

## CO-MORBID PAIN & SUBSTANCE USE DISORDERS SECTION

# Clinical and mental health characteristics among patients receiving medications for opioid use disorder treatment versus patients receiving low- and high-dose opioids when referred for pain management

Jie Yang , MA<sup>1,\*</sup>, Melita Giummarra , PhD<sup>2,3</sup>, Louisa Picco , PhD<sup>1</sup>, Carolyn Arnold, MBBS, FAFRM (RACP)<sup>2,4</sup>, Suzanne Nielsen, PhD<sup>1</sup>

<sup>1</sup>Monash Addiction Research Centre, Eastern Health Clinical School, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria 3199, Australia

<sup>2</sup>Caulfield Pain Management and Research Centre, Caulfield Hospital, Melbourne, Victoria 3162, Australia

<sup>3</sup>Department of Neuroscience, Central Clinical School, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria 3004, Australia

<sup>4</sup>Department of Anaesthesia and Perioperative Medicine, Central Clinical School, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria 3004, Australia

\*Corresponding author: Monash Addiction Research Centre, Monash University, 47-49 Moorooduc Hwy, Frankston, VIC 3199, Australia. Email: Jie.yang@monash.edu.

### Abstract

**Objective:** To examine the demographic and clinical characteristics of patients attending pain management services who were receiving opioid agonist treatment (ie, methadone or buprenorphine for the treatment of opioid use disorder) in comparison with those taking prescription opioid analgesics in oral morphine equivalent daily doses at low (<40 mg) and high doses (>100 mg) in a national database from the electronic Persistent Pain Outcomes Collaboration (ePPOC) in Australia.

**Design:** A cross-sectional study.

**Setting:** Australian pain services.

**Subjects:** Adult patients referred to Australian pain service clinics between 2016 and 2021.

**Methods:** Multinomial and bivariate logistic regression models were conducted to compare the demographic and clinical characteristics of patients on opioid agonist treatment and those taking other prescription opioid analgesics.

**Results:** Among 42 182 participants, most were female (56.8%), with a mean age of 51.7 years. People on opioid agonist treatment ( $n = 1016$ ) and high-dose opioids ( $n = 7122$ ) were similar in that they both had more severe mental health symptoms and longer pain duration than the low-dose group ( $n = 20 517$ ). Compared with the high-dose group, people on opioid agonist treatment had reduced odds of reporting more severe pain intensity but increased odds of having multimorbidity, more severe anxiety, and pain catastrophizing thoughts.

**Conclusions:** These findings highlight the need for mental health treatment and the necessity of tailored multidisciplinary pain management for people in opioid agonist treatment.

**Keywords:** Australia; opioid agonist treatment; opioids; pain management.

### Introduction

Chronic pain is a leading cause of disability, resulting in significant burdens to individuals, society, the economy, and public health.<sup>1,2</sup> It is estimated that around 31.0% (95% CI: 30.8–31.2) of adults suffer from chronic pain worldwide.<sup>3</sup> In Australia, between 2006 and 2016, there was a 67.0% increase in general practice visits related to chronic pain, costing society AU\$139 billion.<sup>4</sup> The prevalence of chronic pain is even higher among certain subpopulations. For example, around 44.0% (95% CI: 40.0–49.0) of people receiving opioid agonist treatment (OAT),<sup>5</sup> a first-line and evidence-based treatment for opioid use disorder (OUD),<sup>6</sup> have chronic pain. OAT medicines

commonly include methadone and buprenorphine, which are prescribed primarily to manage OUD in Australian clinical settings, but in limited situations, specific formulations (eg, buprenorphine patches or methadone tablets) may also be used to treat severe pain.<sup>7</sup> The use of OAT medicines in Australia increased by 50% from 2013 to 2022, rising from 35 733 to 53 501 client-months.<sup>8</sup>

Older age, unemployment, mental health problems, and comorbid physical diseases are common characteristics associated with chronic pain in people receiving OAT.<sup>5,9</sup> Many of these characteristics are also shared vulnerabilities in patients who take prescribed opioids for chronic pain, particularly a

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high prevalence of unemployment, severe depression, and physical problems such as arthritis.<sup>10</sup> Nevertheless, few studies provide a detailed understanding of people on OAT in pain management settings or compare their clinical characteristics with those of people taking other prescription opioid analgesics (excluding buprenorphine and methadone).

Understanding the unique clinical needs of people taking OAT medicines (ie, methadone or buprenorphine for the treatment of OUD) is of great importance for tailoring clinical pain management guidelines in the context of concurrent pain and OUD. Currently, such guidelines for managing concurrent pain and OUD are lacking.<sup>11</sup> The complexity of pain management for people in OAT was identified almost 20 years ago,<sup>12</sup> with undertreated pain still commonly reported in this population.<sup>13–15</sup> However, there has been limited research to drive improved clinical care. Research shows that pain perceptions were significantly associated with OAT, indicating that higher pain intensity scores could result from opioid-induced hyperalgesia due to prolonged exposure to opioids.<sup>12,16</sup> Among people with OUD, methadone doses are negatively correlated with pain intensity,<sup>16–18</sup> but the analgesic efficacy of OAT medicines is deemed to be limited.<sup>12,19</sup> This is why people on OAT are likely to need comprehensive treatment for their pain in a multidisciplinary team-based care.

Currently, limited research has compared pain experiences and characteristics of people receiving OAT for OUD management relative with those of people taking other prescription opioid analgesics. Thus, the present study directly compared demographic and clinical characteristics among 3 distinct patient groups in a sample of people with chronic pain from pain management services in Australia: (1) those on OAT (ie, buprenorphine or methadone), (2) those taking low-dose prescription opioids (<40 mg), and (3) those taking high-dose prescription opioids (>100 mg). The study also presents characteristics for those taking moderate-dose prescription opioids (40–100 mg) in tables. We hypothesized that (1) compared with people on low-dose opioids, people receiving OAT would have higher levels of socioeconomic disadvantage and more severe mental health symptoms and pain intensity and (2) people on OAT would have similar demographic and clinical characteristics to those of people on high-dose opioids.

## Methods

### Study design and setting

This is a cross-sectional study using Australian patient data from the electronic Persistent Pain Outcomes Collaboration (ePPOC), established by the Australian Health Services Research Institute at the University of Wollongong in 2013 for pain service outcome assessment and service benchmarking. The ePPOC database contains information on all patients attending pain management clinics across Australia and New Zealand, including demographics, psychological appraisals of pain, and pain characteristics. A full explanation of this database is published elsewhere.<sup>20</sup> Data were fully deidentified and were limited to adult patients referred between January 1, 2016, and December 31, 2021, in Australia. All data were stored and analyzed on the Monash University Secure Research Platform (SeRP), a secure environment that allows enhanced control over the processes for the analysis and sharing of sensitive research data. This study is reported according to the Strengthening the

Reporting of Observational Studies in Epidemiology (STROBE) statement<sup>21</sup> ([Supplementary Material: STROBE Statement checklist](#)). Ethics approval was obtained from the Monash University Human Research Ethics Committee (Project No. 30987). A protocol was designed and published on the Open Science Framework (OSF) (DOI: 10.17605/OSF.IO/MQTVE/). Notable variations in the updated version of the protocol included insertions of hypotheses and sample size justification. Given the cross-sectional design of this study, the sample selection bias is low because the dataset was derived from a national pain service baseline referral database (ePPOC), in which all cases from 59 Australian adult pain clinics participating in ePPOC by 2021 were included.<sup>22</sup> However, we acknowledge that there are likely to be biases in who is referred to a pain management service. For example, people without resources or transportation might not be able to attend the pain clinic.<sup>23</sup>

### Participants and selection

The dataset contains information for patients meeting the following inclusion criteria: (1) referred to a pain management service in Australia between 2016 and 2021 and completed the ePPOC referral questionnaire; (2) aged 18 years or more at referral; (3) diagnosed with chronic non-cancer pain (defined as having persistent pain for  $\geq 3$  months); (4) not receiving treatment for cancer pain; and (5) taking opioids, identified by OAT status (yes) and oral morphine equivalent daily dose (OMEDD) (>0 mg). All eligible participants were categorized into 4 groups: the OAT group (regardless of opioid dosage), the low-dose group (<40 mg), the moderate-dose group (40–100 mg), and the high-dose group (>100 mg) for those not on OAT, following the recommendations by the Australian and New Zealand College of Anaesthetists (ANZCA).<sup>24</sup>

### Variables and measurement

Self-reported data were collected via questionnaires sent to patients by email, telephone, post, or on-site interview. Collected data were then entered by clinical staff into the ePPOC database. The selection of variables of interest was based on previous research results, indicating that demographics, physical and mental comorbidities, pain experiences, and substance use history are highly associated with the co-occurrence of chronic pain and OUD.<sup>5</sup>

### Demographics

Patient age, sex, country of birth, employment status, and socioeconomic status were used to characterize individual-level demographics. Country of birth was classified into 2 categories: “Oceania and Antarctica” (a standard coding option according to the Standard Australian Classification of Countries [SACC] criteria,<sup>25</sup> which includes countries such as Australia and New Zealand) and “other countries.” Employment status was reported as working (including part-time and full-time work), not working, or retired. If employment status was missing and the patient was 65 years of age or more, the employment status was coded as retired, given that this is the age when people can access the pension in Australia.<sup>26</sup> The national deciles for the Index of Relative Socio-economic Advantage and Disadvantage (IRSAD)<sup>27</sup> were used to characterize socioeconomic status. The IRSAD was summarized into quintiles ranging from 1 to 5, with 1 representing the lowest disadvantage and 5 representing the highest disadvantage.

## Mental health and comorbidities

The short-form version of the Depression Anxiety Stress Scale (DASS-21) was used to characterize depression, anxiety, and stress symptoms. Previous research<sup>28</sup> has shown the validity of using DASS-21 to measure the 3 dimensions in a large nonclinical sample ( $n=1794$ ) by doubling DASS-21 scores. With the use of this established approach,<sup>29</sup> mental health symptoms were classified as mild (depression:  $\leq 13$ ; anxiety:  $\leq 9$ ; stress:  $\leq 18$ ), moderate (depression: 14–20; anxiety: 10–14; stress: 19–25), or severe and extremely severe (depression:  $\geq 21$ ; anxiety:  $\geq 15$ ; stress:  $\geq 26$ ). Cronbach's alpha for the total DASS-21 scale in this sample was 0.95. Comorbidities were calculated by the number of self-reported medical conditions and then reported as multimorbidity when 3 or more conditions were reported, following definitions established in a previous study.<sup>30</sup> Medical conditions included problems related to heart and circulation, blood pressure, cholesterol, respiratory, digestion, liver/kidney and pancreas, mental health, cancer, arthritis, muscle, neurology, thyroid, diabetes, and other unlisted diseases.

## Pain characteristics

The source, duration, severity, interference, and catastrophizing thoughts of pain were measured to characterize patients' pain experiences. Pain sources included (1) injury, (2) surgery, (3) medical condition other than cancer, (4) no obvious cause, and (5) other cause. Pain duration was classified as 3 to 12 months, 1 to 2 years, 2 to 5 years and  $>5$  years. A body map is used in the ePPOC questionnaire to identify which body regions are affected by pain. The Widespread Pain Index (WPI) was calculated to identify whether patients had widespread pain, defined as  $\geq 7$  pain sites according to the American College of Rheumatology (ACR) criteria.<sup>31</sup> Pain in up to 19 body areas was calculated, including head, face, neck, left/right shoulder, chest, left/right upper arm, left/right lower arm (in a combination of left/right elbow, forearm, wrist, and hand), upper and mid back, low back, abdomen, left/right hip, left/right thigh, and left/right lower leg (in a combination of left/right knee, calf, ankle, and foot).

The Brief Pain Inventory (BPI)<sup>32</sup> assessed the severity and interference of pain over the prior week and comprised 2 subscales measured on an 11-point numerical rating scale (scores ranging from 0 ["no pain / does not interfere"] to 10 ["pain as bad as you can imagine / completely interferes"]). The Pain Severity Scale measures pain intensity at its least, average, and worst and at present. The Pain Interference Scale assesses the degree to which pain interferes with 7 aspects of the individual's life and functioning, including general activity, mood, walking ability, normal work, relations with others, sleep, and enjoyment of life. Average scores for pain intensity and interference were calculated and then categorized into mild (0–4), moderate (5–6), and severe (7–10) levels.<sup>32</sup> Cronbach's alpha was 0.86 for pain severity and 0.88 for pain interference in this sample, indicating high levels of internal consistency.

Pain self-efficacy and catastrophizing thoughts were measured with the 10-item Pain Self-Efficacy Questionnaire (PSEQ) (range: 0 to 60)<sup>33</sup> and the 13-item Pain Catastrophizing Scale (PCS) (range: 0 to 52),<sup>34</sup> respectively. PSEQ measures patients' self-assurance in accomplishing everyday duties despite their pain, across 6 dimensions rated on a scale from 0 ("not at all confident") to 6 ("completely confident"). Impairments of pain self-efficacy were

categorized as low/mild ( $>30$ ), moderate (20–30), or severe ( $<20$ ).<sup>35</sup> The PCS was used to assess pain-related catastrophic thoughts and feelings rated on a scale from 0 ("not at all") to 4 ("all the time"). The total PCS rating scores were classified as clinically normal ( $<20$ ), high (20–30), or severe ( $>30$ ).<sup>36</sup> In this sample, Cronbach's alpha was 0.92 for PSEQ and 0.95 for the PCS.

## Opioid use history

Participants' opioid use history was documented from information reported by patients to clinical staff as part of their assessment, which included both prescription and over-the-counter opioids. Clinical staff then recorded the corresponding dosages for all self-reported opioid medications by converting them to OMEDD (in milligrams). In addition, clinical staff recorded patients' OAT status by indicating whether they were on an "opioid replacement/substitution program." The specific types of opioids and different OAT medications used by patients were not recorded in the database.

## Study size

Preliminary sample size checks were requested from the ePPOC data management personnel from 2015 to 2020 to ensure that the dataset was large enough to conduct multinomial logistic regression analysis. The complete dataset was then extracted (before application of exclusion criteria). It contained 1038 patients on OAT and 41 093 on opioids ( $n=7139$  were on high-dose opioids) but not on OAT. According to de Jong et al.,<sup>37</sup> this was likely to meet the threshold for the required number of events per variable for multinomial logistic regression, which is defined as the ratio of the number of observations in the smallest 2 outcome categories.

## Data analysis and approach

Data analyses were conducted in Stata Version 17.<sup>38</sup> Mean and standard deviation (SD) were reported for continuous data. Number, percentage, and relative risk ratio (RRR) or odds ratio (OR) with corresponding 95% confidence interval (CI) were presented for categorical variables. Multinomial logistic regression was conducted to identify the demographic, clinical, and pain-related characteristics associated with OAT and other opioid treatment group membership. In multinomial logistic regression, the risk of belonging to each group was compared with a reference group (the low-dose group, as it was the largest group and most representative of people attending pain specialist services). An additional bivariate logistic regression was conducted to test Hypothesis 2, comparing the characteristics of the OAT group with those of the high-dose group (reference group).

Covariates of interest included in the regression analyses were demographic and clinical characteristics, including age, sex, country of birth, employment status, socioeconomic status, multimorbidity, mental health symptoms (ie, depression, anxiety, and stress), Widespread Pain Index, pain source, pain duration, pain severity, pain interference, and pain self-efficacy.

Multinomial and bivariate logistic regression models with robust standard errors were used to calculate the unadjusted and adjusted RRR/OR of group membership with regard to the demographic, health, and pain-related characteristics. Given the missingness of each variable, descriptive analyses were conducted by creating 2 cohorts to compare their

demographic and clinical characteristics: one with complete data only ( $n = 31\,589$ , 74.9%) and the other with incomplete data (where an observation had a missing value in any of the selected variables) ( $n = 10\,593$ , 25.1%). The descriptive comparison found no significant differences between the two cohorts (Table S1), which allowed us to assume that the data appeared to be missing at random. Multiple imputation by chained equations (MICE), an unbiased method that is able to handle missing data for continuous, binary, and categorical variables,<sup>39</sup> was used to impute missing data and was repeated 20 times.

Multinomial logistic regression assumes the Independence of Irrelevant Alternatives (IIA), meaning that the removal of any category of the dependent variable should not affect the coefficients of the covariates and the remaining categories. Hausman diagnostic tests were performed to test for the IIA, and no violations of the assumption were found, as all  $P$  values were greater than 0.05. To assess multicollinearity, the variance inflation factor (VIF) was examined for each variable, and none had a VIF of 10 or higher (mean VIF = 1.93).

Sensitivity analyses were undertaken to examine whether the multinomial logistic regression results were robust. The adjusted RRR and corresponding 95% CI were qualitatively compared across multinomial regression analyses that used the missing (with missing values categorised), complete, and imputed datasets.

## Results

### Participants' characteristics

A total of 42 182 unique participants met the eligibility criteria (Figure 1). The mean age was 51.7 years (SD = 14.9, range: 18–102). Most participants were female ( $n = 23\,937$ , 56.8%), unemployed ( $n = 30\,640$ , 72.6%), and born in the “Oceania and Antarctica” ( $n = 32\,154$ , 76.2%) region. Most participants were on low-dose opioids ( $n = 20\,517$ , 48.6%), followed by moderate-dose ( $n = 13\,527$ , 32.1%) and high-dose opioids ( $n = 7122$ , 16.9%), with 2.4% ( $n = 1016$ ) taking OAT medicines.

The most common source of pain was reported as “after injury” ( $n = 20\,546$ , 48.7%), followed by “no obvious cause”

( $n = 6363$ , 15.1%), “medical conditions” ( $n = 6109$ , 14.5%), and “after surgery” ( $n = 3433$ , 8.1%) (missing  $n = 1035$ , 2.5%). More than half of the sample reported they had severe pain ( $n = 21\,774$ , 51.6%) and pain interference ( $n = 29\,452$ , 69.8%) and had had pain for more than 5 years ( $n = 21\,522$ , 51.0%). Approximately half of the sample reported having severely impaired self-efficacy ( $n = 23\,839$ , 56.5%), severe pain catastrophizing thoughts ( $n = 20\,796$ , 49.3%), and multimorbidity ( $n = 20\,259$ , 48.0%), with the most common comorbid conditions being mental health problems ( $n = 21\,029$ , 49.9%), arthritis ( $n = 17\,512$ , 41.5%), heart/circulation problems ( $n = 12\,085$ , 28.7%), and respiratory problems ( $n = 9584$ , 22.7%).

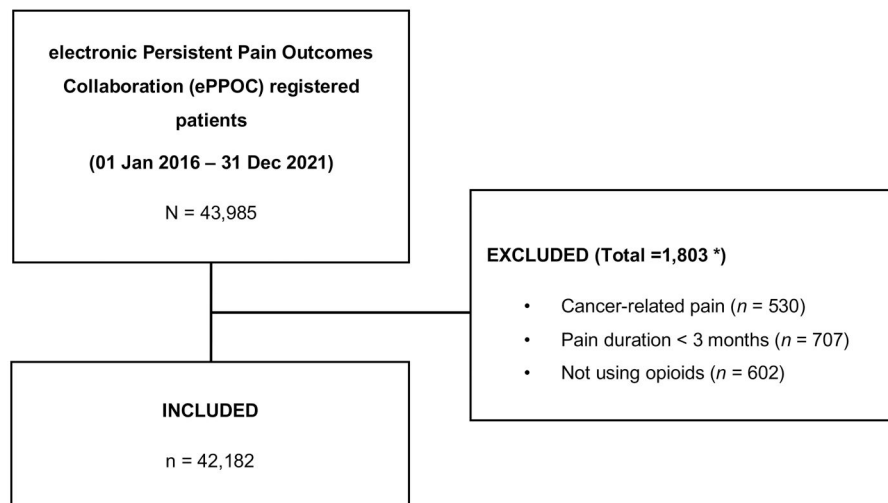
Among those patients on OAT with chronic pain, most were female, with a mean age of 49.9 years (SD = 13.6, range: 18–88). More than half reported that they were unemployed, had multimorbidity, had moderate to extremely severe mental health conditions, had had chronic pain for more than 5 years, and had severe pain intensity and interference (Table 1).

### Hypothesis 1: OAT versus low dose

After adjustment for all covariates in the multinomial logistic regression, compared with the low-dose opioid group, patients on OAT were found to have a higher likelihood of being male and having been born in the “Oceania and Antarctica” region. Patients on OAT also had an increased risk of being unemployed, having multimorbidity, having more severe depression and anxiety, and having a pain duration of more than 5 years, but they had a decreased risk of being more than 65 years of age (relative to being between 18 and 34 years of age). No significant differences in pain severity and interference were found between the 2 groups (Table 2).

### Hypothesis 2: OAT versus high dose

In the multinomial logistic regression, people in the OAT and high-dose groups had relatively similar demographic and clinical characteristics compared with the low-dose group, including low employment, poorer mental health, and longer pain duration (Table 2).



**Figure 1.** Flow chart of participants' eligibility and inclusion. <sup>a</sup>  $n = 36$  patients met multiple exclusion criteria.

**Table 1.** Demographic and clinical characteristics of patients using OAT or opioids ( $n = 42\ 182$ ).

Patient characteristics		OAT $n$ (%)	Low dose $n$ (%)	Moderate dose $n$ (%)	High dose $n$ (%)
$n$		1016 (2.4)	20 517 (48.6)	13 527 (32.1)	7122 (16.9)
Female <sup>a</sup>	No	490 (48.2)	8005 (39.0)	6103 (45.1)	3572 (50.2)
	Yes	526 (51.8)	12 480 (60.8)	7394 (54.7)	3537 (49.7)
	Missing	0 (0.0%)	32 (0.2%)	30 (0.2%)	13 (0.2)
Born in Oceania and Antarctica	No	178 (17.5)	4924 (24.0)	2742 (20.3)	1188 (16.7)
	Yes	811 (79.8)	15 098 (73.6)	10 490 (77.5)	5755 (80.8)
	Missing	27 (2.7)	495 (2.4)	295 (2.2)	179 (2.5)
Employment	Not working	771 (75.9)	14 252 (69.5)	10 016 (74.0)	5601 (78.6)
	Working	178 (17.5)	5019 (24.5)	2568 (19.0)	976 (13.7)
	Retired	13 (1.3)	449 (2.2)	322 (2.4)	170 (2.4)
	Missing	54 (5.3)	797 (3.9)	621 (4.6)	375 (5.3)
Age, years	Mean (SD)	49.9 (13.6)	51.5 (15.3)	52.0 (15.0)	52.0 (13.8)
	18–34	145 (14.3)	3070 (15.0)	1850 (13.7)	804 (11.3)
	35–64	728 (71.7)	13 450 (65.6)	8817 (65.2)	4988 (70.0)
	≥65	143 (14.1)	3997 (19.5)	2860 (21.1)	1330 (18.7)
IRSAD quintiles	5, least disadvantaged	235 (24.3)	4102 (20.0)	2369 (17.5)	1317 (18.5)
	4	169 (16.6)	3520 (17.2)	2214 (16.4)	1131 (15.9)
	3	200 (19.7)	4245 (20.7)	2914 (21.5)	1559 (21.9)
	2	167 (16.4)	3708 (18.1)	2608 (19.3)	1391 (19.5)
	1, most disadvantaged	197 (19.4)	3693 (18.0)	2766 (20.4)	1431 (20.1)
	Missing	48 (4.7)	1249 (6.1)	656 (4.8)	293 (4.1)
Multimorbidity	No	438 (43.1)	10 153 (49.5)	6343 (46.9)	3223 (45.3)
	Yes	562 (55.3)	9464 (46.1)	6673 (49.3)	3560 (50.0)
	Missing	16 (1.6)	900 (4.4)	511 (3.8)	339 (4.8)
DASS—depression	Mild	239 (23.5)	6663 (32.5)	3912 (28.9)	1919 (26.9)
	Mod-extremely severe	741 (72.9)	13 264 (64.6)	9176 (67.8)	4946 (69.4)
	Missing	36 (3.5)	590 (2.9)	439 (3.2)	257 (3.6)
DASS—anxiety	Mild	292 (28.7)	7845 (38.2)	4729 (35.0)	2397 (33.7)
	Mod-extremely severe	687 (67.6)	12 021 (58.6)	8314 (61.5)	4438 (62.3)
	Missing	37 (3.6)	651 (3.2)	484 (3.6)	287 (4.0)
DASS—stress	Mild	379 (37.3)	8777 (42.8)	5589 (41.3)	2935 (41.2)
	Mod-extremely severe	603 (59.4)	11 069 (54.0)	7443 (55.0)	3887 (54.6)
	Missing	34 (3.3)	671 (3.3)	495 (3.7)	300 (4.2)
Widespread Pain Index	No	617 (60.7)	12 645 (61.6)	8186 (60.5)	4175 (58.6)
	Yes	399 (39.3)	7872 (38.4)	5341 (39.5)	2947 (41.4)
Pain source	After injury	505 (49.7)	10 017 (48.8)	6587 (48.7)	3437 (48.3)
	After surgery	78 (7.7)	1569 (7.6)	1167 (8.6)	619 (8.7)
	Medical condition	159 (15.6)	2881 (14.0)	1948 (14.4)	1121 (15.7)
	No obvious cause	123 (12.1)	3361 (16.4)	1968 (14.5)	911 (12.8)
	Other	131 (12.9)	2232 (10.9)	1510 (11.2)	823 (11.6)
	Missing	20 (2.0)	457 (2.2)	347 (2.6)	211 (3.0)
	3–12 months	86 (8.5)	2552 (12.4)	1396 (10.3)	538 (7.6)
Pain duration	1–2 year(s)	117 (11.5)	3127 (15.2)	1732 (12.8)	639 (9.0)
	2–5 years	202 (19.9)	4832 (23.6)	2920 (21.6)	1345 (18.9)
	>5 years	574 (56.5)	9486 (46.2)	7111 (52.6)	4351 (61.1)
	Missing	37 (3.6)	520 (2.5)	368 (2.7)	249 (3.5)
	Mild	120 (11.8)	2199 (10.7)	1186 (8.8)	539 (7.6)
Pain severity	Moderate	353 (34.7)	7603 (37.1)	4634 (34.3)	2314 (32.5)
	Severe	512 (50.4)	10 049 (49.0)	7214 (53.3)	3999 (56.1)
	Missing	31 (3.1)	666 (3.2)	493 (3.6)	270 (3.8)
	Mild	87 (8.6)	1962 (9.6)	1067 (7.9)	499 (7.0)
Pain interference	Moderate	205 (20.2)	4462 (21.7)	2663 (19.7)	1237 (17.4)
	Severe	710 (69.9)	13 865 (67.6)	9601 (71.0)	5276 (74.1)
	Missing	14 (1.4)	228 (1.1)	196 (1.4)	110 (1.5)
	Low/mild impairment	145 (14.3)	3706 (18.1)	1907 (14.1)	914 (12.8)
Pain self-efficacy	Moderate impairment	262 (25.8)	5484 (26.7)	3354 (24.8)	1549 (21.7)
	Severe impairment	582 (57.3)	10 881 (53.0)	7926 (58.6)	4450 (62.5)
	Missing	27 (2.7)	446 (2.2)	340 (2.5)	209 (2.9)
	Clinically normal	196 (19.3)	5075 (24.7)	3101 (22.9)	1637 (23.0)
Pain catastrophizing	Clinically high	222 (21.9)	4797 (23.4)	3035 (22.4)	1564 (22.0)
	Clinically severe	551 (54.2)	9879 (48.2)	6813 (50.4)	3553 (49.9)
	Missing	47 (4.6)	766 (3.7)	578 (4.3)	368 (5.2)

**Abbreviations:** DASS= Depression Anxiety Stress Scale; IRSAD= Index of Relative Socio-Economic Advantage and Disadvantage; mod-extremely severe= moderately severe to extremely severe; SD= standard deviation.

Low dose= patients on low-dose opioids (<40 mg/day); moderate dose= patients on moderate-dose opioids (40–100 mg/day); high dose= patients on high-dose opioids (>100 mg/day).

<sup>a</sup>  $n = 4$  patients reported to be intersex and were coded as not female.

**Table 2.** Adjusted and unadjusted relative risk ratio for multinomial logistic regression on opioid use groups (*n* = 42 182).

Patient characteristics	OAT vs low dose (ref) RRR (95% CI)		Moderate vs low dose (ref) RRR (95% CI)		High vs low dose (ref) RRR (95% CI)	
	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted
Female						
	(reference)					
Yes	1.45 (1.27, 1.65)	1.45 (1.28, 1.65)	1.31 (1.25, 1.37)	1.29 (1.23, 1.34)	1.64 (1.54, 1.73)	1.57 (1.49, 1.66)
No	(reference)					
Born in Oceania and Antarctica						
Yes	1.45 (1.22, 1.72)	1.48 (1.25, 1.75)	1.27 (1.20, 1.34)	1.24 (1.18, 1.31)	1.57 (1.46, 1.69)	1.56 (1.45, 1.67)
Working	(reference)					
Not working	1.40 (1.17, 1.67)	1.51 (1.28, 1.79)	1.19 (1.12, 1.26)	1.37 (1.30, 1.44)	1.63 (1.50, 1.77)	1.97 (1.82, 2.12)
Retired	1.07 (0.58, 1.96)	0.80 (0.45, 1.42)	1.16 (0.98, 1.37)	1.39 (1.19, 1.61)	1.85 (1.49, 2.26)	1.87 (1.55, 2.26)
Age, years						
18–34	(reference)					
35–64	1.00 (0.83, 1.21)	1.15 (1.10, 1.19)	1.00 (0.94, 1.07)	1.09 (1.07, 1.10)	1.18 (1.08, 1.29)	1.42 (1.39, 1.44)
≥65	0.64 (0.49, 0.83)	0.76 (0.72, 0.80)	1.14 (1.04, 1.24)	1.19 (1.17, 1.21)	1.05 (0.94, 1.18)	1.27 (1.24, 1.30)
IRSAD quintiles						
5, least disadvantage	(reference)					
4	0.82 (0.67, 1.00)	0.85 (0.70, 1.04)	1.08 (1.00, 1.16)	1.09 (1.01, 1.17)	0.98 (0.90, 1.08)	1.00 (0.92, 1.10)
3	0.77 (0.63, 0.94)	0.84 (0.69, 1.02)	1.15 (1.07, 1.23)	1.18 (1.10, 1.27)	1.06 (0.97, 1.15)	1.14 (1.05, 1.24)
2	0.70 (0.57, 0.86)	0.81 (0.66, 0.99)	1.14 (1.06, 1.23)	1.21 (1.13, 1.30)	1.02 (0.93, 1.11)	1.17 (1.07, 1.28)
1, most disadvantage	0.81 (0.67, 0.99)	0.95 (0.78, 1.15)	1.20 (1.12, 1.30)	1.29 (1.20, 1.38)	1.03 (0.95, 1.13)	1.21 (1.11, 1.32)
Multimorbidity						
No	(reference)					
Yes	1.31 (1.14, 1.51)	1.39 (1.22, 1.58)	1.01 (0.97, 1.06)	1.12 (1.07, 1.17)	0.97 (0.92, 1.03)	1.19 (1.12, 1.25)
DASS—depression						
Mild	(reference)					
Mod—extremely severe	1.26 (1.03, 1.53)	1.53 (1.32, 1.77)	1.08 (1.01, 1.16)	1.17 (1.12, 1.23)	1.16 (1.07, 1.26)	1.29 (1.22, 1.37)
DASS—anxiety						
Mild	(reference)					
Mod—extremely severe	1.32 (1.11, 1.57)	1.51 (1.31, 1.73)	1.08 (1.02, 1.14)	1.14 (1.09, 1.20)	1.11 (1.03, 1.20)	1.21 (1.14, 1.28)
DASS—stress						
Mild	(reference)					
Mod—extremely severe	0.88 (0.74, 1.04)	1.25 (1.10, 1.43)	0.90 (0.85, 0.96)	1.05 (1.01, 1.10)	0.82 (0.76, 0.88)	1.05 (0.99, 1.11)
Widespread Pain Index						
No	(reference)					
Yes	0.89 (0.77, 1.02)	1.04 (1.01, 1.07)	0.99 (0.94, 1.03)	1.05 (1.04, 1.06)	0.98 (0.92, 1.04)	1.13 (1.12, 1.15)

(continued)

**Table 2.** (continued)

Patient characteristics	OAT vs low dose (ref) RRR (95% CI)		Moderate vs low dose (ref) RRR (95% CI)		High vs low dose (ref) RRR (95% CI)	
	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted
Pain source						
After surgery	(reference)	0.98 (0.76, 1.25)	1.19 (1.09, 1.28)	1.12 (1.03, 1.22)	1.30 (1.17, 1.44)	1.14 (1.03, 1.26)
After surgery	1.07 (0.84, 1.38)					
Medical condition	1.12 (0.92, 1.35)	1.09 (0.91, 1.31)	1.06 (0.99, 1.13)	1.02 (0.96, 1.09)	1.21 (1.11, 1.32)	1.13 (1.04, 1.22)
No obvious cause	0.84 (0.68, 1.03)	0.73 (0.59, 0.89)	0.96 (0.90, 1.03)	0.89 (0.84, 0.95)	0.94 (0.87, 1.03)	0.79 (0.73, 0.86)
Other	1.21 (0.99, 1.48)	1.15 (0.95, 1.40)	1.04 (0.97, 1.12)	1.03 (0.95, 1.10)	1.11 (1.01, 1.22)	1.07 (0.98, 1.17)
Pain duration	(reference)					
3–12 months	1.07 (0.80, 1.42)	1.11 (0.84, 1.48)	0.99 (0.91, 1.08)	1.01 (0.93, 1.10)	0.94 (0.83, 1.07)	0.98 (0.86, 1.11)
1–2 year(s)	1.14 (0.88, 1.48)	1.23 (0.95, 1.59)	1.07 (0.98, 1.16)	1.10 (1.02, 1.19)	1.22 (1.09, 1.37)	1.31 (1.17, 1.46)
2–5 years	1.61 (1.27, 2.05)	1.75 (1.39, 2.21)	1.30 (1.21, 1.40)	1.35 (1.26, 1.46)	1.96 (1.76, 2.17)	2.12 (1.92, 2.34)
>5 years	(reference)					
BPI—pain severity						
Mild	0.81 (0.64, 1.02)	0.86 (0.69, 1.06)	1.08 (1.00, 1.18)	1.13 (1.04, 1.22)	1.17 (1.04, 1.30)	1.24 (1.11, 1.37)
Moderate	0.85 (0.67, 1.07)	0.94 (0.77, 1.16)	1.23 (1.12, 1.34)	1.32 (1.23, 1.43)	1.43 (1.28, 1.61)	1.60 (1.45, 1.77)
Severe	(reference)					
Mild	0.93 (0.71, 1.22)	1.04 (0.80, 1.34)	1.00 (0.91, 1.10)	1.10 (1.01, 1.20)	0.95 (0.84, 1.07)	1.09 (0.97, 1.22)
Moderate	0.87 (0.66, 1.14)	1.16 (0.92, 1.45)	1.01 (0.92, 1.11)	1.27 (1.18, 1.38)	1.05 (0.93, 1.19)	1.49 (1.35, 1.66)
Severe	(reference)					
Pain self-efficacy						
Low/mild impairment	1.07 (0.86, 1.33)	1.21 (0.98, 1.49)	1.16 (1.08, 1.25)	1.18 (1.10, 1.27)	1.08 (0.98, 1.19)	1.14 (1.04, 1.25)
Moderate impairment	1.08 (0.87, 1.34)	1.35 (1.13, 1.63)	1.34 (1.25, 1.44)	1.41 (1.32, 1.50)	1.46 (1.33, 1.61)	1.64 (1.51, 1.78)
Severe impairment	(reference)					
Clinically normal	1.07 (0.87, 1.32)	1.18 (0.97, 1.44)	0.95 (0.89, 1.02)	1.03 (0.97, 1.10)	0.89 (0.82, 0.97)	1.02 (0.94, 1.10)
Clinically high	1.19 (0.96, 1.48)	1.41 (1.20, 1.67)	0.94 (0.87, 1.00)	1.12 (1.06, 1.18)	0.84 (0.77, 0.92)	1.12 (1.05, 1.20)
Clinically severe						

Abbreviations: CI= confidence interval; DASS= Depression Anxiety Stress Scale; IRSAD= Index of Relative Socio-Economic Advantage and Disadvantage; mod-extremely severe= moderately severe to extremely severe; OAT= patients on opioid agonist treatment (n = 1061); RRR= relative risk ratio. Low dose= patients on low-dose opioids (<40 mg/day) (n = 20 517); moderate dose= patients on moderate-dose opioids (40–100 mg/day) (n = 13 527); high dose= patients on high-dose opioids (>100 mg/day) (n = 7122); ref= low-dose group is the reference group in the multinomial logistic regression analysis.

After adjustment for all covariates in the bivariate logistic regression, the OAT group had 40% reduced odds of being 65 years of age or more, 20–30% lower odds of living in disadvantaged areas, 29–39% lower odds of reporting more severe pain, and 26% lower odds of having severely impaired pain self-efficacy, compared with patients on high-dose opioids. Conversely, people on OAT had 33% increased odds of having multimorbidity, 20% increased odds of having moderate to extremely severe anxiety, and 44% increased odds of having severe pain catastrophizing thoughts, compared with the high-dose opioid group. No significant differences were observed for gender, employment status, pain sources, pain duration, or pain interference between the 2 groups (Table 3).

## Sensitivity analyses

Compared with the dataset with missing values (ie, a dataset with missing values categorized) ( $n = 42\,182$ ) and the complete dataset ( $n = 31\,589$ ), the adjusted RRR of the imputed dataset ( $n = 42\,182$ ) showed that most of the results were consistent in direction and significance. Very minor differences were observed in the magnitude of coefficients and corresponding 95% CIs for the variable of pain source (Table S2).

## Discussion

This research examined differences in demographic and clinical characteristics among patients on OAT and those taking

**Table 3.** Adjusted and unadjusted odds ratio for bivariate logistic regression on OAT and high-dose group ( $n = 8138$ ).

Patient characteristics		OAT ( $n = 1016$ ) vs high dose ( $n = 7122$ ) (ref)	
		OR (95% CI)	
		Adjusted	Unadjusted
Female	Yes	(reference)	
	No	0.88 (0.76, 1.01)	0.92 (0.81, 1.05)
Born in Oceania and Antarctica	No	(reference)	
	Yes	0.91 (0.76, 1.09)	0.95 (0.80, 1.13)
Employment	Working	(reference)	
	Not working	0.85 (0.70, 1.03)	0.77 (0.64, 0.92)
	Retired	0.57 (0.30, 1.07)	0.43 (0.24, 0.77)
Age, years	18–34	(reference)	
	35–64	0.84 (0.68, 1.04)	0.81 (0.78, 0.84)
	≥65	0.60 (0.46, 0.80)	0.60 (0.56, 0.63)
IRSAD quintiles	5, least disadvantage	(reference)	
	4	0.84 (0.68, 1.04)	0.85 (0.69, 1.05)
	3	0.73 (0.59, 0.90)	0.74 (0.60, 0.90)
	2	0.70 (0.57, 0.87)	0.69 (0.56, 0.85)
Multimorbidity	1, most disadvantage	0.80 (0.65, 0.98)	0.78 (0.64, 0.96)
	No	(reference)	
DASS—depression	Yes	1.33 (1.15, 1.54)	1.17 (1.02, 1.34)
	Mild	(reference)	
DASS—anxiety	Mod-extremely severe	1.07 (0.87, 1.33)	1.18 (1.02, 1.38)
	Mild	(reference)	
DASS—stress	Mod-extremely severe	1.20 (1.00, 1.45)	1.25 (1.08, 1.44)
	Mild	(reference)	
Widespread Pain Index	Mod-extremely severe	1.06 (0.88, 1.27)	1.19 (1.04, 1.37)
	No	(reference)	
Pain source	Yes	0.91 (0.78, 1.05)	0.92 (0.89, 0.94)
	After injury	(reference)	
	After surgery	0.81 (0.63, 1.05)	0.86 (0.67, 1.10)
	Medical condition	0.92 (0.75, 1.12)	0.96 (0.80, 1.17)
	No obvious cause	0.90 (0.72, 1.11)	0.92 (0.74, 1.13)
	Other	1.08 (0.87, 1.34)	1.08 (0.88, 1.33)
Pain duration	3–12 months	(reference)	
	1–2 year(s)	1.18 (0.87, 1.61)	1.13 (0.84, 1.54)
	2–5 years	0.98 (0.74, 1.30)	0.94 (0.72, 1.23)
	>5 years	0.87 (0.67, 1.13)	0.83 (0.65, 1.05)
BPI—pain severity	Mild	(reference)	
	Moderate	0.71 (0.56, 0.91)	0.70 (0.55, 0.87)
	Severe	0.61 (0.47, 0.78)	0.59 (0.47, 0.73)
BPI—pain interference	Mild	(reference)	
	Moderate	1.00 (0.75, 1.33)	0.95 (0.73, 1.25)
	Severe	0.83 (0.62, 1.12)	0.77 (0.61, 0.98)
Pain self-efficacy	Low/mild impairment	(reference)	
	Moderate impairment	1.01 (0.80, 1.27)	1.06 (0.85, 1.32)
	Severe impairment	0.74 (0.59, 0.93)	0.82 (0.68, 1.00)
Pain catastrophizing	Clinically normal	(reference)	
	Clinically high	1.19 (0.95, 1.48)	1.16 (0.95, 1.42)
	Clinically severe	1.43 (1.14, 1.79)	1.26 (1.06, 1.50)

**Abbreviations:** CI= confidence interval; OAT= patients on opioid agonist treatment; OR= odds ratio.

High dose= patients on high-dose opioids (>100 mg/day); ref= high-dose group is the reference group in the post-hoc bivariate logistic regression analysis.

low and high doses of other prescription opioid analgesics (not methadone or buprenorphine), using a large national pain service database in Australia.

As hypothesized, individuals on OAT had more severe mental health symptoms and pain intensity, but there were no differences in socioeconomic status when compared with people on low-dose opioids. Notably, people on OAT and those on high-dose opioids had relatively similar demographic and clinical characteristics relative to people on low-dose opioids. Given that OUD and experiencing opioid-associated harms are relatively common among people prescribed high-dose opioids,<sup>8,40,41</sup> it is not surprising that there were multiple demographic and clinical similarities to those receiving OAT. These findings are consistent with studies examining people on OAT, indicating the multifactorial complexity of pain management among people receiving OAT, particularly with regard to mental health problems.<sup>9,17,42,43</sup> Although mental health symptoms were prevalent among all patients, a higher risk of having moderate to extremely severe anxiety was observed in the OAT group than in the low- and high-dose groups taking prescription opioid analgesics. A study conducted among US veterans found that people with both OUD and chronic pain had more comorbidities, mental health issues, and psychotropic and opioid medicine prescriptions than did those with either OUD or chronic pain alone.<sup>44</sup> A systematic review also found that the prevalence of chronic pain among OAT participants increased with older age, unemployment, and higher methadone doses.<sup>5</sup> These findings highlight the complex clinical presentations and social situations of people with concurrent chronic pain and OUD and the need for integrated models of care.

Notably, people on OAT were found to report less severe pain compared with those using high-dose opioids. This might be partially explained by the fact that OAT medicines are relatively more potent analgesics than are some conventional opioids.<sup>45</sup> This result is consistent with findings that OAT medicines can be beneficial for managing both chronic pain and OUD.<sup>46</sup> An alternative explanation for the difference in pain intensity between people on OAT and high-dose opioids could be that the primary reason for patients receiving OAT might not have been solely a pain condition. Although it is likely that pain was a relevant part of their presentation, given their referral to a specialist pain clinic, other factors such as the complexity of their overall health status or co-occurring conditions might also have influenced their treatment and pain experiences. Nevertheless, the findings of lower pain intensity reported in people receiving OAT are of note, particularly given that hyperalgesia and increased pain sensitivity are commonly reported in this group because of long-term opioid exposures.<sup>47</sup> As such, further research is needed to examine the analgesic efficacy of OAT medicines in individuals with both pain and OUD.

Overall, half of the sample in OAT reported having multimorbidity, severe pain, long pain duration, and moderate to severe mental health conditions, reflecting the complexity of clinical presentations that are likely to require more comprehensive models of care and multidisciplinary pain management. People with both OUD and chronic pain often have their pain undertreated because of stigma and existing OUD.<sup>48</sup> Combined nonpharmacological approaches (eg, social, behavioral, or psychiatric support) are regarded as more effective than providing medicines alone to manage pain.<sup>49</sup> Our findings highlighted patient characteristics that

could inform clinical care delivery, alongside identifying possible barriers to taking up treatment, such as mental health conditions and multimorbidity.<sup>50</sup> Therefore, concurrent treatment for mental health and multimorbidity is warranted for people with OUD, on OAT, or both.

### Strengths and limitations

This is one of the first Australian studies to compare demographic and clinical characteristics of people on different opioid doses with those of people receiving OAT, among the population seeking specialist chronic pain treatment. Strengths of the ePPOC data include the use of well-validated measures in a structured assessment. Some limitations of the study should, however, be acknowledged. First, as with many studies, generalizability is a consideration. It is standard practice that patients who are referred to the pain clinic services are required to complete the questionnaires, which are then uploaded into ePPOC for inclusion in national benchmarking and outcomes evaluation, so responses are unlikely to have selection bias. This study was conducted with data from only the Australian pain services for adult patients, which might have unique characteristics that influence pain-related outcomes, potentially limiting the applicability of these findings to other regions or health care systems. Therefore, the findings might not represent people who are prescribed opioids or on OAT but who are not seen in pain services. Second, OUD diagnoses are not recorded in this dataset, which prevents us from further exploring the role of OUD in pain management settings. For people prescribed OAT medicines, we can be confident that they meet the criteria for OUD, as this is a prerequisite for receiving OAT in Australian clinical settings. However, it is likely that some patients taking other prescription opioid analgesics not in OAT could also meet the criteria for OUD, and this was not able to be examined within this dataset. In addition, there could be diverse patient experiences, with some patients having experienced chronic pain and subsequently having developed an OUD, whereas others might have developed an OUD first and experienced chronic pain later, which we were not able to examine in this study. Third, the specific opioids and OAT medications a person was using were not recorded in the database, preventing us from comparing demographic and clinical characteristics associated with specific types of opioid medicines. Finally, the ePPOC database collected only one datapoint related to race, which is “whether a person identifies as being of Aboriginal and/or Torres Strait Islander origin,” with no other information on race currently collected. According to the ePPOC Annual Data Report 2021,<sup>22</sup> only 5.9% patients identified as being of Aboriginal and/or Torres Strait Islander origin, which precluded our ability to consider race-related characteristics potentially associated with OAT use.

### Conclusion

We examined the demographic and clinical characteristics of people with chronic pain on OAT with those of people taking other prescription opioid analgesics (not methadone or buprenorphine) in Australian pain management services. People on OAT and high-dose opioids had similar features across most demographics and clinical characteristics (ie, more severe mental health symptoms and longer pain duration) compared with people on low-dose opioids. Although people on OAT and high-dose opioids were similar across

many characteristics, people on OAT reported less severe pain but more severe anxiety. These findings highlight the complexity of clinical presentations of people seeking pain management, especially for patients on OAT and those prescribed higher-dose opioids.

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## Supplementary material

Supplementary material is available at *Pain Medicine* online.

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*Conflicts of interest:* No conflicts of interest to declare.

## Data availability

The data that support the findings of this study can be requested from the electronic Persistent Pain Outcomes Collaboration.

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