Perceptions of injectable opioid agonist treatment (iOAT) among people who regularly use opioids in Australia: Findings from a cross-sectional study in three Australian cities

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ABSTRACT

Background and aims: Not all people experiencing opioid dependence benefit from oral opioid agonist treatment. The aim of this study was to examine perceptions of (supervised) injectable opioid agonist treatment (iOAT) (described as “an opioid similar to heroin self-injected at a clinic several times a day”) among people who regularly use opioids and determine how common iOAT eligibility criteria accord with interest in iOAT.

Design: Cross-sectional survey

Setting: Sydney, Melbourne and Hobart, Australia

Participants: 344 people (63% male) who use opioids regularly and had ever injected opioids, interviewed December 2017- March 2018. The mean age of participants was 41.5 years (SD 8.5).

Measurements: Primary outcome measures were interest in iOAT, factors associated with interest and the proportion of participants who would be eligible using common criteria from trials and guidelines. We examined willingness to travel for iOAT, medication preferences and perspectives on whom should receive iOAT.

Findings: Overall, 53% of participants (n=182) believed that iOAT would be a good treatment option for them. Participants who believed that iOAT was a good treatment option for them were more likely to be male (aOR 1.76, 95%CI 1.10-2.82), have used heroin in the past month (aOR 6.03, 95%CI 2.86-12.71), currently regularly inject opioids (aOR 1.84, 95%CI 1.16-2.91) and have met ICD-10 criteria for opioid dependence (aOR 3.46, 95% CI 1.65-7.24). Those interested in iOAT had commenced more treatment episodes. Among those interested in iOAT (n=182), 26% (n=48) met common eligibility criteria for iOAT.

Conclusions: Interest in injectable opioid agonist treatment does not appear to be universal among people who regularly use opioids. Among study participants who expressed interest in injectable opioid agonist treatment, most did not meet common eligibility criteria.

Keywords: injectable opioid agonist treatment, medication assisted treatment, consumer perceptions

INTRODUCTION

Opioid agonist treatment (OAT) for opioid use disorder is effective for reducing illicit opioid use, and providing personal and societal benefits (1, 2). The clearest benefit is the profound effect of OAT on mortality, roughly halving the risk for people in treatment (3). Retention in OAT is higher than with non-drug treatments (1), but some people who inject opioids are not attracted to, or retained in traditional OAT, and some of those retained in OAT continue to inject opioids (1, 4). It is estimated that approximately 10-15 % of patients in OAT may not receive sufficient benefit from oral OAT (5, 6).

Early forms of injectable OAT (iOAT) in the UK involved a licenced doctor providing unsupervised injectable diamorphine (pharmaceutical heroin) (7). Contemporary iOAT typically consists of diamorphine or hydromorphone, injected under medical supervision up to three times a day (distinct from long-acting injectable buprenorphine, which is administered as a weekly or monthly depot injection by a health professional). Often iOAT is delivered with an additional longer-acting oral opioid agonist (e.g. methadone or slow-release oral morphine) to avoid opioid withdrawal overnight (8). One rationale for iOAT is that providing an injectable medication will retain people in structured treatment where oral OAT has been ineffective (9, 10). In the context of high-potency synthetic opioids, unsupervised hydromorphone has also been proposed as a safer alternative (11, 12), though concerns have been raised with this approach (13).

To date, eight randomised controlled trials have found that supervised iOAT is effective for those 'non-responsive' to conventional treatments (14). Two systematic reviews demonstrated significant reductions in illicit heroin use, increased treatment retention, and health and social benefits from iOAT, and reductions in crime (14, 15). Individual studies showed lower mortality in iOAT, yet the outcomes were not significant in meta-analysis (14, 15). In response to the evidence, iOAT has been implemented in a number of countries including Canada, Denmark, Switzerland, the UK, Germany and the Netherlands (14). In the context of rising opioid-related morbidity and mortality in countries including Australia and the US (16, 17), it seems timely to consider the role of iOAT in these places (18).

Injectable heroin treatment, and to a lesser extent hydromorphone, have increased propensity to cause opioid-induced respiratory depression (19). This has been an important argument for supervised administration of injectable medicines, so adverse events can be safely managed (14, 15). While the patient and societal benefits of iOAT make it cost-effective, the cost of infrastructure, staffing and medication is considerable (20-22). For these reasons, and considering the overall intensity of iOAT, it is considered a second-line treatment with narrow eligibility criteria limiting access to those who do not benefit from oral OAT. Although there is some variation, minimum age, frequency and duration of

opioid use, previous unsuccessful oral OAT, and other indicators of poor health are common criteria (23-27).

Some studies have investigated consumer perspectives of iOAT. Those who had not entered a heroin trial in Belgium gave reasons for non-participation (28). These included fearing making their addiction worse, the one-year limit on treatment in this trial, and disliking supervised injecting with no take-away doses. In Australia, a sample of people who inject drugs did not universally support iOAT - 75% supported a trial of heroin treatment (29, 30). Research has looked into iOAT perceptions among its participants (31-34), though few studies have explored perceptions towards iOAT among broader community samples of people who use opioids. With rising opioid-related mortality in some countries, understanding client preferences may inform efforts to expand treatment engagement.

To address this need, the current study explores attitudes towards iOAT within a diverse Australian sample of people who regularly use opioids and have history of opioid injection. Specifically, this study aimed to examine:

1. The proportion who believe that iOAT is a good treatment option for them (i.e. were interested in iOAT).
2. The correlates of being interested in iOAT.
3. The proportion interested and eligible for iOAT according to published trial and guideline criteria.
4. Perceptions about:
 - (i) Preferences for travel time and medication type (e.g. additional oral methadone etc);
 - (ii) The reasons iOAT would or would not be a good treatment option for them; and
 - (iii) Who should be able to receive iOAT.

METHODS

Study design

This cross-sectional study enrolled participants from capital cities in three Australian states (Sydney, New South Wales; Melbourne, Victoria; and Hobart, Tasmania) between December 2017 and March 2018. The study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement (Table S1).

Ethics

This study was approved by South Eastern Sydney Local Health District Human Research Ethics Committee 17/224 (HREC/17/POWH/486), Tasmania Health and Medical HREC (H0017051) and the Alfred Hospital HREC (515/17).

Participants

Data are drawn from a study of people who were regularly using opioids (35). Eligible participants were: aged 18 years or older; able to provide voluntary informed consent, reported using opioids in the last 6 months and used opioids on at least 21 out of the past 28 days (including heroin use or the extra-medical use of pharmaceutical opioids). Participants were ineligible if intoxication precluded provision of informed consent. For these analysis we limited the sample to those with a lifetime history of injecting who answered questions on iOAT. We purposefully kept the sample broad with respect to current opioid use to understand who might be most interested in iOAT.

Procedure

Participants were recruited from needle-syringe programs, drug treatment services, a supervised injecting facility (Sydney), snowball sampling, and word-of-mouth. The study was advertised at services with posters and fliers, but service staff were not directly involved in recruitment. Interested participants contacted the study team directly and were screened for eligibility over the phone.

Interviewers obtained written informed consent prior to conducting face-to-face interviews using a computer-assisted structured interview schedule. Interviewers had received training in responding to participant distress and suicidal ideation. Interviews took approximately 1-hour and participants were reimbursed AUD\$50.

Measures

Interest in and preferences regarding iOAT

Participants were initially read a description of iOAT: *“Treatment with injectable opioids (pharmaceutical heroin and similar) has been trialled abroad; the aim of the treatment is to stabilise people who don’t benefit from oral treatment options. The treatment requires that participants self-administer all their medication at the clinic; this means coming to the program two to three times per day to self-inject*

(intravenously or intramuscularly) under the supervision of medical staff. No injectable opioid is currently registered for treatment of opioid dependence in Australia". They were then asked questions about their interest in iOAT, medication and travel preferences, reasons for interest in iOAT (if interested) or reasons for being uninterested (See Table S2 for question and response wording).

Demographic characteristics

Participants' age, gender, employment status, main source of income, highest level of education and private health insurance status were recorded. Homelessness, included primary (e.g., sleeping rough), secondary (e.g., couch-surfing or hostel) and tertiary homelessness (e.g., insecure accommodation such as caravan), was measured (36).

Current mental and physical health

Mental health was measured by the Patient Health Questionnaire (PHQ-9) scale for depression and Generalised Anxiety Scale (GAD-7) for anxiety and categorized as none/mild (< 10) and moderate/severe (≥ 10) (37, 38). Poor physical health was defined as being one standard deviation below an Australian population norm for the Visual Analogues Scale rating of overall physical health from the EuroQol five questions standardised measure of health status (EQ-5D) (39).

Substance use

Participants were asked about lifetime and past 28 day substance use. Alcohol use was measured with the Alcohol Use Disorder Identification Test, Version-C (AUDIT-C) (40).

Treatment history

Participants were asked about their lifetime use of treatment for opioid dependence, including current oral/sublingual OAT. Those currently receiving OAT were asked about the characteristics of their current treatment, including medication-type, past 7-day doses (used to calculate an average daily dose), and duration (in weeks).

Opioid dependence

The Composite International Diagnostic Interview 3.0 (CIDI) was used to assess opioid dependence in the past 12 months as per ICD-10 criteria (41).

Eligibility for iOAT

Eligibility criteria for iOAT were taken from the British Columbia Guidelines for iOAT (8), the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) evidence summary (42), and documented eligibility criteria from clinical trials with iOAT (23-25, 27, 42, 43) (See Table S3). Based on common criteria in these papers, iOAT eligibility criteria that were explored in this study were:

- being $\leq$ / $\geq$ 25 years old

- having injected opioids regularly (15/30 days)
- ICD-10 criteria for opioid dependence
- a history of at least 5 years injecting drug use
- least two previous episodes of OAT, with one being methadone
- poor mental or physical health (EQ-5D-5L score < 62 OR GAD-7 score ≥ 10)

Additional exclusion criteria related to other substance use that might increase overdose risk which were defined as:

- benzodiazepine use on ≥ 20 out of the past 28 days
- hazardous alcohol consumption (defined as meeting the cut-point score of 4 for males and 3 for females on the AUDIT-C (40)).

Perceptions on recipients of injectable opioid treatment

Participants were asked who they felt should be offered iOAT, selecting from four options: 'people who are severely dependent on opioids', 'people for whom opioid treatment hasn't worked', 'anyone who injects opioids' or 'no-one'.

Analyses

Descriptive statistics were used to address primary objectives. Correlates of interest in iOAT were assessed. Eligibility criteria were stratified by interest in iOAT, and eligibility and interest in iOAT was considered for the whole sample, and only among those who met ICD-10 criteria for opioid dependence. Independent t-tests were used to compare continuous variables. Fisher's exact test was used to examine associations between categorical variables. Bivariate logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (95% CI) to compare differences in characteristics between those who perceived iOAT might be a good treatment option for them and those who did not. Adjusted ORs (aORs) were used to control for age, gender and state. Missing data were minimal, and are reported in Table S7. Missing data were handled by listwise deletion in logistic regression. To check for heterogeneity in key characteristics across the three survey sites (New South Wales, Victoria and South Australia), we (a) examined differences in the primary outcome ('Perceptions that iOAT was a good treatment option for them') and (b) included any significant interaction terms (state $\times$ characteristic) in the logistic regression model. Analyses were performed using Stata SE 16.1 (44). The analysis was not pre-registered and the results should be considered exploratory.

RESULTS

Participant characteristics

The mean age of the sample was 41.5 years (SD 8.5) and 36% of the sample were females (n = 344) (Tables 1 and 2). After the nature of the treatment was explained, 53% (n= 182) indicated that they believed iOAT would be a good treatment option for them (i.e were interested in iOAT). There was a significant effect of state on interest in iOAT, with those in Victoria being more likely to be interested in iOAT (aOR 1.75, 95%CI 1.02-3.01) and those in Tasmania being less likely to be interested in iOAT (aOR 0.33, 95%CI 0.18-0.60) compared with participants in New South Wales. After adjusting for age, gender, and state, participants who were interested in iOAT were more likely to be male (aOR 1.76, 95%CI 1.10-2.82); experience symptoms of moderate-to-severe depression (aOR 1.61, 95%CI 1.01-2.57), use heroin in the past month (aOR 6.03, 95%CI 2.86-12.71); regularly inject opioids (aOR 1.84, 95%CI 1.16-2.91), and meet ICD-10 criteria for opioid dependence (aOR 3.46, 95% CI 1.65-7.24). Participants who were interested in iOAT were more likely to have engaged in criminal activity in the past 12 months (OR 1.78, 95%CI 1.15-2.78), though after adjusting for age, gender and state this was no longer significant (aOR 1.54, 95%CI 0.96-2.47).

Table 1 and 2 about here

Most study participants (66%) were currently in treatment; receiving methadone (55%) or buprenorphine (+/- naloxone) (11%) (Table 3). People in buprenorphine treatment were less likely to be interested in iOAT (aOR 0.26, 95%CI 0.12-0.58), after adjusting for age, gender and state. In bivariate analysis, those who were interested in iOAT had spent less time in treatment (1.5 [IQR 3.5] vs 3.0 [IQR 6.2] years (non-significant after adjusting for age, gender and state). Those interested in iOAT reported significantly more treatment episodes (4 [IQR 6] vs. 3 [IQR 4] episodes; aOR 1.06, 95%CI 1.00- 1.12) compared with those uninterested in iOAT, after adjusting for age, gender and state.

Table 3 about here

Proportion of participants who would be eligible for iOAT

Of the participants interested in iOAT (n=182), one in four (n=48, 26% of those interested) met common eligibility criteria (Figure 1). If current benzodiazepine use and/or hazardous alcohol use were considered as exclusion criteria, 31 additional participants were excluded leaving 17 participants (9% of those who were interested) considered eligible for iOAT. Of those who were uninterested, one in three (n=28, 37%) were considered eligible. The most common reasons for ineligibility were insufficient frequency of current injected opioid use, and insufficient prior OAT attempts (Table S4). When only those who met ICD-10 criteria for opioid dependence were considered, the proportion interested and eligible in iOAT were similar (Table S5).

Figure 1 about here

Medication regime preferences

Of those interested in iOAT, most (69%) were interested in an injectable substance similar to heroin as the sole treatment (69%) (Table 4). Fewer were interested in an injectable opioid provided in conjunction with oral methadone (35%) or in conjunction with another oral medication (23%) to hold them overnight.

Travel preferences

For those interested in iOAT (n=182), the amount of time that people were willing to travel to administer iOAT varied (Table 4). Most (65%, n=116) were willing to travel between 30-60 minutes, and just over one-in-four (27%, n=49) were willing to travel for ≥ 1 -hour. Fewer than one-in-ten (7%, n=13) were only willing to travel up to 15 minutes.

Insert table 4 around here

Reasons for interest/non-interest in iOAT

Participants reported reasons for interest or non-interest in iOAT (Table 5). The most common reasons expressed for interest in iOAT were to: 'stay off other opioids' (44%, n=80); (2) 'inject opioids in a more healthy way' (42%, n=77); (3) 'stay off injecting illicit drugs' (40%, n=72); and, (4) 'avoid trouble with the police' (40%, n=72). Fewer (19%, n=34) endorsed interest in iOAT because it would 'provide a high that other medications don't'.

Among those uninterested in iOAT, the main reason reported was that participants 'didn't like the idea of coming to a clinic more than once a day' (40%, n=64). Fewer reported that they were uninterested due to 'less flexibility' in their treatment (30%, n=48), and that they did not think they 'could get off injectable medication in the long run' (24%, n=39).

Insert table 5 around here

Opinions regarding who should receive iOAT

All survey participants were asked who they felt should be able to receive iOAT. Being 'severely dependent on opioids' was endorsed by around half (47%, n=164) (Table S6). Fewer participants supported the provision of iOAT for those whom opioid treatment had not worked (38%, n=132) and for anyone who injects opioids (37%, n=128). Twelve percent (n=41) felt that iOAT should not be available to anyone.

DISCUSSION

We examined perceptions of iOAT among people who use opioids. Around half believed that iOAT would be a good treatment option for them. Yet, only one-in-four who were interested in iOAT would be considered eligible to receive it as per common eligibility criteria. Common reasons for ineligibility were insufficient prior OAT attempts, less frequent current opioid use, and concurrent benzodiazepine or alcohol use. The proportion who were both interested in, and eligible for iOAT (14%) is broadly consistent with the estimated proportions of all OAT patients that have been engaged in iOAT in the Netherlands (13%) and Switzerland (9%) (7), and lower than in a Canadian study on people with HIV which found one-in-five (20%) met standard trial criteria (45). Taken together, this highlights that iOAT may be an important option for minority of people who inject opioids.

Those who were interested in iOAT were more likely to: live in Victoria (consistent with elevated numbers of heroin-related deaths, which are double that in New South Wales (46)), be opioid dependent and inject opioids/heroin recently and regularly. They also reported more treatment attempts. These multiple measures of greater opioid-related risk accord with those who might receive most benefit. Motivations for entering iOAT were consistent with the demonstrated benefits of iOAT (42), centring on reducing illicit opioid use, improving health, and reducing contact with law enforcement. Of those interested in iOAT, a minority were willing to travel more than 90 minutes to receive iOAT. This is inconsistent with common iOAT program requirements for participants to reside locally (8), and highlights the importance of locating iOAT programs in areas of need.

In contrast, more than one-in-three meeting eligibility criteria (typically reflecting greater opioid-related risk) were uninterested in iOAT. Among those who were not interested in iOAT, the main barriers were the need for more than daily clinic attendance and the lack of flexibility in treatment. Supervision minimises the risks of medication diversion, and increases safety (e.g. in the event of overdose, with one estimated overdose for every 6,613 heroin injections) (42)). Yet, the structured and supervised nature of iOAT may not be attractive for some patients, and means some remain out of treatment, which also carries risks. Emerging treatments like long-acting buprenorphine may represent a less structured alternative (47).

Most were interested in receiving injectable opioids without supplementary oral medicines. Long-acting opioid agonists (e.g. methadone) are often provided as part of iOAT, or are a requirement to enter iOAT (42). This may highlight a potential gap between iOAT delivery, and preferences. To effectively engage new populations, co-design processes could involve patients in developing new models of care (48).

Other studies have also explored barriers to iOAT. These found reluctance to enter time-limited iOAT (12-months) (28), with the benefits of time-limited iOAT also not maintained after cessation (50). There is divergence as to whether iOAT is offered open-ended, as per current Canadian treatment guidelines

(8), or seen as a time-limited approach with the goal to transition to oral OAT (51). The former option has led to waiting lists (7), and the latter may act as a disincentive to enter treatment. Many trials of iOAT have struggled to meet recruitment targets, or taken longer than planned (43). This might suggest iOAT is not an attractive treatment for some, though there may also be lower willingness to enter an iOAT trial with a 50% chance of receiving a comparator treatment (e.g. oral methadone) (51). Similarly, qualitative research found consumers may be more interested in treatment compared to a research trial (29), and some heroin trial participants have objected to the sterile clinic environment, or found challenges coordinating clinical attendance with employment (52).

These findings highlight the considerations and possible contradictions in iOAT delivery. Previous research has demonstrated iOAT efficacy and explored potential barriers, yet few studies have examined the size of the potential clinical population using a broad sample of people who use opioids. Our study advances knowledge by quantifying the likely treatment demand and the relative importance of barriers to iOAT. This may help inform how iOAT could be made available and how service delivery models could be tailored to reach a broader group of people who might not engage with existing OAT treatment options. Interestingly, participants' perceptions largely reflected policy, where iOAT is limited to those with more severe OUD and for whom other treatments had not worked, though one-in-ten did not support the availability of iOAT at all. That consumers do not unanimously support iOAT is consistent with research where people who inject drugs held mixed views on an iOAT trial (29, 30).

Limitations

There are limitations with the use of hypothetical scenarios, and their generalizability to real world situations. The study was conducted in Australia, where iOAT is not currently available, so participants were unlikely to have any direct experience to inform their preferences. Yet, research shows many already have knowledge and opinions about iOAT (29). The brief description of iOAT provided may mean that assumptions were made about the treatment model. Differing descriptions of iOAT may yield different results, as noted in other research examining the importance of language (53, 54). We are unable to determine the generalisability of the sample. Study sites did not collect information on ineligible participants, and a convenience sampling approach was used, so selection bias may be present. Further, those without telephone access for screening, and those from rural areas were not represented. Nonetheless, participants had a broad range of treatment experiences and came from three Australian jurisdictions. Results may have been influenced by response bias, though participants were assured of confidentiality and there were no negative repercussions for responses. Finally, eligibility criteria were chosen to reflect common criteria in trials and guidelines, though individual programs or trials vary, with some criteria being more or less restrictive than those we explored. Relaxing some criteria, as may happen in clinical practice, may see higher levels of eligibility.

Conclusions

This study provides important insights into iOAT preferences. Those interested in iOAT reflect a higher-risk population with considerable treatment experience. A small proportion of the total treatment population is likely to be eligible according to common criteria.

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Table 1: Demographic and clinical characteristics of the study sample by interest in injectable Opioid Agonist Treatment (iOAT)

		Total ¹ (n=344)	Perceived iOAT was a good treatment option for them		Crude odds ratios		Adjusted odds ratios ²	
		n (%)	No/not sure n=162 (47.09%)	Yes n=182 (52.91%)	OR (95% CI)	p	AOR (95% CI)	p
Demographic and clinical characteristics								
State	New South Wales (ref)	175 (50.9)	81 (46.3)	94 (53.7)				
	Victoria	98 (28.5)	31 (31.6)	67 (68.4)	1.86 (1.11, 3.13)	0.02	1.75 (1.02, 3.01)	0.04
	Tasmania	71 (20.6)	50 (70.4)	21 (29.6)	0.36 (0.20, 0.65)	0.001	0.33 (0.18, 0.60)	< 0.001
Age	≤ 24 years	5 (1.5)	0 (0)	5 (100)	Excluded ³		Excluded ³	
	25 - 34 years (ref)	68 (19.8)	34 (50.0)	34 (50.0)				
	35 - 44 years	142 (41.3)	63 (44.4)	79 (55.6)	1.25 (0.71, 2.24)	0.44	1.16 (0.63, 2.15)	0.63
	45 - 54 years	107 (31.1)	56 (52.3)	51 (47.7)	0.91 (0.50, 1.67)	0.76	0.87 (0.46, 1.66)	0.68
	≥ 55 years	22 (6.4)	9 (40.9)	13 (59.1)	1.44 (0.55, 3.82)	0.46	1.65 (0.60, 4.55)	0.34
Gender	Female (ref)	124 (36.1)	68 (54.8)	56 (45.2)				
	Male	217 (63.1)	92 (42.4)	125 (57.6)	1.65 (1.06, 2.57)	0.03	1.76 (1.10, 2.82)	0.02
Education	Completed <10 years school education (ref)	108 (31.5)	44 (40.7)	64 (59.3)				
	Completed ≥10 years school education	235 (68.5)	118 (50.2)	117 (49.8)	0.68 (0.43, 1.08)	0.10	0.89 (0.54, 1.46)	0.64
Main source of income	Other (ref)	314 (91.5)	147 (46.8)	167 (53.2)				
	Paid employment	29 (8.5)	15 (51.7)	14 (48.3)	0.82 (0.38, 1.76)	0.61	1.13 (0.49, 2.59)	0.78
Homeless ⁴	No (ref)	242 (70.3)	119 (49.2)	123 (50.8)				
	Yes	102 (29.7)	43 (42.2)	59 (57.8)	1.33 (0.83, 2.12)	0.23	0.95 (0.57, 1.59)	0.84
Moderate to severe depression (PHQ-9) ⁵	No (ref)	144 (43.1)	75 (52.1)	69 (47.9)				
	Yes	190 (56.9)	82 (43.2)	108 (56.8)	1.43 (0.93, 2.21)	0.11	1.61 (1.01, 2.57)	0.05
Moderate to severe generalised anxiety disorder (GAD-7) ⁵	No (ref)	182 (54.6)	92 (50.6)	90 (49.5)				
	Yes	151 (45.4)	66 (43.7)	85 (56.3)	1.32 (0.85, 2.03)	0.21	1.45 (0.91, 2.31)	0.12
Current physical health ⁶	Good (ref)	170 (50.0)	84 (49.4)	86 (50.6)				
	Poor	170 (50.0)	77 (45.3)	93 (54.7)	1.18 (0.77, 1.81)	0.45	1.33 (0.84, 2.10)	0.23
Criminal activity past 12 months	No (ref)	211 (61.3)	111 (52.6)	100 (47.4)				
	Yes	133 (38.7)	51 (38.4)	82 (61.7)	1.78 (1.15, 2.78)	0.01	1.54 (0.96, 2.47)	0.08

Percentages are based on all responses (excluding missing data only) and may not sum to 100. Some variables contained minority categories that were not included in the above analysis to assist interpretation (e.g. gender - 3 people identified as non-binary. Therefore n = 341 [99.13%]).

¹See Methods for exact item wording; up to 11 participants were missing data from row variables.

²Adjusted odds ratios (AOR) control for age, gender and state (age, gender and state each control only for the remaining two).

³The first age category was perfectly predictive of the outcome. These observations were therefore excluded from the model due to estimation difficulties.

⁴'Homeless' includes primary, secondary or tertiary homelessness (36)

⁵Measured by the Patient Health Questionnaire (PHQ-9) scale for depression and Generalised Anxiety Scale (GAD-7) for anxiety and categorized as none/mild (< 10) and moderate/severe (≥10) (37, 38).

⁶ Defined as one standard deviation below Australian population norm for the Visual Analogues Scale rating of overall physical health from the EQ-5D (39).

Table 2: Substance use profile of the study sample

		Total ¹ (n=344)	Perceived iOAT was a good treatment option for them		Crude odds ratios		Adjusted odds ratios ²	
		n (%)	No/not sure n=162 (47.1%) n (%)	Yes n=182 (52.9%) n (%)	OR (95% CI)	p	AOR (95% CI)	p
Substance use and use disorders								
Duration of injection drug use (Years)		22.1 (9.5) [†]	21.4 (9.4) [†]	22.7 (9.5) [†]	1.01 (0.99, 1.04)	0.20	1.03 (0.99, 1.07)	0.09
At least 5 years since first injection	No	10 (2.9)	5 (50.0)	5 (50.0)	0.89 (0.25, 3.12)	0.85	1.23 (0.29, 5.21)	0.78
	Yes (ref)	334 (97.1)	157 (47.0)	177 (53.0)				
Regular opioid injection in the past 28 days (at least 14/28 days)	No (ref)	165 (48.0)	91 (55.2)	74 (44.9)				
	Yes	179 (52.0)	71 (39.7)	108 (60.3)	1.87 (1.22, 2.87)	0.004	1.84 (1.16, 2.91)	0.01
Injected opioids in past 12 months	No (ref)	20 (5.9)	17 (85.0)	3 (15.0)				
	Yes	321 (94.1)	144 (44.9)	177 (55.1)	6.97 (2.00, 24.24)	0.002	10.90 (2.37, 50.13)	0.002
Past month cocaine use	No (ref)	311 (90.7)	152 (48.9)	159 (51.1)				
	Yes	32 (9.3)	10 (31.3)	22 (68.8)	2.10 (0.96, 4.59)	0.06	1.74 (0.77, 3.93)	0.19
Past month (meth)amphetamine use	No (ref)	157 (46.5)	79 (50.3)	78 (49.7)				
	Yes	181 (53.5)	81 (44.8)	100 (55.3)	1.25 (0.81, 1.92)	0.31	1.30 (0.81, 2.07)	0.27
Past month heroin use	No (ref)	115 (33.7)	84 (73.0)	31 (27.0)				
	Yes	226 (66.3)	76 (33.6)	150 (66.4)	5.35 (3.26, 8.78)	< 0.001	6.03 (2.86, 12.71)	< 0.001
Past month prescribed opioid use	No (ref)	195 (56.7)	88 (45.1)	107 (54.9)				
	Yes	149 (43.3)	74 (49.7)	75 (50.3)	0.83 (0.54, 1.28)	0.40	1.06 (0.65, 1.70)	0.83
Past month non- prescribed opioid agonist treatment	No (ref)	262 (76.2)	130 (49.6)	132 (50.4)				
	Yes	82 (23.8)	32 (39.0)	50 (61.0)	1.54 (0.93, 2.55)	0.10	1.66 (0.96, 2.86)	0.07
Co-prescribed benzodiazepines	No (ref)	127 (36.9)	55 (43.3)	72 (56.7)				
	Yes	217 (63.1)	107 (49.3)	110 (50.7)	0.79 (0.51, 1.22)	0.28	0.92 (0.58, 1.48)	0.74
Use benzodiazepines (at least 20/28 days)	No (ref)	261 (75.9)	119 (45.6)	142 (54.4)				
	Yes	83 (24.1)	43 (51.8)	40 (48.2)	0.78 (0.48, 1.28)	0.32	0.91 (0.53, 1.56)	0.74
Meet ICD-10 criteria for Opioid Dependence	No (ref)	46 (13.4)	32 (69.6)	14 (30.4)				
	Yes	298 (86.6)	130 (43.6)	168 (56.4)	2.95 (1.51, 5.76)	0.001	3.46 (1.65, 7.24)	0.001
Hazardous drinking ³ (AUDIT-C)	No (ref)	209 (62.8)	102 (48.8)	107 (51.2)			NSW: 0.67 (0.36, 1.26)	0.22
	Yes	124 (37.2)	58 (46.8)	66 (53.2)	1.08 (0.70, 1.69)	0.72	Vic: 3.52 (1.17, 10.57) Tas: 1.63 (0.53, 5.08)	0.03 0.40

¹ See Methods for exact item wording; up to 11 participants were missing data from row variables, See Table S7 for missingness by variable

² Adjusted odds ratios (AOR) control for age, gender and state.

³Adjusted odds ratios estimated by jurisdiction as heterogeneity was noted in the response (statistically significant characteristic x jurisdiction interaction term)

† Mean (SD)

ICD-10: 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD)

AUDIT-C: Alcohol Use Disorders Identification Test

Table 3: Current treatment profile of the study sample and eligibility for injectable Opioid Agonist Treatment (iOAT)

		Total ¹ (n=344)	Perceived iOAT was a good treatment option for them		Crude odds ratios		Adjusted odds ratios ² or z	
		n (%)	No/not sure n=162 (47.09%) n (%)	Yes n=182 (52.91%) n (%)	OR (95% CI)	p	AOR (95% CI)	p
Current treatment								
Any current OAT for opioid dependence	No (ref)	116 (33.8)	44 (37.9)	72 (62.1)				
	Yes	227 (66.2)	117 (51.5)	110 (48.5)	0.57 (0.36, 0.91)	0.02	0.57 (0.34, 0.95)	0.03
Any Current methadone for opioid dependence	No (ref)	153 (44.6)	71 (46.4)	82 (53.6)				
	Yes	190 (55.4)	90 (47.4)	100 (52.6)	0.96 (0.63, 1.47)	0.86	1.02 (0.63, 1.63)	0.94
Methadone dose if current (mg) †		68 (50)	65 (70)	70 (50)	1.00 (0.99, 1.01)	0.93	1.00 (0.99, 1.01)	0.51
Any Current buprenorphine for opioid dependence	No (ref)	306 (89.2)	134 (43.8)	172 (56.2)				
	Yes	37 (10.8)	27 (73.0)	10 (27.0)	0.29 (0.13, 0.62)	0.001	0.25 (0.11, 0.58)	0.001
Buprenorphine dose in in buprenorphine treatment, (mg) †		18 (24)	16 (21)	32 (16)	1.07 (0.99, 1.15)	0.11	1.02 (0.93, 1.13)	0.66
Current duration of OAT treatment, (years) †		2.0 (5.5)	3.0 (6.2)	1.5 (3.5)	0.96 (0.96, 0.99)	0.02	0.97 (0.93, 1.01)	0.16
Number of previous treatment episodes, †		3 (5)	3 (4)	4 (6)	1.08 (1.02, 1.14)	0.004	1.06 (1.00, 1.12)	0.04
Eligibility for iOAT								
Inclusion criteria only [^]	Ineligible	268 (77.9)	134 (50.0)	134 (50.0)				
	Eligible	76 (22.1)	28 (36.8)	48 (63.2)				
Inclusion criteria and benzodiazepine or alcohol use	Ineligible	317 (92.2)	152 (48.0)	165 (52.0)				
	Eligible	27 (7.8)	10 (37.0)	17 (63.0)				

¹See Methods for exact item wording; 1 participant missing data from row variables.

²Adjusted odds ratios (AOR) control for age, gender and state .

† Median (IQR)

[^] Opioid use inclusion criteria for all is 15/30 days use irrespective of if in or out of treatment

OAT: Opioid Agonist Treatment

Table 4: Medication regime and travel preferences among participants interested in iOAT

	n (%)
If injectable opioid treatment was offered in Australia, which medication do you think would be a good treatment for you personally? (n = 182) (Note: options were not mutually exclusive)	
An injectable opioid similar to heroin	126 (69)
An injectable opioid similar to heroin plus oral methadone to hold me over night	64 (35)
An injectable opioid similar to heroin plus a different oral medication to hold me over night (other than methadone)	42 (23)
How far (in travel time) would you be willing to travel for a 2 to 3 times per day self-administered injection? (n = 180)	
Not interested / not willing to travel at all	2 (1)
Less than 15 minutes	13 (7)
15-30 minutes	55 (31)
30-45 minutes	32 (18)
45-60 minutes	29 (16)
60-90 minutes (up to an hour and a half)	9 (5)
More than 90 minutes	40 (22)

Table 5: Reasons for interest/non-interest in injectable Opioid Agonist Treatment (iOAT)

Reasons for interest among those that were interested (n = 182)	n (%)
It would help me stay off other opioids	80 (44)
It would allow me to inject opioids in a more healthy way	77 (42)
It would help me stay off injecting illicit drugs	72 (40)
It would allow to avoid trouble with the police	72 (40)
It would allow me to inject opioids legally	70 (38)
It would allow me to feel more in control of my treatment	70 (38)
It would allow to save money on drugs	67 (37)
It would allow me to reduce or cease criminal behaviour	65 (36)
It would allow me to inject drugs of known dose / potency	55 (30)
It would be something different than the treatments I've already tried	53 (29)
It would help me stay off other drugs than opioids	53 (29)
It would decrease my risk of overdose (safety)	53 (29)
It would allow to avoid regular contact with people on the street	53 (29)
It would give me more time to do other things	53 (29)
It would help me to gradually wean off injecting	50 (27)
It would help me to regain control of my life	50 (27)
It would allow me to improve relationships	50 (27)
It would allow me to improve their mental health and wellbeing	48 (26)
It would allow me to improve my social situation (housing, employment)	44 (24)
It would provide a high that other medications don't	34 (19)
Reasons for non-interest among those that were not interested (n = 162)	
Don't like the idea of coming to a clinic more than once a day	64 (40)
I would feel that there is less flexibility in my treatment	48 (30)
Don't think I could get off the injectable medication in the long run	39 (24)
Would prefer to stay on oral methadone	30 (19)
It would not allow me to travel for work or holidays	30 (19)
I don't like injections (or injection phobia)	24 (15)
I don't have good veins anymore	20 (12)
I don't think I would like to inject drugs under the supervision of medical staff	20 (12)
I don't think any medication-assisted treatment would suit me	20 (12)
Would prefer to try the buprenorphine depot	17 (10)
I don't think the medication provided in the treatment would be as rewarding as the drugs I inject	12 (7)
Would prefer to stay on sublingual buprenorphine	12 (7)
Don't trust it would hold me for the whole period between doses	12 (7)
Don't trust the injectable dose at the clinic would be enough for me	10 (6)
Don't think the treatment would be offered for as long as I need it	10 (6)

Figure 1. Interest and eligibility in injectable Opioid Agonist Treatment (iOAT)

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