

# Best Practices in Tapering Methods in Patients Undergoing Opioid Therapy

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**Abstract** The prescribing of opioids for chronic non-cancer pain has escalated over recent years. This pattern has led to a larger number of patients who require discontinuation of opioid therapy. The purpose of this review was to provide an overview of best practices for tapering opioid therapy in patients. A systematic review of the current literature concerning tapering of opioid therapy was performed from 2000-2013. 24 studies were selected for review. Considerable variation was found with regard to taper rate and duration. Taper rate ranged from an initial 20-50% daily reduction in opioid dose to a 5% reduction in dose every one to four weeks. The most common titration rate was a 10% reduction in the daily dose each day. General themes were to individualize taper parameters to ensure patient compliance and presentation of withdrawal symptoms, to slow the rate of the taper to about 1/3 of the original dose, and advise a referral of addicted and complex patients to appropriate specialists for treatment. The majority of available information on tapering opioid therapy consists of clinical guidelines that have been created based on practice experience. There is a need for additional experimental research to develop a more standardized taper protocol.

**Keywords** Opioid, Opioids, Pain, Pain Management, Tapering, Weaning, Best Practices

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## 1. Introduction

In recent years the use of opioids in the United States has markedly increased.[1] Much of this increase in use can be attributed to the expansion of conditions that opioids are being used to treat. Initially only used in cases of acute pain and severe chronic cancer pain, developments in the last two decades have resulted in greater use of opioids.[2] During the late 1990s there was liberalization of laws governing opioid prescribing by state institutions.[3] In 2000, the Joint Commission on Accreditation of Healthcare Organizations[4]

altered its pain management standards for inpatient and outpatient medical care. Furthermore, there has been increased aggressiveness in pharmaceutical companies' marketing of opioids, greater physician and organization advocacy, and an enhanced patient awareness on the right to pain relief.[5]

Studies have also revealed that the use of opioids has increased in the treatment of chronic non-cancer pain. Between 1980 and 2000 an increase from 8% to 16% was observed in the number of patients receiving opioid prescriptions for chronic musculoskeletal pain.[2] Data from the National Ambulatory Medical Care Survey[1] suggest that opioids are prescribed in about 15-16% of all chronic back pain cases.

The sales of opioid analgesics were found to have quadrupled from 1999 to 2010.[5] Sales in the United States of hydrocodone increased by 280%, methadone rose by 1,293%, and oxycodone expanded by 866% from 1997 to 2007.[5] It was estimated that 2.0% of adults in the United States regularly use opioids and that approximately 2.9% use them occasionally.[1] Additionally the estimated number of opioid prescriptions in the United States was over 256 million in 2009.[5]

The greater prevalence of these agents requires that clinicians be adept at handling potential problems that could arise from this therapy. One of the most common problems clinicians face with opioid therapy is the development of withdrawal symptoms in patients, upon discontinuation. Withdrawal symptoms result from physical tolerance which is closely associated with regular intake of the medication for chronic conditions. These symptoms may include agitation, dysphoria, tachycardia, tachypnea, rhinorrhea, lacrimation, salivation, chills, piloerection, hyperventilation, mydriasis, muscle aches and spasms, bone pain, yawning, restlessness, anxiety, insomnia, diaphoresis, cramps, nausea and vomiting, diarrhea, abdominal cramping, and fever.[6] These symptoms can result in reduced physical function and often lead to a debilitating experience for patients. The most effective way to prevent withdrawal symptoms upon opioid discontinuation is to taper the medication.[7]

There are many other pertinent reasons to consider tapering a patient's opioid therapy. The patient may be unable to tolerate the side effects of an opioid medication. The opioid may not be effective in treating the patient's pain. The patient's condition may improve to the point where he or she no longer requires as high a dose, or can discontinue the therapy altogether. Additional reasons to alter therapy consist of the patient experiencing hyperalgesia from the therapy, to improve the patient's mood, and to prevent further therapy in the case of addiction. In patients in whom such a strategy is desirable; it is beneficial to know the optimal parameters of tapering. The purpose of this review was to provide an overview of the best practices for tapering opioid therapy in patients.

## 2. Methods

A systematic review of the current literature concerning tapering of opioid therapy was performed from 2000-2013 using PubMed, Ovid, Google Scholar, Cochrane Library, and electronic databases. The key search terms were "opioid," "opioids," "taper," "tapering," "detoxification," "detox," "dependence," "withdrawal," and "weaning." Articles which focused on methadone and buprenorphine as detoxification and maintenance treatments in addicted patients were excluded. This omission was due to the complexity and unique aspects of addiction therapy in these patients. Weaning addicted patients off of opioid therapy is significantly different than in non-addicted patients. As addiction is often handled by specialists, it is beyond the scope of this review. Studies cited in the bibliographies of the articles produced by these searches were also included in the review. Articles were selected based upon relevance and quality and included narrative and systematic reviews, prospective and retrospective studies, and clinical guidelines from US government agencies and expert panels. The selected articles were summarized in a table structured by year of publication, author, title, study design, methods, findings, and source. The results were further divided into subgroups: temporal parameters, complex patients with or without behavioral problems (e.g. opioid addiction), and pharmacologic adjuvants.

## 3. Results

Twenty-four articles were selected for this review (see Table 1). Twelve of the articles were clinical guidelines. Of the remaining twelve studies, eight involved pediatric patients in the inpatient setting, and four involved populations that included adults in the inpatient setting.

### Temporal Parameters

Several studies indicated that the overall schedule of the taper should be determined on an individual basis.[8-10] Some experts have suggested that the longer the patient has been on opioid therapy, the longer the taper should

be.[6,8,9,11,12] Patients might require a longer taper because they are more likely to experience withdrawal symptoms.[9] An observational study, conducted by Pederson and colleagues[6], found that the length of the taper was positively correlated with pre-taper dosage ( $r=0.71$ ,  $p=0.001$ ) length of pre-taper opioid therapy ( $r=0.42$ ,  $p=0.001$ ), and the total number of self-reports of taper-related symptoms ( $r=0.48$ ,  $p=0.001$ ). These findings were supported in a later study by the same investigators.[12] Both of these studies were performed in an inpatient setting with patients whose ages ranged from 5 to 64.[6,12] It has also been suggested that patients be placed on medications with long half-lives for the taper, as opposed to short half-lives.[9,10,13,14] Switching patients to agents with long half-lives provides a more stable weaning, as the concentration of the drug is easier to control.

A 2012 review, from American Family Physician, proposed consolidating all of the patient's opioid therapy into a single long-acting medication.[14] However, it has also been suggested that tapering may be performed with short-acting agents.[9] A study by Kral recommended that after conversion to one of the longer half-life medications that a "test dose" or "test regimen" should be implemented with close monitoring. During the first week, dosing should be adjusted to control withdrawal symptoms. The taper regimen should then start after the patient is stabilized.[9] The patient's daily medication schedule should be maintained as long as possible.[9] Furthermore, it was recommended that patients be switched from as needed to scheduled dosing.[9,10] The frequency of the dispensing intervals should vary with the degree of the patient's control over his or her opioid use. Prescriptions should not be refilled if the patient runs out prematurely.[10] Providing the patient and his or her family with information about the taper protocol should help increase the patient's comfort level and compliance.

Findings from the review of the literature also varied with regard to taper rate. A study that utilized information related to weaning in pediatric patients in intensive care units found that the required weaning rate is related to the number of days the child has been on a continuous infusion of opioids and benzodiazepines.[15] The longer the patient has been treated with opioids, the slower the weaning rate should be.[15] A 2012 review by American Family Physician[14] recommended that a rate should be selected that avoids withdrawal symptoms, the loss of patient confidence, or pain escalation. Authors suggested that the rate of opioid tapering should be influenced by specific patient behavior. Rapid tapering, by reducing the original dose by 25% every 3 to 7 days, should be effective in weaning patients that express frequent requests for early refills, despite adequate titration of long-acting opioids.[14] Other reasons for this rate include the patient experiencing major adverse effects or intoxication, opioid-induced hyperalgesia, and non-adherence to the pain medication agreement.[14] Gradual tapering, by reducing the original total dose by 10% every 1 to 4 weeks, was indicated for patients in which

functional goals are not met and in those who experience persistent adverse effects despite opioid rotation (e.g. nausea, refractory constipation, or pruritus).[14]

Guidelines, developed by the Department of Veterans Affairs and the Department of Defense[8], stated that the patient should be tapered at a rate of 20%-50% per week of the original dose, with the goal of minimizing withdrawal effects. It was suggested that the quickest rate of tapering should be 20% of the previous day's dose.[8] Other guidelines from Canadian Family Physician suggested varying the rate of the taper from 10% of the total daily dose every day to 5% every 1 to 4 weeks.[10] Multiple guidelines suggested a 10% reduction in the original dose per week.[16-18] For example, in 2010 a Group Health Cooperative[11] recommended the 10% reduction in all patients except those with complex comorbidities, those whose function has not improved, and those who have received long-term therapy. Specifically, it was suggested that patients should be tapered at a 10% dose reduction every 2 to 4 weeks.[11] Furthermore, slower tapers should be used in patients who are anxious about the tapering process, those that have cardiorespiratory conditions, and those who might be psychologically dependent on opioids.[9,10]

Similarly, a study in which pediatric patients in the intensive care unit were weaned off both opioids and benzodiazepines found that withdrawal symptom onset was related to the speed of the taper.[19] Withdrawal symptoms were more likely to occur early in tapers with quick rates.[19] One study suggested that patients on doses over 200mg/day of morphine or equivalent could be weaned more rapidly than those at lower doses.[20] Patients experiencing severe withdrawal symptoms or worsening of pain or mood should have their dose be held or increased.[10,16] Once the withdrawal, pain, or mood symptoms have subsided, the taper should be resumed.

Several studies cited the last phase of the taper as being the most difficult to accomplish.[9,10,13,20,21] Once the dose reaches 30-45mg of opioid/day, withdrawal symptoms may become more likely.[9,22] Clinical guidelines from the American Pain Society and the Academy of Pain Medicine[20] reported that these effects increase when the patient reaches dosages of 60 to 80mg/day of morphine or equivalent. The reason for this increase in difficulty is due to the poor ability of the body to adapt to the changes in concentration and receptor activity. Findings from an observational study conducted in 2000, focused on transplant patients in the inpatient setting found that patients experienced the most withdrawal effects 4 days after the taper was completed.[6] Additionally, guidelines from Canadian Family Physician[10] suggest that once a third of the original dose is reached, the taper should be slowed to half of the previous rate.[15] Another study stated that if withdrawal symptoms are encountered, it may be necessary to slow rate of dose reduction from a weekly to monthly rate.[16,18] The entire duration of the taper should normally range between 2 to 3 weeks and 3 to 4 months.[10]

In comparison, similar studies from two case reports were

found in which patients were weaned off of long-term opioid use.[22] The first was a 17-year-old male cancer patient who was on 180mg of morphine immediate release (IR) every 4 hours for approximately 8 months. The patient's dose was reduced over 2 weeks to 30mg every 4 hours. Then he was shifted to 60mg sustained release (SR) morphine twice daily. He was subsequently reduced to 10mg SR morphine over the next two weeks. The opioid was then discontinued over the remaining two weeks. The patient did not report any withdrawal symptoms. In the other case, a 65 year-old male cancer patient was taking 90mg of IR morphine every 4 hours for approximately 2 weeks.[22] The patient was then weaned to 30mg IR morphine every 4 hours over 4 months. He was then switched to 60mg SR morphine twice daily, reduced over 2 weeks to 10mg SR morphine, and then discontinued after 1 week. This patient only reported mild self-limiting diarrhea that was not treated.

On the other hand, clinicians have explored methods that combine various recommendations by developing an opioid tapering algorithm.[21] The algorithm was created using non-research-based published guidelines, published research on opioid withdrawal symptoms, clinical experience, and multidisciplinary consultant recommendations.[21] It was designed to be used in patients over the age of five, who were receiving continuous infusion opioids. The investigators stated that key features were that tapering needed to be practical and user-friendly, but would allow for flexibility for taper adjustments based on individual patient response. The investigators felt that only the patient could best determine the acceptable degree of pain relief and side effects. It should be noted that total pre-taper opioid dosage was not used as a basis for determining the length of the taper because it resulted in calculations that were considered to be too complex. Furthermore, the chosen rate of decreasing the dose hourly by 10% was used because it provided for easier calculations and increased the consistency of the taper. The taper was held until the next scheduled decrease if the patient decided not to tolerate the pain or withdrawal symptoms. The investigators felt that holding the taper prevents increases and decreases in the continuous infusion rate, which may cause fluctuations of opioid serum levels and delay the tapering process.

Ongoing assessments of pain and withdrawal symptoms were utilized to determine whether the taper continued to be held at the next scheduled dose decrease or proceeded. If intolerable symptoms continued for two successive scheduled opioid decreases, the taper rate was slowed. If new, persistent, or uncontrolled pain developed, it was treated and the taper was delayed until it resolved. When the patient reached an hourly rate that was at or was lower than 0.5mg of morphine, 0.1mg of hydromorphone, or 5mcg of fentanyl the taper rate was slowed. The rationale for slowing the taper at the end came from suggestions from the literature.[21]

### Complex Patients

Several studies recommended that patients that present with behaviors characteristic of addiction to opioids or other

substances should be referred to an addiction specialist.[8,10,17,18,20] Guidelines created by the Veterans' Administration and Department of Defense[8] suggested that patients with substance use disorders should have their psychiatric conditions and comorbidities identified and documented. These conditions include the presence of infectious diseases, and conditions such as diabetes and cardiovascular disease that may be related to or affected by the patient's substance abuse.[8] The taper will most likely be unsuccessful in patients who are not following the schedule, or are continuing to abuse opioids. The same guideline recommends that these patients be referred to specialists for detoxification treatment in a primary care setting, followed by possible maintenance therapy.[8,17,20]

Guidelines produced by The Agency Medical Director's Group[16] in 2010 suggest that patients whose urine drug screening tests are negative for prescribed opioids, positive for amphetamine or methamphetamine, positive for cocaine or metabolites, positive for non-prescribed prescription drugs, or those positive for alcohol should also be considered for referral to an addiction specialist or drug treatment program. Multiple guidelines recommend that if a patient presents with clearly unsafe or illegal behaviors (e.g. dealing/selling medications, impulse control disorders, or parasuicidal acts), then opioid prescribing should be immediately stopped and withdrawal symptoms should be addressed.[8,10,16,20] They should also be assessed for unmet psychosocial needs or situational stressors.[8] Such stressors include occupational problems, poor social support, problematic family relationships or situations, financial difficulties, inadequate or no housing, and difficulties with the activities of daily living.[8] Guidelines from Canadian Family Physician[10] suggest that patients who are unwilling to comply with the taper should be encouraged to seek medical care at another location.

Additionally the guideline suggested that precaution should be utilized in patients that have unstable medical and psychiatric conditions. These conditions can be exacerbated by tapering, as it can cause anxiety and insomnia.[10] Depending on the circumstances, it may be best to either taper, cease opioid prescribing, or to wait until after consultation for specialty services has been obtained.[10] A pain specialist can help to manage the patients' conditions in addition to their pain management. It was advised that particular caution should be exhibited towards patients with suicidal thoughts. One study on opioid-related overdose deaths in Ontario found that 21% of the deaths were suicides.[23] Therefore, it has been suggested that tapering and discontinuation be initiated in patients if they have no improvement in mood or have decreased pain ratings of at least 30%.[23] Multiple studies also advised that if a patient experiences complex withdrawal symptoms during the taper or cannot tolerate it, then he or she should be referred to a pain specialist or a center specializing in withdrawal treatment.[8,16] It is recommended that the provider remain engaged with the patient through the tapering process and provide psychosocial support as needed. These actions

should help to avoid complex situations involving the patient and should increase the taper's chance of success.[8]

Guidelines by Canadian Family Physician[23] strongly recommended that benzodiazepines and other sedative-hypnotic medications should be discontinued in patients that will undergo opioid tapering. Discontinuation of these medications is particularly important in elderly patients. Cessation of benzodiazepines helps to minimize falls, sedation, and overdose.[23] It was also recommended that pregnant patients or those planning to become pregnant should undergo opioid tapering and discontinuation. These patients should not be taking opioids because acute withdrawal can cause premature labor and spontaneous abortion.[23]

### **Pharmacologic Adjuvants**

Withdrawal symptoms may be a common concern in patients who are physically dependent on opioids.[6] These symptoms should be minimal if the patient is tapered slowly enough. However, should they arise, they will be unpleasant, but are not lethal.[6] Common withdrawal symptoms include anxiety, depression, insomnia, decreased appetite, aching in the bones and joints, chills, runny nose, gastrointestinal discomfort, diarrhea, and a craving for opiates.[6]

Additional medications can be applied to alleviate and minimize withdrawal symptoms. These symptoms should be managed supportively. Antidepressants may be used to manage irritability and sleep disturbances.[8,16] Additionally, antiepileptic medications (AEDs) can be used to treat neuropathic pain in these patients.[8,16,1,2,3] One review studied the use of AEDs in the treatment of central post-stroke pain.[24] Central pain was defined as "pain initiated or caused by a primary lesion or dysfunction of the central nervous system." Central post-stroke pain is due to neuronal excitability, which is caused by damage to the central nervous system. Lamotrigine, gabapentin, carbamazepine, topiramate, and pregabalin have been suggested as a possible adjunct in the treatment of neuropathic pain.[24,25,26] However, there is conflicting literature with regards to their effectiveness and additional research is necessary to judge their effectiveness. These medications are thought to reduce pain by reducing abnormal neuronal hyperexcitability through modulation of voltage-gated ion channels and by their effects on gamma-aminobutyric acidergic and glutamatergic neurotransmission.

One case report, noted that the coadministration of oxycodone and the sodium channel blocker carbamazepine was effective in treating trigeminal neuralgia.[25] The patient's (a 48-year-old woman) neuralgia was initially treated by carbamazepine dosed at 300 mg every 8 hours. However, this treatment was ineffective, and was replaced by a new treatment regimen in which the carbamazepine was reduced to 200 mg every 8 hours and oral oxycodone was added dosed at 5 mg every 12 hours. This regimen was successful in treating the patient's neuralgia.

Another case report suggested that topiramate could be

effective in the treatment of dysaesthetic pain.[26] In this study, a 42-year-old woman with an 8-year history of multiple sclerosis was successfully treated with topiramate dosed at 150 mg/day after unsuccessful attempts to treat the pain with amitriptyline and carbamazepine as monotherapies.

Special care should be taken in the use of these agents in the elderly. These patients are more sensitive to certain secondary effects of AEDs, such as cognitive disturbances, due to pharmacodynamics and pharmacokinetic age-related changes. These changes are significant enough that the use of enzyme-inducing AEDs, such as carbamazepine, phenytoin, phenobarbital, and primidone should be avoided in these patients.

Clonidine can be used to attenuate the autonomic withdrawal symptoms such as hypertension, nausea, cramps, diaphoresis, and tachycardia.[9,11,16] However, a review by American Family Physician[14] suggested that clonidine was ineffective for symptom management. Calcium carbonate and milk of magnesia were offered as treatments for dyspepsia, while promethazine and metoclopramide were also proposed as treatments for nausea.[11] Drugs such as trazodone, hydroxyzine, or diphenhydramine may be used to treat insomnia and restlessness.[9,11] For patients with muscle aches and fever, non-steroidal anti-inflammatory agents can be used to alleviate these issues.[9,11] Furthermore, muscle cramps can be treated with dicyclomine and Pepto-Bismol can be used to treat diarrhea.[9] Finally, it is important to note that withdrawal symptoms should not be treated with opioids or benzodiazepines.[8-10,16]

## 4. Discussion

The purpose of this study was to provide an overview of what are considered to be the best practices for tapering opioid therapy in patients. There was variation in the parameters of the taper between articles. Some guidelines reported that it was necessary to switch the patient to an agent with a long half-life, while others did not.[9,10,13,14] Reasons for the disagreement in findings are difficult to determine. However, these disagreements came from guidelines based upon clinical expertise. A plausible explanation is that the healthcare professionals who developed these documents had varying clinical experiences. The taper rate had the most variation by far. Rates ranged from an initial 20-50% daily reduction in opioid dose to a 5% reduction in dose every one to four weeks.[8,10] Reasoning for these rates was often not provided. Studies that offered their rationale stated that it came from established guidelines, or was per protocol of the institution.[6,12-15,19,27] The one study that experimentally developed its rate, selected it based upon ease of use and consistency.[21]

However, there were several consistencies between the studies. Although the rates varied, tapers were designed with the goal of minimizing the occurrence of withdrawal symptoms.[8-10,14,16] The occurrence and severity of

withdrawal symptoms are the primary means of assessing the taper's success. This practice logically follows into another consistency: the need to be able to individualize tapers. Some patients may be more prone to exhibit these effects, thus, a flexible taper strategy is desirable. Comorbidities, psychological state, functional state, the presence of pain, and anxiety with regards to the taper may fluctuate between patients as well, further enhancing the appeal of a malleable taper strategy. Another consistency was that the length of the taper should reflect the length of the prior opioid therapy.[6,8,9,11,12] This finding was present in several guidelines and was supported by several of the experimental studies. The literature also leaned toward switching the patients onto opioids with long half-lives on a fixed schedule.[9,10,13,14] Another commonality was the recommendation to slow the taper near its end.[9,10,13,15,20,22] Both guidelines and experimental studies supported this advice. However, the exact point that this deceleration should occur was disputed. The suggestion to refer addicted patients or those with complex pain and comorbidities to the indicated specialist was also consistent between guidelines.[8,10,17,18,20] The consensus with addicted patients was that the tapering regimen should be stopped and that the patient should be referred for detoxification treatment. In the guidelines that mentioned pharmacologic adjuvants, clonidine was the most commonly suggested medication.[9,11,16] This finding could be due to clonidine's ability to treat many of the withdrawal symptoms, rather than just one or two.

## Limitations

There were several limitations to this review. Generalization of the results in some of the infant and pediatric studies is limited. This impairment stems from concern that withdrawal symptoms in infants and young children differ from those in older children and adults.[21] These two groups of patients also metabolize the medication differently than others.[21] These differences suggest that the findings from these studies may not be applicable to older patients. Another limitation was the lack of comparative and experimental data in the literature.

Much of what is known regarding opioid tapering is based upon guidelines hedged in clinical experience. In fact, many of the guidelines, themselves, either quote previous guidelines or textbooks as sources for tapering information. This practice may have the effect of creating an echo chamber of sorts where information is restated between studies without any experimental or evidence-based developments. Additionally, there is a lack of comparative data regarding the efficacy of taper strategies. Only one study was found in the literature that included adult patients. This study compared the investigator-made taper to the baseline tapering practices of the large tertiary-care center where the intervention was implemented.[12]

## 5. Conclusion

Over recent years there has been a surge in opioid use in the United States. A review of medication use in the United States found that hydrocodone with acetaminophen was the most common prescription every year from 2007 to 2011.[28] Of the top 25 most commonly prescribed medications in 2011 three were opioids.[28] Due to this prevalent and escalating use there is a greater need to understand the management of opioid therapy. This comprehension includes tapering. There are several guidelines that present recommendations. These guidelines have considerable variations with respect to rate and duration of the taper. However, they have many similarities. These include the valuing of elements that add flexibility and individualization to the taper. These include the option to hold the taper or to change its rate based upon certain patient factors.

Unfortunately, the literature as a whole is limited. This limitation is due to tapering strategies being founded almost completely on clinical experience. Only one quasi-experimental study has been performed in an adult

population.[12] The applicability of a sizable portion of the experimental research is constrained due to its focus on infant and pediatric patients. The downside of these findings is that many of the guidelines cite other guidelines as their source for tapering protocols. The cyclic nature of this practice stagnates progress towards optimizing taper protocols. It also results in greater hardship on the part of the patient. Hopefully more experimental research will be conducted in this area and lead to a standardized protocol.

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**Table 1.** Articles selected from the systematic review.

Year	Author	Title	Study design	Intervention	Findings	Source
2006	Kral, L et al	Opioid Tapering: Safely Discontinuing Opioid Analgesics	Review	None	No single strategy can be universally applied. Each situation is unique. The most important factor is to consider how acutely the taper or conversion is needed. It is suggested 10% decreases every day, 20% decrease every 3-5 days, or 25% decrease per week. For short-acting opioids it is suggested to decrease the dose by 10% every 3-7 days, or decrease the dose 20-50% per day until the lowest dose is reached. After the lowest dose is reached, increase the dosing interval, eliminating one dose ever 2-5 days. For long-acting opioids there are agent-specific guidelines.	Pain treatment topics
2007	Oklahoma. Physician Advisory Committee	Guidelines for Prescription of Opioid Medications for Acute and Chronic Pain	Clinical guidelines	None.	Weaning can be done safely by way of a slower taper. Patients who undergo intensive treatment programs in a pain center or a drug rehabilitation center can be tapered off opioids in 1-2 weeks. Patients being treated in an office-based practice should be tapered more slowly, but the taper should rarely take more than 3 months.	<a href="http://www.digitalprairie.ok.gov/cdm/singleitem/collection/stgovpub/id/3774/rec/47">http://www.digitalprairie.ok.gov/cdm/singleitem/collection/stgovpub/id/3774/rec/47</a>
2010	Washington State Agency Medical Directors Group	Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain	Clinical guidelines.	None.	A decrease by 10% of the original dose per week is usually well tolerated with minimal physiological effects. Some patients can be tapered more rapidly without problems (over 6-8 weeks). In some patients it may be necessary to slow the taper timeline to monthly, rather than weekly dosage adjustments.	AMDG Agency Medical Directors Group
2011	Canadian guideline for safe and effective use of opioids for chronic non-cancer pain Clinical summary for family physicians. Part 1: general population	M. Kahan, et al.	Systematic review and expert panel.	A systematic review of the literature on the effectiveness and safety of opioids for chronic non-cancer pain. A panel of 49 clinicians from across Canada reviewed the draft and achieved consensus on 24 recommendations.	Taper rate can vary from 10% of the total daily dose every day to 5% every 1 to 4 weeks. Slower tapers are recommended for patients who are anxious about tapering, those who might be psychologically dependent on opioids, and those who have cardiorespiratory conditions. Once a third of the original dose is reached, slow the taper to half of the previous rate. Hold or increase the dose if the patient experiences severe withdrawal symptoms or worsening of pain or mood Tapers can usually be completed in between 2 to 3 weeks and 3 to 4 months. Patients who are unable to complete the taper may be maintained at a lower opioid dose if they are compliant with the treatment agreement.	Canadian Family physician
2010	VA/DoD Clinical Practice Guideline for Management	The Management of Opioid	Systematic review and expert panel.	A systematic review of the literature was performed using Ovid	Tapering should be a joint effort on the part of the patient and the physician. Tapering rate and schedule should be individualized. Taper by 20%-50% per week [of original dose], for patients who are not	Department of Veterans Affairs, Department of Defense

	of Opioid Therapy for Chronic Pain	Therapy for Chronic Pain Working Group		MEDLINE, the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials. Electronic searches were supplemented by reference lists and additional citations suggested by experts.	<p>addicted. The goal is to minimize adverse/withdrawal effects. The rapid detoxification literature indicates that a patient needs 20% of the previous day's dose to prevent withdrawal symptoms. Decisions regarding tapering schedule should be made on an individual basis. Sometimes faster or slower tapering may be warranted. Some experts suggest that the longer the person has been on opioids, the slower the taper should be.</p> <p>Remain engaged with the patient through the tapering process, and provide psychosocial support as needed.</p> <p>Consider using adjuvant agents, such as antidepressants to manage irritability, sleep disturbance, or antiepileptics for neuropathic pain. (Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain. Do not treat withdrawal symptoms with opioids or benzodiazepines after discontinuing opioids.</p>	
2009	Clinical Guidelines from the American Pain Society and the American Academy of Pain Medicine on the use of chronic opioid therapy in chronic non-cancer pain: What are the key messages for clinical practice?	R. Chou	Summary of a review of guidelines.	A summary of a review by The American Pain Society and the American Academy of Pain Medicine was performed.	<p>Approaches to weaning range from a slow, 10% dose reduction per week to a more rapid 25–50% reduction every few days. Anecdotal clinical experience suggests that at high doses (e.g., over 200 mg/day of morphine or equivalent), the initial wean can be more rapid. The rate of dose reduction often must be slowed when relatively low daily doses, such as 60 to 80 mg daily of morphine (or equivalent), are reached, due to occurrence of more withdrawal symptoms.</p>	American Pain Society and the American Academy of Pain Medicine, accessed at: <a href="http://pamw.pl/sites/default/files/PAMW_7-8-2009_Chou_0.pdf">http://pamw.pl/sites/default/files/PAMW_7-8-2009_Chou_0.pdf</a>
2013	Evidence-Based Guidelines on the Use of Opioids in Chronic Non-Cancer Pain: A Consensus Statement by the Pain Association of Singapore Task Force.	Ho, Kok et al.	Review of evidence-based clinical guidelines	A multidisciplinary expert panel was convened by the Pain Association of Singapore to develop practical evidence-based recommendations on the use of opioids in the management of chronic non-cancer pain in the local population.	<p>Patients should be tapered or weaned off chronic opioid therapy when they engage in serious or repeated aberrant drug related behaviors or diversion, experience intolerable adverse effects, or make no progress towards meeting therapeutic goals.</p> <p>When a patient is taking more than 200 mg morphine or its equivalent per day without any significant pain relief, discontinuation of opioid therapy should be considered.</p> <p>Tapering can often be achieved in the outpatient setting in patients without severe medical or psychiatric comorbidities</p> <p>Weekly reduction in dose by 10% is generally well tolerated without symptoms of opioid withdrawal.</p> <p>In more complex cases, detoxification in a rehabilitation setting can be helpful, especially for patients unable to reduce their opioid dose in a less structured setting.</p> <p>If the aberrant behaviors are related to addiction, addiction treatment resources should be made available</p>	Annals of the Academy of Medicine, Singapore
2010	Chronic Opioid Therapy (COT)	Group Health	Clinical guidelines	The guidelines systematically	Taper if the medication induces adverse effects, risks outweigh benefit, comorbidities increase the risk of complication, MED exceeds	Group Health Cooperative (Accessed at:

	Safety Guideline for Patients with Chronic Non-Cancer Pain	Cooperative		developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions.	recommended threshold (these patients should be tapered 10% per week). If the indication for tapering opioid therapy is due to function and pain not being improved, or if tolerance has developed with long-term opioid prescription, or if comorbidities are present which increase the risk of complication then the patient should be tapered at a rate of 10% every 2-4 weeks.  There is a list of behavioral indications for the discontinuation of opioid therapy (these patients should be tapered over 3-7 days, or 15-33% per day).	<a href="http://www.ghc.org/all-sites/guidelines/chronicOpioid.pdf">http://www.ghc.org/all-sites/guidelines/chronicOpioid.pdf</a>
2012	When and how to taper opioids	College of Physicians and Surgeons of Ontario	Clinical guidelines	Unspecified.	Taper slowly. Rate may vary from 10% of the total daily dose EVERY DAY to 10% of total daily dose EVERY 1-2 WEEKS (latter for outpatient tapering) Let patient choose which dose is decreased (AM, PM or HS) Taper even more slowly when 1/3 of total dose is reached	The College of Physicians and Surgeons of Ontario, accessed at: ( <a href="http://www.cpso.on.ca/uploadedFiles/members/resources/Opioid-Tapering-Protocols_Dial-I_2012.pdf">http://www.cpso.on.ca/uploadedFiles/members/resources/Opioid-Tapering-Protocols_Dial-I_2012.pdf</a> )
2000	Pederson, C, Parran, L	Opioid Tapering in Hematopoietic Progenitor Cell Transplant Recipients	Descriptive, exploratory, prospective, quantitative, and qualitative. N= 45 (patients between ages 7-64) Daily	interviews, patient reported pain levels and withdrawal symptoms during opioids tapers. Demographic, medication, and nurse documentation data were obtained from patient hospital records.	Length of taper ranged from 1-17 days. There was no difference by disease or transplant type in length of taper cumulative opioids give pre-taper or during taper, or number of self-reports of withdrawal symptoms.  Daily changes in nurse-administered opioid dosage during tapers ranged from a decrease of 67% to an increase in 14%.	Oncology Nursing Forum
2002	Parran, L, Pederson, C	Effects of an Opioid Taper Algorithm in Hematopoietic Progenitor Cell Transplant Recipients	Quasi-experimental. An intervention was used, but there was no random assignment of study participants to groups. N= 106, Phase 1= 45, Phase 2=61	An opioid taper algorithm, developed by the experimenters was used in phase 2, while patients in phase 1 (really just a separate group of patients) received no intervention (i.e. therapy was not directed by the algorithm)	Use of the algorithm decreased taper time by an average of 0.4 days compared to the non-algorithm group.  There was also a significant decrease in withdrawal symptoms, and no significant differences in patient self-reports of worst pain or satisfaction with pain management.	Oncology Nursing Forum
2012	Manchikanti L, et al.	American Society of Interventional Pain Physicians (ASIPP)	Clinical guidelines	Clinical guidelines were developed based on review of previous guidelines and expert panel discussion	Tapering may be carried out slowly with a decrease by 10% of the original dose per week.  Some patients can be tapered or weaned more rapidly without any major problems over a 6 to 8 week period.	Pain Physician

		Guidelines for Responsible Opioid Prescribing in Chronic Non-Cancer Pain: Part 2 – Guidance				
2004	Franck LS, Naughton I, Winter I	Opioid and benzodiazepine withdrawal symptoms in paediatric intensive care patients	Prospective, non-randomized study	<p>For patients with opioid and benzodiazepine administration for greater than 5 days, a 20% daily taper (from the pre-taper dose) was recommended.</p> <p>For patients who had received treatment for greater than 14 days, a 10% daily taper was recommended. If withdrawal symptoms occurred, recommendations were given regarding slowing or suspending the taper and reinitiating opioid treatment, depending on severity.</p>	<p>Thirteen children showed moderate to severe withdrawal symptoms a median 3 days after commencement of tapering.</p> <p>Symptom intensity was not related to prior opioid or benzodiazepine exposure, extracorporeal membrane oxygenation (ECMO) therapy or length of tapering.</p> <p>Withdrawal symptom onset appears related to increment or speed of the taper.</p>	Pain Physician
2005	Ducharme C, Carnevale FA, Clermont M, Shea S.	A prospective study of adverse reactions to the weaning of opioids and benzodiazepines among critically ill children	A prospective multiple case study design was used.	This study followed an earlier investigation that developed a graphical analysis method for examining behavioral signs of withdrawal in relation to changes in opioid and benzodiazepine administration. This method was utilized in this present study for a prospective sample of all patients admitted to a tertiary/quaternary	The findings of this study indicate that the required rate of weaning (in order to prevent withdrawal reactions) is related to the number of days the child has been on a continuous infusion of opioids and/or benzodiazepines.	Intensive Care and Critical Nursing

				level PICU within a 4-week interval (n = 27).		
2007	Ista E, van Kijk M, Gamel C, Tibboel D, de Hoog M.	Withdrawal symptoms in critically ill children after long-term administration of sedatives and/or analgesics: a first evaluation	Systematic review	The literature was reviewed for relevant contributions on the nature of opioid and benzodiazepine withdrawal symptoms and on availability of valid scoring systems to assess the extent of symptoms.	Symptoms of benzodiazepine and opioid withdrawal can be classified in two groups: central nervous system effects and autonomic dysfunction. However, symptoms of the two types show a large overlap for benzodiazepine and opioid withdrawal.	Critical Care Medicine
2007	Jefferies S. A., McGloin R., Pitfield F., & Roxane R. C.	Use of Methadone for Prevention of Opioid Withdrawal in Critically Ill Children	Retrospective chart analysis.	A retrospective analysis of charts was conducted for pediatric patients who had received morphine by continuous IV infusion for 5 days or longer followed by methadone in the PICU between May 2008 and August 2009.	The median duration of weaning was 10 days (range 0–91 days). The conversion ratio for IV morphine to oral methadone was 1:0.78 for anticipated 5-day weaning and 1:0.98 for anticipated 10-day weaning. During the first 10 days of weaning, 18 patients (42%) experienced withdrawal symptoms. The methadone dose was increased for 11 (26%) of the 43 patients.	The Canadian Journal of Hospital Pharmacy
2010	Hooten, W. M., Mantilla C. B., Sandroni P., Townsend C. O.	Associations between Heat Pain Perception and Opioid Dose among Patients with Pain Undergoing Opioid Tapering	Prospective, non-randomized study.	Three-week outpatient multidisciplinary rehabilitation program that incorporates opioid tapering.	Tapering of greater morphine equivalent dosages was associated (P = 0.001) with lower values of HP 5-0.5.	Pain Medicine
2009	Hooten, W. M., Townsend C. O., Bruce B. K., Warner D. O.	The effects of smoking status on opioid tapering among patients	Retrospective, repeated measures design	Pre- and post-treatment outcomes were assessed in a consecutive series of patients admitted to a 3-wk, outpatient pain treatme	The success of opioid tapering did not depend on smoking status, and all groups experienced significant reductions in pain severity at program completion.	Pain Medicine

		with chronic pain		nt program from September 2003 through February 2007. Outcome measures included the frequency of successful opioid tapering, pain severity subscale of the Multidisciplinary Pain Inventory, and program completion status.		
2006	Berens, R. J., Meyer M. T., Theresa A. M., et al.	A Prospective Evaluation of Opioid Weaning in Opioid-Dependent Pediatric Critical Care Patients	Prospective, randomized trial	<p>Opioid-dependent children where enrolled in a prospective, randomized trial of 5-versus 10-day opioid weaning using oral methadone.</p> <p>The 5-daywean protocol was defined by a 20% reduction of the initial methadone dose each of 5-days, followed by a 5-day course of placebo. The 10-day wean protocol was defined by a 10% reduction of the initial methadone dose each of 10 days with no placebo course.</p>	<p>Children exposed to opioids for an average of 3 weeks showed no difference in the number of agitation events requiring opioid rescue in either wean group.</p> <p>Most of the events requiring rescue occurred on day 5 and 6 of the wean in both treatment groups.</p>	Anesthesia and Analgesia
2010	Anand K. J. S., Willson D. F., Berger J., et al.	Tolerance and Withdrawal from Prolonged Opioid Use in Critically Ill Children	Systematic review	<p>Relevant manuscripts published in the English language were searched in Medline by using search terms "opioid," "opiate," "sedation," "analgesia," "child," "infant-newborn," "tolerance," "dependency," "withdrawal,"</p>	<p>Opioid tolerance occurs earlier in the younger age groups, develops commonly during critical illness, and results more frequently from prolonged intravenous infusions of short-acting opioids.</p> <p>Treatment options include slowly tapering opioid doses, switching to longer-acting opioids, or specifically treating the symptoms of opioid withdrawal.</p> <p>Novel therapies may also include blocking the mechanisms of opioid tolerance, which would enhance the safety and effectiveness of opioid analgesia.</p>	Pediatrics

				<p>“analgesic,” “receptor,” and “individual opioid drugs.” Clinical and preclinical studies were reviewed for data synthesis.</p>		
2010	<p>Ahmed A., Khurana H., Gogia V., Mishra S., Bhatnagar S.</p>	<p>Use of Sustained Release Oral Morphine as a Bridge in Withdrawal of Morphine in Patients on High Doses of Oral Immediate Release Morphine for Cancer Pain</p>	<p>Case report.</p>	<p>In one patient, the morphine dose was reduced over 2 weeks to 30mg every 4 hours and then shifted to sustained release morphine (SR) 60g tablets twice daily dose and then reduced further over 2 weeks to 10 mg SR tablets twice daily dose. This schedule was continued for another 2 weeks and then discontinued. The other patient was switched from immediate release morphine to SR morphine tablets 60mg as a twice daily dose and was reduced over 2 weeks to 10mg SR tablets and discontinued after 1 week.</p>	<p>Individual patients may have differing responses to the tapering regimen chosen. Fear or anxiety may be present in the patient regarding the taper. The last stage of tapering is the most difficult.</p>	<p>American Journal of Hospice &amp; Palliative Medicine</p>
2011	<p>Ahmed A., Khurana H., Gogia V., Mishra S., Bhatnagar S.</p>	<p>Canadian guideline for safe and effective use of opioids for chronic non-cancer pain: Clinical summary for family</p>	<p>Systematic review</p>	<p>Researchers for the guideline conducted a systematic review of the literature, focusing on reviews of the effectiveness and safety of opioids in specific populations.</p>	<p>The opioid should be tapered if the patient’s pain remains severe despite an adequate trial of opioid therapy. In the elderly, sedation, falls, and overdose can be minimized through lower initial doses, slower titration, benzodiazepine tapering, and careful patient education. For pregnant women taking daily opioid therapy, the opioids should be slowly tapered and discontinued. If this is not possible, they should be tapered to the lowest effective dose.</p>	<p>Canadian Family Physician</p>

Year	Author	Title	Study design	Intervention	Findings	Source
2000	Parran, L., Pederson, C	Development of an opioid-taper algorithm for hematopoietic cell transplant recipients	Systematic review	An opioid tapering algorithm was created using non-research-based published guidelines, published research on opioid withdrawal symptoms, clinical experience, and multidisciplinary consultant recommendations.	No research-based opioid-tapering guidelines exist in the literature; existing guidelines vary widely and are not specific to HCT recipients. The algorithm addresses a gap in the literature and also provides flexibility when dealing with patient discomfort.	Oncology Nursing Forum
2012	Siniscalchi et al.	Antiepileptic drugs for central post-stroke pain management	Review	None	Central post-stroke pain is due to neuronal excitability, which is caused by damage to the central nervous system. Anti-epileptic drugs have been suggested as a possible adjunct in the treatment of neuropathic pain. There is conflicting research regarding their efficacy in treating this pain. Further research should be performed in order to determine the efficacy of specific anti-epileptic drugs concerning neuropathic pain, as well as how safe they are in specific populations.	Pharmacological Research
2011	Siniscalchi et al.	Effects of carbamazepine/oxycodone coadministration in the treatment of trigeminal neuralgia	Case Report	Carbamazepine 200 mg every 8 hours and oxycodone 5 mg every 12 hours.	The patient's pain resolved within 7 days with no adverse events. During follow-up at 1 and 3 months, the patient did not report any symptoms of trigeminal neuralgia.	The Annals of Pharmacotherapy
2013	Siniscalchi et al.	Effects of topiramate on dysaesthetic pain in a patient with multiple sclerosis	Case Report	Topiramate 50 mg every 12 hours which was increased to 150 mg every day (50 mg in the morning and 100 mg at night) over 7 days.	An initial improvement of pain was observed. After the dose was increased to 150 mg/day great improvement of both pain and sensory loss was observed within 14 days.	Clinical Drug Investigation

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