

The Inclusion of Patients' Reported Outcomes to Inform Treatment Effectiveness Measures in Opioid Use Disorder. A Systematic Review

Nitika Sanger^{1,*}, Balpreet Panesar^{2,*}, Michael Dennis³, Tea Rosic⁴, Myanca Rodrigues⁴, Elizabeth Lovell⁵, Shuling Yang³, Mehreen Butt⁶, Lehana Thabane^{4,7}, Zainab Samaan^{4,5}

¹Medical Science Graduate Program, McMaster University, Hamilton, Ontario, Canada; ²Neuroscience Graduate Program, McMaster University, Hamilton, Ontario, Canada; ³Michael G DeGroote School of Medicine, McMaster University, Hamilton, Ontario, Canada; ⁴Health Research Methodology Graduate Program, McMaster University, Hamilton, Ontario, Canada; ⁵Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, Ontario, Canada; ⁶Accelerated Nursing Program, McMaster University, Hamilton, Ontario, Canada; ⁷Centre for Evaluation of Medicines, Programs for Assessment of Technology in Health (PATH) Research Institute, McMaster University, Hamilton, Ontario, Canada

*These authors contributed equally to this work

Correspondence: Zainab Samaan, Health Research Methodology Graduate Program, McMaster University, Department of Psychiatry and Behavioural Neurosciences, McMaster University, 1280 Main St. West, Hamilton, Ontario, Canada, Tel +1 905-522-1155 ext. 35448, Fax +1 905-381-5629, Email samaanz@mcmaster.ca

Introduction: Patient centred care is needed now more than ever in the treatment of opioid use disorder. Trials, policy makers, and service providers have most often used treatment retention and opioid urine screens as measures of treatment effectiveness. However, patients receiving medication for opioid use disorder treatment (MOUD) may prioritise the use of different ways to assess treatment success.

Objective: The aim of this review is to synthesize literature examining the self-reported goals patients would like to achieve in MOUD for opioid use disorder.

Methods: We searched MEDLINE, EMBASE, PsycINFO, Cumulative Index to Nursing and Allied Health Literature, Web of Science, Cochrane Library, Cochrane Clinical Trials Registry, the National Institutes for Health Clinical Trials Registry, and the WHO International Clinical Trials Registry Platform from inception until April 30th, 2021. No restrictions were placed on language, age, or type of MOUD. A qualitative synthesis is presented given that a meta-analysis was not possible.

Results: The search yielded a total of 21,082 records from which 8 met criteria for inclusion in the qualitative synthesis. We identified a total of 43 patient-reported treatment goals from the 8 studies. Twelve domains were created from the 43 goals reported. These domains cover a range of important areas for patients' goals related to living a normal life, physical health, mental health, treatment, and substance use specific areas.

Conclusion: This review highlights several patient goals that they would like to achieve during treatment for opioid use disorder that are not commonly considered as markers of treatment effectiveness. Goals related to health, living a normal life, and overall substance use concerns by patients should be taken into consideration by clinical trialists, researchers, policy makers, service providers, patients, and communities engaged in developing and tailoring treatment plans for opioid use disorder.

Systematic Review Registration: PROSPERO CRD42018095553.

Keywords: opioid use disorder, patient reported outcomes, patient-centred care, medication for opioid use disorder

Introduction

Problematic opioid use driven by both recreational opioids and diversion of prescription opioids continues to be a crisis across the world.¹ Approximately 70% of the deaths related to drug use in the world are associated with opioids.¹ In 2019, it was reported that 62 million people aged 15–64 had used opioids.² Some countries such as Canada have seen an

increase in the national rate of opioid-related deaths reaching 16.5 (per 100,000) in 2020.³ The Centre of Disease Control and Prevention reported that 128 people overdose on opioids daily in the United States⁷ and approximately 2.1 million people have OUD associated with prescription opioids.⁸ In addition to opioid-related deaths, there has also been an increase in opioid-related hospitalizations.⁴ Simultaneously, there has been an increase in emergency department visits and other healthcare service usage related to opioid use.⁵ Problematic opioid use is associated with opioid use disorder (OUD), a chronic and disabling illness with considerable morbidity and mortality.⁶ Improving treatment outcomes for OUD is thus vital to combat the continually rising opioid-related deaths and associated negative health outcomes.

The main medications used in Medication for Opioid Use Disorder (MOUD) for OUD are methadone and buprenorphine-naloxone.^{9,10} Research has suggested that while methadone is successful in the reduction of opioid use and retaining patients in treatment, there is still a great deal of variation in outcome related to comorbid substance use, social functioning and health status.^{11–15} Buprenorphine-naloxone is most often recommended as first-line treatment for OUD.^{16–18} Buprenorphine works similarly to methadone in reducing opioid cravings but it has less safety concerns, such as sedation and respiratory depression which are associated with methadone.^{19–21} Regardless of the type of medication used in MOUD, trials and clinical care often look at treatment retention, abstinence from opioids, and negative urine drug screen over varying durations as the indicators for successful treatment in OUD.¹⁰

Despite the wide acceptability of these markers of success, recent reports suggest a limited utility of urine drug screen and abstinence in capturing the complexity of individual patient treatment goals.²² Patients' goals for treatment in OUD (and other health conditions) should be considered to improve OUD treatment outcomes.²³ Thus, there is a need to broaden and include patients' goals when assessing treatment outcomes in OUD.¹⁸ Specifically, there has been a movement in various fields through recent years to include the perspective of patients through patient-centred and informed outcomes.²⁴ It is recommended by these movements that clinicians and service providers take patient provided goals into consideration as it will allow patients to incorporate their own values, preferences and health goals into their care decisions.²⁵

Currently, there is no established set of patient important treatment outcomes that standards of care, clinical trials, and guidelines can refer to when providing recommendations to clinicians and patients.¹⁸ Patient important treatment outcomes are goals for treatment success as identified by patients themselves. Trials have used treatment retention, continued substance use, and illegal activity as outcomes of success when assessing the effectiveness of OUD treatment, among many others. Validated tools such as the Maudsley Addiction Profile²⁶ attempt to measure health improvement in those with OUD but are not able to assess patient-important treatment goals. Evidently, there is a clear variation and undecided number of outcomes listed throughout literature, which calls for the establishment of a set of patient-important treatment outcomes that can be considered in the process of determining treatment plans for those with OUD. The first step towards this goal is to provide a synthesis of what has been reported in the literature. Here, we present a qualitative review of patient-reported treatment outcomes identified by studies assessing the perspectives of patients with OUD receiving MOUD have on their treatment goals.

Objectives

The purpose of this systematic review is to identify patient-relevant outcomes to enhance the effectiveness of current treatment options for OUD. Specifically, our study aim is to: summarize the literature reporting patient-reported goals for OUD treatment.

Methods

The protocol for this review has been published²⁷ and is registered in PROSPERO CRD42018095553.

Eligibility Criteria

To be included in the review, studies addressing patient-reported treatment goals in OUD treatment with MOUD were considered. Observational studies, clinical trials, and qualitative research with no restriction on age, sex, or type of treatment were eligible for inclusion. Observational studies selected for this review did not include case studies, case

series, and reviews. Qualitative research included interviews, focus groups, and other methods of data collection for the treatment outcomes and goals reported by patients with OUD receiving MOUDs.

Outcomes and Prioritization

The study objective was to identify goals and markers of treatment success reported as important to patients receiving MOUD. For this review, MOUD was considered any type of medication treatment (traditionally used or not) that was provided to the participants for the OUD treatment such as methadone, buprenorphine, naltrexone, and heroin-assisted treatment. These goals were identified in a variety of ways in the included studies that ranged from qualitative interviews, focus groups and asking open-ended questions during study questionnaires. All the responses related to these goals were captured and categorized accordingly.

Information Sources

The literature search of the selected databases was run from inception until April 30th, 2021. MEDLINE, EMBASE, PsycINFO, Cumulative Index to Nursing and Allied Health Literature, Web of Science, Cochrane Library, Cochrane Clinical Trials Registry, the National Institutes for Health Clinical Trials Registry, and the WHO International Clinical Trials Registry Platform were all searched for this review. Comprehensive search strategies including terms related to patient reported outcomes and MOUD were used and no limit on study year, demographics, or language, was enforced. This search strategy was created with consultation of an experienced health sciences librarian who employed a broad search strategy to capture the data related to patients' goals on the assumption that these goals may not be the primary study objective and therefore a broader approach was needed. Please see [Appendix I](#) for the search strategies of the various databases used.

Data Management

A calibration of 25 articles was completed on Covidence,²⁸ following the team training on how to use the systematic review software platform. This platform allowed the team to collaborate and manage articles during this review.

Selection Process

Six reviewers, working in pairs, referred to inclusion and exclusion criteria to independently screen and conduct title and abstract screening and full-text screening. This process was conducted in duplicate. The two methods used to address disagreements between reviewers were through discussion to consensus and third author consultation if method one was unsuccessful. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines was used to generate a flow chart for the screening and selection process.²⁹ Covidence was used to recognize duplicates and organize full-text extraction articles.

Data Collection Process

Full-text data extraction forms were made for this review to include the following: author, year of study, country, title of journal, type of population, study design, inclusion criteria, exclusion criteria, number of participants, mean age, sex, ethnicity, study objective, type of MOUD received, definition of patient reported goals, measurement of patient reported outcomes, list of patient reported goals, statistical method used for each outcome if applicable, summary of findings, reported limitations, reported conflicts of interest.

Risk of Bias in Individual Studies

Risk of bias was completed in duplicate to assess the quality of the studies included in this review. We used the Critical Appraisal Skills Program (CASP) to assess the risk of bias for qualitative studies.³⁰ The Newcastle-Ottawa Scale was used to assess the risk of bias for observational studies.³¹

Data Synthesis

All results were summarized qualitatively after the patient-reported goals were grouped together using qualitative synthesis. All the goals and categories that were reported for each study (and any breakdowns/definitions provided for

the goals and categories, if applicable) were transcribed into a master document. Two reviewers (NS and BP) performed thematic analysis in which the goals were coded into themes that came up. In cases that studies reported categories that encompasses more than one goal, the individual goals were taken and used in the thematic analysis.

Additionally, in the descriptive synthesis for each theme, we will report the specific goal that the study stated and if available, provide the percentage of participants that identified that as a goal they would like to achieve in each study.

Confidence in the Cumulative Evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) was not used as we were not able to determine the strength of the evidence in the included studies for this review.

Results

Study Selection

Database searches yielded a total of 21,082 studies. Of these, 6328 were removed as duplicates and 14,754 studies went through title and abstract screening. From the title and abstract screening, we were able to remove 11,604 papers and the remaining 3150 underwent full-text screening. A total of 8 studies were included in this review.^{32–39} There were a few studies that appeared to meet the inclusion criteria in the initial steps. However, when they were screened in full text, they either did not focus specifically on the OUD population receiving MOUD, did not report on goals that patients identified, or were case reports or editorials. This process is described using the PRISMA Flow Diagram (Figure 1).

Study Characteristics

The study characteristics are presented in Table 1. A total of eight papers were included in this systematic review, which were comprised of qualitative literature, cross-sectional studies, and secondary analyses from clinical trials. All the included studies captured goals that patients with OUD want to achieve from their treatment. Three of the studies included patients that were receiving methadone treatment,^{34,37,39} two studies included patients that were receiving methadone, buprenorphine, and buprenorphine-naloxone treatment,^{36,38} and one study investigated patients who were receiving methadone and buprenorphine-naloxone treatment.³² Additionally, two of the included studies were examining injectable forms of MOUD, which included injectable diacetylmorphine and hydromorphone treatment,³⁵ supervised injectable heroin, and supervised injectable methadone.³³

The total sample size of the 8 studies was 2711 and majority of the participants were male (59.5%). Four studies were conducted in Europe (United Kingdom, Ireland, and Germany) and 4 were conducted in North America (Canada and United States). The number of goals identified for most studies varied from 2 to 10^{32–37,39} along with one study only reporting the most common goal stated by the participants.³⁸

Risk of Bias in Studies

The quality of the individual studies is shown in Tables 2 and 3. The CASP tool used for qualitative studies does not warrant a scoring arrangement. As such, the observations made are based on the individual labels of “yes”, “no”, and “can’t tell”. Overall, most of the qualitative studies included in this review had a low risk of bias attributed to the numerous “yes” labels given to almost all papers in most categories. Qualitative studies such as O’Reilly 2011 had aspects of risk of bias when assessing the relationship between the participant and the researcher alongside any details surrounding ethical considerations the paper had not reported. These were largely the two categories for which the qualitative papers did not include information for. Both cross-sectional studies included in this review were of fair quality as depicted by the scores on the Newcastle Ottawa Scale (for cross-sectional studies). Lastly, the observational study included in this review is scored as poor quality solely due to the large loss to follow-up in the study.

Results of Individual Studies

The following are the 12 treatment domains that were categorized using the goals mentioned in individual studies summarized in Table 4. Majority of the goals presented in the studies were taken as reported. However, for 2 studies, 2

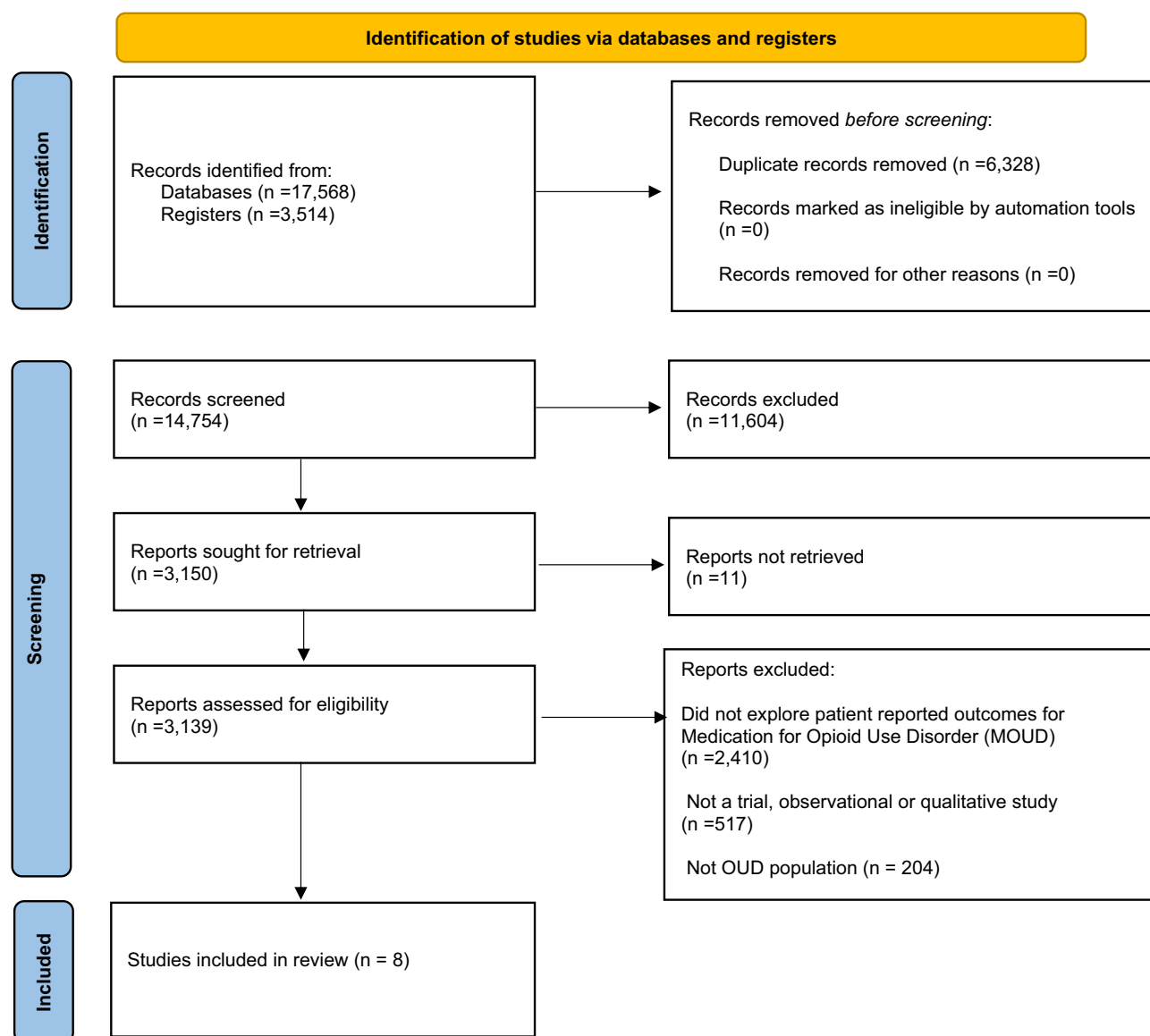


Figure 1 PRISMA Flow Diagram for Study Selection Process.

Notes: PRISMA figure adapted from Page M, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021 Mar 29;372:n71. Common Creative.⁶⁹

goals were further divided. For Gelpi-Acosta et al, 2015, the goal of “desire to quit heroin and observe social norms (licit work and family)” was broken down into three: 1. Desire to quit heroin, 2. Have licit work, and 3. Family. For Sanger et al, 2020, the goal of normal life encompassed of various things and was broken down into: 1. Wanting a stable life, normal life, 2. Get education, job, work, and wanting to support their family, and 3. Good mental health.

Treatment-Related Goals

Treatment Retention

Two studies were categorized under the *treatment retention* theme as a patient reported goal.^{32,37} Sanger et al, 2020 asked the open-ended question of what are the patients desired goals from treatment and 4% of participants responded that they wanted no change from their current treatment and would like to maintain their treatment. O'Reilly et al, 2011 asked their participants what their long-term treatment goals are and 17% reported wanting to remain on

Table 1 Summary of Included Study Characteristics

Author, Year	Study Design	Participant Demographics (Sample Size, Sex, Ethnicity)	Country	Type of MOUD	Inclusion Criteria	Measurement of Patient-Reported Goal	Patient-Reported Goals
Dale-Perera, 2015³⁸	Cross Sectional	N=248 Male=179 Female=69 Ethnicity=NR	United Kingdom	Methadone, buprenorphine, and buprenorphine-naloxone	Participants currently receiving MOUD	Patients of MOUD were asked about "goals of therapy".	Presented most reported response. Treatment goal was to become drug-free (56%).
Gelpi-Acosta, 2014³⁹	Qualitative	Specific population: heroin street users n=28 but only 15 were enrolled in methadone treatment 23 males 16 Hispanic 3 African American 9 Caucasian Mean age=38	United States	Methadone	Participants were 18 years of age or older, able to communicate in English and/or Spanish, currently used heroin, enrolled in methadone treatment, and provided proof of enrollment.	Participants went through a detailed semi-structured interview which was analyzed into themes	Goals were to avoid the "morning sickness", desire to quit heroin and observe social norms (licit work and family)
Groshkova, 2013³³	Secondary analyses of a trial	N=127 Mean age=37.2 Male=93 Female=34 Ethnicity: Caucasian= 122 African-American=4 Mixed=1	United Kingdom	Optimized oral methadone, supervised injectable heroin, and supervised injectable methadone	Participants were chronic heroin users who were on MOUD for at least 6 months but continued to use heroin for 50% of the time in the past 3 months	Asked the open-ended question at baseline: what areas of your life would you most like help with?	Deduce substance misuse (80.5%) achieve stability, normality, routine, and structure (15.9%) improve education and work opportunities (15.0%) improve housing situation (12.4%) improve physical health (11.5%) improve psychological wellbeing (11.5%) improve finances (11.5%) improve relationships with family and friends (7.1%) increase non-drug scene socialization (6.2%) reduce criminal activity (2.7%)
Marchand, 2020³⁵	Qualitative	N=30 Mean age=44.7 Female=14 Male=16 Indigenous=7 Non-Indigenous=23	Canada	Injectable diacetylmorphine and hydromorphone treatments	Participants receiving injectable opioid agonist treatment	In-depth interviews that used open-ended questions relating to various domains of patient-centred care	Theme of self-reported outcomes emerged (outcomes that participants prioritized). Outcomes were reduced street opioid use, reduced involvement in illegal activities, reduced worry and stress related to street opioid use and illegal activities, increased sense of stability and routine, and improved health

Mitchell, 2011 ³⁴	Qualitative	N=6 Mean age=37 Male=5 Female=1 Mean age=37 Ethnicity Caucasian=6 African American=3	United States	Methadone	Participants who were discharged from initial methadone program but re-entered a new one within 12 months	Semi-structured interview with questions relating to treatment attitude and experiences	Theme of initial goals of treatment emerged which included getting a decent place to live, having a job, going back to school raising children, forging meaningful relationships with others, staying off illicit drugs and being abstinent.
O'Reilly, 2011 ³⁷	Mixed Methods	N=41 Mean age=34.5 Male=30 Female=11 Ethnicity = not reported	Ireland	Methadone	Patients receiving methadone treatment	Questionnaire with open and closed-ended questions including long-term treatment goals	Continue methadone treatment into the future (17%) stop methadone treatment in the immediate future (59%) stop taking methadone eventually (22%)
Sanger, 2020 ³²	Mixed methods	n=2031 mean age=39.1 males=1135 females=896 intersex=1 ethnicity: European n=1154 Indigenous n=367 Other= 437	Canada	Methadone and buprenorphine-naloxone	Participants diagnosed with OUD, receiving MOUD, 16 years of age or older and provided written consent	Asked the open-ended question: What are your goals from treatment?	Themes emerged from the responses which were: stop MOUD, avoid illicit drugs, live a "normal" life, manage pain, avoid OUD symptoms, taper off MOUD, and no changes in treatment wanted.
Stover, 2010 ³⁶	Cross-sectional	n=200 males=132 females=68	Germany	Methadone, buprenorphine, and buprenorphine-naloxone	For patients, it was people who are opioid dependent and currently receiving treatment)	Participants were asked a questionnaire on various domains related to their treatment including reasons for starting treatment	Desire to improve their health (71%) change social networks (61%) cease committing crimes, (57%) reduce illicit drug use (52%) improve employment status (51%)

Table 2 Critical Appraisal Skills Program of Included Qualitative Studies

	Was There a Clear Statement of the Aims of Research	Is a Qualitative Methodology Appropriate	Was the Recruitment Strategy Appropriate to the Aims of the Research	Was Data Collected in a Way That Addresses the Research Issue	Has the Relationship Between Researcher and Participant Been Adequately Considered	Have Ethical Issues Been Taken into Considerations	Was the Data Analysis Sufficiently Rigorous	Is There a Clear Statement of Findings	How Valuable is the Research
Marchand 2020	Yes	Yes	Yes	Yes	no	yes	yes	yes	yes
Sanger 2021	Yes	Yes	Yes	Yes	no	yes	yes	yes	yes
Mitchell 2011	Yes	Yes	Yes	Yes	yes	no	yes	yes	yes
Gelpi-Acosta 2015	Yes	Yes	Yes	Yes	yes	no	yes	yes	yes
O'Reilly 2011	Yes	Yes	Yes	Yes	no	no	yes	yes	yes

Table 3 Newcastle-Ottawa Scale Risk of Bias of Included Observational Studies

	Representativeness of the Sample	Sample Size	Non-Respondents	Ascertainment of the Exposure (Risk Factor)	Comparability:	Assessment of the Outcome	Statistical Test		Total
Dale-Perera 2015	*	0	*	0	*	*	*		5
Stover 2010	*	0	0	**	*	*	*		6
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of the exposure (risk factor)	Demonstration that the outcome of interest was not present at beginning of study	Comparability:	Assessment of the outcome	Was the follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Total
Groshkova 2013	*	*	*	*	*	0	*	0	6

Notes: *Indicates one star in the NOS scale. **Indicates two stars in the NOS.

methadone in the future. None of the remaining studies reported any goals that were grouped into the theme of treatment retention.

Stop MOUD

Two studies reported goals that had participants express wanting to *stop their MOUD*. Sanger et al, 2020 had 39% of participants want to stop their treatment and express that they did not want to be dependent on their MOUD. O'Reilly et al, 2011 had 59% of participants say that they wanted to stop their methadone treatment in the immediate future. None of the remaining six studies had participants express goals of wanting to stop their MOUD.

Taper off MOUD

We had two studies that reported goals of wanting to *taper off MOUD* but not necessarily stop it completely. Sanger et al, 2020 had 7% participants say that they wanted to taper off to a small dose or slowly wean off their treatment but had no immediate plans to stop their MOUD completely. O'Reilly et al, 2011 had 22% of participants report that their long-term treatment goal was to eventually stop taking methadone. None of the remaining studies reporting goals relating to the theme of tapering off MOUD.

Substance-Associated Goals

Avoid Withdrawal

Two out of the eight studies reported goals that were categorized into the theme of *avoid withdrawal*. In Sanger et al, 2020, 8% of participants reported wanting to prevent OUD symptoms including OUD withdrawal and cravings. Gelpi-Acosta et al, 2014 reported that one of the reasons of being in methadone treatment is to avoid "morning sickness" which is physical withdrawals. None of the remaining six studies identified any goals that could be grouped into this theme.

Reduce Illicit Drug Use

Seven out of the eight included studies mentioned goals that were categorized into the theme of *reducing illicit drug use*. Sanger et al, 2020 had 25% of participants report that they would like to stop using all illicit drugs, not only opioids. Marchand et al, 2020 had participants report that a goal was to stop using street opioids. Stover 2010 had 52% of participants report that they would like to decrease their illicit substance use. Mitchell et al, 2010 had participants reporting goals of not using illicit substances. The participants in Gelpi-Acosta et al, 2014 reported wanting specifically to quit using heroin. Dale-Perera et al, 2015 reported the goal of 56% of participants was to be drug-free and 80.5% of participants in Groshkova et al, 2013 reported wanting to decrease their substance use.

Health-Related Goals

Physical Health Improvement

Half of the included studies reported patient goals that related to the theme of *physical health improvement*. Marchand et al, 2020 had participants report they would like to improve their health. Stover 2010 had 71% of participants report that they would like to improve their health as well. While 11.5% of the participants in Groshkova et al 2013 reported that they would like to improve their physical health. Sanger et al, 2020 had 8% of participants specifically report that one of their goals from treatment is pain management. None of the remaining studies reported goals that related to improving their physical health.

Mental Health Improvement

Three of the included had patients reporting goals that were associated with the theme of *mental health improvement*. Specifically, 11.5% of the participants in Groshkova et al 2013 reported that they would like to improve their psychological wellbeing. Sanger et al, 2020 had participants report that one of their goals under normal life was to have good mental health. Marchand et al, 2020 also had participants report that they would like to reduce the worry and stress that they experience due to their opioid dependence and criminal activity. This study did separate out the mental

Table 4 Themes Generated from Patient Reported Outcomes of MOUD

THEME GENERATED	REPORTED OUTCOME 1	REPORTED OUTCOME 2	REPORTED OUTCOME 3	REPORTED OUTCOME 4	REPORTED OUTCOME 5	REPORTED OUTCOME 6	REPORTED OUTCOME 7
TREATMENT RETENTION	No change from current treatment	Continue methadone treatment into the future					
AVOID ILLICIT DRUGS	Reduced street opioid use	Become drug-free	Avoid illicit drugs	Staying off illicit drugs	Desire to quit heroin	Reduce substance misuse	Reduce illicit drug use
AVOID WITHDRAWAL	Prevent OUD symptoms	Avoid the “morning sickness”					
REDUCE CRIMINAL ACTIVITY	Reduced involvement in illegal activities	Reduce criminal activity	Cease committing crimes to support their opioid dependence				
MENTAL HEALTH IMPROVEMENT	Reduced worry and stress related to street opioid use and illegal activities	Improve psychological wellbeing	Good mental health				
STABILITY AND NORMALCY	Increased sense of stability and routine	Normal life	Achieve stability, normality, routine, and structure				
PHYSICAL HEALTH IMPROVEMENT	Improved health	Improve physical health	Desire to improve their health	Pain Management			
STOP MOUD	Stop treatment	Stop taking methadone, either in the immediate future					
TAPER OFF MOUD	Taper off treatment	Stop taking methadone, eventually					
IMPROVE HOUSING	Getting a decent place to live	Improve housing situation					

(Continued)

Table 4 (Continued).

THEME GENERATED	REPORTED OUTCOME 1	REPORTED OUTCOME 2	REPORTED OUTCOME 3	REPORTED OUTCOME 4	REPORTED OUTCOME 5	REPORTED OUTCOME 6	REPORTED OUTCOME 7
EDUCATION AND EMPLOYMENT	Having a job	Going back to school	Have licit work	Improve education and work opportunities	Improve finances	Improve employment status	Get education, job, and wanting to support their family
IMPROVED FAMILIAL/SOCIAL RELATIONSHIPS	Raising children	Family	Improve relationships with family and friends	Forging meaningful relationships with others.	Increase non- drug scene socialisation	Change social networks	

health concept from the action of committing criminal activities. None of the remaining five studies included goals that related back to mental health improvement.

Goals Related to Living a Normal Life

Stability and Normalcy

Three of the eight included studies reported goals that were categorized into the theme of *stability and normalcy*. Marchand et al, 2020 reported patients saying that they would like to increase stability and routine in their lives. Sanger et al, 2020 had participants say that a goal they had was to have a stable and normal life. Groshkova et al, 2013 had 15.9% of participants report that they wanted to have a normal, stable with routine and structure.

Reduce Criminal Activity

Three studies identified goals that generated the theme of *reduce criminal activity*. Groshkova et al, 2013 asked their participants through open-ended questions what areas they would like help with and 2.7% wanted to reduce their criminal activity. Marchand et al, 2020 conducted qualitative interviews in which one of the themes that emerged in patient centred care outcomes was to decrease their involvement in illegal activities. Stover 2010 also had 57% of participants say they would like to stop illegal activities come up, but this response was specific to wanting to stop committing crimes to support their opioid dependence. The remaining five studies did not report goals relating to reduction of criminal activity.

Improve Housing

Two studies reported patient goals that related back to *improving their housing*. Groshkova et al, 2013 have 12.4% of participants report that they would like to improve from their current housing condition. Mitchell et al, 2011 had participants report that they would like to get a better place to live in.

Employment and Education

Five studies reported patient goals that related back to *employment and education*. Sanger et al, 2020 had participants express goals of wanting to go back to school, and/or get a job and supporting their family. While 11.5% of the participants in Groshkova et al 2013 reported that they would like to improve their finances. Although this reported goal does not directly use words included in this theme, the concept of improving finances relates to employment. This same study also had 15% of participants state that they would like to improve their education and employment opportunities. Stover 2010 had 51% of participants state that they would like to improve their job status. Gelpi-Acosta et al, 2014 had participants report that they would like to have legal employment. Mitchell et al, 2011 had participants report two goal categories of going back to school and obtaining employment, which were categorized into this one theme.

Improved Social/Familial Relationships

Four studies included patient reported goals relating to *improving social and/or familial relationships*. Stover 2010 had 61% of participants report that they would like to change their current social networks. Groshkova et al, 2013 reported two separate goals in which 7.1% of participants wanted to improve their relationships with friends/family and 6.2% of participants wanted to increase socializing with people that are not in the drug-scene. Gelpi-Acosta et al, 2014 reported a goal of observing social norms, which included the goal of family. Mitchell et al, 2011 also reported two goals, which included raising children and creating meaningful relationships.

Summary of Evidence

There are millions of individuals that have OUD across the world, and this puts enormous burden on the patients, families, communities, healthcare systems, and economic needs of various countries.^{40,41} One of the most common forms of treatment for OUD is MOUD and it is important to understand what treatment goals of MOUD should be considered and what are the goals of patients that are enrolling into these programs. This systematic review identified a total of 43

goals that were categorized into 12 domains. It is known that OUD has a multifaceted impact with concerns related to physical and mental health, social, economic and quality of life.⁶ These concerns are reflected by the treatment goals and domains that patients have identified in this review that extend beyond abstinence from opioids or staying in treatment longer.

The most reported domain across the studies was to reduce all drug use not just opioids. Although patients in two of the studies reported illicit substance use specific to heroin and other opioids, in the remaining five studies, patients reported wanting to stop using substances altogether. It has been suggested that up to 42% of individuals with OUD have other co-morbid substance use.⁴² Reducing all substance use is an important domain in this population and should be addressed in MOUD as polysubstance use is associated with negative treatment outcomes.^{43–45} A study looking at the inclusion criteria of trials for people with OUD reported that 70% of the population with OUD would not be included in studies due to co-substance use, a common exclusion criterion in OUD trials.⁴⁶ Despite the lack of generalizability of treatment, MOUD is indicated for all patients with OUD irrespective of co-substance use.⁴⁶ With polysubstance use being highly prevalent in this population, exclusion of comorbid substance use within the OUD population is creating an evidence base that is not reflective of the actual patient population.

To a lesser extent, the theme of withdrawal avoidance came up in findings as well. Withdrawal from opioids occurs when a person with dependence on opioids significantly reduces or abruptly stops using opioids. Withdrawal symptoms include aches, pains, muscle spasms, irritability, anxiety, GI upset, among others.^{47,48} Suffering from withdrawal symptoms can often lead people with OUD to relapse and continued opioid use. The fear of going into withdrawal may also act as a barrier for getting treatment or reaching their goals. Some patients have expressed preferring methadone over buprenorphine due to fear of precipitated withdrawal.⁴⁹ Guidelines recommend that treatment of withdrawal symptoms is a vital component of OUD management. However, it is only one part of what should be a more comprehensive treatment plan.^{50,51} Discontinuing treatment prematurely once withdrawal symptoms resolve may be associated with increased risk of relapse to opioid use and overdose.⁵²

Improvement of physical health was expressed as a treatment goal by patients with OUD receiving MOUD. Physical health comorbidities are common in OUD with one of the most common being pain.⁵³ Pain management was expressed as a specific goal under this domain and an important goal that needs to be taken into consideration when developing treatment plans. A recent study found that 64% of their participants had chronic pain and majority of them had this chronic pain before they were diagnosed with OUD.⁵⁴ It has been suggested that the increased prescribing of opioids for chronic, noncancer pain is one of the contributing factors in the rise of the opioid epidemic.⁵⁵ With this pain sub-population in OUD, it is important to consider adding the management of pain as a factor that should be assessed concurrently in MOUD. There are also other physical health conditions such as hepatitis C and HIV, which are associated with risk-taking behaviours.⁵⁶ Some substance use disorder treatment clinics do offer hepatitis C treatment on-site but this is not consistent across different services and areas. Physical health plays a major role in overall quality of life⁵⁷ and this review highlights the fact that patients with OUD want to address and improve their overall health, not just their OUD.

Given how prevalent comorbid psychiatric disorders are in OUD, unsurprisingly, mental health improvement was also an area that patients want help with. A previous study suggested that up to 80% of patients with OUD have a comorbid psychiatric illness and although there was no association found between psychiatric comorbidities and abstinence from opioid use during the course of MOUD, there are implications for overall quality of life.⁴² A study found that those with psychiatric comorbidities in methadone treatment had decreased quality of life.⁵⁸ Treating psychiatric comorbidities has shown improvement in psychiatric outcomes⁵⁹ and this may in turn impact overall quality of life. Given the prevalence and impact of mental health comorbidities in patients with OUD, and patients' goals around improving their mental health, integrating psychiatric care into MOUD programs can have implications for treatment outcomes and meeting patients' goals.

One of the most used outcome measures in clinical trials of OUD is retention in treatment. However, in this review only a quarter of the included studies had patients mention that as one of their goals. In contrast to retention, 25% of studies reported participants who wanted to stop MOUD altogether or taper off to a low dose.¹⁸ These findings highlight that patients want different things out of treatment compared to what trial outcomes deem as a success for treatment. This

highlights the need to apply a model of patient centred care in MOUD. OUD management guidelines recommend MOUD as a first line of treatment. However, the length of treatment duration still remains unclear which makes it difficult for policy makers and clinicians to gauge benchmarks of treatment success.⁶⁰ If patients do not want to remain in treatment as a long term goal, this should be discussed with service providers and taken into account by developing tailored treatment programs.

Domains relating to living a normal life were consistently reported across studies. Participants reported goals around employment, education, relationships, housing and avoid criminal activity. Past research reported that OUD increases the risk of unemployment⁶¹ and employment increases likelihood of long-term opioid use abstinence.⁶² This indicates that employment can provide a sense of stability and protective factor for continuing opioid use and perhaps considering how MOUD may impede employment (for example, by requiring daily clinic visits to receive supervised methadone and frequent urine drug screens) should be addressed.⁶³ Trials have found that those on MOUD committed fewer crimes in comparison to those not on MOUD, which suggests that MOUD may be an effective method in reducing criminal activity for some patients.^{64,65} Improved social relationships is also an important goal to address because it has strong implications for treatment outcomes. It has been established that social support is strongly related to retention in treatment, decreased odds of relapse, abstinence, and an overall improved quality of life for those with substance use disorders.^{66–68}

One of the biggest obstacles when creating and providing an intervention for patients with chronic conditions like OUD is to identify what is being achieved by the treatment being implemented and for whom it is being delivered. The current treatments being used for OUD patients are not systematically tailored to the patients' goals but instead investigate objective measures like urine drug screen or treatment retention, which also have a place. However, consideration for other aspects of treatment goals should be included. Despite the urgent needs to manage the opioid crisis, there are no large studies to address the gap of patients' goals in OUD that can inform clinical trials and treatment programs to better support patients with OUD. This paper can serve as an initial step in informing the rationale and methodology for future research in a mixed-methods or qualitative study to further examine what is important for people with OUD and why.

Strengths and Limitations

This study used systematic review methodology to address a knowledge gap around patients' goals during treatment for OUD. Although we were able to identify some literature on this topic, the paucity and variation in the way patients' goals were explored and reported did not allow us to pool these studies and conduct quantitative syntheses. As we have presented a descriptive systematic review, we were unable to assess the certainty of evidence using the GRADE approach. As majority of the studies included in this review were qualitative and observational, the limitations such as social desirability, confirmation and selection bias may have occurred in the individual articles. While we are unable to control for these limitations, we conducted risk of bias assessments and presented the results in a qualitative synthesis to avoid any bias in the methodology of this systematic review. Additionally, given the complex nature of OUD, it is also important to take an approach that meets patients', policy makers' and service providers' expectations. While this review takes on the perspective of patients, it is important to conduct research that examines other stakeholders' perspectives. Despite these limitations, we have presented 12 unique domains that patients have identified as important to them in their treatment goals.

Conclusion

With the continuing effects of the opioid epidemic on the world population, it is important to examine what are patients' goals in treatment. Being able to identify the strengths and limitations of MOUD will allow for of OUD patient care to advance. This will also allow for the revision of treatment guidelines and recommendations to take on a patient-centred approach. We identified domains related to MOUD, normalcy and stability, physical and mental health improvement, which are inconsistent with many clinical trial outcomes of retention and opioid abstinence. These results highlight that patients want to achieve goals from MOUD that are outside of the traditional outcomes measured for treatment success. These results can be used as a stepping stone for further research that can aid in creating tools, which clinicians can use to

incorporate the patient perspective into current addiction treatment models. Future research and trials should include patients' goals in addition to the commonly used measures and identify more inclusive treatment outcome measures to enhance patients' treatment by implementing a more patient centered approach in OUD management.

Funding

Dr. Samaan is supported by research grants from the Canadian Institutes for Health Research (grant numbers PJT-156306 and SHI-155404).

Disclosure

The authors declare no conflicts of interest.

References

1. Opioid overdose. Available from: <https://www.who.int/news-room/fact-sheets/detail/opioid-overdose>. Accessed April 26, 2022.
2. World drug report; 2021. Available from: <https://www.unodc.org/unodc/en/data-and-analysis/wdr2021.html>. Accessed April 26, 2022.
3. Opioid- and stimulant-related harms in Canada. Available from: <https://health-infobase.canada.ca/substance-related-harms/opioids-stimulants/>. Accessed November 10, 2021.
4. Canadian Institute for Health Information. Opioids in Canada. Available from: <https://www.cihi.ca/en/opioids-in-canada>. Accessed November 10, 2021.
5. Interactive Opioid Tool. Public health Ontario. Available from: <https://www.publichealthontario.ca/en/data-and-analysis/substance-use/interactive-opioid-tool>. Accessed November 10, 2021.
6. American Psychiatric Association, American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. Arlington, VA; 2013.
7. CDC. *Centers for Disease Control and Prevention*. U.S.: State Prescribing Rates; 2016.
8. Abuse S Results from the 2012 national survey on drug use and health: summary of national findings, NSDUH series H-46, HHS publication no. (SMA) 13-4795. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013.
9. Rieb LM, Samaan Z, Furlan AD, et al. Canadian guidelines on opioid use disorder among older adults. *Can Geriatr J*. 2020;23(1):123. doi:10.5770/cgj.23.420
10. Sociodemographic Profiles and Clinical Outcomes for Clients. Journal of forensic nursing. Available from: https://journals.lww.com/forensicnursing/Abstract/2019/12000/Sociodemographic_Profiles_and_Clinical_Outcomes.8.aspx. Accessed November 10, 2021.
11. Park TW, Cheng DM, Lloyd-Travaglini CA, Bernstein J, Palfai TP, Saitz R. Changes in health outcomes as a function of abstinence and reduction in illicit psychoactive drug use: a prospective study in primary care. *Addiction*. 2015;110(9):1476–1483. doi:10.1111/add.13020
12. Darke S, Marel C, Slade T, Ross J, Mills KL, Teesson M. Patterns and correlates of sustained heroin abstinence: findings from the 11-year follow-up of the Australian Treatment Outcome Study. *J Stud Alcohol Drugs*. 2015;76(6):909–915. doi:10.15288/jsad.2015.76.909
13. Bertschy G. Methadone maintenance treatment: an update. *Eur Arch Psychiatry Clin Neurosci*. 1995;245(2):114–124. doi:10.1007/BF02190738
14. Bawor M, Dennis BB, Varenbut M, et al. Sex differences in substance use, health, and social functioning among opioid users receiving methadone treatment: a multicenter cohort study. *Biol Sex Differ*. 2015;6(1):21. doi:10.1186/s13293-015-0038-6
15. Zielinski L, Bhatt M, Sanger N, et al. Association between cannabis use and methadone maintenance treatment outcomes: an investigation into sex differences. *Biol Sex Differ*. 2017;8(1):8. doi:10.1186/s13293-017-0130-1
16. Kakko J, Grönbladh L, Svanborg KD, et al. A stepped care strategy using buprenorphine and methadone versus conventional methadone maintenance in heroin dependence: a randomized controlled trial. *Am J Psychiatry*. 2007;164(5):797–803. doi:10.1176/ajp.2007.164.5.797
17. Lions C, Carrieri MP, Michel L, et al. Predictors of non-prescribed opioid use after one year of methadone treatment: an attributable-risk approach (ANRS-Methaville trial). *Drug Alcohol Depend*. 2014;135:1–8. doi:10.1016/j.drugalcdep.2013.10.018
18. Dennis BB, Sanger N, Bawor M, et al. A call for consensus in defining efficacy in clinical trials for opioid addiction: combined results from a systematic review and qualitative study in patients receiving pharmacological assisted therapy for opioid use disorder. *Trials*. 2020;21(1):30. doi:10.1186/s13063-019-3995-y
19. Schuckit MA. Treatment of opioid-use disorders. *N Engl J Med*. 2016;375(4):357–368. doi:10.1056/NEJMra1604339
20. Fiellin DA, Schottenfeld RS, Cutter CJ, Moore BA, Barry DT, O'Connor PG. Primary care-based buprenorphine taper vs maintenance therapy for prescription opioid dependence: a randomized clinical trial. *JAMA Intern Med*. 2014;174(12):1947–1954. doi:10.1001/jamainternmed.2014.5302
21. Cisewski DH, Santos C, Koyfman A, Long B. Approach to buprenorphine use for opioid withdrawal treatment in the emergency setting. *Am J Emerg Med*. 2019;37(1):143–150. doi:10.1016/j.ajem.2018.10.013
22. ScienceDirect. Considering the harms of our habits: the reflexive urine drug screen in opioid use disorder treatment. Available from: <https://www.sciencedirect.com/science/article/abs/pii/S0740547220305158>. Accessed November 11, 2021.
23. Centre for Addiction and Mental Health. Opioid Agonist Therapy: A Synthesis of Canadian Guidelines for Treating Opioid Use Disorder. Published May 2021. Available at <https://www.camh.ca/-/media/files/professionals/canadian-opioid-use-disorder-guideline2021-pdf.pdf>
24. Solberg LI, Asche SE, Butler JC. It is time to ask patients what outcomes are important to them. *Am J Accountable Care*. 2015;3(4):48–54.
25. American Geriatrics Society Expert Panel on Person-Centered Care. Person-centered care: a definition and essential elements. *J Am Geriatr Soc*. 2016;64(1):15–18. doi:10.1111/jgs.13866
26. Marsden J, Gossop M, Stewart D, et al. The Maudsley Addiction Profile (MAP): a brief instrument for assessing treatment outcome. *Addiction*. 1998;93(12):1857–1867. doi:10.1046/j.1360-0443.1998.9312185711.x
27. Sanger N, Shahid H, Dennis BB, et al. Identifying patient-important outcomes in medication-assisted treatment for opioid use disorder patients: a systematic review protocol. *BMJ open*. 2018;8(12):e025059. doi:10.1136/bmjopen-2018-025059

28. Covidence. Covidence systematic review software. Melbourne: Australia. Veritas health innovation; 2019.
29. Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097
30. Long HA, French DP, Brooks JM. Optimising the value of the critical appraisal skills programme (CASP) tool for quality appraisal in qualitative evidence synthesis. *Res Method Med Health Sci*. 2020;1(1):31–42. doi:10.1177/2632084320947559
31. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses; 2000.
32. Sanger N, Panesar B, Rosic T, et al. The future of precision medicine in opioid use disorder: inclusion of patient-important outcomes in clinical trials. *Braz J Psychiatry*. 2020;43:138–146.
33. Groshkova T, Metrebian N, Hallam C, et al. Treatment expectations and satisfaction of treatment-refractory opioid-dependent patients in RIOTT, the R andomised I njectable O piate T reatment T rial, the UK's first supervised injectable maintenance clinics. *Drug Alcohol Rev*. 2013;32(6):566–573. doi:10.1111/dar.12062
34. Mitchell SG, Morioka R, Reisinger HS, et al. Redefining retention: recovery from the patient's perspective. *J Psychoactive Drugs*. 2011;43(2):99–107. doi:10.1080/02791072.2011.587392
35. Marchand K, Foreman J, MacDonald S, Harrison S, Schechter MT, Oviedo-Joekes E. Building healthcare provider relationships for patient-centered care: a qualitative study of the experiences of people receiving injectable opioid agonist treatment. *Subst Abuse Treat Prev Policy*. 2020;15(1):1–9. doi:10.1186/s13011-020-0253-y
36. Stöver H. Barriers to opioid substitution treatment access, entry and retention: a survey of opioid users, patients in treatment, and treating and non-treating physicians. *Eur Addict Res*. 2011;17(1):44–54. doi:10.1159/000320576
37. O'Reilly F, O'Connell D, O'Carroll A, Whitford DL, Long J. Sharing control: user involvement in general practice based methadone maintenance. *Ir J Psychol Med*. 2011;28(3):129–133. doi:10.1017/S079096670001209X
38. Dale-Perera A, Alam F, Barker P. Opioid-dependence treatment in the era of recovery: insights from a UK survey of physicians, patients and out-of-treatment opioid users. *J Subst Use*. 2015;20(5):354–362. doi:10.3109/14659891.2014.923532
39. Gelpi-Acosta C. Challenging biopower: "Liquid cuffs" and the "Junkie" habitus. *Drugs*. 2015;22(3):248–254.
40. Vos T, Abajobir AA, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390(10100):1211–1259.
41. Degenhardt L, Hall W. Extent of illicit drug use and dependence, and their contribution to the global burden of disease. *Lancet*. 2012;379(9810):55–70. doi:10.1016/S0140-6736(11)61138-0
42. Rosic T, Naji L, Bawor M, et al. The impact of comorbid psychiatric disorders on methadone maintenance treatment in opioid use disorder: a prospective cohort study. *Neuropsychiatr Dis Treat*. 2017;13:1399–1408. doi:10.2147/NDT.S129480
43. Peles E, Schreiber S, Adelson M. Factors predicting retention in treatment: 10-year experience of a methadone maintenance treatment (MMT) clinic in Israel. *Drug Alcohol Depend*. 2006;82(3):211–217. doi:10.1016/j.drugalcdep.2005.09.004
44. Zador D, Sunjic S. Deaths in methadone maintenance treatment in New South Wales, Australia 1990–1995. *Addiction*. 2000;95(1):77–84. doi:10.1046/j.1360-0443.2000.951778.x
45. Huang CLC, Lee CW. Factors associated with mortality among heroin users after seeking treatment with methadone: a population-based cohort study in Taiwan. *J Subst Abuse Treat*. 2013;44(3):295–300. doi:10.1016/j.jsat.2012.08.003
46. Dennis BB, Roshanov PS, Naji L, et al. Opioid substitution and antagonist therapy trials exclude the common addiction patient: a systematic review and analysis of eligibility criteria. *Trials*. 2015;16(1):1–18. doi:10.1186/s13063-015-0942-4
47. Kosten TR, Baxter LE. Effective management of opioid withdrawal symptoms: a gateway to opioid dependence treatment. *Am J Addict*. 2019;28(2):55–62. doi:10.1111/ajad.12862
48. Wesson DR, Ling W. The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs*. 2003;35(2):253–259. doi:10.1080/02791072.2003.10400007
49. Pinto H, Maskrey V, Swift L, Rumball D, Wagle A, Holland R. The SUMMIT trial: a field comparison of buprenorphine versus methadone maintenance treatment. *J Subst Abuse Treat*. 2010;39(4):340–352. doi:10.1016/j.jsat.2010.07.009
50. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) national practice guideline for the use of medications in the treatment of addiction involving opioid use. *J Addict Med*. 2015;9(5):358. doi:10.1097/ADM.0000000000000166
51. Abuse S. Medications for opioid use disorder. Treatment Improvement Protocol (TIP) series 63, executive summary. HHS Publication No. (SMA) 18-5063EXSUMM; 2018.
52. Cousins G, Boland F, Courtney B, Barry J, Lyons S, Fahey T. Risk of mortality on and off methadone substitution treatment in primary care: a national cohort study. *Addiction*. 2016;111(1):73–82. doi:10.1111/add.13087
53. Sanger N, Bhatt M, Shams I, et al. Association between socio-demographic and health functioning variables among patients with opioid use disorder introduced by prescription: a prospective cohort study. *Pain Physician*. 2018;21(6):E623–E632.
54. Hser YI, Mooney LJ, Saxon AJ, Miotto K, Bell DS, Huang D. Chronic pain among patients with opioid use disorder: results from electronic health records data. *J Subst Abuse Treat*. 2017;77:26–30. doi:10.1016/j.jsat.2017.03.006
55. Abuse NI on D. As opioid use disorders increased, prescriptions for treatment did not keep pace. National Institute on Drug Abuse. Published July 2; 2018. Available from: <https://www.drugabuse.gov/news-events/nida-notes/2018/07/opioid-use-disorders-increased-prescriptions-treatment-did-not-keep-pace>. Accessed November 21, 2021.
56. Halkitis PN, Parsons JT. Recreational drug use and HIV-risk sexual behavior among men frequenting gay social venues. *J Gay Lesbian Soc Serv*. 2002;14(4):19–38. doi:10.1300/J041v14n04_02
57. Anokye NK, Trueman P, Green C, Pavey TG, Taylor RS. Physical activity and health related quality of life. *BMC Public Health*. 2012;12(1):624. doi:10.1186/1471-2458-12-624
58. Carpentier PJ, Krabbe PFM, van Gogh MT, Knapen LJM, Buitelaar JK, de Jong CAJ. Psychiatric comorbidity reduces quality of life in chronic methadone maintained patients. *Am J Addict*. 2009;18(6):470–480. doi:10.3109/10550490903205652
59. Brooner RK, Kidorf MS, King VL, et al. Managing psychiatric comorbidity within versus outside of methadone treatment settings: a randomized and controlled evaluation. *Addiction*. 2013;108(11):1942–1951. doi:10.1111/add.12269

60. Bruneau J, Ahamad K, Goyer MÈ, et al. Management of opioid use disorders: a national clinical practice guideline. *Can Med Assoc J.* **2018**;190(9):E247–E257. doi:10.1503/cmaj.170958
61. Rhee TG, Rosenheck RA. Association of current and past opioid use disorders with health-related quality of life and employment among US adults. *Drug Alcohol Depend.* **2019**;199:122–128. doi:10.1016/j.drugalcdep.2019.03.004
62. Walton MT, Hall MT. The effects of employment interventions on addiction treatment outcomes: a review of the literature. *J Soc Work Pract Addict.* **2016**;16(4):358–384. doi:10.1080/1533256X.2016.1235429
63. Richardson L, Wood E, Montaner J, Kerr T. Addiction treatment-related Employment barriers: the impact of methadone maintenance. *J Subst Abuse Treat.* **2012**;43(3):276–284. doi:10.1016/j.jsat.2011.12.008
64. Murphy SM, Polsky D, Lee JD, et al. Cost-effectiveness of extended release naltrexone to prevent relapse among criminal justice-involved individuals with a history of opioid use disorder. *Addiction.* **2017**;112(8):1440–1450. doi:10.1111/add.13807
65. Strain EC, Stitzer ML, Liebson IA, Bigelow GE. Methadone dose and treatment outcome. *Drug Alcohol Depend.* **1993**;33(2):105–117. doi:10.1016/0376-8716(93)90052-R
66. Zhou K, Zhuang G. Retention in methadone maintenance treatment in mainland China, 2004–2012: a literature review. *Addict Behav.* **2014**;39(1):22–29. doi:10.1016/j.addbeh.2013.09.001
67. Wasserman DA, Stewart AL, Delucchi KL. Social support and abstinence from opiates and cocaine during opioid maintenance treatment. *Drug Alcohol Depend.* **2001**;65(1):65–75. doi:10.1016/S0376-8716(01)00151-X
68. Lobmaier P, Gossop M, Waal H, Bramness J. The pharmacological treatment of opioid addiction - A clinical perspective. *Eur J Clin Pharmacol.* **2010**;66(6):537–545. doi:10.1007/s00228-010-0793-6
69. Page M, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* **2021** Mar 29;372:n71. doi:10.1136/bmj.n71

Patient Related Outcome Measures

Dovepress

Publish your work in this journal

Patient Related Outcome Measures is an international, peer-reviewed, open access journal focusing on treatment outcomes specifically relevant to patients. All aspects of patient care are addressed within the journal and practitioners from all disciplines are invited to submit their work as well as healthcare researchers and patient support groups. The manuscript management system is completely online and includes a very quick and fair peer-review system. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <http://www.dovepress.com/patient-related-outcome-measures-journal>