available resources, health systems, and policies.

GUIDELINES

International guidelines are generally consistent in their recommendations, but recommendations vary in strength (Tables 1 and 2). It is worth noting that guidelines are evolving quickly. The Australian, U.K., and U.S. guidelines are new or have been updated since the last systematic review of such guidelines was published in 2023[49]; these guidelines provide expanded and more patient-centered deprescribing guidance. For example, the 2022 update of the U.S. Centers for Disease Control and Prevention guidelines removes mention of dose thresholds (because of harms related to their inflexible application)[50] and includes recommendations in favor of shared decision making to assess the benefits and risks of opioid use and determine the appropriateness of deprescribing.[29]

Implementing guidelines into practice has mixed success. A 2024 U.S. trial assessed four strategies to promote guideline-concordant opioid prescribing in primary care and showed that, overall, the most intensive strategy (educational meetings with audit and feedback plus targeting of clinic process and workflows and provision of consultation with an experienced physician to prescribers) was more effective at opioid dose reduction than the least intensive strategy (educational meetings with audit and feedback only).[43] However, this difference was not observed in the subgroup of patients receiving long-term (≥3 months) opioid therapy (Table 3).[43]

CONCLUSIONS AND RECOMMENDATIONS

In the case vignette, the patient is receiving limited benefit from opioids and has opioid-related adverse effects such as constipation and fatigue. Given the limited evidence supporting the long-term efficacy of opioids and because of the known harms, we recommend discussing a trial of opioid deprescribing with the patient using a shared decision-making approach. This conversation should cover the potential benefits and risks of continuing and discontinuing opioid therapy, with emphasis on a gradual reduction (e.g., a 10% reduction in the morphine-milligram-equivalent dose every 4 weeks) to minimize the risk of withdrawal symptoms, especially since the patient has been receiving a high dose for an extended period. If opioid deprescribing is deemed to be appropriate, an individualized deprescribing plan that aligns with the patient's goals and circumstances is recommended (e.g., deciding which formulation of oxycodone to taper first). Because the evidence supporting specific deprescribing interventions is uncertain and the availability of supporting services may vary, we would allow the patient to express preferences for cointerventions (e.g., multidisciplinary pain programs, referrals for mental health support, and simple analgesics to replace opioids). We would ensure ongoing monitoring and support with particular attention paid to her low mood. If outcomes worsen, we would consider pausing the taper, implementing additional supports, and recommencing deprescribing when potential benefits are expected to exceed harms. Because of the increased risk of overdose after a person goes back to taking a previously higher opioid dose, overdose education and naloxone should be offered. We would recommend long-term monitoring to ensure that the patient maintains satisfactory function and quality of life.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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