Pain
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PREVALENCE OF PAIN

Pain is the most common reason people seek healthcare [1]. During their lifetime, 90% of Americans will suffer pain of some kind. Over 25 million people will experience acute pain associated with an injury or trauma in a one year time span. As aging occurs, the incidence of pain and the need for treatment is expected to rise.

Chronic pain (also known as persistent pain) is defined by the International Association for the Study of Pain (IASP) as “pain that persists beyond normal tissue healing time, which is assumed to be three months” [2]. Besides being the leading cause of disability, persistent pain affects a person’s overall quality of life including their ability to function and socialize, as well as impacting their family life [3, 4]. Persistent pain in both the pediatric and adult population is often unrecognized and undertreated [5, 6]. Pain in the pediatric population remains poorly managed due to the misconception that children (including infants and young children) do not feel pain in the same way as adults [7]. On the opposite end of the lifespan, older patients are known to be at risk for poor pain management due to inadequate assessment, intolerance of many medications, the interactions of drugs, and multiple co-morbidities [7].

Those who suffer from pain are not the only ones who bear the burden. Society as a whole suffers when a person experiences pain, including those with a bleeding disorder. When a person experiences and is disabled by pain, even for a short period of time; family, friends, schools, employers, and many others bear the brunt of the impact. Although direct costs can often be measured in missed days from work, school, and decreased productivity, the direct costs to the person in terms of pain and suffering are immeasurable. Quality of life suffers, often leading to serious dysfunction with the family and social life.

Nurses are essential in the management of pain. They are invaluable in the initial and on-going assessment, education, evaluation, and reassessment of the patient, their social support system, level of functioning, and the overall treatment plan. Based on their assessment they can make recommendations to the treatment team [7]. Hemophilia nurses can be strong patient advocates in an area where advocacy is greatly needed. An interdisciplinary pain management approach with the underlying goal of helping the patient live a full life is key to success. Treatment does not focus only on the pain. A multidisciplinary team approach requires the patient to be an active participant. The team of health care providers work directly with the person in pain using a variety of measurements, interventions, and strategies for self-management designed to offer a complete program.

Interdisciplinary treatment programs concentrate on biological, psychological, and social factors that serve to sustain and even intensify pain. The treatment in these programs involves the active
participation and coordination of medical specialists from different disciplines with an emphasis on pain management. Team members generally include: physicians, psychologists, counselors, physical therapists, case managers, occupational therapists, nurses, behavioral health and other health professionals. Treatment typically consists of physical therapy, cognitive behavioral therapy, and instruction in self-regulatory skills, augmented with group educational meetings. The objectives include offering skills to reduce muscle strain and sympathetic nervous system stimulation by recognizing and reframing ideas about pain and coping. The patients are guided in conquering fear and avoidance of behavior associated with pain and in improving physical strengthening and conditioning. [8].

Due to joint bleeds and/or dysmenorrhea, pain is a common occurrence and a known complication in the bleeding disorders population. At a young age persons with hemophilia (PWH) begin experiencing pain. This is often a combination of acute pain secondary to bleeding episodes as well as persistent (chronic) pain as they develop hemarthrosis. The associated pain may accumulate after years of hemarthroses, especially if they have inhibitors or as they age. The use of factor replacement prophylaxis over the past decades has increased the life expectancy for a PWH dramatically. Multiple co-morbidities of aging have accompanied this increase in life span, including persistent pain [9].

PWH frequently experience acute pain concurrently with persistent pain, thus are unusual in their presentation compared to the general population [3, 10, 11]. This leads to the difficult to treat phenomena of acute on persistent pain for which a multimodal approach is recommended [2,6,7]. Multimodal therapy is the use of different classes of drugs with varying mechanisms of action to produce a synergistic effect while minimizing dosing and potential side effects and maximizing efficacy. It also includes utilizing alternative modalities of therapy such as non-pharmacologic strategies along with pharmacologic strategies.

Overall, pain is an undertreated phenomenon. This is true within the general population as well as the bleeding disorders population [1, 12]. Although we can assign many barriers to inadequate pain assessment and treatment, it is the ethical and moral responsibility of all providers to assure that our patients receive the best care possible, including pain management [1, 13]. Untreated and inadequately treated pain has many biopsychosocial as well as financial ramifications. Although staff members of hemophilia treatment centers (HTCs) are generally not trained in advance pain management, that does not excuse them nor relieve them of the responsibility to properly assess pain, initiate a pain management program, and refer to a pain specialist if required. [1; p.10].

As stated by B.E. Cole in Clinical Pain Management: [1] “The failure to relieve pain is national tragedy. Many barriers are described for why this happens, but none excuse the failure to relieve pain. While practitioner, patient, and system-related barriers may increase the challenge for relieving pain all barriers can be overcome and relief provided.”
ACUTE AND PERSISTENT PAIN:

DEFINITION OF PAIN

“An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”

“Pain is always subjective. It is unpleasant and is an emotional experience.” [14, 15]

ACUTE PAIN

- Pain that has lasted less than 3 months.
- Cause is often obvious, such as a surgical intervention or trauma
- Generally results from disease, inflammation, or injury to tissues.
- Onset is quick (ex: after trauma or surgery)
- May be accompanied by anxiety or emotional distress.
- Cause can usually be diagnosed and treated
- Usually analgesic medication can be reduced in a short period and the patient will return to his/her baseline pain status.
- Self-limiting; in rare instances can become chronic.

PERSISTENT PAIN [16]

- Severe discomfort that can extend past 6 months
- Causes may be unknown
- Treatment is focused on pain reduction, increased function, and improved quality of life
- Can be classified as a disease process itself
- Can be worsened by environmental and psychological factors
- May co-exist with other chronic pain conditions
- May not see the actual injury or physical responses such as changes in heart rate, blood pressure, grimacing and crying out
- Maintenance of daily function is important
- Considered non-life threatening

HEMOPHILIA PAIN

Hemophilia pain often starts early in a child’s life, initially presenting as acute pain due to bleeding or to procedures associated with bleed management (ex: intravenous infusions) [11]. Pain in a bleeding joint can result in pressure against the synovial lining and adjacent tissue and from the inflammation caused by trapped blood. Repeated bleeding into the same joint can result in the development of a target joint and progression to hemophilic arthropathy (destruction of the bone), which may cause significant persistent pain. [3]. In some instances, a different type of pain emerges that persists long after bleeding episodes have subsided and appears to be neurogenic in nature. The long-term consequences of persistent pain adversely affect family
dynamics and may be linked to limited job opportunities, low self-esteem, loss of independence, and poor quality of life. Pediatric hemophilic pain can be especially challenging.

Fritz, McKernan and Marandola, [17] surveyed HTC nurses in the U.S. to:

a) Define and quantify, the HTC nurses’ experience in recognizing, evaluating, and managing hemophilic pain in children

b) Develop themes and determine gaps in the overall management of pain by illustrative quotations from HTC nurses.

They reported their findings as:

1. Disparity of perception and understanding of hemophilic pain experience amongst providers (nurses)

2. Disparity of perception and understanding of hemophilic pain experience between provider and patient. It also found a higher percentage of provider (nurse) discomfort in managing chronic pain. The survey concluded that improved two way communication amongst providers and between patient and provider was indicated along with education and preventative techniques.

3. More work is indicated to develop a hemophilic pain management model for the patient.

PATHOPHYSIOLOGY OF PAIN

PAIN PATHWAY

- The science of pain is a complex process.

- Painful stimuli are transmitted from the point of injury through nerves to the spinal cord and ultimately to the brain. However, as that process occurs, there are another complex set of processes that modulate the individual pain experience.

1. Transduction
   a) Process where afferent nerve endings (A-beta, A-delta and C fibers in the skin and tissue) participate in translating noxious stimuli into nociceptive impulses.
   b) A-beta fibers (myelinated, large diameter) respond mostly to light touch and movement – such as vibration.
   c) A-delta fibers (fast, myelinated, small diameter) and C fibers (slower, unmyelinated) respond to painful (noxious) stimuli.
   d) Any fiber that responds to painful (noxious) stimulation is classified as a pain fiber, also known as a nociceptor.

2. Transmission
   a) Movement of impulses from the nerves to the brain (sent through dorsal horn of spinal cord and then along sensory tracts to the brain)
   b) The primary afferent nerves (mostly A-delta and C fibers) in the periphery send and receive chemical and electrical signals to their counterparts in the spinal column.
c) The intensity and quality of pain is determined by the somatosensory cortex (sensory aspect of pain).

d) The emotional response is determined by the frontal cortex and the limbic system.

3. **Modulation**
   a) This is the process of dampening or amplifying the pain signal.
   b) Probably takes place at multiple levels but primarily in the dorsal horn of the spinal cord.
   c) The dorsal horn is rich in opioid receptors (mu, delta, and kappa).
   d) Modulation can be activated by many modalities including the use of opioids (endogenous and non-endogenous), neurotransmitters such as serotonin and norepinephrine, electric stimulation, stress, and suggestion.
   e) The major ascending tract, the spinothalamic tract (STT) ultimately divides in two different pathways as it approaches the thalamus, lending to the sensory/discriminative aspects of pain perception and/or the affective/motivational aspects of pain perception.

4. **Perception**
   a) The conscious awareness and subjective experience of pain.
   b) Results from the interaction of transduction, transmission, modulation, psychological and other characteristics of the individual.

**Gate Control Theory**

- A model of pain modulation that ties all four of the above steps together
- Initially proposed by Melzack and Wall in 1965 [18].
- Proposed the existence of an internal capacity to diminish or intensify the degree of perceived pain through the adjustment of incoming impulses at a neurological gate located in the spinal cord.
- The integration of these inputs (sensory neurons, segmental spinal cord level and the brain) differentiates between types of fibers carrying pain signals, determining whether the gate will be opened or closed.
- The “Gate” can be manipulated by psychological variables (emotions, thoughts, distraction, and stress reaction), pharmacologic measures (altering the transduction, transmission and modulation) or psychological intervention.
- Gate control theory is often used to explain phantom or chronic pain.

**Normal Pain (Nociceptive Pain)**

1. Classified as somatic (bone, joint, muscle, skin or connective tissue) or visceral (organs, such as the GI tract) pain.
2. Nociception
   - When pain receptors (nociceptors) are damaged or irritated they transmit the signal of pain to the brain.
   - Nociceptive pain is usually time limited in that as the tissue heals the pain resolves (except for arthritis pain).
• Often described as well localized, constant, aching and throbbing in quality.
• Usually responds well to opioids

ABNORMAL PAIN

Pain that occurs in the context of a nociceptive system that has been altered by tissue damage or other processes.

1. Inflammatory pain
   • Sensation resulting from injury to a somatic tissue (e.g., skin, muscle, bone) customarily followed by an inflammatory reaction (ex-acute injury).
   • The inflammatory response releases substances that cause “sensitization” of the peripheral pain fibers (nociceptors). Often these pain fibers will develop a lower threshold for firing resulting in more frequent firing than when in a normal state. When this occurs, even normally non-noxious stimuli (light touch or contact with clothing) will cause pain.
   • After tissue healing, the pain generally resolves.
   • However, in states of ongoing inflammation or injury, such as hemophilic joint bleeding, where inflammation may resolve but leave permanent anatomic alterations, (ex: joint damage produced by hemarthropathy) chronic pain may result even though inflammation disappears or becomes unnoticeable.

2. Central sensitization
   • The consequence of continual or frequent and excessive pain signals from the periphery overwhelming the central nervous system.
     o Often referred to as “wind-up”
   • This bombardment of pain signals causes long-term changes in the central nervous system leading to persistent amplification of those pain signals.
   • Central sensitization is one suggested mechanism where a normally harmless stimulus produces pain.

3. Allodynia
   • The phenomenon of normally harmless/painless stimuli (such as light touch) producing pain.

4. Hyperalgesia
   • Exaggerated response to normally painful stimuli.
   • Distinction between primary and secondary is important when deciding on treatment.
   • To effectively treat central sensitization pain, hypersensitivity must be addressed during the clinical assessment of the patient. Therapy that targets the mechanisms of hypersensitivity, if present, rather than mechanisms of nociception, must be used to try to alleviate symptoms
     a) Primary hyperalgesia
        • Occurs at the site of injury
        • Characterized by a lower pain threshold, spontaneous pain, and increased sensitivity.
        • Usually features thermal and mechanical hypersensitivity.
b) **Secondary hyperalgesia**
   - Hyperalgesia occurring outside the area originally injured
   - Thought usually to be a consequence of central sensitization.

c) **Neuropathic pain**
   - Pain due to damaged or dysfunctional nerves.
   - The pathophysiology of neuropathic pain can have both peripheral and central mechanisms that generate abnormal signals with abnormal excitability.

d) **Dysfunctional pain**
   - Pain and abnormal sensitivity not associated with noxious stimulus, tissue damage, inflammation, or identifiable lesion to the nervous system.
   - May include fibromyalgia, tension-type headaches, migraines, irritable bowel syndrome.
   - Individuals with these syndromes share a number of common characteristics, including hyper-vigilance to sensory stimuli, exaggerated experience of a diverse array of sensory stimuli, high prevalence of associated conditions and in some cases abnormal biomarkers (example: high substance P levels in spinal fluid).

e) **Referred pain**
   - The perception of pain in a body part in which it did not originate.
   - The mechanism of referred pain is thought to be convergence of primary afferents from different locations onto the same spinal cord neurons. The spinal nerves serve both deep tissue structures as well as skin structures leading to mislocation of the perception of the pain signal.

Research continues to evolve on the differentiation of the different types of pain and response to treatment associated with specific type of pain. All of these factors are considerations when treating hemophilic pain.

**PAIN ASSESSMENT**

**Goals of Therapy**

1. The first step in pain assessment in the bleeding disorder patient is to identify the goals of therapy which should include:
   a) Increase function
   b) Minimize side effects

2. **Functional pain goal- a goal based on achieving an activity or quality of life issue.** This provides a clear direction as to the planned desired improvement. Keep in mind, if a person with hemophilia has been experiencing persistent pain for many years, a goal of “no pain”, or 0/10 may not be a realistic goal. The goal should be a reduction of the current pain level or, preferably, improvement in the level of functioning [19].

3. Measurable outcomes are necessary to provide a clear goal.
4. It is important to use a pain scale that works for the individual patient and use it consistently. Some patients find that a numeric rating scale (0-10) reduction can be visualized, whereas others may find a decrease in the percentage (%) of pain may be easier to visualize.

5. Suggested measurable outcomes (goals) include:
   a) Pain intensity decreased
   b) Reduction of medications as pain improves
   c) Improved sleep
   d) Improved functional activities
   e) Increased involvement in social activities [15].

6. Development of measurable goals can incorporate the “SMART” mnemonic [20]
   a) Specific
   b) Measurable
   c) Achievable
   d) Realistic
   e) Time-based

**Barriers**

- Barriers to effective pain management should be explored as potential barriers can affect goal achievement.
- The Patient Medication Assessment Questionnaire (PMAQ) barrier assessment can assist in identification of where barriers may occur. [21, 22].
- Identification of potential barriers can provide an opportunity for increased education in the arena of pain management.
- Patient perceived barriers: [15, 23, 24, 25, 26, 27].
  a) Worry about harmful effects
  b) Fear of addiction
  c) Misunderstanding between psychological addiction vs. physical tolerance/dependence vs. tolerance
  d) Fear of side effects
     1. Drowsiness
     2. Nausea
     3. Constipation
     4. Potential mental cloudiness
  e) Immune system harm
  f) Save pain medication until they “really need it”
  g) Pain is “part of being a person with hemophilia”
  h) Hesitant to report pain as may mean progression of disease
  i) “Good patients” do not complain
  j) Pain will distract provider from addressing underlying problems
  k) Inability to afford medication
  l) Lack of insurance
  m) Restrictive insurance formulary
  n) Fear of how perceived by others
o) Family & friends perceptions
   1. Potential negativity, stigma, distain
   2. Pressure from family/friends to halt use of prescribed pain management
p) Colleagues perceptions
q) Fear of reprisals
r) Drug testing
s) Afraid to use sick time

• Provider barriers include: [15, 23, 26].
  • Lack of education regarding pain management strategies
  • Lack of knowledge regarding pain experience
  • Fear of patient addiction/tolerance if opioids are utilized
  • Fear of patient diversion of opioids
  • Fear of prosecution if patients utilize opioids for pain management.

• System/institutional barriers [15, 23]
  • Pharmacy may not have medication in stock
  • Restrictive hours of pharmacy
  • Pharmacist knowledge
  • Cost of medications
  • Provider attitudes
  • Pharmacist attitudes

ADHERENCE

• There are many dimensions of adherence that can affect a patient’s management of pain which can include:
  • Social & economic
  • Healthcare system
  • Condition related
  • Therapy related
  • Patient related

ASSESSMENT

• The first and best assessment is the patient’s reported level of pain [19] This is followed by:
  a) Potential causes of pain
  b) Pain behaviors
  c) Surrogate report
  d) Response to analgesic trial.

• There are 7 steps to appropriate pain assessment: [15]
  a) Location of pain
b) Description-use of words to describe the pain experience  
c) Intensity-pain rating scales, functional pain goals  
d) Duration—how long does it last  
e) Alleviating/aggravating factors—what makes it better, what makes it worse, what previous treatments have been trialed that work or don’t work.  
f) Associative factors—what other symptoms are noted, such as nausea, depression, anxiety  
g) Impact of pain on life—ability to sleep, work, socialization, sexual activity, hobbies, activities of daily living

- The use of assessment tools can be helpful in a patient determining the level of pain and function. A non-exhaustive list includes; [15]  
a) Verbal Descriptor Scale (VDS)  
b) Numeric Rating Scale (NRS)  
c) Revised Faces Pain Scale (FPS-R)  
d) Wong-Baker Faces Scale  
e) Iowa Pain Thermometer (IPT)  
f) Pain Screening Tool Score  
g) Pain logs (See Appendix 2)

PHARMACOLOGIC APPROACH TO PAIN MANAGEMENT

In 2009 a multidisciplinary panel of experts from the American Pain Society (APS) and the American Academy of Pain (AAPM) convened to develop guidelines for the use of opioids in the chronic non cancer pain (CNCP) population [2].
- With so few studies addressing the pharmacologic management of pain in the bleeding disorders population these guidelines, coupled with the stepwise approach for analgesic administration recommended by the World Health Organization (WHO), are the closest recommendations providers currently have to assist them in the management and treatment of pain in the bleeding disorders community [2, 7].
- The World Health Organization (WHO) ladder was originally designed to guide the care of patients with cancer pain through the appropriate section of an analgesic for the pain intensity along with individualized dose titration. In more recent years, it has also been utilized for those with persistent pain [7].
- Cupido, Hayes & Campbell [6] recently released opioid guidelines for CNCP in children and youth that could also be used in the pediatric bleeding disorder setting
- Whenever a patient is being considered for pharmacologic management of pain, universal precautions of pain management should be reviewed (Table 1).
- A multimodal approach referred to as the 3 P’s of Pain Management—psychological, physical, and pharmacologic—is important when treating any type of pain [6].
- Multimodal care addresses the biopsychosocial aspects of pain by targeting both the underlying pain mechanisms as well as the associated symptoms while focusing on the goal of maximizing function and improving quality of life.
- See WHO pain ladder: Diagram 1.
In this section we will focus on the pharmacologic aspect of pain management.

**TREATING MILD PAIN**

*Acetaminophen*

- The first level of the WHO ladder identifies acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) for mild pain.
- The literature shows the most frequently used medications by PWH are acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) [7, 12, 29, 30].
- Both of these analgesics have a ceiling effect (more drug does not equate to increased pain relief – their doses are limited).
- When using acetaminophen, caution needs to be taken in those with co-morbid liver disease (such as hepatitis), with the co-administration of alcohol, or in combination medications that also have acetaminophen to avoid overdose [31].
- In 2006, Watkins et al. [32] studied healthy subjects using acetaminophen for 14 days. He noted significant hepatic transaminase level elevations in more than 30% of the participants. Based on this study, the American Liver Foundation recommended limiting daily dosages of acetaminophen to 4g/day [33].
- Wallny et al. [28] describe an analgesic effect from factor that cannot be explained.

*Non-Steroidal Anti-Inflammatory Drugs*

- NSAID use in the bleeding disorder population remains controversial. Sparse evidence is available evaluating the risks and benefits of standard NSAIDs alone vs. COX-II inhibitors alone vs. NSAIDs compared to COX-II inhibitors.
- As with other studies, COX-II inhibitors have been shown to have less incidence of GI bleeding in the hemophilia population [34].
- A few studies, including some from outside the United States, have demonstrated a reduction in pain, a decrease in factor use, and relief of chronic synovitis with the use of COX-II inhibitors [34, 35, 36, 37].
- If acetaminophen or a NSAID is utilized, the medication should be given on a regular schedule for both pediatric and adult patients experiencing an acute pain crisis or persistent pain [2, 6].
- If NSAIDs (non-COX-II) are used, factor replacement should be adjusted to reflect the use of this medication.
- Liver and kidney studies should be monitored on a regular basis.
- Based on newer clinical trials as well as clinical observation, the American Geriatric Society recommends that NSAIDs and COX-IIIs be considered rarely, and with extreme caution, in highly selected individuals [38].
- The AGS guidelines recommend that all patients with moderate-severe pain or diminished quality of life due to pain should be considered for opioid therapy, which may be safer for many patients than long-term use of NSAIDs [38].
TREATING MODERATE AND SEVERE PAIN

Initiating Opioids

• When pain has become moderate to severe in nature, is adversely impacting a person’s function or quality of life, previous trials of non-opioid strategies have failed, and the benefits of opioid treatment have been determined to outweigh the burdens of treatment, the WHO ladder suggests an opioid trial.
• If the provider and the patient agree that the benefits of opioid therapy outweigh the risks then the option of a trial should be considered.
• This trial involves the use of opioids either as single agents or in combination with adjuvants [2, 6].
• Chou et al. [2] recommend all patients considered for opioid therapy undergo a thorough evaluation including a history and physical, appropriate diagnostic testing and imaging, and screening for the potential of substance abuse or misuse using the Screener and Opioid Assessment for Patients with Pain (SOAPP, Version 1 or R-revised) or the Opioid Risk Tool (ORT) (See Appendix 1).
• Previous unsuccessful trials of non-opioid medications and non-pharmacologic strategies should be documented thoroughly.
• A medication or treatment agreement should be signed outlining the goals of therapy, risks and benefits of treatment (including complications and side effects), and responsibilities and expectations of both the patient, parents (if a pediatric patient) and provider (See Appendix 2).
• The main goals of therapy should be improvement in function (physical, psychological, social, and occupational) as well as improvement in quality of life [37].
• All patients, pediatric as well as adult, exhibit wide variability to opioid dosage and metabolism.

Opioid Dosing

• There are no set rules for establishing a beginning dose, how quickly to escalate the dose, or what the upper dose limits are for each patient.
• It is generally best to “dose to effect” by starting with a low dose of a short acting opioid (exact opioid is up to the provider, there is no evidence that one opioid is superior to another) and slowly increasing the dose until adequate analgesia is obtained or unacceptable side effects require re-evaluation of therapy [2, 6, 37].
• Mu agonist opioids do not have a ceiling effect as do acetaminophen or NSAIDs.
• The upper dose of a mu agonist opioid is limited only by side effects.
• If long term use is warranted, once the patient has achieved a stable dose it may be appropriate (but not a requirement) to convert to a long acting form of an opioid.
• Take the total 24 hour dosage of the short acting medication and convert to the same dose in a sustained release preparation.
• If necessary, a short acting medication may be continued for break-through pain or an acute pain crisis.
• Refer to equianalgesia charts when converting from one opioid to another [2, 6, 37] (See Table 2)
• Studies have shown that many patients must switch opioid medications at least once, sometimes as many as three to four times, before achieving effective analgesia [40]. This is referred to as opioid rotation [2].
• As new research emerges, new drugs and new classifications of drugs are becoming available. These include different formulations, different methods of administration, and different mechanisms of action. It is important to understand the formulation of the long acting drug and educate patients to avoid any potential drug related mishaps (such as cutting or crushing a medication that shouldn’t be cut).

Methadone
• Although methadone is an older drug, its use has increased in recent years.
• Unlike other mu agonist drugs, methadone has both mu and delta receptor agonist activity.
• It is a racemic drug with one isomer acting as an opioid agonist and the other as an NMDA (N-methyl-D-aspartic acid) receptor antagonist.
• NMDA is known to be a “wind-up” protein which can promote pain. If methadone blocks this receptor than it has the potential to block pain at multiple sites – at the mu opioid receptor site as well as at the NMDA antagonist site.
• Thus it is thought to help with treating neuropathic pain [41].
• Methadone is very inexpensive which makes it attractive to patients and providers.
• It does not have any active metabolites so can be used by those with renal and liver disease and it can be given via multiple modalities (sub-q, oral, rectal, and IV).
• The disadvantages to its use are its highly variable half-life (up to 150 hours), slow elimination, multiple drug-drug interactions that affect metabolism, and the potential for cardiac arrhythmias (QT prolongation and torsade de pointes).
• Dose escalation is difficult due to the half-life and elimination issues.
• Converting from one opioid to methadone requires a conversion table specific for methadone [42, 43]. (See Table 2)

Codeine
• Codeine, a pro-drug dependent on the P450 cytochrome for metabolism to morphine, has unpredictable analgesic effect.
• Many pediatric specialists no longer recommended its use.
• Depending on how the patient metabolizes the P450 2D6 cytochrome (slow vs. ultra-rapid) will determine the analgesic benefit (minimal vs. toxic) [37].

Opioid Side Effects
• Most opioid side effects (sleepiness, dizziness, nausea, vomiting, itching, etc.) may resolve with time and are minimized with slow dose escalation.
• Constipation is the most common side effect of chronic opioid use and will not resolve with time.
• It is important to always put the patient on a bowel program with the initiation of opioid therapy [2, 6].

Adjuvants
• Although always thought to be nociceptive in nature, due to the constant irritation of the nervous system from frequent joint bleeds, many PWH may experience neuropathic pain.
• While many drugs are not FDA approved for pain syndromes, adjuvant medications such as tricyclic anti-depressants (amitriptyline, nortriptyline, doxepin), anti-convulsants (gabapentin, pregabalin), and SNRI (duloxetine, venlafaxine) medications have been shown in studies to be effective in various types of neuropathic pain syndromes.
• Anti-depressants and SNRI medications have been shown to be effective in pain management independent of their effect on depression [44].
• When a patient describes pain as sharp, shooting, or burning – a trial of one of these medications may be useful.

MANAGEMENT OF PAIN WITH THE USE OF OPIOIDS

Several definitions need to be understood before the use of opioids in any population. [15, 45, 46].

TOLERANCE

This can occur with the use of medication where decreasing effects are noted of a drug at a constant dose. There is a need for a higher dose of a drug to maintain effect. This is considered a physiological response that is expected. THIS IS NOT ADDICTION [14].

PHYSICAL DEPENDENCE

This is an expected physiologic phenomenon manifested by development of withdrawal syndrome after abrupt discontinuation of therapy. A withdrawal syndrome can be produced by abrupt cessation, rapid dose reduction, and decreasing blood level of the drug. AGAIN, THIS IS NOT ADDICTION.

ADDICTION

Addiction is a primary, chronic neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. Characterized by behaviors that include one or more of the following:
  a) Impaired control over drug use
  b) Compulsive use, craving, continued use despite harm.

PSEUDOADDICTION

Abuse-like behaviors that may develop in response to the under-treatment of pain. When pain is appropriately managed with the correct dosage of medication, this behavior disappears. This is commonly mistaken for addition.

BREAKTHROUGH PAIN
This condition occurs when a patient currently on a pain management program experiences a transient flare of severe pain [47, 48, 49].

1. **Incident Pain** - Pain related to an increase in activity. Treated with a short acting rescue pain medication administered as closely to the event as possible.

2. **Volitional Incident Pain** – pain caused by an activity that can be anticipated and controlled. Ex: To increase activity after an acute bleed, a patient may need to take an immediate release opioid prior to physical therapy knowing it will be painful [47; p 72].

3. **End of Dose Pain** - Pain experienced frequently at the end of a scheduled dose of an opioid. I.e.: A patient on sustained release morphine every 12 hours experiences a pain increase at the 10th hour consistently. This is treated with a dose adjustment.

4. **Idiopathic Pain** - When all other areas are explored and an answer is not forthcoming, occasionally patients can experience higher than usual pain experiences. Disease progression is a consideration that should be investigated.

**Concerns of Substance Abuse (Aberrant Behavior)**

- Pasero and McCafferty [19] report “the likelihood that addictive disease will develop as a result of the administration of opioids to treat pain in a population of patients with no history of addiction or abuse is likely to be below 1%.” (pg, 35). There is no reason to believe this would be different for persons with bleeding disorders. Substance abuse is most often associated with traumatic illness/chronic pain syndrome. Most persistent pain patients on long-term opioid therapy do not develop addiction [50].

- There are many potential predictors of misuse and abuse of opioids. [45]
  1. History of mental health diagnosis
  2. Family history of abuse
  3. Previous history of substance abuse
     a) ETOH, tobacco, cocaine, cannabis
     b) Most consistent predictor of opioid abuse & misuse
  4. Age – literature & validated tools suggest younger age more at risk but does not mean any age is free of risk
  5. Gender is not always a predictor
  6. Chaotic family/social environment – poor support

**Monitoring**

When prescribing an opioid for pain management in any population, close monitoring is essential. Many potential red flags may exist. Repeated behaviors may suggest the need for closer observation and monitoring of the patient. Be alert for inconsistencies in patients’ descriptions and or behaviors. Potential red flags may include: [15, 52]

- Stolen or lost prescriptions
- Resistance to change of medications
- Borrowing medications
- Request early refills
• Escalates dosage without discussion
• Multiple phone calls
• Aggressive complaining
• Use of illicit drugs
• Misuse of prescribed medication (injecting oral formulation)
• Doctor shopping
• Use of multiple pharmacies
• Multiple allergies to pain medications
• Requesting specific pain medications
• Frequent Emergency Department visits for pain issues
• Gross impairment
• Selling prescribed medications
• Violates pain agreement
• Use of pain medication to treat other symptoms such as anxiety and depression

UNIVERSAL PRECAUTIONS

This concept is utilized in the treatment of pain with opioid therapy. Appropriate patient selection, comprehensive benefit-to-harm evaluation, and weighing the potential positive effects of opioids against their potential risks are part of Universal Precautions. Additionally, a thorough risk assessment and stratification should be completed in each and every case [4, 50, 51]. See Table 1.

When preparing to utilize opioids for pain management there are several key points one should become familiar with;

1. Perform due diligence to ensure compliance with regulatory aspects of opioid prescribing
2. Be aware of the ideal steps to ensure due diligence
3. Stay current with State Medical Board rules, federal and local regulations
4. Document ongoing risk management efforts [45]

RISK ASSESSMENT TOOLS

• There are many tools available to assist the clinician in assessing the person at risk for opioid misuse. Find the tool that best works for you and become familiar with its content [45, 50, 51, 52]

1. SOAPP- Screener and opioid assessment for persons in pain
2. ORT- The opioid risk tool
3. STAR-screening tool for addiction risk
4. CAGE- alcohol risk assessment
5. Depressions tools should also be considered as persons with a history of depression may be at higher risk of aberrant use of opioids.
6. A behavioral health or psychiatric evaluation may also be of benefit prior to beginning opioid pain management.
TOOLS FOR MONITORING PATIENTS ON OPIOIDS.

• Any time a person is started on opioid therapy for persistent pain, close monitoring is essential. A commitment on the part of the HTC is necessary to be available for patients as they are assessed and reassessed during therapy [50, 52].

• As always, start low and go slow with close observation

• Pain agreements: This format provides clear guidelines for providers and caregivers with respect to responsibilities of each party. This tool also demonstrates a commitment on the part of the HTC in recognizing the patient’s pain and willingness to address and manage the pain. Key components include:
  a) Clear treatment goals
  b) Use of one provider to order pain medication
  c) Use of one pharmacy to dispense pain medication
  d) Close monitoring will occur
  e) Safe storage of medication
  f) Taking medication only as prescribed
  g) Review the potential side effects of opioid use
  h) Clear consequences if non-adherence is identified

• Pain log—this tool can be particularly helpful for the provider as well as patients to document their pain level, effects of the pain medication prescribed, and the duration of its effects. A written review can help patients visualize the improvement of their pain. It can also help the provider with dose adjustments regarding the frequency or dose of the medications for optimal effects.

• State monitoring programs—these programs provide an electronic monitoring system for quick review of a patient’s opioid use within the state; name of medication, date prescribed, amount prescribed, prescriber information, and which pharmacy filled. Most states have some type of monitoring program.

• Urine drug screening—the use of drug screening can be two-fold; ensure that the medication prescribed is being utilized and screen for other medications or illicit drugs. Drug screenings do carry risks in that false positives can occur. Utilizing an expert in this area should be employed for appropriate interpretation of the results. Decisions should not be made on one positive drug screen due to the possible risk of false positives and should be used to detect ongoing confirmation of diversion of the opioids prescribed [15, 53].

• Pill Counts—regular counting of prescribed medications can ensure that patients are taking the medication as prescribed

• Limited prescriptions with regular office visits—1 month, 2 week supply, 1 week supply. This can be an effective tool for the potential substance abuser.

• REMS (Risk Evaluation Mitigation System) A communication plan developed to inform key audiences about the risks of a drug. Websites are set up to assist providers in a number of areas:
  a) Proper education of the drug being prescribed;
  b) Proper patient selection;
  c) Proper surveillance and monitoring of the medication usage;
  d) Provision of relevant safety messages;
e) An intervention when a signal (deviation from protocol) is detected [4]. Additional information can be obtained: www.fda.gov/drugs/drugsafety/informationbydrugclass/ucml163647.htm

DOCUMENTATION

For optimal management of pain, clear documentation should always occur in the following areas. This also minimizes the potential for censure.

1. Document current pain level utilizing the 7 steps of pain assessment
2. Effectiveness of current management of pain
3. Current pain level – average, highest, lowest
4. Duration of analgesic relief
5. Effect of treatment on sleep/activities
6. Number of office visits/ED visits for pain issues
7. Review of procedures utilized to detect drug diversion

- **Appropriate documentation should include the “6 A’s” of pain management.** [55]
  - What **analgesia** is in use and it **affect**
  - What is the patient’s current **activities of daily living**
  - Are there any **adverse** effects when using the pain medication
  - Are there any **aberrant** activity with the pain medication
  - Regular scheduled **assessment** of the pain
  - Document an **action plan**

ASSESSMENT OF PERSONS ON OPIOID THERAPY

Prior to any refills of medications, a regular scheduled assessment is key. Review of the documentation requirements each and every time will provide necessary information that appropriate effects are achieved as well as monitoring for any potential aberrant behaviors. Persons’ who are at higher risk, should have a more structured environment, providing additional monitoring strategies outlined above and more frequent office visits for closer observation.

NON-PHARMACOLOGICAL PAIN MANAGEMENT STRATEGIES

The exact nature of a patient’s pain experience can be multi-faceted. In order to address these issues, pain management should encompass a “multi-modal” approach [4]. A multimodal approach may include non-pharmacologic interventions, lifestyle changes, complementary and alternative medicine, and physical medicine and rehabilitation [4, 52]. All treatment strategies should include the support of the HTC and be individualized for patients relieve pain.

Non-pharmacological approaches are divided into several categories: [56]

MANIPULATIVE AND BODY-BASED
Massage therapy involves the manipulation of the soft tissues of the body for the purpose of normalizing those tissues.

- There are many techniques which include: applying pressure, holding, and/or causing movement of or to the body.
- There is a concern that deep muscle/tissue massage may increase the risk of bleeding in persons with hemophilia.
- Limited research exists. Explore these options with your patient with an established massage therapist who is familiar with a bleeding disorder. The use of a prophylaxis factor dose prior to initiation of massage may be needed.

1. Chiropractic Therapy

- Very little is known about the use of chiropractic therapy in the bleeding disorders population
- It involves the manipulation of the spine used to treat issues related to the muscles, joints, bone, and connective tissue
- There is a risk of manipulation with the neck
- Patients should discuss this option with their provider and consider if prophylaxis factor may be indicated

**NATURAL PRODUCTS**

Herbal therapies (botanicals), vitamins, minerals, probiotics, etc. can encompass a wide range of oral supplements that can be obtained without a prescription.

- **It is important to ask the patient if these substances are used as they can interfere with other medications or carry an increased risk of bleeding.**
- Natural products do not carry the same rigorous scientific process with testing and development as pharmaceuticals. They have been known to contain a varied strength of the herbal supplement as well as may be contaminated with other supplements.
- Several websites can be used to explore any herbal therapies that patients may trial in an effort to reduce pain:
  a) [http://nccam.nih.gov/health/herbsataglance.htm](http://nccam.nih.gov/health/herbsataglance.htm) [56]
  b) [www.painedu.org](http://www.painedu.org) [57]

**MIND-BODY MEDICINE**

1. Acupuncture is known as Traditional Chinese vs. Western Medicine Theories which “work with natural vital energy inherent within all living things to promote the body’s ability to heal itself”. This therapy can be included in the mind-body, manipulative or energy domains of CAM therapy.

- It is felt that energy flows through pathways call meridians. Each pathway is associated with particular physiological system & internal organs.
- Disease arises due to imbalance of energy or disruption of energy flow.
- A few studies have been performed with persons with hemophilia demonstrating some positives responses [58, 59, 60, 61, 62].
2. **Biofeedback** is initially taught to the patient by a certified specialist.
   • The goals of therapy include: performance of self-relaxation without feedback equipment to use as needed to minimize distress and discomfort.
   • A machine is attached to the patient using audible tones and an immediate digital readout provides instant feedback and control for the patient.
   • It requires frequent sessions that allows the attainment of a general state of relaxation. It is non-invasive, and considered safe in persons with bleeding disorders, although there are no studies to support its use in this population [15, 63].

3. **Spiritual Healing** Rigorous controlled studies indicate there are factors related to spiritual healing beyond suggestion and self-healing that can reduce pain.
   • Spiritual healing is helpful in reducing: headache, back pain, arthritis pain, and postoperative pain.
   • A person’s faith can provide a powerful impact on the pain experience.
   • There are no studies evaluating spiritual healing within the hemophilia population [64, 65].

4. **Cognitive behavioral therapy** The purpose of cognitive behavioral therapy is to examine and clarify the appraisal of pain.
   • With the guidance of a certified therapist, the goal is to change negative beliefs (catastrophizing) to active coping by reviewing past achievements in pain management and encourage ability over disability.
   • This guides the patient to “reframe” the pain experience.

5. **Mind body technique** This technique incorporates the use of guided imagery or distraction to “distract” one’s self from the pain experience.
   • It includes the use of sight, sound, or a combination of senses to imagine a state different than what currently exists.
   • It is completed usually with someone trained in this technique, in a comfortable position in a peaceful setting using the power of the mind to assist with healing.
   • Also incorporated in this technique are relaxation exercises, controlled breathing, and use of distraction. Many of these techniques are available in tape or CD format. With practice, the patient can master this technique [65].

**Energy Medicine**

**Reiki** is based on the idea that there is a universal (or source) energy that supports the body's innate healing abilities.
   • Practitioners seek to access this energy, allowing it to flow to the body and facilitate healing.
   • Reiki appears to be generally safe, and no serious side effects have been reported.
   • There are no reported studies utilizing this method in the hemophilia population [63, 65].
**ADDITIONAL THERAPIES**

1. **Physical therapy** is well known to improve functioning in a variety of ways including:
   - Providing sufficient muscular strengthening & proprioception which can reduce the risk of further joint damage.
   - Specific targeted therapy can focus on:
     - proprioceptive function, gentle strength training with low resistance, improve muscular strength, decrease stress to the joints, restore function & movement

2. **Hydrotherapy** allows the use of exercise in warm water which can decreases pain, decreases muscle spasm, and improves circulation.
   - The buoyancy of the water can also assist with maintenance of range of motion, muscle strengthening, increases exercise tolerance, and improve balance, coordination, and proprioception.

3. **Transcutaneous Nerve Stimulation (TENS)** is a non-invasive method which inhibits transmission of nociceptive information along nerves.
   - TENS provides low intensity electrical impulses to stimulate peripheral nerves allowing the release of endorphins.
   - TENS can provide variable parameters with frequency & intensity. There are limited studies evaluating the use of TENS with hemophilia patients. Anecdotal reports demonstrate some success.

4. **Rest, Ice, Compression, Elevation (RICE)**
   - Resting a joint can reduce pain.
   - The use of ice can provide: superficial vasoconstriction, local anesthesia, decrease rate of conduction of sensory nerves, decrease metabolic rate to specific area, and decrease local circulation

**CONCLUSION**

Chronic, persistent pain affects the physical, psychological, and social dimensions of a patient’s life [4]. It is important to assess a person’s level of stress, anxiety, and/or depression in evaluating the appropriate approach to pain management. Additional therapies may be helpful as you continue to manage the pain experience. There are several tools available for assessment in these areas. See tables and appendices below.
Table 1. Universal Precautions for Pain Management [4, 15, 50]

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>1</td>
<td>Diagnosis with appropriate differential</td>
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<td>2</td>
<td>Psychological assessment, including risk of addictive behaviors</td>
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<td>3</td>
<td>Informed consent</td>
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<td>4</td>
<td>Treatment agreements</td>
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<td>5</td>
<td>Pain and functional assessment</td>
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<td>6</td>
<td>Opioid therapy trial</td>
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<td>7</td>
<td>Reassessment of pain, function and behavior</td>
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<td>8</td>
<td>Regular reassessment of the 6 A’s</td>
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<tr>
<td></td>
<td>a) Analgesia</td>
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<td>b) Activities of daily living</td>
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<td>c) Adverse events</td>
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<td>d) Aberrant drug-taking behavior</td>
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<td>e) Assessment of the current plan</td>
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<td></td>
<td>f) Documentation of the action plan</td>
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<tr>
<td>9</td>
<td>Periodic review of diagnosis and co-morbidities</td>
</tr>
<tr>
<td>10</td>
<td>Documentation</td>
</tr>
</tbody>
</table>
Figure 1. Opioid and Methadone Conversion Tables

Always remember that opioid conversions are only estimates and subject to patient variability. Titration is vital after ANY conversion.

It is recommended to initiate methadone with 50% to 75% of the conversion dose.

If an opioid other than morphine is being converted, first convert that drug to its morphine equivalent dose then to the methadone dose.

TABLE 1: MORPHINE TO METHADONE CONVERSION

<table>
<thead>
<tr>
<th>Oral Morphine Dose in 24 hours (mg)</th>
<th>MS: Methadone</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-99</td>
<td>4:1</td>
</tr>
<tr>
<td>100-299</td>
<td>8:1</td>
</tr>
<tr>
<td>300-499</td>
<td>12:1</td>
</tr>
<tr>
<td>500-999</td>
<td>15:1</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>20:1</td>
</tr>
</tbody>
</table>

TABLE 2: OPIOID ANALGESIC EQUIVALENTS

<table>
<thead>
<tr>
<th>Medication</th>
<th>Oral</th>
<th>Parental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>30 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Hydromorphone (Dilaudid)</td>
<td>7.5 mg</td>
<td>1.5 mg</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>20 mg</td>
<td>N/A</td>
</tr>
<tr>
<td>Hydrocodone (Vicodin)</td>
<td>20 mg</td>
<td>N/A</td>
</tr>
<tr>
<td>Methadone (Dolophine)</td>
<td>Varies depending on previous opioid use (please consult pharmacy)</td>
<td></td>
</tr>
</tbody>
</table>
### TABLE 3: ORAL 24 HOUR MORPHINE TO FENTANYL CONVERSION\(^3\)

<table>
<thead>
<tr>
<th>Oral 24 hour Morphine (in mg/day)</th>
<th>Transdermal Fentanyl (Duragesic) (mcg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-134</td>
<td>25</td>
</tr>
<tr>
<td>135-224</td>
<td>50</td>
</tr>
<tr>
<td>225-314</td>
<td>75</td>
</tr>
<tr>
<td>315-404</td>
<td>100</td>
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<tr>
<td>405-494</td>
<td>125</td>
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<tr>
<td>495-584</td>
<td>150</td>
</tr>
<tr>
<td>585-674</td>
<td>175</td>
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<tr>
<td>675-764</td>
<td>200</td>
</tr>
<tr>
<td>765-854</td>
<td>225</td>
</tr>
<tr>
<td>855-944</td>
<td>250</td>
</tr>
<tr>
<td>945-1034</td>
<td>275</td>
</tr>
<tr>
<td>1035-1124</td>
<td>300</td>
</tr>
</tbody>
</table>

1. Adopted from “Methadone use in the hospice setting: safe, effective, cost efficient” by Toombs, JD
2. Adopted from Principles of Analgesic Use in the Treatment of Acute Pain and Cancer pain, American Pain Society, Fifth Edition
APPENDIX 1. METHOD TO CONVERT AN OPIOID TO METHADONE

Always remember that opioid conversions are only estimates and subject to patient variability. Titration is vital after ANY conversion.

1. Calculate the morphine equivalent daily dose (MEDD)* by converting the current medication used by whatever route to oral morphine in 24 hours (Table 2).
2. Divide the MEDD* by the factor in Table 1 to get the 24 hour methadone dose.
3. Divide the 24 hour methadone dose by three to determine the q 8 hour dose (or divide by two to determine the q 12 hour dose).
4. After determining the conversion dose, discontinue current opioid and begin with the calculated methadone dose and dosing schedule (q 8 hours or q 12 hours).
5. Continue patient’s current breakthrough pain medication (ex. hydromorphone, Oxyfast® etc.) as needed and instruct patient/family to record dose and time given.
6. If pain persists, titrate methadone every 3 days by recalculating dose:
   a. Add up breakthrough medication
   b. Convert to methadone (table 1)
   c. Divide the converted 24 hour dose to determine dose and dosing schedule (refer to step 3)
   d. Add the dose calculated to the current methadone dose
7. Once a stable methadone dose is established, the clinician may wish to use methadone for breakthrough pain.
8. The breakthrough pain dose is calculated by using 1/10th of the total 24 hour methadone dose
9. It is also reasonable and appropriate to use a different short-acting opioid (rapid onset) for breakthrough pain. The short-acting breakthrough dose is calculated using roughly 10% of the MEDD*. 

Sample Opioid to Methadone Conversion:
Patient is currently on Duragesic® (fentanyl) transdermal patch 50 mcg/hr every 3 days
1. Calculate the MEDD*.
2. Using table 3, a 50 mcg/hr patch is equal to 135-224 mg/day morphine.
3. Calculate the average (224+135)/2 = 180 mg of oral morphine. (This is the MEDD*)
4. Convert morphine to methadone by using table 1. Table 1 indicates 180 mg morphine to be an 8:1 ratio.
5. Convert morphine to methadone by using table 1. Table 1 indicates 180 mg morphine to be an 8:1 ratio.
6. Divide 180 mg by 8 to determine the daily dose of methadone (180mg/8 = 22.5 mg/day methadone).
7. To determine the dosing interval divide 22.5 mg by 3 (7.5 mg q 8 hour) or by 2 (11.25 mg q12 hours).
8. Round this dose to nearest 5 or 10 mg depending on individual patient circumstance.

Sample Opioid to Opioid Conversion
Patient is currently taking Oxycontin® (oxycodone controlled release) 100mg po q 12 hours and is being switched to a Duragesic (fentanyl) transdermal patch. What would be an approximate equal analgesic dose of fentanyl (patch)?
1. Calculate MEDD*
   a. Oxycodone po 20 mg=morphine 30 mg (table 2)
   b. Patient is on 200 mg/day oxycodone=300 mg MEDD
2. Using table 3, determine the equal analgesic dose of fentanyl
   a. The MEDD*=300mg.
   b. Table 3 indicates that 225-314 oral morphine/day equals 75 mcg/hr fentanyl.
   c. The approximate conversion from po Oxycontin® 100mg q 12 hour to transdermal Duragesic® is 75mcg/hr q 3 days.
*Morphine equivalent daily dose=MEDD
APPENDIX 2. Opioid Risk Tool Calculator (ORT)

Sex
☐ Male  ☐ Female

Family history of substance abuse
☐ Alcohol
☐ Illegal drugs
☐ Prescription drugs

Personal history of substance abuse
☐ Alcohol
☐ Illegal drugs
☐ Prescription drugs

Age
☐ 16 - 45

History of preadolescent sexual abuse
☐ History of preadolescent sexual abuse

Psychological disease
☐ Attention deficit disorder, obsessive-compulsive disorder, bipolar, schizophrenia
☐ Depression

Total: 0

Total score risk category
Low risk: 0 - 3
Moderate risk: 4-7
High risk: >= 8

How to use Opioid Risk Tool

The Opioid Risk Tool (ORT) provides clinicians with a brief screening method to predict which individuals may develop aberrant behaviors when prescribed opioids for chronic pain. Clinicians can use the ORT to assess and score the following risk factors associated in scientific literature.
with substance abuse: personal and family history of substance abuse; age; history of preadolescent sexual abuse; and certain psychological diseases.

Patients’ scores can be entered on the sticker and posted on their charts, with 0–3 (low risk), 4–7 (moderate risk), or 8 (high risk) indicating the probability of their displaying opioid-related aberrant behaviors.

For further information, please visit www.painbalance.org.

APPENDIX 3. SAMPLE OF PAIN AGREEMENT

Patient/Provider Agreement for Management of Pain

1. I, ____________________________ agree that Dr. ____________________________ will be the only provider that prescribes opioid (also known as Narcotic) pain medications for me. I will not obtain pain medications (opioids) from any other providers.

2. I will use only one pharmacy for my pain medication.

3. I will take the medication at the dose and frequency prescribed by my provider. I agree not to change the dose of pain medication without first discussing it with my provider.

4. I will attend all reasonable follow up appointments, treatments, and consultations as requested by my provider to assist with the management of my pain including:

5. I understand that the common side effects of opioid therapy may include nausea, constipation, sweating, and skin itching. Drowsiness may occur when starting opioid therapy or when increasing the dosage. I agree to refrain from driving a motor vehicle or operating dangerous machinery, until such drowsiness disappears and my provider agrees that I am fit to resume these activities.

6. I understand that using long-term opioids to treat chronic pain may result in the development of physical dependence on this medication, and that a sudden decrease or stopping of this medicine may lead to symptoms of opioid withdrawal. I understand that opioid withdrawal is uncomfortable but not life-threatening. I understand that when I no longer require pain management, I will work with my provider to gradually decrease the dosage to prevent physical withdrawal symptoms.

7. I understand that there is a small risk that I may discover an addiction to the opioids I am being prescribed. I understand that the use of any mood-modifying substances, such as tranquilizers, sleeping pills, alcohol, or illegal drugs (pot, cocaine, heroin) can have adverse effects or interfere with opioid therapy. I agree not to take any of these types of substances while receiving opioid medication for my pain. As such, my provider may require that I have blood or urine drug testing.

8. I agree to be responsible for the safe storage of my medication at all times. I will not give or sell my pain medication to any other person. I will store all pain medications out of reach of children. I understand that lost, misplaced, or stolen medications may not be replaced and that a police report may be required.

9. I consent to open communication between my provider and any other health care professional involved in the management of my pain, such as pharmacists, other specialists, emergency department, etc.

10. I understand that if I break this agreement, my provider reserves the right to stop prescribing opioid medications for me. At that point, I would be tapered safely off the opioids, and if required, referred for specialist treatment with a chemical dependency professional.

11. I will sign a release of information to access records from providers outside of ________ for continuity of care.

12. I will contact the: ______________ during normal business hours; Monday-Friday, 8:00 am to 5:00 pm at the telephone number ________________. I will allow at least 3 working days prior to picking up my prescription. Refills will not be given prior to the planned refill date.

I understand and have reviewed each statement above with my provider.

Patient:_________________ Patient signature: ______________ Date: _____________

Guardian: _______________ Guardian Signature: ______________ Date: _____________

(if applicable) Print

Provider: _______________ Provider Signature: ______________ Date: _____________
APPENDIX 4. SAMPLE PAIN LOG

<table>
<thead>
<tr>
<th>Date and Time</th>
<th>Pain level Scale 0 – 10 (0= none 10 = severe)</th>
<th>Location of pain</th>
<th>Name and Dose of pain medicine</th>
<th>Pain level after 30 minutes (Scale 1-10)</th>
<th>After 1 hour</th>
<th>After 2 hours</th>
<th>Comments</th>
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DIAGRAM 1. WHO PAIN LADDER

- Pain
  - Pain persisting or increasing
    - Non opioid +/- adjuvant
  - Pain persisting or increasing
    - Opioid for mild to moderate pain +/- non opioid +/- adjuvant
  - Pain persisting or increasing
    - Opioid for moderate to severe pain +/- non opioid +/- adjuvant
  - Freedom from cancer pain
REFERENCES


53. REMS www.fda.gov/drugs/drugsafety/informationbydrugclass/ucml163647.htm