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Exploring goals in treatment for opioid use disorder: Are patients' goals associated with expected treatment outcomes?

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Exploring goals in treatment for opioid use disorder: Are patients' goals associated with expected treatment outcomes?

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ABSTRACT

Objectives: Existing methods of measuring effectiveness of pharmacological treatment for opioid use disorder (OUD) are highly variable. Therefore, understanding patients' treatment goals is an integral part of patient-centered care. Our objective is to explore whether patients' treatment goals align with a frequently used clinical outcome, opioid abstinence.

Design: Prospective cohort design

Setting and Participants: We collected prospective data from 2,030 participants who were required to be receiving pharmacological treatment for a diagnosis of OUD in order to meet study inclusion criteria. We asked, "What are your goals in treatment?" and used Nvivo software to identify common themes.

Primary outcome measure: Urine drug screens were collected for 3 months post-study enrolment in order to identify abstinence versus ongoing opioid use. We used logistic regression to examine the association between treatment goals and opioid abstinence.

Results: Participants had a mean age of 39.2 years (standard deviation = 10.7), 44% were female, and median duration in treatment was 2.6 years (interquartile range 5.2). Six overarching goals were identified from patient responses, including "stop or taper off of treatment" (68%), "stay or get clean" (37%), and "live a normal life" (14%). Participants reporting the goal "stay or get clean" had lower odds of abstinence at 3 months than those who did not report this goal (OR = 0.73, 95% CI 0.59-0.91, $p = 0.005$). Although the majority of patients wanted to taper off or stop medication, this goal was not associated with opioid abstinence, nor were any of their other goals.

Conclusions: Patient goals in OUD treatment do not appear to be associated with program measures of outcome (i.e., abstinence from opioids). Future studies are needed to examine outcomes related to patient-reported treatment goals found in our study;

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3 pain management, employment, and stopping/tapering treatment
4 should all be explored.
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6 Strengths and limitations of this study:

- 7 • This study is strengthened by its large sample size (2,000
8 participants) and multisite design.
- 9 • Participating clinics follow a harm-reduction approach to
10 treatment and these findings may not generalize to
11 abstinence-based treatment settings.
- 12 • The goals and treatment outcomes of patients newly entering
13 treatment may differ from those of patients who have been
14 in treatment longer and may not be captured in this study.

15 Key words: opioid agonist treatment, patient-centred care,
16 methadone, buprenorphine, treatment goals
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INTRODUCTION

Opioid use disorder (OUD) remains a clinical and public health challenge, with ongoing high rates of opioid use and overdose deaths.¹ Consequently, growing numbers of patients are enrolled in pharmacological treatment for OUD.^{2,3} Methadone, a full opioid agonist, and buprenorphine, a partial opioid agonist, are the two most commonly used medications in the management of OUD; they act to reduce cravings and withdrawal, and support abstinence from ongoing opioid use.⁴ Evidence from systematic reviews of experimental studies indicates that both medications reduce opioid use.^{5,6} However, not all patients have favorable outcomes,^{7,8} and patients who continue to use opioids during treatment have a high risk of overdose and death.^{9,10}

Better understanding patients' goals in treatment is considered increasingly important within the field of substance use and addiction.¹¹⁻¹³ The now well-known concept of *patient-centered care* was originally coined with the definition of "care that is respectful of, and responsive to, individual patient preferences, needs, and values",^{14,15} and is demonstrated to have a significant impact on patients' outcomes and satisfaction in treatment.¹⁶ Increasing attention is being paid to patients' goals and the implementation of patient-centred care principles in addiction treatment.¹⁷

Identifying core treatment outcomes is an active area of investigation within the field of Addiction Medicine. Unfortunately, there is still significant variability in the outcomes used to evaluate the effectiveness of pharmacological treatment for OUD.¹⁸ How to best measure and assess treatment outcomes remains uncertain, and current practices risk being based upon convenience. Opioid use, measured by urine drug screens (UDS), and retention in treatment are the most commonly used primary outcomes measured in clinical studies and treatment programs;¹⁸ however, it is unknown how well these outcomes are associated with patients' goals in treatment. Personal and social functioning outcomes are, in contrast, much less commonly assessed.¹⁸ As core endpoints and outcome sets for studies of OUD are developed, it is critical to understand which goals in treatment are important to patients and how to best measure them.

In a recent study by Sanger et al., 2020, we used qualitative analysis methods to examine patient-reported treatment goals in a cohort of more than 2,000 patients receiving outpatient pharmacological treatment for OUD.¹⁹ We identified six distinct

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3 goals in treatment from patient responses, including to control
4 cravings or withdrawal, to maintain or stabilize medication
5 dose, to stop or taper off treatment, to "stay or get clean", to
6 manage pain, and to "live a normal life".¹⁹
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9 The objective of the present study was to explore whether these
10 patient-reported treatment goals are associated with abstinence
11 from opioid use (a frequently measured program outcome). We
12 hypothesized that patient goals related to drug use would be
13 associated with opioid use during treatment; meanwhile, goals
14 unrelated to drug use would have no association with UDS
15 results.
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17 METHODS

18 *Data*

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20 We collected prospective observational data from 2,030
21 participants recruited from 45 outpatient clinics in the
22 Pharmacogenetics of Opioid Substitution Treatment Response
23 (POST) study. To meet study inclusion criteria, participants
24 were required to be receiving pharmacological treatment (for any
25 length of time) for a diagnosis of OUD, as per the Diagnostic
26 and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)²⁰.
27 No other inclusion or exclusion criteria were applied in order
28 to increase the generalizability of this study. Participants
29 completed face-to-face interviews at study entry to collect
30 information on demographic and clinical characteristics.
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35 At study intake, all participants were asked the open-ended
36 question, "What are your goals in treatment".¹⁹ We used NVivo
37 software QSR International [Americas] Inc., Burlington,
38 Massachusetts, USA) for qualitative analysis to identify common
39 themes from patient answers.²¹ We began by reviewing the open-
40 ended question data in Microsoft Excel to minimize typographical
41 errors present in the free text responses and to get a better
42 understanding of the data present. We then imported the data
43 onto the NVivo platform and began cataloguing main ideas,
44 phrases, and patterns into nodes using word and text queries,
45 and a review of the transcribed data. Word and text queries
46 helped us capture the patterns in data and improve analytic
47 accuracy by identifying stemmed variants. This was followed by
48 regular housekeeping of nodes which included the collapsing of
49 related nodes into one node. These steps were completed
50 iteratively, eventually allowing well researched nodes to become
51 themes. Ultimately, we identified six distinct "themes" or
52 "goals" in treatment: 1) to control cravings or withdrawal, 2)
53 to maintain or stabilize medication dose, 3) to stop or taper
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3 off treatment, 4) to "stay or get clean", 5) to manage pain, and
4 6) to "live a normal life".¹⁹
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6 We collected the results of UDSs for opioids for three months
7 following study entry to assess treatment outcome. The FaStep
8 Assay (Trimedica Supply Network Ltd, Concord, Ontario, Canada)
9 was used to detect morphine, oxycodone, fentanyl, methadone
10 metabolite, and buprenorphine, as well as other non-opioid
11 substances.²² UDSs were collected following clinic protocol
12 (typically weekly or biweekly). This study was conducted in
13 accordance with the ethical guidelines of the Hamilton
14 Integrated Research Ethics Board (project ID 4556) and all
15 participants provided informed consent. We report methods and
16 results in accordance with the Strengthening the Reporting of
17 Observational Studies in Epidemiology (STROBE) guidelines.²³
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20 21 *Statistical analysis*

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23 We conducted all quantitative analyses using Stata Version 15.1
24 (StataCorp LP, College Station, TX, USA). We report demographic
25 and clinical data using mean and standard deviation (SD) for
26 normally distributed continuous variables and median with
27 quartiles 1 and 3 or interquartile range (IQR) for skewed data.
28 We report categorical variables as frequency with percentage. We
29 summarize the results of UDSs in three ways: 1) the mean number
30 of UDSs collected; 2) the percentage of opioid-positive UDSs; and
31 3) abstinence from opioid use, defined as no opioid-positive
32 UDSs during the 3-month time period.
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36 We used logistic regression analysis to examine the association
37 between patient goals in treatment and abstinence from opioid
38 use, adjusting for other important covariates. We constructed a
39 logistic regression model, using the dependent variable
40 abstinence from opioid use throughout the 3 months following
41 study entry. We included the six identified treatment goals in
42 the model and controlled for other factors believed to impact
43 ongoing opioid use in treatment, including age, sex,^{24,25} type of
44 treatment (methadone or buprenorphine-naloxone), medication
45 dose,²⁶ length of time in treatment,²⁷ and abstinence from opioids
46 at baseline. We also conducted an additional logistic regression
47 to determine whether the number of goals reported by
48 participants was associated with opioid abstinence, as patients
49 who report more treatment needs tend to have more opioid use.²⁸
50 Results are reported as odds ratios (OR) with 95% confidence
51 intervals (CI) and associated *p* values. We report the estimates
52 of effect for our main variables of interest (treatment goals)
53 in the results table and describe all variables adjusted for in
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3 a footnote in the table in order to focus solely on the
4 variables of interest to our specific study question. We
5 assessed for multicollinearity using variance inflation factor
6 and examined model diagnostics using the Hosmer-Lemeshow
7 statistic and deviance residuals. We conducted a sensitivity
8 analysis after excluding observations with a deviance residual
9 lower than -2 or higher than 2. Our sample size of 2,030
10 participants and event rate of more than 1,000 participants
11 abstinent from opioids is adequate, based on the rule of thumb
12 for number of events needed ($n = 10$) per covariate included in
13 logistic regression analysis.²⁹
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17 Missing data were identified and reported for each variable of
18 interest. There were less than 5 cases with missing data for
19 baseline demographic or clinical variables. For 3-month UDS,
20 missing data affected 34 participants (1.7%). Reasons for
21 missing 3-month UDS data included: results not yet available ($n =$
22 6), transfer to another clinic ($n = 8$), treatment failure ($n =$
23 10), incarceration ($n = 3$), completion of treatment ($n=2$), and
24 other ($n = 4$), such as hospitalization, moving, or never
25 starting treatment. Due to the low percentage of missing data,
26 all missing data were handled by available case analysis.
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29 RESULTS

30 *Participant characteristics and goals in treatment*

31
32 Altogether, 2,030 participants were included in the analyses
33 (Figure 1; Study flow diagram), with a mean age of 39.2 years
34 (SD = 10.7) and 44% were female (Table 1). The majority of
35 participants were receiving treatment with methadone (78.9%)
36 compared to buprenorphine-naloxone (21.1%) and the median length
37 of time in treatment was 2.6 years (IQR 5.2). UDSs collected for
38 the three months of study duration were available for 1,996
39 participants. Among these participants, 57% were abstinent from
40 opioid use during those 3 months. The most common patient-
41 reported goal was to "stop or taper off treatment" (68%; see
42 Table 1 for all goals). Other goals included to "stay or get
43 clean" (37%), to "live a normal life" (14%), and to control
44 cravings or withdrawal (12%). Most participants (60.2%) reported
45 one treatment goal (mean number of goals = 1.49, SD = 0.67).
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50 *Association between patients' goals in treatment and 3-month* 51 *abstinence from opioid use (MAT program goal)*

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54 We examined the association between patient goals and abstinence
55 from opioid use for 3 months following study entry, adjusting
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3 for other characteristics previously shown to be associated with
4 ongoing opioid use (Table 2). Paradoxically, participants
5 reporting the goal "to stay or get clean" had 27% lower odds of
6 abstinence from opioids at 3 months (OR = 0.73, 95% CI 0.59-
7 0.91, $p = 0.005$), even after adjusting for baseline abstinence
8 from opioid use. No other patient-reported goals in treatment
9 were significantly associated with 3-month abstinence.

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12 Good model fit was assessed using the Hosmer-Lemeshow statistic
13 ($\chi^2 = 5.93$, $p = 0.656$) and multicollinearity was not a concern
14 (mean VIF 1.19). Using deviance residuals, we detected 14
15 outliers with deviance residuals greater than an absolute value
16 of 2. We conducted a post-hoc sensitivity analysis removing
17 outliers and found that participants who reported the goal "to
18 control cravings or withdrawal" also had significantly lower
19 odds of opioid abstinence at 3 months (OR = 0. .2, 95% CI 0.54-
20 0.99, $p = 0.044$; data not shown). There were no other
21 significant changes to the results upon removing outliers.

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24 Finally, the number of goals reported by participants was not
25 significantly associated with 3-month abstinence (data not
26 shown).

27 28 29 DISCUSSION

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31 In this prospective cohort study, we examined treatment goals
32 reported by more than 2,000 patients receiving pharmacological
33 treatment for OUD to determine their association with the
34 frequently measured treatment outcome, opioid use. Participants
35 reporting the goals to "stay or get clean" and to control
36 cravings or withdrawal were less likely to be abstinent from
37 opioids during the next 3 months of treatment than participants
38 who did not report those goals. Other goals related to
39 termination of treatment, pain or personal or social functioning
40 were not associated with opioid use. These findings suggest that
41 abstinence from opioids, a commonly used treatment outcome
42 measured in clinical trials, does not reflect what patients want
43 out of treatment.

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47 We found that patients who identified goals related to stopping
48 drug use or controlling OUD symptoms had worse outcomes in
49 treatment as measured by UDS. One possible explanation is that
50 patients who were experiencing worse outcomes in treatment or
51 higher severity of illness were more likely to report goals
52 regarding management of substance use symptoms and abstinence
53 from drug use, thus also increasing the likelihood that they
54 experienced ongoing opioid use. Another possibility is that
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3 participants who had achieved abstinence or had improvements in
4 OUD withdrawal symptoms may have been less likely to identify
5 the same goals.
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8 Although the majority of patients wanted to taper off or stop
9 treatment, this goal had no association with abstinence from
10 opioid use. This finding calls into question the rationale for
11 entering and continuing pharmacological treatment while
12 continuing to use opioids for this group of patients.
13 Furthermore, this is a particularly important finding, given
14 that retention in treatment is amongst the most consistently
15 measured outcomes,¹⁸ and guidance around taper and
16 discontinuation of long-term opioid agonist treatments for
17 opioid use disorder is limited.^{4,33} Studies examining opioid
18 agonist tapers have identified challenges and risks of poor
19 outcomes^{34,35} including withdrawal symptoms, return to drug use,
20 pain, psychiatric symptoms, hospitalization, and death.^{36,37} A
21 previous study found that patients' interest in stopping
22 treatment was associated with shorter duration of treatment and
23 lack of concern about relapse to opioid use.³⁸ This is concerning
24 as one would hope patients planning to stop treatment would be
25 reliably abstinent from opioids. What distinguishes this group
26 of patients who wish to discontinue treatment? Whether some of
27 these patients are mandated to be in treatment is unknown.
28 Better understanding patients' reasons for wanting to stop or
29 taper treatment and examining outcomes for patients who initiate
30 an opioid agonist taper is imperative.
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35 Other patient identified goals in treatment that were not
36 associated with the results of their UDS, included goals around
37 pain management, and the goal "to live a normal life". This
38 suggests that clinicians and researchers may require additional
39 tools to measure outcomes related to those patient-important
40 treatment goals. Tools validated to assess pain in this
41 population include the Brief Pain Inventory^{30,31} and social
42 functioning may be examined using the Maudsley Addiction
43 Profile.³² A more nuanced understanding of specific goals around
44 personal and social functioning, on a population and individual
45 level, is required in order to be able to appropriately assess
46 and address these goals during treatment.
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50 This study has a number of potential limitations. There may be a
51 healthy user/volunteer bias,³⁹ such that individuals with better
52 outcomes in treatment may have been more likely to participate.
53 Additionally, the goals and treatment outcomes of patients newly
54 entering treatment may differ from those of patients who have
55 been in treatment longer. Patients who may have successfully
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3 achieved their goal of termination of treatment were not
4 captured by this study since they would no longer be on OUD thus
5 not recruited. The findings in this study may not generalize to
6 settings in which opioid agonist medications take on a primarily
7 abstinence-based role in treatment. In Canada, pharmacological
8 treatment for OUD is provided largely in a harm-reduction model,
9 in which retention in treatment is not contingent on abstinence
10 from opioids or non-opioid substances. This study did not
11 measure patient's satisfaction or perception of treatment
12 success or perception of meeting their goals. Future studies
13 that examine patient satisfaction in treatment may wish to
14 determine whether perception of treatment success correlates
15 with program-measured outcomes such as opioid abstinence.
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19 CONCLUSION

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21 Patients report a number of different goals in their treatment
22 for OUD, which are not associated with traditional goals of
23 treatment programs and outcomes measured in clinical settings
24 (abstinence from opioid use measured by UDS). We found that
25 patients who identified goals related to stopping drug use or
26 controlling OUD symptoms were more likely to have ongoing opioid
27 use. However, goals unrelated to drug use carried no significant
28 association with opioid use status. Patients reporting the goal
29 of wanting to stop treatment were no more likely to be abstinent
30 from opioids. The patient-identified goals to manage pain or
31 "live a normal life" had no association with ongoing opioid use.
32 Future studies are needed to examine outcomes related to the
33 goals in treatment identified in our study. Are these goals
34 being met in treatment? For example, do patients feel their pain
35 is well managed? Do they achieve employment? Can they achieve
36 the goal of stopping treatment without adverse consequences? As
37 core outcome sets are developed, patient-important outcomes
38 remain essential to consider and may help with implementing
39 patient-centered approaches to treatment.
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45
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47 Substitution Treatment Response (POST) study participants for
48 their time and contributions, without which this study would not
49 be possible.
50

51 **Authors' contributions**

52 TR, LN, BP, NS, BBD, and ZS are responsible for the study
53 concept and design. TR, BP, LT and ZS developed the methods and
54 data analysis. TR conducted quantitative analysis and BP
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3 conducted qualitative analysis. TR wrote the first draft of the
4 manuscript, and TR, LN, BP, DBC, NS, BBD, DCM, LR, AW, LT, and
5 ZS, contributed to writing and critically revising the final
6 manuscript. All authors reviewed and approved the final
7 manuscript.
8
9

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11
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15 analysis, interpretation, or publication of results.
16
17

18 **Patient and Public Involvement**

19
20 Patients or the public were not involved in the design, or
21 conduct, or reporting, or dissemination plans of our research.
22
23

24 **Declaration of interests**

25 Dr. Marsh reports Salary income as Chief Medical Director,
26 Canadian Addiction Treatment Centres and as Associate Dean
27 Research, Innovation and International Relations, Northern
28 Ontario School of Medicine. The other study authors declare no
29 conflicts of interest.
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References

1. Special Advisory Committee on the Epidemic of Opioid Overdoses. National report: Apparent opioid-related deaths in Canada (January 2016 to December 2018). Web Based Report. Ottawa: Public Health Agency of Canada; June 2019.
2. Fischer B, Kurdyak P, Goldner E, et al. Treatment of prescription opioid disorders in Canada: looking at the 'other epidemic'? *Subst Abuse Treat Prev Policy*. 2016;11:12.
3. Ontario Drug Policy Research Network. Ontario Prescription Opioid Tool. Toronto, ON; July 2018. DOI: 10.31027/ODPRN.2018.01. Available from: <https://odprn.ca/ontario-opioid-drug-observatory/ontario-prescription-opioid-tool/>
4. Bruneau J, Ahamad K, Goyer ME, et al. Management of opioid use disorders: a national clinical practice guideline. *CMAJ*. 2018 Mar 5;190(9):E247-E257.
5. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database Syst Rev*. 2009;3:CD002209.
6. Nielsen S, Larance B, Degenhardt L, Gowing L, Kehler C, Lintzeris N. Opioid agonist treatment for pharmaceutical opioid dependent people. *Cochrane Database Syst Rev*. 2016 May 9; (5):CD011117.
7. Dennis BB, Naji L, Bawor M, et al. The effectiveness of opioid substitution treatments for patients with opioid dependence: a systematic review and multiple treatment comparison protocol. *Syst Rev*. 2014;3:105.
8. Li Y, Kantelip J-P, Gerritsen-van Schieveen P, Davani S. Interindividual variability of methadone response. *Mol Diagn Ther*. 2008;12:109-24.
9. Huang CL, 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.
10. Zador D, Sunjic S. Deaths in methadone maintenance treatment in New South Wales, Australia 1990-1995. *Addiction*. 2000;95(1):77-84.
11. Deshpande PR, Rajan S, Sudeepthi BL, Abdul Nazir CP. Patient-reported outcomes: a new era in clinical research. *Perspect Clin Res*. 2011;2:137-44.
12. Marchand K, Beaumont S, Westfall J, et al. Patient-centred care for addiction treatment: a scoping review protocol. *BMJ Open*. 2018 Dec; 8(12):e024588

13. Kolind T, Hesse M. Patient-centred care-perhaps the future of substance abuse treatment. *Addiction*. 2017 Mar;112(3):465-466.
14. National Research Council. Crossing the quality chasm: a new health system for the 21st century. Washington, DC: National Academies Press, 2001.
15. Barry MJ, Edgman-Levitan S. Shared decision making-pinnacle of patient-centred care. *N Engl J Med*. 2012 Mar 1;366(9):780-781.
16. Stewart M, Brown JB, Donner A, et al. The impact of patient-centered care on outcomes. *J Fam Pract*. 2000 Sep;49(9):796-804.
17. Marchand K, Beaumont S, Westfall J, et al. Conceptualizing patient-centered care for substance use disorder treatment: findings from a systematic scoping review. *Subst Abuse Traet Prev Policy*. 2019 Sep 11;14(1):37.
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;21:30.
19. Sanger N, Panesar B, Rosic T, et al. The future of precision medicine in opioid use disorder: the inclusion of patient important outcomes in clinical trials. *Braz J Psychiatry*. 2020;00:000-000. <http://dx.doi.org/10.1590/1516-4446-2019-0734>
20. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th edn. Arlington, VA: American Psychiatric Publishing, 2013.
21. NVivo qualitative data analysis software; QSR International Pty Ltd. Version 12, 2018.
22. FaStep Assay. Trimedic Supply Network Ltd. Available from: <https://www.trimedic-inc.com/wp-content/uploads/2018/04/Fastep-Package-Insert.pdf>
23. Elm Ev, Altman DG, Egger M, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007; 335: 806-8.
24. Bawor M, Dennis BB, Bhalerao A, et al. Sex differences in outcomes of methadone maintenance treatment for opioid use disorder: a systematic review and meta-analysis. *CMAJ Open*. 2015;3(3):E344-E351. Published 2015 Jul 17. doi:10.9778/cmajo.20140089
25. 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;6:21. Published 2015 Nov 10. doi:10.1186/s13293-015-0038-6
26. Strain EC, Bigelow GE, Liebson IA, Stitzer ML. Moderate- vs High-Dose Methadone in the Treatment of Opioid Dependence: A Randomized Trial. *JAMA*. 1999;281(11):1000-1005
27. Eastwood B, Strang J, Marsden J. Effectiveness of treatment for opioid use disorder: A national, five-year, prospective, observational study in England. *Drug Alcohol Depend*. 2017 Jul 1;176:139-147.
28. Kelly SM, O'Grady KE, Brown BS, Mitchell SG, Schwartz RP. The role of patient satisfaction in methadone treatment. *Am J Drug Alcohol Abuse*. 2010;36(3):150-154.
29. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996; 49: 1373-9.
30. Cleeland C. The Brief Pain Inventory: User Guide. Texas, USA 1991.
31. Dennis BB, Roshanov PS, Bawor M, et al. Usefulness of the Brief Pain Inventory in patient with opioid addiction receiving methadone maintenance treatment. *Pain Physician*. 2016 Jan;19(1):E181-95.
32. Marsden J, Gossop M, Stewart D, et al. The Maudsley Addiction Profile (MAP): a brief instrument for assessing treatment outcome. *Addiction*. 1998;93(12):1857-68.
33. College of Physicians and Surgeons of British Columbia. Methadone Maintenance Program: Clinical Practice Guidelines. Updated September 2015. Accessed on April 11, 2020 from: http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Publications/Epid/Other/02_CPSBC-Methadone_Maintenance_Program_Clinical%20_Practice_Guideline.pdf
34. Magura S, Rosenblum A. Leaving methadone treatment: Lessons learned, lessons forgotten, lessons ignored. *Mount Sinai Journal of Medicine*. 2001;68:62-74.
35. Latowsky M. Improving detoxification outcomes from methadone maintenance treatment: The interrelationships of affective states and protracted withdrawal. *Journal of Psychoactive Drugs*. 1996;28:251-257.
36. Calsyn DA, Malcy JA, Saxon AJ. Slow tapering from methadone maintenance in a program encouraging indefinite maintenance. *J Subst Abuse Treat*. 2006 Mar;30(2):159-163
37. Nosyk B, Sun H, Evans E, et al. Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: results from a population-

1
2
3 based retrospective cohort study. *Addiction*. 2012
4 Sep;107(9):1621-1629.

- 5
6 38. Winstock AR, Lintzeris N, Lea T. "Should I stay or
7 should I go?" Coming off methadone and buprenorphine
8 treatment. *Int J Drug Policy*. 2011 Jan;22(1):77-81.
9
10 39. Shrank WH, Patrick AR, Brookhart MA. Healthy user and
11 related biases in observational studies of preventive
12 interventions: a primer for physicians. *J Gen Intern Med*.
13 2011;26(5):546-550. doi:10.1007/s11606-010-1609-1
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Table 1. Characteristics of participants at study entry (N = 2,030).

Characteristic	Statistic
Demographic and clinical	
Age in years; mean (SD)	39.2 (10.7)
Female sex ^a ; n (%)	894 (44.1)
Type of treatment; n (%)	
Methadone	1601 (78.9)
Buprenorphine-naloxone	429 (21.1)
Dose in mg/day; mean (SD)	
Methadone	70.5 (41.4)
Buprenorphine-naloxone	12.0 (6.7)
Years in treatment ^a ; median (IQR)	2.6 (5.2)
Abstinence from opioid use at baseline ^b ; n (%)	646 (31.9)
Number of opioid urine drug screens at 3 months ^c ; mean (SD)	12.6 (5.3)
Median percentage of opioid-positive urine drug screens at 3 months ^c ; median (Q1, Q3)	0 (0, 20)
Abstinence from opioid use at 3 months ^c ; n (%)	1,127 (56.5)
Patient-reported goals in treatment ^d	
Number of goals reported; n (%)	
One	1222 (60.2%)
Two	643 (31.7%)
Three	150 (7.4%)
Four	13 (0.64%)
Five	2 (0.1%)
Control cravings/withdrawal	247 (12.17%)

Maintain or stabilize medication dose	122 (6.01%)
"Live a normal life"	283 (13.94%)
Manage pain	240 (11.82%)
"Stay or get clean"	742 (36.55%)
Stop or taper off treatment	1386 (68.28%)
SD = Standard Deviation, Q1 = 25 th percentile, Q3 = 75 th percentile	
^a Data available for 2,029 participants.	
^b Data available for 2,028 participants.	
^c Data available for 1,996 participants (missing for 34 participants).	
^d Percentages sum to more than 100% as patients could report multiple goals in treatment.	

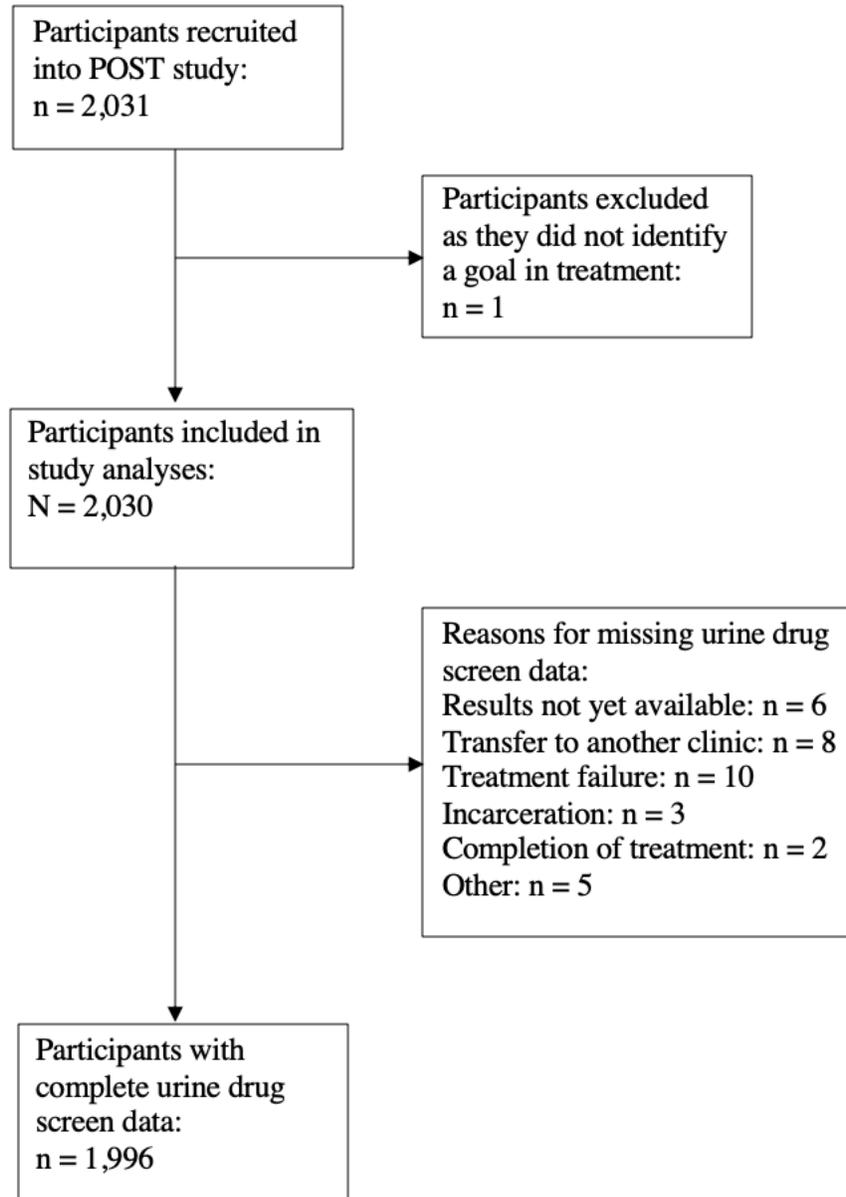
Table 2. Multivariable model of the association between patient goals and abstinence from opioid use for 3 months following study entry.

Covariate	Complete case analysis ^a (n = 1, 994 ^b)			Sensitivity analysis excluding outliers (n = 1,980) ^{a,c}		
	OR	95% CI	p	OR	95% CI	p
Control cravings/withdrawal	0.76	0.56, 1.03	0.078	0.73	0.54, 0.99	0.044
Maintain or stabilize medication dose	1.15	0.74, 1.79	0.523	1.24	0.79, 1.95	0.354
“Live a normal life”	1.02	0.77, 1.35	0.879	0.98	0.74, 1.31	0.902
Manage pain	1.0	0.73, 1.36	0.976	0.96	0.70, 1.32	0.806
“Stay or get clean”	0.73	0.59, 0.91	0.005	0.70	0.56, 0.87	0.001
Stop or taper off treatment	1.0	0.80, 1.27	0.974	1.01	0.80, 1.27	0.954

OR = Odds Ratio, CI = Confidence Interval
 Variance inflation factor = 1.19
 Hosmer-Lemeshow χ^2 5.93, p = 0.656
^a Model is adjusted for age, sex, type of treatment (methadone or buprenorphine-naloxone), dose, length of time in treatment, and opioid abstinence at baseline.
^b Participants with missing data in any of the included covariates are excluded due to complete case analysis (missing urine drug screen data: n = 36, missing sex: n = 1, missing length of time in treatment: n = 1).

^c Excluding 14 outliers detected using deviance residuals less than -2 from the analysis

For peer review only

Figure 1. Study flow diagram.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Included on page:
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3 (intro, paragraphs 1-3)
Objectives	3	State specific objectives, including any pre-specified hypotheses	3 (intro, paragraph 5)
Methods			
Study design	4	Present key elements of study design early in the paper	3-4 (Methods, Data section)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4 (Methods, Data section)
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3 (Methods, paragraph 1, 3)
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4 (Statistical analysis, paragraph 2)
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4 (Methods)

Bias	9	Describe any efforts to address potential sources of bias	Methods (Data), Limitations (page 7)
Study size	10	Explain how the study size was arrived at	Figure 1 Study Flow Diagram
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods, Statistical analysis page 4
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Methods, Statistical analysis page 4
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	Page 5 first paragraph
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
(e) Describe any sensitivity analyses			
Continued on next page			
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Study flow diagram Figure 1
		(b) Give reasons for non-participation at each stage	Study flow diagram Figure 1
		(c) Consider use of a flow diagram	Study flow diagram Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1

		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Table 1
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Table 1
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Results page 5, paragraph 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	Discussion page 6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Discussion page 7
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion page 6
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion page 7
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Title page

Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
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Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses

Continued on next page

Results

BMJ Open

Are patients' goals in treatment associated with expected treatment outcomes? Findings from a mixed-methods study on outpatient pharmacological treatment for opioid use disorder.

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Are patients' goals in treatment associated with expected treatment outcomes? Findings from a mixed-methods study on outpatient pharmacological treatment for opioid use disorder.

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10
11 ABSTRACT
12

13 Objectives: Existing methods of measuring effectiveness of
14 pharmacological treatment for opioid use disorder (OUD) are
15 highly variable. Therefore, understanding patients' treatment
16 goals is an integral part of patient-centered care. Our
17 objective is to explore whether patients' treatment goals align
18 with a frequently used clinical outcome, opioid abstinence.
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20

21 Design: Triangulation mixed-methods design
22

23 Setting and Participants: We collected prospective data from
24 2,030 participants who were receiving methadone or
25 buprenorphine-naloxone treatment for a diagnosis of OUD in order
26 to meet study inclusion criteria. Participants were recruited
27 from 45 centrally-managed outpatient opioid agonist therapy
28 clinics in Ontario, Canada. At study entry, we asked, "What are
29 your goals in treatment?" and used Nvivo software to identify
30 common themes.
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33 Primary outcome measure: Urine drug screens (UDS) were collected
34 for 3 months post-study enrolment in order to identify
35 abstinence versus ongoing opioid use (mean number of UDS over 3
36 months = 12.6, standard deviation (SD) = 5.3). We used logistic
37 regression to examine the association between treatment goals
38 and opioid abstinence.
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41 Results: Participants had a mean age of 39.2 years (SD = 10.7),
42 44% were female, and median duration in treatment was 2.6 years
43 (interquartile range 5.2). Six overarching goals were identified
44 from patient responses, including "stop or taper off of
45 treatment" (68%), "stay or get clean" (37%), and "live a normal
46 life" (14%). Participants reporting the goal "stay or get clean"
47 had lower odds of abstinence at 3 months than those who did not
48 report this goal (OR = 0.73, 95% CI 0.59-0.91, $p = 0.005$).
49 Although the majority of patients wanted to taper off or stop
50 medication, this goal was not associated with opioid abstinence,
51 nor were any of their other goals.
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3 Conclusions: Patient goals in OUD treatment do not appear to be
4 associated with program measures of outcome (i.e., abstinence
5 from opioids). Future studies are needed to examine outcomes
6 related to patient-reported treatment goals found in our study;
7 pain management, employment, and stopping/tapering treatment
8 should all be explored.
9

10
11 Strengths and limitations of this study:

- 12 • This study is strengthened by its large sample size (2,000
13 participants) and multisite design.
- 14 • Participating clinics follow a harm-reduction approach to
15 treatment and these findings may not generalize to
16 abstinence-based treatment settings.
- 17 • The goals and treatment outcomes of patients newly entering
18 treatment may differ from those of patients who have been
19 in treatment longer and may not be captured in this study.
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21

22
23 Key words: opioid agonist treatment, patient-centred care,
24 methadone, buprenorphine, treatment goals

25 INTRODUCTION

26
27 Opioid use disorder (OUD) remains a clinical and public health
28 challenge, with ongoing high rates of opioid use and overdose
29 deaths.¹ Consequently, growing numbers of patients are enrolled
30 in pharmacological treatment for OUD.^{2,3} Methadone, a full opioid
31 agonist, and buprenorphine, a partial opioid agonist, are the
32 two most commonly used medications in the management of OUD;
33 they act to reduce cravings and withdrawal, and support
34 abstinence from ongoing opioid use.⁴ Evidence from systematic
35 reviews of experimental studies indicates that both medications
36 reduce opioid use.^{5,6} However, not all patients have favorable
37 outcomes,^{7,8} and patients who continue to use opioids during
38 treatment have a high risk of overdose and death.^{9,10} Other
39 treatments, including heroin-assisted treatment, are available
40 in some jurisdictions for patients who have limited response to
41 treatment with first-line medications.¹¹
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46 Better understanding patients' goals in treatment is considered
47 increasingly important within the field of substance use and
48 addiction.¹²⁻¹⁴ The now well-known concept of *patient-centered*
49 *care* was originally coined with the definition of "care that is
50 respectful of, and responsive to, individual patient
51 preferences, needs, and values",^{15,16} and is demonstrated to have
52 a significant impact on patients' outcomes and satisfaction in
53 treatment.¹⁷ Increasing attention is being paid to patients'
54 goals and the implementation of patient-centred care principles
55 in addiction treatment.¹⁸
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4 Identifying core treatment outcomes is an active area of
5 investigation within the field of Addiction Medicine.¹⁹
6 Unfortunately, there is still significant variability in the
7 outcomes used to evaluate the effectiveness of pharmacological
8 treatment for OUD.^{20, 21} How to best measure and assess treatment
9 outcomes remains uncertain, and current practices risk being
10 based upon convenience. Opioid use, measured by urine drug
11 screens (UDS), and retention in treatment are the most commonly
12 used primary outcomes measured in clinical studies and treatment
13 programs;²¹ however, it is unknown how well these outcomes are
14 associated with patients' goals in treatment. Personal and
15 social functioning outcomes are, in contrast, much less commonly
16 assessed.²¹ As core endpoints and outcome sets for studies of OUD
17 are developed, it is critical to understand which goals in
18 treatment are important to patients and how to best measure
19 them.
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24 In a recent study by Sanger et al., 2020, we used qualitative
25 analysis methods to examine patient-reported treatment goals in
26 a cohort of more than 2,000 patients receiving outpatient
27 pharmacological treatment for OUD.²² We identified six distinct
28 goals in treatment from patient responses, including to control
29 cravings or withdrawal, to maintain or stabilize medication
30 dose, to stop or taper off treatment, to "stay or get clean", to
31 manage pain, and to "live a normal life".²²
32

33
34 The objective of the present study was to explore whether these
35 patient-reported treatment goals are associated with abstinence
36 from opioid use (a frequently measured program outcome). We
37 hypothesized that patient goals related to drug use would be
38 associated with opioid use during treatment; meanwhile, goals
39 unrelated to drug use would have no association with UDS
40 results.
41

42 METHODS

43 *Data*

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45 We collected prospective observational data from 2,030
46 participants recruited from 45 outpatient clinics in the
47 Pharmacogenetics of Opioid Substitution Treatment Response
48 (POST) study. To meet study inclusion criteria, participants
49 were required to be at least 16 years of age and receiving
50 pharmacological treatment with methadone or buprenorphine-
51 naloxone (for any length of time) for a diagnosis of OUD, as per
52 the Diagnostic and Statistical Manual of Mental Disorders, 5th
53 Edition (DSM-5).²³ The diagnosis of OUD was made by treating
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3 physicians according to DSM-5 criteria and is an eligibility
4 criterion for treatment entry and clinical follow up at the
5 outpatient clinics included in this study. No other inclusion or
6 exclusion criteria were applied in order to increase the
7 generalizability of this study. Participants completed face-to-
8 face interviews at study entry to collect information on
9 demographic and clinical characteristics.
10

11
12 We used a triangulation mixed-methods design to combine
13 quantitative and qualitative data collection, where both
14 quantitative and qualitative data were collected within one
15 study instrument using closed- and open-ended questions.^{24,25} At
16 study intake, participants were interviewed by trained research
17 staff to obtain information on sociodemographic and clinical
18 information, medical history, and substance use history.
19 Research staff have a background in addiction research, as they
20 have previously participated in recruitment of participants for
21 a study investigating genetic influences on methadone
22 treatment.²⁶ Their experience allowed for familiarity of
23 addiction related terms used in interview responses, but they
24 were not known to the participants of this research study. Study
25 interviews were conducted in-person at the CATC. The interview
26 data used in this study is from participants recruited from May
27 2018 until August 2019. During the interview, all participants
28 who met the inclusion and exclusion criteria above were asked
29 the open-ended question, "What are your goals in treatment".
30 Details regarding the study settings and data collection are
31 outlined in a previous study looking at OUD-related patient
32 important outcomes.²² Verbal responses, in their entirety, were
33 transcribed by research staff word-for-word in online anonymized
34 records, where each participant was given an anonymized record
35 number.
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41 We collected the results of UDSs for opioids for each
42 participant for three months following study entry to assess
43 treatment outcome. The FaStep Assay (Trimedec Supply Network
44 Ltd, Concord, Ontario, Canada) was used to detect morphine,
45 oxycodone, fentanyl, methadone metabolite, and buprenorphine, as
46 well as other non-opioid substances.²⁷ Though other methods may
47 be used to assess ongoing opioid use during treatment, such as
48 saliva and hair tests, as well as self-report,²⁸ UDSs are
49 collected as part of routine clinical protocol in the clinics
50 participating in this study and are a recommended method of
51 assessment based on Canadian Guidelines.⁴ UDSs were collected
52 following clinic protocol (typically weekly or biweekly). For
53 each participant, we calculated the percentage of opioid-
54 positive UDSs by dividing the number of opioid-positive urines
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3 by the number of urine samples taken. Abstinence from opioids
4 was selected as our primary study outcome as it is a routinely
5 measured treatment outcome in both clinical practice and
6 research studies.
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9 Another commonly studied treatment outcome, retention in
10 treatment, was not formally assessed in the present study for
11 two reasons. First, treatment retention is not equivalent to the
12 duration of time enrolled in this study (as our study used a
13 naturalistic design and enrolled patients in various stages of
14 their treatment). Second, with the exception of patients who
15 have entered treatment for the first time, there exists some
16 uncertainty in defining treatment retention because patients
17 frequently enter and discontinue treatment at various points in
18 their course of illness. Instead, we asked participants to
19 report their length of time enrolled in this treatment episode
20 (as a proxy for treatment retention) and adjusted all study
21 analyses for length of time in treatment.
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25 This study was reviewed and approved by the Hamilton Integrated
26 Research Ethics Board (project ID 4556) and conducted in
27 accordance with its ethical guidelines. We report methods and
28 quantitative results in accordance with the Strengthening the
29 Reporting of Observational Studies in Epidemiology (STROBE)
30 guidelines.²⁹
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33 34 *Qualitative analysis* 35

36 The qualitative approach used to analyze the data was data-
37 driven thematic analysis.³⁰ We began by familiarizing ourselves
38 with the data through active, repeated reading of the interview
39 responses and began to recognize emerging patterns. This phase
40 of data familiarization also allowed us to minimize
41 typographical errors present in the free text responses. We
42 began phase two by generating initial codes using NVivo software
43 QSR International [Americas] Inc., Burlington, Massachusetts,
44 USA) for qualitative analysis to identify common themes from
45 patient answers.³¹ We began cataloguing main ideas, phrases, and
46 patterns into meaningful nodes using word and text queries, and
47 a review of the transcribed data. Word and text queries helped
48 us capture the patterns in data and improve analytic accuracy by
49 identifying stemmed variants. Each data item was given equal
50 attention and in addition to text and word queries, key phrases
51 were tagged within each data item. This phase is characterized
52 by the generation of a codebook that provided specific
53 definitions of the key phrases, words and patterns. The next
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3 phase consisted of the labelling of some nodes as themes and the
4 collapsing of related nodes into one node, eventually being
5 labelled as a themes or sub-themes. The final phase consisted of
6 a review of identified themes and resultant reworking of themes
7 to better establish coherent patterns within each theme.
8 Defining and refining of each theme followed this phase, where
9 patterns and content were considered before choosing relevant
10 and reflective theme names.^{30,32} To increase rigour in our
11 analysis we used investigator triangulation, where phases
12 concerning the generation of themes involved the consultation of
13 four investigators to ensure incorporation of diverse
14 perspectives. This was reflected in the iterative review of
15 nodes and patterns, where meaningfulness of coding was discussed
16 and was reassessed at every identified phase. We report
17 qualitative methods and results in accordance with the Standards
18 of Reporting Qualitative Research (SRQR).³³
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23 *Quantitative analysis*

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25 We conducted all quantitative analyses using Stata Version 15.1
26 (StataCorp LP, College Station, TX, USA). We report demographic
27 and clinical data using mean and standard deviation (SD) for
28 normally distributed continuous variables and median with
29 quartiles 1 and 3 or interquartile range (IQR) for skewed data.
30 We report categorical variables as frequency with percentage. We
31 summarize the results of UDSs in three ways: 1) the mean number
32 of UDSs collected; 2) the percentage of opioid-positive UDSs; and
33 3) abstinence from opioid use, defined as no opioid-positive
34 UDSs during the 3-month time period.
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38 We used logistic regression analysis to examine the association
39 between patient goals in treatment and abstinence from opioid
40 use, adjusting for other important covariates. We constructed a
41 logistic regression model, using the dependent variable
42 abstinence from opioid use throughout the 3 months following
43 study entry. We included the six identified treatment goals in
44 the model and controlled for other factors believed to impact
45 ongoing opioid use in treatment, including age, sex,^{34,35} type of
46 treatment (methadone or buprenorphine-naloxone), medication
47 dose,³⁶ length of time in treatment,³⁷ and abstinence from opioids
48 at baseline. We also conducted an additional logistic regression
49 to determine whether the number of goals reported by
50 participants was associated with opioid abstinence, as patients
51 who report more treatment needs tend to have more opioid use.³⁸
52 Results are reported as odds ratios (OR) with 95% confidence
53 intervals (CI) and associated *p* values. We report the estimates
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of effect for our main variables of interest (treatment goals) in the results table and describe all variables adjusted for in a footnote in the table in order to focus solely on the variables of interest to our specific study question. We assessed for multicollinearity using variance inflation factor and examined model diagnostics using the Hosmer-Lemeshow statistic and deviance residuals. We conducted a sensitivity analysis after excluding observations with a deviance residual lower than -2 or higher than 2. Our sample size of 2,030 participants and event rate of more than 1,000 participants abstinent from opioids is adequate, based on the rule of thumb for number of events needed ($n = 10$) per covariate included in logistic regression analysis.³⁹

Missing data were identified and reported for each variable of interest. There were less than 5 cases with missing data for baseline demographic or clinical variables. For 3-month UDS, missing data affected 34 participants (1.7%). Reasons for missing 3-month UDS data included: results not yet available ($n = 6$), transfer to another clinic ($n = 8$), treatment failure ($n = 10$), incarceration ($n = 3$), completion of treatment ($n=2$), and other ($n = 4$), such as hospitalization, moving, or never starting treatment. Due to the low percentage of missing data, all missing data were handled by available case analysis.

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

Participant characteristics and goals in treatment

Altogether, 2,030 participants were included in the analyses (Figure 1; Study flow diagram), with a mean age of 39.2 years ($SD = 10.7$) and 44% were female (Table 1). The majority of participants were receiving treatment with methadone (78.9%) compared to buprenorphine-naloxone (21.1%) and the median length of time in treatment was 2.6 years (IQR 5.2). UDSs collected for the three months of study duration were available for 1,996 participants. Among these participants, 57% were abstinent from opioid use during those 3 months. Ultimately, we identified six distinct "themes" or "goals" in treatment: 1) to control cravings or withdrawal, 2) to maintain or stabilize medication dose, 3) to stop or taper off treatment, 4) to "stay or get

clean", 5) to manage pain, and 6) to "live a normal life", as presented by our previous paper looking at patient important outcomes in the OUD population receiving MAT.²² The "control cravings or withdrawal" theme consisted of participants responses stating they would like to avoid withdrawal or control their cravings. Participant responses grouped in the second theme of "no changes in treatment" were made up of responses indicating that they wanted to maintain OSAT doses, stabilize their OSAT dose, or did not have any reported goals. The third goal to "stop OSAT treatment" had goals to stop treatment completely, to not be dependent on OSAT, to taper off, or reduce dose. Participant goals such as wanting to get clean, stay clean, achieve abstinence, or achieve sobriety from all drugs were included in the fourth goal of "avoiding illicit drugs". The fifth theme of "pain management" either mentioned chronic pain, or pain management in general. The sixth theme of "living a normal life" consisted of responses such as wanting a stable life, normal life, to get qualifications related to education, job or work, to achieve good mental health, or wanting to support their family.²²

The most common patient-reported goal was to "stop or taper off treatment" (68%; see Table 1 for all goals). Other goals included to "stay or get clean" (37%), to "live a normal life" (14%), and to control cravings or withdrawal (12%). Most participants (60.2%) reported one treatment goal (mean number of goals = 1.49, SD = 0.67).

Association between patients' goals in treatment and 3-month abstinence from opioid use (MAT program goal)

We examined the association between patient goals and abstinence from opioid use for 3 months following study entry, adjusting for other characteristics previously shown to be associated with ongoing opioid use (Table 2). Paradoxically, participants reporting the goal "to stay or get clean" had 27% lower odds of abstinence from opioids at 3 months (OR = 0.73, 95% CI 0.59-0.91, $p = 0.005$), even after adjusting for baseline abstinence from opioid use. No other patient-reported goals in treatment were significantly associated with 3-month abstinence.

Good model fit was assessed using the Hosmer-Lemeshow statistic ($\chi^2 = 5.93$, $p = 0.656$) and multicollinearity was not a concern (mean VIF 1.19). Using deviance residuals, we detected 14 outliers with deviance residuals greater than an absolute value of 2. We conducted a post-hoc sensitivity analysis removing outliers and found that participants who reported the goal "to control cravings or withdrawal" also had significantly lower odds of opioid abstinence at 3 months (OR = 0.73, 95% CI 0.54-0.99, $p = 0.044$; Supplementary Table 1). There were no other significant changes to the results upon removing outliers.

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3 Finally, we examined the association between number of reported
4 goals and abstinence from opioid use for 3 months (Supplementary
5 Table 2). As compared to reporting one goal in treatment,
6 reporting two goals was not associated with opioid use (OR =
7 0.93, 95% CI = 0.75, 1.15, $p = 0.497$), however reporting three
8 or more goals may be associated with lower odds of abstinence
9 from opioids (OR = 0.70, 95% CI = 0.49, 1.0, $p = 0.049$).

12 DISCUSSION

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14 In this mixed-methods study, we examined treatment goals
15 reported by more than 2,000 patients receiving pharmacological
16 treatment for OUD to determine their association with the
17 frequently measured treatment outcome, opioid use. Participants
18 reporting the goals to "stay or get clean" and to control
19 cravings or withdrawal were less likely to be abstinent from
20 opioids during the next 3 months of treatment than participants
21 who did not report those goals. Other goals related to
22 termination of treatment, pain or personal or social functioning
23 were not associated with opioid use. These findings suggest that
24 abstinence from opioids, a commonly used treatment outcome
25 measured in clinical trials, does not reflect what patients want
26 out of treatment, and raises questions about the alignment
27 between treatment outcomes and patient goals.⁴⁰

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29 We found that patients who identified goals related to stopping
30 drug use or controlling OUD symptoms had worse outcomes in
31 treatment as measured by UDS. There is a rich literature
32 examining the apparent contradiction between abstinence-related
33 goals and subsequent drug-taking behaviors. This is in essence
34 the focus of motivational interviewing⁴¹ in which clinicians help
35 patients develop motivation through recognizing discrepancies
36 between their current situation and their goals, shifting the
37 balance towards change.⁴² One possible explanation is that
38 patients who were experiencing worse outcomes in treatment or
39 higher severity of illness were more likely to report goals
40 regarding management of substance use symptoms and abstinence
41 from drug use, thus also increasing the likelihood that they
42 experienced ongoing opioid use. Another possibility is that
43 participants who had achieved abstinence or had improvements in
44 OUD withdrawal symptoms may have been less likely to identify
45 the same goals. Nonetheless, exploring why patients wishing to
46 abstain from opioid use are not achieving this goal is an area
47 requiring further study. Beyond quantitatively examining factors
48 associated with ongoing substance use, previous qualitative
49 studies that explore patient perceptions of barriers and
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3 facilitators to achieving abstinence are illuminating and may
4 inform future interventions and study.⁴³⁻⁴⁵
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7 Although the majority of patients wanted to taper off or stop
8 treatment, this goal had no association with abstinence from
9 opioid use. One possible explanation is that participants may
10 have been unhappy with treatment and therefore non-adherent.
11 Factors associated with non-adherence to opioid agonist
12 treatments have been previously studied.⁴⁶⁻⁴⁹ There is a vast
13 literature on factors affecting patient adherence to treatment
14 in general and, notably, no single explanation sufficiently
15 accounts for variation in adherence.⁵⁰ Authors in this field have
16 suggested considering the patient's experience of illness and
17 its meaning as important factors to study in understanding
18 adherence to treatment.^{50, 51} This finding calls into question the
19 rationale for entering and continuing pharmacological treatment
20 while continuing to use opioids for this group of patients.
21 Furthermore, this is a particularly important finding, given
22 that retention in treatment is amongst the most consistently
23 measured outcomes,¹⁹ and guidance around taper and
24 discontinuation of long-term opioid agonist treatments for
25 opioid use disorder is limited.^{4,52} Studies examining opioid
26 agonist tapers have identified challenges and risks of poor
27 outcomes^{53,54} including withdrawal symptoms, return to drug use,
28 pain, psychiatric symptoms, hospitalization, and death.^{55,56} A
29 previous study found that patients' interest in stopping
30 treatment was associated with shorter duration of treatment and
31 lack of concern about relapse to opioid use.⁵⁷ This is concerning
32 as one would hope patients planning to stop treatment would be
33 reliably abstinent from opioids. What distinguishes this group
34 of patients who wish to discontinue treatment? Whether some of
35 these patients are mandated to be in treatment is unknown.
36 Better understanding patients' reasons for wanting to stop or
37 taper treatment and examining outcomes for patients who initiate
38 an opioid agonist taper is imperative.
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44 Other patient identified goals in treatment that were not
45 associated with the results of their UDS, included goals around
46 pain management, and the goal "to live a normal life". This
47 suggests that clinicians and researchers may require additional
48 tools to measure outcomes related to those patient-important
49 treatment goals. Tools validated to assess pain in this
50 population include the Brief Pain Inventory^{58,59} and social
51 functioning may be examined using the Maudsley Addiction
52 Profile.⁶⁰ A more nuanced understanding of specific goals around
53 personal and social functioning, on a population and individual
54 level, is required in order to be able to appropriately assess
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3 and address these goals during treatment. Overall, our finding
4 that results of UDSs are not associated with all patient goals
5 in treatment is expected as UDSs results would not be expected
6 to be a proxy for all of the different goals. However, this
7 study adds evidence to the notion that traditional metrics of
8 success in opioid use disorder treatment are insufficient in
9 isolation. It is important to note that although patient goals
10 appear to have limited predictive value on opioid use during
11 treatment, this does not imply that clinicians should not ask
12 patients about their treatment goals. It is not uncommon that
13 patients have goals that are not achieved in treatment (e.g.,
14 weight loss, increased physical activity) and this does not mean
15 that clinicians or patients should give up on these goals or
16 should not enquire about them. Rather, we must consider how well
17 traditional metrics of treatment success align with desired
18 treatment outcomes for all stakeholders, especially patients,
19 and consider additional ways to evaluate and improve treatment
20 success based on patients' self-reported goals.
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25 Finally, in a previous paper, we examined group differences
26 between participants selecting each treatment goal.²² Females
27 were more likely to report the goal of stopping treatment. Older
28 age, first exposure to opioids through physician prescription,
29 and unemployment were all associated with greater odds of
30 reporting goals related to pain management.²² These findings
31 indicated that, unsurprisingly, patients' characteristics are
32 associated with their treatment goals and may help to guide
33 focused questioning and evaluation of patients' goals in
34 treatment.
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37 This study has a number of potential limitations. First, this
38 study interprets and summarizes the patients' narrative when
39 expressing their goals in treatment using qualitative methods;
40 however, this interpretation carries limitations related to the
41 potential influence social desirability bias and the influence
42 of contextual factors on patients' responses that have not been
43 explored in this study. Though beyond the scope of this paper,
44 sociological approaches to qualitative analysis include critical
45 appraisal of the circumstances of the participant and the
46 context in which statements are expressed. Furthermore, there
47 may be a healthy user/volunteer bias,⁶¹ such that individuals
48 with better outcomes in treatment may have been more likely to
49 participate. Additionally, the goals and treatment outcomes of
50 patients newly entering treatment may differ from those of
51 patients who have been in treatment longer. Patients who may
52 have successfully achieved their goal of termination of
53 treatment were not captured by this study since they would no
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3 longer be on OUD thus not recruited. The findings in this study
4 may not generalize to settings in which opioid agonist
5 medications take on a primarily abstinence-based role in
6 treatment. In Canada, pharmacological treatment for OUD is
7 provided largely in a harm-reduction model, in which retention
8 in treatment is not contingent on abstinence from opioids or
9 non-opioid substances. This study did not measure patient's
10 satisfaction or perception of treatment success or perception of
11 meeting their goals. Future studies that examine patient
12 satisfaction in treatment may wish to determine whether
13 perception of treatment success correlates with program-measured
14 outcomes such as opioid abstinence.
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17 18 CONCLUSION

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20 Patients report a number of different goals in their treatment
21 for OUD, which are not associated with traditional goals of
22 treatment programs and outcomes measured in clinical settings
23 (abstinence from opioid use measured by UDS). We found that
24 patients who identified goals related to stopping drug use or
25 controlling OUD symptoms were more likely to have ongoing opioid
26 use. However, goals unrelated to drug use carried no significant
27 association with opioid use status. Patients reporting the goal
28 of wanting to stop treatment were no more likely to be abstinent
29 from opioids. The patient-identified goals to manage pain or
30 "live a normal life" had no association with ongoing opioid use.
31 Future studies are needed to examine outcomes related to the
32 goals in treatment identified in our study. Are these goals
33 being met in treatment? For example, do patients feel their pain
34 is well managed? Do they achieve employment? Can they achieve
35 the goal of stopping treatment without adverse consequences? As
36 core outcome sets are developed, patient-important outcomes
37 remain essential to consider and may help with implementing
38 patient-centered approaches to treatment.
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43 ACKNOWLEDGMENTS

44
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46 Substitution Treatment Response (POST) study participants for
47 their time and contributions, without which this study would not
48 be possible.
49

50 51 **Authors' contributions**

52 TR, LN, BP, NS, BBD, and ZS are responsible for the study
53 concept and design. TR, BP, LT and ZS developed the methods and
54 data analysis. TR conducted quantitative analysis and BP
55 conducted qualitative analysis. TR wrote the first draft of the
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3 manuscript, and TR, LN, BP, DBC, NS, BBD, DCM, LR, AW, LT, and
4 ZS, contributed to writing and critically revising the final
5 manuscript. All authors reviewed and approved the final
6 manuscript.
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8 **Data availability**

9 Data are available upon reasonable request
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12 **Role of funding source**

13 This study was supported by research grants from the Canadian
14 Institutes for Health Research (grant numbers PJT-156306 and
15 SHI-155404). The funding bodies had no role in the design,
16 analysis, interpretation, or publication of results.
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19 **Declaration of interests**

20 Dr. Marsh reports Salary income as Chief Medical Director,
21 Canadian Addiction Treatment Centres and as Associate Dean
22 Research, Innovation and International Relations, Northern
23 Ontario School of Medicine. The other study authors declare no
24 conflicts of interest.
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References

1. Special Advisory Committee on the Epidemic of Opioid Overdoses. National report: Apparent opioid-related deaths in Canada (January 2016 to December 2018). Web Based Report. Ottawa: Public Health Agency of Canada; June 2019.
2. Fischer B, Kurdyak P, Goldner E, et al. Treatment of prescription opioid disorders in Canada: looking at the 'other epidemic'? *Subst Abuse Treat Prev Policy*. 2016;11:12.
3. Ontario Drug Policy Research Network. Ontario Prescription Opioid Tool. Toronto, ON; July 2018. DOI: 10.31027/ODPRN.2018.01. Available from: <https://odprn.ca/ontario-opioid-drug-observatory/ontario-prescription-opioid-tool/>
4. Bruneau J, Ahamad K, Goyer ME, et al. Management of opioid use disorders: a national clinical practice guideline. *CMAJ*. 2018 Mar 5;190(9):E247-E257.
5. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database Syst Rev*. 2009;3:CD002209.
6. Nielsen S, Larance B, Degenhardt L, Gowing L, Kehler C, Lintzeris N. Opioid agonist treatment for pharmaceutical opioid dependent people. *Cochrane Database Syst Rev*. 2016 May 9; (5):CD011117.
7. Dennis BB, Naji L, Bawor M, et al. The effectiveness of opioid substitution treatments for patients with opioid dependence: a systematic review and multiple treatment comparison protocol. *Syst Rev*. 2014;3:105.
8. Li Y, Kantelip J-P, Gerritsen-van Schieveen P, Davani S. Interindividual variability of methadone response. *Mol Diagn Ther*. 2008;12:109-24.
9. Huang CL, 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.
10. Zador D, Sunjic S. Deaths in methadone maintenance treatment in New South Wales, Australia 1990-1995. *Addiction*. 2000;95(1):77-84.
11. Ferri M, Davoli M, Perucci CA. Heroin maintenance for chronic heroin-dependent individuals. *Cochrane Database of Systematic Reviews* 2011, Issue 12. Art. No.: CD003410. DOI: 10.1002/14651858.CD003410.pub4
12. Deshpande PR, Rajan S, Sudeepthi BL, Abdul Nazir CP. Patient-reported outcomes: a new era in clinical research. *Perspect Clin Res*. 2011;2:137-44.

13. Marchand K, Beaumont S, Westfall J, et al. Patient-centred care for addiction treatment: a scoping review protocol. *BMJ Open*. 2018 Dec; 8(12):e024588
14. Kolind T, Hesse M. Patient-centred care—perhaps the future of substance abuse treatment. *Addiction*. 2017 Mar;112(3):465–466.
15. National Research Council. *Crossing the quality chasm: a new health system for the 21st century*. Washington, DC: National Academies Press, 2001.
16. Barry MJ, Edgman-Levitan S. Shared decision making—pinnacle of patient-centred care. *N Engl J Med*. 2012 Mar 1;366(9):780–781.
17. Stewart M, Brown JB, Donner A, et al. The impact of patient-centered care on outcomes. *J Fam Pract*. 2000 Sep;49(9):796–804.
18. Marchand K, Beaumont S, Westfall J, et al. Conceptualizing patient-centered care for substance use disorder treatment: findings from a systematic scoping review. *Subst Abuse Treat Prev Policy*. 2019 Sep 11;14(1):37.
19. International Consortium for Health Outcomes Measurement. *ICHOM Standard Set for Addiction*. Accessed on October 26, 2020, from: <https://www.ichom.org/portfolio/addiction/>.
20. Wiessing L, Ferri M, Darke S, Simon R, Griffiths P. Large variation in measures used to assess outcomes of opioid dependence treatment: A systematic review of longitudinal observational studies. *Drug Alcohol Rev*. 2018 Apr;37 Suppl 1:S323–S338. doi:10.1111/dar.12608.
21. 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;21:30.
22. Sanger N, Panesar B, Rosic T, et al. The future of precision medicine in opioid use disorder: the inclusion of patient important outcomes in clinical trials. *Braz J Psychiatry*. 2020;00:000-000. <http://dx.doi.org/10.1590/1516-4446-2019-0734>
23. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5th edn. Arlington, VA: American Psychiatric Publishing, 2013.
24. Plano Clark VL, Huddleston-Casas CA, Churchill SL, et al. Mixed Methods Approaches in Family Science Research. *Journal of Family Issues*. 2008;29(11):1543–1566. doi:10.1177/0192513X08318251
25. Doyle L, Brady AM, Byrne G. An overview of mixed methods research. *Journal of Research in Nursing*. 2009;14(2):175–185. <https://doi.org/10.1177/1744987108093962>
26. Samaan Z, Bawor M, Dennis BB, et al. Genetic influence on methadone treatment outcomes in patients undergoing methadone maintenance treatment for opioid addiction: a pilot study. *Neuropsychiatr Dis Treat*. 2014;19(10):1503–1508.

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59
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27. FaStep Assay. Trimedica Supply Network Ltd. Available from: <https://www.trimedica-inc.com/wp-content/uploads/2018/04/Fastep-Package-Insert.pdf>
 28. Donovan DM, Bigelow GE, Brigham GS, et al. Primary outcome indices in illicit drug dependence treatment research: systematic approach to selection and measurement of drug use end-points in clinical trials. *Addiction*. 2012;107(4):694-708. doi:10.1111/j.1360-0443.2011.03473.x
 29. Elm Ev, Altman DG, Egger M, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007; 335: 806-8.
 30. Braun V, Clarke V. Using thematic analysis in psychology. *Qualitative Research in Psychology*. 2006;3(2):77-101. DOI: 10.1191/1478088706qp063oa
 31. NVivo qualitative data analysis software; QSR International Pty Ltd. Version 12, 2018.
 32. Guest G, MacQueen KM, Namey EE. *Applied thematic analysis*. Thousand Oaks, CA: SAGE Publications, Inc. 2012.
 33. O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. *Acad Med* 2014;89:1245-51. doi:10.1097/ACM.0000000000000388.
 34. Bawor M, Dennis BB, Bhalerao A, et al. Sex differences in outcomes of methadone maintenance treatment for opioid use disorder: a systematic review and meta-analysis. *CMAJ Open*. 2015;3(3):E344-E351. Published 2015 Jul 17. doi:10.9778/cmajo.20140089
 35. 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;6:21. Published 2015 Nov 10. doi:10.1186/s13293-015-0038-6
 36. Strain EC, Bigelow GE, Liebson IA, Stitzer ML. Moderate- vs High-Dose Methadone in the Treatment of Opioid Dependence: A Randomized Trial. *JAMA*. 1999;281(11):1000-1005
 37. Eastwood B, Strang J, Marsden J. Effectiveness of treatment for opioid use disorder: A national, five-year, prospective, observational study in England. *Drug Alcohol Depend*. 2017 Jul 1;176:139-147.
 38. Kelly SM, O'Grady KE, Brown BS, Mitchell SG, Schwartz RP. The role of patient satisfaction in methadone treatment. *Am J Drug Alcohol Abuse*. 2010;36(3):150-154.
 39. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996; 49: 1373-9.

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40. Liberati A. Need to re-align patient-oriented and commercial and academic research. *Cochrane Database of Systematic Reviews* 2011, Issue 12. Art. No.: ED000094. DOI: 10.1002/14651858.ED000094
41. Miller WR, Rose GS. Toward a theory of motivational interviewing. *Am Psychol.* 2009;64(6):527-537. doi:10.1037/a0016830
42. Westra HA, Aviram A. Core skills in motivational interviewing. *Psychotherapy (Chic)*. 2013 Sep;50(3):273-8. doi: 10.1037/a0032409. PMID: 24000834.
43. Herbeck, D. M., Brecht, M. L., Christou, D., & Lovinger, K. (2014). A qualitative study of methamphetamine users' perspectives on barriers and facilitators of drug abstinence. *Journal of psychoactive drugs*, 46(3), 215-225.
44. Moran, L., Keenan, E. & Elmusharaf, K. Barriers to progressing through a methadone maintenance treatment programme: perspectives of the clients in the Mid-West of Ireland's drug and alcohol services. *BMC Health Serv Res* 18, 911 (2018).
45. Notley C, Blyth A, Maskrey V, Craig J, Holland R. The experience of long-term opiate maintenance treatment and reported barriers to recovery: a qualitative systematic review. *Eur Addict Res.* 2013;19(6):287-98. doi: 10.1159/000346674.
46. Roux P, Lions C, Michel L, Cohen J, Mora M, Marcellin F, Spire B, Morel A, Carrieri PM, Karila L; ANRS Methaville Study Group. Predictors of non-adherence to methadone maintenance treatment in opioid-dependent individuals: implications for clinicians. *Curr Pharm Des.* 2014;20(25):4097-105. doi: 10.2174/13816128113199990623.
47. Tran BX, Nguyen LH, Tran TT, Latkin CA. Social and structural barriers for adherence to methadone maintenance treatment among Vietnamese opioid dependence patients. *PLoS One.* 2018 Jan 18;13(1):e0190941. doi: 10.1371/journal.pone.0190941.
48. Fareed A, Eilender P, Ketchen B, Buchanan-Cummings AM, Scheinberg K, Crampton K, Nash A, Shongo-Hiango H, Drexler K. Factors affecting noncompliance with buprenorphine maintenance treatment. *J Addict Med.* 2014 Sep-Oct;8(5):345-50. doi: 10.1097/ADM.0000000000000057.
49. Launonen E, Wallace I, Kotovirta E, Alho H, Simojoki K. Factors associated with non-adherence and misuse of opioid maintenance treatment medications and intoxicating drugs among Finnish maintenance treatment patients. *Drug Alcohol Depend.* 2016 May 1;162:227-35. doi: 10.1016/j.drugalcdep.2016.03.017.

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50. Vermeire E, Hearnshaw H, Van Royen P, Denekens J. Patient adherence to treatment: three decades of research. A comprehensive review. *J Clin Pharm Ther.* 2001 Oct;26(5):331-42. doi: 10.1046/j.1365-2710.2001.00363.x.
 51. Conrad P. The meaning of medications: another look at compliance. *Soc Sci Med.* 1985;20(1):29-37. doi: 10.1016/0277-9536(85)90308-9.
 52. College of Physicians and Surgeons of British Columbia. Methadone Maintenance Program: Clinical Practice Guidelines. Updated September 2015. Accessed on April 11, 2020 from: http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Publications/Epid/Other/02_CPSBC-Methadone_Maintenance_Program_Clinical%20_Practice_Guideline.pdf
 53. Magura S, Rosenblum A. Leaving methadone treatment: Lessons learned, lessons forgotten, lessons ignored. *Mount Sinai Journal of Medicine.* 2001;68:62-74.
 54. Latowsky M. Improving detoxification outcomes from methadone maintenance treatment: The interrelationships of affective states and protracted withdrawal. *Journal of Psychoactive Drugs.* 1996;28:251-257.
 55. Calsyn DA, Malcy JA, Saxon AJ. Slow tapering from methadone maintenance in a program encouraging indefinite maintenance. *J Subst Abuse Treat.* 2006 Mar;30(2):159-163
 56. Nosyk B, Sun H, Evans E, et al. Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: results from a population-based retrospective cohort study. *Addiction.* 2012 Sep;107(9):1621-1629.
 57. Winstock AR, Lintzeris N, Lea T. "Should I stay or should I go?" Coming off methadone and buprenorphine treatment. *Int J Drug Policy.* 2011 Jan;22(1):77-81.
 58. Cleeland C. *The Brief Pain Inventory: User Guide.* Texas, USA 1991.
 59. Dennis BB, Roshanov PS, Bawor M, et al. Usefulness of the Brief Pain Inventory in patient with opioid addiction receiving methadone maintenance treatment. *Pain Physician.* 2016 Jan;19(1):E181-95.
 60. Marsden J, Gossop M, Stewart D, et al. The Maudsley Addiction Profile (MAP): a brief instrument for assessing treatment outcome. *Addiction.* 1998;93(12):1857-68.
 61. Shrank WH, Patrick AR, Brookhart MA. Healthy user and related biases in observational studies of preventive interventions: a primer for physicians. *J Gen Intern Med.* 2011;26(5):546-550. doi:10.1007/s11606-010-1609-1

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Table 1. Characteristics of participants at study entry (N = 2,030).

Characteristic	Statistic
Demographic and clinical	
Age in years; mean (SD)	39.2 (10.7)
Female sex ^a ; n (%)	894 (44.1)
Type of treatment; n (%)	
Methadone	1601 (78.9)
Buprenorphine-naloxone	429 (21.1)
Dose in mg/day; mean (SD)	
Methadone	70.5 (41.4)
Buprenorphine-naloxone	12.0 (6.7)
Years in treatment ^a ; median (IQR)	2.6 (5.2)
Abstinence from opioid use at baseline ^b ; n (%)	646 (31.9)
Number of opioid urine drug screens at 3 months ^c ; mean (SD)	12.6 (5.3)
Median percentage of opioid-positive urine drug screens at 3 months ^c ; median (Q1, Q3)	0 (0, 20)
Abstinence from opioid use at 3 months ^c ; n (%)	1,127 (56.5)
Patient-reported goals in treatment ^d	
Number of goals reported; n (%)	
One	1222 (60.2%)
Two	643 (31.7%)
Three	150 (7.4%)
Four	13 (0.64%)
Five	2 (0.1%)
Control cravings/withdrawal	247 (12.17%)

Maintain or stabilize medication dose	122 (6.01%)
"Live a normal life"	283 (13.94%)
Manage pain	240 (11.82%)
"Stay or get clean"	742 (36.55%)
Stop or taper off treatment	1386 (68.28%)
SD = Standard Deviation, Q1 = 25 th percentile, Q3 = 75 th percentile	
^a Data available for 2,029 participants.	
^b Data available for 2,028 participants.	
^c Data available for 1,996 participants (missing for 34 participants).	
^d Percentages sum to more than 100% as patients could report multiple goals in treatment.	

Table 2. Multivariable model of the association between patient goals and abstinence from opioid use for 3 months following study entry.

Covariate	Complete case analysis ^a (n = 1, 994 ^b)			Sensitivity analysis excluding outliers (n = 1,980) ^{a,c}		
	OR	95% CI	p	OR	95% CI	p
Control cravings/withdrawal	0.76	0.56, 1.03	0.078	0.73	0.54, 0.99	0.044
Maintain or stabilize medication dose	1.15	0.74, 1.79	0.523	1.24	0.79, 1.95	0.354
“Live a normal life”	1.02	0.77, 1.35	0.879	0.98	0.74, 1.31	0.902
Manage pain	1.0	0.73, 1.36	0.976	0.96	0.70, 1.32	0.806
“Stay or get clean”	0.73	0.59, 0.91	0.005	0.70	0.56, 0.87	0.001
Stop or taper off treatment	1.0	0.80, 1.27	0.974	1.01	0.80, 1.27	0.954

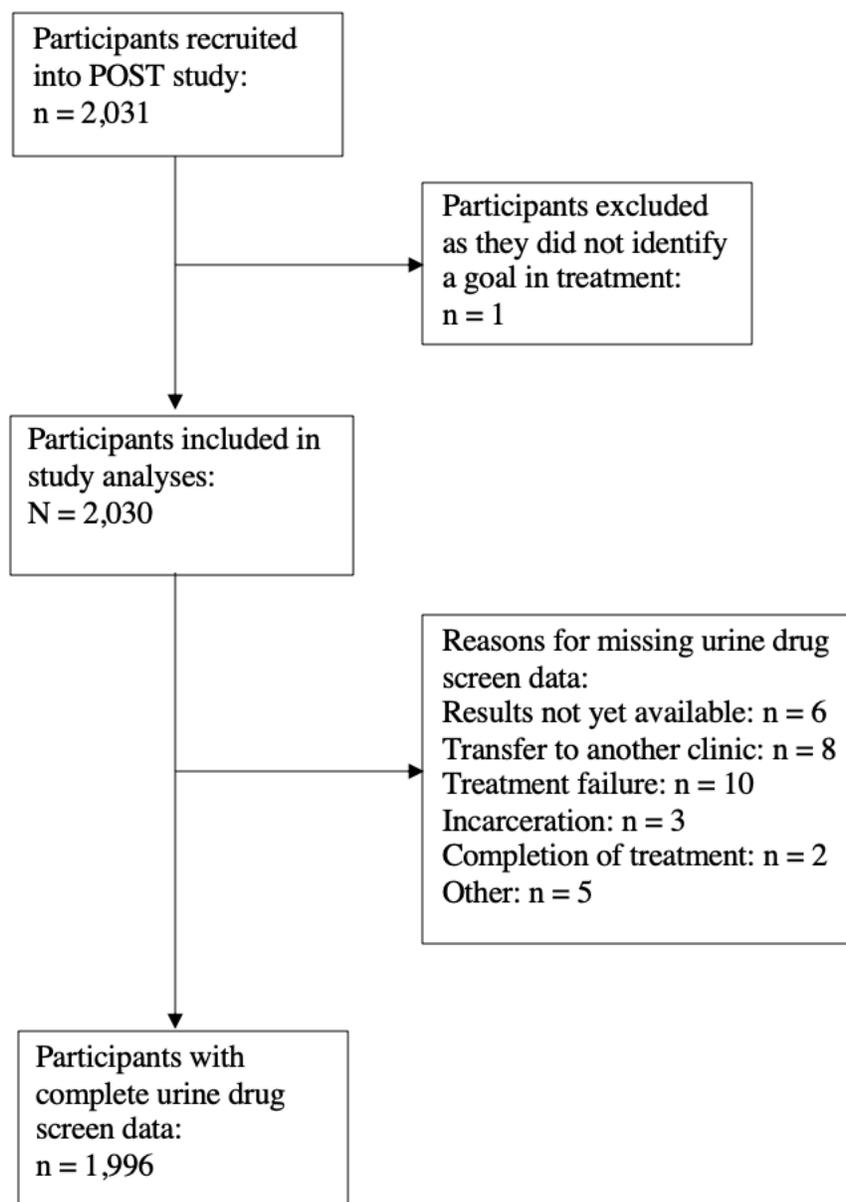
OR = Odds Ratio, CI = Confidence Interval
 Variance inflation factor = 1.19
 Hosmer-Lemeshow χ^2 5.93, p = 0.656
^a Model is adjusted for age, sex, type of treatment (methadone or buprenorphine-naloxone), dose, length of time in treatment, and opioid abstinence at baseline.
^b Participants with missing data in any of the included covariates are excluded due to complete case analysis (missing urine drug screen data: n = 36, missing sex: n = 1, missing length of time in treatment: n = 1).

^c Excluding 14 outliers detected using deviance residuals less than - 2 from the analysis

Figure 1 Legend:

Study Flow Diagram. POST = Pharmacogenetics of Opioid Substitution Treatment Response

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Figure 1. Study flow diagram.

Supplementary Table 1 for Peer-Review. Multivariable model of the association between patient goals and abstinence from opioid use for 3 months following study entry including all covariates.

Covariate	Complete case analysis ^a (n = 1,994 ^b)			Sensitivity analysis excluding outliers (n = 1,980) ^{a,c}		
	OR	95% CI	p	OR	95% CI	p
Control cravings/withdrawal	0.76	0.56, 1.03	0.078	0.73	0.54, 0.99	0.044
Maintain or stabilize medication dose	1.15	0.74, 1.79	0.523	1.24	0.79, 1.95	0.354
“Live a normal life”	1.02	0.77, 1.35	0.879	0.98	0.74, 1.31	0.902
Manage pain	1.0	0.73, 1.36	0.976	0.96	0.70, 1.32	0.806
“Stay or get clean”	0.73	0.59, 0.91	0.005	0.70	0.56, 0.87	0.001
Stop or taper off treatment	1.0	0.80, 1.27	0.974	1.01	0.80, 1.27	0.954
Age in years	1.0	0.99, 1.01	0.730	1.0	0.99, 1.01	0.715
Female sex	1.13	0.93, 1.37	0.223	1.14	0.94, 1.39	0.194
Type of treatment						
Methadone	[ref]			[ref]		
Buprenorphine-naloxone	1.88	1.40, 2.50	< 0.001	2.13	1.58, 2.86	< 0.001
Medication dose (mg/day)	1.0	0.99, 1.01	0.057	1.0	1.0, 1.0	0.015
Years in treatment	1.03	1.01, 1.04	0.013	1.03	1.01, 1.05	0.006
Opioid abstinence at baseline	5.34	4.23, 6.74	<0.001	6.15	4.83, 7.84	< 0.001

OR = Odds Ratio, CI = Confidence Interval
Variance inflation factor = 1.19
Hosmer-Lemeshow χ^2 5.93, p = 0.656
^a Model is adjusted for age, sex, type of treatment (methadone or buprenorphine-naloxone), dose, length of time in treatment, and opioid abstinence at baseline.
^b Participants with missing data in any of the included covariates are excluded due to complete case analysis (missing urine drug screen data: n = 36, missing sex: n = 1, missing length of time in treatment: n = 1).

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° Excluding 14 outliers detected using deviance residuals less than -2 from the analysis

Supplementary Table 2 for Peer-Review. Multivariable model of the association between number of self-reported goals and abstinence from opioid use for 3 months following study entry.

	(n = 1,994^b)		
Covariate	OR	95% CI	p
Number of goals reported			
One	[ref]		
Two	0.93	0.75, 1.15	0.497
Three or more	0.70	0.49, 1.0	0.049
Age in years	1.0	0.99, 1.01	0.600
Female sex	1.14	0.94, 1.38	0.197
Type of treatment			
Methadone	[ref]		
Buprenorphine-naloxone	1.88	1.41, 2.52	< 0.001
Medication dose (mg/day)	1.0	0.99, 1.01	0.055
Years in treatment	1.03	1.01, 1.05	0.004
Opioid abstinence at baseline	5.41	4.30, 6.82	<0.001
OR = Odds Ratio, CI = Confidence Interval			

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Included on page:
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3 (intro, paragraphs 1-3)
Objectives	3	State specific objectives, including any pre-specified hypotheses	3 (intro, paragraph 5)
Methods			
Study design	4	Present key elements of study design early in the paper	3-4 (Methods, Data section)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4 (Methods, Data section)
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3 (Methods, paragraph 1, 3)
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4 (Statistical analysis, paragraph 2)
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4 (Methods)

Bias	9	Describe any efforts to address potential sources of bias	Methods (Data), Limitations (page 7)
Study size	10	Explain how the study size was arrived at	Figure 1 Study Flow Diagram
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods, Statistical analysis page 4
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Methods, Statistical analysis page 4
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	Page 5 first paragraph
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
(e) Describe any sensitivity analyses			
Continued on next page			
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Study flow diagram Figure 1
		(b) Give reasons for non-participation at each stage	Study flow diagram Figure 1
		(c) Consider use of a flow diagram	Study flow diagram Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1

		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Table 1
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Table 1
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Results page 5, paragraph 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	Discussion page 6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Discussion page 7
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion page 6
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion page 7
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Title page

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Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses

Continued on next page

Results

BMJ Open

Are patients' goals in treatment associated with expected treatment outcomes? Findings from a mixed-methods study on outpatient pharmacological treatment for opioid use disorder.

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Are patients' goals in treatment associated with expected treatment outcomes? Findings from a mixed-methods study on outpatient pharmacological treatment for opioid use disorder.

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10
11 ABSTRACT
12

13 Objectives: Existing methods of measuring effectiveness of
14 pharmacological treatment for opioid use disorder (OUD) are
15 highly variable. Therefore, understanding patients' treatment
16 goals is an integral part of patient-centered care. Our
17 objective is to explore whether patients' treatment goals align
18 with a frequently used clinical outcome, opioid abstinence.
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21 Design: Triangulation mixed-methods design
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23 Setting and Participants: We collected prospective data from
24 2,030 participants who were receiving methadone or
25 buprenorphine-naloxone treatment for a diagnosis of OUD in order
26 to meet study inclusion criteria. Participants were recruited
27 from 45 centrally-managed outpatient opioid agonist therapy
28 clinics in Ontario, Canada. At study entry, we asked, "What are
29 your goals in treatment?" and used Nvivo software to identify
30 common themes.
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33 Primary outcome measure: Urine drug screens (UDS) were collected
34 for 3 months post-study enrolment in order to identify
35 abstinence versus ongoing opioid use (mean number of UDS over 3
36 months = 12.6, standard deviation (SD) = 5.3). We used logistic
37 regression to examine the association between treatment goals
38 and opioid abstinence.
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41 Results: Participants had a mean age of 39.2 years (SD = 10.7),
42 44% were female, and median duration in treatment was 2.6 years
43 (interquartile range 5.2). Six overarching goals were identified
44 from patient responses, including "stop or taper off of
45 treatment" (68%), "stay or get clean" (37%), and "live a normal
46 life" (14%). Participants reporting the goal "stay or get clean"
47 had lower odds of abstinence at 3 months than those who did not
48 report this goal (OR = 0.73, 95% CI 0.59-0.91, $p = 0.005$).
49 Although the majority of patients wanted to taper off or stop
50 medication, this goal was not associated with opioid abstinence,
51 nor were any of their other goals.
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3 Conclusions: Patient goals in OUD treatment do not appear to be
4 associated with program measures of outcome (i.e., abstinence
5 from opioids). Future studies are needed to examine outcomes
6 related to patient-reported treatment goals found in our study;
7 pain management, employment, and stopping/tapering treatment
8 should all be explored.
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11 Strengths and limitations of this study:

- 12 • This study is strengthened by its large sample size (2,000
13 participants) and multisite design.
- 14 • Participating clinics follow a harm-reduction approach to
15 treatment and these findings may not generalize to
16 abstinence-based treatment settings.
- 17 • The goals and treatment outcomes of patients newly entering
18 treatment may differ from those of patients who have been
19 in treatment longer and may not be captured in this study.
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23 Key words: opioid agonist treatment, patient-centred care,
24 methadone, buprenorphine, treatment goals

25 INTRODUCTION

26
27 Opioid use disorder (OUD) remains a clinical and public health
28 challenge, with ongoing high rates of opioid use and overdose
29 deaths.¹ Consequently, growing numbers of patients are enrolled
30 in pharmacological treatment for OUD.^{2,3} Methadone, a full opioid
31 agonist, and buprenorphine, a partial opioid agonist, are the
32 two most commonly used medications in the management of OUD;
33 they act to reduce cravings and withdrawal, and support
34 abstinence from ongoing opioid use.⁴ Evidence from systematic
35 reviews of experimental studies indicates that both medications
36 reduce opioid use.^{5,6} However, not all patients have favorable
37 outcomes,^{7,8} and patients who continue to use opioids during
38 treatment have a high risk of overdose and death.^{9,10} Other
39 treatments, including heroin-assisted treatment, are available
40 in some jurisdictions for patients who have limited response to
41 treatment with first-line medications.¹¹
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46 Better understanding patients' goals in treatment is considered
47 increasingly important within the field of substance use and
48 addiction.¹²⁻¹⁴ The now well-known concept of *patient-centered*
49 *care* was originally coined with the definition of "care that is
50 respectful of, and responsive to, individual patient
51 preferences, needs, and values",^{15,16} and is demonstrated to have
52 a significant impact on patients' outcomes and satisfaction in
53 treatment.¹⁷ Increasing attention is being paid to patients'
54 goals and the implementation of patient-centred care principles
55 in addiction treatment.¹⁸
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4 Identifying core treatment outcomes is an active area of
5 investigation within the field of Addiction Medicine.¹⁹
6 Unfortunately, there is still significant variability in the
7 outcomes used to evaluate the effectiveness of pharmacological
8 treatment for OUD.^{20, 21} How to best measure and assess treatment
9 outcomes remains uncertain, and current practices risk being
10 based upon convenience. Opioid use, measured by urine drug
11 screens (UDS), and retention in treatment are the most commonly
12 used primary outcomes measured in clinical studies and treatment
13 programs;²¹ however, it is unknown how well these outcomes are
14 associated with patients' goals in treatment. Personal and
15 social functioning outcomes are, in contrast, much less commonly
16 assessed.²¹ As core endpoints and outcome sets for studies of OUD
17 are developed, it is critical to understand which goals in
18 treatment are important to patients and how to best measure
19 them.
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24 In a recent study by Sanger et al., 2020, we used qualitative
25 analysis methods to examine patient-reported treatment goals in
26 a cohort of more than 2,000 patients receiving outpatient
27 pharmacological treatment for OUD.²² We identified six distinct
28 goals in treatment from patient responses, including to control
29 cravings or withdrawal, to maintain or stabilize medication
30 dose, to stop or taper off treatment, to "stay or get clean", to
31 manage pain, and to "live a normal life".²²
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34 The objective of the present study was to explore whether these
35 patient-reported treatment goals are associated with abstinence
36 from opioid use (a frequently measured program outcome). We
37 hypothesized that patient goals related to drug use would be
38 associated with opioid use during treatment; meanwhile, goals
39 unrelated to drug use would have no association with UDS
40 results.
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42 METHODS

43 *Data*

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45 We collected prospective observational data from 2,030
46 participants recruited from 45 outpatient clinics in the
47 Pharmacogenetics of Opioid Substitution Treatment Response
48 (POST) study. To meet study inclusion criteria, participants
49 were required to be at least 16 years of age and receiving
50 pharmacological treatment with methadone or buprenorphine-
51 naloxone (for any length of time) for a diagnosis of OUD, as per
52 the Diagnostic and Statistical Manual of Mental Disorders, 5th
53 Edition (DSM-5).²³ The diagnosis of OUD was made by treating
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3 physicians according to DSM-5 criteria and is an eligibility
4 criterion for treatment entry and clinical follow up at the
5 outpatient clinics included in this study. No other inclusion or
6 exclusion criteria were applied in order to increase the
7 generalizability of this study. Participants completed face-to-
8 face interviews at study entry to collect information on
9 demographic and clinical characteristics.
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12 We used a triangulation mixed-methods design to combine
13 quantitative and qualitative data collection, where both
14 quantitative and qualitative data were collected within one
15 study instrument using closed- and open-ended questions.^{24,25} At
16 study intake, participants were interviewed by trained research
17 staff to obtain information on sociodemographic and clinical
18 information, medical history, and substance use history.
19 Research staff had a background in addiction research, as they
20 previously participated in recruitment of participants for a
21 study investigating genetic influences on methadone treatment.²⁶
22 Their experience allowed for familiarity of addiction-related
23 terms used in interview responses; however, research staff were
24 not known to the participants of this study. Study interviews
25 were conducted in-person at the CATC. The interview data used in
26 this study is from participants recruited from May 2018 until
27 August 2019. During the interview, all participants who met the
28 inclusion and exclusion criteria above were asked the open-ended
29 question, "What are your goals in treatment". Details regarding
30 the study settings and data collection are outlined in a
31 previous study looking at OUD-related patient important
32 outcomes.²² Verbal responses, in their entirety, were transcribed
33 by research staff word-for-word in online anonymized records,
34 where each participant was given an anonymized record number.
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39 We collected the results of UDSs for opioids for each
40 participant for three months following study entry to assess
41 treatment outcome. The FaStep Assay (Trimed Supply Network
42 Ltd, Concord, Ontario, Canada) was used to detect morphine,
43 oxycodone, fentanyl, methadone metabolite, and buprenorphine, as
44 well as other non-opioid substances.²⁷ Though other methods may
45 be used to assess ongoing opioid use during treatment, such as
46 saliva and hair tests, as well as self-report,²⁸ UDSs are
47 collected as part of routine clinical protocol in the clinics
48 participating in this study and are a recommended method of
49 assessment based on Canadian Guidelines.⁴ UDSs were collected
50 following clinic protocol (typically weekly or biweekly). For
51 each participant, we calculated the percentage of opioid-
52 positive UDSs by dividing the number of opioid-positive urines
53 by the number of urine samples taken. Abstinence from opioids
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3 was selected as our primary study outcome as it is a routinely
4 measured treatment outcome in both clinical practice and
5 research studies.
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8 Another commonly studied treatment outcome, retention in
9 treatment, was not formally assessed in the present study for
10 two reasons. First, treatment retention is not equivalent to the
11 duration of time enrolled in this study (as our study used a
12 naturalistic design and enrolled patients in various stages of
13 their treatment). Second, with the exception of patients who
14 have entered treatment for the first time, there exists some
15 uncertainty in defining treatment retention because patients
16 frequently enter and discontinue treatment at various points in
17 their course of illness. Instead, we asked participants to
18 report their length of time enrolled in this treatment episode
19 (as a proxy for treatment retention) and adjusted all study
20 analyses for length of time in treatment.
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24 This study was reviewed and approved by the Hamilton Integrated
25 Research Ethics Board (project ID 4556) and conducted in
26 accordance with its ethical guidelines. We report methods and
27 quantitative results in accordance with the Strengthening the
28 Reporting of Observational Studies in Epidemiology (STROBE)
29 guidelines.²⁹
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31 32 33 *Qualitative analysis*

34
35 The qualitative approach used to analyze the data was data-
36 driven thematic analysis.³⁰ We began by familiarizing ourselves
37 with the data through active, repeated reading of the interview
38 responses and began to recognize emerging patterns. This phase
39 of data familiarization also allowed us to minimize
40 typographical errors present in the free text responses. We
41 began phase two by generating initial codes using NVivo software
42 QSR International [Americas] Inc., Burlington, Massachusetts,
43 USA) for qualitative analysis to identify common themes from
44 patient answers.³¹ We began cataloguing main ideas, phrases, and
45 patterns into meaningful nodes using word and text queries, and
46 a review of the transcribed data. Word and text queries helped
47 us capture the patterns in data and improve analytic accuracy by
48 identifying stemmed variants. Each data item was given equal
49 attention and in addition to text and word queries, key phrases
50 were tagged within each data item. This phase is characterized
51 by the generation of a codebook that provided specific
52 definitions of the key phrases, words and patterns. The next
53 phase consisted of the labelling of some nodes as themes and the
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3 collapsing of related nodes into one node, eventually being
4 labelled as a themes or sub-themes. The final phase consisted of
5 a review of identified themes and resultant reworking of themes
6 to better establish coherent patterns within each theme.
7 Defining and refining of each theme followed this phase, where
8 patterns and content were considered before choosing relevant
9 and reflective theme names.^{30,32} To increase rigour in our
10 analysis we used investigator triangulation, where phases
11 concerning the generation of themes involved the consultation of
12 four investigators to ensure incorporation of diverse
13 perspectives. This was reflected in the iterative review of
14 nodes and patterns, where meaningfulness of coding was discussed
15 and was reassessed at every identified phase. We report
16 qualitative methods and results in accordance with the Standards
17 of Reporting Qualitative Research (SRQR).³³
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22 *Quantitative analysis*

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24 We conducted all quantitative analyses using Stata Version 15.1
25 (StataCorp LP, College Station, TX, USA). We report demographic
26 and clinical data using mean and standard deviation (SD) for
27 normally distributed continuous variables and median with
28 quartiles 1 and 3 or interquartile range (IQR) for skewed data.
29 We report categorical variables as frequency with percentage. We
30 summarize the results of UDSs in three ways: 1) the mean number
31 of UDSs collected; 2) the percentage of opioid-positive UDSs; and
32 3) abstinence from opioid use, defined as no opioid-positive
33 UDSs during the 3-month time period.
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37 We used logistic regression analysis to examine the association
38 between patient goals in treatment and abstinence from opioid
39 use, adjusting for other important covariates. We constructed a
40 logistic regression model, using the dependent variable
41 abstinence from opioid use throughout the 3 months following
42 study entry. We included the six identified treatment goals in
43 the model and controlled for other factors believed to impact
44 ongoing opioid use in treatment, including age, sex,^{34,35} type of
45 treatment (methadone or buprenorphine-naloxone), medication
46 dose,³⁶ length of time in treatment,³⁷ and abstinence from opioids
47 at baseline. We also conducted an additional logistic regression
48 to determine whether the number of goals reported by
49 participants was associated with opioid abstinence, as patients
50 who report more treatment needs tend to have more opioid use.³⁸
51 Results are reported as odds ratios (OR) with 95% confidence
52 intervals (CI) and associated *p* values. We report the estimates
53 of effect for our main variables of interest (treatment goals)
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3 in the results table and describe all variables adjusted for in
4 a footnote in the table in order to focus solely on the
5 variables of interest to our specific study question. We
6 assessed for multicollinearity using variance inflation factor
7 and examined model diagnostics using the Hosmer-Lemeshow
8 statistic and deviance residuals. We conducted a sensitivity
9 analysis after excluding observations with a deviance residual
10 lower than -2 or higher than 2. Our sample size of 2,030
11 participants and event rate of more than 1,000 participants
12 abstinent from opioids is adequate, based on the rule of thumb
13 for number of events needed ($n = 10$) per covariate included in
14 logistic regression analysis.³⁹
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18 Missing data were identified and reported for each variable of
19 interest. There were less than 5 cases with missing data for
20 baseline demographic or clinical variables. For 3-month UDS,
21 missing data affected 34 participants (1.7%). Reasons for
22 missing 3-month UDS data included: results not yet available ($n = 6$),
23 transfer to another clinic ($n = 8$), treatment failure ($n = 10$),
24 incarceration ($n = 3$), completion of treatment ($n=2$), and
25 other ($n = 4$), such as hospitalization, moving, or never
26 starting treatment. Due to the low percentage of missing data,
27 all missing data were handled by available case analysis.
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30 **Patient and Public Involvement**

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32 Patients or the public were not involved in the design, or
33 conduct, or reporting, or dissemination plans of our research.
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36 RESULTS

37 *Participant characteristics and goals in treatment*

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39 Altogether, 2,030 participants were included in the analyses
40 (Figure 1; Study flow diagram), with a mean age of 39.2 years
41 (SD = 10.7) and 44% were female (Table 1). The majority of
42 participants were receiving treatment with methadone (78.9%)
43 compared to buprenorphine-naloxone (21.1%) and the median length
44 of time in treatment was 2.6 years (IQR 5.2). UDSs collected for
45 the three months of study duration were available for 1,996
46 participants. Among these participants, 57% were abstinent from
47 opioid use during those 3 months. Ultimately, we identified six
48 distinct "themes" or "goals" in treatment: 1) to control
49 cravings or withdrawal, 2) to maintain or stabilize medication
50 dose, 3) to stop or taper off treatment, 4) to "stay or get
51 clean", 5) to manage pain, and 6) to "live a normal life", as
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presented by our previous paper looking at patient important outcomes in the OUD population receiving MAT.²² The “control cravings or withdrawal” theme consisted of participants responses stating they would like to avoid withdrawal or control their cravings. Participant responses grouped in the second theme of “no changes in treatment” were made up of responses indicating that they wanted to maintain OSAT doses, stabilize their OSAT dose, or did not have any reported goals. The third goal to “stop OSAT treatment” had goals to stop treatment completely, to not be dependent on OSAT, to taper off, or reduce dose. Participant goals such as wanting to get clean, stay clean, achieve abstinence, or achieve sobriety from all drugs were included in the fourth goal of “avoiding illicit drugs”. The fifth theme of “pain management” either mentioned chronic pain, or pain management in general. The sixth theme of “living a normal life” consisted of responses such as wanting a stable life, normal life, to get qualifications related to education, job or work, to achieve good mental health, or wanting to support their family.²²

The most common patient-reported goal was to “stop or taper off treatment” (68%; see Table 1 for all goals). Other goals included to “stay or get clean” (37%), to “live a normal life” (14%), and to “control cravings or withdrawal” (12%). Most participants (60.2%) reported one treatment goal (mean number of goals = 1.49, SD = 0.67). We reported demographic and clinical characteristics associated with different treatment goals in a previously published paper.²²

The proportion of participants treated with methadone (as compared to buprenorphine-naloxone) was 79% for the goal “stop or taper off treatment”, 78% for “stay or get clean”, 84% for “live a normal life”, 86% for “manage pain”, 81% for “control cravings or withdrawal”, and 75% for “maintain or stabilize medication dose”. The median length of time in treatment at the time of study recruitment was 3 years (IQR = 5) for the goal “stop or taper off treatment”, 2 years (IQR = 4.5) for “stay or get clean”, 3 years (IQR = 6.2) for “live a normal life”, 4 years (IQR = 8) for “manage pain”, 2 years (IQR = 5.4) for “control cravings or withdrawal”, and 5 years (IQR = 8) for “maintain or stabilize medication dose”. Abstinence from opioid use at study entry was observed in 33% of participants reporting the goal to “stop or taper off treatment”, 28% for “stay or get clean”, 31% for “live a normal life”, 30% for “manage pain”, 31% for “control cravings or withdrawal”, and 45% for “maintain or stabilize medication dose”.

Association between patients' goals in treatment and 3-month abstinence from opioid use (MAT program goal)

We examined the association between patient goals and abstinence from opioid use for 3 months following study entry, adjusting for other characteristics previously shown to be associated with ongoing opioid use (Table 2). Paradoxically, participants

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3 reporting the goal "to stay or get clean" had 27% lower odds of
4 abstinence from opioids at 3 months (OR = 0.73, 95% CI 0.59-
5 0.91, $p = 0.005$), even after adjusting for baseline abstinence
6 from opioid use. No other patient-reported goals in treatment
7 were significantly associated with 3-month abstinence.
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10 Good model fit was assessed using the Hosmer-Lemeshow statistic
11 ($\chi^2 = 5.93$, $p = 0.656$) and multicollinearity was not a concern
12 (mean VIF 1.19). Using deviance residuals, we detected 14
13 outliers with deviance residuals greater than an absolute value
14 of 2. We conducted a post-hoc sensitivity analysis removing
15 outliers and found that participants who reported the goal "to
16 control cravings or withdrawal" also had significantly lower
17 odds of opioid abstinence at 3 months (OR = 0.73, 95% CI 0.54-
18 0.99, $p = 0.044$; Supplementary Table 1). There were no other
19 significant changes to the results upon removing outliers.
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22 Finally, we examined the association between number of reported
23 goals and abstinence from opioid use for 3 months (Supplementary
24 Table 2). As compared to reporting one goal in treatment,
25 reporting two goals was not associated with opioid use (OR =
26 0.93, 95% CI = 0.75, 1.15, $p = 0.497$), however reporting three
27 or more goals may be associated with lower odds of abstinence
28 from opioids (OR = 0.70, 95% CI = 0.49, 1.0, $p = 0.049$).
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31 DISCUSSION

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33 In this mixed-methods study, we examined treatment goals
34 reported by more than 2,000 patients receiving pharmacological
35 treatment for OUD to determine their association with the
36 frequently measured treatment outcome, opioid use. Participants
37 reporting the goals to "stay or get clean" and to control
38 cravings or withdrawal were less likely to be abstinent from
39 opioids during the next 3 months of treatment than participants
40 who did not report those goals. Other goals related to
41 termination of treatment, pain, or personal or social
42 functioning were not associated with opioid use. These findings
43 suggest that abstinence from opioids, a commonly used treatment
44 outcome measured in clinical trials, does not reflect what
45 patients want out of treatment, and raises questions about the
46 alignment between treatment outcomes and patient goals.⁴⁰
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50 We found that patients who identified goals related to stopping
51 drug use or controlling OUD symptoms had worse outcomes in
52 treatment as measured by UDS. There is a rich literature
53 examining the apparent contradiction between abstinence-related
54 goals and subsequent drug-taking behaviors. This is in essence
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3 the focus of motivational interviewing⁴¹ in which clinicians help
4 patients develop motivation through recognizing discrepancies
5 between their current situation and their goals, shifting the
6 balance towards change.⁴² One possible explanation is that
7 patients who were experiencing worse outcomes in treatment or
8 higher severity of illness were more likely to report goals
9 regarding management of substance use symptoms and abstinence
10 from drug use, thus also increasing the likelihood that they
11 experienced ongoing opioid use. Another possibility is that
12 participants who had achieved abstinence or had improvements in
13 OUD withdrawal symptoms may have been less likely to identify
14 the same goals. Nonetheless, exploring why patients wishing to
15 abstain from opioid use are not achieving this goal is an area
16 requiring further study. Beyond quantitatively examining factors
17 associated with ongoing substance use, previous qualitative
18 studies that explore patient perceptions of barriers and
19 facilitators to achieving abstinence are illuminating and may
20 inform future interventions and research.⁴³⁻⁴⁵

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25 Although the majority of patients wanted to taper off or stop
26 treatment, this goal had no association with abstinence from
27 opioid use. One possible explanation is that participants may
28 have been unhappy with treatment and therefore non-adherent.
29 Factors associated with non-adherence to opioid agonist
30 treatments have been previously studied.⁴⁶⁻⁴⁹ There is a vast
31 literature on factors affecting patient adherence to treatment
32 in general and, notably, no single explanation sufficiently
33 accounts for variation in adherence.⁵⁰ Authors in this field have
34 suggested considering the patient's experience of illness and
35 its meaning as important factors to study in understanding
36 adherence to treatment.^{50, 51} This finding calls into question the
37 rationale for entering and continuing pharmacological treatment
38 while continuing to use opioids for this group of patients.
39 Furthermore, this is a particularly important finding, given
40 that retention in treatment is amongst the most consistently
41 measured outcomes,¹⁹ and guidance around taper and
42 discontinuation of long-term opioid agonist treatments for
43 opioid use disorder is limited.^{4,52} Studies examining opioid
44 agonist tapers have identified challenges and risks of poor
45 outcomes^{53,54} including withdrawal symptoms, return to drug use,
46 pain, psychiatric symptoms, hospitalization, and death.^{55,56} A
47 previous study found that patients' interest in stopping
48 treatment was associated with shorter duration of treatment and
49 lack of concern about relapse to opioid use.⁵⁷ This is concerning
50 as one would hope patients planning to stop treatment would be
51 reliably abstinent from opioids. What distinguishes this group
52 of patients who wish to discontinue treatment? Whether some of

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3 these patients are mandated to be in treatment is unknown.
4 Better understanding patients' reasons for wanting to stop or
5 taper treatment and examining outcomes for patients who initiate
6 an opioid agonist taper is imperative.
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9 Other patient identified goals in treatment that were not
10 associated with the results of their UDS, included goals around
11 pain management, and the goal "to live a normal life". This
12 suggests that clinicians and researchers may require additional
13 tools to measure outcomes related to those patient-important
14 treatment goals. Tools validated to assess pain in this
15 population include the Brief Pain Inventory^{58,59} and social
16 functioning may be examined using the Maudsley Addiction
17 Profile.⁶⁰ A more nuanced understanding of specific goals around
18 personal and social functioning, on a population and individual
19 level, is required in order to be able to appropriately assess
20 and address these goals during treatment. Overall, our finding
21 that results of UDSs are not associated with all patient goals
22 in treatment is expected as UDSs results would not be expected
23 to be a proxy for all of the different goals. However, this
24 study adds evidence to the notion that traditional metrics of
25 success in opioid use disorder treatment are insufficient in
26 isolation. It is important to note that although patient goals
27 appear to have limited predictive value on opioid use during
28 treatment, this does not imply that clinicians should not ask
29 patients about their treatment goals. It is not uncommon that
30 patients have goals that are not achieved in treatment (e.g.,
31 weight loss, increased physical activity) and this does not mean
32 that clinicians or patients should give up on these goals or
33 should not enquire about them. Rather, we must consider how well
34 traditional metrics of treatment success align with desired
35 treatment outcomes for all stakeholders, especially patients,
36 and consider additional ways to evaluate and improve treatment
37 success based on patients' self-reported goals.
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43 Finally, in a previous paper, we examined group differences
44 between participants selecting each treatment goal.²² Females
45 were more likely to report the goal of stopping treatment. Older
46 age, first exposure to opioids through physician prescription,
47 and unemployment were all associated with greater odds of
48 reporting goals related to pain management.²² These findings
49 indicated that, unsurprisingly, patients' characteristics are
50 associated with their treatment goals and may help to guide
51 focused questioning and evaluation of patients' goals in
52 treatment.
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3 This study has a number of potential limitations. First, this
4 study interprets and summarizes the patients' narrative when
5 expressing their goals in treatment using qualitative methods;
6 however, this interpretation carries limitations related to the
7 potential influence of social desirability bias and the
8 influence of contextual factors on patients' responses that have
9 not been explored in this study. Though beyond the scope of this
10 paper, sociological approaches to qualitative analysis include
11 critical appraisal of the circumstances of the participant and
12 the context in which statements are expressed. Furthermore,
13 there may be a healthy user/volunteer bias,⁶¹ such that
14 individuals with better outcomes in treatment may have been more
15 likely to participate. Additionally, the goals and treatment
16 outcomes of patients newly entering treatment may differ from
17 those of patients who have been in treatment longer. Patients
18 who may have successfully achieved their goal of treatment
19 termination were not captured by this study since they would no
20 longer be on OUD thus not recruited. The findings in this study
21 may not generalize to settings in which opioid agonist
22 medications take on a primarily abstinence-based role in
23 treatment. In Canada, pharmacological treatment for OUD is
24 provided largely in a harm-reduction model, in which retention
25 in treatment is not contingent on abstinence from opioids or
26 non-opioid substances. This study did not measure patient's
27 satisfaction or perception of treatment success or perception of
28 meeting their goals. Future studies that examine patient
29 satisfaction in treatment may wish to determine whether
30 perception of treatment success correlates with program-measured
31 outcomes such as opioid abstinence.
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36 37 CONCLUSION

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39 Patients report a number of different goals in their treatment
40 for OUD, which are not associated with traditional goals of
41 treatment programs and outcomes measured in clinical settings
42 (abstinence from opioid use measured by UDS). We found that
43 patients who identified goals related to stopping drug use or
44 controlling OUD symptoms were more likely to have ongoing opioid
45 use. However, goals unrelated to drug use carried no significant
46 association with opioid use status. Patients reporting the goal
47 of wanting to stop treatment were no more likely to be abstinent
48 from opioids. The patient-identified goals to manage pain or
49 "live a normal life" had no association with ongoing opioid use.
50 Future studies are needed to examine outcomes related to the
51 goals in treatment identified in our study. Are these goals
52 being met in treatment? For example, do patients feel their pain
53 is well managed? Do they achieve employment? Can they achieve
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3 the goal of stopping treatment without adverse consequences? As
4 core outcome sets are developed, patient-important outcomes
5 remain essential to consider and may help with implementing
6 patient-centered approaches to treatment.
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8 9 ACKNOWLEDGMENTS

10
11 We would like to thank the Pharmacogenetics of Opioid
12 Substitution Treatment Response (POST) study participants for
13 their time and contributions, without which this study would not
14 be possible.
15

16 17 **Authors' contributions**

18 TR, LN, BP, NS, BBD, and ZS are responsible for the study
19 concept and design. TR, BP, LT and ZS developed the methods and
20 data analysis. TR conducted quantitative analysis and BP
21 conducted qualitative analysis. TR wrote the first draft of the
22 manuscript, and TR, LN, BP, DBC, NS, BBD, DCM, LR, AW, LT, and
23 ZS, contributed to writing and critically revising the final
24 manuscript. All authors reviewed and approved the final
25 manuscript.
26

27 28 **Data availability**

29 Data are available upon reasonable request
30

31 32 **Role of funding source**

33 This study was supported by research grants from the Canadian
34 Institutes for Health Research (grant numbers PJT-156306 and
35 SHI-155404). The funding bodies had no role in the design,
36 analysis, interpretation, or publication of results.
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38 39 **Declaration of interests**

40 Dr. Marsh reports Salary income as Chief Medical Director,
41 Canadian Addiction Treatment Centres and as Associate Dean
42 Research, Innovation and International Relations, Northern
43 Ontario School of Medicine. The other study authors declare no
44 conflicts of interest.
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References

1. Special Advisory Committee on the Epidemic of Opioid Overdoses. National report: Apparent opioid-related deaths in Canada (January 2016 to December 2018). Web Based Report. Ottawa: Public Health Agency of Canada; June 2019.
2. Fischer B, Kurdyak P, Goldner E, et al. Treatment of prescription opioid disorders in Canada: looking at the 'other epidemic'? *Subst Abuse Treat Prev Policy*. 2016;11:12.
3. Ontario Drug Policy Research Network. Ontario Prescription Opioid Tool. Toronto, ON; July 2018. DOI: 10.31027/ODPRN.2018.01. Available from: <https://odprn.ca/ontario-opioid-drug-observatory/ontario-prescription-opioid-tool/>
4. Bruneau J, Ahamad K, Goyer ME, et al. Management of opioid use disorders: a national clinical practice guideline. *CMAJ*. 2018 Mar 5;190(9):E247-E257.
5. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database Syst Rev*. 2009;3:CD002209.
6. Nielsen S, Larance B, Degenhardt L, Gowing L, Kehler C, Lintzeris N. Opioid agonist treatment for pharmaceutical opioid dependent people. *Cochrane Database Syst Rev*. 2016 May 9; (5):CD011117.
7. Dennis BB, Naji L, Bawor M, et al. The effectiveness of opioid substitution treatments for patients with opioid dependence: a systematic review and multiple treatment comparison protocol. *Syst Rev*. 2014;3:105.
8. Li Y, Kantelip J-P, Gerritsen-van Schieveen P, Davani S. Interindividual variability of methadone response. *Mol Diagn Ther*. 2008;12:109-24.
9. Huang CL, 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.
10. Zador D, Sunjic S. Deaths in methadone maintenance treatment in New South Wales, Australia 1990-1995. *Addiction*. 2000;95(1):77-84.
11. Ferri M, Davoli M, Perucci CA. Heroin maintenance for chronic heroin-dependent individuals. *Cochrane Database of Systematic Reviews* 2011, Issue 12. Art. No.: CD003410. DOI: 10.1002/14651858.CD003410.pub4
12. Deshpande PR, Rajan S, Sudeepthi BL, Abdul Nazir CP. Patient-reported outcomes: a new era in clinical research. *Perspect Clin Res*. 2011;2:137-44.

13. Marchand K, Beaumont S, Westfall J, et al. Patient-centred care for addiction treatment: a scoping review protocol. *BMJ Open*. 2018 Dec; 8(12):e024588
14. Kolind T, Hesse M. Patient-centred care—perhaps the future of substance abuse treatment. *Addiction*. 2017 Mar;112(3):465–466.
15. National Research Council. *Crossing the quality chasm: a new health system for the 21st century*. Washington, DC: National Academies Press, 2001.
16. Barry MJ, Edgman-Levitan S. Shared decision making—pinnacle of patient-centred care. *N Engl J Med*. 2012 Mar 1;366(9):780–781.
17. Stewart M, Brown JB, Donner A, et al. The impact of patient-centered care on outcomes. *J Fam Pract*. 2000 Sep;49(9):796–804.
18. Marchand K, Beaumont S, Westfall J, et al. Conceptualizing patient-centered care for substance use disorder treatment: findings from a systematic scoping review. *Subst Abuse Treat Prev Policy*. 2019 Sep 11;14(1):37.
19. International Consortium for Health Outcomes Measurement. *ICHOM Standard Set for Addiction*. Accessed on October 26, 2020, from: <https://www.ichom.org/portfolio/addiction/>.
20. Wiessing L, Ferri M, Darke S, Simon R, Griffiths P. Large variation in measures used to assess outcomes of opioid dependence treatment: A systematic review of longitudinal observational studies. *Drug Alcohol Rev*. 2018 Apr;37 Suppl 1:S323–S338. doi:10.1111/dar.12608.
21. 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;21:30.
22. Sanger N, Panesar B, Rosic T, et al. The future of precision medicine in opioid use disorder: the inclusion of patient important outcomes in clinical trials. *Braz J Psychiatry*. 2020;00:000-000. <http://dx.doi.org/10.1590/1516-4446-2019-0734>
23. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5th edn. Arlington, VA: American Psychiatric Publishing, 2013.
24. Plano Clark VL, Huddleston-Casas CA, Churchill SL, et al. Mixed Methods Approaches in Family Science Research. *Journal of Family Issues*. 2008;29(11):1543–1566. doi:10.1177/0192513X08318251
25. Doyle L, Brady AM, Byrne G. An overview of mixed methods research. *Journal of Research in Nursing*. 2009;14(2):175–185. <https://doi.org/10.1177/1744987108093962>
26. Samaan Z, Bawor M, Dennis BB, et al. Genetic influence on methadone treatment outcomes in patients undergoing methadone maintenance treatment for opioid addiction: a pilot study. *Neuropsychiatr Dis Treat*. 2014;19(10):1503–1508.

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27. FaStep Assay. Trimedica Supply Network Ltd. Available from: <https://www.trimedica-inc.com/wp-content/uploads/2018/04/Fastep-Package-Insert.pdf>
 28. Donovan DM, Bigelow GE, Brigham GS, et al. Primary outcome indices in illicit drug dependence treatment research: systematic approach to selection and measurement of drug use end-points in clinical trials. *Addiction*. 2012;107(4):694-708. doi:10.1111/j.1360-0443.2011.03473.x
 29. Elm Ev, Altman DG, Egger M, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007; 335: 806-8.
 30. Braun V, Clarke V. Using thematic analysis in psychology. *Qualitative Research in Psychology*. 2006;3(2):77-101. DOI: 10.1191/1478088706qp063oa
 31. NVivo qualitative data analysis software; QSR International Pty Ltd. Version 12, 2018.
 32. Guest G, MacQueen KM, Namey EE. *Applied thematic analysis*. Thousand Oaks, CA: SAGE Publications, Inc. 2012.
 33. O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. *Acad Med* 2014;89:1245-51. doi:10.1097/ACM.0000000000000388.
 34. Bawor M, Dennis BB, Bhalerao A, et al. Sex differences in outcomes of methadone maintenance treatment for opioid use disorder: a systematic review and meta-analysis. *CMAJ Open*. 2015;3(3):E344-E351. Published 2015 Jul 17. doi:10.9778/cmajo.20140089
 35. 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;6:21. Published 2015 Nov 10. doi:10.1186/s13293-015-0038-6
 36. Strain EC, Bigelow GE, Liebson IA, Stitzer ML. Moderate- vs High-Dose Methadone in the Treatment of Opioid Dependence: A Randomized Trial. *JAMA*. 1999;281(11):1000-1005
 37. Eastwood B, Strang J, Marsden J. Effectiveness of treatment for opioid use disorder: A national, five-year, prospective, observational study in England. *Drug Alcohol Depend*. 2017 Jul 1;176:139-147.
 38. Kelly SM, O'Grady KE, Brown BS, Mitchell SG, Schwartz RP. The role of patient satisfaction in methadone treatment. *Am J Drug Alcohol Abuse*. 2010;36(3):150-154.
 39. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996; 49: 1373-9.

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40. Liberati A. Need to re-align patient-oriented and commercial and academic research. *Cochrane Database of Systematic Reviews* 2011, Issue 12. Art. No.: ED000094. DOI: 10.1002/14651858.ED000094
 41. Miller WR, Rose GS. Toward a theory of motivational interviewing. *Am Psychol.* 2009;64(6):527-537. doi:10.1037/a0016830
 42. Westra HA, Aviram A. Core skills in motivational interviewing. *Psychotherapy (Chic)*. 2013 Sep;50(3):273-8. doi: 10.1037/a0032409. PMID: 24000834.
 43. Herbeck, D. M., Brecht, M. L., Christou, D., & Lovinger, K. (2014). A qualitative study of methamphetamine users' perspectives on barriers and facilitators of drug abstinence. *Journal of psychoactive drugs*, 46(3), 215-225.
 44. Moran, L., Keenan, E. & Elmusharaf, K. Barriers to progressing through a methadone maintenance treatment programme: perspectives of the clients in the Mid-West of Ireland's drug and alcohol services. *BMC Health Serv Res* 18, 911 (2018).
 45. Notley C, Blyth A, Maskrey V, Craig J, Holland R. The experience of long-term opiate maintenance treatment and reported barriers to recovery: a qualitative systematic review. *Eur Addict Res.* 2013;19(6):287-98. doi: 10.1159/000346674.
 46. Roux P, Lions C, Michel L, Cohen J, Mora M, Marcellin F, Spire B, Morel A, Carrieri PM, Karila L; ANRS Methaville Study Group. Predictors of non-adherence to methadone maintenance treatment in opioid-dependent individuals: implications for clinicians. *Curr Pharm Des.* 2014;20(25):4097-105. doi: 10.2174/13816128113199990623.
 47. Tran BX, Nguyen LH, Tran TT, Latkin CA. Social and structural barriers for adherence to methadone maintenance treatment among Vietnamese opioid dependence patients. *PLoS One.* 2018 Jan 18;13(1):e0190941. doi: 10.1371/journal.pone.0190941.
 48. Fareed A, Eilender P, Ketchen B, Buchanan-Cummings AM, Scheinberg K, Crampton K, Nash A, Shongo-Hiango H, Drexler K. Factors affecting noncompliance with buprenorphine maintenance treatment. *J Addict Med.* 2014 Sep-Oct;8(5):345-50. doi: 10.1097/ADM.0000000000000057.
 49. Launonen E, Wallace I, Kotovirta E, Alho H, Simojoki K. Factors associated with non-adherence and misuse of opioid maintenance treatment medications and intoxicating drugs among Finnish maintenance treatment patients. *Drug Alcohol Depend.* 2016 May 1;162:227-35. doi: 10.1016/j.drugalcdep.2016.03.017.

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50. Vermeire E, Hearnshaw H, Van Royen P, Denekens J. Patient adherence to treatment: three decades of research. A comprehensive review. *J Clin Pharm Ther.* 2001 Oct;26(5):331-42. doi: 10.1046/j.1365-2710.2001.00363.x.
51. Conrad P. The meaning of medications: another look at compliance. *Soc Sci Med.* 1985;20(1):29-37. doi: 10.1016/0277-9536(85)90308-9.
52. College of Physicians and Surgeons of British Columbia. Methadone Maintenance Program: Clinical Practice Guidelines. Updated September 2015. Accessed on April 11, 2020 from: http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Publications/Epid/Other/02_CPSBC-Methadone_Maintenance_Program_Clinical%20_Practice_Guideline.pdf
53. Magura S, Rosenblum A. Leaving methadone treatment: Lessons learned, lessons forgotten, lessons ignored. *Mount Sinai Journal of Medicine.* 2001;68:62-74.
54. Latowsky M. Improving detoxification outcomes from methadone maintenance treatment: The interrelationships of affective states and protracted withdrawal. *Journal of Psychoactive Drugs.* 1996;28:251-257.
55. Calsyn DA, Malcy JA, Saxon AJ. Slow tapering from methadone maintenance in a program encouraging indefinite maintenance. *J Subst Abuse Treat.* 2006 Mar;30(2):159-163
56. Nosyk B, Sun H, Evans E, et al. Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: results from a population-based retrospective cohort study. *Addiction.* 2012 Sep;107(9):1621-1629.
57. Winstock AR, Lintzeris N, Lea T. "Should I stay or should I go?" Coming off methadone and buprenorphine treatment. *Int J Drug Policy.* 2011 Jan;22(1):77-81.
58. Cleeland C. *The Brief Pain Inventory: User Guide.* Texas, USA 1991.
59. Dennis BB, Roshanov PS, Bawor M, et al. Usefulness of the Brief Pain Inventory in patient with opioid addiction receiving methadone maintenance treatment. *Pain Physician.* 2016 Jan;19(1):E181-95.
60. Marsden J, Gossop M, Stewart D, et al. The Maudsley Addiction Profile (MAP): a brief instrument for assessing treatment outcome. *Addiction.* 1998;93(12):1857-68.
61. Shrank WH, Patrick AR, Brookhart MA. Healthy user and related biases in observational studies of preventive interventions: a primer for physicians. *J Gen Intern Med.* 2011;26(5):546-550. doi:10.1007/s11606-010-1609-1

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Table 1. Characteristics of participants at study entry (N = 2,030).

Characteristic	Statistic
Demographic and clinical	
Age in years; mean (SD)	39.2 (10.7)
Female sex ^a ; n (%)	894 (44.1)
Type of treatment; n (%)	
Methadone	1601 (78.9)
Buprenorphine-naloxone	429 (21.1)
Dose in mg/day; mean (SD)	
Methadone	70.5 (41.4)
Buprenorphine-naloxone	12.0 (6.7)
Years in treatment ^a ; median (IQR)	2.6 (5.2)
Abstinence from opioid use at baseline ^b ; n (%)	646 (31.9)
Number of opioid urine drug screens at 3 months ^c ; mean (SD)	12.6 (5.3)
Median percentage of opioid-positive urine drug screens at 3 months ^c ; median (Q1, Q3)	0 (0, 20)
Abstinence from opioid use at 3 months ^c ; n (%)	1,127 (56.5)
Patient-reported goals in treatment ^d	
Number of goals reported; n (%)	
One	1222 (60.2%)
Two	643 (31.7%)
Three	150 (7.4%)
Four	13 (0.64%)
Five	2 (0.1%)
Control cravings/withdrawal	247 (12.17%)

Maintain or stabilize medication dose	122 (6.01%)
"Live a normal life"	283 (13.94%)
Manage pain	240 (11.82%)
"Stay or get clean"	742 (36.55%)
Stop or taper off treatment	1386 (68.28%)
SD = Standard Deviation, Q1 = 25 th percentile, Q3 = 75 th percentile ^a Data available for 2,029 participants. ^b Data available for 2,028 participants. ^c Data available for 1,996 participants (missing for 34 participants). ^d Percentages sum to more than 100% as patients could report multiple goals in treatment.	

Table 2. Multivariable model of the association between patient goals and abstinence from opioid use for 3 months following study entry.

Covariate	Complete case analysis ^a (n = 1, 994 ^b)			Sensitivity analysis excluding outliers (n = 1,980) ^{a,c}		
	OR	95% CI	p	OR	95% CI	p
Control cravings/withdrawal	0.76	0.56, 1.03	0.078	0.73	0.54, 0.99	0.044
Maintain or stabilize medication dose	1.15	0.74, 1.79	0.523	1.24	0.79, 1.95	0.354
“Live a normal life”	1.02	0.77, 1.35	0.879	0.98	0.74, 1.31	0.902
Manage pain	1.0	0.73, 1.36	0.976	0.96	0.70, 1.32	0.806
“Stay or get clean”	0.73	0.59, 0.91	0.005	0.70	0.56, 0.87	0.001
Stop or taper off treatment	1.0	0.80, 1.27	0.974	1.01	0.80, 1.27	0.954

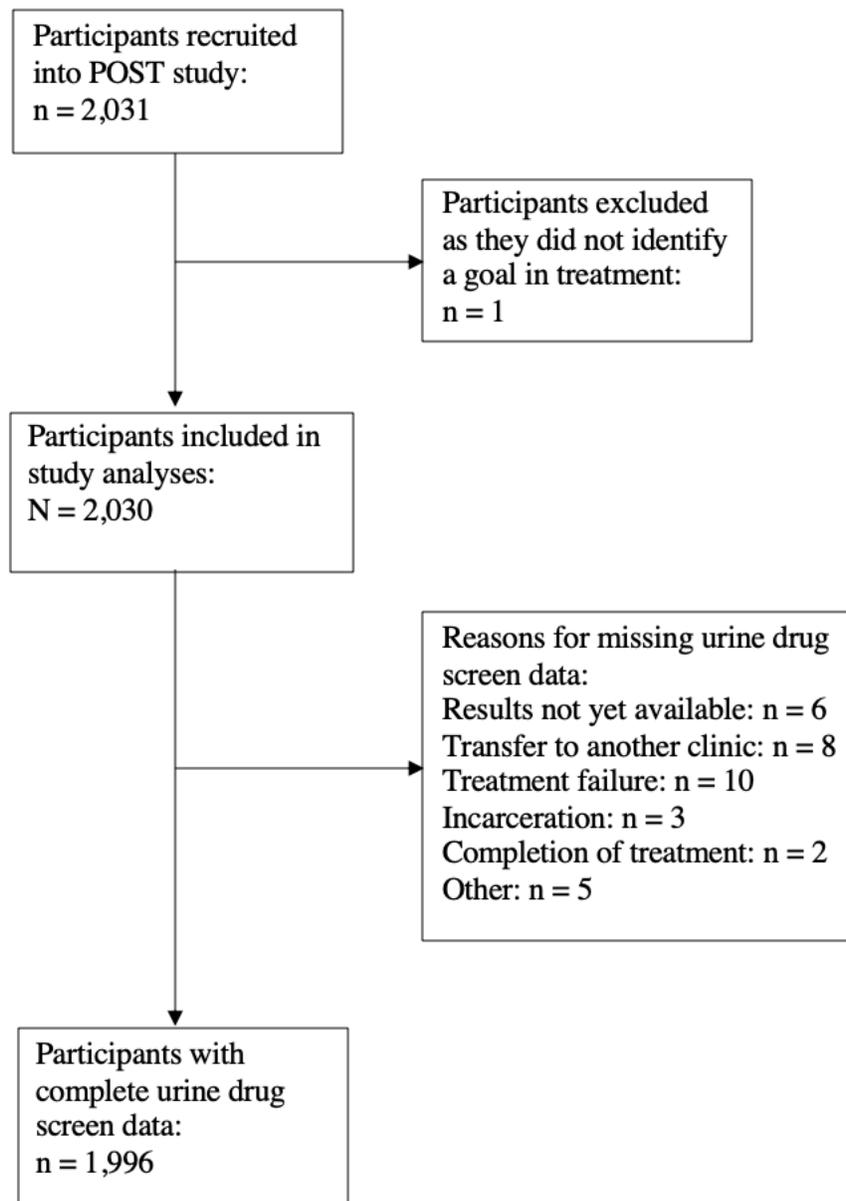
OR = Odds Ratio, CI = Confidence Interval
 Variance inflation factor = 1.19
 Hosmer-Lemeshow χ^2 5.93, p = 0.656
^a Model is adjusted for age, sex, type of treatment (methadone or buprenorphine-naloxone), dose, length of time in treatment, and opioid abstinence at baseline.
^b Participants with missing data in any of the included covariates are excluded due to complete case analysis (missing urine drug screen data: n = 36, missing sex: n = 1, missing length of time in treatment: n = 1).

^c Excluding 14 outliers detected using deviance residuals less than - 2 from the analysis

Figure 1 Legend:

Study Flow Diagram. POST = Pharmacogenetics of Opioid Substitution Treatment Response

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Figure 1. Study flow diagram.

Supplementary Table 1 for Peer-Review. Multivariable model of the association between patient goals and abstinence from opioid use for 3 months following study entry including all covariates.

Covariate	Complete case analysis ^a (n = 1,994 ^b)			Sensitivity analysis excluding outliers (n = 1,980) ^{a,c}		
	OR	95% CI	p	OR	95% CI	p
Control cravings/withdrawal	0.76	0.56, 1.03	0.078	0.73	0.54, 0.99	0.044
Maintain or stabilize medication dose	1.15	0.74, 1.79	0.523	1.24	0.79, 1.95	0.354
“Live a normal life”	1.02	0.77, 1.35	0.879	0.98	0.74, 1.31	0.902
Manage pain	1.0	0.73, 1.36	0.976	0.96	0.70, 1.32	0.806
“Stay or get clean”	0.73	0.59, 0.91	0.005	0.70	0.56, 0.87	0.001
Stop or taper off treatment	1.0	0.80, 1.27	0.974	1.01	0.80, 1.27	0.954
Age in years	1.0	0.99, 1.01	0.730	1.0	0.99, 1.01	0.715
Female sex	1.13	0.93, 1.37	0.223	1.14	0.94, 1.39	0.194
Type of treatment						
Methadone	[ref]			[ref]		
Buprenorphine-naloxone	1.88	1.40, 2.50	< 0.001	2.13	1.58, 2.86	< 0.001
Medication dose (mg/day)	1.0	0.99, 1.01	0.057	1.0	1.0, 1.0	0.015
Years in treatment	1.03	1.01, 1.04	0.013	1.03	1.01, 1.05	0.006
Opioid abstinence at baseline	5.34	4.23, 6.74	<0.001	6.15	4.83, 7.84	< 0.001

OR = Odds Ratio, CI = Confidence Interval
Variance inflation factor = 1.19
Hosmer-Lemeshow χ^2 5.93, p = 0.656
^a Model is adjusted for age, sex, type of treatment (methadone or buprenorphine-naloxone), dose, length of time in treatment, and opioid abstinence at baseline.
^b Participants with missing data in any of the included covariates are excluded due to complete case analysis (missing urine drug screen data: n = 36, missing sex: n = 1, missing length of time in treatment: n = 1).

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° Excluding 14 outliers detected using deviance residuals less than -2 from the analysis

Supplementary Table 2 for Peer-Review. Multivariable model of the association between number of self-reported goals and abstinence from opioid use for 3 months following study entry.

	(n = 1, 994^b)		
Covariate	OR	95% CI	<i>p</i>
Number of goals reported			
One	[ref]		
Two	0.93	0.75, 1.15	0.497
Three or more	0.70	0.49, 1.0	0.049
Age in years	1.0	0.99, 1.01	0.600
Female sex	1.14	0.94, 1.38	0.197
Type of treatment			
Methadone	[ref]		
Buprenorphine-naloxone	1.88	1.41, 2.52	< 0.001
Medication dose (mg/day)	1.0	0.99, 1.01	0.055
Years in treatment	1.03	1.01, 1.05	0.004
Opioid abstinence at baseline	5.41	4.30, 6.82	<0.001
OR = Odds Ratio, CI = Confidence Interval			

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Included on page:
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3 (intro, paragraphs 1-3)
Objectives	3	State specific objectives, including any pre-specified hypotheses	3 (intro, paragraph 5)
Methods			
Study design	4	Present key elements of study design early in the paper	3-4 (Methods, Data section)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4 (Methods, Data section)
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3 (Methods, paragraph 1, 3)
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4 (Statistical analysis, paragraph 2)
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4 (Methods)

Bias	9	Describe any efforts to address potential sources of bias	Methods (Data), Limitations (page 7)
Study size	10	Explain how the study size was arrived at	Figure 1 Study Flow Diagram
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods, Statistical analysis page 4
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Methods, Statistical analysis page 4
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	Page 5 first paragraph
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
(e) Describe any sensitivity analyses			
Continued on next page			
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Study flow diagram Figure 1
		(b) Give reasons for non-participation at each stage	Study flow diagram Figure 1
		(c) Consider use of a flow diagram	Study flow diagram Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1

		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Table 1
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Table 1
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Results page 5, paragraph 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	Discussion page 6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Discussion page 7
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion page 6
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion page 7
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Title page

Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses

Continued on next page

Results

