

## Chronic and Acute Pain and Pain Management for Patients in Methadone Maintenance Treatment

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**Background and Objectives:** Many individuals receiving methadone maintenance treatment (MMT) for opioid addiction also require treatment for acute or chronic pain, and the presence of pain is known to have a negative impact on patient health and function. However, effective pain management in this population is complicated by many factors, including heightened pain sensitivity, high opioid tolerance, illicit substance use, and variable cross-tolerance to opioid pain medications. This article reviews the recent literature on acute and chronic pain among, and pain treatment of, patients receiving MMT for opioid addiction and discusses the implications for effective pain management. Acute pain management among women maintained on methadone during and after labor and delivery is also discussed, as well as common concerns held by patients and providers about appropriate pain management strategies in the context of methadone maintenance and addiction treatment.

**Methods:** One hundred nine articles were identified in a PubMed/MEDLINE electronic database search using the following search terms: methadone, methadone maintenance, methadone addiction, pain, pain management, chronic pain, and acute pain. Abstracts were reviewed for relevance, and additional studies were extracted from the reference lists of articles identified in the original search.

**Results:** The pain sensitivity and pain responses of MMT patients differ significantly from those of patients not maintained on opioids, and few data are available to guide patient care.

**Conclusions and Scientific Significance:** Rigorous studies are needed to identify and evaluate effective pain management approaches for this unique patient population and to improve patient treatment outcomes. (*Am J Addict* 2013;22:75–83)

abuse of or dependence on heroin or prescription pain drugs.<sup>2</sup> Prescription pain drug abuse in particular has risen significantly in recent years and is a major contributor to the rising national incidence in accidental, drug-induced fatalities.<sup>2–4</sup> Fueling this rise in the abuse of prescription pain drugs is a dramatic increase in the prescription and purchases of opioid analgesics, including methadone, for the treatment of acute and chronic pain.<sup>2–4</sup> This increase presents several unique challenges for patients recovering from opioid addiction, because many patients receiving long-term methadone maintenance treatment (MMT), one of the most successful and frequently used treatments for this condition,<sup>5</sup> also require treatment for co-occurring acute and chronic pain. The number of MMT patients with co-occurring pain is likely to increase as these patients age<sup>6,7</sup> making effective pain management for these individuals an increasing concern.

Unfortunately, few studies have systematically evaluated pain treatment strategies and pain responses in individuals receiving MMT. As a result, pain treatment in this population has largely been guided by clinical experience and expert opinion rather than by controlled experimental evidence.<sup>8–12</sup> Existing research indicates that effective pain management in MMT patients is complicated by numerous factors, including heightened pain sensitivity (hyperalgesia) induced by long-term opioid use,<sup>13–19</sup> increased opioid tolerance,<sup>8,12,13,15,20–22</sup> high rates of licit and illicit drug use by patients to manage their pain,<sup>7,23–26</sup> and conflicting attitudes about pain and addiction treatment held by patients and medical providers.<sup>8,10,12,27</sup> This review summarizes the recent literature addressing these and other issues as they relate to the acute and chronic pain and pain treatment of MMT patients. The implications for pain management in this population are also discussed, and areas where additional research is needed are identified.

This review focuses on recent updates to the field and includes articles published in English from January 2005 to July 2011. A PubMed/MEDLINE electronic database search identified 109 articles using the following search terms: methadone, methadone maintenance, methadone addiction, pain, pain management, chronic pain, and acute pain. All

### INTRODUCTION

Opioid addiction is a chronic illness,<sup>1</sup> with approximately 2.25 million Americans older than age 12 reporting past-year

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relevant studies conducted in humans were included following a review of article abstracts. Older studies were extracted from the reference lists of articles identified in the original search.

## **THE IMPACT OF CHRONIC AND ACUTE PAIN AMONG MMT PATIENTS**

Several studies have indicated that patients receiving MMT for opioid addiction have high rates of pain, with 24–39% of patients reporting moderate to severe pain and 55–61% reporting a current chronic pain condition.<sup>6,7,22,25,26,28</sup> In addition, up to 80–88% of individuals enrolled in<sup>7</sup> or seeking entry to<sup>25</sup> MMT have reported experiencing pain in the past week. In comparison, a nationally representative survey estimated that close to 31% of U.S. adults in the general population have a current chronic pain condition<sup>29</sup> and approximately 26% have experienced pain in the past month.<sup>30</sup> These rates, although significant, are much lower than those reported among MMT patients.

The presence of pain significantly impacts MMT patient health and quality of life, which in turn can affect addiction treatment outcomes.<sup>31,32</sup> Pain, particularly chronic pain, among MMT patients is associated with high rates of healthcare utilization and psychiatric and physical illnesses, including depression, anxiety, somatization, surgeries, and chronic illness.<sup>6,7,22,25,26,28,33,34</sup> In addition, MMT patients with chronic pain report lower social and physical functioning and greater interference with their relationships, work, and daily activities than do those without chronic pain.<sup>6,7,28,33,34</sup> These effects on mental and physical health and activity are associated with an increased likelihood of continued drug abuse during and after opioid addiction treatment<sup>31</sup> and with decreased treatment retention.<sup>32</sup> Moreover, MMT patients with pain are less likely to report satisfaction with treatment than are patients without pain and are less likely to feel that they are receiving an adequate methadone dose.<sup>26,34</sup> Despite these obstacles, individuals with pain conditions can be successfully treated for addiction in MMT programs. One study found that MMT patients with and without pain showed similar declines in illicit substance use over 1 year of treatment and found no significant differences in patient dropout rates or treatment length.<sup>34</sup> However, because of the many negative effects of poorly managed pain on patient health and function, effective pain management is an important consideration in improving patient treatment experiences and outcomes.

## **PAIN SENSITIVITY IN MMT PATIENTS**

### **Opioid Use Induces Heightened Pain Sensitivity**

Not only do individuals formerly addicted to opioids experience high rates of acute and chronic pain, they may also exhibit heightened pain sensitivity resulting from opioid exposure. This phenomenon, called opioid-induced hyperalgesia, is distinct from opioid tolerance and is a known

complication of opioid treatment for chronic pain<sup>35,36</sup> that may develop within a month of initiating opioid use.<sup>37</sup> Several studies report that MMT patients exhibit lower pain thresholds and tolerance levels than do non-MMT controls.<sup>13–18</sup> In addition, one study found a positive association between maintenance methadone dose and patient pain severity and duration, suggesting that MMT patients with pain may receive higher average methadone doses than those without pain.<sup>22</sup> Although pain sensitivity was not assessed, the observed correlation between methadone dose and chronic pain severity may reflect the development of opioid-induced hyperalgesia in some patients.

Interestingly, MMT patients are not hypersensitive to all touch or pain sensations, suggesting that the effects of prolonged opioid exposure on pain result from effects on specific pain pathways. Multiple studies have shown few or no differences between MMT patients and controls in their response to pressure, pain in response to a non-painful stimulus (allodynia), and electrical pain, but have shown differences in sensitivity to hot, cold, and cold pressor pain.<sup>13–18</sup> The cold pressor test is a commonly used experimental pain model in which subjects immerse their hands in a temperature-controlled ice water bath and researchers record the first reported perception of pain (threshold) and the time of hand withdrawal (tolerance). In agreement with earlier reports, a recent study observed that MMT patients had significantly lower tolerances than did control subjects to cold pressor pain but did not exhibit allodynia or differ from controls in cold pressor pain threshold or in electrical stimulation pain threshold or tolerance.<sup>17</sup> Interestingly, this study further reported that non-addicted chronic pain patients receiving long-term opioid therapy with either methadone or morphine exhibited pain responses identical to those of patients receiving MMT. Although the study size was small, and no mention was made of controlling for non-opioid illicit drug use among MMT patients, these results indicate that the opioid-induced alterations in pain sensitivity commonly observed in MMT patients are generally associated with long-term opioid treatment but are not specific to opioid addiction. This suggests that treatment recommendations developed for chronic pain patients receiving long-term opioid therapy may be useful in guiding pain management practices for patients in MMT programs.

### **Opioid-Induced Changes in Patient Pain Sensitivity Are Long-Lasting**

Recent evidence has indicated that differences in pain perception following chronic opioid use may persist for weeks to months following cessation of MMT or opioid exposure. One study of 60 opioid-addicted individuals entering a detoxification program reported that patients exhibited alterations in pain sensitivity that persisted throughout the 4-week program.<sup>38</sup> Specifically, patients undergoing opioid detoxification had lower tolerances for cold pressor pain than did controls and reported lower maximal pain intensities at the time of hand withdrawal, suggesting heightened sensitivity to pain. Although this study did not control for the possible influence of

withdrawal pain on patient pain sensitivity and pain responses, this finding is similar to other reports of increased pain sensitivity in MMT patients. These pain responses are also similar to those observed in chronic pain patients tapered from long-term opioid analgesic treatment<sup>39</sup> in whom the observed reduction in tolerance for cold pressor pain was not associated with changes in clinical pain severity or withdrawal pain. Interestingly, despite exhibiting increased sensitivity to cold pressor pain, patients participating in the opioid detoxification program reported longer times to initial pain perception at the time of hand withdrawal than did control subjects.<sup>38</sup> This observation, together with the finding that patients also reported lower subjective pain scores at the time of hand withdrawal, may suggest that individuals formerly addicted to opioids do not perceive pain more quickly or intensely than do controls but instead react more strongly to the pain they perceive.

A second study<sup>19</sup> evaluating the heat and pain perception of 23 MMT patients who had been detoxified from methadone for at least 6 months supports this interpretation. This study found that former MMT patients exhibited higher heat and pain thresholds than did controls, suggesting decreased pain sensitivity following detoxification. However, former MMT patients reported greater perceived pain unpleasantness than did controls, despite their apparently reduced pain sensitivity and despite reporting similar pain intensity scores as controls. Although former MMT patients were significantly older than control subjects, which could have influenced their pain responses, reported pain unpleasantness, pain intensity, and pain threshold did not vary as a function of age. The observation that former MMT patients subjectively associate more negativity with their pain experience than do non-MMT patients may partially explain the previously reported divergence between objective measurements of pain sensitivity (ie, pain threshold and tolerance) and subjective indicators of pain experience (ie, patient-reported pain intensity scores and perceived pain unpleasantness).<sup>19,38</sup> Although limited in sample size, these reports also indicate that alterations in pain perception and response following opioid addiction or methadone maintenance are long-lasting, even following prolonged opioid abstinence. Importantly, hypersensitivity to the subjective experience of pain may not be caused directly by opioid use or addiction and may reflect the influence of other underlying psychological, physical, or social factors on pain perception. However, regardless of their origin, these altered pain responses should be carefully considered for the treatment of current MMT patients and those undergoing opioid detoxification, and also for patients fully detoxified from opioid use.

### **The Presence or Absence of Chronic Pain Affects Pain Perception among MMT Patients**

One caveat regarding the studies that have examined the pain threshold and tolerance levels of MMT patients is that nearly all specifically excluded patients with pain conditions or did not differentiate between patients with and without pain. However,

the presence or absence of chronic pain in patients maintained on methadone may have a significant effect on their pain perception. In a study of 31 MMT patients who were formerly addicted to heroin and stably maintained on methadone for at least 6 months, researchers examined the relationship between methadone dose and the presence or absence of chronic pain to patient pain sensitivity.<sup>18</sup> Although methadone dose had no effect on sensitivity to hot or cold pain in MMT patients, the presence of chronic pain had a significant effect on pain perception. Similar to previous reports, MMT patients without chronic pain demonstrated decreased cold pain tolerance, but patients with chronic pain had cold pain thresholds similar to controls. In addition, MMT patients with chronic pain had higher thresholds for hot pain than did controls, whereas patients without chronic pain had lower thresholds for hot pain. Importantly, groups of patients with and without chronic pain did not differ significantly in terms of gender, prevalence of diseases, prevalence of drug abuse, duration in MMT, or age of onset of opioid abuse, all of which could potentially affect pain perception. However, the presence or initial development of chronic pain may possibly be associated with inherent differences in pain perception in these individuals that preceded opioid addiction or methadone maintenance. Regardless, these findings indicate that MMT patients with chronic pain lack the heightened pain sensitivity previously reported for this population, perhaps because the presence of chronic pain inhibited sensation of additional painful stimuli<sup>40</sup> or made other pain sensations harder to distinguish. Thus, the presence or absence of chronic pain should be taken into account in future studies of pain perception among MMT patients.

### **Increased Pain Catastrophizing May Magnify Pain Responses among MMT Patients**

Interestingly, although MMT patients with chronic pain exhibited higher pain thresholds than those without pain, they also reported higher experimental pain ratings.<sup>18</sup> This is similar to the results reported by Prosser et al.,<sup>19</sup> in which MMT patients who were detoxified from methadone reported higher pain thresholds than controls but greater perceived pain unpleasantness. This raises the possibility that MMT patients with chronic pain may exhibit increased pain catastrophizing, a response associated with adverse pain-related clinical outcomes and characterized by magnification of the threat or negativity of painful experiences, feelings of helplessness, and preoccupation with pain-related thoughts.<sup>41,42</sup> This interpretation is supported by a cross-sectional survey that found higher levels of pain catastrophizing in MMT patients reporting chronic severe pain than in those reporting recent pain that was not chronic.<sup>43</sup> Greater pain catastrophizing in MMT patients with chronic pain was also associated with greater pain intensity and increased likelihood of recent pain-related interference with normal work, relationships, and daily activities. These findings suggest that addressing pain catastrophizing and enhancing patient pain coping skills may be an important component in addressing the pain concerns of MMT patients.

## PHARMACOLOGICAL TREATMENT OF PAIN IN MMT PATIENTS

### Licit and Illicit Drug Use for Pain Management Is High among MMT Patients

Pain and addiction are often closely intertwined. Although pain is usually not the primary force motivating initial drug abuse,<sup>7,22,44</sup> MMT patients frequently describe a relationship between drug use and pain,<sup>44</sup> and MMT patients with chronic severe pain are more likely than patients without pain to report pain as a reason for initial drug use.<sup>7</sup> In addition, some studies have observed a connection between high rates of prescription opioid abuse and chronic pain,<sup>45,46</sup> although this correlation is confounded by the fact that opioid use can itself induce heightened pain sensitivity, as mentioned previously. Distinguishing between legitimate and illegitimate opioid use as well as between opioid-induced pain and pain originating from other causes can become an extremely complicated task.

In addition to prescription opioids, MMT patients use over-the-counter drugs, non-opioid drugs, and benzodiazepines, both medically (as prescribed) and non-medically (eg, more than prescribed, prescribed to another individual), as well as alcohol and illicit drugs (eg, heroin, street methadone, marijuana), to treat their recent and ongoing pain.<sup>7,25,26</sup> Data from two studies examining the pain and pain treatment utilization practices of newly enrolled and current MMT patients with recent pain indicated that between 44% and 55% of patients reported having used over-the-counter drugs to manage their pain within the past week,<sup>23,24</sup> compared with approximately 20% of the general population.<sup>47</sup> In addition, 5–30% reported the recent medical use of prescription opioids, non-opioid drugs, or benzodiazepines for pain, with chronic pain patients generally reporting higher rates of use.<sup>23,24</sup> Some reports have also indicated that MMT patients with pain have higher rates of recent heroin use,<sup>6</sup> illicit opioid use,<sup>28,34</sup> and cannabis use<sup>6,28,34</sup> than do patients without pain, which may reflect efforts at pain self-treatment. The potential pain-relieving effects of cannabinoids<sup>6,28,34,48,49</sup> may particularly complicate studies of pain in MMT patients, especially in light of a report indicating that vaporized cannabis may augment the analgesic effects of opioids in patients with chronic pain.<sup>48</sup> Except as noted, the studies discussed in this review attempted to control for the influence of cannabis and other substance use by excluding MMT patients with positive urine or serum toxicology tests or by including the rates of substance use between groups of patients in their analyses.

Notably, although MMT patients with pain have higher overall rates of prescription and over-the-counter drug use to treat pain than do non-pain patients, the rates of licit and illicit drug use for pain management are substantial and largely equivalent for MMT patients both with and without a pain condition.<sup>7,22–26,33,34</sup> Assessing current and past history of drug use for pain management is therefore critical for all MMT patients, with and without documented pain, to minimize potential drug–drug interactions with methadone and other medications.<sup>50,51</sup>

### Opioid Cross-Tolerance Decreases the Effectiveness of Opioid Analgesics for Pain Management of MMT Patients

The pharmacological treatment of pain in patients maintained on methadone is further complicated by the potential for opioid cross-tolerance, which reduces the analgesic effects of opioids used for pain treatment. One study,<sup>13</sup> consistent with earlier findings,<sup>15</sup> reported that administering morphine to MMT patients had no effect on their cold pressor or electrical pain threshold or tolerance levels. Furthermore, this absence of pain relief was observed at morphine concentrations nearly five times higher than those shown to be effective in controls. Similarly, another report<sup>21</sup> showed that treatment with the rapid onset/rapid offset opioid analgesic remifentanyl decreased sensitivity to cold pressor pain in MMT patients in a dose-dependent manner, but only at concentrations 10–20 times higher than those normally used in non-MMT patients. Although no mention is made of controlling for drug use other than opioids, the difference in effective analgesic dose is dramatic. Importantly, administration of high-dose remifentanyl also led to a dose-dependent decrease in patient respiratory rate. Respiratory rates were similarly depressed following administration of high-dose morphine, particularly in patients maintained on high methadone doses.<sup>13</sup> Prescription of opioid pain medications at high doses is still recommended for MMT patients, because patients generally develop tolerance to the respiratory depressive as well as to the pain-relieving effects of these medications.<sup>8,12</sup> However, larger controlled studies are needed to determine rigorously at what dose ranges these and other analgesic opioids can be administered to relieve pain safely and effectively in these individuals.

Methadone has also been evaluated for its potential to treat pain as well as addiction in MMT patients. One study has shown that additional methadone for pain can be administered safely and effectively every 6–8 hours to patients maintained on stable, daily doses of methadone for opioid addiction.<sup>20</sup> In this study, patient pain scores were significantly reduced within 1 month following methadone treatment for pain relief and stabilized after 6 months. Although the average total daily methadone dose, including the doses for both addiction and analgesia, was relatively high (nearly three times the maintenance methadone dose), side effects were minimal and rates of substance abuse decreased significantly over the 12-month study period. This suggests that reducing patient pain may also lead to improvements in substance abuse treatment outcomes. Importantly, this was a retrospective, non-randomized study, and patients were treated with multiple opioid and non-opioid medications for pain, so the observed effects on pain relief cannot be attributed solely to methadone. However, as discussed previously, MMT patients commonly take both opioid and non-opioid medications for pain management, and this study may therefore reflect likely real-world clinical circumstances. As with administration of other analgesic opioids, additional studies are needed to determine the appropriate timing and dosing of additional methadone to achieve effective pain relief in MMT patients while minimizing

potential side effects like respiratory depression and opioid-induced hyperalgesia.

### **Non-Opioid Analgesics May Offer Promising Alternatives for Pain Management**

Interestingly, a recent study<sup>52</sup> showed that gabapentin, a non-opioid anticonvulsant used to treat neuropathic pain, may reduce the heightened pain sensitivity commonly observed in MMT patients. Continuous administration of gabapentin over a 5-week period significantly increased the cold pressor pain thresholds and tolerance levels of MMT patients compared with administration of a placebo. Furthermore, these effects were observed within a typical clinical dose range, with minimal side effects, at both peak and trough blood levels of methadone. These findings suggest that additional research should be conducted to assess whether gabapentin, and other medications used to treat neuropathic pain, can be used safely and effectively to manage clinical pain in MMT patients.

In contrast, another report indicated that chronic treatment with high doses of dextromethorphan, an NMDA receptor antagonist that relieves pain through a different mechanism from that of gabapentin, had no significant effect on electrical or cold pressor pain thresholds or tolerances in MMT patients.<sup>53</sup> Additional research into the specific pain pathways affected by long-term opioid therapy will provide insight into which kinds of medications provide the most effective pain relief for patients in MMT. Studies are also needed that specifically evaluate pain relief in MMT patients with current pain conditions and the effectiveness of different treatments in relieving clinical as well as experimental pain. Currently, very few studies have examined the effects of different medications on reducing pain in MMT patients, and these studies have been conducted primarily with small samples of MMT patients without pain, using experimental pain models. Distinguishing between effective pain management strategies for MMT patients with and without chronic pain may also be critical, in light of the findings indicating that the pain responses of these patients may differ.<sup>18</sup> Also, given the potential influence of pain catastrophizing or other psychological factors in magnifying patient pain responses, investigation of non-pharmacological treatments to address the psychosocial aspects of co-occurring pain and opioid addiction would be valuable.<sup>54</sup>

### **Acute Intrapartum and Postpartum Pain Can Be Managed Effectively for Pregnant Women Receiving MMT**

Women in MMT during and after labor and delivery are one subpopulation of MMT patients in which more extensive research has been done to evaluate the effective clinical management of acute pain. One study found that acute pain following vaginal or cesarean delivery could be managed effectively using routine postpartum pain medication procedures in patients stably maintained on methadone or buprenorphine, another medication approved for the medication-assisted treatment of opioid addiction.<sup>55</sup> Specifically,

patients were administered a combination acetaminophen/oxycodone pain reliever as needed every 4–6 hours for moderate or severe pain and ibuprofen as needed every 4–6 hours for mild or moderate pain. The authors note that buprenorphine, which is known to block the effects of other opioids,<sup>56</sup> might be expected to hinder pain management with opioid medications like oxycodone. Opioid cross-tolerance might also be expected to reduce the effectiveness of opioid medications for pain relief in these women. However, both methadone- and buprenorphine-maintained patients appeared to respond to combination medications for pain control, suggesting that ibuprofen and combination acetaminophen/oxycodone can effectively relieve pain in these individuals, although the pain-relieving effects of the combination medication may have been mediated primarily by the acetaminophen. Regardless of mechanism, both mean patient pain ratings and use of opioid pain medication decreased over a 5-day observation period, indicating that patient pain was effectively managed using standard procedures and that prescription of opioid analgesics did not trigger drug-seeking behavior.

An earlier, retrospective study similarly found that pain treatment responses during and after labor and delivery were similar for MMT patients and controls.<sup>57</sup> Reported pain scores were higher for MMT patients than for controls following both vaginal and cesarean delivery. However, following vaginal delivery, the number of patients requesting opioids for pain relief and the amount of opioid medication used for pain were similar. Following cesarean delivery, MMT patients exhibited a 70% increase in analgesic opioid use compared with control patients and required doses or potencies in excess of routine standards more frequently than controls did. However, this increased opioid use occurred primarily in the first 24 hours following delivery. Despite continued higher pain scores, the use of opioids for pain declined similarly in MMT patients and controls in the postpartum period, and use of acetaminophen and ibuprofen was similar for all patients. Although these results may not generalize to acute pain management situations outside labor and delivery, they suggest that acute pain in MMT patients can be successfully managed using opioid and non-opioid pain medications administered through routine procedures. However, MMT patients may require more frequent or higher doses of opioid pain medications than do non-MMT patients, and their pain status should be monitored closely throughout treatment.

### **MMT Patient Pain Is Frequently Managed Inadequately**

Perhaps because MMT patients may have significantly different pain medication requirements than are typical for non-MMT patients, findings from several studies indicate that MMT patient pain may often be under-treated.<sup>58,59</sup> A small, retrospective study of 12 MMT patients referred to palliative care services for cancer pain found that all of them required opioids and additional adjuvant medications to manage their pain, but 5 patients had not been prescribed opioids for pain

relief at referral.<sup>59</sup> Moreover, nearly all of these patients had documented pain upon referral and documented difficulty in managing their pain. These findings indicate that analgesic opioids for patient pain relief were initially under-prescribed and further suggest that the doses that were prescribed originally may have been insufficient.

The high rates of acute and chronic pain reported for this population also suggest that pain among MMT patients may frequently be managed inadequately or inappropriately. As mentioned previously, one complication is that opioid-induced hyperalgesia can sometimes paradoxically cause opioids prescribed for pain relief to exacerbate rather than alleviate pain symptoms. Some studies also suggest that pain in MMT patients is often treated identically to pain in non-MMT patients, which may be insufficient in light of studies indicating that MMT patients exhibit heightened pain sensitivity and frequently require higher opioid doses than do non-MMT patients to achieve pain relief. For instance, a retrospective study of 67 MMT patients and 67 matched controls admitted to a hospital for acute care found no significant differences in the median doses of opioid or non-opioid pain medications prescribed to either group.<sup>58</sup> This study also found that MMT patients had significantly more reported behavioral problems than did non-MMT patients and were more likely to be discharged from the hospital against medical advice. Although pain scores were not directly assessed in this report, these findings may reflect actual or perceived inadequacies in acute pain management for these patients. However, other potentially confounding circumstances such as higher rates of co-occurring Axis I or Axis II disorders, lack of medical insurance, or greater distrust between patients and medical providers could also account for these findings. Identifying and standardizing effective pain treatment strategies for MMT patients will hopefully lead to improved patient outcomes and experiences and reduce the incidence of poorly managed pain.

## **PROVIDER AND PATIENT BARRIERS TO EFFECTIVE PAIN MANAGEMENT**

### **Provider Perspectives**

In addition to the pharmacological challenges complicating treatment, attitudes and beliefs held by physicians and MMT patients can also present barriers to effective pain management. One difficulty commonly experienced by medical providers who treat MMT patients with pain is the inherent ambiguity in attempting to manage both patient pain and opioid addiction. A series of semi-structured interviews with 16 physicians and physician assistants in an integrated medical and substance abuse treatment program revealed a prevalent feeling of provider uncertainty surrounding the prescription of opioids for pain to patients who were simultaneously receiving treatment for opioid addiction.<sup>27</sup> An underlying tension was also evident between treatment approaches that emphasized pain management and those emphasizing addiction management, with wide practice variations emerging between

providers depending on their treatment perspectives. Although these results were qualitative, they indicate that providers' perspectives and attitudes toward pain and addiction can significantly impact their approaches to pain management and may therefore affect patients' treatment experiences.

This study also identified several common provider concerns that may lead to the under-treatment of pain in MMT patients. Similar concerns have been cited in reviews and clinical guidelines for acute and chronic pain treatment of patients with opioid addiction or other substance use disorders.<sup>8,10,12</sup> These include misunderstandings about methadone, such as the belief that methadone used for maintenance treatment will provide adequate pain relief without additional medication, and concerns about the additive effects of analgesic and maintenance opioids on respiratory and central nervous system function. As mentioned earlier, although methadone can be used to treat pain as well as addiction, the duration of methadone's effects on pain suppression are much shorter (6–8 hours) than the duration of its effects on opioid withdrawal and craving (24–36 hours). Therefore, patients typically require more frequent methadone doses to achieve pain relief than the once-daily dose used for MMT.<sup>5,20,60</sup> In addition, as already discussed, MMT patients frequently exhibit increased opioid tolerance and heightened pain sensitivity compared with non-MMT patients, causing them to require more, not less, opioid pain medication. Although the risk of depressed respiratory or central nervous system function is a valid concern at higher opioid doses, patients generally develop tolerance for these adverse side effects and may be able to tolerate higher than usual opioid doses to achieve pain relief. Other frequently cited provider concerns related to the use of opioids for pain management in MMT patients include fears about patient deception and drug-seeking behavior, the risk of drug diversion, disciplinary action for inappropriate opioid prescription, and the risk of triggering addiction relapse. These factors may also contribute to provider reluctance to prescribe opioids for pain treatment to patients in MMT and could weaken the patient-provider relationship, leading to inadequate pain management.

### **Patient Perspectives**

Patient perspectives can also have a significant impact on the actual and perceived effectiveness of pain and addiction treatment in this population. MMT patients frequently harbor apprehensions about increased drug craving and addiction relapse similar to those of treatment providers.<sup>10,12,26,44</sup> Many MMT patients also believe that prescription opioids administered for pain management caused their addiction problems<sup>26</sup> or that methadone itself contributes to their pain.<sup>44</sup> In addition, many individuals hope eventually to leave MMT treatment and are fearful of addiction or dependence on methadone.<sup>44</sup> This fear is even more prevalent in MMT patients with chronic pain.<sup>26</sup> These factors may prevent MMT patients with pain from seeking or accepting high doses of opioid pain medications, even if these medications are recommended by a physician. A qualitative study of MMT patients with

unmanaged chronic pain further found that MMT patients are very sensitive to being perceived as drug-seeking, and some admitted never having spoken to a physician about their pain.<sup>44</sup> Several reports have also indicated that MMT patients are suspicious of medical providers after previous negative experiences and feel that their pain has been or will be ignored or under-treated because of their opioid addiction.<sup>10,12,44</sup> Moreover, MMT patients frequently fear having their pain medication or their methadone withdrawn and suffering from unmanaged pain or withdrawal symptoms as a result. These fears may be heightened by the increased pain sensitivity and pain catastrophizing commonly experienced by MMT patients. As with the concerns frequently cited by providers, these factors may hamper effective patient-provider communication and the development of mutual trust, leading to inefficient or inadequate pain management.

Another complication that may become more common as long-term opioid therapy for chronic pain becomes increasingly prevalent is that some patients may wish to reduce or discontinue MMT program participation in favor of treatment in a pain management clinic.<sup>12,61</sup> Although a potentially attractive and viable option, MMT patients should be made fully aware that pain clinics are not structured to provide the same addiction treatment expertise or support services as an MMT program. In a review of four patient cases,<sup>61</sup> the article's authors emphasized that individual circumstances must be considered to determine whether MMT services can be safely and successfully discontinued or whether dual treatment in MMT and in a pain clinic will better manage both patient pain and addiction. The authors further discussed the importance of clear and consistent communication between pain and addiction specialists in making treatment decisions and suggested that co-location of pain and addiction services could improve treatment outcomes. One study indicates that, in addition to facilitating consultation between specialists in different disciplines, co-located pain and addiction treatment services would be well received by MMT patients with pain.<sup>23</sup> However, state licensing and other regulations for opioid treatment programs may restrict or complicate the establishment of co-located facilities for pain and addiction management.

## CONCLUSION

Acute and chronic pain are common among patients receiving long-term MMT for opioid addiction and negatively affect patient health, function, and quality of life. However, effective pain management for this population is complicated by many factors. Illegal substance use and both the medical and non-medical use of prescription pain drugs are prevalent among MMT patients, raising the risk of adverse interactions with methadone and other medications. In addition, MMT patients exhibit heightened pain sensitivity compared with patients without long-term opioid exposure and may exhibit increased pain catastrophizing. The presence or absence of a

chronic pain condition may also affect patient pain sensitivity and pain response. Furthermore, MMT patients frequently demonstrate significant cross-tolerance to opioids used for pain treatment and generally require higher or more frequent doses of opioid analgesics than do non-MMT patients to treat their pain. However, few systematic studies have been conducted to evaluate the effectiveness of different pain treatments in this population, and those studies that have been performed are small and have examined primarily experimental rather than clinical pain outcomes. Larger, randomized clinical trials are needed to provide a strong evidence base to guide treatment recommendations and allow clinicians to offer more standardized and effective pain management to patients in MMT. In addition, efforts to foster open communication between MMT patients and providers may promote mutual understanding of patient needs and available treatment options, leading to improved pain treatment experiences.

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## Declaration of Interest

The author reports no conflicts of interest. The author alone is responsible for the content and writing of this paper.

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