

Introduction to chronic pain

Definitions of chronic pain

Chronic, noncancer, pain (CP) is a diverse group of clinical entities that have two important components:

1. the presence of pain and
2. the persistence of the pain over an extended period of time.

The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” [1]. CP is further defined as pain that has lasted longer than 3–6 months [2]; however, some authors prefer a definition of CP that does not use a time limit and define CP as “pain that extends beyond the expected period of healing” [2].

Prevalence of chronic pain

The reported prevalence rates of CP have varied widely due to numerous variations in the definitions of CP, the severity required for reporting, and other variables between studies. In a survey of CP that assessed 46,000 individuals in Europe, one in five people reported suffering from CP. On average, individuals reported having CP for 7 years and some individuals reported pain that persisted for more than 20 years [3]. The 2011 American Institute of Medicine report estimated that CP affects approximately 100 million Americans each year [4].

Effect of chronic pain

CP is increasingly being thought of as a disease unto itself and a serious disease at that [5]. CP impairs physical, social, and psychological well-being, resulting in a decreased quality of life for patients, their family members, and caregivers [6–8]. Not only does CP cause suffering, but there is often a financial burden as well; for example, CP can cause a decrease in productive time at work, which may result in financial difficulties for patients and their families with subsequent emotional distress [9].

The nociceptive system is the body's pain signaling system, transmitting information from parts of the body that are experiencing pain to various brain centers. Transmission to the discriminatory part of the brain results in a cognitive reaction (eg, localization such as: “my finger hurts”), activation of the motor system results in a physical reaction (eg, removal of the finger from what is causing pain), and the limbic system produces an emotional response (eg, anger, fear) [10]. The emotional response from a short episode of pain can cause fear or anger; however, when the pain persists and becomes chronic, these emotions may transform into anxiety, frustration, and depression. From an adaptive learning perspective, linking an unpleasant emotion to a painful memory helps us avoid repeating potentially harmful activities. For example, if fear is linked to the pain that is caused by a specific action, a person is less likely to repeat the painful activity (eg, if a person burns themselves by touching fire, they will remember that pain, and will not touch the fire again due to the fear of pain) [11]. This is part of the learning–avoidance process. However, if learning cannot result in avoidance, as is the case for patients with CP, then the learning–avoidance process may not function properly. In this setting, the aversive, unpleasant emotional response to pain can intensify and may result in suffering, depression [12], and at times suicide [13]. It is possible that alterations in the mesolimbic reward system in patients with CP may play a role in the increased suicide rate seen in these patients [13]. The intimate association between CP and the limbic system has led to the concept of the ‘limbically augmented pain syndrome’. Patients with this syndrome are reported to have atypical and treatment-refractory pain complaints, which are associated with disturbances of mood, sleep, energy, libido, memory/concentration,

behavior, and stress intolerance [14]. In my practice, negative affective states, such as depression and anxiety, are often observed as part of the presentation of CP. The fact that CP signals may continuously activate the limbic system may explain why these emotions are so commonly expressed by these patients and perhaps why they are so difficult to treat in this population.

Additionally, the limbic system is the home of the nucleus accumbens (among other structures), which is part of the mesolimbic reward pathway involved with the development of addiction; therefore, the systems that are known to play a role in addiction also play a role in CP.

Introduction to management: managing expectations of patients with chronic pain

When managing a patient with CP, the physician, multidisciplinary team, patient, family, and caregivers must be aware that while complete pain relief may occur, it is rare. The patient's expectations must be managed appropriately. The most frequently used treatments for CP consist of physical therapy, antidepressants, antiepileptics or anticonvulsants*, and injections, such as epidurals; however, there is no panacea. Cognitive behavioral therapy (CBT) and other behavioral therapies or psychological interventions can help reduce pain and improve daily functioning [15] and, for some patients, may be the only treatments that are tolerated. However, the pain reduction with CBT is often of small magnitude [16]. Even opioids, called “God’s own medicine” by the great 19th century physician Sir William Osler [17], often do not provide complete relief. No drug or procedure will work for all patients, and even achieving partial pain relief may require multiple approaches, such as physical modalities, rational polypharmacy [18], and invasive procedures, including surgery [19]. Even advanced pain management techniques, such as spinal cord stimulation, intrathecal medications, and radiofrequency ablations, may not provide adequate pain relief. Furthermore, I have witnessed patients who have undergone deep-brain stimulation, nerve ablations, amputations, spinothalamic tract, and dorsal root entry zone spinal cord

**The term ‘antiepileptics’ will be used to refer to these drugs throughout the text*

lesioning without obtaining significant pain relief. While one or more of these approaches provide adequate pain relief for certain patients, some patients have little response to any treatment.

Complete pain relief is usually not possible. Some of the procedures used to treat CP are quite invasive and some of the medications carry significant risks. By attempting to provide a patient complete pain relief, a physician and team may bring harm to the patient (an old adage in medicine is that “the enemy of good is better”); additionally, the patient’s inappropriate expectations for pain relief might lead to treatment failure. The physician and team must provide the patient with realistic expectations. When a patient has intractable pain, it is critical that physicians and their teams help patients understand that *managing* their pain is the ultimate goal, not curing the pain completely, hence the term ‘pain management’. Based on my clinical experience, I often must remind patients that CP is called ‘*chronic* pain’ because it is chronic (persistent).

Introduction to medical management of patients with chronic pain

As previously mentioned, there are various options for CP management, but the backbone of managing severe CP is chronic opioid therapy (COT). Since these medications have an inherent risk for developing addictions, patients must be closely observed and monitored while on COTs (see Chapter 3). Most authors would agree that nonopioid treatments and medications should be tried prior to considering COT. These include physical therapy (eg, for myofascial pain), CBT, nonsteroidal anti-inflammatory drugs, low-dose tricyclic medications (or other antidepressants that increase norepinephrine levels), antiepileptics, nerve blocks (eg, medial branch block and radiofrequency ablation for facet joint pain), and treatment of co-occurring psychiatric illnesses [20]. Although these approaches should be tried before prescribing COT, opioids should be considered for the many patients with CP who do not obtain adequate relief from these treatments (see Figure 2.1 for an algorithm for CP management).

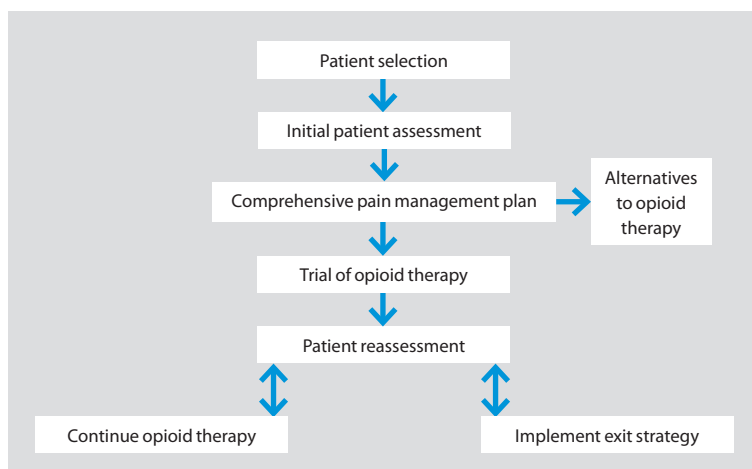


Figure 2.1 Algorithm for chronic pain management.

Initial patient assessment and comprehensive pain management plan

The first step in CP management is patient assessment: the patient should be evaluated to confirm or make a diagnosis through history, physical examination, and evaluation of laboratory and imaging data. It is not uncommon for patients to be sent to pain specialists with an incorrect diagnosis, thus it is important to assess the patient regardless of prior diagnosis. For example, a patient might be referred for sciatica when they have meralgia paresthetica. Although it is important to determine and diagnose the source of pain or ‘pain generator’, the patient’s psychosocial history should also be assessed before beginning pain management.

Patient assessment should also include screening for the risk of addiction or aberrant drug-related behavior. Using a tool, such as the Opioid Risk Tool, is reasonable (see Appendix, page 109, for Opioid Risk Tool). Opioids are not the most appropriate choice for all patients. For example, patients at high risk for addiction might be better candidates for spinal cord stimulation. Another option for the patient at high risk of aberrant drug-related behavior is buprenorphine, which will be discussed in the following chapters of this book.

Expert insight from the clinic

When assessing CP in the patient with addiction, the patient's addiction must be addressed before pain can be rationally managed. In my experience the patient with addiction will use their pain as a mechanism for allowing themselves to abuse their opioids. This is not necessarily a conscious act by the patient. Some patients with CP and addiction at my clinic have found that once their addiction is under control they state: "I do have pain but I don't have as much pain as I told myself." This type of self-realization can occur if the addiction is brought under control. It is important to understand that addiction creates a drive in the patient's primal brain centers that prioritizes drug use over basic human needs, like eating. Effectively, their addiction can 'hijack their brain' and the need for the drug overrides fear of consequence and harm. With this in mind, a patient can exaggerate their pain to get more opioids since they are not thinking rationally but are focusing on their current need for more drugs. Thus, once an addiction is under control, the patient will often more accurately assess their pain levels.

Studies have shown that addiction affects not only the reward circuit, but also circuits involved with memory (conditioning/habits), motivation (energy, drive), executive function (inhibitory control, salience attribution, decision making), mood (stress reactivity and hedonic state), and interoception (internal awareness) [21]. Thus, it is not surprising that the treatment of addiction is complex, requiring biological and psychosocial approaches. Likewise, CP is a complex illness and it requires a similar approach. Therefore, it should not be surprising that many of the techniques used to manage addiction are also used in CP management (eg, medications, psychological approaches [CBT, physical exercise and modalities, spiritual and family counseling and support groups]).

Treatment of pain and/or addiction can also depend upon the patient's ability to understand and adhere to the treatment plan. For example, if a patient has difficulty following directions on how to use their medications, a physician might consider minimizing the use of regular release opioids for COT. Likewise, with patients who have a history of drug and/or alcohol abuse, the physician may plan to shorten the length of time between follow-up visits. Similarly, psychiatric disorders, such as depression, bipolar disorder, or schizophrenia, may change the pain management plan due to the patient's behaviors or current therapeutic regimens. Thus, treatment of CP begins with taking a biological and psychosocial history followed by development of a comprehensive pain management plan. Such a plan will address psychosocial issues that might affect treatment outcome while addressing the biological source of pain (eg, inflammation, nerve damage, central sensitization).

Trial of opioid therapy

Before a patient begins a trial of opioid therapy for CP, the physician must decide whether or not the patient is an appropriate candidate for

long-term opioid therapy (ie, COT). In general, patients who are candidates for COT will have exhausted all other avenues of treatment. They will have failed to achieve adequate pain relief with nonopioid medications and procedures. Often a patient will be referred to the pain clinic on low-dose opioids but without having ever been trialed on antidepressants or antiepileptics. Their current opioid medications can be maintained while antiepileptics and/or antidepressants are titrated. If not already done, physical therapy, CBT, and interventional procedures can be undertaken to ensure that nonopioid pain management is optimized before proceeding to a trial of opioids. Additionally, the physician must arrive at a working diagnosis first before beginning an opioid trial, as discussed above.

Once a patient has been deemed appropriate for a trial of opioids, the physician should emphasize to the patient that the trial is being conducted to ascertain whether the patient obtains enough pain relief to make long-term treatment with opioids an acceptable risk. During the opioid trial, side effects such as constipation or nausea should be treated appropriately. If patients do not achieve adequate pain relief or if side effects are unacceptable (cannot be controlled), opioid treatment should be stopped (ie, the trial has failed).

If the patient is opioid naïve, it is customary to initiate treatment with a short-acting opioid (SAO) or with the lowest dose of transdermal buprenorphine if a continuous around-the-clock opioid is needed. Tramadol, a weak mu-agonist and serotonin-norepinephrine reuptake inhibitor, or the stronger mu-agonist tapentadol (which additionally has prominent norepinephrine reuptake inhibition and minimal serotonin effect) can also be used [22]. In many cases, the patient will have tried one or more mu-agonists prior to being referred to a pain specialist for CP management. Knowledge of the effects of these previously tried opioids can be used as a guide for choosing an initial drug and dose. If the patient is already taking a SAO on a daily basis and around-the-clock opioid therapy is indicated, then the physician can proceed directly to a long-acting opioid (LAO).

The medication must be tailored to the patient's pain pattern and to the patient's individual needs. For example, if the patient mainly has

pain during their waking hours, when they are most active, then the majority of the opioid dose can be delivered during the day. This use of different doses in the morning and evening is often referred to as ‘asymmetrical dosing’. Other factors may suggest asymmetrical dosing as well, for example, if a patient has sleep apnea, a physician might consider prescribing a LAO with an 8- or 12-hour duration in the morning while omitting the night-time dose. If the patient has minimal pain at rest and significant pain with activity, a SAO given on an as-needed basis might better match the patient’s pain pattern. If the patient has had severe nausea with a particular opioid in the past but has tolerated another, then starting the trial with the well-tolerated opioid would make sense. Constructing the patient’s opioid regimen requires attention to the pain (temporal pattern) and to the patient’s individual needs.

Expert insight from the clinic

If the patient is in severe distress, the physician can consider early initiation of opioid therapy; however, the physician may want to treat this severe pain as an episode of acute pain in addition to CP, and may use a time-limited course of opioids while initiating nonopioid therapies. Physicians must remember that CP, by definition, is a long-lasting (chronic) disorder, and if a patient has, for instance, had this same severe pain for the past 5 years, then this pain is not suddenly an emergency. In my experience it is not uncommon for patients with CP to rate their pain as a 10 of 10 on the Numerical Rating Scale (Table 2.1) [23], where 0 represents no pain and 10 represents the worst imaginable pain, and demand immediate relief even though their pain has not changed in years. These patients are prone to catastrophizing, and they often need CBT as part of their treatment plan. If the patient’s thoughts, feelings, and behaviors about their symptoms are disproportionate or excessive this can lead to inappropriately aggressive medical or surgical treatment. The physician and multidisciplinary team may need to protect such patients from harm from other physicians who may perform surgery, interventions, or provide inappropriate doses of drugs in an attempt to relieve symptoms that are unlikely to respond to medical or surgical interventions [24]. Some of these patients may have what was in the past known as somatoform pain disorder, now known as somatic symptom disorder. Other patients may not meet the full criteria for somatic symptom disorder but their presentation may have features that suggest there is a significant psychological component to their pain (resulting from limbic amplification). This ‘psychological component’ does not mean that the patient is consciously faking their pain (malingering) or that the patient is not experiencing pain. Although the healthcare professional may see their symptoms as magnified, the pain is real to the patient. Even when no physiologic or anatomic etiology for the pain can be found and the pain may be suspected to be an expression of an underlying emotional distress, it is still pain to the patient. When managing these patients it is best to describe the condition to the patient in a manner that avoids any implication of a psychosomatic illness. They should be told that there is no cure for their illness but that treatment can help them to feel better and to lead a more productive and functional life. Their distress should be acknowledged and CBT may be arranged. The patient may be told that though their pain may not be cured, the CBT may help them cope with it better.

Opioids are titrated until the desired effect is achieved or until side effects limit further dose increases. The rapidity of the dose escalation depends upon the patient's response to opioids, the drug's recommended titration scheme and its limitations, and the patient's needs. Based on pharmacokinetics, some drugs can be titrated daily (eg, morphine) and others should only be increased weekly (eg, methadone, transdermal fentanyl). The patient should be assessed for side effects prior to each

Numeric pain level	Description of pain for patients
0	No pain. Feeling perfectly normal.
Minor: Does not interfere with most activities. Able to adapt to pain psychologically and with medication or devices, such as cushions.	
1 (very mild)	Very light barely noticeable pain, like a mosquito bite or a poison ivy itch. Most of the time you never think about the pain.
2 (discomforting)	Minor pain, like lightly pinching the fold of skin between the thumb and first finger with the other hand, using the fingernails.
3 (tolerable)	Very noticeable pain, like an accidental cut, a blow to the nose causing a bloody nose, or a doctor giving you an injection. The pain is not so strong that you cannot get used to it. Eventually, most of the time you do not notice the pain. You have <i>adapted</i> to it.
Moderate: Interferes with many activities. Requires lifestyle changes but patient remains independent. Unable to adapt to pain.	
4 (distressing)	Strong, deep pain, like an average toothache, the initial pain from a bee sting, or minor trauma to part of the body, such as stubbing your toe. So strong you notice the pain all the time and <i>cannot completely adapt</i> .
5 (very distressing)	Strong, deep, piercing pain, such as a sprained ankle or mild back pain. Not only do you notice the pain all the time, you are now so preoccupied with managing it that your normal lifestyle is curtailed. Temporary personality disorders are frequent.
6 (intense)	Strong, deep, piercing pain so strong it seems to partially dominate your senses, causing you to think somewhat unclearly. At this point you begin to have trouble holding a job or maintaining normal social relationships. Comparable to a bad non-migraine headache combined with several bee stings or a bad back pain.

Table 2.1 Comparative pain scale for patients (continues overleaf).

Numeric pain level	Description of pain for patients
Severe: Unable to engage in normal activities. Patient is disabled and unable to function independently.	
7 (very intense)	Same as 6 except the pain completely dominates your senses, causing you to think unclearly about half the time. At this point you are effectively disabled and frequently cannot live alone. Comparable to an average migraine headache.
8 (utterly horrible)	Pain so intense you can no longer think clearly at all, and have often undergone severe personality changes if the pain has been present for a long time. Suicide is frequently contemplated and sometimes tried. Comparable to childbirth or a severe migraine headache.
9 (excruciating unbearable)	Pain so intense you cannot tolerate it and demand pain killers or surgery, no matter what the side effects or risk. If this does not work, suicide attempts are frequent.
10 (unimaginable, unspeakable)	Pain so intense you will go unconscious shortly. Most people have never experienced this level of pain. Those who have suffered a severe accident, such as a crushed hand, and lost consciousness as a result of the pain and not blood loss, have experienced level 10.

Table 2.1 Comparative pain scale for patients (continued). Scale developed by Jack Harich [23].

dose escalation. It is beyond the scope of this book to provide detailed titration schedules or to discuss the management of opioid side effects during the trial; readers should always refer to the opioid’s prescribing information for further details. Titration regimens for each opioid vary, and physicians should review specific titration plans per opioids when treating a patient with COTs. It should be noted that when dealing with CP there is rarely a need for rapid dose escalation.

Reassessing the patient

Opioid trials may take several weeks to several months to complete. During this time, the physician should monitor pain relief and function versus opioid dose. Generally speaking, as the opioid dose increases pain should decrease, function increase, and quality of life should improve. However, it is common for pain relief to plateau, and further dose increases produce little or no decrease in pain. If there is inadequate pain relief or unacceptable side effects at the plateau point, the trial has failed.

On the other hand, if adequate pain relief is achieved, side effects are minimal or manageable, and function is increased, then the trial may be considered successful. Monitoring for a plateau requires that the physician compare pain relief and function with opioid dose at each visit. If there have been several up-titrations in dose without improvement in pain scores or functional capacity, then a plateau has been reached. On occasion, pain may improve significantly but side effects, such as nausea, mental clouding, or severe constipation, may make the quality of life decline. If these side effects can be managed then the net quality of life may be improved; if they are intractable then the trial will be a failure even though the opioids significantly improved pain.

Currently, there is no scientific definition of ‘adequate pain relief’. As with pain, adequate pain relief is what the patient says it is. If the patient is able to achieve some of their functional goals, they may be happy with a reduction in pain from an 8 of 10 to a 6 of 10. Indeed, a reduction of 2 points on the Numerical Rating Scale is thought to be clinically meaningful [25]. To determine whether the patient’s pain relief is adequate, patients can be asked how much pain relief their medication provides and whether the pain medication improves their quality of life in a meaningful way. If the patient feels that the medication is providing a meaningful improvement in their quality of life, then it can be continued. It is helpful at this point to have a patient’s ‘significant other’ give their opinion on the patient’s self-assessment. Sometimes the patient will think that they are doing well on the medications, but the significant other might report otherwise. The patient may not be aware that they are having side effects, such as slurred speech, sedation, or mental clouding, whereas the patient’s family might be well aware of these symptoms.

While there is no formal definition of ‘adequate pain relief’, it may be conceptualized by using the idea of ‘good enough pain relief’, described by Twycross for palliative care patients. In the hospice setting, Twycross developed the practical concept of ‘good enough pain relief’ where pain relief is ‘good enough’ when the patient can accomplish desired rational goals without undue suffering [26]. ‘Adequate’ or ‘good enough’ pain relief embodies the fact that physicians are not seeking complete pain relief,

which is an important point for the patient to understand. This simple, functional definition can be used to explain to the patient with CP and their family what the physician is looking for during an opioid trial. This can be done by first determining what the patient wants to or needs to do that they currently cannot do because of pain. If these activities are rational for the patient (ie, they can be potentially accomplished by the patient), then they become the functional goals for the opioid trial. During the trial, opioids are titrated until the patient can accomplish these goals, pain relief plateaus, or intolerable (unmanageable) side effects ensue. If the functional goals are accomplished, then the opioids are providing meaningful pain relief and it is reasonable to consider long-term opioid therapy. Since this approach provides an externally observable endpoint, some physicians prefer to use this ‘goal directed’ approach to opioid trials, with pain relief assuming lesser importance than improved function. Surprisingly, some patients have functional improvement (accomplish their goals) but do not report lower pain scores (see Expert insight from the clinic box below). Thus, measuring pain relief alone does not tell the whole story. My typical approach is similar to the goal-oriented trial. However, not all patients who present to the pain clinic for treatment are particularly limited in what they can do by their pain. They work and function despite their pain. They push through their pain to accomplish their goals. These patients are active and engaged in life but they still experience pain, they still suffer, and they want pain relief. With this group, the physician must rely more on the patient’s self-report and less on the achievement of functional goals in deciding whether an opioid trial is successful. In my practice, I try to address this issue by asking the patient: “Is your pain significantly better and is your quality of life improved?” An improved ‘quality of life’ suggests that the patient not only has pain relief but that any side effects from the opioid are trivial or controlled. If the patient answers these questions in the affirmative, the trial is a success.

Failing an opioid trial

If the patient fails the opioid trial, the medication should be tapered off slowly enough to avoid withdrawal. At this point, spinal cord stimulation

or other advanced pain management techniques might be considered.* Sometimes there is no medication or procedure that will significantly reduce the patient's pain. In this situation, physicians can only offer psychological interventions to improve coping skills and they should ensure that comorbid conditions, such as depression, are maximally treated. This aspect of treatment should not be left as a 'last resort' but rather these issues should be addressed from the initiation of treatment. Due to the time it takes for psychological interventions (behavioral or pharmacologic) to achieve maximal impact, these treatments should be initiated as soon as possible in the treatment paradigm. Unfortunately, many patients cannot afford behaviorally oriented treatment. However, where possible, after a patient fails an opioid trial, the pain specialist can continue nonopioid treatments, offering reassurance that if any new treatments come forth that they will be offered to the patient. Thus, the patient is not abandoned and by guiding the patient's treatment, the physician can help the patient avoid wasting time and money on ineffective treatments. Some patients may even come to harm if they relentlessly seek surgery or interventions in desperate attempts to obtain pain relief. This is particularly a risk for patients with significant somatization. Compassionate physicians can share the patient's journey – their *via dolorosa* – and help them avoid coming to harm at the hands of other well-meaning physicians.

Expert insight from the clinic

I have seen some patients who seem to experience a reduction in pain and then increase their activity level until their pain level returns to their previous baseline. These patients may be more interested in the medications empowering effect, where the pain medication allows them to be more active without experiencing more pain than that which they had already become accustomed. In assessing this group's response to opioid therapy, it is important to determine the patient's function and overall quality of life, not just their pain scores.

**It should be noted that due to the risks associated with long-term opioid use, some pain management experts would argue that spinal cord stimulation should be considered before considering long-term opioid treatment. However, each case should be evaluated individually. If a patient's pain is controlled with low-dose opioids (eg, 10–40 mg per day of oxycodone [or equivalent]), then the invasiveness and expense of a spinal cord stimulator does not seem warranted. Other patients might lack adequate insurance coverage and expensive procedures may not be an option. If patients fail to achieve adequate pain relief with NSAIDs, antiepileptic drugs, or antidepressants, opioids may be the only financially viable option for relief. Nevertheless, not every patient will obtain adequate relief from opioids.*

The importance of continual care

Without adequate pain control, many patients with CP drift into meaningless unproductive lives, as they become consumed by their pain. The pain becomes the sole focus of their lives and their main method of manipulating their family and friends into providing the support they need to maintain their sick role. All patients with CP should therefore be encouraged to find something meaningful to do with their time (eg, volunteer work). The more they occupy their time, the less time they have to dwell on their pain; distraction is a well-recognized technique for pain management. Part of the ongoing care of patients with CP is to encourage them to find meaning in their lives and to help families understand how to avoid enabling the sick role; co-dependency and enabling are as much issues in patients with CP as they are in patients with addiction.

Expert insight from the clinic

I have seen patients who left pain clinics after failed medication trials or interventions and subsequently were able to convince surgeons or interventionists that they deserved one more operation or procedure in an attempt to relieve their pain. Some of these patients had amputations, others suffered paralysis, and others had less dramatic complications but none obtained pain relief and all suffered at the hands of well-meaning physicians. Physicians must remember what Dr Arthur Bloomfield (1888–1962) stated so well: “There are some patients whom we cannot help...there are none whom we cannot harm.” It is just as important to manage the patient well who fails an opioid trial as it is to manage the opioid therapy of a patient who had a successful trial.

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