Treatment Guidelines for the Pharmacological Management of Pain in Older Persons

Perry G. Fine, MD

Pain Research Center, School of Medicine, University of Utah, Salt Lake City, Utah, USA

Reprint requests to: Perry G. Fine, MD, Pain Research Center, School of Medicine, University of Utah, Salt Lake City, UT 84108, USA. Tel: 801-585-7690; Fax: 801-585-7694; E-mail: perry.fine@hsc.utah.edu.

Abstract

Background. Chronic or persistent pain is a common problem in older adults and is often associated with significant physical disability and psychosocial problems. The potential benefits, risks, and costs of pharmacotherapy as a mainstay in the treatment of moderate to severe pain in this population must be well-understood and weighed accordingly. Recent treatment guidelines have been introduced that can guide decision making to optimize pain-related treatment outcomes in older individuals

Objectives and Results. This review article describes and summarizes key evidence-based recommendations that were derived by a committee convened by the American Geriatrics Society in order to provide guidance to optimize pharmacotherapy in the management of persistent pain in older individuals.

Conclusions. It is postulated that ongoing education of clinicians who treat older patients with persistent moderate to severe pain will lead to improved outcomes in this vulnerable population.

Key Words. Guidelines; Pain; Pharmacotherapy; Older Patients

Introduction

Chronic or persistent pain is a common problem in older adults, and is often associated with significant physical disability and psychosocial problems. Many persons over the age of 65 are contending with some degree of frailty and chronic illness, while others may have multiple comorbidities that cause pain [1] (Table 1). A particularly challenging comorbidity in older patients is cognitive impairment leading to significant barriers in diagnosis and treatment of pain [2]. In this rapidly growing population, practitioners must become sensitive to and skilled at recognizing behavioral manifestations of pain, employing empirically based analgesic strategies to treat putative pain, and evaluating outcomes of treatment based upon behavioral change rather than verbal self-report (Table 2).

These combined issues—demographic shift to an older population [3]; high prevalence of pain and its impact on older adults; cognitive, expressive, and care-giving challenges—make pain an extremely important public health issue. As such, the potential benefits, risks, and costs of pharmacotherapy as a mainstay in the treatment of moderate to severe pain in this population must be well-understood and weighed accordingly. Recent treatment guidelines have been introduced that can guide decision making to optimize pain-related treatment outcomes in older individuals [1].

Combining pharmacologic and nonpharmacologic strategies has been found to enhance the relief of pain for many patients [1,4]. Nondrug approaches include such modalities as exercise, cognitive-behavioral therapies, physical therapy, and acupuncture. One analysis of older adults found that acetaminophen (61%), regular exercise (58%), prayer (53%), and heat and cold (48%) were the most frequently used pain management strategies [5]. Although the number of randomized controlled trials of nonpharmacologic interventions in older adults is limited, there is sufficient evidence to support the use of selected nonpharmacological approaches [6]. With the premise that optimal care involves such an integrated approach, this review will focus on pharmacotherapy.

Barriers to Appropriate Utilization of Analgesics

Substantial barriers to the proper management of chronic pain in older adults stem both from the patient and provider perspectives. Patients may fail to report pain because they think that it is a normal part of aging, or their perception of pain may be different from that of younger individuals [7]. They may also withhold reports of pain to avoid additional testing or medication. In particular, they

Table 1 Common causes of pain in older adults [1,24,27]

Nociceptive pain
  Low back pain from facet joint arthritis and spondylosis
  Osteoarthritis
  Osteoporosis and bone fractures
  Rheumatoid arthritis
  Coronary artery disease
  Gout
  Degenerative disk disease
  Chronic tendonitis
Neuropathic pain
  Herpes zoster
  Postherpetic neuralgia
  Trigeminal neuralgia
  Peripheral neuropathies (caused by diabetes, HIV infection, chemotherapy, etc)
  Central poststroke pain
  Radicular pain
  Trauma
Mixed
  Myofascial pain
  Fibromyalgia
  Chronic low back pain episodic pain

may fear receiving opioids because of heightened concerns about addiction, tolerance, and adverse effects [8,9].

One survey of cancer patients found that some respondents believed that pain was inevitable, thus indicating that they did not expect medication would be effective [9].

In addition, pain was associated with a worsening of their disease.

A label of dementia may also bias the interpretation of pain cues of demented patients, and complaints from cognitively impaired patients may be taken for granted. Nygaard and Jarland [10] found that mentally intact nursing home residents were more likely to receive unscheduled pain medication (33%), compared with cognitively impaired residents (27%), and those with a diagnosis of dementia (12%).

In a larger and more recent analysis, Reynolds et al. [11] reported similar results. Data collected from six nursing homes, with a total of 551 residents, found that reports of pain decreased as cognitive abilities declined. While 80% of residents who were cognitively intact received pain medications, only 56% of those with severe impairments did ($P < 0.001$). Even though the diagnoses likely to cause pain were similar among all residents, those with severe cognitive impairments had fewer orders for scheduled pain medications.

Among older adults, physical accessibility to treatment, the cost of drug therapy, the presence of comorbidities, and the use of concomitant medication may represent barriers to effective pain management [7]. Sensory impairments, such as those affecting vision and hearing, memory difficulties, and lack of social backup can all interfere with the diagnosis and treatment of pain. Vision problems, for example, can affect an individual's ability to read the pharmacy labels for dose and frequency, and a patient living alone may be unable to obtain assistance with drug administration. These factors can also make assessment difficult; a uniform approach to assessment through use of validated tools is recommended [1] (Table 3).

For prescribers, fear of regulatory actions regarding opioid prescribing, and reports of diversion and abuse have also affected the use of these agents [8]. A survey of California physicians reported that 40% of respondents limited their use of opioids for noncancer chronic pain because they feared legal investigations [12]. Concerns about regulatory scrutiny can result in clinicians prescribing lower and potentially ineffective doses of opioids, or selecting less effective analgesics [9].

Table 2 Common pain behaviors in cognitively impaired older adults [24,27,28]

Behavior	Example
Facial expressions	Slight frown, sad, frightened face
	Grimacing, wrinkled forehead, closed or tightened eyes
	Distorted expression
Verbalizations, vocalizations	Sighing, moaning, groaning
	Grunting, chanting, calling out
	Noisy breathing
	Asking for help
	Verbal abusiveness
Body movements	Rigid, tense body posture, guarding
	Fidgeting
	Increased pacing, rocking
	Restricted movement
	Gait or mobility changes
Changes in interpersonal interactions	Aggressive, combative, resists care
	Decreased social interactions
	Socially inappropriate, disruptive
	Withdrawn
Changes in activity patterns or routines	Refusing food, appetite change
	Increase in rest periods
	Sleep, rest pattern changes
	Sudden cessation of common routines
	Increased wandering
Mental status changes	Crying or tears
	Increased confusion
	Irritability or distress

Table 3 Pain assessment tools for cognitively intact adults [5,24,29,30]

Name of Measure	Description	Validity/Usage
Numeric rating scales	Available in various scale ranges (0–10, 0–20, etc) with 0 being no pain and the highest number the most severe	Validated in a wide variety of settings, sensitive to changes in pain, and preferred by many older adults
Verbal descriptor scales or pain thermometer	Also available in various scale types and scenarios	Shown to be the most preferred and easiest to understand tools
Facial pain scale	Consists of six or seven faces, beginning with a neutral face (no pain) to one that is wincing/contorted	An alternative that is useful for some adults, most preferred by Black and Asian adults
Brief pain inventory	Assesses pain history, location, intensity, and interference with activities	Simple and easy to use, has been translated and validated in many languages
Geriatric pain measure	Multidimensional questionnaire that includes self-reported demographic and clinical information. Was developed specifically for older adults	Validity and reliability established in European and US populations of older adults

The respective same tool should be used each time an assessment takes place, and also when the patient's condition is reevaluated after treatment is initiated. This is important as the various pain tools are not interchangeable with comparable findings.

Pharmacology and Aging

Differences in pharmacokinetics and pharmacodynamics between older and younger adults affect pain management. Increasing age is associated with physiological changes, such as increased body fat, reduced muscle mass, and a reduction in the body's fluid balance [7,13]. This combination of factors increases the volume of distribution of lipophilic drugs, which in turn delays the onset of action and elimination rate while leaving plasma concentrations unaffected. At the same time, the volume of distribution of hydrophilic drugs declines, which may elevate plasma levels of these agents.

With increasing age comes a reduction in renal and hepatic function, which means progressively diminishing efficacy in drug clearance [7,13]. With reduced hepatic function, the bioavailability of drugs with high first-pass elimination, such as lidocaine and opioid analgesics, will be increased. The presence of chronic hepatic disease will generally require reductions in drug dosages or longer intervals between doses to prevent increased plasma concentrations and a higher risk of side effects.

Reduced renal function, particularly a decrease in the glomerular filtration rate, can increase the half-life of agents that are primarily excreted through the kidneys. Dosing levels may need to be adjusted to prevent drug toxicity, especially drugs with active metabolites, such as morphine [7,13] (see Table 4).

Pharmacologic Therapies

Choosing an analgesic treatment will largely depend on the cause and intensity of pain and other individual patient factors, such as the presence of comorbidities, drug–drug interactions, drug–disease interactions, adherence to therapy, and cost. Even though older patients are generally at a heightened risk of adverse events, pharmacologic therapy can be safely initiated, and be effective, when all risk factors are taken into consideration [1]. Clinicians must assume, however, that there may be age-associated differences in the effectiveness and toxicity of the therapy, and that pharmacokinetic and pharmacodynamic drug properties will be altered in the older population.

Selecting Appropriate Medication and Dosing

Among older adults, the clinical manifestations of persistent pain are often complex and multifactorial, and comorbidities and other health issues make both evaluation and treatment more difficult [1]. In addition, older adults have a heightened potential for drug-related adverse events and a higher risk for complications.

The optimal treatment regimen is one that has a good probability of reducing pain and associated disability, and improving function and quality of life. However, guidelines from the American Geriatrics Society (AGS) note that it is unrealistic for clinicians to imply, or for patients to expect, that pain will be completely eliminated in all cases [1]. Instead, the patient and practitioner need to establish mutual and realistic goals to manage pain, and reach a level of comfort that can improve quality of life.

Older adults use an average of two to five prescription medications on a regular basis [13]. It is estimated that polypharmacy, defined as the use or five or more medications, exists in 20–40% of the older population. Therefore, drug–disease and drug–drug interactions often have to be considered when selecting an analgesic therapy.

In addition, age-related alterations in drug absorption, distribution, metabolism, and excretion can result in greater

Table 4 Physiology and effect on drug therapy [1,7,13,14]

Physiological Change	Age-Related Physiologic Change	Effect on Pharmacology
Volume of distribution	Body fat increases by 20–40% and body water decreases by 10–15% in old age	Leads to an increased concentration of water-soluble drugs and a prolonged elimination half-life for lipid-soluble drugs
Hepatic function	Arterial hepatic blood flow may decline with aging, but splenic and venous blood flow does not change with normal aging. The effect of a decline in arterial blood flow has not been well characterized. Decreased cardiac index can result in stiffening vasculature, increasing systolic blood pressure, and reduced myocardial reserve and reduce both hepatic and renal function.	Decreased hepatic function only applies to those drugs that are largely metabolized by oxidation mechanisms. Oxidative enzyme function may change with aging and some liver diseases in some individuals. Most opioid medications are metabolized by conjugation, which is usually not affected by aging or many liver disease processes. May cause a 30–40% reduction in elimination of drugs metabolized by the liver. Bioavailability of drugs with high first-pass elimination will be increased; decreased activity of certain drug metabolizing enzymes
Renal function	Glomerular filtration rate and renal blood flow decreases with advancing age in many patients	Can increase the half-life of drugs eliminated via the kidneys; accumulation of drug or active drug metabolites increases the risk of toxicity and the severity of adverse events
Gastrointestinal absorption or function	Gastrointestinal transit time may slow down	Can lengthen effects of continuous release enteral agents; bowel dysmotility related to opioids might be enhanced

variability in duration of action and plasma concentration for many analgesics; therefore, lower initial dosing and slower titration are recommended to optimize safety [1,14].

Most analgesics do not have recommendations for age-adjusted dosing, and because older adults comprise a very heterogeneous group, it is difficult to predict common side effects or derive an optimum dose [1]. The dosing adage of "start low and go slow" is largely based on pharmacokinetic considerations and the desire to avoid adverse reactions, and not data from clinical trials [13,15–17]. But in the absence of dosage guidelines that can be generalized to a wide population, the initiation of therapy at a low dosage followed by careful upward titration, with frequent monitoring and follow-up, is advisable for older adults.

The least-invasive method of drug administration should also be used. For most patients, the oral route is the most convenient and provides relatively steady blood concentrations of the drug [1]. Other routes, such as intravenous, subcutaneous, and intramuscular, provide a more rapid onset but shorter duration than oral, and are also more invasive, require more technical skill, and are less convenient for the patient. Individuals with swallowing difficulties may benefit from transdermal, rectal, and oral transmucosal routes of administration.

Timing of medication administration is another important consideration. For example, rapid-onset, short-acting analgesics are required for severe episodic pain, while for continuous pain, medications should be provided around the clock [1]. Medication can also be prescribed on an "as needed" basis, but for cognitively impaired patients, who may be unable to request pain relief, scheduled administration is recommended.

The integration of one or more pharmacologic agents that have a synergistic effect may be more effective than monotherapy in managing a painful condition [1]. While monotherapy eliminates potential competing mechanisms of metabolism and drug–drug interactions, a single therapeutic agent may require dose escalation for adequate pain control. This increases the risk of adverse events, drug discontinuance, and switching agents. A multidrug approach may be more effective and efficient when two or more drugs with complementary mechanisms of action work synergistically to give greater relief with less toxicity. This strategy of "rational polypharmacy" may be an important intervention for some patients.

Available Agents: Benefits and Risks in Older Patients

Pharmacotherapy for managing persistent pain can be divided into three categories: nonopioid, opioid, and adjuvant therapies [1,15–17].

Nonopioid

Acetaminophen

Acetaminophen is an effective analgesic, particularly for musculoskeletal pain, including osteoarthritis and low

back pain. AGS guidelines recommend acetaminophen as initial and ongoing pharmacotherapy in the treatment of persistent pain [1]. Compared with traditional nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen is associated with less gastrointestinal (GI) and renal toxicity, fewer drug interactions, and importantly, no age-related differences in drug clearance [14].

If pain relief is unsatisfactory, clinicians should consider raising the dose before prescribing a more potent agent [1]. However, very high doses can cause toxicity and patients and/or caregivers need to be educated about the maximum safe dose (currently, 4 g/24 hours) of acetaminophen from all sources. An advisory board of the United States Food and Drug Administration has urged that this maximum daily dose be lowered because of concerns that the drug can cause liver damage, even death, if used improperly [18]. Many patients may take more than the recommended dose because they are unaware of the potential risks of what they perceive as a "safe" drug. They may also be unaware that acetaminophen is found as an ingredient in numerous over-the-counter agents, including cold remedies, which may lead them to exceed the recommended maximum dose unintentionally.

Acetaminophen is less effective than NSAIDs in relieving inflammatory conditions, such as rheumatoid arthritis, and is contraindicated in patients with liver failure. It should be used cautiously, if at all, in patients with hepatic insufficiency and chronic alcohol abuse or dependence. For such patients, the maximum dose should be reduced from 50% to 75% [1].

NSAIDs

Nonselective NSAIDs are widely used to treat common musculoskeletal and inflammatory pain conditions, and in general, over-the-counter agents have a good safety profile. Particular caution must be exercised if used in patients with low creatinine clearance, gastropathy, cardiovascular disease, or intravascularly depleted states such as congestive heart failure [1]. While adverse drug reactions are a significant cause of morbidity and mortality among older adults, one study found that of older adults hospitalized for adverse drug reactions, nearly one-quarter (23.7%) were attributed to NSAID use [19].

Compared with younger patients, those older than age 60 have a threefold risk of GI complications [14]. The incidence of GI toxicity induced by NSAIDs also appears to be more time- and dose-dependent, rather than associated with the specific drug utilized [20]. A meta-analysis found that the relative risks of GI adverse reactions in persons using NSAIDs vs untreated controls, varied from 1.2 to 5.6 [20].

Several studies have found that combining NSAIDs with other drugs has led to an increase in serious adverse reactions. The risk of hemorrhagic peptic ulcer disease increases almost 13-fold when NSAIDs are used with the common anticoagulant warfarin [14]. Heerdink et al. [21]

also found that the concomitant use of diuretics and NSAIDs was associated with a twofold increased risk of hospitalization for congestive heart failure in persons aged 55 years and older. This was particularly pronounced for patients with existing serious congestive heart failure. In addition, the risk for GI bleeding is increased when NSAIDs are used concomitantly with low-dose aspirin, often administered as a cardioprotective agents [1]. These agents may also interfere with antihypertensive agents and exacerbate heart failure [1].

*Cyclooxygenase-2 (COX-2) selective inhibitor*s were introduced with the hope of reducing GI toxicity. While their use has been associated with fewer significant GI adverse events, the protection incurred is not complete. In addition, the other types of NSAID-related toxicities are the same [1]. Celecoxib is currently the only COX-2 inhibitor remaining on the market, as both rofecoxib and valdecoxib were withdrawn due to concerns about unacceptable risks of adverse cardiovascular events.

Topical NSAIDs, such as diclofenac or salicylate derivatives and compounded topicals, have also been introduced as an alternative to traditional oral agents. A number of studies support the efficacy and safety of these agents in relieving chronic painful musculoskeletal conditions [22], but as insufficient numbers of older persons have participated in trials, the risks to this population are still unclear [14]. One agent, diclofenac sodium 1% gel, approved for the treatment of osteoarthritis pain, has demonstrated greatly reduced systemic levels compared with oral equivalent doses. There are no long-term comparative studies for GI or cardiovascular safety. For specific recommendations related to NSAID use in older patients, refer to Table 5.

Opioids

Opioid analgesics are widely accepted for first-line treatment of severe acute pain and chronic pain-related to cancer or at the end of life [23]; however, the use of opioids to treat noncancer pain remains controversial. Although there are diverse opinions on the subject, opioid analgesics can be an effective therapy for selected patients with persistent noncancer pain [1,23].

No studies have evaluated the long-term efficacy and safety of opioids for noncancer pain in older adults. The American Pain Society and American Academy of Pain Medicine have recently issued joint guidelines regarding the use of opioids for persistent noncancer pain, but they address the entire adult population [23].

The AGS includes the use of opioid analgesics in its updated guidelines on persistent pain in older adults [1]. In addition, a recent consensus statement from a multidisciplinary group of experts, which reviewed and evaluated the efficacy and tolerability of the six most commonly used World Health Organization step III opioids for older patients, also provides practical recommendations for use in this population [13].

Table 5 AGS recommendations for classes of pharmacologic agents [1]

Non-opioid analgesics

   I.   Acetaminophen should be considered as initial and ongoing pharmacotherapy in the treatment of persistent pain, particularly musculoskeletal pain, owing to its demonstrated effectiveness and good safety profile (high quality of evidence; strong recommendation).

      A. Absolute contraindications: liver failure (high quality of evidence, strong recommendation).

      B. Relative contraindications and cautions: hepatic insufficiency, chronic alcohol abuse/dependence (moderate quality of evidence, strong recommendation).

      C. Maximum daily recommended dosages should not be exceeded and must include "hidden sources" such as from combination pills (moderate quality of evidence, strong recommendation).

   II.   Nonselective NSAIDs and COX-2 selective inhibitors may be considered rarely, and with extreme caution, in highly selected individuals (high quality of evidence, strong recommendation).

      A. Patient selection: other (safer) therapies have failed; evidence of continuing therapeutic goals met; ongoing assessment of risks/complications outweighed by therapeutic benefits (low quality of evidence, strong recommendation).

      B. Absolute contraindications: current active peptic ulcer disease (low quality of evidence, strong recommendation), chronic kidney disease (moderate level of evidence, strong recommendation), heart failure (moderate level of evidence, weak recommendation).

      C. Relative contraindications and cautions: hypertension, H. pylori, history of peptic ulcer disease, concomitant use of steroids or SSRIs (moderate quality of evidence, strong recommendation).

   III. Older persons taking nonselective NSAIDs should use a proton pump inhibitor or misoprostol for gastrointestinal protection (high quality of evidence, strong recommendation).

   IV. Patients taking a COX-2 selective inhibitor with aspirin should use a proton pump inhibitor or misoprostol for gastrointestinal protection (high quality of evidence, strong recommendation).

   V.   Patients should not take more than one nonselective NSAID/COX-2 selective inhibitor for pain control (low quality of evidence, strong recommendation).

   VI. Patients taking ASA for cardioprophylaxis should not use ibuprofen (moderate quality of evidence, weak recommendation).

   VII. All patients taking nonselective NSAIDs and COX-2 selective inhibitors should be routinely assessed for gastrointestinal and renal toxicity, hypertension, heart failure, and other drug-drug and drug-disease interactions (weak quality of evidence, strong recommendation).

Opioid analgesics

   VIII. All patients with moderate-severe pain, pain-related functional impairment or diminished quality of life due to pain should be considered for opioid therapy (low quality of evidence, strong recommendation).

   IX. Patients with frequent or continuous pain on a daily basis should be treated with ATC time-contingent dosing aimed at achieving steady state opioid therapy (low quality of evidence, weak recommendation).

   X.   Clinicians should anticipate, assess for, and identify potential opioid-associated adverse effects (moderate quality of evidence, strong recommendation).

   XI. Maximal safe doses of acetaminophen or NSAIDs should not be exceeded when using fixed-dose opioid combination agents as part of an analgesic regimen (moderate quality of evidence, strong recommendation).

   XII. When long-acting opioid preparations are prescribed, breakthrough pain should be anticipated, assessed, prevented and/or treated using short acting immediate opioid medications (moderate quality of evidence, strong recommendation).

   XIII. Methadone should be initiated and titrated cautiously only by clinicians well versed in its use and risks (moderate quality of evidence, strong recommendation).

   XIV. Patients taking opioid analgesics should be reassessed for ongoing attainment of therapeutic goals, adverse effects, and safe and responsible medication use (moderate quality of evidence, strong recommendation).

Adjuvant analgesics

   XV. All patients with neuropathic pain are candidates for adjuvant analgesics (strong quality of evidence, strong recommendation).

   XVI. Patients with fibromyalgia are candidates for a trial of approved adjuvant analgesics (moderate quality of evidence, strong recommendation).

   XVII. Patients with other types of refractory persistent pain may be candidates for certain adjuvant analgesics (e.g., back pain, headache, diffuse bone pain, temporomandibular disorder) (low quality of evidence, weak recommendation).

   XVIII. Tertiary tricyclic antidepressants (amitriptyline, imipramine, doxepin) should be avoided because of higher risk for adverse effects (e.g., anticholinergic effects, cognitive impairment) (moderate quality of evidence, strong recommendation).

Table 5 Continued

XIX. Agents may be used alone, but often the effects are enhanced when used in combination with other pain analgesics and/or non-drug strategies (moderate quality of evidence, strong recommendation).

XX. Therapy should begin with the lowest possible dose and increase slowly based on response and side effects, with the caveat that some agents have a delayed onset of action and therapeutic benefits are slow to develop. For example, gabapentin may require 2–3 weeks for onset of efficacy (moderate quality of evidence, strong recommendation).

XXI. An adequate therapeutic trial should be conducted before discontinuation of a seemingly ineffective treatment (weak quality of evidence, strong recommendation).

Other drugs

XXII. Long-term systemic corticosteroids should be reserved only for patients with pain-associated inflammatory disorders or metastatic bone pain. Osteoarthritis should not be considered an inflammatory disorder (moderate quality of evidence, strong recommendation).

XXIII. All patients with localized neuropathic pain are candidates for topical lidocaine (moderate quality of evidence, strong recommendation).

XXIV. Patients with localized non-neuropathic pain may be candidates for topical lidocaine (low quality of evidence, weak recommendation).

XXV. All patients with other localized non-neuropathic persistent pain may be candidates for topical NSAIDs (moderate quality of evidence, weak recommendation).

XXVI. Other topical agents may be considered for regional pain syndromes including capsaicin or menthol (moderate quality of evidence, weak recommendation).

XXVII. Many other agents for specific pain syndromes may require caution in older persons and merit further research (e.g., glucosamine, chondroitin, cannabinoids, botulinum toxin, alpha-2 adrenergic agonists, calcitonin, vitamin D, bisphosphonates, ketamine) (low quality of evidence, weak recommendation).

ASA = acetyl salicylic acid (aspirin); ATC = around the clock; COX-2 = cyclo-oxygenase-2 selective inhibitors; NSAIDs = nonsteroidal anti-inflammatory drugs; SSRI = serotonin selective uptake inhibitor.

Long-term use of opioids for persistent pain may be associated with fewer potential life-threatening risks compared with long-term NSAID use, but opioids have their own set of potential risks [14]. They can cause constipation, nausea and vomiting, sedation, impaired cognition and psychomotor function, and respiratory depression [13]. While most adverse events do decline over time, extended use of opioids may suppress the production of several hypothalamic, pituitary, gonadal, and adrenal hormones [1]. Thus, long-term use requires careful monitoring for the development of adverse events.

Clinical trials have established the efficacy of numerous opioid agents in the treatment of persistent pain associated with musculoskeletal conditions, such as osteoarthritis and low back pain, along with painful neuropathic conditions such as diabetic peripheral neuropathy. However, long-term effectiveness in all age groups has not been clearly established [1].

Opioid diversion and misuse and abuse can also become a concern, especially among patients with a history of substance-use disorder [1,23]. While the incidence of addictive behavior, and misuse and abuse are significantly lower in the older population, few long-term studies have been conducted [1,14]. Therefore, caution should be exercised when prescribing opioid therapy over several years since, due to certain genetic and environmental factors, some patients are likely to abuse these drugs.

Opioids should be prescribed only with clearly defined therapeutic goals, after weighing the potential positive effects on pain and function against potential risks [1,23]. The selected agent should be provided on a trial basis initially, starting at a low dose and then titrated slowly.

An initial risk assessment, using tools such as the opioid risk tool or the revised version of the Screener and Opioid Assessment for Patients with Pain (SOAPP-R), can assist the clinician determine the presence of risk factors known to be associated with abuse/misuse of these agents [1]. Once opioids have been prescribed, the Current Opioid Misuse Measure, a self-assessment tool, can be used to identify patient misuse [23]. A positive score on these screening tools does not positively diagnose an abuse disorder, but it should trigger further evaluation and increase awareness of potential risk that requires more rigorous monitoring. This may include a written treatment agreement, smaller prescribed amounts with more frequent visits and "pill counts," urine drug testing on a recurrent basis, among other structured, ongoing evaluative and therapeutic approaches.

Although vigilance regarding misuse or abuse of opioids is important in all patients irrespective of age, some experts suggest that *underuse* may be a larger problem among the elderly [1]. Many older patients may never fill their prescriptions or may use their opioid medication sparingly because of concerns that include fears of addiction, the discomfort of associated constipation, social stigma, and cost. Therefore, it is important for clinicians to discuss these issues with their patients, and investigate their beliefs and prior experiences with this class of

Table 6 Adjuvant analgesic drugs [1,14]

Drug Class	Indication	Issues*
Antidepressants—tricyclics, SSRIs and mixed SNRIs	Neuropathic pain conditions and fibromyalgia. SRNI duloxetine is FDA-approved for managing pain associated with diabetic peripheral neuropathy and fibromyalgia	Tricyclics have a higher adverse event profile than the other classes, which often contraindicates their use in this population
Anticonvulsants	Used for neuropathic pain. Gabapentin is considered first line and is FDA-approved for pain associated with postherpetic neuralgia; pregabalin is FDA-approved for diabetic peripheral neuropathy, postherpatic neuralgia, and fibromyalgia	Should be monitored frequently for adverse events and for therapeutic effects
Muscle relaxants†	May relieve skeletal muscle pain	Associated dizziness and somnolence may increase risk for falls in older persons. After long use, discontinuation requires gradual tapering because of potential for delirium and seizures
Benzodiazepines	Efficacy in the management of persistent pain is limited	The high-risk profile in older adults generally obviates any potential benefit; use may be justified in a trial for relief of muscle spasm
Corticosteroids	Analgesic effects have been described for a wide range of different conditions including rheumatoid arthritis, polymyalgia rheumatica, giant cell arteritis, some neuropathic pain syndromes, and cancer pain	Side effects and serious toxicity of both short- and long-term use often limit their overall safety
Topical analgesics (lidocaine patch 5%, capsaicin, topical NSAIDs)	Data has shown that these agents can be effective for neuropathic pain syndromes and osteoarthritis	Local skin reactions may occur; systemic adverse events are not common with these agents

* Please consult full prescribing information for complete discussion of potential adverse effects.
† Note: the term "muscle relaxant" is used conventionally, but pharmacologically it is a misnomer. The analgesic mechanisms of action of these drugs are not specifically known.
FDA = Food and Drug Administration; NSAIDs = nonsteroidal antiinflammatory drugs; SNRIs = serotonin- and norepinephrine-uptake inhibitors; SSRIs = selective serotonin-reuptake inhibitors.

medications before beginning opioid therapy [1]. For specific recommendations related to opioid therapy in older individuals, refer to Table 5.

Adjuvant Analgesic Drugs

Adjuvant drugs can be used alone or in combination with an opioid or a nonopioid analgesic to treat persistent pain conditions. Some of these agents are indicated for specific pain problems, such as neuropathic pain and fibromyalgia. Others are not specifically developed or indicated for pain relief nor classically categorized as analgesics but found to be effective in attenuating certain pain syndromes such as chronic low back pain. Drug classes that fall into this category include antidepressants, anticonvulsants, corticosteroids, muscle

relaxants, benzodiazepines, and topical analgesics (see Table 6).

Moving Toward "Best Practices"

Effective treatment begins with a comprehensive assessment, and all older adults should be screened for persistent pain in all types of health care settings [24]. If pain is identified, then a comprehensive evaluation should be conducted that includes pain history, medical history, complete physical examination, and a functional assessment.

Older adults with persistent pain that causes functional impairment and/or adversely affects quality of life should be considered for pharmacologic therapy. The type of

therapy selected will largely depend on the intensity and cause of pain, and individual patient's characteristics. Response to therapy should be reassessed periodically, with interventions revised if pain is not being adequately controlled. Likewise, if the pain is resolved, medication can sometimes be tapered, switched, or stopped completely.

A number of guidelines are now available to help health care professionals in the assessment and particularly the treatment of persistent pain in older adults. AGS guidelines urge caution in the use of NSAIDs, and recommend the least invasive route for giving medication [1]. The AGS, along with other professional organizations, affirms that opioids are effective for relieving moderate to severe pain and are associated with a low potential for addiction in older patients who do not have a history of abuse or addiction. In older persons with persistent pain, relatively low-dose opioid therapy can be associated with fewer long-term risks than other drug regimens, such as NSAIDs [1].

Pharmacotherapy is usually needed, particularly when pain interferes with physical and psychological function and quality of life. However, nonpharmacologic therapies, including exercise, massage, physical therapy, biofeedback, cognitive-behavioral therapy, acupuncture, and transcutaneous electrical nerve stimulation, can optimize and enhance the effects of drug therapy [1,15–17,25]. Interventional techniques, such as joint and muscle injections of local anesthetics or steroids, can also play an important role in managing selected chronic pain conditions [26]. Referral to specialists may be necessary for diagnosis and treatment of complex conditions.

Because of the often complex nature of their health care needs, older patients require the coordinated and comprehensive services that can be offered through a patient-centered primary care medical home [23]. In the medical home model, the primary care clinician provides most of the patient's health care needs, taking responsibility for appropriately arranging care with other qualified professionals as needed. Patient care is coordinated and/or integrated across all elements of the health care system, both in institutional and community settings.

Persistent pain in the older population generally requires a multidisciplinary approach in formulating a pain management plan that is appropriate and effective for the individual patient.

Conclusion

Pharmacotherapy should be considered for all patients with pain that negatively impacts quality of life. Understanding the pharmacology of all potentially useful agents and patient-specific factors, coupled with ongoing monitoring of therapeutic goals and adverse effects will greatly help to optimize outcomes. Currently available evidence-based clinical guidelines should be referred to as a means of improving clinical practice.

References

1 American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. J Am Geriatr Soc 2009;57: 1331–46.

2 Bjoro K, Herr K. Assessment of pain in the nonverbal or cognitively impaired older adult. Clin Geriatr Med 2008;24:237–62.

3 Vincent GK, Velkoff VA. The Next Four Decades: The Older Population in the United States: 2010 to 2050, Current Population Reports. P25-1138, U.S. Census Bureau, Washington, DC: May 2010.

4 Cavalieri TA. Pain management in the elderly. J Am Osteopath Assoc 2002;102:481–5.

5 Kemp CA, Ersek M, Turner JA. A descriptive study of older adults with persistent pain: Use and perceived effectiveness of pain management strategies (ISRCTN11899548). BMC Geriatr 2005;5:12.

6 Schneider H, Cristian A. Role of rehabilitation medicine in the management of pain in older adults. Clin Geriatr Med 2008;24:313–34. vii.

7 McCleane G. Pharmacological pain management in the elderly patient. Clin Interv Aging 2007;2(4):637–43.

8 Agin CW, Glass PS. Tolerance and aging: Optimizing analgesia in pain management. Anesth Analg 2005; 100:1731–2.

9 Glajchen M. Chronic pain: Treatment barriers and strategies for clinical practice. J Am Board Fam Pract 2001;14:211–8.

10 Nygaard HA, Jarland M. Are nursing home patients with dementia diagnosis at increased risk for inadequate pain treatment? Int J Geriatr Psychiatry 2005;20:730–7.

11 Reynolds KS, Hanson LC, DeVellis RF, et al. Disparities in pain management between cognitively intact and cognitively impaired nursing home residents. J Pain Symptom Manage 2008;35:388–96.

12 Morley-Forster PK, Clark AJ, Speechley M, Moulin DE. Attitudes toward opioid use for chronic pain: A Canadian physician survey. Pain Res Manag 2003;8:189–94.

13 Pergolizzi J, Böger RH, Budd K, et al. Opioids and the management of chronic severe pain in the elderly: Consensus statement of an International Expert Panel with focus on the six clinically most often used World Health Organization Step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). Pain Pract 2008;8(4):287–313.

14 Fine PG, Herr KA. Pharmacologic management of persistent pain in older persons. Clin Geriatr 2009;17(4):25–32.

15 Bonnewyn A, Katona C, Bruffaerts R, et al. Pain and depression in older people: Comorbidity and patterns of help seeking. J Affect Disord 2009;117(3):193–6.

16 Landi F, Russo A, Liperoti R, et al. Daily pain and functional decline among old-old adults living in the community: Results from the ilSIRENTE Study. J Pain Symptom Manage 2009;38(3):350–7.

17 Snow AL, Chandler JF, Kunik ME, et al. Self-reported pain in persons with dementia predicts subsequent decreased psychosocial functioning. Am J Geriatr Psychiatry 2009;17(10):873–80.

18 US Food and Drug Aministration Advisory Committee Calendar. June 29–30, 2009: Joint Meeting of the Drug Safety and Risk Management Advisory Committee with the Anesthetic and Life Support Drugs Advisory Committee and the Nonprescription Drugs Advisory Committee: Meeting Announcement; 2011. Available at: http://www.fda.gov/advisorycommittees/calendar/ucm143083.htm (accessed November 2011).

19 Franceschi M, Scarcelli C, Niro V, et al. Prevalence, clinical features and avoidability of adverse drug reactions as cause of admission to a geriatric unit: A prospective study of 1,756 patients. Drug Saf 2008;31:545–56.

20 Richy F, Bruyere O, Ethgen O, et al. Time dependent risk of gastrointestinal complications induced by non-steroidal anti-inflammatory drug use: A consensus statement using a meta-analytic approach. Ann Rheum Dis 2004;63:759–66.

21 Heerdink ER, Leufkens HG, Herings RM, et al. NSAIDs associated with increased risk of congestive heart failure in elderly patients taking diuretics. Arch Intern Med 1998;158:1108–12.

22 Mason L, Moore RA, Edwards JE, et al. Topical NSAIDs for chronic musculoskeletal pain: Systematic review and meta-analysis. BMC Musculoskelet Disord 2004;5:28.

23 Chou R, Fanciullo GJ, Fine PG, et al. American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain 2009;10:113–30.

24 Hadjistavropoulos T, Herr K, Turk DC, et al. An inter-disciplinary expert consensus statement of assessment of pain in older persons. Clin J Pain 2007;23(1 suppl):S1–43.

25 Morone NE, Greco CM. Mind-body interventions for chronic pain in older adults: A structured review. Pain Med 2007;8:359–75.

26 Christo PF, Li S, Gibson S, Fine PG. Effective treatments for pain in the older patient. Curr Pain Headache Rep 2011;15(1):22–34.

27 Bruckenthal P. Assessment of pain in the elderly adult. Clin Geriatr Med 2008;24:213–36, v–vi.

28 Herr K, Bursch H, Ersek M, et al. Use of pain-behavioral assessment tools in the nursing home: Expert consensus recommendations for practice. J Gerontol Nurs 2010;36:18–31.

29 Blozik E, Stuck AE, Niemann S, et al. Geriatric Pain Measure short form: Development and initial evaluation. J Am Geriatr Soc 2007;55(12):2045–50.

30 Geriatric Pain web site; 2011. Available at: http://www.geriatricpain.org/Pages/home.aspx (accessed November 2011).