



# Opioids and Falls Risk in Older Adults: A Narrative Review

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## Abstract

Pain treatment is important in older adults but may result in adverse events such as falls. Opioids are effective for nociceptive pain but the evidence for neuropathic pain is weak. Nevertheless, both pain and opioids may increase the risk of falls. This narrative literature review aims to summarize the existing knowledge on the opioid-related fall risk in older adults, including the pharmacokinetics and pharmacodynamics, and assist clinicians in prescribing and deprescribing opioids in older persons. We systematically searched relevant literature on opioid-related fall risk in older adults in PubMed and Scopus in December 2020. We reviewed the literature and evaluated fall-related adverse effects of opioids, explaining how to optimally approach deprescribing of opioids in older adults. Opioid use increases fall risk through drowsiness, (orthostatic) hypotension and also through hyponatremia caused by weak opioids. When prescribing, opioids should be started with low dosages if possible, keeping in mind their metabolic genetic variation. Falls are clinically significant adverse effects of all opioids, and the risk may be dose dependent and highest with strong opioids. The risk is most prominent in older adults prone to falls. To reduce the risk of falls, both pain and the need for opioids should be assessed on a regular basis, and deprescribing or changing to a lower dosage or safer alternative should be considered if the clinical condition allows. Deprescribing should be done by reducing the dosage gradually and by assessing and monitoring the pain and withdrawal symptoms at the same time. Weighing the risks and benefits is necessary before prescribing opioids, especially to older persons at high risk of falls. Clinical decision tools assist prescribers in clinical decisions regarding (de-) prescribing.

## 1 Introduction

Falls are the most frequent cause of injuries in older adults [1]. In 2012–2014, almost four million individuals over 65 years old annually required medical care after falling in the European Union. The total number of falls (including falls that do not result in injury requiring medical care) is higher. Falling constitutes an important cause of morbidity in older adults because falls can cause serious injuries, such as hip fractures or traumatic brain injuries, potentially leading to permanent decline of functional and cognitive abilities, need for institutional care or even death [2, 3]. It is important to

prevent falls among older people to preserve their functional capacity and quality of life and also to reduce health care costs for societies.

Falls are often multifactorial and one person may have several risk factors simultaneously. Over 400 risk factors for falls have been identified, including several diseases, cognitive disorder, fall-risk-increasing drugs (FRID), difficulties in mobility and psychological and sociodemographic factors [4, 5]. With regard to FRID, according to systematic reviews and meta-analyses, several central nervous system drugs, such as psychotropics, antiepileptics and opioids, increase the risk of falls [6].

Pain is one of the risk factors for falling and, conversely, injurious falls cause pain [4, 7]. According to the meta-analyses, pain was associated with falls and recurrent falls [4, 8]. More than 50% of US older adults reported pain and the majority of them had multiple pain sites [9]. The most prevalent painful conditions affecting older adults are arthritis related (for example hips, knees), although chronic diseases like diabetic complications, cancer-related pain and post-stroke pain are also seen among older individuals [10].

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### Key Points

We summarize existing knowledge on the risk of opioid-related falls in older adults, including aspects of pharmacokinetics and pharmacodynamics, and assist clinicians in (de-)prescribing opioids.

Opioid use increases the risk of falls in older adults due to sedation, orthostatic hypotension and also hyponatremia caused by weak opioids.

Decisions regarding both opioid prescribing and de-prescribing in fall-prone older persons need to be individualized as adverse drug events may lead to falls, but adequate pain treatment is also warranted. Clinical decision tools can support prescribers in rational (de-)prescribing decision making.

Among community-dwelling older persons aged over 74 years, musculoskeletal pain was reported by 61% and about a quarter had daily pain that hindered their activities [11].

It is essential to assess pain and define its cause, type (nociceptive, neuropathic) and intensity by using a pain rating scale designed for older adults. A comprehensive pain assessment in older persons is challenging due to under-reporting of pain, sensory impairments and cognitive impairment [12]. As a result, pain in older persons is often assessed and treated inadequately [13–15]. Pain should be treated with an effective pharmacological approach if pain is a significant problem and affects physical functioning or quality of life [16]. The importance of nonpharmacological treatment options should not be overlooked in the treatment of pain but instead combining pharmacotherapy with non-pharmacological treatments, such as physiotherapy or cognitive behavioral therapy, can alleviate pain [17]. However, in clinical practice, it is not always possible to completely eliminate the pain, but then the goal of treatment should be a level at which quality of life and daily activities improve. Different classes of drugs are used to treat nociceptive and neuropathic pain. Paracetamol is recommended as a first-line pain medication in older adults for nociceptive pain [16] and long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided in older adults due to their adverse gastrointestinal, renal and cardiovascular effects [14, 18]. If paracetamol is not sufficiently effective and NSAIDs are contraindicated or long-term treatment is indicated, the next step is opioids.

The proportion of the older population using opioids and strong opioids has been increasing for more than a decade. In the Netherlands, the proportion of opioid users more than doubled from the year 2005 (4.2%) to 2017 (11.4%) and the proportion of strong opioid users increased even more

from 1.3 to 7.0% [19]. The increase was highest among persons aged 85 years and over. In addition, 70% of these oldest persons had more than one strong opioid prescription. This is concerning, because in a meta-analysis, opioids have been associated with an increased risk of falls and European guidelines suggested that opioids have the highest risk of falling at the initiation of use [6, 20]. Opioids are also associated with recurrent falls [21]. In this clinical review, we focus on opioid use in older adults in different settings. However, we do not address opioid use in cancer treatment or terminal care, as these are large entities with specific problems.

Our aims were firstly to perform a systematic literature search on opioid use and falls risk in older adults; secondly to provide an overview of the literature on pharmacokinetic and pharmacodynamic mechanisms regarding opioids use and falls; and thirdly to provide information and tools to clinicians for weighing the benefits and harms of (de-)prescribing opioids.

## 2 Search Strategy

A systematic literature search was carried out in December 2020 using PubMed and Scopus. Search terms are described in Supplement Table 1 of the electronic supplementary material (ESM). The search was restricted to English language and original articles but not restricted regarding publication date or status or study design. We excluded studies focusing on palliative/terminal/hospice care. All identified studies were screened based on titles and abstracts and further clustered to meet the aims: pharmacokinetic and pharmacodynamic mechanisms regarding opioids and falls and (de-)prescribing tools needed in narrative review.

## 3 Medication Review and Reconciliation

Medication review should be done for all patients presenting with acute falls, recurrent falls during the past year, or problems with walking or balance as recommended by the European Geriatric Medicine Society (EuGMS) Falls and Fracture Special Interest Group and American Geriatrics Society/British Geriatrics Society guidelines [22, 23]. Medication review for risk of falling is recommended at least annually and every 6 months if the older individual is frail or vulnerable [22]. This medication review in older adults should be part of a comprehensive geriatric assessment or a holistic assessment.

In the medication review, clinicians need to thoroughly review all current medication and check that all medications, including opioids, have a current appropriate indication for their use. Before prescribing opioids, there should

be an evidence-based clinical indication and the duration of opioid treatment should be well defined [24].

In the medication review, deprescribing of opioids should be initiated if the drug no longer has a current indication and consideration should be given to whether it is causing serious adverse events such as falls or injurious falls [20, 25]. In addition, the doses, possible drug–drug interactions (DDIs) and renal function should be assessed.

### 3.1 Match Opioid Use to an Appropriate Indication

Opioids are strong analgesics and their indications include moderate pain and severe acute pain, postoperative pain and pain in palliative care [26]. The efficacy of opioid use in chronic non-cancer pain is under discussion. In older people, opioids are recommended for use with moderate to severe pain, pain-related functional impairment or reduced quality of life due to pain [14, 16]. Short-term efficacy has been demonstrated in persistent musculoskeletal pain, such as osteoarthritis and low back pain, and also in post-herpetic neuralgia and diabetic peripheral neuropathy, but long-term evidence of efficacy and safety are lacking. There are several tools available to help appropriate prescribing of opioids. According to Screening Tool to Alert to Right Treatment (START) criteria, strong opioids should be used for severe pain or when treatment with paracetamol, NSAIDs or mild and moderate opioids are ineffective [24]. In addition, laxatives or peripherally acting  $\mu$ -opioid receptor antagonists such as oral naloxone should be used regularly with opioids to avoid constipation [27]. Sometimes vomiting may also require a therapeutic approach. Weak opioids (tramadol, codeine and dihydrocodeine) are recommended for use in moderate pain in the World Health Organization (WHO) pain ladder [14], but can have an unfavorable profile in the older population with higher risk of adverse drug events in comparison with its efficacy.

The role of opioids in neuropathic pain is controversial because of inconsistent evidence of benefits [28]. Nevertheless, opioids are commonly used in neuropathic pain conditions and their use has been somewhat accepted by guidelines [14, 28]. In older adults, first-line treatment for neuropathic pain includes serotonin norepinephrine reuptake inhibitors (SNRIs), gabapentinoids and transdermal lidocaine or capsaicin [29]. Tramadol is considered a suitable second-line treatment due to its multiple mechanisms of action but is primarily recommended for short-term use, and it should not be combined with SNRIs due to serotonergic effects. Based on a meta-analysis, there was only a weak recommendation for the use of strong opioids in neuropathic pain [30]. The guidelines recommended that the use of strong opioids should be carefully considered due to significant adverse effects and lack of data on long-term efficacy [16].

Long-term opioid therapy for chronic musculoskeletal pain is common in older adults; the risk for long-term opioid prescribing was nearly five times higher in older persons aged 80 years or over compared with young adults [31]. After hip fracture surgery in opioid-naïve older adults, the risk of become a long-term user was especially increased in persons with chronic diseases like dementia [32]. On the other hand, long-term oral opioid therapy was discontinued due to adverse events (23%) or insufficient pain relief (10%) [26]. In the case of long-term opioid therapy for chronic musculoskeletal pain, deprescribing should be initiated in close collaboration with the patient to avoid harms like falls.

Opioids have several adverse effects and, according to Beers Criteria for Potentially Inappropriate Medication Use in Older Adults, opioids should be avoided for the treatment of pain except in acute pain [33]. In addition, according to the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) Criteria, opioids should be avoided as first-line therapy for mild to moderate pain for >2 weeks [24].

### 3.2 Opioid Dosage

Dosing of opioids should be individualized [33]. Adverse effects and pain intensity should be monitored regularly during opioid therapy. Doses in older adults should generally be lower than those used by younger adults. Initially, opioids should be started at a low dose, then uptitrated gradually on an individual basis guided by the intensity of pain. Slow dose titration can also help in reducing typical initial adverse effects such as nausea and vomiting [28]. In addition, a low dose of a more potent opioid such as morphine may be better tolerated than weak opioids at a higher dose. In long-term opioid use, the dose is likely to increase due to opioid tolerance [34]. In addition to dose titration, there might be a need for opioid rotation in order to identify an opioid with an appropriate therapeutic effect and tolerability for the patient [35]. Sustained-release preparations, including transdermal formulations, appear to increase patient compliance [28]. In challenging cases, when adequate pain relief is not provided, a specialized pain specialist/unit should be consulted. Then other therapies like interventional therapies can also be considered [14].

Age-related changes in pharmacokinetics and pharmacodynamics may increase the risk of adverse effects such as falls [33, 36]. The half-life of the active drug and metabolites is prolonged in older people with renal impairment. Many active opioid metabolites are completely or partially eliminated by the kidneys, so the doses must be reduced, and a longer time interval used between doses to prevent the accumulation of metabolites. For example, codeine and oxycodone should be used with caution even in mild renal insufficiency [37]. Too-high doses in relation to renal

function may increase the risk of falling. Dose reduction or switching to a less fall-risk-increasing drug (a less potent analgesic, if the clinical condition allows) would maintain effectiveness while minimizing harms. When switching one opioid to another, a morphine equivalent dose (MED) calculator may be used to assist in dose calculation [38, 39]. The new opioid should be started with a 25–50% lower dose to avoid problems related to incomplete cross-tolerance and individual differences in opioid pharmacokinetics [33].

### 3.3 Pharmacodynamics and Pharmacogenetics

Most opioids are metabolized via combinations of different cytochrome P450 (CYP) enzymes [40]. Codeine, hydrocodone and tramadol are metabolized completely or partially via CYP2D6 enzyme [40, 41]. These prodrugs are metabolized via the CYP2D6 enzyme to active metabolites, which means that their analgesic effect is poor without metabolism [33]. Buprenorphine, fentanyl and oxycodone are metabolized completely or partially via CYP3A4 and they do not need to be activated in order to be effective. Morphine, hydromorphone and oxymorphone are primarily metabolized by glucuronidation instead of CYP metabolism [28].

Polymorphism of CYP2D6 enzymes has been studied in relation to the clinical effects and safety of opioids [41]. Over 130 alleles of CYP2D6 enzymes have been identified, and the most common alleles have been classified into normal function, impaired function and no function. Activity level of CYP2D6 phenotypes vary by individual as persons can be ultrarapid, normal, intermediate and poor metabolizers of CYP2D6 enzymes. These levels of activity affect the rate of metabolism and thereby changes in concentration, efficacy and the occurrence of adverse effects such as falls.

The label-recommended starting dose for codeine and tramadol is recommended for normal and intermediate CYP2D6 metabolizer types [41]. The use of these drugs should be avoided in poor and ultrarapid metabolizers, as ultrarapid metabolizers are at risk for toxicity at the doses recommended on the label and, conversely, those doses are not sufficiently effective for poor metabolizers. Therefore, opioid prescribing should always be carefully monitored and initiated at very low doses if the patient's genotype is unknown, or the person is a new opioid user.

### 3.4 Drug–Drug Interactions

Possible drug–drug interactions (DDIs) and risk of adverse effects should be checked, for instance by using drug interaction databases and/or evidence-based decision aids [18, 36]. The risk of adverse effects may develop with inappropriately high dosing or DDIs. The adverse effects

caused by DDIs are different from the adverse effects caused by a single drug.

DDIs associated with opioids are mainly based on pharmacokinetics or sedation. CYP2D6 and CYP3A4 enzymes are the most common metabolic pathways for opioids and interactions with other drugs via the metabolic pathway may lead to changes in opioid concentrations [42].

Being prodrugs, codeine, hydrocodone and tramadol are metabolized via CYP2D6 to active metabolites [33, 42]. Drugs that inhibit CYP2D6, such as fluoxetine and duloxetine, reduce the analgesic effect of these opioids due to inhibition of active metabolite production, whereas drugs that induce CYP2D6, such as rifampicin and dexamethasone, increase analgesic effects by inducing faster metabolism to active metabolites [42]. DDIs with inducer drugs can lead to adverse effects such as dizziness and sedation due to higher concentrations of active metabolites.

Buprenorphine, fentanyl and oxycodone are metabolized via CYP3A4, but they do not have clinically significant active metabolites [33]. CYP3A4-inhibiting drugs, such as simvastatin and sertraline, are increasing and CYP3A4-inducer drugs, such as dexamethasone and carbamazepine, are decreasing the concentration and effect of those opioids [42]. Adverse effects of opioids, including the risk of falls, increase with changes in concentration.

The combination of opioids with benzodiazepines should be avoided due to an increased risk of high sedative load and respiratory depression [18]. Concomitant alcohol use further increases the risk. However, concomitant use of opioids and benzodiazepines appears to exist, and extensive sedation further increased the risk of falls [43]. Although older adults might have both severe nociceptive and neuropathic pain, concomitant use of opioids and gabapentinoids (gabapentin and pregabalin) should be avoided due to the increased sedation [18]. Gabapentinoids can be used with opioids if there is ongoing switch to opioid use or if there is an aim to reduce the dose of opioids by using gabapentinoids.

Increased serotonergic effects or even serotonin syndrome can lead to falls through agitation, hypertension and delirium [44]. DDI with tramadol and psychotropics such as monoamine oxidase inhibitors, tricyclic antidepressants, selective serotonin reuptake inhibitors and SNRIs may increase the risk of serotonin syndrome and seizures. In addition, many of these psychotropics inhibit the enzyme CYP2D6, which prevents the conversion of tramadol to the active metabolite and increases its concentration. Tramadol inhibits serotonin and norepinephrine reuptake, but its metabolite *o*-desmethyltramadol is the major  $\mu$ -opioid receptor agonist causing analgesic effects.

## 4 Fall-Related Adverse Effects of Opioids

Fall-risk-increasing adverse effects of opioids are caused by sedation, dizziness and cognitive impairment [6]. The use of opioids has been associated with increased risk of falling in the meta-analysis (pooled odds ratio [OR] 1.60, 95% confidence interval [CI] 1.35–1.91). According to the Screening Tool of Older Persons Prescriptions in older adults with high fall risk (STOPPFall) recommendation, strong opioids increase the risk of falls more than weak opioids [20]. However, debate is ongoing between strong and weak opioids with regard to efficacy and risk of adverse drug effects. The prevalence of fall-related adverse effects of opioids based on summaries of product characteristics are presented in Table 1.

### 4.1 Sedation and Anticholinergic Effects

One of the most common adverse effects associated with opioids is sedation [28, 45, 46]. Sedation can lead to falls through daytime drowsiness, reduced alertness and impaired psychomotor functioning. Sedation as an adverse effect of

opioids is more frequent among older adults [47]. Risk is additive and dose dependent. Risk of sedation is high during the first days after opioid initiation. However, some tolerance to sedation develops during use [6, 34].

Fall-related anticholinergic effects of drugs include cognitive impairment, confusion and blurred vision [48]. Opioids were classified as low-potency anticholinergics in the systematic review. Opioids have only a mild anticholinergic effect and, together with other effects of opioids, may lead to dizziness, drowsiness and falling.

### 4.2 Orthostatic Hypotension and Dizziness

Orthostatic hypotension is highly prevalent in older adults and includes symptoms of light-headedness, general weakness and even loss of consciousness [49, 50]. Orthostatic hypotension can be defined as an impaired blood pressure response to the upright position when there is at least 20 mmHg reduction of systolic blood pressure or 10 mmHg reduction of diastolic blood pressure within 3 minutes of standing [49, 51].

Buprenorphine, fentanyl, hydromorphone, morphine and oxycodone use has been associated with orthostatic

**Table 1** Prevalence of fall-related side effects of opioids based on summaries of product characteristics (Finnish Medicine Agency)

Opioids	(Orthostatic) hypotension	Drowsiness or somnolence	Dizziness or vertigo	Sedation	Confusion	Delirium or confusional state	Eye disorders	Muscle problems (e.g. rigidity)
Codeine (tablet)	Unknown	Unknown	Unknown	No data	No data	No data	Unknown	No data
Dihydrocodeine (tablet)	No data	No data	No data	No data	No data	No data	No data	No data
Tramadol (capsule)	++	+++	++++	No data	+	+	+	+
Buprenorphine (sublingual tablet)	+++	+++	+++	No data	No data	No data	+++	+++
Buprenorphine (transdermal patch)	++	++++	++++	++	+++	No data	++	+++
Fentanyl (sublingual tablet)	++	+++	+++	No data	No data	++	++	No data
Fentanyl (transdermal patch)	++	++++	+++	+++	No data	+++	++	+++
Hydromorphone (capsule)	++	++++	++++	+	No data	+++	++	No data
Methadone (tablet)	+++	+++	+++	+++	++++	Unknown	Unknown	No data
Morphine (tablet)	++	+++	+++	No data	+++	No data	++	No data
Oxycodone (capsule)	+	++++	++++	+++	No data	+++	++	++
Pethidine (tablet)	Unknown	Unknown	Unknown	Unknown	No data	No data	Unknown	Unknown

++++: > 1/10 (very common:  $\geq 1/10$ )

+++ : 1/10–1/100 (common:  $\geq 1/100$  to  $< 1/10$ )

++ : 1/100–1/1000 (uncommon:  $\geq 1/1000$  to  $< 1/100$ )

+ :  $< 1/1000$  (Rare:  $\geq 1/10,000$  to  $< 1/1000$ ) and (very rare:  $< 1/10,000$ )

Unknown: cannot be estimated from the available data

hypotension [52]. Risk of hypotension increased with concomitant use of other drugs such as benzodiazepines [51]. Opioids can induce histamine release, resulting in a decrease in blood pressure [52].

### 4.3 Hyponatremia

In older adults, hyponatremia is a common problem in electrolyte balance found in clinical practice [53]. Mild hyponatremia is defined as a serum sodium concentration < 135 mmol/L and severe hyponatremia < 125 mmol/L [54]. Fall-related symptoms of hyponatremia are drowsiness, lethargy, confusion and seizures [54, 55]. Drug-induced hyponatremia is often caused by SIADH (syndrome of inappropriate anti-diuretic hormone secretion).

The only opioid causing hyponatremia is tramadol as a result of its serotonergic properties [55]. According to the Beers criteria, tramadol causes hyponatremia and should be used with caution in older adults [18]. In addition, the Beers criteria recommends monitoring sodium levels when starting tramadol or changing the dose in older adults.

The use of tramadol was associated with a twofold increased risk of hospitalization for hyponatremia when compared with codeine during the first 30 days of use (adjusted HR 2.05, 95% CI 1.08–3.86) [55]. In another study, weak opioids were associated with hospitalization due to hyponatremia compared with controls (tramadol OR 1.17, 95% CI 1.08–1.26 and codeine OR 1.14, 95% CI 1.03–1.26) [54]. In addition, the use of tramadol posed the highest risk of hospitalization due to hyponatremia at the beginning of tramadol use (adjusted OR 2.34, 95% CI 2.01–2.72).

### 4.4 Injurious Falls and Fracture Risk

Opioid use among older adults was associated with the occurrence of falls, fall injuries and fractures in the meta-analysis [3]. Injurious falls can cause different kinds of fractures, and persons with Alzheimer's disease are particularly vulnerable to these fractures [56]. The risk of hip fractures in community-dwelling persons with Alzheimer's disease was almost double compared with nonusers of opioids (HR 1.96, 95% CI 1.27–3.02) and strong opioids increased hip fracture risk more (HR 2.89, 95% CI 1.32–6.32) than weak opioids (HR 1.75, 95% CI 0.91–3.35).

In a Colombian study, opioid use in the previous month was associated with an increased risk of fall with hip fracture (OR 4.49, 95% CI 2.72–7.42) [57]. In a study of old (mean age 81 years) incident users of opioids with arthritis in the United States, the incidence rate of fractures per 1000 person years (PYs) was 25 among NSAID initiators and 120 for opioid initiators and the incidence rate increased with the increasing dose; the rates were 53/1000 PYs for low opioid dose, 115/1000 PYs for medium dose and 126/1000 PYs for high dose [58].

## 5 Deprescribing Opioids to Reduce Fall Risk

### 5.1 Decision Aids in Deprescribing Opioids to Reduce Fall Risk

There are several tools available to assist clinicians in deprescribing medications including FRIDs. Some of those tools are STOPPFall, MedStopper and Deprescribing.org [20, 59, 60]. Scott et al. [61] has described the process of deprescribing. The STOPPFall deprescribing tool was developed by the European Geriatric Medicine Society (EuGMS) Task and Finish Group on FRIDs in collaboration with the EuGMS Special Interest Group on Pharmacology through a European expert Delphi consensus effort [20]. The expert group has planned a decision tree for opioid withdrawal, focusing on fall prevention, and it includes algorithms for practical deprescribing (<https://kik.amc.nl/falls/decision-tree/>).

Regardless of the drug in question, deprescribing should always be considered if there are no indications for prescribing the drug or if there are safer alternatives available [20]. Opioid withdrawal should be considered if prescribed for chronic non-cancer pain or if adverse symptoms such as slow reaction times, impaired balance or sedative symptoms exist. If adverse effects occur and dose reduction is not an option, withdrawal should be considered. If deprescribing is impossible, balance and other symptoms such as sedation should be monitored.

### 5.2 Taper and Timing of Deprescribing

Deprescribing opioids should be planned. According to the STOPPFall tool, opioid deprescribing should be done in a stepwise manner [20]. In general, the dose should be reduced by 5–25% of the daily dose every 1–4 weeks and even more slowly if adverse effects occur during deprescribing. Deprescribing should be done very slowly if the dose is high, or the opioid has been used for a long time. According to MedStopper (medstopper.com) [59], if an opioid is used daily for more than 4 weeks, the dose should be reduced by 25% every 3–4 days. If withdrawal symptoms occur, it is recommended to reduce the dose back to 75% of the previous tolerated dose.

### 5.3 Monitoring During and After Deprescribing

During deprescribing the physician should contact the patient and monitor their clinical condition [36]. Patients should be informed about possible withdrawal symptoms and advised to contact their physician if withdrawal symptoms occur. After deprescribing, adverse effects and the recurrence of pain should be closely monitored [20]. Symptoms that should be monitored for after deprescribing

include musculoskeletal symptoms, restlessness, gastrointestinal symptoms, anxiety, insomnia, diaphoresis, anger and chills.

## 6 Conclusions

Pain is common in older adults and it should be properly assessed and treated by considering both pharmacological and nonpharmacological treatments. Opioid use is common in the treatment of pain in older adults and they are at increased risk of falling. Opioids increase the risk of falls through sedation, orthostatic hypotension and dizziness. Tramadol also increases the risk of falling through hyponatremia, which can cause symptoms such as dizziness, drowsiness and confusion. Drug–drug interactions may increase the risk of falls with opioids due to increased sedation and changes in pharmacokinetics (CYP2D6 and CYP3A4 enzymes).

When prescribing opioids, start slow, go slow and monitor efficacy and adverse effects carefully. It is important to carefully weigh risks and benefits before prescribing opioids to older persons at high risk of falling and deprescribe opioids without a current indication. In addition, deprescribing should be considered if an opioid is prescribed to treat chronic pain or if it causes adverse effects such as sedation or impaired balance. Deprescribing should be performed in a stepwise manner and withdrawal symptoms should be closely monitored. A newly developed expert-based decision aid (STOPPFall tool) can assist in clinical decision making in deprescribing.

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