Care of the Patient with Chronic Pain 63

Kelly Bossenbroek Fedoriw

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Definition and Scope of Chronic Pain

Chronic pain is pain that persists beyond the typical healing time of 3–6 months. The Institute of Medicine estimates that 100 million people in the United States suffer from chronic noncancer pain (CNCP) which is more than the number of people with diabetes, coronary heart disease, stroke, and cancer combined [1]. The annual health care costs for patients with CNCP are estimated at $635 billion (in 2010 dollars), but despite the high prevalence, CNCP remains undertreated [2].

Paralleling the incidence of CNCP, prescriptions for opioid pain medications have skyrocketed over the past 15 years, with approximately 259 million opioid prescriptions written by providers in 2012 [3]. This increase in prescriptions has been associated with an alarming increase in accidental overdose deaths involving prescription opioids but shown to have little impact on effectively reducing pain [3, 2].

Patients with CNCP frequently are seen in primary care offices where their treatment is often coordinated by a family physician. While these patients and their pain can often be seen as challenging to manage, using a stepwise approach and collaborative care model can safely and successfully mitigate pain and improve function.

K. Bossenbroek Fedoriw (✉)
Department of Family Medicine, UNC – Chapel Hill, Chapel Hill, NC, USA
e-mail: kelly_fedoriw@med.unc.edu

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Treating Acute Pain

Acute pain tends to have an easily identifiable cause and typically resolves when the inciting injury heals. Nonopioid medications should be considered first line for acute pain [4]. However, when opioids are indicated for an acute injury, providers must discuss the risks of treatment as well as the expectations for healing and engage the patient in mutual decision-making. The transition from acute pain to chronic pain is not always obvious. Providers can easily find themselves refilling opioid prescriptions long after the acute injury should have healed and without having discussed the risks of long-term opioids with patients.

Patient Assessment

Every patient in pain requires a thorough initial history and physical exam to assess pain characteristics including location, intensity, quality, duration, and relieving and exacerbating factors. Previous investigations and treatments tried will help guide treatment options and social history; substance use history and any psychiatric comorbidities need to be explored as well [5, 6]. Categorizing the type of chronic pain will help determine possible treatment options.

A functional assessment is essential for patients in chronic pain [6]. Tools for use in primary care include the Pain, Enjoyment, and General Activity questionnaire (see Fig. 1) and the Physical Functional Ability Questionnaire by the Institute for Clinical Systems Improvement. The goal of therapy for chronic pain is to improve function and quality of life as well as control pain. Patients should be aware of these goals, and function should be tracked over time.

In addition to assessing the patient, providers must set expectations for pain management at the first visit. Chronic pain by definition is a chronic disease and must be managed similarly to other chronic diseases. Many patients will require multiple modalities, self-management skills, and more than one medication trial to achieve improvement in their function.

Types of Pain and Treatment Options

Pain can be classified as nociceptive or neuropathic. Nociceptive pain is caused by tissue injury and includes inflammatory, muscular, and mechanical pain. Neuropathic pain is caused by damage to or dysfunction of the central or peripheral nervous system. Importantly, the categories are not mutually exclusive, and patients can be affected by both types of pain. However, classification of mechanism for a given patient can be helpful in guiding therapy [5].

Inflammatory pain – Arthritis, surgery, and infection are potential causes of inflammatory pain. Hallmarks on physical exam are edema, heat, erythema, and pain at the site of an injury. Treatment typically involves NSAIDS, corticosteroids, or immune-modulating agents to control the inflammation.

Muscular pain – Muscle soft tissue pain typically occurs after an injury and involves pain in one or more areas of muscle, loss of range of motion, as well as tenderness over the affected muscle groups. Myofascial pain is a common cause of chronic pain and is best managed by physical therapy and restoring muscle balance and not medication [5]. Trigger point injections or acupuncture may be useful.

1. What number best describes your Pain on average in the past week? (No pain - Pain as bad as you can imagine)

2. What number best describes how, during the past week, pain has interfered with your Enjoyment of life? (Does not interfere-Completely interferes)

3. What number best describes how, during the past week, pain has interfered with your General activity? (Does not interfere – Completely interferes)

Fig. 1 Pain, enjoyment, and general activity (Scale 1–10) [7]

Mechanical pain – Mechanical pain is often caused by compression due to a cyst or tumor, fracture, degeneration, or dislocation. Pain is aggravated by activity and can be relieved by rest [5]. Most chronic neck pain and visceral pain fall into this category. Chronic low back pain can also be in this category but is often multifactorial. Treatment may be surgical in the case of cysts, fractures, and impingement.

Neuropathic pain – Common examples of neuropathic pain include diabetic neuropathy, postherpetic neuralgia, carpal tunnel, multiple sclerosis, and poststroke pain. Neuropathic pain is often described as "shooting" or "stabbing" but can also present as numbness, tingling, and increased sensitivity to benign touch (allodynia) [5]. Neuropathic pain is less responsive to opioid analgesics [8]. Treatment options for neuropathic pain are numerous and can be divided into two categories: disease-specific treatments such as improved glucose control for diabetic neuropathy or surgery for nerve decompression and symptom management. First-line treatment options for symptom management include anticonvulsants, tricyclic antidepressants (TCAs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) [5].

Chronic Pain Treatment Algorithm

See Refs. [5, 6, 8] (Fig. 3, Table 1)

Muscle Relaxants

Little evidence exists to support the use of muscle relaxants such as cyclobenzaprine (Flexeril) and tizanidine (Zanaflex) for chronic low back pain [5, 9]. Carisoprodol (Soma) is structurally similar to alprazolam, has little utility in the management of chronic pain and can be habit forming [5]. If used chronically, muscle relaxants cause central relaxation and may carry the risk of physical dependence [9]. Baclofen is a commonly used antispasmodic agent which may improve neuropathic pain and may be less habit forming than muscle relaxants [9, 5].

Multiple Modalities

Treatment plans for chronic noncancer pain must include more than just medications. Exercise therapy is recommended for chronic low back pain as well as other types of chronic pain and can reduce functional limitations [5]. Patients with CNCP are often deconditioned due to inactivity, and providers should recommend gradually increasing general activity levels as well as formal exercise [5]. In addition, massage has been shown to reduce for chronic pain due to low back pain, knee osteoarthritis, and fibromyalgia [5].

Psychotherapy is an additional treatment modality for patients with CNCP. Psychotherapy focuses on improving the patient's quality of life, social functioning, and mood rather than decreasing the level of pain [11]. Cognitive-behavioral therapy (CBT) and mindfulness-based stress reduction are two psychological interventions that therapists can use to teach patients how to manage their pain and engage in a full life despite their pain. Unfortunately many patients struggle with the cost of these services, but mindfulness and diaphragmatic breathing are methods that can also be taught in primary care settings. Providers can also utilize modified CBT techniques when working with patients (see Fig. 2).

Surgical interventions are sometimes warranted but are beyond the scope of this chapter (Table 2).

Opioid Trial Algorithm

See Refs. [4–6, 12, 13] (Fig. 4)

Indications/Contraindications and Risks of Opioids

Guidelines have been developed to help clinicians safely and effectively treat CNCP with opioids [6, 13–15]. However, many of the recommendations are based on limited data. Most trials involving CNCP are short (<3 months) and evaluate pain scores and not patient function [14]. While the

Table 1 Selected analgesics [8–10]

Drug name	Usual dose	Maximum dose	Comments
Acetaminophen (Tylenol, others)	500–1,000 mg po q6-8 h	3,000 mg/day	Recommended for noninflammatory osteoarthritis. May require maximum dose for 1 week for chronic pain trial. Avoid with chronic alcoholism. Monitor OTC medications for risk of accidental overdose
NSAID			
Ibuprofen (Motrin, others)	400–800 mg po q4–6 h	3,200 mg/day	NSAIDs in recommended doses usually provide superior analgesia compared with aspirin, but do not produce the same analgesic effect in all patients. Major adverse effects are: 1. Elevated blood pressure especially in the elderly and in conjunction with beta-blockers or angiotensin-converting enzyme inhibitors 2. Fluid retention in patients with congestive heart failure 3. Acute renal failure or renal insufficiency 4. Drowsiness and confusion 5. Reversible inhibition of platelet aggregation 6. Anaphylaxis in aspirin-sensitive patients 7. Peptic ulcer disease, regardless of mode of administration, especially in the first month of therapy Adding a proton pump inhibitor, H2-receptor antagonist or misoprostol may decrease GI toxicity Use with caution and for the shortest time possible in the elderly
Naproxen (Naprosyn)	500 mg po q12h	1,000 mg/day	
Indomethacin (Indocin)	25–50 mg po q8h or SR–75 mg po q12h	200 mg/day	
Ketoralac (Toradol, others)	10 mg po q4–6 h	40 mg/day	
	Pts <65 years: 30 mg IM/IV q6h	120 mg/day	
	Pts ≥65 years: 15 mg IM/IV q6h	60 mg/day 60 mg/day	
Diclofenac (Cataflam, Voltaren)	50 mg po q8h or SR-75 mg po q12h	200 mg/day	
Meloxicam (Mobic)	7.5–15 mg daily	15 mg/day	May be more selective for COX-2 at low dose (7.5 mg)
Nabumetone (Relafen)	500–750 mg po q8-12 h	2,000 mg/day	
Celecoxib (Celebrex)	200 mg po q12h	400 mg/day	Selective COX-2 inhibitors and NSAIDs have demonstrated decreased gastrointestinal complications compared with nonselective NSAIDs. They do not inhibit platelet aggregation Less effective than full doses of ibuprofen or naproxen Less effective treatment for acute pain
TCA			Analgesia achieved at lower dose (20–100 mg/day) than antidepressant dose (150–300 mg/day). Contraindications include heart failure, ischemic heart disease and arrhythmias. Side effects include confusion, urinary retention, orthostatic hypotension, dry mouth, drowsiness, nightmares Use cautiously in patients at risk for suicide or accidental overdose due to potential for lethal cardiotoxicity Nortriptyline and desipramine are better tolerated than amitriptyline and imipramine
Nortriptyline (Pamelor)	10–100 mg qHS	300 mg/day	
Desipramine (Norpramin)	50–150 mg daily	150 mg/day	
SNRI			Taper over 2 weeks to discontinue. Better tolerated than TCA Common SE of HA and nausea
Venlafaxine (Effexor)	75–150 mg po daily	225 mg	
Milnacipran (Savella)	50 mg po BID	200 mg/day	
Duloxetine (Cymbalta)	60 mg daily	60 mg/day	Specifically approved for diabetic neuropathy, fibromyalgia, chronic low back pain. No known cardiovascular risk. Nausea is a common side effect

(*continued*)

Table 1 (continued)

Drug name	Usual dose	Maximum dose	Comments
Anticonvulsant			Typically used for neuropathic pain and chronic headaches. Can be added to TCA. Similar efficacy to TCA
Gabapentin (Neurontin)	600–1,200 mg TID	3,600 mg/day	Start at 100–300 mg qHS and titrate to effective dose. Common side effects include dizziness, fatigue, impaired concentration, and peripheral edema. Reduce dose in renal impairment
Pregabalin (Lyrica)	75–300 mg po BID	600 mg/day	FDA approved for fibromyalgia. May have anxiolytic benefits
Carbamazepine (Tegretol)	200–400 mg BID	1,200 mg/day	Effective for trigeminal neuralgia, painful diabetic neuropathy and postherpetic neuralgia
Oxcarbazepine (Trileptal)	300–600 mg po BID	1,200 mg/day	May have fewer side effects than carbamazepine
Topical Agent			
Lidocaine patch (Lidoderm)	1–3 patches for 12 h per day	3 patches/day	Approved for postherpetic neuralgia. Minimal evidence to support other use
Diclofenac (Voltaren gel)	2–4g topical q6-8 h	32 g/day	Topical NSAID with low risk of systemic side effects

OTC over the counter, *COX* cyclooxygenase, *NSAID* nonsteroidal antiinflammatory drug, *SR* sustained release, *TCA* tricyclic antidepressant, *SNRI* serotonin-norepinephrine reuptake inhibitor

Encourage your patient to take an active role in their pain management

Tell your patient that you believe the pain is real and you will work together to manage it

Do not let pain dictate activity or appointments. Schedule regular visits and medications at regular intervals instead of as needed

Fig. 2 Cognitive behavioral techniques [5]

risk of overdose death with high-dose opioids has been well established, there are no high-quality controlled trials that evaluate the effectiveness of opioid therapy for longer than 1 year [14].

There is no evidence in favor of one opioid over another for the treatment of CNCP [14, 15]. Opioid selection is primarily based on cost, side effects, and patient comorbidities. Specifically, there is no compelling evidence to prescribe a long-acting medication accompanied by a short-acting medication for "break-through pain" [15]. Patients who are well controlled and functional on a short-acting medication four times a day do not necessarily need the addition of a long-acting medication.

Methadone deserves specific mention due to the unique risks associated with chronic methadone use [16]. Methadone should be a medication of last resort given the significant risk of QTc prolongation and long, variable half-life which can make titration difficult. Patients who require a trial of methadone can be started at 2.5 mg orally every 8 h. Dosage increases should occur no more frequently than once a week [15]. The starting dose of methadone, even in a patient on high doses of other opioids, should not be higher than 30–40 mg per day [15]. The QTc interval should be monitored with electrocardiograms prior to starting methadone, after 1 month, and yearly while therapy continues. Providers should avoid the use of other medications that prolong QTc and increase monitoring if necessary. Methadone should not be used to treat breakthrough pain or on an as-needed basis [15].

Given the well-established risks of opioids high-dose therapy, in particular, should be reconsidered. Not surprisingly, limiting dosage is associated with decreased number of overdose deaths [13]. Multiple guidelines support opioid dosage limits, but there is inconsistency over

Table 2 Selected opioid analgesics [8, 9]

Drug name	Usual adult starting dose	Duration of action	Comments
Don't use Meperidine (Demerol) due to toxic metabolite			
Many opioids are available in multiple formulations: immediate release, sustained release or extended release formulations. This will affect the starting dosage as well as the dosing interval			
Codeine	15–60 mg po q4h	4 h	Avoid in children
Fentanyl (Duragesic)	Depends on previous opioid dosage[a]	72 h/patch	Warn patients that exposing the patch to heat can increase release of fentanyl and increase risk of respiratory depression Keep away from children. Exposure to patch can be fatal CYP3A4 inhibitors (eg ketoconazole, clarithromycin) can dangerously increase serum fentanyl levels
Hydrocodone (Norco)	5–10 mg po q4-6 h	4 h	
Hydromorphone (Dilaudid)	2 mg po q6-8 h	4–6 h	
Methadone (Dolophine)	2.5–10 mg po q8-12 h	8–12 h	Monitor the initial titration period carefully as the half-life is variable (up to 5 days). Serious arrhythmias can occur and are dose dependent
Morphine (MS Contin)	10–30 mg po q4h (IR)	4 h (IR)	Use with caution in patients with renal impairment.
	15–30 mg po q8-12 h (ER)	8-12 h (ER)	
Oxycodone (Roxicodone, Oxycontin)	5–15 mg po q4-6 h (IR)	4–6 h (IR)	1.5 times as potent as oral morphine
	10 mg po q12 (ER)	12 h (ER)	
Oxymorphone (Opana)	5–15 mg po q4-6 h (IR) 10 mg po q12 (ER)	4–6 h (IR) 12 h (ER)	3 times as potent as oral morphine
Tapentadol (Nucynta)	50–100 mg po q4-6 h (IR) 50 mg po q12 (ER)	4–6 h (IR) 12 h (ER)	Less potent than morphine but fewer GI side effects
Tramadol (Ultram)	50–100 mg po q4-6 h (IR) 100 mg po q24 (ER)	4–6 h (IR) 24 h (ER)	Maximum dose is 400 mg/day (IR) and 300 mg/day (ER)

OTC over the counter, COX cyclooxygenase, NSAID nonsteroidal antiinflammatory drug, SR sustained release, TCA tricyclic antidepressant, IR immediate release, ER extended release
[a]Not recommended for opioid naïve patients

specific threshold recommendations [14]. Patients who do not experience a response to low-dose opioids (up to 40 mg morphine equivalent dose (MED)) or moderate doses (40–90 mg MED) are unlikely to respond to higher doses [13]. Patients requiring high doses (>100 mg MED) should be re-evaluated for the cause of their pain, and providers should consider more frequent monitoring, evaluation of adherence to the treatment plan, and consider referral to pain specialists [13, 15].

Mitigating Risks

In addition to establishing a diagnosis, patients should be stratified according to risk. Mitigating the hazards of opioid misuse and addiction requires routine and ongoing risk assessment. Multiple patient screening tools are available, but unfortunately the effectiveness of these tools is not well studied [14]. However, this should not preclude screening patients. Tools that are often used include

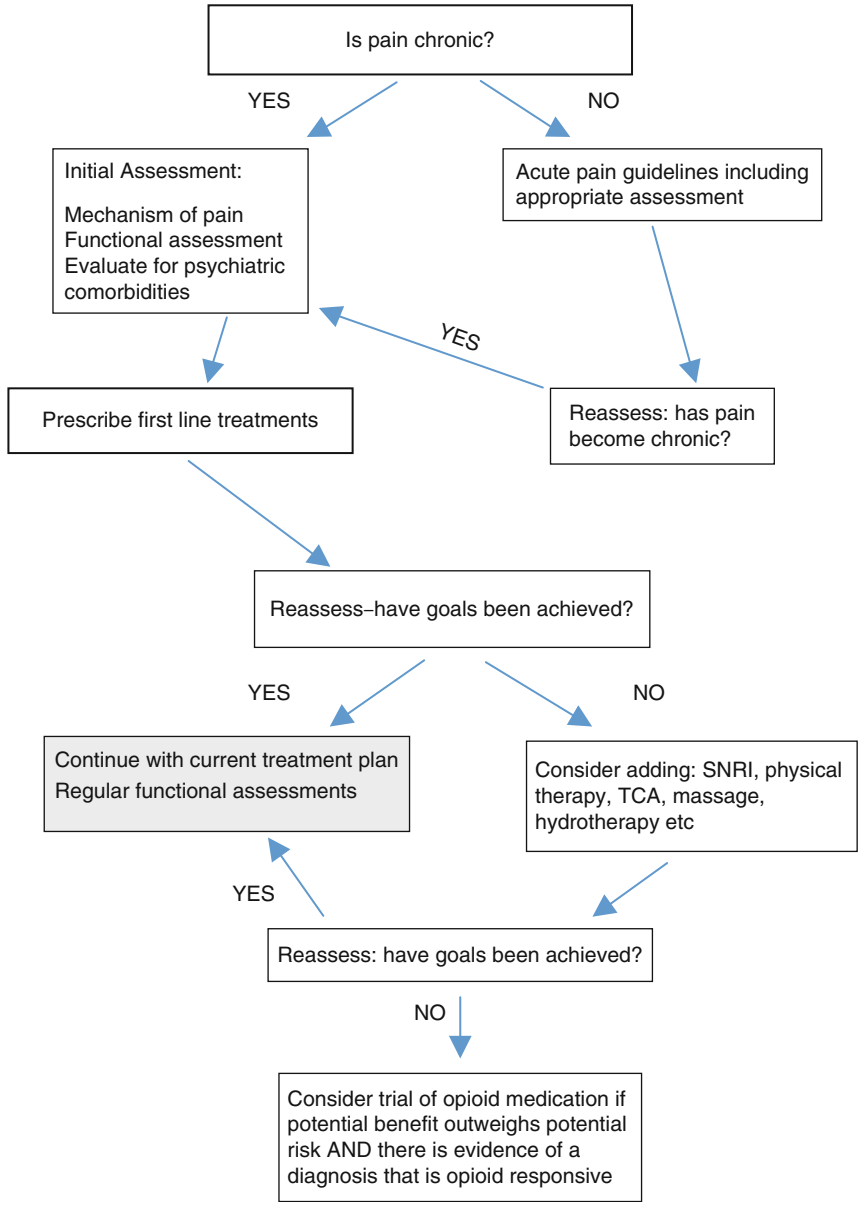

Fig. 3 Chronic Pain Treatment Algorithm, *SNRI* = serotonin-norepinephrine reuptake inhibitor, *TCA* = tricyclic antidepressant

the Opioid Risk Tool, Addiction Behaviors Checklist, and the Screener and Opioid Assessment for Patients with Pain [6]. Categorizing patients into high, moderate, or low risk groups can help guide management. High-risk patients and those with significant psychiatric comorbidities or history of drug abuse should be managed only by providers experienced with this population, and comanagement with psychiatry or an addiction specialist is strzongly recommended [15].

Patients must give informed consent prior to starting an opioid trial. Providers should plan for the common adverse effects of opioids at the start of treatment. Even patients on short-term opioids should be warned about constipation and prescribed a stool softener. Chronic opioid users do

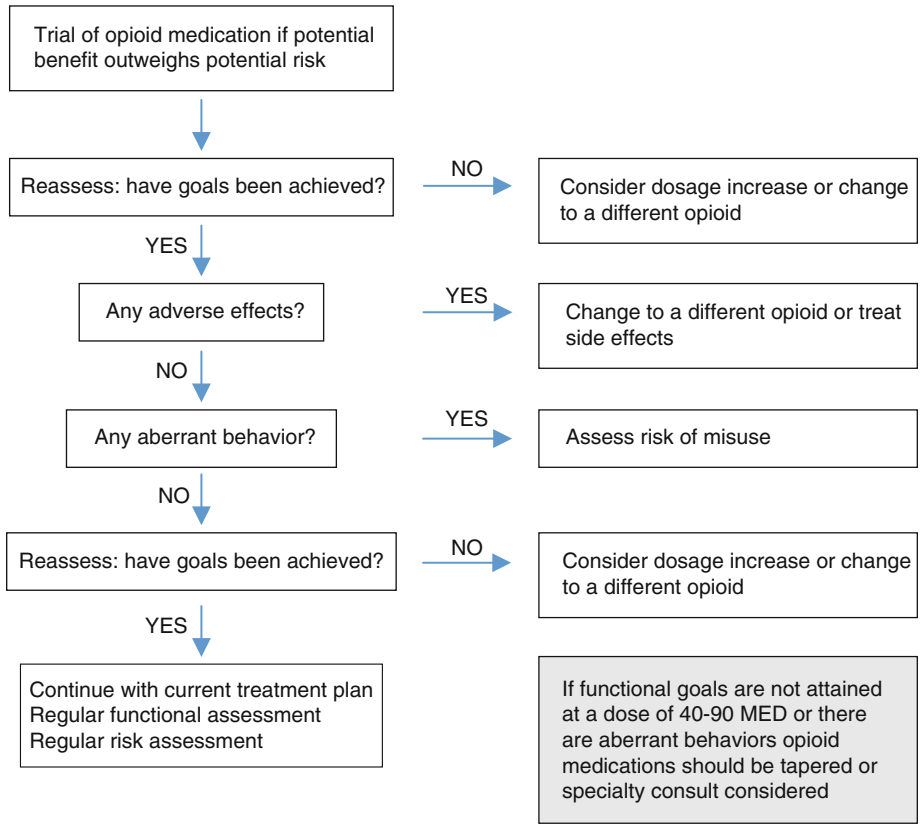

Fig. 4 Opioid Treatment Algorithm for Patients with Chronic Pain, MED = morphine equivalent dose

not develop tolerance to constipation and may also require a stimulant laxative. Nausea is common and typically resolves with time, however antihistamines or metoclopramide will also relieve symptoms [17]. Cognitive impairment or sedation is a major risk when starting or increasing medications or when taken with other sedating substances including benzodiazepines and alcohol. Patients should be instructed not to drive at any time when they feel impaired [15]. The risk of respiratory depression and death is much higher when a patient's dose is increased or when combined with other drugs such as benzodiazepines. A discussion of the risks of physical dependence and withdrawal is also necessary.

Patients and providers should establish reasonable expectations at the start of an opioid trial. Total pain relief with opioids is not realistic. The average benefit on a 10 point pain scale is 2–3 points [15]. A successful opioid trial typically results in a 30 % reduction in pain or a 30 % improvement in function [13].

Documenting informed consent and expectations is crucial and can be accomplished using treatment agreements (pain contracts). There is some evidence that treatment agreements may improve compliance [13]. Using these agreements, providers can also discuss expectations of random urine drug testing, pill counts, replacement of lost/stolen prescriptions and counsel to avoid excessive amounts of alcohol.

Prescription monitoring programs are active in at least 48 states and can reduce doctor shopping and prescription drug abuse [13, 14] Unfortunately these programs are grossly underutilized [13, 14].

Every patient on chronic opioid therapy should have periodic urine drug screening (UDS)

[13]. The frequency of testing can be based on the patient's overall risk of misuse. Using these screens is important, however the interpretation of results is not always straightforward. Results should be considered in the context of patient behavior and overall compliance [15]. Unexpected positive results should be confirmed by more specific means, and a discussion with the laboratory may be helpful to determine concentrations necessary for a positive result when the prescribed opioid is not present. Furthermore, numerous assays and platforms for UDS are available, each with variable test characteristics not equivalent across all drug classes. Not infrequently, pseudoephedrine may result in a false-positive amphetamine screen, while testing positive for cocaine is far more specific.

Discontinuation of Opioids

If patients are not progressing toward established treatment goals, show repeated aberrant behaviors, or are suffering intolerable adverse effects, discontinuation of therapy should be considered [15]. A conservative opioid taper, with weekly decreases of 10 % of the original dose, is usually well tolerated although more aggressive decreases are possible [13]. While not life threatening, opioid withdrawal can be unpleasant, and symptoms can be managed with clonidine 0.1–0.2 mg orally every 6 h or by transdermal patch at 0.1 mg weekly. Patients on clonidine should be monitored for hypotension [13]. Benzodiazepines should not be used to control symptoms during tapering [6]. Patients who are abusing the medication or noncompliant with the taper schedule should be referred for detoxification [13].

All patients with aberrant behavior should be offered addiction resources [15]. Office-based treatment with buprenorphine/naloxone may be appropriate for patients with opioid dependence. This treatment is an alternative to methadone maintenance and can be offered by primary care providers after obtaining further education and a special licensure from the DEA. More information can be found at http://buprenorphine.samhsa.gov.

Chronic Disease Model

Chronic noncancer pain is complex and following current treatment guidelines requires significant clinical resources. However, this is not unlike other chronic illnesses. Using a chronic care model within primary care has clearly improved the care of patients with chronic illnesses such as diabetes, congestive heart failure, and asthma [18]. Chronic noncancer pain must be approached in the same manner. A comprehensive approach that includes risk assessment, treatment agreement, patient self-management, and care coordination can improve adherence to guidelines, pain disability, and pain intensity [19].

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