Table S1: Cross-sectional Risk of Bias Assessment using National Institute of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

	Peles, 2005	Dhingra, 2013	Barry, 2009	Chakrabarti, 2009	Dennis, 2014	Dreifuss, 2012	Dunn, 2014	Jamison, 2000	Rosenblum, 2003	Trafton, 2004
Was the study population clearly specified and defined?	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Was the participation rate of eligible persons at least 50%?	Yes	Not Reported	Not Reported	Not Reported	No	Not Reported	Yes	Not Reported	Not Reported	Not Reported
Was the research question or objective in this paper clearly stated?	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes
Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Yes	Yes	Yes	No	Yes	Cannot Determine	Yes	Yes	Yes	Yes
Was a sample size justification, power description, or variance and effect estimates provided?	No	No	Not Reported	Yes	Yes	No	Not Reported	Not Reported	Yes	No
For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	No	Cannot Determine	No	Yes	No	Yes	No	No	No	No
Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Yes	Cannot Determine	No	Yes	Yes	Yes	No	No	Yes	No
For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	Yes	No	Yes	Yes	No	No	No	No	Yes	Yes
Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Cannot Determine	Yes	No	Yes	Yes
Was the exposure(s) assessed more than once over time?	No	No	No	Yes	No	No	No	No	No	No
Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Were the outcome assessors blinded to the	Not	Not	Not	Not Reported	Yes	Not	Not	Not	Not	Not

exposure status of participants?	Reported	Reported	Reported			Reported	Reported	Reported	Reported	Reported
Was loss to follow-up after baseline 20% or less?	Not Reported	Not Reported	Not Reported	Not Reported	Yes	Not Reported	Not Reported	Not Reported	Yes	Not Reported
Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	No	Yes	No	Yes	Yes	No	Yes	No	No	No
How would you rate the quality of this article?	**Good**	**Fair**	**Fair**	**Good**	**Good**	**Fair**	**Good**	**Poor**	**Good**	**Fair**

Table S2: Newcastle Ottawa Scale Risk of Bias Assessment for Cohort Studies

	Bounes, 2013	Fox, 2012	Potter, 2015
Were cohorts drawn from the same population?	3	3	3
Is the source population (sampling frame) representative of the cohort of interest?	3	2	3
Was the outcome analysis of high quality and the methodology of the outcome assessment explicitly detailed?	2	3	2
Did the study use statistical analysis methods to adjust for prognostic variables across participant groups?	3	3	3
Is there little missing data?	1	2	1
Were all outcome assessors blinded to the treatment group (i.e. methadone or buprenorphine) information of the participant?	1	1	1
Was there an objective assessment of the outcome of interest?	3	3	2
Did the study identify and adjust for any possible influence a concurrent therapy or unintended exposure might have on the results of the investigation?	1	2	2
Risk of Bias Score	17	19	17

*Risk of bias score minimum of 8 and maximum of 24, higher scores indicate lower risk of bias

Table S3: Risk of Bias Assessment for Randomized Controlled Trials Using the Cochrane Risk of Bias Tool

Author Last Name, Year	Was the allocation sequence adequately generated?	Was allocation adequately concealed?	Was knowledge of the allocated intervention adequately prevented during the study?	Were incomplete outcome data adequately addressed?	Are reports of the study free of suggestion of selective outcome reporting?	Was the study apparently free of other problems that could put it at a high risk of bias?	Cochrane Score
Neumann, 2013	1	1	1	3	3	2	11

*Cochrane risk of bias scores are summed from individual ranking among multiple subdomains, giving a total score out of 18. Higher scores indicate increasing risk of bias

Table S4: Summary of Findings for Studies Evaluating Psychiatric Health Outcomes

Author Last Name	Outcome	Measurement of Psychiatric Symptoms	Findings
Dhingra	Evaluated whether severe depressive symptoms were associated with the presence of chronic pain, using clinically significant pain as the dependent variable in a multi-variable logistic regression model.	Beck Depression Inventory (used to assess depressive symptoms)	Using a dependent variable of presence or absence of clinically significant pain, the model was significant (Wald score $2(8, N = 480) = 85.55$, $p < 0.0001$) and four variables remained independently associated with pain: current use of prescribed opioid therapy for pain, higher methadone dose, higher level of comorbid medical conditions, and more severe depressive symptoms.
Barry	The study evaluated the association between pain and psychiatric symptoms, using t-tests to assess for differences in psychiatric rating scale scores across pain categories.	Measured psychiatric symptoms using the Brief Symptom Inventory 18 (BSI-18; (14))—the BSI-18 is an 18-item instrument, designed to screen for psychiatric disorders, that contains 3 subscales: depression, somatization and anxiety, and a total global severity index (GSI) score.	Using ANOVA to assess the differences in psychiatric symptoms scores, Barry et. al (2009) found significant differences ($p<0.05$) across all groups indicating the presence of pain is associated with a higher severity of psychiatric symptoms.
Jaimison	Jamison et. al evaluated whether participants reporting pain have a higher incidence of mental health diagnoses, Jamison et. al found that 67.1% of the participants categorized as having pain reported a mental health diagnosis and 51% of the non-pain group reported a mental health diagnosis ($x2$: 6.38, $p<0.05$). Jamison also evaluated the differences in the absence of anxiety (% of participant reporting no anxiety; pain: 5.3%, No pain 9.4%; $x2$, 22.41 $p<0.001$), no depression (pain 6.0%, no pain 17.7%; $x2$, 32.53 $p<0.001$), and no irritability (Pain 5.9%, no pain 9.4%; $x2$ 10.08, $p<0.05$), all of which showed patients with pain to have lower rates of reporting no psychiatric symptoms.	Self-report to a mood questionnaire generated for study	Evaluated the differences in proportions using chi-square
Rosenblum	Evaluated the history of psychiatric diagnosis among patients, finding the prevalence of CSP participants reporting yes to be 112 52.7%, while the percentage of non-chronic pain patients reporting a psychiatric medical history to be 247 (28.3%). These results indicate an increased risk of psychiatric comorbidity among patients reporting pain.	Self-report (psychiatric comorbidity), Symptom Checklist-90 (SCL-90) for psychiatric distress	When evaluating the differences in psychiatric in the presence of illness between patients with and without pain, the OR was shown to be 2.82 (95%CI 1.77-4.47), indicating an increased risk for psychiatric comorbidity among patients reporting pain. Rosenblum also showed participants with chronic severe pain to have higher ratings for moderate and high levels of psychiatric distress ($p<0.05$)
Trafton	Evaluated psychiatric functioning over a 30-day period by	Addiction Severity Index: Measures	Trafton (2004) report a significant effect of pain on psychiatric

	evaluating the differences in the percentage of participants reporting depression, anxiety, hallucinations, trouble understanding, serious thoughts of suicide, violent behaviour, attempted suicide, and prescribed psychiatric symptoms.	psychological problems in the last month	symptoms, showing patients with pain to have a statistically significantly higher prevalence of 30-day depression, anxiety, hallucinations, trouble understanding, violent behaviour serious thoughts of suicide ($p<0.05$ for all chi-square tests evaluating differences in proportions). However, the reporting of actual suicide attempt was not found to statistically differ between groups (only one participant reported this)
Dennis (unpublished)	Using author requested data, we evaluated the prevalence of self-reported psychiatric diagnoses among patients reporting pain.	Dennis et. al used a self-report tool to determine the presence of psychiatric comorbidity, which was measured as composite outcome for depression, anxiety, schizophrenia, bipolar, and personality disorder	Among the GENOA sample of opioid dependent patients (n=250), 64 participants reported having chronic pain, whereby 186 report no pain. Among those reporting chronic pain, 37 report any history of psychiatric illness, where only 85 of the non-chronic pain patients report a history of psychiatric comorbidity. Evaluating the differences in proportions between groups showed a trending effect.

Table S5 - The Impact of Pain on Substitute Opioid Therapy Treatment Outcomes

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pain	No Pain	Relative (95% CI)	Absolute (95% CI)		
Illicit Opioid Use (assessed with: self-report measures and urine toxicology screening)												
2	observational studies	serious [1][2][3][4][5]	not serious [6]	not serious [7]	serious [8]	all plausible residual confounding would suggest spurious effect, while no effect was observed [9]	62/153 (40.5%)	163/252 (64.7%)	**OR 0.70** (0.41 to 1.17)	85 fewer per 1000 (from 35 more to 218 fewer)	⨁◯◯◯ VERY LOW	IMPORTANT
Illicit Substance Use (cocaine, methamphetamine) (assessed with: self-report, urine toxicology screening, addiction severity index)												
2	observational studies	serious [1][2][3][4][5]	not serious [6]	not serious [7]	not serious [8]	all plausible residual confounding would reduce the demonstrated effect	125/276 (45.3%)	211/341 (61.9%)	**OR 0.57** (0.41 to 0.79)	138 fewer per 1000 (from 57 fewer to 219 fewer)	⨁⨁◯◯ LOW	IMPORTANT
Psychiatric Comorbidity: Do Patients With Pain Report Higher Rates of Psychiatric Disorders? (assessed with: Self-report)												
3	observational studies	serious [1][2][3][4][5]	not serious [6]	not serious [7]	not serious [8]	none	198/345 (57.4%)	187/512 (36.5%)	**OR 2.16** (1.60 to 2.90)	189 more per 1000 (from 114 more to 260 more)	⨁⨁◯◯ LOW	IMPORTANT

MD – mean difference, OR - odds ratio

1. Lack of demonstration of dose-response with pain severity
2. Chronic pain measurement, BPI not validated in the OST setting
3. No reported sample size calculation (Peeles)
4. Serious reporting issues: follow-up of participants, missing data, and blinding of outcome assessors
5. Exposure of Interest not measured prior to outcome, also no repeated assessment of exposure
6. Results were consistent across studies, low I2 estimates and overlapping confidence intervals
7. All treatments were evaluated in a representative observational sample (minimally restrictive eligibility criteria applied)
8. Wide confidence intervals
9. No explanation was provided