

Examining the association between pain and opioid agonist treatment status

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Disclosure of Interest

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Study Overview

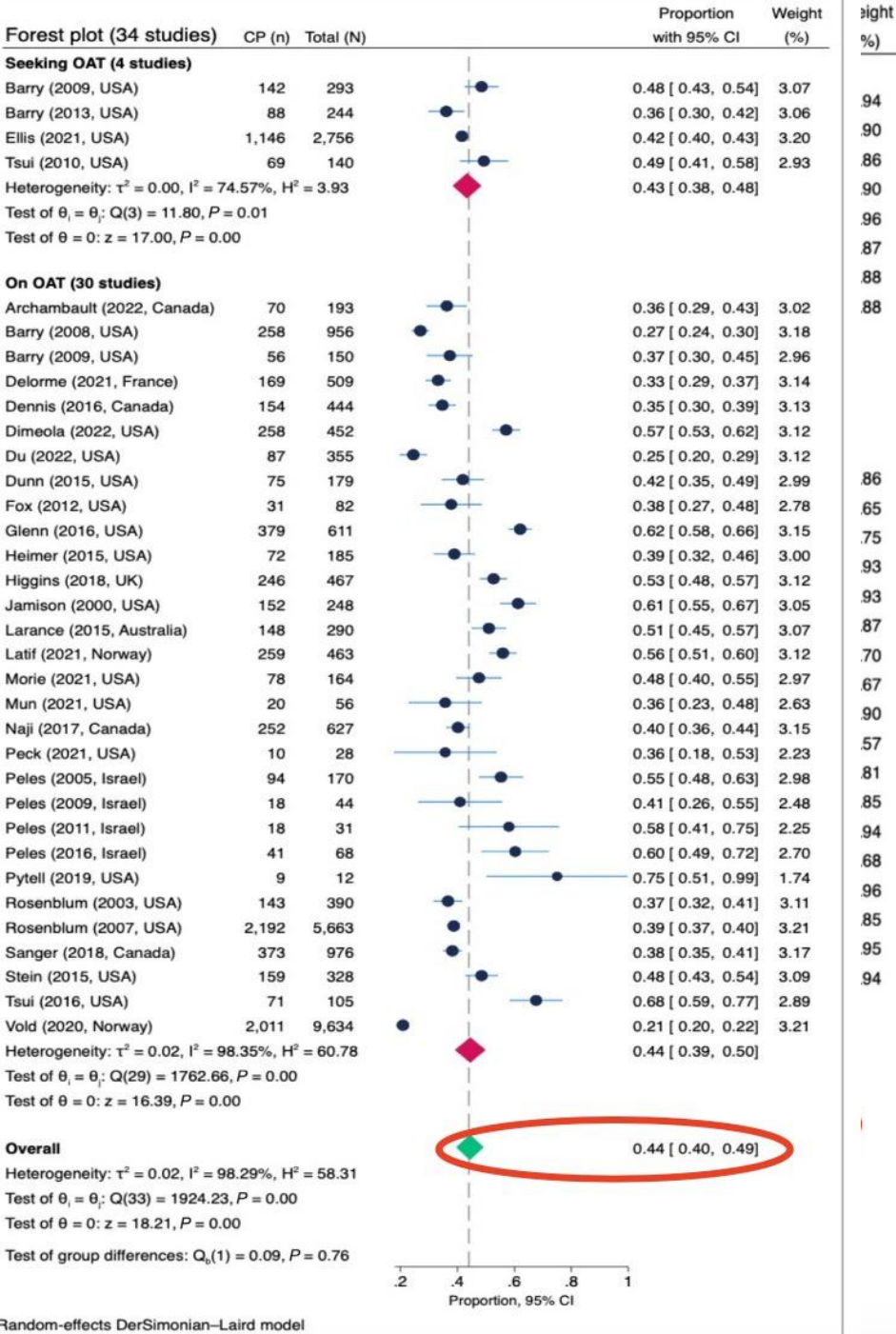
Study background:

- Pain is highly prevalent among people seeking/receiving OAT
- Pain is often undertreated as a comorbid condition among people seeking/receiving OAT
- Pain relief efficacies of OAT medicines remain unclear

1.6.2 Mean dose of methadone (mg/day)

Delorme (2021, France)	66.1	38.3	108	62.5	41.6	235	6.4%	3.60 [-5.37, 12.57]
Dennis (2014, Canada)	84.6	51.5	58	85.7	50.1	177	2.9%	-1.10 [-16.27, 14.07]
Dimeola (2022, USA)	80.5	31.7	258	74.1	31.7	194	10.3%	6.40 [0.50, 12.30]
Jamison (2000, USA)	82.3	34.5	152	65.7	28.3	96	7.6%	16.60 [8.72, 24.48]
Latif (2021, Norway)	98.5	35.8	161	89.6	26.9	84	7.4%	8.90 [0.92, 16.88]
Peles (2005, Israel)	164.2	59.6	94	147.1	52.8	76	2.4%	17.10 [0.19, 34.01]
Peles (2009, Israel)	160.3	74.4	18	139.9	65.9	25	0.4%	20.40 [-22.60, 63.40]
Subtotal (95% CI)			849			887	37.3%	8.74 [4.19, 13.29]

Heterogeneity: $\tau^2 = 10.46$; $\chi^2 = 8.52$, $df = 6$ ($P = 0.20$); $I^2 = 30\%$
Test for overall effect: $Z = 3.76$ ($P = 0.0002$)



Reference:
Yang, J., Jung, M., Picco, L., Grist, E., Lloyd-Jones, M., Giummarra, M., & Nielsen, S. (2024). Pain in people seeking and receiving opioid agonist treatment: A systematic review and meta-analysis of prevalence and correlates. *Addiction*.

Study Overview

Study aim:

- To explore the correlates of pain and how pain severity changes in people with OUD as they move in and out of opioid agonist treatment (OAT)

Study questions:

- What are the correlates of pain?
- Does pain severity change with current OAT status?
- Does pain severity vary with using different OAT medicines (i.e. buprenorphine vs methadone)?

Longitudinal cohort:

- Melbourne Injecting Drug User Cohort Study (SuperMIX) cohort data



Research Design

Participant eligibility:

- Ever been in OAT for at least one time point (2008-2024)

Analysis methods:

- Baseline dataset: Ordinal logistic regression
- Longitudinal dataset: Multilevel ordinal logistic regression

Outcome variable:

- Current pain was measured by a 6-point Likert Scale (none to very severe pain in the past 4 weeks)

Covariates of interest:

- Demographics
 - Gender, age
 - Country of birth, employment (yes/no)
 - Homelessness (yes/no)



Covariates of interest:

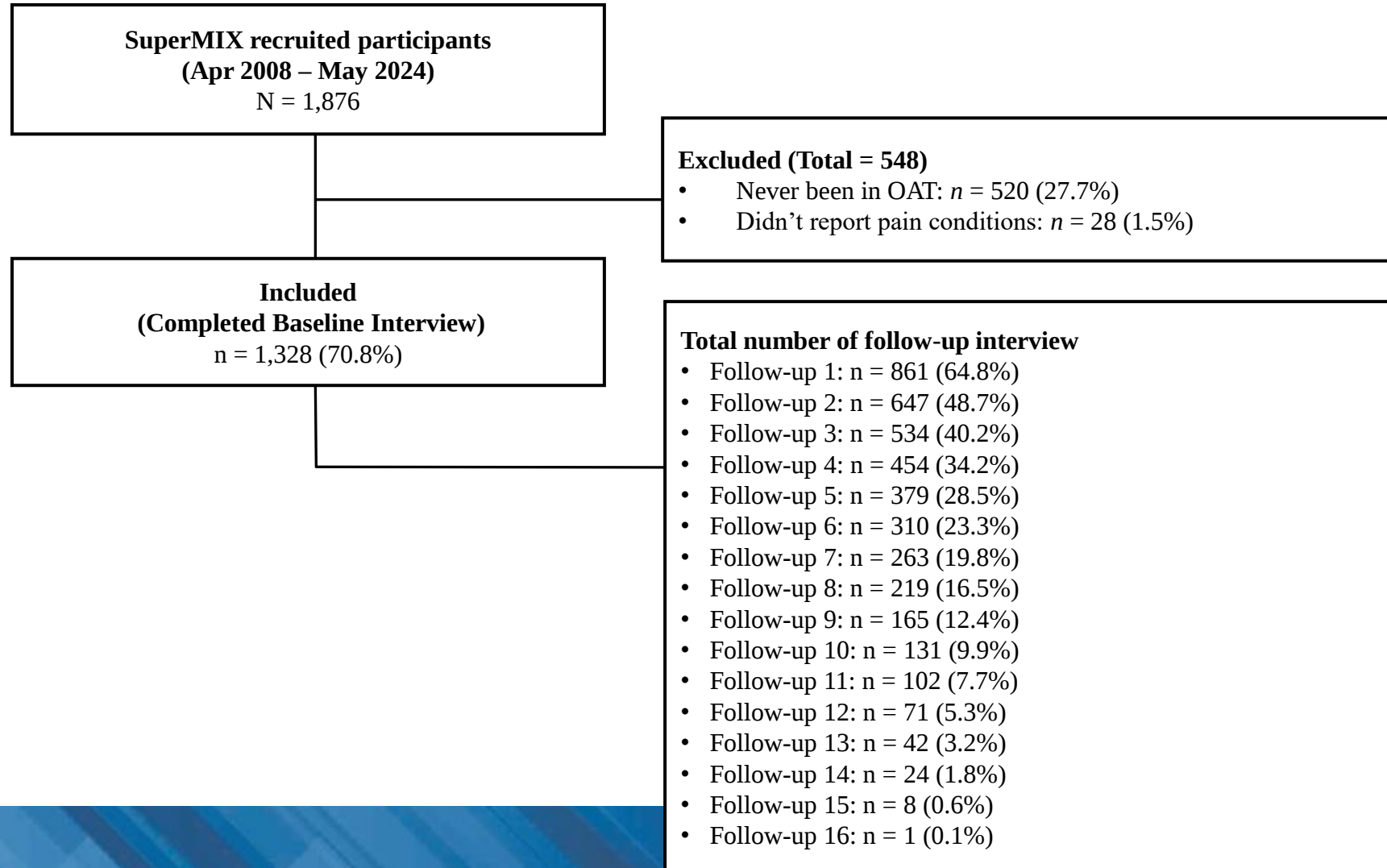
- Physical and mental health
 - Overall physical health (measured by a 6-point Likert Scale)
 - Physical activity interference (measured by a 5-point Likert Scale)
 - Daily work interference (measured by a 5-point Likert Scale)
 - Social activity interference (measured by a 5-point Likert Scale)
 - Emotional problems (measured by a 5-point Likert Scale)
 - Sleep difficulties (yes/no)

Covariates of interest:

- Substance use history
 - Current prescribed buprenorphine and methadone use (yes/no) (last month)
 - Times of injecting non-prescribed opioids (last week)
 - Heroin use (yes/no) (last month)
 - Other non-prescribed opioid use (i.e., methadone, buprenorphine, morphine, and oxycodone) (last month)
 - Benzodiazepine, antipsychotic, antidepressant use (yes/no) (last month)



Participant Recruitment Flow Chart



Baseline analysis: Ordinal regression

TABLE 1 Baseline demographic and clinical characteristics of participants (N=1,328), and factors associated with pain severity using ordinal regression model (N=1168)

Variables		No pain n (%)	Mild pain n (%)	Moderate pain n (%)	Severe pain n (%)	Odds ratio with 95% CI	
N		452 (34.0)	367 (27.6)	257 (19.4)	252 (19.0)	Unadjusted	Adjusted
Male ^a	No	121 (26.8)	124 (33.8)	85 (33.1)	99 (39.3)	Ref	Ref
	Yes	330 (73.2)	243 (66.2)	172 (66.9)	153 (60.7)	0.71 (0.57, 0.87)	0.77 (0.60, 0.98)
Age at baseline ^b	Mean (SD), years	34.8 (9.7)	35.4 (10.2)	38.8 (11.6)	39.6 (10.7)	1.03 (1.02, 1.04)	1.03 (1.02, 1.04)
Born in Australia ^c	No	87 (19.3)	56 (15.3)	46 (17.9)	28 (11.1)	Ref	Ref
	Yes	364 (80.7)	311 (84.7)	211 (82.1)	224 (88.9)	1.37 (1.05, 1.78)	1.11 (0.82, 1.50)
Education, ≥Year 12 ^d	No	409 (90.5)	321 (87.5)	220 (85.6)	205 (81.7)	Ref	Ref
	Yes	43 (9.5)	46 (12.5)	37 (14.4)	46 (18.3)	1.64 (1.23, 2.19)	1.06 (0.75, 1.50)
Employment ^e	No	395 (87.4)	320 (87.4)	230 (89.5)	228 (90.5)	Ref	Ref
	Yes	57 (12.6)	46 (12.6)	27 (10.5)	24 (9.5)	0.82 (0.60, 1.10)	1.11 (0.78, 1.57)
Homelessness ^f	No	414 (92.2)	337 (92.3)	229 (89.1)	219 (87.3)	Ref	Ref
	Yes	35 (7.8)	28 (7.7)	28 (10.9)	32 (12.7)	1.49 (1.07, 2.09)	1.25 (0.83, 1.88)
HIV status ^g	Negative	393 (93.1)	326 (94.2)	217 (93.9)	218 (92.0)	Ref	Ref
	Positive	2 (0.5)	3 (0.9)	4 (1.7)	2 (0.8)	1.66 (0.61, 4.51)	2.19 (0.72, 6.67)
	Never had a test	27 (6.4)	17 (4.9)	10 (4.3)	17 (7.2)	0.99 (0.63, 1.54)	1.22 (0.75, 2.00)
Overall physical health rating ^h	Good	332 (73.5)	208 (56.8)	95 (37.0)	61 (24.2)	Ref	Ref
	Fair	90 (19.9)	112 (30.6)	99 (38.5)	81 (32.1)	2.95 (2.34, 3.72)	1.89 (1.44, 2.47)
	Poor	30 (6.6)	46 (12.6)	63 (24.5)	110 (43.7)	7.89 (5.94, 10.48)	2.69 (1.89, 3.82)
Physical activity interference ⁱ	Not at all/Minimal	422 (93.8)	254 (69.6)	108 (42.0)	78 (31.1)	Ref	Ref
	Moderate	12 (2.7)	84 (23.0)	88 (34.2)	59 (23.5)	5.89 (4.52, 7.67)	2.97 (2.08, 4.24)
	Quite a lot/Extremely	16 (3.6)	27 (7.4)	61 (23.7)	114 (45.4)	15.00 (11.00, 20.45)	3.94 (2.41, 6.44)
Daily work interference ^j	Not at all/Minimal	413 (91.6)	265 (72.8)	126 (49.0)	75 (30.0)	Ref	Ref
	Moderate	21 (4.7)	64 (17.6)	64 (24.9)	44 (17.6)	4.47 (3.36, 5.93)	1.66 (1.13, 2.43)
	Quite a lot/Extremely	17 (3.8)	35 (9.6)	67 (26.1)	131 (52.4)	13.34 (9.96, 17.88)	2.76 (1.73, 4.40)
Social activity interference ^k	Not at all/Minimal	309 (69.0)	168 (46.4)	69 (27.1)	66 (26.4)	Ref	Ref
	Moderate	69 (15.4)	114 (31.5)	88 (34.5)	59 (23.6)	2.96 (2.31, 3.78)	1.29 (0.95, 1.76)
	Quite a lot/Extremely	70 (15.6)	80 (22.1)	98 (38.4)	125 (50.0)	5.08 (3.96, 6.51)	1.23 (0.85, 1.78)
Emotional problems ^l	Not at all/Minimal	288 (64.4)	160 (44.1)	87 (34.3)	56 (22.6)	Ref	Ref
	Moderate	55 (12.3)	70 (19.3)	54 (21.3)	41 (16.5)	2.50 (1.89, 3.31)	1.72 (1.21, 2.44)
	Quite a lot/Extremely	104 (23.3)	133 (36.6)	113 (44.5)	151 (60.9)	3.74 (2.98, 4.68)	1.67 (1.18, 2.35)
Sleep difficulties ^m	No	397 (88.0)	297 (81.4)	205 (79.8)	192 (76.2)	Ref	Ref
	Yes	54 (12.0)	68 (18.6)	52 (20.2)	60 (23.8)	1.70 (1.32, 2.19)	1.22 (0.91, 1.63)
Current methadone use ⁿ	No	308 (68.1)	230 (62.8)	159 (61.9)	163 (64.9)	Ref	Ref
	Yes	144 (31.9)	136 (37.2)	98 (38.1)	88 (35.1)	1.14 (0.93, 1.40)	1.13 (0.88, 1.46)

- Mean age: 36.7 years
- Male (67.7%) and unemployed (88.4%)
- Half were currently in OAT
- Pain at any levels: 66%; severe pain: 19%

Baseline analysis: Ordinal regression

Variables		No pain n (%)	Mild pain n (%)	Moderate pain n (%)	Severe pain n (%)	Odds ratio with 95% CI	
Current buprenorphine use ^o	No	381 (85.4)	312 (85.7)	216 (84.4)	204 (82.9)	Ref	Ref
	Yes	65 (14.6)	52 (14.3)	40 (15.6)	42 (17.1)	1.13 (0.86, 1.48)	1.16 (0.83, 1.61)
Non-prescribed opioid injection, times	0	101 (22.3%)	69 (18.8%)	45 (17.5%)	52 (20.6%)	Ref	Ref
	1~7	206 (45.6%)	176 (48.0%)	119 (46.3%)	125 (49.6%)	1.16 (0.89, 1.51)	1.36 (0.94, 1.98)
	>7	145 (32.1%)	122 (33.2%)	93 (36.2%)	75 (29.8%)	1.11 (0.84, 1.46)	1.08 (0.73, 1.59)
Heorin use	No	69 (15.3)	42 (11.4)	26 (10.1)	44 (17.5)	Ref	Ref
	Yes	383 (84.7)	325 (88.6)	231 (89.9)	208 (82.5)	1.01 (0.76, 1.36)	0.90 (0.59, 1.37)
Other non-prescribed opioid use ^p	No	335 (74.8)	245 (67.5)	148 (58.5)	137 (55.5)	Ref	Ref
	Yes	113 (25.2)	118 (32.5)	105 (41.5)	110 (44.5)	1.85 (1.50, 2.27)	2.13 (1.67, 2.73)
Benzodiazepine use ^q	No	230 (50.9)	157 (42.9)	90 (35.2)	89 (35.3)	Ref	Ref
	Yes	222 (49.1)	209 (57.1)	166 (64.8)	163 (64.7)	1.62 (1.33, 1.98)	1.16 (0.92, 1.47)
Antipsychotics use ^r	No	383 (84.9)	297 (81.1)	222 (86.7)	199 (79.6)	Ref	Ref
	Yes	68 (15.1)	69 (18.9)	34 (13.3)	51 (20.4)	1.16 (0.89, 1.50)	0.98 (0.72, 1.34)
Antidepressant use ^s	No	381 (84.9)	306 (83.4)	216 (84.4)	182 (72.2)	Ref	Ref
	Yes	68 (15.1)	61 (16.6)	40 (15.6)	70 (27.8)	1.56 (1.21, 2.02)	1.06 (0.78, 1.44)

Abbreviation: CI, Confidence interval; SD, standard deviation.

^an = 1 missing, ^bn = 2 missing, 3 participants reported to be non-binary and were coded as not male.

^cn = 1 missing, ^dn = 1 missing, ^en = 1 missing, ^fn = 6 missing, ^gn = 92 missing, ^hn = 1 missing, ⁱn = 5 missing, ^jn = 6 missing, ^kn = 13 missing, ^ln = 16 missing, ^mn = 3 missing

ⁿn = 2 missing, ^on = 16 missing, ^pn = 17 missing, ^qn = 2 missing, ^rn = 5 missing, ^sn = 4 missing



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Longitudinal Analysis: Multilevel regression

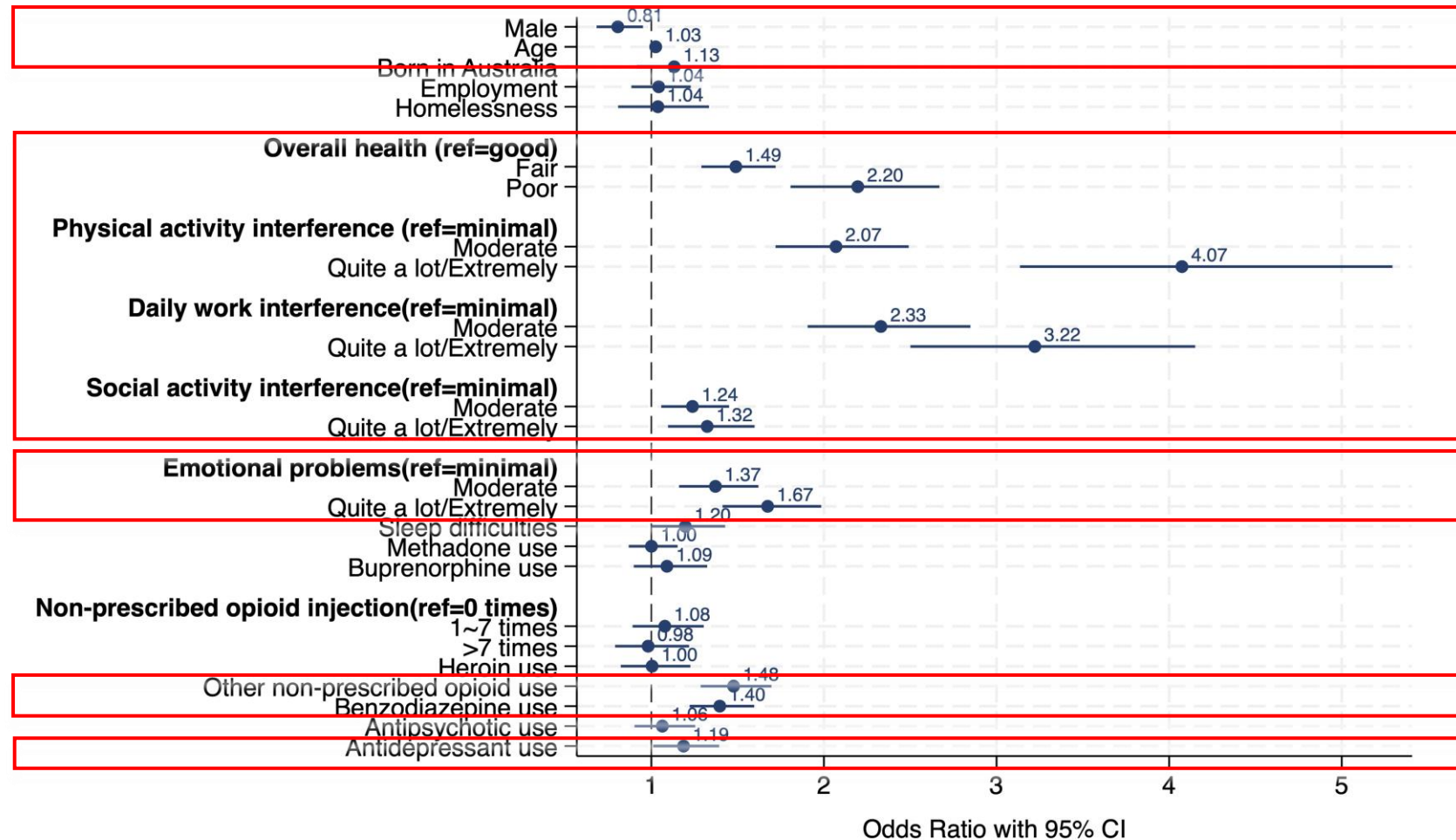


Figure 2. Forest plot showing factors associated with changes of pain severity using multilevel ordinal logistic regression
Abbreviations: CI, confidence interval.

WHY no associations between pain severity and OAT status?



An ongoing qualitative study.....

Exploring the pain treatment barriers and needs among people with chronic pain and in OAT

Q: Methadone tapering & pain experience

“What I’d say is, it’s [pain] always there. But I noticed, since I had my methadone 20 minutes later, I don’t think it goes away, sort of... I don’t... [pain] is there. I know it’s there, but I don’t think about that until probably at night time, and I go to bed it starts getting uncomfortable again, it keep growing until I find a comfortable spot and go to sleep.” (Male, 52 years)

Q: Buprenorphine vs Methadone re pain relief

“It [methadone] works better. It works better to a point. It works better till tonight I’ll wake up in the middle of the night at two or three in the morning, and I’ll have to have my methadone, you know, to... to be normal, to not be sick, you know what I mean...[drinking alcohol]. That’s why I drink, too. I have my fridge full of beer.” (Male, 58 years)



Conclusions

Gender, age, physical and mental health, and substance use were associated with changes in pain severity



No association was observed between pain severity and current OAT status



OAT medicines are not enough to manage concurrent opioid dependence and pain



Need for co-designing a pain management program with consumers and healthcare providers



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Thank You!

Q&A

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Research protocol: <https://osf.io/m5ws2/>

