

**Management of Opioid Withdrawal in the Emergency Setting:
A case presentation and literature review.**

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Home for the Summer Program – June 2019 Pinawa, MB

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Introduction:

Opioid Use Disorder (OUD) is a common reason for patient presentation to Emergency Departments (ED). On average, 16 Canadians were hospitalized each day due to opioid-related poisonings in Canada in 2016. ((CIHI), n.d.) Addictions and deaths related to opioids are increasing in all age groups, sexes, and income brackets. (Gomes, 2017)

Buprenorphine and methadone are effective for treating opioid use disorder (OUD).

Buprenorphine has been shown to be advantages over methadone as it results in less respiratory depression at higher doses, and fewer withdrawal symptoms upon discontinuation.

Buprenorphine also has evidence for improved efficacy in relieving withdrawal symptoms and has fewer adverse effects than other symptomatic treatments for opioid withdrawal in the ED.

(Berg et al., 2007). Previous randomized controlled trails have shown that patients with OUD

are more likely to continue treatment if opioid maintenance therapy in the form of

buprenorphine/naloxone (Suboxone) is started in the ED rather than referral only for

treatment. (D'Onofrio et al., 2015) Despite the increasing amount of evidence for induction of

Suboxone in the ED setting for presentations of acute OUD and associated opioid withdrawal,

the uptake to practice doesn't always occur for numerous reasons. There is also wide variability

in practice of Emergency physicians when prescribing opioids and managing opioid-related ED

presentations.(Tamayo-Sarver, 2004) This paper will demonstrate a case related to this scenario

and present a literature review for evidence-based management of this type of ED

presentation. Finally, a discussion of OUD in the rural ED specific to the Interlake Eastern

Regional Health Authority (IERHA) will be given.

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Case Presentation:

Mr. A is a 38 year old male that presented to the Pinawa Emergency Department at 09:47 am with abdominal pain. At approximately 02:00 am earlier that day the pain began diffusely around his mid-abdomen, later moving to his right lower quadrant with radiation to his back. The pain was gradually shifting and was described as a stabbing pain upon presentation. Associated symptoms of diarrhea began the day prior and the patient described emesis of a yellow color three times approximately three hours after the onset of diarrhea. He felt slightly diaphoretic and experienced mild pain with joint movement.

Mr. A had a past medical history of left renal cancer and subsequent left nephrectomy as well as chronic pain with an unknown cause. Mr. A takes Oxycodone/Acetaminophen (5mg/325mg) 4 tablets/day, Esomeprazole 40 mg PO daily, and Indomethacin 50 mg PO BID. He later admitted to not having taken Oxycodone for the past 3 days prior to admission. He described allergies to Codeine (rash and feeling of doom), Morphine, Tramacet, Tramadol (reaction unknown). A past history of non-prescribed opioid use was not mentioned in the patients chart.

On physical exam upon admission Mr. A's vital signs were as follows. Temperature of 36.8, heart rate (HR) 108 and regular, Blood pressure (BP) 170/91, and SpO2 96% on room air. His pain was described as 10/10. He appeared restless and irritable and anxious. The patient was rocking back and forth and was wincing in pain at first appearance. He was alert and oriented, lungs were clear with bilateral air entry, and heart sounds were normal. Abdomen was soft and tender in all four quadrants however patient demonstrated guarding, rebound tenderness, and

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a positive McBurney's sign upon palpation of right lower quadrant. A differential diagnosis of appendicitis vs. diverticulitis was considered and subsequent bloodwork was ordered.

A CBC and electrolytes was ordered for bloodwork. Results came back normal for all but a few markers. The WBC count was slightly elevated at $11.9 \times 10^9/L$ as well as his neutrophil count at 92.1% ($10.99 \times 10^9/L$). The remainder of findings on bloodwork were unremarkable. Due to the slight elevation of WBC and neutrophils associated with symptoms discovered on history and physical, a CT scan was ordered.

At 10:45 the attending physician ordered 2 tablets of Oxycodone/Acetaminophen (5mg/325mg) PO for pain relief and at 11:20 the patient was given 1L of normal saline IV and 50 mg Gravol IV in attempt to relieve the retching the patient was experiencing. At 12:15 patient continued to have stabbing pain but nausea was better. By 12:45 patient experienced minor alleviation of pain and appeared comfortable. IV solution of normal saline was reduced to an infusion at 100 cc/hr. At 14:30 a dose of hydromorphone 2 mg was given IV as patient waits for CT scan as his stabbing abdominal pain had not ceased. Mr. A's BP had also resolved at this point to 109/73. 16:00 patient was transported by EMS for closest CT scan 1 hours drive away in stable condition. At 18:40 the patients vitals were normal upon return from CT scan via EMS.

The CT scan results reported the liver and spleen appearing normal with no pancreatic abnormality seen. Left nephrectomy had been performed and left renal bed is normal. There was compensatory hypertrophy of right kidney but otherwise appears normal. The appendix and ileocecal area were well imaged and normal and there was no evidence of appendicitis or

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enteritis. No pelvic abnormality was seen. The overall impression was that no acute process was identified and no evidence of appendicitis.

Based off presentation, all available testing was performed in order to rule out severe gastrointestinal pathology. With no evidence from the CT scan, a diagnosis of appendicitis or diverticulitis could safely be ruled out. A new differential of opioid-withdrawal pain or functional abdominal pain was considered. The diagnosis of opioid withdrawal was not confirmed, however considering the patients chronic prescription opioid use and lack of opioid intake for the previous three days, the diagnosis was a valid consideration. At 20:45 Mr. A, now in stable condition, was re-assessed by the attending physician and discharge from the ED was ordered.

There are multiple signs and symptoms that Mr. A described that would be consistent with an opioid withdrawal including initial tachycardia, vomiting, diarrhea, sweating, restlessness, irritability, bone or joint aching. Other signs and symptoms of opioid withdrawal such as tremor, yawning, pupillary size, gooseflesh skin, or runny nose were not noted in the patients chart. The attending ED physician performed excellent management with the patients care and stabilizing treatment; however at the time of presentation, the systems for the most beneficial and efficacious treatment (if Mr. A was confirmed to be in opioid withdrawal) were not in place for the physician to utilize.

Methods:

A literature review utilizing a systematic search strategy was performed on June 14, 2019 in order to examine previously reported evidence for the most efficacious management of OUD

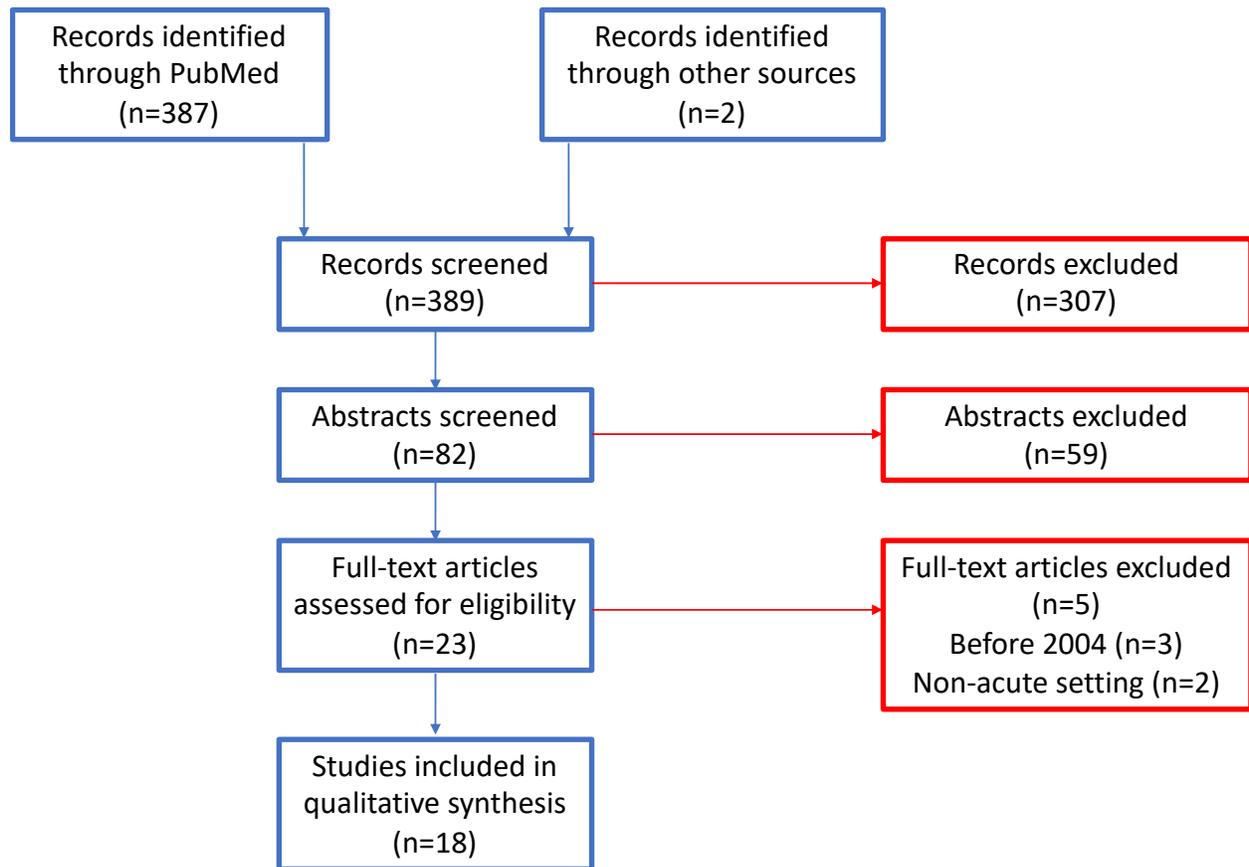
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and opioid withdrawal in the ED setting. The database PubMed was searched using the search terms presented in Appendix 1. Inclusion criteria was any type of study that described a management strategy for opioid presentations to the ED. Exclusion criteria was any paper published before 2004, and management given outside the acute ED setting. No language restrictions were applied.

Results:

A flow diagram summarising the systematic search and study selection process is given in Fig. 1. 389 records were screened for eligibility, and 19 articles were included for qualitative synthesis. Appendix 2 displays the articles included in the literature review. A common theme was noticed in 12 of the articles included in the qualitative synthesis which directly utilized Buprenorphine as their described management; while 6 studies described other forms of management. Figure 2 demonstrates the accumulated evidence provided in 5 studies plus a separate reference that presented algorithms for management of opioid withdrawal presentations to the ED. (Bridge, 2018; Cisewski, Santos, Koyfman, & Long, 2019; Duber et al., 2018; Herring, Perrone, & Nelson, 2019; Hu, Snider-Adler, Nijmeh, & Pyle, 2019; Melnick et al., 2019)

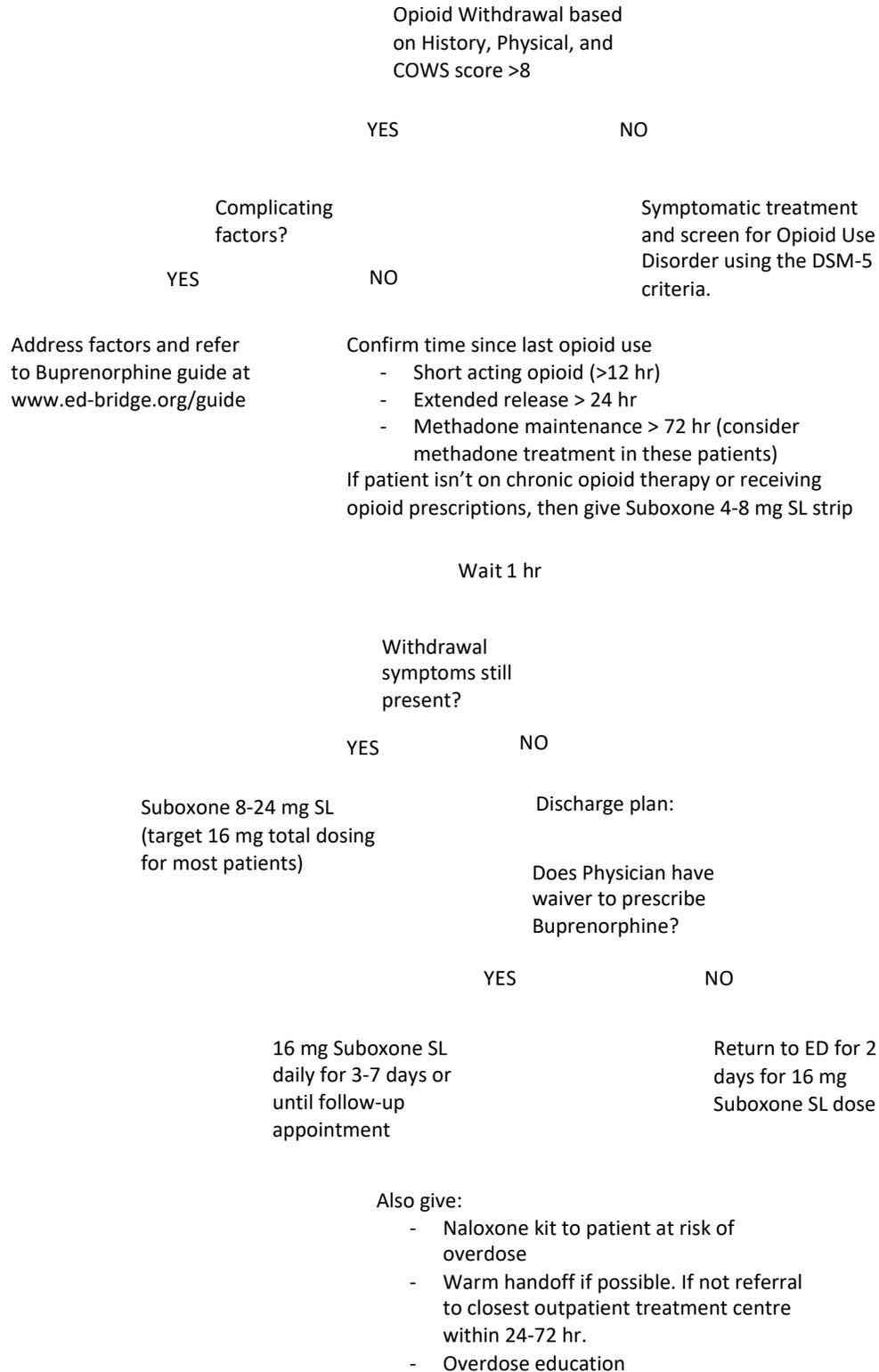
Figure 1: Flow Diagram of systematic search



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Figure 2: Management Algorithm for Presentation of Opioid Withdrawal to Emergency

Department



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Discussion:

The topic of opioid management in the ED setting is an increasing area of research with many recent studies being published in the last few years. The majority of studies included in the qualitative synthesis of the literature review focused on providing evidence for the efficacious use of Buprenorphine in the ED setting. Buprenorphine is a partial agonist with high affinity and low intrinsic activity for the mu-opioid receptor creating a longer duration of action compared to other opioids.(Cisewski et al., 2019) Buprenorphine is rarely abused by individuals as the addictive opioid effects are countered by the combined delivery of naloxone under the trade name “Suboxone” taken through a sublingual route. Multiple studies showed evidence for Buprenorphine having effective use in the ED setting. (Cisewski et al., 2019; Crane, 2013; D’Onofrio et al., 2017, 2015; Dunkley et al., 2019; Hu et al., 2019; Love, Perrone, & Nelson, 2018; Srivastava, Kahan, Njoroge, & Sommer, 2019) Although Methadone and Buprenorphine have similar treatment success, Buprenorphine was shown to be safer, and easier to administrate and refer, making it a more beneficial option for ED initiation. (Love et al., 2018) ED initiated Buprenorphine was associated with increased engagement in addiction treatment, reduced illicit opioid use, and decreased the use of inpatient addiction treatment services when Buprenorphine was continued in primary care. (D’Onofrio et al., 2017, 2015) Srivastava showed that when opioid withdrawal is treated with Buprenorphine in the ED, patients were more likely to be receiving opioid agonist treatment and be connected with addiction treatment 1 month later. (Srivastava et al., 2019) Suggestions were made for outpatients being prescribed Suboxone in the ED settings to have adjunctive treatment with counselling, social work, and connection to pharmacy, laboratory, and medical staff to address their social causes for

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addiction. (Sittambalam, Vij, & Ferguson, 2014) Along with being an efficacious treatment for patients with OUD, Buprenorphine was also shown to be cost-effective. (Busch, Fiellin, & Chawarski, 2017)

Other forms of therapies for managing opioid-related presentations to the ED include the following. Although a weak predictor, screening questionnaires such as the Prescription Drug Use Questionnaire for patients (PDUQp) are being tested for their use for predicting opioid misuse and prescription opioid use disorder. (Beaudoin, Merchant, & Clark, 2016). Bellew showed that implementing an opioid detoxification management pathway reduces ED length of stay and utilization of resources. (Bellew et al., 2018) Recommendations were made for the most efficacious screening tools to use for OUD in the ED as well as overall recommendations for symptomatic treatment and management for transition from ED to a medication assisted treatment center. (Duber et al., 2018). Hawkins suggests that ED implement a chart-flagging system for patients with repeated opioid-seeking visits for pain management, in order to decrease the physicians time reviewing previous records and rather apply an acceptable treatment plan specific to the patient. (Hawkins, Smeeks, & Hamel, 2008) Health care providers in the ED may wish to utilize a brief negotiation interview adherence scale for opioid use disorders (BAS-O) which is a 38 item list to guide patient discussion and was extensively studied. (Pantalon et al., 2017). Alternatively, patients who are already on a Methadone treatment plan who present in a withdrawal state might benefit instead from a single IM dose of 10 mg methadone which has been shown to reduce the severity of acute mild to moderate withdrawal symptoms by 30 minutes. (Su, Lopez, Crossa, & Hoffman, 2018)

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Considering all the evidence synthesized in this literature review, an algorithm was developed to summarize the recommendations made and is shown in Fig. 2. The most widely used scale to assess for opioid withdrawal is the Clinical Opioid Withdrawal Scale (COWS) with a score >8 being considered moderate to severe opioid withdrawal. (Wesson & Ling, 2003) Similarly, the DSM-V criteria is the reference standard when assessing a patient for OUD. (*Diagnostic and statistic manual for mental disorders*, 2013) Patients with complicating factors such as methadone use, intoxication, prescription opioids, or decompensated cirrhosis require specific considerations when initiating Buprenorphine in which case the Emergency Buprenorphine Treatment Guide should be referred to. (Bridge, 2018) Once a diagnosis is made and factors are accounted for, Buprenorphine provides the most evidence-based therapy when combined with a warm handoff to a nearby outpatient treatment centre within 24-72 hours of ED discharge. A warm handoff refers to a transfer of care between members of different healthcare teams where the handoff occurs in front of patients and their family and is shown to lead to better uptake of outpatient resources if the service is available. (Herring et al., 2019) A naloxone kit and education about prevention of overdosing to at-risk patients is also important to prevent overdose situations in drug-abusing patients.

Commentary on Rural ED setting specific to IERHA:

In 2014 the IERHA had a population of 126,674 to serve with a median age of 42.8 and 17 First Nations communities. (*Strategic Plan 2016-2021*, 2015) Figure 3 displays the region of Manitoba that is covered by this health authority on the map. The IERHA has two physicians at

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present time that have obtained a license to prescribe Methadone and Suboxone, however there are more physicians in the process. The need for alcohol and drug addiction specialists greatly exceeds the capacity this region has to accommodate at the moment. Limiting factors to the lack of physicians prescribing opioid maintenance therapy include the stressful and emotional burden of the work, the time and effort required to receive additional training and exemption. Along with these factors, the majority of rural family physicians practice using a fee-for-service pay model which doesn't financially accommodate the time-consuming practice required for the proper care of patients with OUD. (Neufeld, 2018)

Figure 3: Map of IERHA



(Strategic Plan 2016-2021, 2015)

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The physicians prescribing opioid maintenance therapy typically practice from the town of Powerview-Pine Falls which services a number of nearby indigenous reserves. This marginalized population has a high prevalence of unemployment, substance abuse issues, crime and widespread poverty. (Neufeld, 2018) This creates a large prevalence of OUD presentations to ED and walk-in clinics. A recent Rapid Access to Addictions Medicine (RAAM) clinic has also opened up in Selkirk which is a centre that doesn't require any referral and can treat many substance use conditions.

If Mr. A's management were to be applied to the opioid withdrawal management algorithm presented in Figure 2, the changes to care would be as follows. The treatments that he received wouldn't have changed drastically as every ED physician would first need to rule out other causes of abdominal pain. He would be considered to have complicating factors due to his chronic opioid prescription but according to the ED-bridge guidelines(Bridge, 2018), he would still be a candidate for Buprenorphine with a prescription of a much smaller doses (ex. 2 mg SL QID) and require care coordination. The algorithm would continue to be followed as presented and the patient would have been referred to the closest outpatient opioid maintenance therapy treatment centre within 24-72 hours if the ED physician did not have a waiver to prescribe Buprenorphine themselves. These outpatient centre options would include the option of Pine Falls Primary Health Care Center or Selkirk's RAAM clinic in the IERHA district.

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The number of ED physicians in the IERHA with a waiver to prescribe Suboxone is quite minimal which prompts the question: what are the necessary steps involved for a physician to receive their waiver to prescribe Buprenorphine? According to the College of Physicians and Surgeons of Manitoba a physician must apply in writing to the Registrar for approval to prescribe Suboxone for OUD and have completed a recognized course for prescribing Suboxone approved by the College. These online courses are typically 8 hours in length and can be completed over time. A similar process is required for a physician to obtain license to prescribe Methadone, however an additional 4 half-days working directly with a supervising physician is required prior to approval by the College. ("Prescribing Methadone or Suboxone," 2018) The time requirement for a physician to be able to prescribe Suboxone is reasonable; though the IERHA must be willing to provide incentive potentially through the role of financial contracts in order to attract physicians to attain this ever-needed license. Otherwise, the IERHA will continue to experience even more drastic presentations then described in Mr. A's case, and with no plan in place for providing the most beneficial and efficacious treatment as demonstrated in this literature review.

Limitations:

Some limitations to this project include the lack of a second reviewer and explicit search criteria. Searching more than one database would expand the review to include more evidence that wasn't obtained through PubMed solely. The majority of studies in the review were conducted in the setting of large urban tertiary care centers which may produce results that may not be applicable to the rural setting and its population.

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Conclusions:

This review of literature demonstrates evidence for efficacious management of patients with opioid withdrawal who present to ED settings. Buprenorphine provides many benefits to patients both symptomatically as well as for post-discharge management. This evidence should be applied to the IERHA's ED to combat the ongoing problem of individuals suffering with OUD and opioid withdrawals. The need for more physicians with the ability to prescribe Suboxone is indicated and could greatly benefit many patients including Mr. A's whose case was presented in this paper. Further research is needed to determine the extent of the prevalence of OUD in the IERHA that would benefit from referral to an addictions and drug abuse specialist; as well as research specific to the rural ED setting.

Acknowledgements:

I would like to thank the supervision and teaching provided by Dr. Garg and Dr. Sayfee as well as all the individuals I interacted with at the Pinawa Hospital. Thank you to the Home for the Summer Program and everyone involved in its organizing that provided an amazing summer exposure experience for myself and colleagues.

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Appendix 1: Search Strategy for Literature Review

("Drug-Seeking Behavior"[Mesh] OR "drug-seeking" OR "drug-dependence" OR "withdrawal" OR "substance abuse") AND ("Analgesics, Opioid"[Mesh] OR "opioids" OR "opioid-maintenance-therapy" OR "buprenorphine" OR "Suboxone" OR "opioid-use" OR "opioid-withdrawal") AND ("Emergency Service, Hospital"[Mesh] OR "emergency" OR "emergency department" OR "ER" OR "ED" OR "rural" OR "post-discharge treatment")

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Appendix 2: Table of articles included for final literature review

Studies involving Buprenorphine specifically:

Author	Title	Year	Study Type
Berg(Berg et al., 2007)	Evaluation of the use of buprenorphine for opioid withdrawal in an emergency department	2006	Retrospective chart review
Cisewski(Cisewski et al., 2019)	Approach to buprenorphine use for opioid withdrawal treatment in the emergency setting.	2019	Narrative review
Crane(Crane, 2013)	Emergency Department visits involving buprenorphine	2013	Report
D'Onofrio(D'Onofrio et al., 2015)	Emergency Department-Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence	2015	Randomized Controlled Trial
D'Onofrio(D'Onofrio et al., 2017)	Emergency Department-Initiated Buprenorphine for Opioid Dependence with Continuation in Primary Care: Outcomes During and After Intervention	2017	Cohort study
Dunkley(Dunkley et al., 2019)	Retrospective Review of a novel approach to buprenorphine induction in the Emergency Department	2019	Retrospective review
Herring(Herring et al., 2019)	Managing Opioid Withdrawal in the Emergency Department with Buprenorphine	2018	Review
Hu(Hu et al., 2019)	Buprenorphine/Naloxone induction in a Canadian Emergency Department with rapid access to community-based addictions providers.	2019	Retrospective chart review
Love(Love et al., 2018)	Should Buprenorphine be administered to patients with	2018	Systematic Review

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	opioid withdrawal in the Emergency Department?		
Melnick(Melnick et al., 2019)	User-centred clinical decision support to implement Emergency Department initiated Buprenorphine for Opioid Use Disorder: Protocol for the pragmatic group Randomised EMBED Trial.	2019	Protocol of parallel cluster randomized study
Sittambalam(Sittambalam et al., 2014)	Buprenorphine outpatient outcomes project: can suboxone be a viable outpatient option for heroin addiction?	2014	Prospective cohort study
Srivastava(Srivastava et al., 2019)	Buprenorphine in the ED	2019	Randomized Controlled Trial

Studies involving other management strategies

Author	Title	Year	Study type
Beaudoin(Beaudoin et al., 2016)	Prevalence and Detection of Prescription Opioid Misuse and Prescription opioid use disorder among emergency department patients 50 years of age and older: performance of the prescription drug use questionnaire, patient version	2016	Cross-sectional study
Bellew(Bellew et al., 2018)	Implementation of an opioid detoxification management pathway reduces ED length of stay.	2017	Uncontrolled before-and-after study
Duber(Duber et al., 2018)	Identification, Management, and Transition of care for patients with opioid use disorder in the emergency department.	2018	clinical review
Hawkins(Hawkins et al., 2008)	Emergency Management of Chronic Pain and Drug-seeking behaviour: An alternate perspective	2008	opinion
Pantalon(Pantalon et al., 2017)	an interventionist adherence scale for a specialized brief negotiation interview focused on treatment engagement for opioid use disorders.	2017	Randomized Controlled Trial evaluation

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Su(Su et al., 2018)	Low dose intramuscular methadone for acute mild to moderate opioid withdrawal syndrome.	2018	prospective observational study
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