# Supplementary Online Content

Santo T Jr, Clark B, Hickman M, et al. Association of opioid agonist treatment with all-cause mortality and specific causes of death among people with opioid dependence: a systematic review and meta-analysis. *JAMA Psychiatr*. Published online June 2, 2021. doi:10.1001/jamapsychiatry.2021.0976

This supplementary material has been provided by the authors to give readers additional information about their work.

## eTable 1: GATHER checklist

| Item # | Checklist item | Section Reported |
|---|---|---|
| **Objectives and funding** | | |
| 1 | Define the indicator(s), populations (including age, sex, and geographic entities), and time period(s) for which estimates were made. | Introduction (pg1) |
| 2 | List the funding sources for the work. | Article Information (pg 12) |
| **Data Inputs** | | |
| *For all data inputs from multiple sources that are synthesized as part of the study:* | | |
| 3 | Describe how the data were identified and how the data were accessed. | Methods (pg 2-3), eTable 4-5 |
| 4 | Specify the inclusion and exclusion criteria. Identify all ad-hoc exclusions. | eAppendix, eTable3 |
| 5 | Provide information on all included data sources and their main characteristics. For each data source used, report reference information or contact name/institution, population represented, data collection method, year(s) of data collection, sex and age range, diagnostic criteria or measurement method, and sample size, as relevant. | Results (pg3-10), eTables 6-14 |
| 6 | Identify and describe any categories of input data that have potentially important biases (e.g., based on characteristics listed in item 5). | Methods (pg 2-3), eAppendix, eFigures 37-49 |
| *For data inputs that contribute to the analysis but were not synthesized as part of the study:* | | |
| 7 | Describe and give sources for any other data inputs. | eAppendix, eTable5 |
| *For all data inputs:* | | |
| 8 | Provide all data inputs in a file format from which data can be efficiently extracted (e.g., a spreadsheet rather than a PDF), including all relevant meta-data listed in item 5. For any data inputs that cannot be shared because of ethical or legal reasons, such as third-party ownership, provide a contact name or the name of the institution that retains the right to the data. | eTable 6 |
| **Data analysis** | | |
| 9 | Provide a conceptual overview of the data analysis method. A diagram may be helpful. | Methods (pg 2-3), eAppendix |
| 10 | Provide a detailed description of all steps of the analysis, including mathematical formulae. This should cover, as relevant, data cleaning, data pre-processing, data adjustments and weighting of data sources, and mathematical or statistical model(s). | Methods (pg2-3), eAppendix |
| 11 | Describe how candidate models were evaluated and how the final model(s) were selected. | Methods (pg 2-3), eAppendix, eFigure46-49 |
| 12 | Provide the results of an evaluation of model performance, if done, as well as the results of any relevant sensitivity analysis. | N/A, eFigure 46-49 |
| 13 | Describe methods for calculating uncertainty of the estimates. State which sources of uncertainty were, and were not, accounted for in the uncertainty analysis. | Methods (pg 2-3) |
| 14 | State how analytic or statistical source code used to generate estimates can be accessed. | Methods (pg 2-3) |
| **Results and Discussion** | | |
| 15 | Provide published estimates in a file format from which data can be efficiently extracted. | Tables 1-4, eFigures 2-36, eTables 16-20 |
| 16 | Report a quantitative measure of uncertainty of the estimates (e.g. uncertainty intervals). | Tables 1-4 |
| 17 | Interpret results in light of existing evidence. If updating a previous set of estimates, describe the reasons for changes in estimates. | Discussion (pg 10-13) |
| 18 | Discuss limitations of the estimates. Include a discussion of any modelling assumptions or data limitations that affect interpretation of the estimates. | Discussion (Limitations, pg 13) |

**eTable 2: PRISMA checklist**

| Section/topic | # | Checklist item | Reported Section |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | Title (pg1) |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | Abstract (pg1) |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | Introduction (pg2) |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | Introduction (pg2) |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, where it can be accessed, and, if available, provide registration information including registration number. | Methods (pg 2-3) |
| Eligibility criteria | 6 | Specify study characteristics and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | Methods (pg 2-3), eTable 4-5 |
| Information sources | 7 | Describe all information sources in search and date last searched. | Methods (pg 2-3), eAppendix |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | eAppendix |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | Methods (pg 2-3), eFigure3, eTable3 |
| Data collection process | 10 | Describe method of data extraction (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | Methods (pg 2-3), Results (pg3) |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | Methods (pg 2-3), eTable 4-5 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | Methods (pg 2-3), eAppendix, eFigures 37-49 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | Methods (pg. 2) |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | Methods (pg 2-3), eTable 4-5 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | Methods (pg 2-3), eAppendix, eFigures 37-49 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | Methods (pg 2-3), Table 1, eFigures 46-49 |

| Section/topic | # | Checklist item | Reported Section |
|---|---|---|---|
| **RESULTS** | | | |
| Study selection | 17 | Give no. studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | eFigure3 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | Results (pg3-10), eTables 6-14 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Methods (pg 2-3), eAppendix, eFigures 37-49 |
| Results of individual studies | 20 | For all outcomes, present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals | Table 1-3, Results (pg 3-10) |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | Tables 1-3, eFigures 2-36, eTables 16-20 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | Methods (pg 2-3), eAppendix, eFigures 37-49 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | Methods (pg 2-3), eAppendix, eFigures 37-49 |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups | Discussion (pg 10-13) |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | Discussion (Limitations, pg 13) |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | Discussion (pg 10-13) |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | Article Information (pg 12) |

# eAppendix: Peer Reviewed Literature Search

## Database searches

| **Medline** | | | |
|---|---|---|---|
| Group | | Search terms | |
| | | MeSH | *Non MeSH* |
| #1 | Opiate Substitution Treatment | Opiate Substitution Treatment | *(opioid OR opiate) adj (substitut* OR maint*) adj (treatment OR therapy))* |
| | | Substance Abuse Treatment | *Methadone* |
| | | Buprenorphine | *LAAM* |
| | | Methadone | *Substance Abuse Treatment* |
| | | Methadyl Acetate | *Dextropropoxyphene* |
| | | | *Naltrexone* |
| | | | *Buprenorphine*<br>*Methadone* |
| | | | *(opiate OR opioid OR heroin) adj (treatment OR substitut* OR replacement OR maint*)* |
| | | | *BMT or MMT* |
| | | | *Suboxone* |
| | | | *Subutex* |
| #2 | Mortality | Mortality | *Mortal** |
| | | Cause of Death | *Fatal** |
| | | Fatal Outcome | *Death** |
| | | Mortality, Premature | *Die** |
| #3 | Cohorts Studies | Cohort Studies | *Cohort* |
| | | Follow-Up Studies | *Longitudinal* |
| | | Longitudinal Studies | *Prospective* |
| | | Prospective Studies | *Follow-up* |
| | | Retrospective Studies<br>Clinical Trial | *Retrospective*<br>*Rate* |
| | | | *RCT* |
| #1 AND #2 AND #3 | | | |

| **Embase** | | |
|---|---|---|
| Group | Search terms | |
| | EMTREE | *Non EMTREE* |
| #1 Opioid Substitution Treatment | Drug dependence treatment<br>Methadone treatment<br>Opiate substitution treatment<br>Methadone<br>Buprenorphine<br>Buprenorphine plus naloxone<br>Methadone plus naloxone | *(opioid OR opiate) adj2 (substitut* OR maint*) adj2 (treatment OR therapy))*<br>*Methadone*<br>*Methadyl Acetate OR LAAM*<br>*Substance Abuse Treatment*<br>*Buprenorphine*<br>*Naltrexone*<br>*Dextropropoxyphene*<br>*Methadone*<br>*(opiate OR opioid OR heroin) adj (treatment OR substitut* OR replacement OR maint*)*<br>*BMT or MMT*<br>*Suboxone*<br>*Subutex* |
| #2 Mortality | Mortality<br>Death<br>Accidental death<br>"Cause of death"<br>Sudden death | *Mortal**<br>*Fatal**<br>*Death**<br>*Die** |
| #3 Cohorts Studies | Cohort analysis<br>Follow up<br>Longitudinal study<br>Prospective study<br>Retrospective study<br>"Clinical trial (topic)" | *Cohort*<br>*Longitudinal*<br>*Prospective*<br>*Follow-up*<br>*Retrospective*<br>*Rate*<br>*RCT* |
| #1 AND #2 AND #3 | | |

**Limits:** Humans

| **PsycINFO** | | | |
|---|---|---|---|
| Group | | Search terms | |
| | | THESAURUS | *Non THESAURUS* |
| #1 | Opioid Substitution Treatment | Maintenance Therapy<br>Methadone<br>Buprenorphine<br>Methadone Maintenance<br>"Substance Use Treatment" | *(opioid OR opiate) adj2 (substitut* OR maint*) adj2 (treatment OR therapy))*<br>*Methadone*<br>*Methadyl Acetate OR LAAM* |
| | | | *Substance Abuse Treatment* |
| | | | *Buprenorphine* |
| | | | *Naltrexone* |
| | | | *Dextropropoxyphene* |
| | | | *Methadone* |
| | | | *(opiate OR opioid OR heroin) adj (treatment OR substitut* OR replacement OR maint*)* |
| | | | *BMT or MMT*<br>*Suboxone*<br>*Subutex* |
| #2 | Mortality | "Death and Dying"<br>Mortality Rate<br>Sudden Death | *Mortal**<br>*Fatal**<br>*Death**<br>*Die** |
| #3 | Cohorts Studies | Cohort Analysis<br>Followup Studies<br>Longitudinal studies<br>Prospective studies<br>Retrospective studies<br>Clinical Trials | *Cohort*<br>*Longitudinal*<br>*Prospective*<br>*Follow-up*<br>*Retrospective*<br>*Rate*<br>*RCT* |
| #1 AND #2 AND #3 | | | |

**Additional hand searches**

- Mattick 2009 Cochrane review
    - Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2009). Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane database of systematic reviews*, (3).
- Mattick 2014 Cochrane review
    - Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane database of systematic reviews*, (2).
- Search through Cochrane Reviews website
    - Topic: tobacco, drugs, & alcohol
- Moore 2019 review
    - Moore, K. E., Roberts, W., Reid, H. H., Smith, K. M., Oberleitner, L. M., & McKee, S. A. (2019). Effectiveness of medication assisted treatment for opioid use in prison and jail settings: *A meta-analysis and systematic review. Journal of substance abuse treatment, 99*, 32-43.
- Search through Clinical registries (see **eTable 4** for details)
    - Completed & ongoing studies

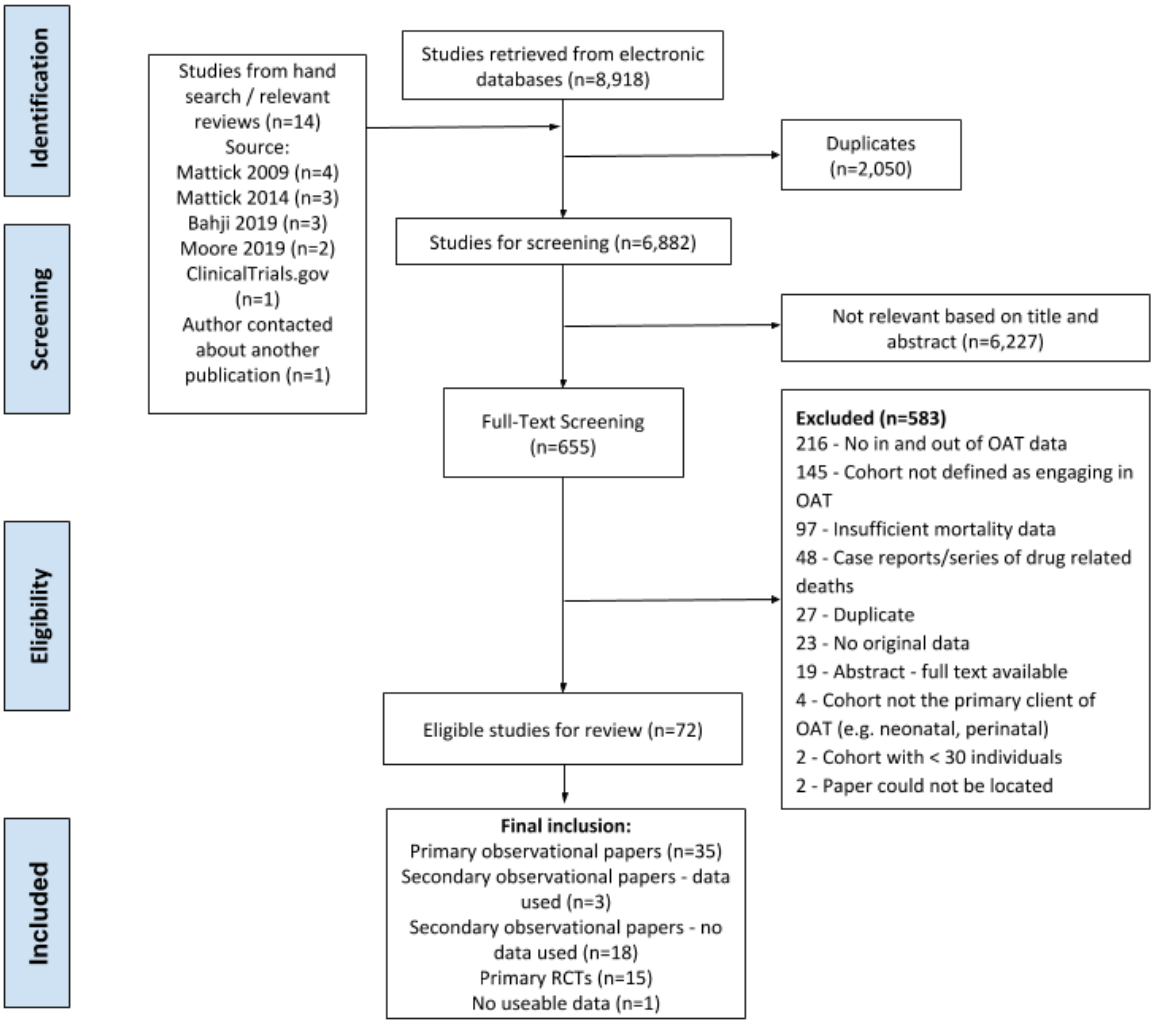
**Prespecified exclusion criteria**

The prespecified exclusion criteria were as follows:

- No data in humans or no original research (e.g. reviews, editorials, protocols)
- Study designs other than observational cohort studies or RCTs (e.g. case-control studies, cross sectional surveys, case reports, case series, qualitative research)
- Study not focused on people with opioid dependence
- Treatment unknown or other than methadone or buprenorphine maintenance (e.g. methadone detoxification, opioid antagonist therapy, therapeutic community)
- No all cause or cause-specific mortality as outcome or no deaths over follow-up
- Insufficient data to compute mortality rates during periods in and out of treatment

For cohorts where several papers were located, we used data from non-overlapping follow-up periods from each report whenever possible or selected the publication with the longest follow-up.

**eFigure 1: PRISMA flow diagram**



**eTable 3: List of studies excluded at full text review stage and reasons for exclusion**

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 1. | Aalto, M.; Visapaa, J. P.; Halme, J. T.; Fabritius, C.; Salaspuro, M. (2011). Effectiveness of buprenorphine maintenance treatment as compared to a syringe exchange program among buprenorphine misusing opioid-dependent patients. *Nordic Journal of Psychiatry, 65*(4), 238-43. | No/insufficient mortality data |
| 2. | Abdel-Mawgoud, M.; al-Haddad, M. K. (1996). Heroin addiction in Bahrain: 15 years experience. Addiction, 91(12), 1859-64. | Review |
| 3. | Accurso, A. J.; Rastegar, D. A.; Ghazarian, S. R.; Fingerhood, M. I. (2015). Impact of hepatitis C status on 20-year mortality of patients with substance use disorders. Addiction science & clinical practice, 1020. | Cohort not defined as engaging in opioid agonist treatment |
| 4. | Alexandridis, Apostolos Alexander (2019). Longitudinal cohort studies of addiction treatment initiation and opioid overdose prevention efforts in North Carolina. Dissertation Abstracts International: Section B: The Sciences and Engineering, 80 No Pagination Specified. | No/insufficient mortality data |
| 5. | Ali, R.; Auriacombe, M.; Casas, M.; Cottler, L.; Farrell, M.; Kleiber, D.; Kreuzer, A.; Ogborne, A.; Rehm, J.; Ward, P. (1999). Report of the external panel on the evaluation of the Swiss scientific studies of medically prescribed narcotics to drug addicts. *Sucht, 45*(3), 160-170. | No original data |
| 6. | Alim, T.; Richardson, F.; Settles-Reaves, B.; Kumari, S.; Akinfiresoye, E.; Chapman, E.; Bland, W.; Johnson, M. (2017). Buprenorphine integrated care delivery project: Correlates of mental health screening and primary care outcomes. Neuropsychopharmacology, 43 (Supplement 1)S256-S257. | No/insufficient mortality data |
| 7. | Anonymous, (1996). Observational analysis of German injecting drug users (IDU): survival with and without methadone maintenance treatment. German AIDS Study Group GASG/IdkF. European journal of medical research, 1(4), 209-214. | Paper could not be located |
| 8. | Anonymous, (2011). Risk of death during and after opiate substitution treatment. Australian Journal of Pharmacy, 92(1090), 78. | Abstract - full text available |
| 9. | Anonymous, (2016). 12th Congress of European Opiate Addiction Treatment Association, EUROPAD 2016. Heroin Addiction and Related Clinical Problems. Conference: 12th Congress of European Opiate Addiction Treatment Association, EUROPAD, 18(3 Supplement 1), . | No original data |
| 10. | Apelt, S.; Scherbaum, N.; Golz, J.; Backmund, M.; Soyka, M. (2013). Safety, effectiveness and tolerance of buprenorphine-naloxone in the treatment of opioid dependence: Results from a nationwide non-interventional study in routine care. Pharmacopsychiatry, 46(3), 94-107. | No/insufficient mortality data |
| 11. | Arendt, Mikkel; Munk-Jorgensen, Povl; Sher, Leo; Jensen, Signe O. (2011). Mortality among individuals with cannabis, cocaine, amphetamine, MDMA, and opioid use disorders: A nationwide follow-up study of Danish substance users in treatment. Drug and Alcohol Dependence, 114(43892), 134-139. | No in/out treatment data available |
| 12. | Asharani, P. V.; Wen, T. J.; Karuvetil, M. Z.; Cheong, A.; Cheok, C.; Kandasami, G. (2019). Unnatural death among treatment seeking substance users in Singapore: A retrospective study. International Journal of Environmental Research and Public Health, 16 (15) (no pagination)(2743), . | Cohort not defined as engaging in opioid agonist treatment |
| 13. | Auriacombe, M.; Apelt, S. M.; Scherbaum, N.; Mankabady, B. (2017). The association between buprenorphine/naloxone and all-cause mortality in the United Kingdom (UK): An interim report. Value in Health, 20 (9)A716. | No in/out treatment data available |
| 14. | Baghazal, A. A.; Tariko, L.; Shikely, K.; Patta, S.; Omar, B.; Musyoki, H.; Bertrand, S.; Abdallah, S. (2016). Preliminary experience with medically assisted therapy for people who inject drugs in Mombasa County, Kenya. Journal of the International AIDS Society, 19 (Supplement 5)51. | No/insufficient mortality data for OAT group |
| 15. | Bahji, A.; Cheng, B.; Gray, S.; Stuart, H. (2019). Reduction in mortality risk with opioid agonist therapy: a systematic review and meta-analysis. Acta Psychiatrica Scandinavica, 140(4), 313-339. | Review |

| Excluded reference | | Exclusion Reason |
|---|---|---|
| 16. | Bandiera, F. C.; Anteneh, B.; Le, T.; Delucchi, K.; Guydish, J. (2015). Tobacco-related mortality among persons with mental health and substance abuse problems. PLoS ONE [Electronic Resource], 10(3), e0120581. | Cohort not defined as engaging in opioid agonist treatment |
| 17. | Bansback, Nick; Guh, Daphne; Oviedo-Joekes, Eugenia; Brissette, Suzanne; Harrison, Scott; Janmohamed, Amin; Krausz, Michael; MacDonald, Scott; Marsh, David C.; Schechter, Martin T.; Anis, Aslam H. (2018). Cost-effectiveness of hydromorphone for severe opioid use disorder: Findings from the SALOME randomized clinical trial. Addiction, 113(7), 1264-1273. | No/insufficient mortality data for OAT group |
| 18. | Bargagli, Anna Maria; Sperati, A.; Davoli, M.; Forastiere, F.; Perucci, C. (2001). Mortality among problem drug users in Rome: An 18-year follow-up study, 1980-97. Addiction, 96(10), 1455-1463. | No in/out treatment data available |
| 19. | Bargagli, A. M.; Hickman, M.; Davoli, M.; Perucci, C. A.; Schifano, P.; Buster, M.; Brugal, T.; Vicente, J. (2006). Drug-related mortality and its impact on adult mortality in eight European countries. European Journal of Public Health, 16(2), 198-202. | No in/out treatment data available |
| 20. | Barnett, Paul G. (1999). The cost-effectiveness of methadone maintenance as a health care intervention. Addiction, 94(4), 479-488. | Review |
| 21. | Barocas, J. A.; Morgan, J. R.; Fiellin, D. A.; Schackman, B. R.; Eftekhari Yazdi, G.; Stein, M. D.; Freedberg, K. A.; Linas, B. P. (2019). Cost-effectiveness of integrating buprenorphine-naloxone treatment for opioid use disorder into clinical care for persons with HIV/hepatitis C co-infection who inject opioids. International Journal of Drug Policy, 72160-168. | No original data |
| 22. | Barr, Harriet L.; Antes, Derry; Ottenberg, Donald J.; Rosen, Alvin (1984). Mortality of treated alcoholics and drug addicts: The benefits of abstinence. Journal of Studies on Alcohol, 45(5), 440-452. | Cohort not defined as engaging in opioid agonist treatment |
| 23. | Bart, G.; Wyman, Z.; Wang, Q.; Hodges, J. S.; Karim, R.; Bart, B. A. (2017). Methadone and the QTc Interval: Paucity of Clinically Significant Factors in a Retrospective Cohort. Journal of Addiction Medicine, 11(6), 489-493. | No/insufficient mortality data for OAT group |
| 24. | Bartu, Anne; Freeman, Nerelie C.; Gawthorne, Geoff S.; Codde, James P.; Holman, C. (2004). Mortality in a cohort of opiate and amphetamine users in Perth, Western Australia. Addiction, 99(1), 53-60. | No in/out treatment data available |
| 25. | Basu, Debasish; Mattoo, Surendra K.; Malhotra, Anil; Gupta, Nitin; Malhotra, Rama (2000). A longitudinal study of male buprenorphine addicts attending an addiction clinic in India. Addiction, 95(9), 1363-1372. | No in/out treatment data available |
| 26. | Bauer, Susanne M.; Loipl, Rita; Jagsch, Reinhold; Gruber, Diego; Risser, Daniele; Thau, Kenneth; Fischer, Gabriele (2008). Mortality in opioid-maintained patients after release from an addiction clinic. European Addiction Research, 14(2), 82-91. | No in/out treatment data available |
| 27. | Bazazi, A. R.; Culbert, G.; Kamarulzaman, A.; Altice, F. (2018). High mortality unaffected by within-prison methadone among men with hiv leaving prison. Journal of Addiction Medicine, 12 (3)E11. | Conference abstract - have full text |
| 28. | Bech, A. B.; Clausen, T.; Waal, H.; Saltyte Benth, J.; Skeie, I. (2019). Mortality and causes of death among patients with opioid use disorder receiving opioid agonist treatment: a national register study. BMC health services research, 19(1), 440. | Case reports/case series of drug-related deaths |
| 29. | Beijer, Ulla; Andreasson, Sven; Agren, Gunnar; Fugelstad, Anna (2011). Mortality and causes of death among homeless women and men in Stockholm. Scandinavian journal of public health, 39(2), 121-127. | Cohort not defined as engaging in opioid agonist treatment |
| 30. | Bell, J.; Butler, B. (2008). Health care utilization and morbidity associated with methadone and buprenorphine treatment. Heroin Addiction and Related Clinical Problems, 10(2), 21-26. | No original data |
| 31. | Bell, James R.; Butler, Bethany; Lawrance, Anne; Batey, Robert; Salmelainen, Pia (2009). Comparing overdose mortality associated with methadone and buprenorphine treatment. Drug and Alcohol Dependence, 104(43862), 73-77. | OAT engagement and mortality not reported for the same sample of people |
| 32. | Ben Bassat, O. K.; Peles, E.; Schreiber, S.; Adelson, M.; Zeltser, D.; Viskin, S.; Adler, A. (2013). Response of QT interval in methadone maintenance treated patients to the rapid | No in/out treatment data available |

| Excluded reference | | Exclusion Reason |
|---|---|---|
| | changes in heart rate provoked by brisk standing: comparison to healthy controls and patients with long QT syndrome. Journal of Electrocardiology, 46(6), 519-23. | |
| 33. | Benson, G.; Holmberg, M. (1984). Drug-related mortality in young people. Acta Psychiatrica Scandinavica, 70(6), 525-534. | Cohort not defined as engaging in opioid agonist treatment |
| 34. | Berg, John E.; Andersen, Steinar (2001). Mortality 5 years after detoxification and counseling as indicated by psychometric tests. Substance abuse, 22(1), 44105. | Cohort not defined as engaging in opioid agonist treatment |
| 35. | Bernstein, Judith; Derrington, Taletha M.; Belanoff, Candice; Cabral, Howard J.; Babakhanlou-Chase, Hermik; Diop, Hafsatou; Evans, Stephen R.; Jacobs, Hilary; Kotelchuck, Milton (2015). Treatment outcomes for substance use disorder among women of reproductive age in Massachusetts: A population-based approach. Drug and Alcohol Dependence, 147151-159. | No in/out treatment data available |
| 36. | Bertin, C.; Delorme, J.; Riquelme, M.; Peyriere, H.; Brousse, G.; Eschalier, A.; Ardid, D.; Chenaf, C.; Authier, N. (2019). Risk assessment of using off-label morphine sulfate in a population-based retrospective cohort of opioid-dependent patients. British Journal of Clinical Pharmacology., . | No in/out treatment data available |
| 37. | Bewley, Thomas H.; James, I.; Le Fevre, C.; Maddocks, P.; Mahon, T. (1972). Maintenance treatment of narcotic addicts: Not British nor a system, but working now. International Journal of the Addictions, 7(4), 597-611. | No in/out treatment data available |
| 38. | Bhatraju, E. P.; Grossman, E.; Tofighi, B.; McNeely, J.; DiRocco, D.; Flannery, M.; Garment, A.; Goldfeld, K.; Gourevitch, M. N.; Lee, J. D. (2017). Public sector low threshold office-based buprenorphine treatment: outcomes at year 7. Addiction science & clinical practice, 12(1), 7. | No/insufficient mortality data for OAT group |
| 39. | Biggar, R. J.; Buskell-Bales, Z.; Yakshe, P. N.; Caussy, D.; Gridley, G.; Seeff, L. (1991). Antibody to human retroviruses among drug users in three east coast American cities, 1972-1976. Journal of Infectious Diseases, 163(1), 57-63. | No in/out treatment data available |
| 40. | Bird, S. M.; Hutchinson Sharon, J. S. J.; Hay, G.; King, R. (2010). Missing targets on drugs-related deaths, and a Scottish paradox. International Journal of Drug Policy, 21(3), 155-159. | Cohort not defined as engaging in opioid agonist treatment |
| 41. | Bird, Sheila M.; Fischbacher, Colin M.; Graham, Lesley; Fraser, Andrew (2015). Impact of opioid substitution therapy for scotland's prisoners on drug-related deaths soon after prisoner release. Addiction, 110(10), 1617-1624. | Cohort not defined as engaging in opioid agonist treatment |
| 42. | Blix, O.; Bruvik, S.; Waal, H. (1999). The Oslo methadone project. [Norwegian]. Tidsskrift for den Norske Laegeforening, 119(2), 242-246. | No in/out treatment data available |
| 43. | Blix, O.; Bruvik, S.; Waal, H. (1999). [The Oslo methadone project]. Tidsskrift for den Norske Laegeforening, 119(2), 242-6. | Duplicate |
| 44. | Bogdanowicz, K. M.; Stewart, R.; Chang, C. K.; Downs, J.; Khondoker, M.; Shetty, H.; Strang, J.; Hayes, R. D. (2016). Identifying mortality risks in patients with opioid use disorder using brief screening assessment: Secondary mental health clinical records analysis. Drug and Alcohol Dependence, 16482-88. | No in/out treatment data available |
| 45. | Bogdanowicz, K. M.; Stewart, R.; Chang, C. K.; Shetty, H.; Khondoker, M.; Day, E.; Hayes, R. D.; Strang, J. (2018). Excess overdose mortality immediately following transfer of patients and their care as well as after cessation of opioid substitution therapy. Addiction, 113(5), 946-951. | No/insufficient mortality data for OAT group |
| 46. | Boglione, L.; Mornese Pinna, S.; De Nicolo, A.; Cusato, J.; Cariti, G.; Di Perri, G.; D'Avolio, A. (2017). Treatment with direct-acting antiviral agents of hepatitis C virus infection in injecting drug users: A prospective study. Journal of Viral Hepatitis, 24(10), 850-857. | No in/out treatment data available |
| 47. | Bostwick, A. D.; Gebhart, B.; Wolfe, B.; Holtey, A.; Carr, J.; Gordon, A.; Cook, P. J.; Howell, E.; Boltax, J. P. (2019). Implementation of an addiction consult protocol improves access to addiction services for patients admitted to a medical intensive care unit. American Journal of Respiratory and Critical Care Medicine. Conference, 199(9), . | No/insufficient mortality data for OAT group |
| 48. | Bouab, O.; Lahmek, P.; Meunier, N.; Aubin, H. J.; Michel, L. (2013). [Maintaining opioid abstinence long after inpatient treatment with opioid substitution in an addictology hospital unit]. Revue Medicale de Bruxelles, 34(3), 132-40. | Cohort not defined as engaging in opioid agonist treatment |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 49. | Bouab, O.; Lahmek, P.; Meunier, N.; Aubin, H. J.; Michel, L. (2013). Opioid abstinence after inpatient opioid substitution treatment withdrawal: A retrospective study. [French]. Revue Medicale de Bruxelles, 34(3), 132-140. | Cohort not defined as engaging in opioid agonist treatment |
| 50. | Boucher, Lisa M.; Bayoumi, Ahmed M.; Mark, Amy E.; Cooper, Curtis; Martin, Alana; Marshall, Zack; Boyd, Rob; Oickle, Pam; Diliso, Nicola; Pineau, Dave; Renaud, Brad; LeBlanc, Sean; Tyndall, Mark; Lee, Olivia M.; Kendall, Claire E. (2019). Hepatitis C testing, status and treatment among marginalized people who use drugs in an inner city setting: An observational cohort study. Substance use & misuse, 54(1), 18-30. | Cohort not defined as engaging in opioid agonist treatment |
| 51. | Boucherie, Q.; Frauger, E.; Thirion, X.; Mallaret, M.; Micallef, J. (2014). New methadone formulation in france: Results from 5 years of utilization. Therapie, 70(2), 229-234. | Duplicate |
| 52. | Boucherie, Q.; Frauger, E.; Thirion, X.; Mallaret, M.; Micallef, J. (2015). New methadone formulation in France: results from 5 years of utilization. Therapie, 70(2), 223-34. | No/insufficient mortality data for OAT group |
| 53. | Boyd, J.; Randell, T.; Luurila, H.; Kuisma, M. (2003). Serious overdoses involving buprenorphine in Helsinki. Acta Anaesthesiologica Scandinavica, 47(8), 1031-3. | Case reports/case series of drug-related deaths |
| 54. | Boyle, A.; Marra, F.; Peters, E.; Heydtmann, M.; Cairns, H.; Datta, S.; Barclay, S. (2018). 8 weeks sofosbuvir/velpatasvir in genotype 3 patients with significant fibrosis: Highly effective amongst an OST cohort. Journal of Hepatology, 68 (Supplement 1)(), S20. | No in/out treatment data available |
| 55. | Bozinoff, N.; DeBeck, K.; Milloy, M. J.; Nosova, E.; Fairbairn, N.; Wood, E.; Hayashi, K. (2018). Utilization of opioid agonist therapy among incarcerated persons with opioid use disorder in Vancouver, Canada. Drug & Alcohol Dependence, 19342-47. | No/insufficient mortality data for OAT group |
| 56. | Braback, Martin; Ekstrom, Lars; Troberg, Katja; Nilsson, Suzan; Isendahl, Pernilla; Bradvik, Louise; Hakansson, Anders (2017). Malmo treatment referral and intervention study-High 12-month retention rates in patients referred from syringe exchange to methadone or buprenorphine/naloxone treatment. Frontiers in Psychiatry Vol 8 2017, ArtID 161, 8. | No/insufficient mortality data for OAT group |
| 57. | Brennan, L. V. (2019). Medication for opioid use disorder after nonfatal opioid overdose and mortality. Annals of Internal Medicine, 170(6), 430. | No original data |
| 58. | Brett, J.; Wylie, C. E.; Raubenheimer, J.; Isbister, G. K.; Buckley, N. A. (2019). The relative lethal toxicity of pharmaceutical and illicit substances: A 16-year study of the Greater Newcastle Hunter Area, Australia. British Journal of Clinical Pharmacology, 85(9), 2098-2107. | Cohort not defined as engaging in opioid agonist treatment |
| 59. | Brinkley-Rubinstein, L.; McKenzie, M.; Macmadu, A.; Larney, S.; Zaller, N.; Dauria, E.; Rich, J. (2018). A randomized, open label trial of methadone continuation versus forced withdrawal in a combined US prison and jail: Findings at 12 months post-release. Drug & Alcohol Dependence, 18457-63. | No/insufficient mortality data for OAT group |
| 60. | Britton, P. C.; Wines Jr, J. D.; Conner, K. R. (2010). Non-fatal overdose in the 12 months following treatment for substance use disorders. Drug and Alcohol Dependence, 107(1), 51-55. | No/insufficient mortality data for OAT group |
| 61. | Bronstein, A. C.; Spyker, D. A. (2010). National poison data system: Methadone exposures 2000-2008. Clinical Toxicology, 48 (3)261. | Case reports/case series of drug-related deaths |
| 62. | Brown, Sandra A.; D'Amico, Elizabeth J.; McCarthy, Denis M.; Tapert, Susan F. (2001). Four-year outcomes from adolescent alcohol and drug treatment. Journal of Studies on Alcohol, 62(3), 381-388. | Cohort not defined as engaging in opioid agonist treatment |
| 63. | Brugal, M.; Domingo-Salvany, A.; Puig, R.; Barrio, G.; de Olalla, P.; de la Fuente, L. (2005). Evaluating the impact of methadone maintenance programmes on mortality due to overdose and AIDS in a cohort of heroin users in Spain. Addiction, 100(7), 981-989. | No in/out treatment data available |
| 64. | Brugal, M.; Molist, Gemma; Sarasa-Renedo, Ana; de la Fuente, Luis; Espelt, Albert; Mesias, Beatriz; Puerta, Carmen; Guitart, Anna M.; Barrio, Gregorio (2016). Assessing gender disparities in excess mortality of heroin or cocaine users compared to the general population. International Journal of Drug Policy, 3836-42. | Cohort not defined as engaging in opioid agonist treatment |
| 65. | Brunet, L.; Moodie, E.; Cox, J.; Gill, J.; Cooper, C.; Walmsley, S.; Rachlis, A.; Hull, M.; Klein, M.; Cohen, J.; Conway, B.; Cote, P.; Haider, S.; Sadr, A.; Johnston, L.; Montaner, J.; Pick, N.; Rouleau, D.; Sandre, R.; Tyndall, J. M.; Vachon, M. L.; Sanche, S.; Skinner, S.; Wong, D. (2016). Opioid use and risk of liver fibrosis in HIV/hepatitis C virus-coinfected patients in Canada. HIV Medicine, 17(1), 36-45. | Cohort not defined as engaging in opioid agonist treatment |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 66. | Bruno, T.; Pharr, J. R. (2017). Retrospective case series analysis of characteristics and trends in unintentional pharmaceutical drug poisoning by methadone, opioid analgesics, antidepressants and benzodiazepines in Clark County, NV 2009-13. Journal of Public Health, 39(2), 304-311. | Case reports/case series of drug-related deaths |
| 67. | Bucknall, A. B. V.; Robertson, J. R. (1986). Deaths of heroin users in a general practice population. Journal of the Royal College of General Practitioners, 36(284), 120-122. | No in/out treatment data available |
| 68. | Buhl, L.; Saelan, H.; Sorensen, T. M. (2004). Adverse events due to change in organization of problem drug users' treatment?. Scandinavian journal of public health, 32(2), 130-5. | No in/out treatment data available |
| 69. | Bukten, A.; Roislien, J.; Skurtveit, S.; Waal, H.; Gossop, M.; Clausen, T. (2013). A day-by-day investigation of changes in criminal convictions before and after entering and leaving opioid maintenance treatment: A national cohort study. BMC Psychiatry, 13 (no pagination)(262), . | No/insufficient mortality data for OAT group |
| 70. | Bukten, Anne; Stavseth, Marianne Riksheim; Skurtveit, Svetlana; Tverdal, Aage; Strang, John; Clausen, Thomas (2017). High risk of overdose death following release from prison: Variations in mortality during a 15-year observation period. Addiction, 112(8), 1432-1439. | Cohort not defined as engaging in opioid agonist treatment |
| 71. | Bunn, T. L.; Yu, L.; Spiller, H. A.; Singleton, M. (2010). Surveillance of methadone-related poisonings in Kentucky using multiple data sources. Pharmacoepidemiology & Drug Safety, 19(2), 124-31. | Cohort not defined as engaging in opioid agonist treatment |
| 72. | Burke, L. G.; Zhou, X.; Boyle, K.; Orav, E. J.; Bernson, D.; Hood, M. E.; Land, T.; Frakt, A. (2018). Association between opioid prescribing and opioid use disorder and overdose among opioid naive individuals. Academic Emergency Medicine, 25 (Supplement 1)S25-S26. | Abstract - full text available |
| 73. | Burke, L. G.; Zhou, X.; Boyle, K. L.; Orav, E. J.; Bernson, D.; Hood, M. E.; Land, T.; Bharel, M.; Frakt, A. B. (2019). Trends in Opioid Use Disorder and overdose among opioid-naive individuals receiving an opioid prescription in Massachusetts from 2011-2014. Addiction, 6. | Cohort not defined as engaging in opioid agonist treatment |
| 74. | Burns, Lucy; Gisev, Natasa; Larney, Sarah; Dobbins, Timothy; Gibson, Amy; Kimber, Jo; Larance, Briony; Mattick, Richard P.; Butler, Tony; Degenhardt, Louisa (2015). A longitudinal comparison of retention in buprenorphine and methadone treatment for opioid dependence in New South Wales, Australia. Addiction, 110(4), 646-655. | No/insufficient mortality data for OAT group |
| 75. | Butler, Bethany; Rubin, George; Lawrance, Anne; Batey, Robert; Bell, James (2011). Estimating the risk of fatal arrhythmia in patients in methadone maintenance treatment for heroin addiction. Drug and alcohol review, 30(2), 173-180. | Case reports/case series of drug-related deaths |
| 76. | Byrne, Andrew (2000). Nine-year follow-up of 86 consecutive patients treated with methadone in general practice, Sydney, Australia. Drug and alcohol review, 19(2), 153-158. | No/insufficient mortality data for OAT group |
| 77. | Calcaterra, S.; Glanz, J.; Binswanger, I. A. (2013). National trends in pharmaceutical opioid related overdose deaths compared to other substance related overdose deaths: 1999-2009. Drug and Alcohol Dependence, 131(3), 263-270. | Case reports/case series of drug-related deaths |
| 78. | Callaghan, Russell C.; Cunningham, James K.; Verdichevski, Marina; Sykes, Jenna; Jaffer, Sukaina R.; Kish, Stephen J. (2012). All-cause mortality among individuals with disorders related to the use of methamphetamine: A comparative cohort study. Drug and Alcohol Dependence, 125(3), 290-294. | Cohort not defined as engaging in opioid agonist treatment |
| 79. | Cao, X.; Wu, Z.; Li, L.; Pang, L.; Rou, K.; Wang, C.; Luo, W.; Yin, W.; Li, J.; McGoogan, J. M. (2013). Mortality among methadone maintenance clients in China: A six-year cohort study. PLoS ONE, 8 (12) (no pagination)(e82476), . | No in/out treatment data available |
| 80. | Cao, X.; Wu, Z.; Li, L.; Pang, L.; Rou, K.; Wang, C.; Luo, W.; Yin, W.; Li, J.; McGoogan, J. M.; National Methadone Maintenance Treatment Program Working, Group (2013). Mortality among methadone maintenance clients in China: a six-year cohort study. PLoS ONE [Electronic Resource], 8(12), e82476. | Duplicate |
| 81. | Cao, T.; Nguyen, T.; Nguyen, H.; Nguyen, D.; Boeke, C. E.; Sacks, J.; Tebor, J.; Ramers, C.; Van Kinh, N. (2018). Preliminary cure rates from the national HCV pilot program in Vietnam. Journal of Viral Hepatitis, 25 (Supplement 2)143. | Cohort not defined as engaging in opioid agonist treatment |
| 82. | Caplehorn, J. R. M. (1996). Risk factors for non-HIV-related death among methadone maintenance patients. European Addiction Research, 2(1), 49-52. | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 83. | Caplehorn, John R. (1998). Deaths in the first two weeks of maintenance treatment in NSW in 1994: Identifying cases of iatrogenic methadone toxicity. Drug and alcohol review, 17(1), 42979. | No in/out treatment data available |
| 84. | Carreno, J. E.; Bobes, J.; Brewer, C.; Alvarez, C. E.; San Narciso, G. I.; Bascaran, M. T.; Sanchez del Rio, J. (2002). 24-Hour opiate detoxification and antagonist induction at home--the 'Asturian method': a report on 1368 procedures. Addiction Biology, 7(2), 243-50. | Cohort not defined as engaging in opioid agonist treatment |
| 85. | Carter, J. A.; Dammerman, R.; Tiberg, F.; Jensen, R. (2017). Cost-effectiveness of long acting injectable buprenorphine versus sublingual buprenorphine to treat opioid use disorder in sweden and the united kingdom. Value in Health, 20 (5)A304. | No original data |
| 86. | Carter, J.; Zevin, B.; Lum, P. J. (2019). Low barrier buprenorphine treatment for persons experiencing homelessness and injecting heroin in San Francisco. Addiction science & clinical practice, 14(1), 20. | No in/out treatment data available |
| 87. | Caudarella, A.; Dong, H.; Milloy, M. J.; Kerr, T.; Wood, E.; Hayashi, K. (2016). Non-fatal overdose as a risk factor for subsequent fatal overdose among people who inject drugs. Drug and Alcohol Dependence, 16251-55. | No in/out treatment data available |
| 88. | Cerovecki, V.; Tiljak, H.; Adzic, Z. O.; Krizmaric, M.; Pregelj, P.; Kastelic, A. (2013). Risk factors for fatal outcome in patients with opioid dependence treated with methadone in a family medicine setting in Croatia. Croatian Medical Journal, 54(1), 42-48. | No in/out treatment data available |
| 89. | Chang, K. C.; Chen, C. Y.; Wang, J. D.; Lu, T. H. (2015). Estimation of life expectancy and the expected years of life loss among heroin users in the era of opiate substitution treatment in Taiwan. Drug and Alcohol Dependence, 156e41. | Abstract - full text available |
| 90. | Chang, K. C.; Wang, J. D.; Saxon, A.; Matthews, A. G.; Woody, G.; Hser, Y. I. (2017). Causes of death and expected years of life lost among treated opioid-dependent individuals in the United States and Taiwan. International Journal of Drug Policy, 4343983. | No in/out treatment data available |
| 91. | Chang, Kun-Chia; Lee, Kuan-Ying; Lu, Tsung-Hsueh; Hwang, Jing-Shiang; Lin, Chia-Ni; Ting, Shuo-Yen; Chang, Chih-Cheng; Wang, Jung-Der (2019). Opioid agonist treatment reduces losses in quality of life and quality-adjusted life expectancy in heroin users: Evidence from real world data. Drug and Alcohol Dependence, 201197-204. | No in/out treatment data available |
| 92. | Chappel, J. N.; Mays, V. M.; Senay, E. C. (1973). Death and the treatment of drug addiction: a five year study of deaths occurring to members of the Illinois Drug Abuse Program. Proceedings - National Conference on Methadone Treatment, 1530-7. | No in/out treatment data available |
| 93. | Chatterjee, Avik; Larochelle, Marc R.; Xuan, Ziming; Wang, Na; Bernson, Dana; Silverstein, Michael; Hadland, Scott E.; Land, Thomas; Samet, Jeffrey H.; Walley, Alexander Y.; Bagley, Sarah M. (2019). Non-fatal opioid-related overdoses among adolescents in Massachusetts 2012-2014. Drug and Alcohol Dependence, 19428-31. | Cohort not defined as engaging in opioid agonist treatment |
| 94. | Chen, A.; Xia, Y. H.; Chen, W.; Ling, L.; Tan, W. K.; Zheng, R. J. (2009). [Predictors of retention related factors at the initial methadone maintenance treatment clinics in Guangdong province]. Chung-Hua Liu Hsing Ping Hsueh Tsa Chih Chinese Journal of Epidemiology, 30(12), 1230-3. | No/insufficient mortality data for OAT group |
| 95. | Chen, A.; Xia, Y. H.; Chen, W.; Ling, L.; Tan, W. K.; Zheng, R. J. (2009). [Predictors of retention related factors at the initial methadone maintenance treatment clinics in Guangdong province]. [Chinese]. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi, 30(12), 1230-1233. | Duplicate |
| 96. | Chen, Y.; Song, X.; Yao, Y.; Huang, I.; An, Z.; Yuan, J.; Xumg, H.; Liu, Y.; Zhang, Y. (2019). Mortality and influencing factors on injecting drug users with HIV/AIDS in Guizhou province, 1996-2015. [Chinese]. Chinese Journal of Endemiology, 40(7), 765-769. | No in/out treatment data available |
| 97. | Chen, Y.; Song, X. T.; Yao, Y. M.; Huang, L.; An, Z.; Yuan, J.; Xiong, B.; Liu, Y. H.; Zhang, Y. Q. (2019). [Mortality and influencing factors on injecting drug users with HIV/AIDS in Guizhou province, 1996-2015]. Chung-Hua Liu Hsing Ping Hsueh Tsa Chih Chinese Journal of Epidemiology, 40(7), 765-769. | Duplicate |
| 98. | Christensen, P. B.; Hammerby, E.; Smith, E.; Bird, S. (2006). Mortality among Danish drug users released from prison. International journal of prisoner health, 2(1), 13-19. | Cohort not defined as engaging in opioid agonist treatment |

| Excluded reference | | Exclusion Reason |
|---|---|---|
| 99. | Christoffersen, P. J.; Boesen, K.; Drenck, N. E. (1985). Deaths among patients discharged after acute drug and alcohol poisoning. A follow-up investigation of 615 patients discharged from the Municipal Hospital in Copenhagen in 1980. [Danish]. Ugeskrift for Laeger, 147(13), 1133-1137. | Cohort not defined as engaging in opioid agonist treatment |
| 100. | Clausen, T.; Asland, R.; Kristensen, O. (2014). Patients who terminate OMT--how do they fare?. Tidsskrift for den Norske Laegeforening, 134(11), 1146-50. | No in/out treatment data available |
| 101. | Cottrell, David; Childs-Clarke, Adrian; Ghodse, A. (1985). British opiate addicts: An 11-year follow-up. The British Journal of Psychiatry, 146448-450. | Cohort not defined as engaging in opioid agonist treatment |
| 102. | Cousien, A.; Tran, V. C.; Deuffic-Burban, S.; Jauffret-Roustide, M.; Mabileau, G.; Dhersin, J. S.; Yazdanpanah, Y. (2015). Effectiveness and cost-effectiveness of improvements in harm reduction interventions, a better cascade of care, and treat as prevention of chronic hepatitis C in people who inject drugs (PWID) in France (ANRS 95146). Hepatology, 1)1109A. | No original data |
| 103. | Cousins, G.; Boland, F.; Barry, J.; Lyons, S.; Bennett, K.; Fahey, T. (2016). Retention in Methadone Maintenance Treatment (MMT) in primary care: National cohort study using proportional hazards frailty model for recurrent MMT episodes. Pharmacoepidemiology and Drug Safety, 25 (Supplement 3)228. | No/insufficient mortality data for OAT group |
| 104. | Croxford, S.; Miller, R.; Post, F.; Figueroa, J.; Harrison, I.; Harding, R.; Delpech, V.; Lucas, S.; Dhoot, S.; Sullivan, A. (2018). Cause of death among HIV patients in London in 2016: A retrospective audit. HIV Medicine, 19 (Supplement 2)S130. | Case reports/case series of drug-related deaths |
| 105. | Cruts, Guus; Buster, Marcel; Vicente, Julian; Deerenberg, Ingeborg; Van Laar, Margriet (2008). Estimating the total mortality among problem drug users. Substance use & misuse, 43(5), 733-747. | No in/out treatment data available |
| 106. | Cui, N.; Cao, X. B.; Wang, C. H.; Luo, W.; Pang, L.; Rou, K. M.; Wu, Z. Y. (2013). [Factors associated with overdose-caused mortality of HIV-positive patients who were on methadone maintenance treatment program]. Chung-Hua Liu Hsing Ping Hsueh Tsa Chih Chinese Journal of Epidemiology, 34(10), 961-3. | Case reports/case series of drug-related deaths |
| 107. | Cui, N.; Cao, X.; Wang, C.; Luo, W.; Pang, L.; Rou, K.; Wu, Z. (2013). Factors associated with overdose-caused mortality of HIV-positive patients who were on methadone maintenance treatment program. [Chinese]. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi, 34(10), 961-963. | Duplicate |
| 108. | Cullen, W.; Griffin, S.; Bury, G.; Plunkett, P. K. (2003). Opiate overdose in Dublin [1]. Irish Journal of Medical Science, 172(1), 46. | No/insufficient mortality data for OAT group |
| 109. | Cunningham, E.; Litwin, A. H.; Dalgard, O.; Amin, J.; Powis, J.; Bruneau, J.; Feld, J.; Hellard, M.; Bruggmann, P.; Read, P.; Cooper, C.; Conway, B.; Dunlop, A.; Gane, E.; Fraser, C.; Hajarizadeh, B.; Philippa, M.; Sophie, Q.; Siriragavan, S.; Lacalamita, M.; Dore, G. J.; Grebely, J. (2018). Efficacy and adherence to sofosbuvir and velpatasvir among people with chronic hepatitis C virus infection and recent injection drug use: the SIMPLIFY study. Canadian Liver Journal, 1 (1)49-50. | Cohort not defined as engaging in opioid agonist treatment |
| 110. | Dalgard, O.; Grebely, J.; Conway, B.; Cunningham, E.; Bruggmann, P.; Hajarizadeh, B.; Amin, J.; Marks, P.; Quiene, S.; Applegate, T. L.; Swan, T.; Byrne, J.; Lacalamita, M.; Dunlop, A.; Bruneau, J.; Hellard, M. E.; Matthews, G. V.; Powis, J.; Shaw, D.; Thurnheer, M. C.; Weltman, M.; Kronborg, I.; Cooper, C.; Feld, J. J.; Fraser, C.; Litwin, A.; Dillon, J.; Read, P.; Gane, E.; Dore, G. J. (2018). Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injecting drug use (simplify): An open-label, single-arm, phase 4, multicentre trial. Heroin Addiction and Related Clinical Problems, 20 (Supplement 1)14. | Conference abstract - have full text |
| 111. | Dao, A. T. M.; Nguyen, H. T. T.; Nguyen, L. H. (2018). Variation Overtime among Patients of the Six Methadone Maintenance Treatment Clinics in Thai Nguyen from 2011 to 2015. BioMed Research International, 20189081968. | No in/out treatment data available |
| 112. | Darke, S.; Ross, J.; Williamson, A.; Teesson, M. (2005). The impact of borderline personality disorder on 12-month outcomes for the treatment of heroin dependence. Addiction, 100(8), 1121-1130. | No/insufficient mortality data for OAT group |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 113. | Darke, S.; Ross, J.; Teesson, M. (2007). The Australian Treatment Outcome Study (ATOS): what have we learnt about treatment for heroin dependence?. Drug & Alcohol Review, 26(1), 49-54. | No original data |
| 114. | Darke, Shane; Mills, Katherine L.; Ross, Joanne; Teesson, Maree (2011). Rates and correlates of mortality amongst heroin users: Findings from the Australian Treatment Outcome Study (ATOS), 2001-2009. Drug and Alcohol Dependence, 115(3), 190-195. | No in/out treatment data available |
| 115. | Darke, Shane; Marel, Christina; Mills, Katherine L.; Ross, Joanne; Slade, Tim; Tessson, Maree (2016). Years of potential life lost amongst heroin users in the Australian Treatment Outcome Study cohort, 2001-2015. Drug and Alcohol Dependence, 162206-210. | No in/out treatment data available |
| 116. | Darke, S.; Farrell, M.; Duflou, J.; Larance, B.; Lappin, J. (2019). Circumstances of death of opioid users being treated with naltrexone. Addiction (Abingdon, England), 114(11), 2000-2007. | Case reports/case series of drug-related deaths |
| 117. | Dasgupta, N.; Funk, M. J.; Proescholdbell, S.; Hirsch, A.; Ribisl, K. M.; Marshall, S. (2016). Cohort study of the impact of high-dose opioid analgesics on overdose mortality. Pain Medicine (United States), 17(1), 85-98. | Cohort not defined as engaging in opioid agonist treatment |
| 118. | Davison, J. W.; Sweeney, M. L.; Bush, K. R.; Correale, T. M. D.; Calsyn, D. A.; Reoux, J. P.; Sloan, K. L.; Kivlahan, D. R. (2006). Outpatient treatment engagement and abstinence rates following inpatient opioid detoxification. Journal of Addictive Diseases, 25(4), 27-35. | Cohort not defined as engaging in opioid agonist treatment |
| 119. | Davoli, M.; Perucci, C. A.; Forastiere, F.; Doyle, P.; Rapiti, E.; Zaccarelli, M.; Abeni, D. D. (1993). Risk factors for overdose mortality: a case-control study within a cohort of intravenous drug users. International Journal of Epidemiology, 22(2), 273-7. | Cohort not defined as engaging in opioid agonist treatment |
| 120. | Davstad, Ingrid; Stenbacka, Marlene; Leifman, Anders; Romelsjo, Anders (2009). An 18-year follow-up of patients admitted to methadone treatment for the first time. Journal of Addictive Diseases, 28(1), 39-52. | No in/out treatment data available |
| 121. | de Bernardis, E.; Busa, L. (2014). Can the buprenorphine-naloxone association outperform buprenorphine alone?. Heroin Addiction and Related Clinical Problems, 16(1), 63-64. | No original data |
| 122. | de Dios, Marcel A.; Cano, Miguel Angel; Vaughan, Ellen L.; McNeel, Morgan M.; Childress, Sarah; Niaura, Raymond (2019). Nicotine maintenance for smokers in methadone treatment: A new direction. Addiction Research & Theory, 27(4), 269-276. | No original data |
| 123. | Degenhardt, L.; Larney, S.; Kimber, J.; Gisev, N.; Farrell, M.; Dobbins, T.; Weatherburn, D. J.; Gibson, A.; Mattick, R.; Butler, T.; Burns, L. (2014). The impact of opioid substitution therapy on mortality post-release from prison: A retrospective data linkage study. Pharmacoepidemiology and Drug Safety, 1)346. | Abstract - full text available |
| 124. | Degenhardt, Louisa; Larney, Sarah; Randall, Deborah; Burns, Lucy; Hall, Wayne (2014). Causes of death in a cohort treated for opioid dependence between 1985 and 2005. Addiction, 109(1), 90-99. | No in/out treatment data available |
| 125. | Degenhardt, L.; Larney, S.; Kimber, J.; Gisev, N.; Farrell, M.; Dobbins, T.; Weatherburn, D. J.; Gibson, A.; Mattick, R.; Butler, T.; Burns, L. (2015). The impact of opioid substitution therapy on mortality post-release from prison. Drug and Alcohol Dependence, 146e260. | Abstract - full text available |
| 126. | De Giovanni, N.; Fucci, N. (2013). The role of methadone in fatalities. Forensic Toxicology, 31(2), 347-350. | Case reports/case series of drug-related deaths |
| 127. | De Gottardi, A.; Hilleret, M.; Gelez, P.; La Mura, V.; Guillaud, O.; Majno, P.; Hadengue, A.; Morel, P.; Zarski, J.; Fontana, M.; Moradpour, D.; Mentha, G.; Boillot, O.; Leroy, V.; Giostra, E.; Dumortier, J. (2010). Injection drug use before and after liver transplantation: A retrospective multicenter analysis on incidence and outcome. Clinical Transplantation, 24(4), 564-571. | Cohort with less than 30 individuals |
| 128. | Deheul, S.; Plancke, L.; Bordet, R.; Gautier, S. (2011). Is the mortality of drug users in France under-estimated? A survey of the nord-pas de Calais region. Fundamental and Clinical Pharmacology, 1)44. | Case reports/case series of drug-related deaths |
| 129. | de la Fuente, Luis; Molist, Gemma; Espelt, Albert; Barrio, Gregorio; Guitart, Anna; Bravo, Maria J.; Brugal, M. (2014). Mortality risk factors and excess mortality in a cohort of cocaine users admitted to drug treatment in Spain. Journal of Substance Abuse Treatment, 46(2), 219-226. | Cohort not defined as engaging in opioid agonist treatment |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 130. | DeLorenze, Gerald N.; Weisner, Constance; Tsai, Ai-Lin; Satre, Derek D.; Quesenberry, Charles P., Jr. (2011). Excess mortality among HIV-infected patients diagnosed with substance use dependence or abuse receiving care in a fully integrated medical care program. Alcoholism: Clinical and Experimental Research, 35(2), 203-210. | Cohort not defined as engaging in opioid agonist treatment |
| 131. | Delorme, J.; Chenaf, C.; Kabore, J. L.; Pereira, B.; Mulliez, A.; Tremey, A.; Brousse, G.; Zenut, M.; Laporte, C.; Authier, N. (2016). Incidence of high dosage buprenorphine and methadone shopping behavior in a retrospective cohort of opioid-maintained patients in France. Drug & Alcohol Dependence, 16299-106. | No in/out treatment data available |
| 132. | Desai, N. (2012). Review of six years of buprenorphine treatment in an addiction program. American Journal on Addictions, 21 (4)392-393. | No in/out treatment data available |
| 133. | Des Jarlais, D. C.; Friedman, S. R.; Sotheran, J. L.; Wenston, J.; Marmor, M.; Yancovitz, S. R.; Frank, B.; Beatrice, S.; Mildvan, D. (1994). Continuity and change within an HIV epidemic. Injecting drug users in New York City, 1984 through 1992. JAMA, 271(2), 121-7. | Cohort not defined as engaging in opioid agonist treatment |
| 134. | Devlin, J.; Duprey, M.; Roberts, R.; Jacobson, J.; Wakeman, S.; Moreno, J. (2018). Epidemiology, opioid exposure, and outcomes for ICU patients admitted with known opioid use disorder. Critical Care Medicine, 46 (Supplement 1)214. | No/insufficient mortality data for OAT group |
| 135. | Dines, A. M.; Dargan, P. I.; Archer, J. R. H.; Hovda, K. E.; Heyerdahl, F.; Yates, C.; Giraudon, I.; Wood, D. M. (2017). Patterns of use of licensed medicines in Emergency Department acute recreational drug toxicity presentations reported to the European Drug Emergencies Network Plus (Euro-DEN Plus). Clinical Toxicology, 55 (5)450. | Cohort not defined as engaging in opioid agonist treatment |
| 136. | Dooley, J.; Gerber-Finn, L.; Antone, I.; Guilfoyle, J.; Blakelock, B.; Balfour-Boehm, J.; Hopman, W. M.; Jumah, N.; Kelly, L. (2016). Buprenorphine-naloxone use in pregnancy for treatment of opioid dependence: Retrospective cohort study of 30 patients. Canadian Family Physician, 62(4), e194-e200. | No/insufficient mortality data for OAT group |
| 137. | D'Orban, P. T. (1973). Female narcotic addicts: a follow-up study of criminal and addiction careers. British Medical Journal, 4(5888), 345-7. | Cohort not defined as engaging in opioid agonist treatment |
| 138. | d' Orban, P. T. (1974). A follow-up study of female narcotic addicts: variables related to outcome. The British journal of psychiatry : the journal of mental science, 125(0), 28-33. | Cohort not defined as engaging in opioid agonist treatment |
| 139. | D'Orban, P. (1974). A follow-up study of female narcotic addicts: Variables related to outcome. The British Journal of Psychiatry, 12528-33. | Cohort not defined as engaging in opioid agonist treatment |
| 140. | Druce, H.; Lowrie, R.; Ritchie, C.; Morrison, D.; Sainsbury, C. A. R.; Jones, G. C. (2017). Diabetes and opiate replacement therapy (ORT): A retrospective cohort study of health care usage and clinical outcomes. Diabetologia, 60 (1 Supplement 1)S345. | No in/out treatment data available |
| 141. | Duburque, C.; Canva, V.; Auriacombe, M.; Djomboue, P.; Hernout, B.; Lucidarme, D.; Harbonnier, J. (2015). A 3 year follow-up of HCV infection in opioid use disorder patients in treatment. Drug and Alcohol Dependence, 156e60. | No in/out treatment data available |
| 142. | Dundas, P.; English, S.; Bailey, L.; Mukhopadhya, A.; Vijayan, B.; Fraser, A.; McLeman, L. (2015). Real life experience of direct acting anti-viral therapy for hepatitis C infection in north east of Scotland. Hepatology, 1)753A. | No in/out treatment data available |
| 143. | Dvoriak, Sergii; Karachevsky, Andrey; Chhatre, Sumedha; Booth, Robert; Metzger, David; Schumacher, Joseph; Chychula, Nina; Pecoraro, Anna; Woody, George (2014). Methadone maintenance for HIV positive and HIV negative patients in Kyiv: Acceptability and treatment response. Drug and Alcohol Dependence, 13762-67. | No in/out treatment data available |
| 144. | Eastwood, B.; Strang, J.; Marsden, J. (2017). Effectiveness of treatment for opioid use disorder: A national, five-year, prospective, observational study in England. Drug & Alcohol Dependence, 176139-147. | No/insufficient mortality data for OAT group |
| 145. | Eibl, Joseph K.; Gomes, Tara; Martins, Diana; Camacho, Ximena; Juurlink, David N.; Mamdani, Muhammad M.; Dhalla, Irfan A.; Marsh, David C. (2015). Evaluating the effectiveness of first-time methadone maintenance therapy across Northern, Rural, and Urban regions of Ontario, Canada. Journal of Addiction Medicine, 9(6), 440-446. | No in/out treatment data available |
| 146. | Eibl, J. K.; Wilton, A. S.; Franklyn, A. M.; Kurdyak, P.; Marsh, D. C. (2019). Evaluating the Impact of Prescribed Versus Nonprescribed Benzodiazepine Use in Methadone | No/insufficient mortality data for OAT group |

| Excluded reference | | Exclusion Reason |
|---|---|---|
| | Maintenance Therapy: Results From a Population-based Retrospective Cohort Study. Journal of Addiction Medicine, 13(3), 182-187. | |
| 147. | Elias, H. (1990). Treatment of drug dependence by substitution in the doctor's office. [German]. Fortschritte der Medizin, 108(13), 50-54. | No in/out treatment data available |
| 148. | Elias, H. (1990). [Substitute drug-assisted treatment of drug dependent patients in general practice]. Fortschritte der Medizin, 108(13), 256-8. | Duplicate |
| 149. | Elias, H. (1990). Substitute drug-assisted treatment of drug dependent patients in general practice. [German]. Fortschritte der Medizin, 108(13), 256-258. | Duplicate |
| 150. | Elmer, J.; Lynch, M. J.; Kristan, J.; Morgan, P.; Gerstel, S. J.; Callaway, C. W.; Rittenberger, J. C.; Dezfulian, C.; Doshi, A. A.; Guyette, F. X. (2015). Recreational drug overdose-related cardiac arrests: Break on through to the other side. Resuscitation, 89(C), 177-181. | Case reports/case series of drug-related deaths |
| 151. | Emmanuelli, Julien; Desenclos, Jean-Claude (2005). Harm reduction interventions, behaviours and associated health outcomes in France, 1996-2003. Addiction, 100(11), 1690-1700. | No original data |
| 152. | Ernst, E.; Bartu, A.; Popescu, A.; Ileutt, K. F.; Hansson, R.; Plumley, N. (2002). Methadone-related deaths in Western Australia 1993-99. Australian & New Zealand Journal of Public Health, 26(4), 364-70. | Case reports/case series of drug-related deaths |
| 153. | Esteban, J., Gimeno, C., Barril, J., Aragonés, A., Climent, J. M., & de la Cruz Pellín, M. (2003). Survival study of opioid addicts in relation to its adherence to methadone maintenance treatment. *Drug and alcohol dependence*, *70*(2), 193–200. https://doi.org/10.1016/s0376-8716(03)00002-4 | No in/out treatment data available |
| 154. | Ettner, Susan L.; Huang, David; Evans, Elizabeth; Ash, Danielle Rose; Hardy, Mary; Jourabchi, Mickel; Hser, Yih-Ing (2006). Benefit-Cost in the California Treatment Outcome Project: Does Substance Abuse Treatment "Pay for Itself"?. Health Services Research, 41(1), 192-213. | No/insufficient mortality data for OAT group |
| 155. | Evans, E.; Kelleghan, A.; Li, L.; Min, J.; Huang, D.; Urada, D.; Hser, Y. I.; Nosyk, B. (2015). Gender differences in mortality among treated opioid dependent patients. Drug and Alcohol Dependence, 155228-235. | No in/out treatment data available |
| 156. | Fang, S. Y.; Huang, N.; Tsay, J. H.; Chang, S. H.; Chen, C. Y. (2018). Excess mortality in children born to opioid-addicted parents: A national register study in Taiwan. Drug & Alcohol Dependence, 183118-126. | Cohort not the primary client of treatment (e.g., neonatal/perinatal) |
| 157. | Fareed, Ayman; Casarella, Jennifer; Amar, Richard; Vayalapalli, Sreedevi; Drexler, Karen (2009). Benefits of retention in methadone maintenance and chronic medical conditions as risk factors for premature death among older heroin addicts. Journal of Psychiatric Practice, 15(3), 227-234. | No in/out treatment data available |
| 158. | Fareed, Ayman; Vayalapalli, Sreedevi; Byrd-Sellers, Johnita; Casarella, Jennifer; Drexler, Karen (2011). Safety and efficacy of long-term buprenorphine maintenance treatment. Addictive Disorders & Their Treatment, 10(3), 123-130. | No in/out treatment data available |
| 159. | Fareed, Ayman; Vayalapalli, Sreedevi; Scheinberg, Kelly; Gale, Robin; Casarella, Jennifer; Drexler, Karen (2013). QTc interval prolongation for patients in methadone maintenance treatment: A five years follow-up study. The American journal of drug and alcohol abuse, 39(4), 235-240. | No in/out treatment data available |
| 160. | Fareed, A.; Patil, D.; Scheinberg, K.; Blackinton Gale, R.; Vayalapalli, S.; Casarella, J.; Drexler, K. (2013). Comparison of QTc interval prolongation for patients in methadone versus buprenorphine maintenance treatment: a 5-year follow-up. Journal of Addictive Diseases, 32(3), 244-51. | No in/out treatment data available |
| 161. | Farrell, Michael; Marsden, John (2008). Acute risk of drug-related death among newly released prisoners in England and Wales. Addiction, 103(2), 251-255. | Cohort not defined as engaging in opioid agonist treatment |
| 162. | Farsi, D.; Mirafzal, A.; Hassanian-Moghaddam, H.; Azizi, Z.; Jamshidnejad, N.; Zehtabchi, S. (2014). The correlation between prolonged corrected QT interval with the frequency of respiratory arrest, endotracheal intubation, and mortality in acute methadone overdose. Cardiovascular Toxicology, 14(4), 358-67. | Case reports/case series of drug-related deaths |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 163. | Faul, M.; Bohm, M.; Alexander, C. (2017). Methadone Prescribing and Overdose and the Association with Medicaid Preferred Drug List Policies - United States, 2007-2014. MMWR - Morbidity & Mortality Weekly Report, 66(12), 320-323. | Cohort not defined as engaging in opioid agonist treatment |
| 164. | Favrod-Coune, T.; Baroudi, M.; Casillas, A.; Rieder, J. P.; Getaz, L.; Barro, J.; Gaspoz, J. M.; Broers, B.; Wolff, H. (2013). Opioid substitution treatment in pretrial prison detention: a case study from Geneva, Switzerland. Swiss Medical Weekly, 143w13898. | No/insufficient mortality data for OAT group |
| 165. | Ferri, M.; Bargagli, A. M.; Faggiano, F.; Belleudi, V.; Salamina, G.; Vigna-Taglianti, F.; Davoli, M.; Perucci, C. A. (2007). Mortality of drug users attending public treatment centers in Italy 1998-2001: a cohort study. [Italian]. Epidemiologia e prevenzione, 31(5), 276-282. | No in/out treatment data available |
| 166. | Ferri, M.; Bargagli, A. M.; Faggiano, F.; Belleudi, V.; Salamina, G.; Vigna-Taglianti, F.; Davoli, M.; Perucci, C. A.; Gruppo di studio, VEdeTTE (2007). [Mortality of drug users attending public treatment centers in Italy 1998-2001: a cohort study]. Epidemiologia e prevenzione, 31(5), 276-82. | Duplicate |
| 167. | Fhima, A.; Henrion, R.; Lowenstein, W.; Charpak, Y. (2001). Two-year follow-up of an opioid-user cohort treated with high-dose buprenorphine (Subutex). Results of the SPESUB study. [French]. Annales de Medecine Interne, 152(3 SUPPL.), 1S26-1S36. | No in/out treatment data available |
| 168. | Fhima, A.; Henrion, R.; Lowenstein, W.; Charpak, Y. (2001). Two-year follow-up of an opioid-user cohort treated with high-dose buprenorphine (Subutex). [French]. Annales de Medecine Interne, 152 Suppl 3IS26-36. | Duplicate |
| 169. | Fhima, A.; Henrion, R.; Lowenstein, W.; Charpak, Y. (2001). [Two-year follow-up of an opioid-user cohort treated with high-dose buprenorphine (Subutex)]. Annales de Medecine Interne, 152 Suppl 3IS26-36. | Duplicate |
| 170. | Filippovych, S.; Burgay, O. (2015). Development of treatment model for HIV/HCV co-infected OST patients as the basis for scaling up access to HCV treatment for key populations in Ukraine. Journal of Viral Hepatitis, 2)89. | No in/out treatment data available |
| 171. | Fine, D. R.; Chang, Y.; Triant, V.; Baggett, T. P.; Metlay, J. (2019). Predictors of mortality in patients treated with buprenorphine for opioid use disorder. Journal of General Internal Medicine, 34 (2 Supplement)S322. | Abstract - full text available |
| 172. | Fischer, Benedikt; Rehm, Jurgen; Patra, Jayadeep; Cruz, Michelle Firestone (2006). Changes in illicit opioid use across Canada. Canadian Medical Association Journal, 175(11), 1385-1387. | Cohort not defined as engaging in opioid agonist treatment |
| 173. | Fogh, K. (2010). Leg ulcers in intravenous drug addicts: Clinical characteristics, complications and challenges. Wound Repair and Regeneration, 18 (2)A45. | Cohort not defined as engaging in opioid agonist treatment |
| 174. | Fox, Lindsay M.; Hoffman, Robert S.; Vlahov, David; Manini, Alex F. (2018). Risk factors for severe respiratory depression from prescription opioid overdose. Addiction, 113(1), 59-66. | Case reports/case series of drug-related deaths |
| 175. | Franklyn, Alexandra M.; Eibl, Joseph K.; Gauthier, Graham; Pellegrini, David; Lightfoot, Nancy E.; Marsh, David C. (2017). The impact of benzodiazepine use in patients enrolled in opioid agonist therapy in Northern and rural Ontario. Harm Reduction Journal Vol 14 2017, ArtID 6, 14. | No/insufficient mortality data for OAT group |
| 176. | Fridell, Mats; Hesse, M. (2006). Psychiatric severity and mortality in substance abusers a 15-year follow-up of drug users. Addictive Behaviors, 31(4), 559-565. | Cohort not defined as engaging in opioid agonist treatment |
| 177. | Friedmann, P. D.; Wilson, D.; Hoskinson, R., Jr.; Poshkus, M.; Clarke, J. G. (2018). Initiation of extended release naltrexone (XR-NTX) for opioid use disorder prior to release from prison. Journal of Substance Abuse Treatment, 8545-48. | Cohort not defined as engaging in opioid agonist treatment |
| 178. | Fugelstad, Anna; Annell, A.; Rajs, J.; Agren, G. (1997). Mortality and causes and manner of death among drug addicts in Stockholm during the period 1981-1992. Acta Psychiatrica Scandinavica, 96(3), 169-175. | No in/out treatment data available |
| 179. | Fugelstad, Anna; Thiblin, Ingmar; Johansson, Lars Age; Agren, Gunnar; Sidorchuk, Anna (2019). Opioid-related deaths and previous care for drug use and pain relief in Sweden. Drug and Alcohol Dependence, 201253-259. | Case reports/case series of drug-related deaths |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 180. | Fulton-Kehoe, D.; Sullivan, M.; Turner, J.; Garg, R.; Bauer, A.; Wickizer, T.; Franklin, G. (2015). Opioid poisonings in Washington state medicaid: Trends, dosing, and guidelines. Journal of Pain, 1)S83. | Case reports/case series of drug-related deaths |
| 181. | Gao, Lu; Dimitropoulou, Polyxeni; Robertson, J.; McTaggart, Stuart; Bennie, Marion; Bird, Sheila M. (2016). Risk-factors for methadone-specific deaths in Scotland's methadone-prescription clients between 2009 and 2013. Drug and Alcohol Dependence, 167214-223. | No in/out treatment data available |
| 182. | Gao, Lu; Robertson, J.; Bird, Sheila M. (2019). Non drug-related and opioid-specific causes of 3262 deaths in Scotland's methadone-prescription clients, 2009-2015. Drug and Alcohol Dependence, 197262-270. | No in/out treatment data available |
| 183. | Gerlach, K. K.; Veley, K.; Schnoll, S. (2018). Btod rems program surveillance findings: Buprenorphine and benzodiazepine concomitant use. Journal of Addiction Medicine, 12 (3)E4. | Cohort not defined as engaging in opioid agonist treatment |
| 184. | Gertner, Alex K.; Grabert, Brigid; Domino, Marisa Elena; Cuddeback, Gary S.; Morrissey, Joseph P. (2019). The effect of referral to expedited Medicaid on substance use treatment utilization among people with serious mental illness released from prison. Journal of Substance Abuse Treatment, 9942248. | Cohort not defined as engaging in opioid agonist treatment |
| 185. | Gibson, Amy; Randall, Deborah; Degenhardt, Louisa (2011). The increasing mortality burden of liver disease among opioid-dependent people: Cohort study. Addiction, 106(12), 2186-2192. | No in/out treatment data available |
| 186. | Giraudon, Isabelle; Vicente, Julian; Matias, Joao; Mounteney, Jane; Griffiths, Paul (2012). Reducing drug related mortality in Europe - A seemingly intractable public health issue. Adicciones, 24(1), 44046. | No original data |
| 187. | Gisev, N.; Larney, S.; Gibson, A.; Kimber, J.; Burns, L.; Butler, T.; Mattick, R.; Weatherburn, D.; Degenhardt, L. (2015). The effect of treatment and retention with opioid substitution therapy in reducing crime among opioid-dependent people. Pharmacoepidemiology and Drug Safety, 1)28-29. | Abstract - full text available |
| 188. | Gisev, Natasa; Shanahan, Marian; Weatherburn, Don J.; Mattick, Richard P.; Larney, Sarah; Burns, Lucy; Degenhardt, Louisa (2015). A cost-effectiveness analysis of opioid substitution therapy upon prison release in reducing mortality among people with a history of opioid dependence. Addiction, 110(12), 1975-1984. | No in/out treatment data available |
| 189. | Gisev, N.; Shanahan, M.; Weatherburn, D. J.; Mattick, R. P.; Larney, S.; Burns, L.; Degenhardt, L. (2015). A cost-effectiveness analysis of opioid substitution therapy upon release in reducing mortality among prisoners with a history of opioid dependence. Pharmacoepidemiology and Drug Safety, 1)481-482. | Abstract - full text available |
| 190. | Gisev, N.; Bharat, C.; Larney, S.; Dobbins, T.; Weatherburn, D.; Hickman, M.; Farrell, M.; Degenhardt, L. (2019). The effect of entry and retention in opioid agonist treatment on contact with the criminal justice system among opioid-dependent people: a retrospective cohort study. The Lancet Public Health, 4(7), e334-e342. | No in/out treatment data available |
| 191. | Gjersing, L.; Bretteville-Jensen, A. L. (2014). Gender differences in mortality and risk factors in a 13-year cohort study of street-recruited injecting drug users. BMC public health, 14440. | No in/out treatment data available |
| 192. | Gjersing, Linn; Bretteville-Jensen, Anne Line (2015). Are overdoses treated by ambulance services an opportunity for additional interventions? A prospective cohort study. Addiction, 110(11), 1767-1774. | No in/out treatment data available |
| 193. | Gjersing, Linn; Bretteville-Jensen, Anne Line (2018). Patterns of substance use and mortality risk in a cohort of 'hard-to-reach' polysubstance users. Addiction, 113(4), 729-739. | No in/out treatment data available |
| 194. | Gladstone, E. J.; Smolina, K.; Weymann, D.; Rutherford, K.; Morgan, S. G. (2015). Geographic variations in prescription opioid dispensations and deaths among women and men in British Columbia, Canada. Medical Care, 53(11), 954-959. | Case reports/case series of drug-related deaths |
| 195. | Glaizal, M.; Gazin, V.; Aymard, I.; Messina-Gourlot, C.; Richard, N.; Mallaret, M.; Saviuc, P.; de Haro, L. (2012). Suicidal poisonings with methadone in France: results of a two year national survey by the Toxicovigilance network. Clinical Toxicology: The Official Journal of the American Academy of Clinical Toxicology & European Association of Poisons Centres & Clinical Toxicologists, 50(9), 841-6. | Case reports/case series of drug-related deaths |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 196. | Glynn, R. W.; Lynn, E.; Griffin, E.; Fitzgerald, M.; Ward, M. (2017). Self-harm, methadone use and drug-related deaths amongst those registered as being of no fixed abode or homeless in Ireland. Irish Medical Journal, 110(9), 631. | Cohort not defined as engaging in opioid agonist treatment |
| 197. | Goldstein, Avram; Herrera, James (1995). Heroin addicts and methadone treatment in Albuquerque: A 22-year follow-up. Drug and Alcohol Dependence, 40(2), 139-150. | No in/out treatment data available |
| 198. | Golz, J.; Moll, A.; Nzimegne, S.; Klausen, G.; Schleehauf, D. (2001). Comparison of antiretroviral therapy in IVDU and MSM - A retrospective study 1996-2000. Suchtmedizin in Forschung und Praxis, 3(1), 25-33. | No in/out treatment data available |
| 199. | Gordon, Alistair M. (1978). Drugs and delinquency: A four year follow-up of drug clinic patients. The British Journal of Psychiatry, 13221-26. | No in/out treatment data available |
| 200. | Gordon, Alistair M. (1983). Drugs and delinquency: A ten year follow-up of drug clinic patients. The British Journal of Psychiatry, 142169-173. | No in/out treatment data available |
| 201. | Goren, L.; Carmel, Z.; Marchevsky, S. (2014). Buprenorphine for opiate dependence: clinic based therapy in Israel. Israel Journal of Psychiatry & Related Sciences, 51(4), 281-4. | No/insufficient mortality data for OAT group |
| 202. | Gottfredsson, M.; Tyrfngsson, T.; Runarsdottir, V.; Bergmann, O. M.; Bjornsson, E. S.; Johannsson, B.; Sigurdardottir, B.; Fridriksdottir, R. H.; Love, A.; Love, T. J.; Sigmundsdottir, G.; Heimisdottir, M.; Olafsson, S. (2017). Treatment as prevention for hepatitis C (trap hepc). A real-world experience from the first 12 months of a nationwide elimination program in iceland. Open Forum Infectious Diseases, 4 (Supplement 1)S42. | No in/out treatment data available |
| 203. | Graf, S.; Brunner, N.; Falcato, L.; Bruggmann, P. (2013). Causes of death among patients in opioid maintenance treatment and association with HCV infections: A retrospective analysis. Suchtmedizin in Forschung und Praxis, 15 (4)254. | Case reports/case series of drug-related deaths |
| 204. | Grebely, J.; Dalgard, O.; Conway, B.; Cunningham, E.; Bruggmann, P.; Hajarizadeh, B.; Amin, J.; Marks, P.; Quiene, S.; Applegate, T. L.; Swan, T.; Byrne, J.; Lacalamita, M.; Dunlop, A. J.; Bruneau, J.; Hellard, M. E.; Matthews, G. V.; Powis, J.; Shaw, D.; Thurnheer, C. M.; Weltman, M.; Kronborg, I.; Cooper, C.; Feld, J. J.; Fraser, C.; Litwin, A.; Dillon, J.; Read, P.; Gane, E.; Dore, G. J. (2017). Efficacy and safety of sofosbuvir/velpatasvir in people with chronic hepatitis C virus infection and recent injecting drug use: The SIMPLIFY study. Journal of Hepatology, 66 (1 Supplement 1)S513. | Abstract - full text available |
| 205. | Grebely, J.; Dalgard, O.; Conway, B.; Cunningham, E. B.; Bruggmann, P.; Hajarizadeh, B.; Amin, J.; Bruneau, J.; Hellard, M.; Litwin, A. H.; Marks, P.; Quiene, S.; Siriragavan, S.; Applegate, T. L.; Swan, T.; Byrne, J.; Lacalamita, M.; Dunlop, A.; Matthews, G. V.; Powis, J.; Shaw, D.; Thurnheer, M. C.; Weltman, M.; Kronborg, I.; Cooper, C.; Feld, J. J.; Fraser, C.; Dillon, J. F.; Read, P.; Gane, E.; Dore, G. J.; Simplify Study Group (2018). Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY): an open-label, single-arm, phase 4, multicentre trial. The Lancet. Gastroenterology & Hepatology, 3(3), 153-161. | No/insufficient mortality data for OAT group |
| 206. | Grebely, J.; Conway, B.; Cunningham, E. B.; Fraser, C.; Moriggia, A.; Gane, E.; Stedman, C.; Cooper, C.; Castro, E.; Schmid, P.; Petoumenos, K.; Hajarizadeh, B.; Marks, P.; Erratt, A.; Dalgard, O.; Lacombe, K.; Feld, J. J.; Bruneau, J.; Daulouede, J. P.; Powis, J.; Bruggmann, P.; Matthews, G. V.; Kronborg, I.; Shaw, D.; Dunlop, A.; Hellard, M.; Applegate, T. L.; Crawford, S.; Dore, G. J.; D. Feat Study Group (2018). Paritaprevir, ritonavir, ombitasvir, and dasabuvir with and without ribavirin in people with HCV genotype 1 and recent injecting drug use or receiving opioid substitution therapy. International Journal of Drug Policy, 6294-103. | No in/out treatment data available |
| 207. | Green, Traci C.; Clarke, Jennifer; Brinkley-Rubinstein, Lauren; Marshall, Brandon D.; Alexander-Scott, Nicole; Boss, Rebecca; Rich, Josiah D. (2018). Postincarceration fatal overdoses after implementing medications for addiction treatment in a statewide correctional system. JAMA Psychiatry, 75(4), 405-407. | Case reports/case series of drug-related deaths |
| 208. | Greene, M. H.; Luke, J. L.; DuPont, R. L. (1974). Opiate overdose deaths in the District of Columbia. II. Methadone-related fatalities. Journal of forensic sciences, 19(3), 575-84. | Case reports/case series of drug-related deaths |
| 209. | Greig, Renay L.; Baker, Amanda; Lewin, Terry J.; Webster, Rosemary A.; Carr, Vaughan J. (2006). Long-term follow-up of people with co-existing psychiatric and substance use disorders: Patterns of use and outcomes. Drug and alcohol review, 25(3), 249-258. | Cohort not defined as engaging in opioid agonist treatment |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 210. | Gronbladh, Leif; Gunne, Lars (1989). Methadone-assisted rehabilitation of Swedish heroin addicts. Drug and Alcohol Dependence, 24(1), 31-37. | No/insufficient mortality data for OAT group |
| 211. | Gronbladh, L.; Ohlund, L. S. (2010). Adherence and social antecedents in relation to outcome in methadone maintenance treatment (MMT). Heroin Addiction and Related Clinical Problems, 12(2), 43344. | No/insufficient mortality data for OAT group |
| 212. | Groth, A. (1975). [Mortality and attempted suicide among young hospitalized addicts]. Ugeskrift for Laeger, 137(39), 2295-300. | Cohort not defined as engaging in opioid agonist treatment |
| 213. | Gunne, L. (2009). Swedish use and misuse of the Dole & Nyswander treatment. Heroin Addiction and Related Clinical Problems, 11(2), 44048. | No original data |
| 214. | Gutierrez, E.; Saiz, P. A.; Garcia, N.; Fernandez, P.; Gonzalez, M. P.; Fernandez, J. J.; Bobes, J. (2001). Evolution of the severity of addiction after two years of treatment in heroin addicts. [Spanish]. Adicciones, 13(1), 51-60. | No in/out treatment data available |
| 215. | Haarr, D.; Nessa, J. (2007). [Treatment of opiate-dependent patients in a general practice]. Tidsskrift for den Norske Laegeforening, 127(13), 1770-2. | Duplicate |
| 216. | Haastrup, Soren; Jepsen, P. (1984). Seven year follow-up of 300 young drug abusers. Acta Psychiatrica Scandinavica, 70(5), 503-509. | No in/out treatment data available |
| 217. | Haastrup, Soren; Jepsen, P. (1988). Eleven year follow-up of 300 young opioid addicts. Acta Psychiatrica Scandinavica, 77(1), 22-26. | Duplicate |
| 218. | Haggerty, Kevin P.; Fleming, Charles B.; Catalano, Richard F.; Petrie, Renee S.; Rubin, Ronald J.; Grassley, Mary H. (2008). Ten years later: Locating and interviewing children of drug abusers. Evaluation and Program Planning, 31(1), 44075. | Cohort not defined as engaging in opioid agonist treatment |
| 219. | Hampton, S.; Blomgren, D.; Roberts, J.; Mackinnon, T.; Nicholls, G. (2015). Prescribing for people in custody. Australian Prescriber, 38(5), 160-163. | No original data |
| 220. | Harris, A. H.; Gupta, S.; Bowe, T.; Ellerbe, L. S.; Phelps, T. E.; Rubinsky, A. D.; Finney, J. W.; Asch, S. M.; Humphreys, K.; Trafton, J. (2015). Predictive validity of two process-of-care quality measures for residential substance use disorder treatment. Addiction science & clinical practice, 1022. | Cohort not defined as engaging in opioid agonist treatment |
| 221. | Hartel, D. M.; Schoenbaum, E. E. (1998). Methadone treatment protects against HIV infection: two decades of experience in the Bronx, New York City. Public Health Reports, 113 Suppl 1107-15. | No/insufficient mortality data for OAT group |
| 222. | Hartman, L.; Barnes, E.; Bachmann, L.; Schafer, K.; Lovato, J.; Files, D. C. (2016). Opiate Injection-associated Infective Endocarditis in the Southeastern United States. American Journal of the Medical Sciences, 352(6), 603-608. | Cohort not defined as engaging in opioid agonist treatment |
| 223. | Hassanian-Moghaddam, H.; Zamani, N.; Rahimi, M.; Shadnia, S.; Pajoumand, A.; Sarjami, S. (2014). Acute adult and adolescent poisoning in Tehran, Iran; the epidemiologic trend between 2006 and 2011. Archives of Iranian Medicine, 17(8), 534-8. | Case reports/case series of drug-related deaths |
| 224. | Hassanian-Moghaddam, H.; Afzali, S.; Pooya, A. (2014). Withdrawal syndrome caused by naltrexone in opioid abusers. Human & Experimental Toxicology, 33(6), 561-7. | Cohort not defined as engaging in opioid agonist treatment |
| 225. | Hayashi, K.; Milloy, M. J.; Wood, E.; Dong, H.; Montaner, J. S. G.; Kerr, T. (2014). Predictors of liver-related death among people who inject drugs in Vancouver, Canada: A 15-year prospective cohort study. Journal of the International AIDS Society, 17 (no pagination)(A97), . | Cohort not defined as engaging in opioid agonist treatment |
| 226. | Hayashi, Kanna; Milloy, M.; Lysyshyn, Mark; DeBeck, Kora; Nosova, Ekaterina; Wood, Evan; Kerr, Thomas (2018). Substance use patterns associated with recent exposure to fentanyl among people who inject drugs in Vancouver, Canada: A cross-sectional urine toxicology screening study. Drug and Alcohol Dependence, 18343983. | Cohort not defined as engaging in opioid agonist treatment |
| 227. | He, J.; Apelt, S. M. (2016). Association between buprenorphine/naloxone sublingual tablet and all-cause mortality in patients receiving medication assisted treatment for opioid addiction in UK. Pharmacoepidemiology and Drug Safety, 25 (Supplement 3)579-580. | No/insufficient mortality data for OAT group |
| 228. | Heinemann, A.; Iwersen-Bergmann, S.; Stein, S.; Schmoldt, A.; Puschel, K. (2000). Methadone-related fatalities in Hamburg 1990-1999: implications for quality standards in maintenance treatment?. Forensic Science International, 113(43891), 449-55. | Case reports/case series of drug-related deaths |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 229. | Herbeck, D. M.; Brecht, M. L.; Lovinger, K. (2015). Mortality, causes of death, and health status among methamphetamine users. Journal of Addictive Diseases, 34(1), 88-100. | Cohort not defined as engaging in opioid agonist treatment |
| 230. | Hesse, Morten; Pedersen, Mads U. (2008). Easy-access services in low-threshold opiate agonist maintenance. International Journal of Mental Health and Addiction, 6(3), 316-324. | No/insufficient mortality data for OAT group |
| 231. | Hickman, M.; Carnwath, Z.; Madden, P.; Farrell, M.; Rooney, C.; Ashcroft, R.; Judd, A.; Stimson, G. (2003). Drug-related mortality and fatal overdose risk: pilot cohort study of heroin users recruited from specialist drug treatment sites in London. Journal of Urban Health, 80(2), 274-87. | No in/out treatment data available |
| 232. | Hilbig, A.; Cheng, A. (2020). Infective Endocarditis in the Intravenous Drug Use Population at a Tertiary Hospital in Melbourne, Australia. Heart Lung and Circulation, 29(2), 246-253. | Cohort not defined as engaging in opioid agonist treatment |
| 233. | Hjorther, A. B.; Andersen, L. B.; Hetmar, O.; Jepsen, P. W. (1994). HIV-positive drug addicts treated at the Copenhagen City Drug Dependency Clinic 1986-1992. [Danish]. Ugeskrift for Laeger, 156(20), 3028-3032. | No in/out treatment data available |
| 234. | Hjorther, A. B.; Andersen, L. B.; Hetmar, O.; Jepsen, P. W. (1994). [HIV-positive drug addicts treated at the Copenhagen City Drug Dependency Clinic 1986-1992]. Ugeskrift for Laeger, 156(20), 3028-32. | Duplicate |
| 235. | Hodgins, S.; Larm, P.; Molero-Samuleson, Y.; Tengstrom, A.; Larsson, A. (2009). Multiple adverse outcomes over 30 years following adolescent substance misuse treatment. Acta Psychiatrica Scandinavica, 119(6), 484-93. | Cohort not defined as engaging in opioid agonist treatment |
| 236. | Hodgins, Sheilagh; Lovenhag, Sara; Rehn, Mattias; Nilsson, Kent W. (2014). A 5-year follow-up study of adolescents who sought treatment for substance misuse in Sweden. European Child & Adolescent Psychiatry, 23(5), 347-360. | Cohort not defined as engaging in opioid agonist treatment |
| 237. | Hogan, B. J.; Shepherd, E.; Webzell, I.; Webb, K.; Agarwal, K.; Aldersley, M.; Bathgate, A.; Ferguson, J.; Griffiths, W. J. H.; Hope, M.; Wood, J.; Masson, S.; Rothwell, K.; Thorburn, D. (2011). The uk experience of liver transplantation in patients receiving opiate replacement therapy. Gut, 1)A58-A59. | No in/out treatment data available |
| 238. | Holstege, C.; Rege, S.; Ngo, A. D.; Rizer, J.; Sharma, S.; Ait-Daoud Tiouririne, N. (2018). Comparison of buprenorphine and methadone exposures reported to U.S. poison centers 2013-2016. European Psychiatry, 48 (Supplement 1)S308-S309. | Case reports/case series of drug-related deaths |
| 239. | Honer, W. G.; Cervantes-Larios, A.; Jones, A. A.; Vila-Rodriguez, F.; Montaner, J. S.; Tran, H.; Nham, J.; Panenka, W. J.; Lang, D. J.; Thornton, A. E.; Vertinsky, T.; Barr, A. M.; Procyshyn, R. M.; Smith, G. N.; Buchanan, T.; Krajden, M.; Krausz, M.; Macewan, G. W.; Gicas, K. M.; Leonova, O.; Langheimer, V.; Rauscher, A.; Schultz, K. (2017). The Hotel Study - Clinical and Health Service Effectiveness in a Cohort of Homeless or Marginally Housed Persons. Canadian Journal of Psychiatry, 62(7), 482-492. | Cohort not defined as engaging in opioid agonist treatment |
| 240. | Hser, Y. I.; Anglin, M. D.; Powers, K. (1990). Longitudinal patterns of alcohol use by narcotics addicts. Recent Developments in Alcoholism, 8145-71. | No original data |
| 241. | Hser, Y. I.; Anglin, D.; Powers, K. (1993). A 24-year follow-up of California narcotics addicts. Archives of General Psychiatry, 50(7), 577-84. | Cohort not defined as engaging in opioid agonist treatment |
| 242. | Hser, Y. I.; McCarthy, W. J.; Anglin, M. D. (1994). Tobacco use as a distal predictor of mortality among long-term narcotics addicts. Preventive Medicine, 23(1), 61-9. | No in/out treatment data available |
| 243. | Hser, Yih-Ing; Hoffman, Valerie; Grella, Christine E.; Anglin, M. (2001). A 33-year follow-up of narcotics addicts. Archives of General Psychiatry, 58(5), 503-508. | Cohort not defined as engaging in opioid agonist treatment |
| 244. | Hser, Y. I.; Kagihara, J.; Huang, D.; Evans, E.; Messina, N. (2012). Mortality among substance-using mothers in California: a 10-year prospective study. Addiction, 107(1), 215-22. | Cohort not defined as engaging in opioid agonist treatment |
| 245. | Hser, Y. I.; Evans, E.; Huang, D.; Weiss, R.; Saxon, A.; Carroll, K. M.; Woody, G.; Liu, D.; Wakim, P.; Matthews, A. G.; Hatch-Maillette, M.; Jelstrom, E.; Wiest, K.; McLaughlin, P.; Ling, W. (2016). Long-term outcomes after randomization to buprenorphine/naloxone versus methadone in a multi-site trial. Addiction, 111(4), 695-705. | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 246. | Huber, M.; Stahelin, C.; Castro Batanjer, E.; Bregenzer, A.; Schoeni-Affolter, F.; Aubert, V.; Barth, J.; Battegay, M.; Bernasconi, E.; Boni, J.; Bucher, H. C.; Burton-Jeangros, C.; Calmy, A.; Cavassini, M.; Egger, M.; Elzi, L.; Fehr, J.; Fellay, J.; Furrer, H.; Fux, C. A.; Gorgievski, M.; Gunthard, H.; Haerry, D.; Hasse, H.; Hirsch, H. H.; Hosli, I.; Kahlert, C.; Kaiser, L.; Keiser, O.; Klimkait, T.; Kovari, H.; Kouyos, R.; Ledergerber, B.; Martinetti, G.; Martinez de Tejada, B.; Metzner, K.; Muller, N.; Nadal, D.; Pantaleo, G.; Rauch, A.; Regenass, S.; Rickenbach, M.; Rudin, C.; Schmid, P.; Schultze, D.; Schoni-Affolter, F.; Schupbach, J.; Speck, R.; Staehelin, C.; Tarr, P.; Telenti, A.; Trkola, A.; Vernazza, P.; Weber, R.; Yerly, S. (2015). Influence of noninjecting and injecting drug use on mortality, retention in the cohort, and antiretroviral therapy, in participants in the Swiss HIV Cohort Study. HIV Medicine, 16(3), 137-151. | No in/out treatment data available |
| 247. | Hurt, Richard D.; Offord, Kenneth P.; Croghan, Ivana T.; Gomez-Dahl, Leigh; Kottke, Thomas E.; Morse, Robert M.; Melton, L. (1996). Mortality following inpatient addictions treatment: Role of tobacco use in a community-based cohort. JAMA: Journal of the American Medical Association, 275(14), 1097-1103. | Cohort not defined as engaging in opioid agonist treatment |
| 248. | Jackson, C. T.; Covell, N. H.; Drake, R. E.; Essock, S. M. (2007). Relationship between diabetes and mortality among persons with co-occurring psychotic and substance use disorders. Psychiatric Services, 58(2), 270-2. | Cohort not defined as engaging in opioid agonist treatment |
| 249. | Janjua, N.; Islam, N.; Wong, J.; Yoshida, E. M.; Ramji, A.; Samji, H.; Butt, Z. A.; Chong, M.; Cook, D.; Alvarez, M.; Tyndall, M.; Krajden, M. (2017). Are DAAs reducing barriers for HIV co-infected and people who inject drugs? A population based cohort study. Journal of Hepatology, 66 (1 Supplement 1)S726-S727. | Cohort not defined as engaging in opioid agonist treatment |
| 250. | Javanbakht, M.; Mirahmadizadeh, A.; Mashayekhi, A. (2014). The long-term effectiveness of methadone maintenance treatment in prevention of hepatitis c virus among illicit drug users: A modeling study. Iranian Red Crescent Medical Journal, 16 (2) (no pagination)(e13484), . | No/insufficient mortality data for OAT group |
| 251. | Jerkeman, A.; Westin, J.; Lagging, M.; Norkrans, G.; Lidman, C.; Frimand, J.; Simonsberg, C.; Kakko, J.; Widell, A.; Bjorkman, P. (2014). Chronic hepatitis C in Swedish subjects receiving opiate substitution therapy-Factors associated with advanced fibrosis. Scandinavian Journal of Infectious Diseases, 46340-347. | No/insufficient mortality data for OAT group |
| 252. | Jerkeman, A.; Norkrans, G.; Lidman, C.; Westin, J.; Lagging, M.; Frimand, J.; Simonsberg, C.; Kakko, J.; Widell, A.; Bjorkman, P. (2014). Treatment for chronic hepatitis C in a cohort of opiate substitution therapy recipients in three Swedish cities - completion rates and efficacy. European Journal of Gastroenterology & Hepatology, 26(5), 523-31. | No in/out treatment data available |
| 253. | Jerkeman, Anna; Hakansson, Anders; Rylance, Rebecca; Wagner, Philippe; Alanko Blome, Marianne; Bjorkman, Per (2017). Death from liver disease in a cohort of injecting opioid users in a Swedish city in relation to registration for opioid substitution therapy. Drug and alcohol review, 36(3), 424-431. | No in/out treatment data available |
| 254. | Jimenez Trevino, L.; Saiz Martinez, P. A.; Gutierrez Cienfuegos, E.; Bascaran Fernandez, M. T.; Carreno Rendueles, E.; Gonzalez-Quiros Menendez de Luarca, M.; Gonzalez Garcia-Portilla, M. P.; Bobes Garcia, J. (2000). A cross-sectional evaluation after fifteen years of a sample of opioid addicts in Asturias. [Spanish]. Adicciones, 12(4), 507-513. | No in/out treatment data available |
| 255. | Jimenez-Trevino, Luis; Saiz, Pilar A.; Garcia-Portilla, M.; Diaz-Mesa, Eva M.; Sanchez-Lasheras, Fernando; Buron, Patricia; Casares, M.; Marina, Pedro; Gutierrez, Eduardo; Bobes, Julio (2011). A 25-year follow-up of patients admitted to methadone treatment for the first time: Mortality and gender differences. Addictive Behaviors, 36(12), 1184-1190. | No in/out treatment data available |
| 256. | Joe, G. W.; Lehman, W.; Simpson, D. D. (1982). Addict death rates during a four-year posttreatment follow-up. American journal of public health, 72(7), 703-9. | No in/out treatment data available |
| 257. | Johnson, Jennifer E.; Finney, John W.; Moos, Rudolf H. (2005). Predictors of 5-year mortality following inpatient/residential group treatment for substance use disorders. Addictive Behaviors, 30(7), 1300-1316. | Cohort not defined as engaging in opioid agonist treatment |
| 258. | Jones, Andrew; Pierce, Matthias; Sutton, Matt; Mason, Thomas; Millar, Tim (2018). Does paying service providers by results improve recovery outcomes for drug misusers in treatment in England?. Addiction, 113(2), 279-286. | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 259. | Jongbloed, K.; Zhang, H.; Thomas, V.; Pearce, M.; Christian, W.; Schechter, M. T.; Spittal, P. M. (2014). The cedar project: Predictors of mortality among young aboriginal people who use drugs in British Columbia. Canadian Journal of Infectious Diseases and Medical Microbiology, SA)31A. | No in/out treatment data available |
| 260. | Kalkman, G. A.; Kramers, C.; van Dongen, R. T.; van den Brink, W.; Schellekens, A. (2019). Trends in use and misuse of opioids in the Netherlands: a retrospective, multi-source database study. The Lancet Public Health, 4(10), e498-e505. | Cohort not defined as engaging in opioid agonist treatment |
| 261. | Kamien, J. B., Branstetter, S. A., & Amass, L. (2008). Buprenorphine-naloxone versus methadone maintenance therapy: A randomised double-blind trial with opioid-dependent patients. *Heroin Addict Relat Clin Probl, 10*(4), 5-18. | No in/out treatment data available |
| 262. | Kastelic, A.; Rihtar, T. K. (2007). Agonist opioid treatment in prisons. Heroin Addiction and Related Clinical Problems, 9(4), 21-30. | No original data |
| 263. | Katz, M.; Link, A. R.; Sherman, S.; Wang, B.; Grossman, E. (2018). A secondary analysis of hospitalized smokers who use opioids: Demographics, comorbidities, and cessa-tion strategies. Journal of General Internal Medicine, 33 (2 Supplement 1)101. | Cohort not defined as engaging in opioid agonist treatment |
| 264. | Kauhanen, J.; Tiihonen, J. (2017). Health risks of drugs in Finland - can the risks be managed?. Duodecim, 133(1), 34-42. | No in/out treatment data available |
| 265. | Kawasaki, Sarah; Francis, Erica; Mills, Sara; Buchberger, Glenn; Hogentogler, Ruth; Kraschnewski, Jennifer (2019). Multi-model implementation of evidence-based care in the treatment of opioid use disorder in Pennsylvania. Journal of Substance Abuse Treatment, 10658-64. | No/insufficient mortality data for OAT group |
| 266. | Keenan, E.; Dorman, A.; O'Connor, J. (1993). Six year follow up of forty five pregnant opiate addicts. Irish Journal of Medical Science, 162(7), 252-5. | No in/out treatment data available |
| 267. | Kelty, Erin; Hulse, Gary (2012). Examination of mortality rates in a retrospective cohort of patients treated with oral or implant naltrexone for problematic opiate use. Addiction, 107(10), 1817-1824. | Cohort not defined as engaging in opioid agonist treatment |
| 268. | Kelty, E.; Hulse, G. (2017). Fatal and non-fatal opioid overdose in opioid dependent patients treated with methadone, buprenorphine or implant naltrexone. International Journal of Drug Policy, 4654-60. | No/insufficient mortality data for OAT group |
| 269. | Kelty, E.; Dobbins, T.; Hulse, G. (2017). Incidence of cancer and cancer related mortality in opiate dependent patients treated with methadone, buprenorphine or implant naltrexone as compared with non-opiate using controls. Heroin Addiction and Related Clinical Problems, 19(3), 65-72. | No in/out treatment data available |
| 270. | Kelty, E.; Hulse, G. (2018). Morbidity and mortality in opioid dependent patients after entering an opioid pharmacotherapy compared with a cohort of non-dependent controls. Journal of Public Health, 40(2), 409-414. | No in/out treatment data available |
| 271. | Kerr, Thomas; Marsh, David; Li, Kathy; Montaner, Julio; Wood, Evan (2005). Factors associated with methadone maintenance therapy use among a cohort of polysubstance using injection drug users in Vancouver. Drug and Alcohol Dependence, 80(3), 329-335. | No in/out treatment data available |
| 272. | Khue, P. M.; Tham, N. T.; Thanh Mai, D. T.; Thuc, P. V.; Thuc, V. M.; Han, P. V.; Lindan, C. (2017). A longitudinal and case-control study of dropout among drug users in methadone maintenance treatment in Haiphong, Vietnam. Harm Reduction Journal, 14(1), 59. | No/insufficient mortality data for OAT group |
| 273. | Kielland, K. B.; Amundsen, E. J.; Dalgard, O. (2013). Hepatitis C treatment uptake in a Norwegian cohort of people who inject drugs. Suchtmedizin in Forschung und Praxis, 15 (4)264-265. | Cohort not defined as engaging in opioid agonist treatment |
| 274. | Kimber, J.; Copeland, L.; Hickman, M.; Macleod, J.; McKenzie, J.; De Angelis, D.; Robertson, J. R. (2010). Survival and cessation in injecting drug users: prospective observational study of outcomes and effect of opiate substitution treatment. Bmj, 341c3172. | No in/out treatment data available |
| 275. | Kimmel, S.; Walley, A. Y.; Berson, D.; Larochelle, M. (2019). Medications for Opioid Use Disorder Following Injection Drug-associated Endocarditis. Journal of Addiction Medicine, 13 (3)E12. | No in/out treatment data available |
| 276. | Klein, Audrey A.; Seppala, Marvin D. (2019). Medication-assisted treatment for opioid use disorder within a 12-step based treatment center: Feasibility and initial results. Journal of Substance Abuse Treatment, 10451-63. | No/insufficient mortality data for OAT group |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 277. | Klimas, J.; O'Reilly, M.; Egan, M.; Tobin, H.; Bury, G. (2014). Urban overdose hotspots: a 12-month prospective study in Dublin ambulance services. American Journal of Emergency Medicine, 32(10), 1168-73. | Case reports/case series of drug-related deaths |
| 278. | Klimas, J.; Keane, A.; Cullen, W.; O'Kelly, F.; Bury, G. (2016). Seventeen year mortality in a cohort of patients attending opioid agonist treatment in Ireland. Commentary on methadone-maintained patients in primary care have higher rates of chronic disease (OToole et al., European Journal of General Practice 2014;20:275-80). European Journal of General Practice, 22(1), 64-65. | No in/out treatment data available |
| 279. | Klimas, J.; Dong, H.; Dobrer, S.; Milloy, M. J.; Kerr, T.; Wood, E.; Hayashi, K. (2017). Alcohol Use among Persons on Methadone Treatment. Addictive Disorders and their Treatment, 16(1), 36-37. | No in/out treatment data available |
| 280. | Kline-Simon, A. H.; Chi, F. W.; Mertens, J. R.; Weisner, C. (2017). Trajectories of remission and mortality over 13 years after intake to substance use treatment. American Journal of Drug and Alcohol Abuse, 43(5), 583-590. | Cohort not defined as engaging in opioid agonist treatment |
| 281. | Klobucar, I.; Potocnjak, I.; Dumancic, J.; Stemberger, K.; Cupic, M.; Kokotovic, T.; Kucijan, Z.; Degoricija, V. (2019). Acute poisonings in Croatia: differences in epidemiology, associated comorbidities and final outcomes-a single-centre 15-year follow-up. Clinical Toxicology, 57(3), 181-188. | Case reports/case series of drug-related deaths |
| 282. | Knobel, H.; Vallecillo, G.; Guelar, A.; Pedrol, E.; Soler, A.; Carmona, A.; Saballs, P.; Gonzalez, A.; Gimeno, J. L.; Colomes, J. L. (2004). Simplified therapy with zidovudine, lamivudine, and abacavir for very nonadherent, treatment-failing patients. HIV Clinical Trials, 5(2), 65-73. | No in/out treatment data available |
| 283. | Knudsen, Hannah K.; Havens, Jennifer R.; Lofwall, Michelle R.; Studts, Jamie L.; Walsh, Sharon L. (2017). Buprenorphine physician supply: Relationship with state-level prescription opioid mortality. Drug and Alcohol Dependence, 173(Suppl 1), S55-S64. | Cohort not defined as engaging in opioid agonist treatment |
| 284. | Kohli, R.; Lo, Y.; Howard, A. A.; Buono, D.; Floris-Moore, M.; Klein, R. S.; Schoenbaum, E. E. (2005). Mortality in an urban cohort of HIV-infected and at-risk drug users in the era of highly active antiretroviral therapy. Clinical Infectious Diseases, 41(6), 864-72. | No in/out treatment data available |
| 285. | Kornor, H.; Waal, H.; Ali, R. L. (2006). Abstinence-orientated buprenorphine replacement therapy for young adults in out-patient counselling. Drug & Alcohol Review, 25(2), 123-30. | Cohort not defined as engaging in opioid agonist treatment |
| 286. | Koustenis, K. R.; Koutli, E.; Kranidioti, H.; Antonakaki, P.; Pantsas, P.; Anagnostou, O.; Deutsch, M.; Manolakopoulos, S. (2019). Adherence to Follow-up of People Who Inject Drugs (Pwid) after the Successful Treatment of Chronic Hepatitis C with Direct-Acting Antivirals (Daa). Gastroenterology, 156 (6 Supplement 1)S-1346. | No in/out treatment data available |
| 287. | Krebs, E.; Urada, D.; Evans, E.; Huang, D.; Hser, Y. I.; Nosyk, B. (2017). The costs of crime during and after publicly funded treatment for opioid use disorders: a population-level study for the state of California. Addiction, 112(5), 838-851. | No/insufficient mortality data for OAT group |
| 288. | Kyrychenko, T. (2018). Antiretroviral therapy retention times and predictors of retention to care among HIV-infected patients in Ukraine. Journal of the International AIDS Society, 21 (Supplement 8)69. | Cohort not defined as engaging in opioid agonist treatment |
| 289. | Lam, S. K.; To, W. K.; Duthie, S. J.; Ma, H. K. (1992). Narcotic addiction in pregnancy with adverse maternal and perinatal outcome. Australian & New Zealand Journal of Obstetrics & Gynaecology, 32(3), 216-21. | Cohort not the primary client of treatment (e.g., neonatal/perinatal) |
| 290. | Lam, Tai Hing; Li, Zhi Bin; Ho, Sai Yin; Chan, Wai Man; Ho, Kin Sang; Tham, May Ked; Cowling, Benjamin J.; Schooling, C.; Leung, Gabriel M. (2007). Smoking, quitting and mortality in an elderly cohort of 56,000 Hong Kong Chinese. Tobacco Control: An International Journal, 16(3), 182-189. | Cohort not defined as engaging in opioid agonist treatment |
| 291. | Lambdin, B. H.; Masao, F.; Chang, O.; Kaduri, P.; Mbwambo, J.; Magimba, A.; Sabuni, N.; Bruce, R. D. (2014). Methadone treatment for HIV prevention-feasibility, retention, and predictors of attrition in Dar es Salaam, Tanzania: a retrospective cohort study. Clinical Infectious Diseases, 59(5), 735-42. | No in/out treatment data available |
| 292. | Larm, P.; Hodgins, S.; Larsson, A.; Samuelson, Y. M.; Tengstrom, A. (2008). Long-term outcomes of adolescents treated for substance misuse. Drug & Alcohol Dependence, 96(43862), 79-89. | Cohort not defined as engaging in opioid agonist treatment |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 293. | Larney, Sarah; Randall, Deborah; Gibson, Amy; Degenhardt, Louisa (2013). The contributions of viral hepatitis and alcohol to liver-related deaths in opioid-dependent people. Drug and Alcohol Dependence, 131(3), 252-257. | No in/out treatment data available |
| 294. | Larney, Sarah; Bohnert, Amy S.; Ganoczy, Dara; Ilgen, Mark A.; Hickman, Matthew; Blow, Fred C.; Degenhardt, Louisa (2015). Mortality among older adults with opioid use disorders in the Veteran's Health Administration, 2000-2011. Drug and Alcohol Dependence, 14732-37. | No in/out treatment data available |
| 295. | Larney, Sarah; Grebely, Jason; Falster, Michael; Swart, Alexander; Amin, Janaki; Degenhardt, Louisa; Burns, Lucinda; Vajdic, Claire M. (2015). Opioid substitution therapy is associated with increased detection of hepatitis C virus infection: A 15-year observational cohort study. Drug and Alcohol Dependence, 148213-216. | No/insufficient mortality data for OAT group |
| 296. | Larney, S.; Gisev, N.; Farrell, M.; Dobbins, T.; Burns, L.; Gibson, A.; Kimber, J.; Degenhardt, L. (2015). Opioid substitution therapy as a strategy to reduce deaths in prison: Retrospective cohort study. Drug and Alcohol Dependence, 146e168. | Abstract - full text available |
| 297. | Larochelle, M.; Bernson, D.; Land, T.; Stopka, T.; Walley, A. Y. (2017). Mortality after nonfatal opioid overdose: Medications for opioid use disorder are associated with lower risk. Journal of General Internal Medicine, 32 (2 Supplement 1)S250. | Abstract - full text available |
| 298. | Lavignasse, P.; Lowenstein, W.; Batel, P.; Constant, M. V.; Jourdain, J. J.; Kopp, P.; Reynaud-Maurupt, C.; Riff, B.; Videau, B.; Mucchielli, A. (2002). Economic and social effects of high-dose buprenorphine substitution therapy. Six-month results. Annales de Medecine Interne, 153(3 Suppl), 1S20-6. | No/insufficient mortality data for OAT group |
| 299. | Lee, S.; Doyon, S.; Klein-Schwartz, W. (2011). Comparison of toxicity of nonmedical use of buprenorphine and methadone. Clinical Toxicology, 49 (6)523-524. | Case reports/case series of drug-related deaths |
| 300. | Lee, S.; Klein-Schwartz, W.; Welsh, C.; Doyon, S. (2013). Medical outcomes associated with nonmedical use of methadone and buprenorphine. Journal of Emergency Medicine, 45(2), 199-205. | Case reports/case series of drug-related deaths |
| 301. | Lee, C. T.; Chen, V. C.; Tan, H. K.; Chou, S. Y.; Wu, K. H.; Chan, C. H.; Gossop, M. (2013). Suicide and other-cause mortality among heroin users in Taiwan: a prospective study. Addictive Behaviors, 38(10), 2619-23. | No in/out treatment data available |
| 302. | Lee, Samantha C.; Klein-Schwartz, Wendy; Doyon, Suzanne; Welsh, Christopher (2014). Comparison of toxicity associated with nonmedical use of benzodiazepines with buprenorphine or methadone. Drug and Alcohol Dependence, 138118-123. | Case reports/case series of drug-related deaths |
| 303. | Lee, J. D.; Friedmann, P. D.; Kinlock, T. W.; Nunes, E. V.; Boney, T. Y.; Hoskinson, R. A.; Wilson, D.; McDonald, R.; Rotrosen, J.; Gourevitch, M. N.; Gordon, M.; Fishman, M.; Chen, D. T.; Bonnie, R. J.; Cornish, J. W.; Murphy, S. M.; O'Brien, C. P. (2016). Extended-release naltrexone to prevent opioid relapse in criminal justice offenders. New England Journal of Medicine, 374(13), 1232-1242. | Cohort not defined as engaging in opioid agonist treatment |
| 304. | Lejeune, C.; Ropert, J. C.; Montamat, S.; Floch-Tudal, C.; Mazy, F.; Wijkhuisen, N.; Froment, H. (1997). Medicosocial outcome in 59 infants born to drug-addicted mothers. [French]. Journal de Gynecologie Obstetrique et Biologie de la Reproduction, 26(4), 395-404. | Cohort not the primary client of treatment (e.g., neonatal/perinatal) |
| 305. | Lejeune, C.; Ropert, J. C.; Montamat, S.; Floch-Tudal, C.; Mazy, F.; Wijkhuisen, N.; Froment, H. (1997). [Medical-social outcome of 59 infants born to addicted mothers]. Journal de Gynecologie, Obstetrique et Biologie de la Reproduction, 26(4), 395-404. | Cohort not the primary client of treatment (e.g., neonatal/perinatal) |
| 306. | Lev, R.; Petro, S.; Lee, A.; Lee, O.; Lucas, J.; Castillo, E. M.; Egnatios, J.; Vilke, G. M. (2015). Methadone related deaths compared to all prescription related deaths. Forensic Science International, 257347-352. | Case reports/case series of drug-related deaths |
| 307. | Levy, Barry S. (1972). Five years after: A follow-up of 50 narcotic addicts. The American journal of psychiatry, 128(7), 868-872. | No/insufficient mortality data for OAT group |
| 308. | Levy, R. B.; Nissly, T.; Hooker, S. (2019). Predictors of retention in a primary-care-based MAT Program for opioid use disorder. Journal of Addiction Medicine, 13 (3)E15. | No/insufficient mortality data for OAT group |
| 309. | Liao, D. L.; Chen, P. C.; Chen, C. H.; Hsieh, C. J.; Huang, Y. F.; Shih, W. Y.; Cheng, J. J. (2013). Higher methadone doses are associated with lower mortality in patients of opioid dependence in Taiwan. Journal of Psychiatric Research, 47(10), 1530-4. | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 310. | Lin, C. K.; Hung, C. C.; Peng, C. Y.; Chao, E.; Lee, T. S. (2015). Factors associated with methadone treatment duration: a Cox regression analysis. PLoS ONE [Electronic Resource], 10(4), e0123687. | Duplicate |
| 311. | Lin, C. K.; Hung, C. C.; Peng, C. Y.; Chao, E.; Lee, T. S. H. (2015). Factors associated with methadone treatment duration: A Cox regression analysis. PLoS ONE, 10 (4) (no pagination)(e0123687), . | No in/out treatment data available |
| 312. | Lin, L. A.; Peltzman, T.; McCarthy, J. F.; Oliva, E. M.; Trafton, J. A.; Bohnert, A. S. B. (2019). Changing Trends in Opioid Overdose Deaths and Prescription Opioid Receipt Among Veterans. American Journal of Preventive Medicine, 57(1), 106-110. | Cohort not defined as engaging in opioid agonist treatment |
| 313. | Lincoln, Thomas; Johnson, Benjamin D.; McCarthy, Patrick; Alexander, Ellen (2018). Extended-release naltrexone for opioid use disorder started during or following incarceration. Journal of Substance Abuse Treatment, 8597-100. | Cohort not defined as engaging in opioid agonist treatment |
| 314. | Lindblad, R.; Hu, L.; Campanella, M.; Kondapaka, R.; Rosa, C.; Allen, C.; Van Paul, V. (2012). Estimating death rates in substance use disorder clinical trials. Clinical Trials, 9 (4)506. | Cohort not defined as engaging in opioid agonist treatment |
| 315. | Lindblad, Robert; Hu, Lian; Oden, Neal; Wakim, Paul; Rosa, Carmen; VanVeldhuisen, Paul (2016). Mortality rates among substance use disorder participants in clinical trials: Pooled analysis of twenty-two clinical trials within the National Drug Abuse Treatment Clinical Trials Network. Journal of Substance Abuse Treatment, 7073-80. | No in/out treatment data available |
| 316. | Ling, W.; Charuvastra, C.; Collins, J. F.; Batki, S.; Brown, L. S., Jr.; Kintaudi, P.; Wesson, D. R.; McNicholas, L.; Tusel, D. J.; Malkerneker, U.; Renner, J. A., Jr.; Santos, E.; Casadonte, P.; Fye, C.; Stine, S.; Wang, R. I.; Segal, D. (1998). Buprenorphine maintenance treatment of opiate dependence: a multicenter, randomized clinical trial. Addiction, 93(4), 475-86. | No in/out treatment data available |
| 317. | Liu, E. W.; Wang, S. J.; Liu, Y.; Liu, W.; Chen, Z. S.; Li, X. Y.; A, L. Y.; Wu, Z. Y. (2011). [Mortality of HIV infected clients treated with methadone maintenance treatment in Yili Kazakh autonomous prefecture]. Chung-Hua Yu Fang i Hsueh Tsa Chih [Chinese Journal of Preventive Medicine], 45(11), 979-84. | Duplicate |
| 318. | Liu, E. W.; Wang, S. J.; Liu, Y.; Liu, W.; Chen, Z. S.; Li, X. Y.; A, L. Y.; Wu, Z. Y. (2011). [Mortality of HIV infected clients treated with methadone maintenance treatment in Yili Kazakh autonomous prefecture]. [Chinese]. Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine], 45(11), 979-984. | No in/out treatment data available |
| 319. | Lloyd, Belinda; Barratt, Monica J.; Ferris, Jason; Best, David; Lubman, Dan I. (2013). Factors influencing mortality among alcohol and drug treatment clients in Victoria, Australia: The role of demographic and substance use characteristics. Australian and New Zealand Journal of Psychiatry, 47(9), 859-867. | Cohort not defined as engaging in opioid agonist treatment |
| 320. | Lloyd, B.; Zahnow, R.; Barratt, M. J.; Best, D.; Lubman, D. I.; Ferris, J. (2017). Exploring mortality among drug treatment clients: The relationship between treatment type and mortality. Journal of Substance Abuse Treatment, 8222-28. | Cohort not defined as engaging in opioid agonist treatment |
| 321. | Lobmaier, P. P.; Kunoe, N.; Gossop, M.; Katevoll, T.; Waal, H. (2010). Naltrexone implants compared to methadone: outcomes six months after prison release. European Addiction Research, 16(3), 139-45. | No/insufficient mortality data for OAT group |
| 322. | Lovrecic, B.; Semerl, J. S.; Tavcar, R.; Maremmani, I. (2011). Sociodemographic and clinical differences among deceased and surviving cohort members of opioid maintenance therapy. Heroin Addiction and Related Clinical Problems, 13(3), 39-48. | No in/out treatment data available |
| 323. | Lovrecic, B. (2016). Overdoses and other drug related deaths: Comparison between outpatient treatment registered and not-registered patients. Heroin Addiction and Related Clinical Problems, 18 (3 Supplement 1)37. | No in/out treatment data available |
| 324. | Lovrecic, M. (2016). Suicide mortality in illicit drug users: Comparison between outpatient treatment registered and not-registered patients. Heroin Addiction and Related Clinical Problems, 18 (3 Supplement 1)37. | No in/out treatment data available |
| 325. | Lovrecic, M.; Lovrecic, B.; Semerl, J. S.; Maremmani, I.; Maremmani, A. G. I. (2016). The filing of addicted patients at addiction units is correlated with a reduction in mortality due to illicit opioids, but also to prescribed opioids and other substances of abuse. Heroin Addiction and Related Clinical Problems, 18(3), 15-22. | Case reports/case series of drug-related deaths |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 326. | Lowder, E. M.; Amlung, J.; Ray, B. R. (2020). Individual and county-level variation in outcomes following non-fatal opioid-involved overdose. Journal of epidemiology and community health., 9. | Cohort not defined as engaging in opioid agonist treatment |
| 327. | Lucas, Gregory M.; Beauchamp, Geetha; Aramrattana, Apinun; Shao, Yiming; Liu, Wei; Fu, Liping; Jackson, J.; Celentano, David D.; Richardson, Paul; Metzger, David (2012). Short-term safety of buprenorphine/naloxone in hiv-seronegative opioid-dependent chinese and thai drug injectors enrolled in hiv prevention trials network 058. International Journal of Drug Policy, 23(2), 162-165. | No/insufficient mortality data for OAT group |
| 328. | Lucas, G. M.; Mullen, B. A.; Galai, N.; Moore, R. D.; Cook, K.; McCaul, M. E.; Glass, S.; Oursler, K. K.; Rand, C. (2013). Directly administered antiretroviral therapy for HIV-infected individuals in opioid treatment programs: results from a randomized clinical trial. PLoS ONE [Electronic Resource], 8(7), e68286. | No in/out treatment data available |
| 329. | Macias, J.; Morano, L. E.; Tellez, F.; Granados, R.; Rivero-Juarez, A.; Palacios, R.; Rios, M. J.; Merino, D.; Perez-Perez, M.; Collado, A.; Figueruela, B.; Morano, A.; Freyre-Carrillo, C.; Martin, J. M.; Rivero, A.; Garcia, F.; Pineda, J. A. (2019). Response to direct-acting antiviral therapy among ongoing drug users and people receiving opioid substitution therapy. Journal of Hepatology, 71(1), 45-51. | No in/out treatment data available |
| 330. | MacLeod, John; Whittaker, Anne; Robertson, J. (1998). Changes in opiate treatment during attendance at a community drug service-Findings from a clinical audit. Drug and alcohol review, 17(1), 19-25. | No in/out treatment data available |
| 331. | Macleod, J.; Steer, C.; Tilling, K.; Cornish, R.; Marsden, J.; Millar, T.; Strang, J.; Hickman, M. (2019). Prescription of benzodiazepines, z-drugs, and gabapentinoids and mortality risk in people receiving opioid agonist treatment: Observational study based on the UK Clinical Practice Research Datalink and Office for National Statistics death records. PLoS Medicine, 16 (11) (no pagination)(e1002965), . | Duplicate |
| 332. | Madruga, A.; Escribano, Juan Jose Avila; Treceno, M.; Paniagua, C.; Perez, J. (1998). Retrospective and follow-up analysis on opiate dependent patients, attending from 1985 to 1990. Psiquis: Revista de Psiquiatria, Psicologia y Psicosomatica, 19(1), 31-36. | Paper could not be located |
| 333. | Mamakwa, S.; Kahan, M.; Kanate, D.; Kirlew, M.; Folk, D.; Cirone, S.; Rea, S.; Parsons, P.; Edwards, C.; Gordon, J.; Main, F.; Kelly, L. (2017). Evaluation of 6 remote First Nations community-based buprenorphine programs in northwestern Ontario: Retrospective study. Canadian Family Physician, 63(2), 137-145. | No/insufficient mortality data for OAT group |
| 334. | Marks, L.; Schwarz, E.; Liss, D.; Satish, M.; Warren, D. K.; Stephen, L.; Durkin, M. (2019). A comparison of medication assisted therapy treatment strategies for opioid use disorder in persons who inject drugs and are hospitalized with serious infections. Open Forum Infectious Diseases, 6 (Supplement 2)S126. | No/insufficient mortality data for OAT group |
| 335. | Marmor, M.; Alcabes, P.; Titus, S.; Frenkel, K.; Krasinski, K.; Penn, A.; Pero, R. W. (1997). Low serum thiol levels predict shorter times-to-death among HIV-infected injecting drug users. Aids, 11(11), 1389-93. | No in/out treatment data available |
| 336. | Marra, F.; Boyle, A.; Peters, E.; Morris, J.; Priest, M.; McDonald, N.; Barclay, S. (2019). Real world outcomes for Genotype 3 patients treated with glecaprevir/pibrentasvir: Real world outcomes from an unselected cohort. Journal of Hepatology, 70 (1 Supplement)e230-e231. | No in/out treatment data available |
| 337. | Marsden, J.; Stillwell, G.; Jones, H.; Cooper, A.; Eastwood, B.; Farrell, M.; Lowden, T.; Maddalena, N.; Metcalf, C.; Shaw, J.; Hickman, M. (2016). Does exposure to opioid substitution treatment at prison release reduce the risk of death? A prospective, observational study in England. The Lancet, 388 (SPEC.ISS 1)11. | Abstract - full text available |
| 338. | Marsden, John; Stillwell, Garry; James, Kirsty; Shearer, James; Byford, Sarah; Hellier, Jennifer; Kelleher, Michael; Kelly, Joanna; Murphy, Caroline; Mitcheson, Luke (2019). Efficacy and cost-effectiveness of an adjunctive personalised psychosocial intervention in treatment-resistant maintenance opioid agonist therapy: A pragmatic, open-label, randomised controlled trial. The Lancet Psychiatry, 6(5), 391-402. | No in/out treatment data available |
| 339. | Martell, B. A.; Arnsten, J. H.; Krantz, M. J.; Gourevitch, M. N. (2005). Impact of methadone treatment on cardiac repolarization and conduction in opioid users. American Journal of Cardiology, 95(7), 915-918. | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 340. | Martin, C.; Pehrsson, P.; Osterberg, A.; Sonnerborg, A.; Hansson, P. (1999). Pain in ambulatory HIV-infected patients with and without intravenous drug use. European Journal of Pain, 3(2), 157-164. | Cohort not defined as engaging in opioid agonist treatment |
| 341. | Marzo, J. N.; Rotily, M.; Meroueh, F.; Varastet, M.; Hunault, C.; Obradovic, I.; Zin, A. (2009). Maintenance therapy and 3-year outcome of opioid-dependent prisoners: a prospective study in France (2003-06). Addiction, 104(7), 1233-40. | No in/out treatment data available |
| 342. | Maughan, B. C.; Becker, E. A. (2019). Drug-related mortality after discharge from treatment: A record-linkage study of substance abuse clients in Texas, 2006-2012. Drug and Alcohol Dependence, 204 (no pagination)(107473), . | No in/out treatment data available |
| 343. | Maxwell, S. (2002). Optimizing long-term response to methadone maintenance treatment: A 152-week follow-up using higher-dose methadone. Journal of Addictive Diseases, 21(3), 44166. | No/insufficient mortality data for OAT group |
| 344. | Maxwell, Jane Carlisle; Pullum, Thomas W.; Tannert, Karen (2005). Deaths of clients in methadone treatment in Texas: 1994-2002. Drug and Alcohol Dependence, 78(1), 73-81. | Case reports/case series of drug-related deaths |
| 345. | Maynard, Charles; Cox, Gary B.; Krupski, Antoinette; Stark, Kenneth (2000). Utilization of services by persons discharged from involuntary chemical dependency treatment. Journal of Addictive Diseases, 19(2), 83-93. | Cohort not defined as engaging in opioid agonist treatment |
| 346. | McCowan, C.; Kidd, B.; Fahey, T. (2009). Factors associated with mortality in Scottish patients receiving methadone in primary care: retrospective cohort study. BMJ: British Medical Journal, 338(7710), No Pagination Specified. | No in/out treatment data available |
| 347. | McLellan, A.; Skipper, Gregory S.; Campbell, Michael; DuPont, Robert L. (2008). Five year outcomes in a cohort study of physicians treated for substance use disorders in the United States. BMJ: British Medical Journal, 337(7679), No Pagination Specified. | Cohort not defined as engaging in opioid agonist treatment |
| 348. | Mega, J.; Lougee, M.; Gaines, E.; Hermerding-Lim, M. (2019). Low-threshold street outreach buprenorphine for homeless patients with opioid use disorder. Journal of Addiction Medicine, 13 (3)E33-E34. | No in/out treatment data available |
| 349. | Merrall, Elizabeth L.; Bird, Sheila M.; Hutchinson, Sharon J. (2012). Mortality of those who attended drug services in Scotland 1996-2006: Record-linkage study. International Journal of Drug Policy, 23(1), 24-32. | No in/out treatment data available |
| 350. | Merrall, Elizabeth; Bird, Sheila; Hutchinson, Sharon (2013). A record linkage study of hospital episodes for drug treatment clients in Scotland, 1996-2006. Addiction Research & Theory, 21(1), 52-61. | No in/out treatment data available |
| 351. | Merrall, E. L.; Bird, S. M.; Hutchinson, S. J. (2013). A record-linkage study of drug-related death and suicide after hospital discharge among drug-treatment clients in Scotland, 1996-2006. Addiction, 108(2), 377-84. | No in/out treatment data available |
| 352. | Metcalfe, R.; Proctor, G.; Schofield, J.; Thomson, E. (2017). Cause & predictors of mortality in an HIV/hepatitis-c-coinfected cohort in Scotland. Topics in Antiviral Medicine, 25 (1 Supplement 1)218s. | Cohort not defined as engaging in opioid agonist treatment |
| 353. | Metcalfe, R.; Martin, T.; Glover, C.; Peters, S. E.; Priyadarshi, S. (2018). A high mortality rate amongst HIV-infected homeless people who inject drugs: Reviewing cause of death and engagement with services. HIV Medicine, 19 (Supplement 2)S42. | Case reports/case series of drug-related deaths |
| 354. | Michel, L.; Giorgi, R.; Villes, V.; Poizot-Martin, I.; Dellamonica, P.; Spire, B.; Protopopescu, C.; Carrieri, M. P. (2009). Withdrawal symptoms as a predictor of mortality in patients HIV-infected through drug use and receiving highly active antiretroviral therapy (HAART). Drug and Alcohol Dependence, 99(43891), 96-104. | No in/out treatment data available |
| 355. | Midgard, H.; Hajarizadeh, B.; Cunningham, E. B.; Conway, B.; Backmund, M.; Bruggmann, P.; Bruneau, J.; Bourgeois, S.; Dunlop, A.; Foster, G. R.; Hellard, M.; Robaeys, G.; Thurnheer, M. C.; Weltman, M.; Amin, J.; Marks, P. S.; Quiene, S.; Dore, G. J.; Dalgard, O.; Grebely, J. (2017). Changes in risk behaviours during and following treatment for hepatitis C virus infection among people who inject drugs: The ACTIVATE study. International Journal of Drug Policy, 47230-238. | Cohort not defined as engaging in opioid agonist treatment |
| 356. | Midgard, H.; Kjersti, U.; Oystein, B.; Foshaug, T.; Wusthoff, L. E. C.; Dalgard, O. (2019). The hepatitis C cascade of care and treatment outcomes among people who inject drugs in a Norwegian low-threshold setting: A real life experience. Journal of Hepatology, 70 (1 Supplement)e41. | Cohort not defined as engaging in opioid agonist treatment |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 357. | Mientjes, G. H.; Van Ameijden, E. J.; Van den Hoek, A. J. A. R.; Coutinho, R. A. (1992). Increasing morbidity without rise in non-AIDS mortality among HIV-infected intravenous drug users in Amsterdam. Aids, 6(2), 207-212. | Cohort not defined as engaging in opioid agonist treatment |
| 358. | Mientjes, G. H.; van Ameijden, E. J.; van den Hoek, A. J.; Coutinho, R. A. (1992). Increasing morbidity without rise in non-AIDS mortality among HIV-infected intravenous drug users in Amsterdam. Aids, 6(2), 207-12. | Cohort not defined as engaging in opioid agonist treatment |
| 359. | Miller, C. L.; Kerr, T.; Strathdee, S. A.; Li, K.; Wood, E. (2007). Factors associated with premature mortality among young injection drug users in Vancouver. Harm Reduction Journal, 4 (no pagination)(1), . | No in/out treatment data available |
| 360. | Miller, William C.; Hoffman, Irving F.; Hanscom, Brett S.; Ha, Tran V.; Dumchev, Kostyantyn; Djoerban, Zubairi; Rose, Scott M.; Latkin, Carl A.; Metzger, David S.; Lancaster, Kathryn E.; Go, Vivian F.; Dvoriak, Sergii; Mollan, Katie R.; Reifeis, Sarah A.; Piwowar-Manning, Estelle M.; Richardson, Paul; Hudgens, Michael G.; Hamilton, Erica L.; Sugarman, Jeremy; Eshleman, Susan H.; Susami, Hepa; Chu, Viet Anh; Djauzi, Samsuridjal; Kiriazova, Tetiana; Bui, Duong D.; Strathdee, Steffanie A.; Burns, David N. (2018). A scalable, integrated intervention to engage people who inject drugs in HIV care and medication-assisted treatment (HPTN 074): A randomised, controlled phase 3 feasibility and efficacy study. The Lancet, 392(10149), 747-759. | No in/out treatment data available |
| 361. | Miotto, Karen; McCann, Michael J.; Rawson, Richard A.; Frosch, Dominick; Ling, Walter (1997). Overdose, suicide attempts and death among a cohort of naltrexone-treated opioid addicts. Drug and Alcohol Dependence, 45(43862), 131-134. | Cohort not defined as engaging in opioid agonist treatment |
| 362. | Mogford, D. V.; Lawrence, R. J. (2016). Medical comorbidity and projected survival in patients admitted to a specialist addictions in-patient unit. Psychiatric Bulletin, 40(5), 255-260. | Cohort not defined as engaging in opioid agonist treatment |
| 363. | Moller, L.; Matic, S.; van den Bergh, B.; Moloney, K.; Hayton, P.; Gatherer, A. (2010). Acute drug-related mortality of people recently released from prisons. Public Health, 124(11), 637-639. | Cohort not defined as engaging in opioid agonist treatment |
| 364. | Monwell, B.; Gerdner, A. (2019). Opioid maintenance treatment: trajectories in and out of treatment. Nordic Journal of Psychiatry, 73(1), 24-30. | No in/out treatment data available |
| 365. | Moreno, J.; Duprey, M.; Wakeman, S.; Roberts, R.; Jacobson, J.; Devlin, J. (2018). Predictors for hospital readmission for patients with opioid use disorder administered opioids during initial hospitalization. JACCP Journal of the American College of Clinical Pharmacy, 1 (2)276. | No/insufficient mortality data for OAT group |
| 366. | Morgan, O.; Griffiths, C.; Hickman, M. (2006). Association between availability of heroin and methadone and fatal poisoning in England and Wales 1993-2004. International Journal of Epidemiology, 35(6), 1579-85. | Case reports/case series of drug-related deaths |
| 367. | Morrow, R. L.; Bassett, K.; Maclure, M.; Dormuth, C. R. (2019). Outcomes associated with hospital admissions for accidental opioid overdose in British Columbia: A retrospective cohort study. BMJ Open, 9 (5) (no pagination)(e025567), . | Case reports/case series of drug-related deaths |
| 368. | Muga, R.; Tor, J.; Ginesta, C.; Melus, R.; Jacas, C.; Rey-Joly, C.; Foz, M. (1990). Natural history of parenteral drug addicts treated in a general hospital. British Journal of Addiction, 85(6), 775-8. | Cohort not defined as engaging in opioid agonist treatment |
| 369. | Muga, R.; Langohr, K.; Tor, J.; Sanvisens, A.; Serra, I.; Rey-Joly, C.; Munoz, A. (2007). Survival of HIV-infected injection drug users (IDUs) in the highly active antiretroviral therapy era, relative to sex- and age-specific survival of HIV-uninfected IDUs. Clinical Infectious Diseases, 45(3), 370-6. | No in/out treatment data available |
| 370. | Naderi-Heiden, A.; Gleiss, A.; Backer, C.; Bieber, D.; Nassan-Agha, H.; Kasper, S.; Frey, R. (2012). Mortality and employment after in-patient opiate detoxification. European Psychiatry, 27(4), 294-300. | Cohort not defined as engaging in opioid agonist treatment |
| 371. | Nadler, J.; Fumia, F.; Cherubin, C. (1973). Deaths of narcotic addicts in New York City in 1971: those reported to be using methadone. Proceedings - National Conference on Methadone Treatment, 1324-9. | Case reports/case series of drug-related deaths |
| 372. | Nambiar, D.; Agius, P. A.; Stoove, M.; Hickman, M.; Dietze, P. (2015). Mortality in the Melbourne injecting drug user cohort study (MIX). Harm Reduction Journal, 12 (1) (no pagination)(55), . | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 373. | Nelwan, E. J.; Indrati, A. K.; Isa, A.; Triani, N.; Alam, N. N.; Herlan, M. S.; Husen, W.; Pohan, H. T.; Alisjahbana, B.; Meheus, A.; Van Crevel, R.; van der Ven, A. J. (2015). Effect of Hiv Prevention and Treatment Program on Hiv and Hcv Transmission and Hiv Mortality at an Indonesian Narcotic Prison. Southeast Asian Journal of Tropical Medicine & Public Health, 46(5), 880-91. | Cohort not defined as engaging in opioid agonist treatment |
| 374. | Ngo, Hanh T.; Tait, Robert J.; Hulse, Gary K. (2008). Comparing drug-related hospital morbidity following heroin dependence treatment with methadone maintenance or naltrexone implantation. Archives of General Psychiatry, 65(4), 457-465. | No/insufficient mortality data for OAT group |
| 375. | Nguyen, T. L.; Boudemaghe, T.; Leguelinel-Blache, G.; Eiden, C.; Kinowski, J. M.; Le Manach, Y.; Peyriere, H.; Landais, P. (2017). Identifying Life-Threatening Admissions for Drug Dependence or Abuse (ILIADDA): Derivation and Validation of a Model. Scientific reports, 744428. | Case reports/case series of drug-related deaths |
| 376. | Nguyen, H. H.; Bui, D. D.; Dinh, T. T.; Pham, L. Q.; Nguyen, V. T.; Tran, T. H.; Pham, T. H.; Nguyen, S. M.; Suthar, A. B.; Do, N. T.; Ford, N.; Lo, Y. R.; Nguyen, L. H.; Giang, L. M.; Kato, M.; team for the implementation research project "Vietnam, H. I. V. early antiretroviral therapy with regular H. I. V. testing (2018). A prospective "test-and-treat" demonstration project among people who inject drugs in Vietnam. Journal of the International AIDS Society, 21(7), e25151. | Cohort not defined as engaging in opioid agonist treatment |
| 377. | Nguyen, H. H.; Bui, D. D.; Dinh, T. T. T.; Pham, L. Q.; Nguyen, V. T. T.; Tran, T. H.; Pham, T. H.; Nguyen, S. M.; Suthar, A. B.; Do, N. T.; Ford, N.; Lo, Y. R.; Nguyen, L. H.; Giang, L. M.; Kato, M. (2018). A prospective "test-and-treat" demonstration project among people who inject drugs in Vietnam. Journal of the International AIDS Society, 21 (7) (no pagination)(e25151), . | Duplicate |
| 378. | Noe, Shelly R. (2014). Office-based buprenorphine treatment: Identifying factors that promote retention in opioid dependent patients. Dissertation Abstracts International: Section B: The Sciences and Engineering, 74(7-B(E)), No Pagination Specified. | No/insufficient mortality data for OAT group |
| 379. | Nolan, Seonaid; Hayashi, Kanna; Milloy, M.; Kerr, Thomas; Dong, Huiru; Lima, Viviane Dias; Lappalainen, Leslie; Montaner, Julio; Wood, Evan (2015). The impact of low-threshold methadone maintenance treatment on mortality in a Canadian setting. Drug and Alcohol Dependence, 15657-61. | No in/out treatment data available |
| 380. | Nolla-Salas, J.; Garcia-Villanueva, M.; Teijeira, R.; de la Torre, R. (2003). [Morbidity and mortality related to methadone]. Medicina Clinica, 121(7), 276-7. | Case reports/case series of drug-related deaths |
| 381. | Nordt, C.; Wiessing, L.; Kuijpers, W.; Wisselink, J.; Espelt, A.; Brugal, M. T.; Mravcik, V.; Nechanska, B.; Seifritz, E.; Herdener, M. (2018). Long-Term Opioid Agonist Treatment Participation after First Treatment Entry is Similar across 4 European Regions but Lower in Non-Nationals. European Addiction Research, 24(4), 173-183. | No/insufficient mortality data for OAT group |
| 382. | Norton, B.; Fleming, J.; Steinman, M.; Yu, K.; Deluca, J.; Cunningham, C. O.; Litwin, A. (2016). High HCV cure rates for drug users treated with daas at an urban primary care clinic. Topics in Antiviral Medicine, 24 (E-1)235. | No in/out treatment data available |
| 383. | Norton, B. L.; Beitin, A.; Glenn, M.; DeLuca, J.; Litwin, A. H.; Cunningham, C. O. (2017). Retention in buprenorphine treatment is associated with improved HCV care outcomes. Journal of Substance Abuse Treatment, 7538-42. | No/insufficient mortality data for OAT group |
| 384. | Nosyk, B.; MacNab, Y. C.; Sun, H.; Fischer, B.; Marsh, D. C.; Schechter, M. T.; Anis, A. H. (2009). Proportional hazards frailty models for recurrent methadone maintenance treatment. American Journal of Epidemiology, 170(6), 783-92. | No/insufficient mortality data for OAT group |
| 385. | Nosyk, Bohdan; Sun, Huiying; Evans, Elizabeth; Marsh, David C.; Anglin, M.; Hser, Yih-Ing; Anis, Aslam H. (2012). Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: Results from a population-based retrospective cohort study. Addiction, 107(9), 1621-1629. | Cohort not defined as engaging in opioid agonist treatment |
| 386. | Nosyk, B.; Min, J. E.; Evans, E.; Li, L.; Liu, L.; Lima, V. D.; Wood, E.; Montaner, J. (2015). The effects of opioid substitution treatment and highly active antiretroviral therapy on the cause-specific risk of mortality among opioid-dependent individuals with HIV/AIDS. Drug and Alcohol Dependence, 156e164. | Abstract - full text available |
| 387. | Nosyk, B.; Min, J. E.; Evans, E.; Li, L.; Liu, L.; Lima, V.; Wood, E.; Montaner, J. (2015). The effects of opioid substitution treatment and highly active antiretroviral therapy on the | Abstract - full text available |

| Excluded reference | | Exclusion Reason |
|---|---|---|
| | cause-specific risk of mortality among injection drug using people living with HIV/AIDS. Journal of the International AIDS Society, 4)97-98. | |
| 388. | Novick, D. M.; Joseph, H.; Salsitz, E. A.; Kalin, M. F.; Keefe, J. B.; Miller, E. L.; Richman, B. L. (1994). Outcomes of treatment of socially rehabilitated methadone maintenance patients in physicians' offices (medical maintenance): follow-up at three and a half to nine and a fourth years. Journal of General Internal Medicine, 9(3), 127-30. | No/insufficient mortality data for OAT group |
| 389. | Nunes, E.; Bickel, W.; Luderer, H.; Maricich, Y. (2019). Prescription digital therapeutics: A new treatment modality for substance use disorders. Journal of Addiction Medicine, 13 (3)E35-E36. | No in/out treatment data available |
| 390. | Nyhagen, Hege Tollefsen; Waal, Helge (2017). The ageing OMT patient. NAT Nordisk alkohol & narkotikatidskrift, 34(1), 72-79. | No in/out treatment data available |
| 391. | Odegard, E.; Amundsen, E. J.; Kielland, K. B. (2007). Fatal overdoses and deaths by other causes in a cohort of Norwegian drug abusers--a competing risk approach. Drug & Alcohol Dependence, 89(43892), 176-82. | No in/out treatment data available |
| 392. | O'Hara, R.; Murphy, L.; Metcalfe, R.; Peters, E.; Harrison, A.; Brown, K. (2018). Providing HIV ARVs via community pharmacies alongside opiate replacement therapy (ORT) during an HIV outbreak amongst people who inject drugs (PWIDs). Journal of the International AIDS Society, 21 (Supplement 8)64-65. | No/insufficient mortality data for OAT group |
| 393. | Ohlin, Leif; Fridell, Mats; Nyhlen, Anna (2015). Buprenorphine maintenance program with contracted work/education and low tolerance for non-prescribed drug use: A cohort study of outcome for women and men after seven years. BMC Psychiatry Vol 15 2015, ArtID 56, 15. | No in/out treatment data available |
| 394. | Oppenheimer, Edna; Stimson, Gerry V. (1982). Seven year follow-up of heroin addicts: Life histories summarised. Drug and Alcohol Dependence, 9(2), 153-159. | No in/out treatment data available |
| 395. | Oppenheimer, E.; Tobutt, C.; Taylor, C.; Andrew, T. (1994). Death and survival in a cohort of heroin addicts from London clinics: a 22-year follow-up study. Addiction, 89(10), 1299-308. | No in/out treatment data available |
| 396. | Ouzan, D.; Larrey, D. G.; Guyader, D.; Remy, A. J.; Riachi, G.; Heluwaert, F.; Truchi, R.; Combis, J. M.; Bailly, F.; Rosa, I.; Zourbas, S.; Petour, P.; Libert, O. P.; Asselah, T.; Thiefin, G.; Roulot, D.; Roche, B.; Hezode, C.; Dumortier, J.; Thabut, D.; Pol, S. (2017). Effectiveness and safety of sofosbuvir-based therapy in patients with chronic hepatitis C virus infection: Results from the prospective french multicenter real-world cohort (helios). Hepatology, 66 (Supplement 1)808A-809A. | Cohort not defined as engaging in opioid agonist treatment |
| 397. | Ovrehus, A.; Nielsen, S.; Hansen, J. F.; Holm, D. K.; Christensen, P. (2019). Test uptake and hepatitis C prevalence in 5483 Danish people in drug use treatment from 1996 to 2015: a registry-based cohort study. Addiction (Abingdon, England), 114(3), 494-503. | No in/out treatment data available |
| 398. | Oyefeso, Adenekan; Ghodse, Hamid; Clancy, Carmel; Corkery, John M. (1999). Suicide among drug addicts in the UK. The British Journal of Psychiatry, 175277-282. | Case reports/case series of drug-related deaths |
| 399. | Oyefeso, A.; Ghodse, H.; Clancy, C.; Corkery, J.; Goldfinch, R. (1999). Drug abuse-related mortality: A study of teenage addicts over a 20-year period. Social Psychiatry and Psychiatric Epidemiology: The International Journal for Research in Social and Genetic Epidemiology and Mental Health Services, 34(8), 437-441. | No in/out treatment data available |
| 400. | Pagels Mardhed, E.; Hakansson, A. (2016). Opioid maintenance treatment and mortality in opiate users leaving prison - A naturalistic follow-up study. Heroin Addiction and Related Clinical Problems, 18 (3 Supplement 1)18-19. | No in/out treatment data available |
| 401. | Palatkin, V.; Yaroslavtseva, T.; Blokhina, E.; Krupitsky, E.; Verbitskaya, E.; Zvartau, E.; Gnatienko, N.; Walley, A.; Gross, R.; Samet, J.; Woody, G. (2019). Fatal overdose in recently detoxified Russian HIV-positive persons with opioid use disorder: The role of naltrexone in prevention. European Neuropsychopharmacology, 29 (Supplement 1)S487-S488. | Cohort not defined as engaging in opioid agonist treatment |
| 402. | Park, T. W. (2018). The use of gabaergic substances in buprenorphine maintenance treatment. Alcoholism: Clinical and Experimental Research, 42 (Supplement 2)113A. | Abstract - full text available |
| 403. | Park, T. W.; Larochelle, M. R.; Saitz, R.; Wang, N.; Bernson, D.; Walley, A. Y. (2020). Associations between prescribed benzodiazepines, overdose death, and buprenorphine discontinuation among people receiving buprenorphine. Addiction, 8. | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 404. | Parmenter, J.; Mitchell, C.; Keen, J.; Oliver, P.; Rowse, G.; Neligan, I.; Keil, C.; Mathers, N. (2013). Predicting biopsychosocial outcomes for heroin users in primary care treatment: a prospective longitudinal cohort study. British Journal of General Practice, 63(612), e499-505. | No in/out treatment data available |
| 405. | Parpouchi, Milad; Moniruzzaman, Akm; Rezansoff, Stefanie N.; Russolillo, Angela; Somers, Julian M. (2017). Characteristics of adherence to methadone maintenance treatment over a 15-year period among homeless adults experiencing mental illness. Addictive Behaviors Reports, 6106-111. | No/insufficient mortality data for OAT group |
| 406. | Pauchard, Denis; Calanca, A. (1983). Catamnestic study (5-12 years follow up) of 76 cases of heroin toxicomania among young adults. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie, 133(2), 321-345. | No in/out treatment data available |
| 407. | Pauchard, D.; Calanca, A. (1983). Catamnestic study (5-12 years follow up) of 76 cases of heroin toxicomania among young adults. [French]. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie, 133(2), 321-345. | Duplicate |
| 408. | Pauchard, D.; Calanca, A. (1983). [Catamnestic study of 76 cases of heroin addiction among young adults (5 to 12 year follow-up)]. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie, 133(2), 321-45. | Duplicate |
| 409. | Pavarin, R. M.; Berardi, D. (2011). Mortality risk in a cohort of subjects reported by authorities for cannabis possession for personal use. Results of a longitudinal study. Epidemiologia e prevenzione, 35(2), 89-93. | Duplicate |
| 410. | Pavarin, R. M. (2015). Mortality Risk Among Heroin Abusers: Clients and Non-clients of Public Treatment Centers for Drug Addiction. Substance use & misuse, 50(13), 1690-6. | Cohort not defined as engaging in opioid agonist treatment |
| 411. | Pavarin, R. M.; Fioritti, A. (2018). Mortality Trends among Cocaine Users Treated between 1989 and 2013 in Northern Italy: Results of a Longitudinal Study. Journal of Psychoactive Drugs, 50(1), 72-80. | Cohort not defined as engaging in opioid agonist treatment |
| 412. | Pearson, E. C.; Woosley, R. L. (2005). QT prolongation and torsades de pointes among methadone users: reports to the FDA spontaneous reporting system. Pharmacoepidemiology & Drug Safety, 14(11), 747-53. | Case reports/case series of drug-related deaths |
| 413. | Pedersen, M. U.; Hesse, M.; Bloomfield, K. (2011). Abstinence-orientated residential rehabilitation of opioid users in Denmark: do changes in national treatment policies affect treatment outcome?. Scandinavian journal of public health, 39(6), 582-589. | No/insufficient mortality data for OAT group |
| 414. | Peles, Einat; Schreiber, Shaul; Adelson, Miriam (2010). 15-year survival and retention of patients in a general hospital-affiliated methadone maintenance treatment (MMT) center in Israel. Drug and Alcohol Dependence, 107(43892), 141-148. | No in/out treatment data available |
| 415. | Peles, Einat; Linzy, Shirley; Kreek, Mary Jeanne; Adelson, Miriam (2013). Prospective study of QTc changes among former opiate addicts since admission to methadone maintenance treatment: Benzodiazepine risk. Journal of Addiction Medicine, 7(6), 428-434. | No in/out treatment data available |
| 416. | Peles, E.; Linzy, S.; Kreek, M. J.; Adelson Dr, M. (2013). Prospective study of QTc changes among former opiate addicts since admission to methadone maintenance treatment. Journal of Addiction Medicine, 7(6), 428-434. | Duplicate |
| 417. | Peles, Einat; Schreiber, Shaul; Adelson, Miriam (2013). Opiate-dependent patients on a waiting list for methadone maintenance treatment are at high risk for mortality until treatment entry. Journal of Addiction Medicine, 7(3), 177-182. | No in/out treatment data available |
| 418. | Peles, Einat; Schreiber, Shaul; Sason, Anat; Adelson, Miriam (2018). Similarities and changes between 15- and 24-year survival and retention rates of patients in a large medical-affiliated methadone maintenance treatment (MMT) center. Drug and Alcohol Dependence, 185112-119. | No in/out treatment data available |
| 419. | Perkins, Marvin E.; Bloch, Harriet I. (1971). A study of some failures in methadone treatment. The American journal of psychiatry, 128(1), 47-51. | No/insufficient mortality data for OAT group |
| 420. | Perucci, Carlo A.; Davoli, Marina; Rapiti, Elisabetta; Abeni, Damiano D.; Forastiere, Francesco (1991). Mortality of intravenous drug users in Rome: A cohort study. American journal of public health, 81(10), 1307-1310. | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 421. | Petry, N. M.; Bickel, W. K.; Badger, G. J. (1998). A 12-year study (1975-1986) of mortality in methadone-maintenance patients: selected demographic characteristics and drug-use patterns of AIDS and non-AIDS-related deaths. Substance use & misuse, 33(12), 2521-34. | Case reports/case series of drug-related deaths |
| 422. | Pierce, M.; Millar, T.; Robertson, T.; Bird, S. (2018). Ageing opioid users' increased risk of methadone-specific death in the UK. International Journal of Drug Policy, 55, 121-127. | No in/out treatment data available |
| 423. | Pirrie, G. (1977). Deaths among users of dangerous drugs. British Journal of Addiction, 72(4), 365-369. | Case reports/case series of drug-related deaths |
| 424. | Pombo, S.; Felix Da Costa, N. (2018). On the long-term status of treatment-seeking, heroin addicted patients: A 22-year follow-up study on mortality and drug use in Portugal. Heroin Addiction and Related Clinical Problems, 20(1), 21-30. | No in/out treatment data available |
| 425. | Popa, I. C.; Erscoiu, S.; P. Atru C; Burcos, O.; Stoicev, T.; Ceausu, E.; Pirvu, N.; Oncel, D.; Loghin, R.; Mehedinti, A. M. (2014). Antiretroviral treatment in adult ethnobotanical intravenous drug users recently infected with HIV. BMC Infectious Diseases. Conference: 7th Romanian National HIV/AIDS Congress and the 2nd Central European HIV Forum. Romania., 14(Supplement 4), . | Cohort not defined as engaging in opioid agonist treatment |
| 426. | Price, L.; Manuel, J.; Kurz, D.; Delate, T. (2013). Methadone and cardiac adverse outcomes: A retrospective study of patients in a managed care organization (S750). Journal of Pain and Symptom Management, 45 (2)448. | Cohort not defined as engaging in opioid agonist treatment |
| 427. | Radley, A.; de Bruin, M.; Inglis, S.; Donnan, P.; Beer, L.; Dillon, J. (2019). Preliminary analysis of SuperDOT-C: A cluster randomised controlled trial of pharmacy-led versus conventional treatment for HCV positive patients receiving daily opioid substitution therapy-The Tayside sites. Journal of Hepatology, 70 (1 Supplement)e155. | No in/out treatment data available |
| 428. | Rafful, Claudia; Orozco, Ricardo; Rangel, Gudelia; Davidson, Peter; Werb, Dan; Beletsky, Leo; Strathdee, Steffanie A. (2018). Increased non-fatal overdose risk associated with involuntary drug treatment in a longitudinal study with people who inject drugs. Addiction, 113(6), 1056-1063. | No/insufficient mortality data for OAT group |
| 429. | Ranapurwala, Shabbar I.; Shanahan, Meghan E.; Alexandridis, Apostolos A.; Proescholdbell, Scott K.; Naumann, Rebecca B.; Edwards, Daniel, Jr.; Marshall, Stephen W. (2018). Opioid overdose mortality among former North Carolina inmates: 2000-2015. American journal of public health, 108(9), 1207-1213. | Cohort not defined as engaging in opioid agonist treatment |
| 430. | Randall, D.; Degenhardt, L.; Vajdic, C. M.; Burns, L.; Hall, W. D.; Law, M.; Butler, T. (2011). Increasing cancer mortality among opioid-dependent persons in Australia: a new public health challenge for a disadvantaged population. Australian & New Zealand Journal of Public Health, 35(3), 220-5. | No in/out treatment data available |
| 431. | Rathod, Nehkant H.; Addenbrooke, W.; Rosenbach, Alan F. (2005). Heroin dependence in an English town: 33-year follow-up. The British Journal of Psychiatry, 187(5), 421-425. | No in/out treatment data available |
| 432. | Ravndal, Edle; Vaglum, Per (1998). Psychopathology, treatment completion and 5 years outcome: A prospective study of drug abusers. Journal of Substance Abuse Treatment, 15(2), 135-142. | No/insufficient mortality data for OAT group |
| 433. | Ravndal, E.; Lauritzen, G. (2004). Opiate users in methadone-assisted rehabilitation: Follow-up after one and two years. [Norwegian]. Tidsskrift for den Norske Laegeforening, 124(3), 329-331. | No in/out treatment data available |
| 434. | Ravndal, E.; Lauritzen, G. (2004). [Opiate users in methadone-assisted rehabilitation one year and two years after admission]. Tidsskrift for den Norske Laegeforening, 124(3), 329-31. | Duplicate |
| 435. | Ravndal, E.; Amundsen, E. J. (2010). Mortality among drug users after discharge from inpatient treatment: an 8-year prospective study. Drug & Alcohol Dependence, 108(43862), 65-9. | No in/out treatment data available |
| 436. | Rawson, R.; Cousins, S. J.; McCann, M.; Pearce, R.; Van Donsel, A. (2019). Assessment of medication for opioid use disorder as delivered within the Vermont hub and spoke system. Journal of Substance Abuse Treatment, 9784-90. | No/insufficient mortality data for OAT group |
| 437. | Reddon, Hudson; Ho, Joel; DeBeck, Kora; Milloy, M.; Liu, Yang; Dong, Huiru; Ahamad, Keith; Wood, Evan; Kerr, Thomas; Hayashi, Kanna (2018). Increasing diversion of methadone in Vancouver, Canada, 2005-2015. Journal of Substance Abuse Treatment, 8542644. | No/insufficient mortality data for OAT group |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 438. | Reece, A. S. (2009). Comparative treatment and mortality correlates and adverse event profile of implant naltrexone and sublingual buprenorphine. Journal of Substance Abuse Treatment, 37(3), 256-65. | No in/out treatment data available |
| 439. | Rehm, Jurgen; Frick, Ulrich; Hartwig, Christina; Gutzwiller, Felix; Gschwend, Patrick; Uchtenhagen, Ambros (2005). Mortality in heroin-assisted treatment in Switzerland 1994-2000. Drug and Alcohol Dependence, 79(2), 137-143. | No in/out treatment data available |
| 440. | Rezai-Zadeh, K.; Engstrom, Richard N.; Sharma, Andy; Chen, Yiming; Chu, Jun; Cox, Robin Parker; Lee, Mei-Ling Ting (2019). Generational trends and patterns in readmission within a statewide cohort of clients receiving heroin use disorder treatment in Maryland, 2007-2013. Journal of Substance Abuse Treatment, 9682-91. | No/insufficient mortality data for OAT group |
| 441. | Rezansoff, S. N.; Moniruzzaman, A.; Somers, J. M. (2019). Temporal associations between medication adherence for patients with schizophrenia and opioid dependence: A 17-year Canadian Cohort Study. Schizophrenia Research, 210157-163. | No in/out treatment data available |
| 442. | Riblet, N. B.; Kenneally, L.; Shiner, B.; Watts, B. V. (2019). Health Care Processes Contributing to Suicide Risk in Veterans During and After Residential Substance Abuse Treatment. Journal of Dual Diagnosis, 15(4), 217-225. | Cohort not defined as engaging in opioid agonist treatment |
| 443. | Rich, J. D.; Holmes, L.; Salas, C.; Macalino, G.; Davis, D.; Ryczek, J.; Flanigan, T. (2001). Successful linkage of medical care and community services for HIV-positive offenders being released from prison. Journal of Urban Health, 78(2), 279-89. | Cohort not defined as engaging in opioid agonist treatment |
| 444. | Riggins, Daniel P.; Cunningham, Chinazo O.; Ning, Yuming; Fox, Aaron D. (2017). Recent incarceration and buprenorphine maintenance treatment outcomes among human immunodeficiency virus-positive patients. Substance abuse, 38(3), 297-302. | No/insufficient mortality data for OAT group |
| 445. | Risser, Daniele; Honigschnabl, Selma; Stichenwirth, Martin; Pfudl, Susanne; Sebald, Dieter; Kaff, Alfred; Bauer, Georg (2001). Mortality of opiate users in Vienna, Austria. Drug and Alcohol Dependence, 64(3), 251-256. | No in/out treatment data available |
| 446. | Rivas, I.; Sanvisens, A.; Faure, E.; Fuster, D.; Trinidad, M.; Rubio, M.; Muga, R. (2015). Early mortality after entering a methadone treatment program in Badalona, Spain. Drug and Alcohol Dependence, 156e191. | No in/out treatment data available |
| 447. | Rivero-Juarez, A.; Tellez, F.; Castano, M.; Merino, D.; Espinosa, N.; Santos, J.; Macias, J.; Paniagua-Garcia, M.; Zapata-Lopez, A.; Collado, A.; Gomez-Vidal, A.; Stachowski, J. P.; Munoz-Medina, L.; Fernandez-Fuertes, E.; Rivero, A. (2018). Daa implementation rate in HIV/HCV patients in Spain: 2 years of unrestricted access. Topics in Antiviral Medicine, 26 (Supplement 1)258s. | No in/out treatment data available |
| 448. | Robertson, J. R.; Ronald, P. J. M.; Raab, G. M.; Ross, A. J.; Parpia, T. (1994). Deaths, HIV infection, abstinence, and other outcomes in a cohort of injecting drug users followed up for 10 years. British Medical Journal, 309(6951), 369-372. | No in/out treatment data available |
| 449. | Romelsjo, Anders; Engdahl, Barbro; Stenbacka, Marlene; Fugelstad, Anna; Davstad, Ingrid; Leifman, Anders; Thiblin, Ingemar (2010). Were the changes to Sweden's maintenance treatment policy 2000-06 related to changes in opiate-related mortality and morbidity?. Addiction, 105(9), 1625-1632. | Case reports/case series of drug-related deaths |
| 450. | Rosca, Paula; Haklai, Ziona; Goldberger, Nehama; Zohar, Peres; Margolis, Anatoly; Ponizovsky, Alexander M. (2012). Mortality and causes of death among users of methadone maintenance treatment in Israel, 1999-2008. Drug and Alcohol Dependence, 125(43862), 160-163. | No in/out treatment data available |
| 451. | Rosca, P.; Neumark, Y. (2018). Infectious diseases among omt patients in Israel-results of a historical cohort study and the new treatment policy. Heroin Addiction and Related Clinical Problems, 20 (Supplement 1)43-44. | No in/out treatment data available |
| 452. | Rosenthal, E. S.; Karchmer, A. W.; Theisen-Toupal, J.; Castillo, R. A.; Rowley, C. F. (2016). Suboptimal Addiction Interventions for Patients Hospitalized with Injection Drug Use-Associated Infective Endocarditis. American Journal of Medicine, 129(5), 481-485. | Cohort not defined as engaging in opioid agonist treatment |
| 453. | Rosenthal, E. S.; Nussdorf, L.; D'Amore, A.; Brokus, C.; Silk, R.; Eyasu, R.; Mathur, P.; Bijole, P.; Jones, M.; Kier, R.; Sternberg, D.; Masur, H.; Kottilil, S.; Kattakuzhy, S. (2019). High rates of experienced and witnessed opioid overdose in PWID receiving HCV treatment: Data from the anchor study. Open Forum Infectious Diseases, 6 (Supplement 2)S83. | No in/out treatment data available |

| Excluded reference | | Exclusion Reason |
|---|---|---|
| 454. | Ruadze, E.; Todadze, K. (2016). Retention in Georgia opioid substitution therapy program and associated factors. Harm Reduction Journal, 13(1), 35. | No/insufficient mortality data for OAT group |
| 455. | Russolillo, A.; Moniruzzaman, A.; Somers, J. M. (2019). Association of Methadone Treatment With Substance-Related Hospital Admissions Among a Population in Canada With a History of Criminal Convictions. JAMA Network Open, 2(3), e190595. | No/insufficient mortality data for OAT group |
| 456. | Saitz, R.; Gaeta, J.; Cheng, D. M.; Richardson, J. M.; Larson, M. J.; Samet, J. H. (2007). Risk of mortality during four years after substance detoxification in urban adults. Journal of Urban Health, 84(2), 272-82. | Cohort not defined as engaging in opioid agonist treatment |
| 457. | Salsitz, Edwin A.; Holden, Christopher C.; Tross, Susan; Nugent, Ann (2010). Transitioning stable methadone maintenance patients to buprenorphine maintenance. Journal of Addiction Medicine, 4(2), 88-92. | No/insufficient mortality data for OAT group |
| 458. | Samji, H.; O'Brien, N.; Wang, H.; Shen, A.; Palmer, A. K.; Montaner, J. S.; Hogg, R. S. (2011). Correlates of HIV treatment interruption in a cohort of HIV-positive individuals in British Columbia, Canada. Canadian Journal of Infectious Diseases and Medical Microbiology, SB)39B-40B. | Cohort not defined as engaging in opioid agonist treatment |
| 459. | Sanvisens, A.; Fuster, D.; Serra, I.; Tor, J.; Tural, C.; Rey-Joly, C.; Muga, R. (2011). Estimated liver fibrosis and its impact on all-cause mortality of HCV Monoinfected and HCV/HIV-coinfected drug users. Current HIV Research, 9(4), 256-262. | Cohort not defined as engaging in opioid agonist treatment |
| 460. | Sanvisens, Arantza; Vallecillo, Gabriel; Bolao, Ferran; Rivas, Inmaculada; Fonseca, Francina; Fuster, Daniel; Torrens, Marta; Perez-Hoyos, Santiago; Pujol, Ramon; Tor, Jordi; Muga, Roberto (2014). Temporal trends in the survival of drug and alcohol abusers according to the primary drug of admission to treatment in Spain. Drug and Alcohol Dependence, 136115-120. | Cohort not defined as engaging in opioid agonist treatment |
| 461. | Satre, D. D.; Mertens, J. R.; Arean, P. A.; Weisner, C. (2004). Five-year alcohol and drug treatment outcomes of older adults versus middle-aged and younger adults in a managed care program. Addiction, 99(10), 1286-97. | Cohort not defined as engaging in opioid agonist treatment |
| 462. | Satre, Derek D.; Chi, Felicia W.; Mertens, Jennifer R.; Weisner, Constance M. (2012). Effects of age and life transitions on alcohol and drug treatment outcome over nine years. Journal of Studies on Alcohol and Drugs, 73(3), 459-468. | Cohort not defined as engaging in opioid agonist treatment |
| 463. | Saxon, A. J.; Hser, Y. I.; Woody, G.; Ling, W. (2013). Medication-assisted treatment for opioid addiction: Methadone and buprenorphine. Journal of Food and Drug Analysis, 21(4 SUPPL.), S69-S72. | No original data |
| 464. | Schackman, B. R.; Teixeira, P. A.; Beeder, A. B. (2007). Offers of hepatitis C care do not lead to treatment. Journal of Urban Health, 84(3), 455-8. | Cohort not defined as engaging in opioid agonist treatment |
| 465. | Scherbaum, N.; Specka, M.; Hauptmann, G.; Gastpar, M. (2002). Does maintenance treatment reduce the mortality rate of opioid addicts?. [German]. Fortschritte der Neurologie Psychiatrie, 70(9), 455-461. | Duplicate |
| 466. | Schiff, D. M.; Nielsen, T.; Terplan, M.; Hood, M.; Bernson, D.; Diop, H.; Bharel, M.; Wilens, T. E.; LaRochelle, M.; Walley, A. Y.; Land, T. (2018). Fatal and Nonfatal Overdose Among Pregnant and Postpartum Women in Massachusetts. Obstetrics & Gynecology, 132(2), 466-474. | No in/out treatment data available |
| 467. | Schmid, Petra; Uhlmann, Carmen (2019). Open doors of a psychiatric intensive care unit with addiction patients: A 3-year Follow up study. Fortschritte der Neurologie, Psychiatrie, 87(9), 493-498. | No/insufficient mortality data for OAT group |
| 468. | Schuckit, M. A. (2016). Treatment of opioid-use disorders. New England Journal of Medicine, 375(4), 357-368. | Review |
| 469. | Schwartz, Robert P.; Brooner, Robert K.; Montoya, Ivan D.; Currens, Marian; Hayes, Michael (1999). A 12-year follow-up of a methadone medical maintenance program. The American Journal on Addictions, 8(4), 293-299. | Cohort with less than 30 individuals |
| 470. | Schwartz, Robert P.; Gryczynski, Jan; O'Grady, Kevin E.; Sharfstein, Joshua M.; Warren, Gregory; Olsen, Yngvild; Mitchell, Shannon G.; Jaffe, Jerome H. (2013). Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995-2009. American journal of public health, 103(5), 917-922. | Case reports/case series of drug-related deaths |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 471. | Schwartz, R. P.; Kelly, S. M.; Mitchell, S. G.; O'Grady, K. E.; Sharma, A.; Jaffe, J. H. (2020). Methadone treatment of arrestees: A randomized clinical trial. Drug and Alcohol Dependence, 206 (no pagination)(107680), . | Cohort not defined as engaging in opioid agonist treatment |
| 472. | Scordato, M. (1982). [1967-82, an evaluation of the Swedish experience with maintenance methadone therapy of morphine addicts]. Minerva Medica, 73(47), 3353-8. | No in/out treatment data available |
| 473. | Scott, C. K.; Dennis, M. L.; Laudet, A.; Funk, R. R.; Simeone, R. S. (2011). Surviving drug addiction: the effect of treatment and abstinence on mortality. American journal of public health, 101(4), 737-44. | Cohort not defined as engaging in opioid agonist treatment |
| 474. | Seewald, R.; Bruce, R. D.; Elam, R.; Tio, R.; Lorenz, S.; Friedmann, P.; Rabin, D.; Garger, Y. B.; Bonilla Jr, V.; Perlman, D. C. (2013). Effectiveness and feasibility study of routine HIV rapid testing in an urban methadone maintenance treatment program. American Journal of Drug and Alcohol Abuse, 39(4), 247-251. | No/insufficient mortality data for OAT group |
| 475. | Segest, Erling; Mygind, Ole; Bay, Hans (1989). The allocation of drug addicts to different types of treatment: An evaluation and a two-year follow-up. The American journal of drug and alcohol abuse, 15(1), 41-53. | No in/out treatment data available |
| 476. | Segest, Erling; Mygind, Ole; Bay, Hans (1990). The influence of prolonged stable methadone maintenance treatment on mortality and employment: An 8-year follow-up. International Journal of the Addictions, 25(1), 53-63. | No in/out treatment data available |
| 477. | Selling, Daniel; Lee, David; Solimo, Angela; Venters, Homer (2015). A Road Not Taken: Substance abuse programming in the New York City jail system. Journal of Correctional Health Care, 21(1), 44142. | Cohort not defined as engaging in opioid agonist treatment |
| 478. | Sells, S. B.; Chatham, L. R.; Retka, R. L. (1972). A study of differential death rates and causes of death among 9276 opiate addicts during 1970-1971. Contemporary Drug Problems, 1(4), 665-706. | No in/out treatment data available |
| 479. | Selwyn, P. A.; Feingold, A. R.; Hartel, D.; Schoenbaum, E. E.; Alderman, M. H.; Klein, R. S.; Friedland, G. H. (1988). Increased risk of bacterial pneumonia in HIV-infected intravenous drug users without AIDS. Aids, 2(4), 267-72. | No in/out treatment data available |
| 480. | Selwyn, P. A.; Alcabes, P.; Hartel, D.; Buono, D.; Schoenbaum, E. E.; Klein, R. S.; Davenny, K.; Friedland, G. H. (1992). Clinical manifestations and predictors of disease progression in drug users with human immunodeficiency virus infection. New England Journal of Medicine, 327(24), 1697-703. | No in/out treatment data available |
| 481. | Seymour, Alison; Black, Majorie; Jay, Jane; Cooper, Gail; Weir, Christopher; Oliver, John (2003). The role of methadone in drug-related deaths in the west of Scotland. Addiction, 98(7), 995-1002. | Case reports/case series of drug-related deaths |
| 482. | Shah, Nina; Lathrop, Sarah L.; Landen, Michael G. (2005). Unintentional methadone-related overdose death in New Mexico (USA) and implications for surveillance, 1998-2002. Addiction, 100(2), 176-188. | Case reports/case series of drug-related deaths |
| 483. | Shah, A.; Atreja, N.; Duncan, M.; Tai, K.; Gore, M. (2017). Health care utilization and costs associated with pharmacological therapy versus nonpharmacological therapy for opioid dependence. Journal of Managed Care and Specialty Pharmacy, 23 (10-A SUPPL.)S42. | No/insufficient mortality data for OAT group |
| 484. | Shah, A.; Atreja, N.; Tai, K. S.; Gore, M.; Duncan, M. (2018). Health care utilization and costs associated with opioid dependence treatments. American Journal on Addictions, 27 (4)321-322. | No/insufficient mortality data for OAT group |
| 485. | Shah, A.; Atreja, N.; Tai, K. S.; Gore, M.; Duncan, M. (2018). Health care utilization and costs associated with pharmacological vs. non-pharmacological therapy for opioid dependence. American Journal on Addictions, 27 (4)326-327. | No/insufficient mortality data for OAT group |
| 486. | Shannon, K.; Kerr, T.; Lai, C.; Ishida, T.; Wood, E.; Montaner, J. S.; Hogg, R. S.; Tyndall, M. W. (2005). Nonadherence to antiretroviral therapy among a community with endemic rates of injection drug use. Journal of the International Association of Physicians in AIDS Care: JIAPAC, 4(3), 66-72. | Cohort not defined as engaging in opioid agonist treatment |
| 487. | Singh, J.; Dalal, P. K.; Arya, A.; Agarwal, M.; Sinha, P. K. (2018). A follow up study of opioid injecting drug users registered in opioid substitution therapy center-after three years. Indian Journal of Psychiatry, 60 (5 Supplement 1)S84. | No in/out treatment data available |
| 488. | Singhal, N.; Sanger, N.; Samaan, Z. (2018). Changes in polysubstance use among patients on methadone for opioid use disorder. Journal of Addiction Medicine, 12 (3)E5. | No/insufficient mortality data for OAT group |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 489. | Skeie, I.; Brekke, M.; Lindbaek, M.; Waal, H. (2008). Somatic health among heroin addicts before and during opioid maintenance treatment: a retrospective cohort study. BMC public health, 843. | No/insufficient mortality data for OAT group |
| 490. | Skidmore, C. A.; Robertson, J. R.; Robertson, A. A.; Elton, R. A. (1990). After the epidemic: follow up study of HIV seroprevalence and changing patterns of drug use. Bmj, 300(6719), 219-23. | Cohort not defined as engaging in opioid agonist treatment |
| 491. | Skinner, Martie L.; Haggerty, Kevin P.; Fleming, Charles B.; Catalano, Richard F.; Gainey, Randy R. (2011). Opiate-addicted parents in methadone treatment: Long-term recovery, health, and family relationships. Journal of Addictive Diseases, 30(1), 17-26. | No in/out treatment data available |
| 492. | Smart, Reginald G. (1974). The probable value of heroin maintenance for Canadian narcotic addicts. Canada's Mental Health, 22(3), 44046. | No original data |
| 493. | Smart, Reginald G.; Mann, Robert; Suurvali, Helen (1997). Do increased levels of drug abuse treatment lead to fewer drug-related problems?. The American journal of drug and alcohol abuse, 23(3), 421-429. | Cohort not defined as engaging in opioid agonist treatment |
| 494. | Smink, B.; Ruiter, B.; Lusthof, K.; de Gier, J.; Uges, D.; Egberts, A. (2005). Drug use and the severity of a traffic accident. Accident Analysis and Prevention, 37(3), 427-433. | Cohort not defined as engaging in opioid agonist treatment |
| 495. | Smyth, Bobby P.; Barry, Joe; Lane, Alison; Cotter, Mary; O'Neill, Mary; Quinn, Caroline; Keenan, Eamon (2005). In-patient treatment of opiate dependence: medium-term follow-up outcomes. The British Journal of Psychiatry, 187(4), 360-365. | Cohort not defined as engaging in opioid agonist treatment |
| 496. | Smyth, B. P.; Barry, J.; Keenan, E.; Ducray, K. (2010). Lapse and relapse following inpatient treatment of opiate dependence. Irish Medical Journal, 103(6), 176-9. | Cohort not defined as engaging in opioid agonist treatment |
| 497. | Smyth, Bobby P.; Fagan, John; Kernan, Kathy (2012). Outcome of heroin-dependent adolescents presenting for opiate substitution treatment. Journal of Substance Abuse Treatment, 42(1), 35-44. | No/insufficient mortality data for OAT group |
| 498. | Socias, M. E.; Wood, E.; Lake, S.; Nolan, S.; Fairbairn, N.; Hayashi, K.; Shulha, H. P.; Liu, S.; Kerr, T.; Milloy, M. J. (2018). High-intensity cannabis use is associated with retention in opioid agonist treatment: a longitudinal analysis. Addiction, 113(12), 2250-2258. | No/insufficient mortality data for OAT group |
| 499. | Soyka, Michael; Apelt, Sabine M.; Lieb, Martin; Wittchen, Hans-Ulrich (2006). One-year Mortality Rates of Patients Receiving Methadone and Buprenorphine Maintenance Therapy: A Nationally Representative Cohort Study in 2694 Patients. Journal of Clinical Psychopharmacology, 26(6), 657-660. | No in/out treatment data available |
| 500. | Soyka, Michael; Trader, Anna; Klotsche, Jens; Backmund, Markus; Buhringer, Gerhard; Rehm, Jurgen; Wittchen, Hans-Ulrich (2011). Six-year mortality rates of patients in methadone and buprenorphine maintenance therapy: Results from a nationally representative cohort study. Journal of Clinical Psychopharmacology, 31(5), 678-680. | No in/out treatment data available |
| 501. | Soyka, M.; Trader, A.; Klotsche, J.; Backmund, M.; Buhringer, G.; Rehm, J. T.; Wittchen, H. U. (2011). Mortality in long-term opioid maintenance treatment in Germany: Frequency, causes and predictors. [German]. Suchtmedizin in Forschung und Praxis, 13(5), 247-252. | Duplicate |
| 502. | Soyka, Michael; Trader, Anna; Klotsche, Jens; Haberthur, Annina; Buhringer, Gerhard; Rehm, Jurgen; Wittchen, Hans-Ulrich (2012). Criminal behavior in opioid-dependent patients before and during maintenance therapy: 6-year follow-up of a nationally representative cohort sample. Journal of forensic sciences, 57(6), 1524-1530. | No in/out treatment data available |
| 503. | Soyka, Michael; Strehle, Jens; Rehm, Jurgen; Buhringer, Gerhard; Wittchen, Hans-Ulrich (2017). Six-year outcome of opioid maintenance treatment in heroin-dependent patients: Results from a naturalistic study in a nationally representative sample. European Addiction Research, 23(2), 97-105. | No in/out treatment data available |
| 504. | Stang, Hans J. (1977). Three-year follow-up of 100 vagrant adolescent drug abusers in Oslo. Acta Psychiatrica Scandinavica, 55(5), 381-390. | No in/out treatment data available |
| 505. | Stankiewicz, B.; Montalvo, C. (2018). Buprenorphine retention in outpatient mental health: Comparing primary care and mental health outcomes in a large urban safety net hospital. American Journal on Addictions, 27 (4)293. | No/insufficient mortality data for OAT group |

| Excluded reference | | Exclusion Reason |
|---|---|---|
| 506. | Stenbacka, M.; Leifman, A.; Romelsjo, A. (1998). The impact of methadone on consumption of inpatient care and mortality, with special reference to HIV status. Substance use & misuse, 33(14), 2819-34. | No in/out treatment data available |
| 507. | Stevenson, Erin (2014). Examining chronic non-cancer pain among a sample of individuals in opioid treatment programs. Dissertation Abstracts International Section A: Humanities and Social Sciences, 75(5-A(E)), No Pagination Specified. | No/insufficient mortality data for OAT group |
| 508. | Stewart, Duncan; Gossop, Michael; Marsden, John (2002). Reductions in non-fatal overdose after drug misuse treatment: Results from the National Treatment Outcome Research Study (NTORS). Journal of Substance Abuse Treatment, 22(1), 44075. | No/insufficient mortality data for OAT group |
| 509. | Stillwell, G.; Jones, H.; Shaw, J.; Farrell, M.; Marsden, J. (2017). An evaluation of opioid substitution treatment in prison on risk of mortality in period immediately after prison: Does leaving prison on OST reduce the risk of death?. Drug and Alcohol Dependence, 171e197. | Abstract - full text available |
| 510. | Stimson, G. V.; Oppenheimer, E.; Thorley, A. (1978). Seven-year follow-up of heroin addicts: drug use and outcome. British Medical Journal, 1(6121), 1190-2. | No in/out treatment data available |
| 511. | Stoklosa, T.; Haber, P.; Gounder, P.; Youssef, H. (2017). Hepatitis C and liver disease in opioid treatment program patients. Journal of Gastroenterology and Hepatology (Australia), 32 (Supplement 2)81. | No/insufficient mortality data for OAT group |
| 512. | Stone, Andrew C.; Carroll, Jennifer J.; Rich, Josiah D.; Green, Traci C. (2018). Methadone maintenance treatment among patients exposed to illicit fentanyl in Rhode Island: Safety, dose, retention, and relapse at 6 months. Drug and Alcohol Dependence, 19294-97. | No in/out treatment data available |
| 513. | Stone, A. C.; Carroll, J. J.; Rich, J.; Green, T. C. (2018). Methadone maintenance treatment for fentanyl use; Dose, retention in treatment and relapse. Journal of Addiction Medicine, 12 (3)E17-E18. | Abstract - full text available |
| 514. | Stone, A. C.; Carroll, J. J.; Rich, J. D.; Green, T. C. (2019). Fentanyl use and outcomes in a methadone treatment program: 1-year follow-up. Journal of Addiction Medicine, 13 (3)E28. | No in/out treatment data available |
| 515. | Storbjork, Jessica; Ullman, Sara (2012). A prospective study of mortality up to eight years after starting treatment for alcohol and drug problems in Stockholm county: 2000-2008. Addiction Research & Theory, 20(5), 402-413. | Cohort not defined as engaging in opioid agonist treatment |
| 516. | Strang, John; McCambridge, Jim; Best, David; Beswick, Tracy; Bearn, Jenny; Rees, Sian; Gossop, Michael (2003). Loss of tolerance and overdose mortality after inpatient opiate detoxification: Follow up study. BMJ: British Medical Journal, 326(7396), 959-960. | Cohort not defined as engaging in opioid agonist treatment |
| 517. | Strang, J.; Manning, V.; Mayet, S.; Best, D.; Titherington, E.; Santana, L.; Offor, E.; Semmler, C. (2008). Overdose training and take-home naloxone for opiate users: Prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses. Addiction, 103(10), 1648-1657. | No/insufficient mortality data for OAT group |
| 518. | Sullivan, M.; Mannelli, P.; Yu, M.; Nangia, N.; Graham, C.; Webster, I.; Andrew Tompkins, D.; Kosten, T.; Akerman, S.; Silverman, B. (2018). Outpatient transition to extended-release naltrexone in patients with opioid-use disorder. American Journal on Addictions, 27 (4)323. | Cohort not defined as engaging in opioid agonist treatment |
| 519. | Sutlovic, D.; Kljucevic, Z.; Sliskovic, L.; Susnjar, H.; Viskovic, I.; Definis-Gojanovic, M. (2018). Methadone Maintenance Treatment: A 15-year Retrospective Study in Split-Dalmatia County, Croatia. Therapeutic Drug Monitoring, 40(4), 486-494. | No in/out treatment data available |
| 520. | Swart, A.; Burns, L.; Mao, L.; Grulich, A. E.; Amin, J.; O'Connell, D. L.; Meagher, N. S.; Randall, D. A.; Degenhardt, L.; Vajdic, C. M. (2012). The importance of blood-borne viruses in elevated cancer risk among opioid-dependent people: A population-based cohort study. BMJ Open, 2 (5) (no pagination)(e001755), . | No in/out treatment data available |
| 521. | Tait, R. J.; Hulse, G. K. (2008). Hospital morbidity associated with the natural history of heroin use. Journal of Opioid Management, 4(5), 321-327. | No/insufficient mortality data for OAT group |
| 522. | Tait, R. J.; Ngo, H. T.; Hulse, G. K. (2008). Mortality in heroin users 3 years after naltrexone implant or methadone maintenance treatment. Journal of Substance Abuse Treatment, 35(2), 116-24. | No in/out treatment data available |
| 523. | Tait, J.; Stephens, B. P.; Evans, M.; Cleary, S.; Dillon, J. F. (2013). People who inject drugs (PWID): Difficult to get into services, easy to cure. Hepatology, 1)1102A-1103A. | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 524. | Takeda, M.; Katzman, J. G.; Balasch, M. M.; Greenberg, N. (2018). Take-home naloxone for patients with opioid use disorder-successful opioid reversals. Journal of Addiction Medicine, 12 (3)E23. | No/insufficient mortality data for OAT group |
| 525. | Tamraz, B.; Reisner, L.; French, A. L.; King, S. T.; Fischl, M. A.; Ofotokun, I.; Kashuba, A.; Milam, J.; Murphy, K.; Augenbraun, M.; Liu, C.; Finley, P. R.; Aouizerat, B.; Cocohoba, J.; Gange, S.; Bacchetti, P.; Greenblatt, R. M. (2019). Association between Use of Methadone, Other Central Nervous System Depressants, and QTc Interval-Prolonging Medications and Risk of Mortality in a Large Cohort of Women Living with or at Risk for Human Immunodeficiency Virus Infection. Pharmacotherapy, 39(9), 899-911. | Cohort not defined as engaging in opioid agonist treatment |
| 526. | Teoh, J.; Yee, A.; Danaee, M. (2018). Predictors of retention and mortality among patients on methadone maintenance therapy. Heroin Addiction and Related Clinical Problems, 20(4), 19-28. | No/insufficient mortality data for OAT group |
| 527. | Termorshuizen, F.; Krol, A.; Prins, M.; van Ameijden, E. J. (2005). Long-term outcome of chronic drug use: the Amsterdam Cohort Study among Drug Users. American Journal of Epidemiology, 161(3), 271-9. | Cohort not defined as engaging in opioid agonist treatment |
| 528. | Thakarar, K.; Rokas, K. E.; Lucas, F. L.; Powers, S.; Andrews, E.; DeMatteo, C.; Mooney, D.; Sorg, M. H.; Valenti, A.; Cohen, M. (2019). Mortality, morbidity, and cardiac surgery in Injection Drug Use (IDU)-associated versus non-IDU infective endocarditis: The need to expand substance use disorder treatment and harm reduction services. PLoS ONE, 14 (11) (no pagination)(e0225460), . | No in/out treatment data available |
| 529. | Thomas, D. B.; Whysner, J. A.; Newmann, M. C. (1979). The phase III clinical evaluation of LAAM: I. Comparative epidemiology of mortality in LAAM and methadone. NIDA Research Monograph, 27289-295b. | No in/out treatment data available |
| 530. | Thomas, D.; Elizabeth, A.; Patrick, P.; Bruno, M. (2018). Report from the Paris supervised injection site: Is it this facility, the recent harm reduction approach towards drug use, safe?. Annals of Intensive Care. Conference: French Intensive Care Society, International Congress Reanimation, 8(1 Supplement 1), . | Cohort not defined as engaging in opioid agonist treatment |
| 531. | Thorpe, L. E.; Frederick, M.; Pitt, J.; Cheng, I.; Watts, D. H.; Buschur, S.; Green, K.; Zorrilla, C.; Landesman, S. H.; Hershow, R. C. (2004). Effect of hard-drug use on CD4 cell percentage, HIV RNA level, and progression to AIDS-defining class C events among HIV-infected women. Journal of Acquired Immune Deficiency Syndromes: JAIDS, 37(3), 1423-30. | Cohort not defined as engaging in opioid agonist treatment |
| 532. | Thylstrup, Birgitte; Bloomfield, Kim; Hesse, Morten (2018). Incremental predictive validity of the Addiction Severity Index psychiatric composite score in a consecutive cohort of patients in residential treatment for drug use disorders. Addictive Behaviors, 76201-207. | Cohort not defined as engaging in opioid agonist treatment |
| 533. | Thylstrup, B.; Seid, A. K.; Tjagvad, C.; Hesse, M. (2020). Incidence and predictors of drug overdoses among a cohort of >10,000 patients treated for substance use disorder. Drug and Alcohol Dependence, 206 (no pagination)(107714), . | No in/out treatment data available |
| 534. | Truszkowska, E.; McCarron, P.; Konovalov, P.; Galander, T.; Lyons, S.; Keenan, E.; Smyth, B. P. (2015). Case-control study of risks and causes of death amongst opioid dependent patients on methadone maintenance treatment. Canadian Journal of Addiction, 6(3), 18-26. | No in/out treatment data available |
| 535. | Tyndall, M. W.; Craib, K. J.; Currie, S.; Li, K.; O'Shaughnessy, M. V.; Schechter, M. T. (2001). Impact of HIV infection on mortality in a cohort of injection drug users. Journal of Acquired Immune Deficiency Syndromes: JAIDS, 28(4), 351-7. | Cohort not defined as engaging in opioid agonist treatment |
| 536. | Uchtenhagen, A.; Gutzwiller, F.; Dobler-Mikola, A.; Steffen, T.; Blattler, R.; Dreifuss, R.; Gschwend, P.; Kaufmann, B.; Kressig, M. M.; Lory, B. N.; Pfeifer, S.; Nyman, A. S.; Schmidlin, C.; Wulschleger, S.; Ernst, M.; Stocker, C.; Metzler, V.; Gasser, M.; Knierim-Keul, C.; Kummerle, U.; Ryser, H.; Schmied, M.; Stierli, M.; Brenneisen, R.; Christen, S.; Frei, A.; Dinkel, R.; Greiner, R. A.; Mehnert, A.; Fluck, C.; Geistlich, S.; Hammig, R.; Hug, I.; Kilhas, M.; Rabasa, J.; Seidenberg, A.; Uehlinger, C.; Basel, J.; Bern, K. I.; Freiburg, P.; Olten, H.; Thun, P. H.; Zug, Z.; Gallen, M. S. H. I. St; Solothurn, G.; Winterthur, I.; Zurcher, H.; Uster, O.; Horgen, D. B. B.; Biel, S.; Luzern, D. I.; Genf, P.; Oberschongrun, S. (1998). Economic evaluation in a trial of medically controlled prescription of narcotics to dependent users (PROVE). [German]. Sozial- und Praventivmedizin, 43(4), 185-194. | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 537. | Uosukainen, Hanna; Kauhanen, Jussi; Bell, J.; Ronkainen, Kimmo; Tiihonen, Jari; Fohr, Jaana; Onyeka, Ifeoma N.; Korhonen, Maarit J. (2013). Mortality among clients seeking treatment for buprenorphine abuse in Finland. Drug and Alcohol Dependence, 133(2), 391-397. | No in/out treatment data available |
| 538. | Uosukainen, Hanna; Kauhanen, Jussi; Bell, J.; Ronkainen, Kimmo; Tiihonen, Jari; Fohr, Jaana; Onyeka, Ifeoma N.; Korhonen, Maarit J. (2014). "Mortality among clients seeking treatment for buprenorphine abuse in Finland": Corrigendum. Drug and Alcohol Dependence, 142361. | No in/out treatment data available |
| 539. | Vaillant, George E. (1966). A twelve-year follow-up of New York narcotic addicts: I. The relation of treatment to outcome. The American journal of psychiatry, 122(7), 727-737. | Cohort not defined as engaging in opioid agonist treatment |
| 540. | Vaillant, George E. (1973). A 20-year follow-up of New York narcotic addicts. Archives of General Psychiatry, 29(2), 237-241. | Cohort not defined as engaging in opioid agonist treatment |
| 541. | Vajdic, C. M.; Marashi Pour, S.; Olivier, J.; Swart, A.; O'Connell, D. L.; Falster, M. O.; Meagher, N. S.; Mao, L.; Grulich, A. E.; Randall, D. A.; Amin, J.; Burns, L.; Degenhardt, L. (2015). The impact of blood-borne viruses on cause-specific mortality among opioid dependent people: An Australian population-based cohort study. Drug & Alcohol Dependence, 152264-71. | No in/out treatment data available |
| 542. | Valcarce Pardeiro, N.; Alvarez, H.; Santalla, J.; Garcia, J. F.; Rodriguez, I.; Marino, A. (2018). Collaborative approach to improve adherence and retention in care among illicit drug users with HIV/AIDS. European Journal of Hospital Pharmacy, 25 (Supplement 1)A84-A85. | Cohort not defined as engaging in opioid agonist treatment |
| 543. | van Ameijden, E. J.; Krol, A.; Vlahov, D.; Flynn, C.; van Haastrecht, H. J.; Coutinho, R. A. (1999). Pre-AIDS mortality and morbidity among injection drug users in Amsterdam and Baltimore: an ecological comparison. Substance use & misuse, 34(6), 845-65. | Cohort not defined as engaging in opioid agonist treatment |
| 544. | van Ameijden, E.; Langendam, M.; Coutinho, R. (1999). Dose-effect relationship between overdose mortality and prescribed methadone dosage in low-threshold maintenance programs. Addictive Behaviors, 24(4), 559-563. | No in/out treatment data available |
| 545. | van Ameijden, E. J.; Coutinho, R. A. (2001). Large decline in injecting drug use in Amsterdam, 1986-1998: explanatory mechanisms and determinants of injecting transitions. Journal of Epidemiology & Community Health, 55(5), 356-63. | Cohort not defined as engaging in opioid agonist treatment |
| 546. | van Haastrecht, H. J.; van Ameijden, E. J.; van den Hoek, J. A.; Mientjes, G. H.; Bax, J. S.; Coutinho, R. A. (1996). Predictors of mortality in the Amsterdam cohort of human immunodeficiency virus (HIV)-positive and HIV-negative drug users. American Journal of Epidemiology, 143(4), 380-91. | No in/out treatment data available |
| 547. | VanVeldhuisen, P.; Hu, L.; Lindblad, R.; Oden, N.; Wakim, P.; Rosa, C. (2017). Mortality rates among substance use disorder participants in clinical trials: Pooled analysis of 22 NIDA CTN studies. Drug and Alcohol Dependence, 171e206. | Duplicate of Lindbald et al. 2016 |
| 548. | Vest, Bridgette Helms (2014). Substance abuse cessation for Veterans coping with mental illness. Dissertation Abstracts International: Section B: The Sciences and Engineering, 74(9-B(E)), No Pagination Specified. | Cohort not defined as engaging in opioid agonist treatment |
| 549. | Vlahov, D.; Wang, C. I.; Galai, N.; Bareta, J.; Mehta, S. H.; Strathdee, S. A.; Nelson, K. E. (2004). Mortality risk among new onset injection drug users. Addiction, 99(8), 946-954. | No in/out treatment data available |
| 550. | Vlahov, D.; Galai, N.; Safaeian, M.; Galea, S.; Kirk, G. D.; Lucas, G. M.; Sterling, T. R. (2005). Effectiveness of highly active antiretroviral therapy among injection drug users with late-stage human immunodeficiency virus infection. American Journal of Epidemiology, 161(11), 999-1012. | No in/out treatment data available |
| 551. | Wachsman, M. (2019). Mathematically modeling attrition from buprenorphine/naloxone treatment: Finding the lost. American Journal on Addictions, 28 (3)211-212. | No/insufficient mortality data for OAT group |
| 552. | Wakeman, S. E.; Rich, J. D. (2015). Substance use disorders and avoidable mortality after prison. The Lancet Psychiatry, 2(5), 369-370. | No original data |
| 553. | Walley, A. Y.; Cheng, D. M.; Quinn, E. K.; Blokhina, E.; Gnatienko, N.; Chaisson, C. E.; Krupitsky, E.; Coffin, P. O.; Samet, J. H. (2017). Fatal and non-fatal overdose after narcology hospital discharge among Russians living with HIV/AIDS who inject drugs. International Journal of Drug Policy, 39114-120. | Cohort not defined as engaging in opioid agonist treatment |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 554. | Wang, C.; Vlahov, D.; Galai, N.; Bareta, J.; Strathdee, S. A.; Nelson, K. E.; Sterling, T. R. (2004). Mortality in HIV-seropositive versus -seronegative persons in the era of highly active antiretroviral therapy: implications for when to initiate therapy. Journal of Infectious Diseases, 190(6), 1046-54. | Cohort not defined as engaging in opioid agonist treatment |
| 555. | Wang, C.; Vlahov, D.; Galai, N.; Cole, S. R.; Bareta, J.; Pollini, R.; Mehta, S. H.; Nelson, K. E.; Galea, S. (2005). The effect of HIV infection on overdose mortality. Aids, 19(9), 935-42. | No in/out treatment data available |
| 556. | Watterson, Olive; Simpson, D.; Sells, S. (1975). Death rates and causes of death among opioid addicts in community drug treatment programs during 1970-1973. The American journal of drug and alcohol abuse, 2(1), 99-111. | No in/out treatment data available |
| 557. | Weaver, T.; Metrebian, N.; Hellier, J.; Pilling, S.; Charles, V.; Little, N.; Poovendran, D.; Mitcheson, L.; Ryan, F.; Bowden-Jones, O.; Dunn, J.; Glasper, A.; Finch, E.; Strang, J. (2014). Use of contingency management incentives to improve completion of hepatitis B vaccination in people undergoing treatment for heroin dependence: A cluster randomised trial. The Lancet, 384(9938), 153-163. | No in/out treatment data available |
| 558. | Webber, M. P.; Schoenbaum, E. E.; Gourevitch, M. N.; Buono, D.; Chang, C. J.; Klein, R. S. (1998). Temporal trends in the progression of human immunodeficiency virus disease in a cohort of drug users. Epidemiology, 9(6), 613-7. | No in/out treatment data available |
| 559. | Webber, Mayris P.; Schoenbaum, Ellie E.; Gourevitch, Marc N.; Bouno, Donna; Klein, Robert S. (1999). A prospective study of HIV disease progression in female and male drug users. Aids, 13(2), 257-262. | No in/out treatment data available |
| 560. | Weiner, S. G.; Baker, O.; Bernson, D.; Schuur, J. D. (2017). One-year mortality of opioid overdose victims who received naloxone by emergency medical services. Annals of Emergency Medicine, 70 (4 Supplement 1)S158. | Cohort not defined as engaging in opioid agonist treatment |
| 561. | Weiner, S. G.; Baker, O.; Bernson, D.; Schuur, J. D. (2020). One-Year Mortality of Patients After Emergency Department Treatment for Nonfatal Opioid Overdose. Annals of Emergency Medicine, 75(1), 13-17. | Cohort not defined as engaging in opioid agonist treatment |
| 562. | Weintraub, E. (2018). TELE-BUP: Prescribing buprenorphine to patients in underserved areas using tele-medicine. Heroin Addiction and Related Clinical Problems, 20 (Supplement 1)27. | No/insufficient mortality data for OAT group |
| 563. | Westermeyer, Joseph (1979). Medical and nonmedical treatment for narcotic addicts: A comparative study from Asia. Journal of Nervous and Mental Disease, 167(4), 205-211. | Cohort not defined as engaging in opioid agonist treatment |
| 564. | White, S. R.; Bird, S. M.; Merrall, E. L.; Hutchinson, S. J. (2015). Drugs-Related Death Soon after Hospital-Discharge among Drug Treatment Clients in Scotland: Record Linkage, Validation, and Investigation of Risk-Factors. PLoS ONE [Electronic Resource], 10(11), e0141073. | No in/out treatment data available |
| 565. | Wiepert, G. D.; Bewley, T. H.; d'Orban, P. T. (1978). Outcomes of 575 British opiate addicts entering treatment between 1968 and 1975. Bulletin on Narcotics, 30(1), 21-32. | No in/out treatment data available |
| 566. | Willems, R.; Gouda, A. S.; Jaffal, K.; Buisine, A.; Labat, L.; Megarbane, B. (2019). Opioid overdoses admitted to the intensive care unit over a 10-year period: Clinical features and opioids involved. Clinical Toxicology, 57 (6)437. | Case reports/case series of drug-related deaths |
| 567. | Williams, A. R.; Samples, H.; Crystal, S.; Olfson, M. (2020). Acute Care, Prescription Opioid Use, and Overdose Following Discontinuation of Long-Term Buprenorphine Treatment for Opioid Use Disorder. The American journal of psychiatry, 177(2), 117-124. | No/insufficient mortality data for OAT group |
| 568. | Willis, J.; Osbourne, A. (1978). What happens to heroin addicts? A follow-up study. British Journal of Addiction, 73(2), 189-198. | No in/out treatment data available |
| 569. | Winograd, R. P.; Wood, C. A.; Stringfellow, E. J.; Presnall, N.; Duello, A.; Horn, P.; Rudder, T. (2020). Implementation and evaluation of Missouri's Medication First treatment approach for opioid use disorder in publicly-funded substance use treatment programs. Journal of Substance Abuse Treatment, 108(), 55-64. | No/insufficient mortality data for OAT group |
| 570. | Wittchen, H. U.; Apelt, S. M.; Soyka, M.; Gastpar, M.; Backmund, M.; Golz, J.; Kraus, M. R.; Tretter, F.; Schafer, M.; Siegert, J.; Scherbaum, N.; Rehm, J.; Buhringer, G. (2008). Feasibility and outcome of substitution treatment of heroin-dependent patients in specialized substitution centers and primary care facilities in Germany: a naturalistic study in 2694 patients. Drug & Alcohol Dependence, 95(3), 245-57. | No in/out treatment data available |

| | Excluded reference | Exclusion Reason |
|---|---|---|
| 571. | Wittchen, H. U.; Buhringer, G.; Rehm, J. T.; Soyka, M.; Trader, A.; Mark, K.; Trautmann, S. (2011). The 6-years course and outcome of opioid maintenance treatment of 1.624 patients in the German substitution system. [German]. Suchtmedizin in Forschung und Praxis, 13(5), 232-246. | No/insufficient mortality data for OAT group |
| 572. | Wolff, H.; Favrod-Coune, T.; Baroudi, M.; Pierre Rieder, J.; Getaz, L.; Barro, J.; Gaspoz, J. M. T.; Broers, B. (2012). Substitution treatment for all dependent opioid users is possible in jail: A case study of Switzerland. Journal of General Internal Medicine, 2)S304-S305. | No in/out treatment data available |
| 573. | Wood, E.; Hogg, R. S.; Kerr, T.; Palepu, A.; Zhang, R.; Montaner, J. S. G. (2005). Impact of accessing methadone on the time to initiating HIV treatment among antiretroviral-naive HIV-infected injection drug users. Aids, 19(8), 837-839. | No/insufficient mortality data for OAT group |
| 574. | Woody, George E.; Kane, Vince; Lewis, Kimberly; Thompson, Richard (2007). Premature deaths after discharge from methadone maintenance: A replication. Journal of Addiction Medicine, 1(4), 180-185. | No in/out treatment data available |
| 575. | Wright, N. M.; French, C.; Allgar, V. (2014). The safe implementation of a prison-based methadone maintenance programme: 7 year time-series analysis of primary care prescribing data. BMC family practice, 1564. | No in/out treatment data available |
| 576. | Yule, A. M.; Carrellas, N. W.; DiSalvo, M.; Lyons, R. M.; McKowen, J. W.; Nargiso, J. E.; Bergman, B. G.; Kelly, J. F.; Wilens, T. E. (2019). Risk Factors for Overdose in Young People Who Received Substance Use Disorder Treatment. American Journal on Addictions, 28(5), 382-389. | No in/out treatment data available |
| 577. | Zador, D. A.; Sunjic, S. D. (2002). Methadone-related deaths and mortality rate during induction into methadone maintenance, New South Wales, 1996. Drug & Alcohol Review, 21(2), 131-6. | No in/out treatment data available |
| 578. | Zanis, D. A.; McLellan, A. T.; Alterman, A. I.; Cnaan, R. A. (1996). Efficacy of enhanced outreach counseling to reenroll high-risk drug users 1 year after discharge from treatment. American Journal of Psychiatry, 153(8), 1095-6. | No in/out treatment data available |
| 579. | Zanis, D. A.; Woody, G. E. (1998). One-year mortality rates following methadone treatment discharge. Drug & Alcohol Dependence, 52(3), 257-60. | No in/out treatment data available |
| 580. | Zhao, Min; Hao, Wei; Yang, Desen; Zhang, Yalin; Li, Lingjiang (2001). A prospective study of factors related to relapse in heroin addicts. Chinese Journal of Clinical Psychology, 9(2), 81-83, 89. | No in/out treatment data available |
| 581. | Zhao, Y.; Shi, C. X.; McGoogan, J. M.; Rou, K.; Zhang, F.; Wu, Z. (2013). Methadone maintenance treatment and mortality in HIV-positive people who inject opioids in China. Bulletin of the World Health Organization, 91(2), 93-101. | No in/out treatment data available |
| 582. | Zhao, Yan; Shi, Cynthia X.; McGoogan, Jennifer M.; Rou, Keming; Zhang, Fujie; Wu, Zunyou (2015). Predictors of accessing antiretroviral therapy among HIV-positive drug users in China's National Methadone Maintenance Treatment Programme. Addiction, 110(Suppl 1), 40-50. | No/insufficient mortality data for OAT group |
| 583. | Zhao, Yan; Zhang, Mingjie; Shi, Cynthia X.; Huang, Jie; Zhang, Fujie; Rou, Keming; Wu, Zunyou (2017). Mortality and virological failure among HIV-infected people who inject drugs on antiretroviral treatment in China: An observational cohort study. Drug and Alcohol Dependence, 170189-197. | No in/out treatment data available |

**eTable 4: Cause of death categories**

| | ICD-9 | ICD-10 | Sources |
|---|---|---|---|
| **All injury and poisoning** | 304, 305.2-305.9, E800-E869, E880-E929, E950-E999 | F11-F16, F19, F55, V00-X99, Y00-Y39, Y85-Y87, Y89 | CHO injury and poisoning indicator (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_diag.htm)<br>- *NB: F codes added to ICD-10 to include drug related deaths in circumstances of dependence (likewise 300 codes for ICD-9) and to encapsulate all deaths in subcategories below* |
| Drug-induced deaths | 304, 305.2-305.9, E850-E858, E950.0-E950.5, E962.0, E980.0-E980.5 | F11- F16, F19, F55, X40- X44, X60-X64, X85, Y10-Y14 | ABS definitions of drug induced deaths (http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/3321.0.55.001Explanatory%20Notes11991-2001?OpenDocument) |
| Accidental drug-induced deaths | 304, E850-E858 | F11-F16, F19, F55, X40-X44 | ICD10 codes from: Barker B and Degenhardt L. Accidental drug-induced deaths in Australia 1997-2001. NDARC Technical Report No. 163. Sydney, National Drug and Alcohol Research Centre, University of New South Wales. |
| Accidental opioid deaths | 304.0, 304.7, E850.0-E850.2 | F11; F19 & F11;<br>X42 & T40.0-T40.4 or T40.6;<br>X44 & T40.0-T40.4 or T40.6;<br>F19 & T40.0-T40.4 or T40.6 | Barker B and Degenhardt L. Accidental drug-induced deaths in Australia 1997-2001. NDARC Technical Report No. 163. Sydney, National Drug and Alcohol Research Centre, University of New South Wales.<br>Added E850.2 in the ICD9 definition – Accidental poisoning by other opiates and related narcotics. |
| **Suicide** | E950-E959 | X60- X84, Y87.0 | CHO suicide indicator (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_diag.htm) |
| **Violence** | E960-E969 | X85-Y09, Y87.1 | CHO violence indicator (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_avm.htm) |
| **Motor vehicle and transport accidents** | E810-E825, E929.0 | V01-V99 | CHO motor vehicle crash injury indicator (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_diag.htm) and CHO unintentional injuries indicators (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_avm.htm)<br>- *NB: modified to only the ICD-10 chapter 'Transport Accidents' including all codes in this chapter* |
| **Falls/fires/burns/drownings** | E880-E886, E888; E890-E899; E910 | W00-W19, W65-W74, X00-X09 | CHO unintentional injuries indicators (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_avm.htm) |
| **All liver-related** | 070, 155, 570, 571, 572-573 | B15–B19, B94.2, C22, I85.0, K70–K77, O98.4, P35.3 | Amin J, Law M, Bartlett M, Kaldor J, Dore G. Causes of death after diagnosis of hepatitis B or hepatitis C infection: a large community-based linkage study. Lancet 2006; 368: 938–45.<br>Added obstetric and neonatal hepatitis codes from CHO viral hepatitis indicator. |

| | ICD-9 | ICD-10 | Sources |
|---|---|---|---|
| | | | - *NB: I85.0 (Oesophageal varices with bleeding) added* |
| Viral hepatitis | 070 | B15-B19, B94.2, I85.0, O98.4, P35.3 | CHO potentially avoidable mortality table (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_avm.htm) and diagnosis table (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_diag.htm)<br>- *NB: I85.0 (Oesophageal varices with bleeding) added* |
| **All alcohol-related** | 291, 303.0, 303.9, 305.0, 357.5, 425.5, 535.3, 571.0-571.3, E860.0-E860.2 | E24.4, F10, G31.2, G62.1, G72.1, I42.6, K29.2, K70, K86.0, R78.0, X45, X65, Y15 | ABS alcohol-induced deaths indicator in 3303.0 - Causes of Death, Australia, 2006 (http://www.abs.gov.au/AUSSTATS/abs@.nsf/Latestproducts/3303.0Appendix32006?opendocument&tabname=Notes&prodno=3303.0&issue=2006&num=&view=)<br>ICD9 translation assisted by Chikritzhs et al 2002 'Alcohol-related codes: Mapping ICD-9 to ICD-10' Technical Report from NDRI and Dept of Health, Western Australia (http://espace.lis.curtin.edu.au/archive/00000406/01/T128_ICD9-ICD10.pdf) |
| **Cancer** | 140-208 | C00-C97 | CHO indicator for cancer (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_diag.htm) |
| **Cardiovascular disease** | 390-459 | I00-I99, G45, G46 | CHO cardiovascular disease indicator (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_diag.htm) |
| **Chronic respiratory disease** | 491, 492, 493, 496 | J41-J46 | CHO chronic respiratory disease indicator (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_diag.htm) |
| **Digestive disorders** *(including chronic liver disease)* | 531-534, 540-543, 550-553, 571.4-571.9, 574-577 | K25-K28, K35-K38, K40-K46, K73, K74, K80-K83, K85-K86, K91.5 | CHO potentially avoidable mortality table (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_avm.htm) |
| **HIV-related** | 042-044, 279.10 | B20-B24 | ABS definition in 3303.0 - Causes of Death, Australia, 2006, explanatory notes point 42 (http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/3303.0Explanatory%20Notes12006?OpenDocument) |
| **Influenza and pneumonia** | 480-487 | J10-J18 | CHO indicator (http://www.health.nsw.gov.au/public-health/chorep/toc/app_icd_diag.htm) |
| **Injection-related injuries and diseases** *(including osteomyelitis)* | 1128, 11281, 421*, 424*,038*, 4151, 41512, 4229, 42292, 449*, 7855*, 7907*, 9959, 99590-2, 7300*-7302*, | B376, I33*-I37*, I38, I39*, A40*, A41*, I269, I400, R572, R651, R659, M86*, M899*, I80*, L97*, L988, | Janjua NZ, Islam N, Kuo M, et al. Identifying injection drug use and estimating population size of people who inject drugs using healthcare |

| | ICD-9 | ICD-10 | Sources |
|---|---|---|---|
| | 7309*, 0400*, 324*, 326*, 451*, 5672, 56722, 56731, 56738, 5695*, 5720*, 5901*, 681*, 682*, 7071*, 7078*, 7079*, 7098*, 7236*, 72886, 7293, 72930, 72939, 7854*, 7300*-7302*, 7309* | M793*, A480, G06*, G09, K630, K650, K750, L02*, L03*, M5402, M726*, N10, R02 | administrative datasets. *The International journal on drug policy* 2018; **55**: 31-9. |
| Endocarditis | 1128, 11281, 421*, 424* | B376, I33*-I37*, I38, I39* | Janjua NZ, Islam N, Kuo M, et al. Identifying injection drug use and estimating population size of people who inject drugs using healthcare administrative datasets. *The International journal on drug policy* 2018; **55**: 31-9. |
| Bacteraemia or sepsis | 038*, 4151, 41512, 4229, 42292, 449*, 7855*, 7907*, 9959, 99590-2 | A40*, A41*, I269, I400, R572, R651, R659 | Janjua NZ, Islam N, Kuo M, et al. Identifying injection drug use and estimating population size of people who inject drugs using healthcare administrative datasets. *The International journal on drug policy* 2018; **55**: 31-9. |
| Skin or soft tissue infections | 0400*, 324*, 326*, 451*, 5672, 56722, 56731, 56738, 5695*, 5720*, 5901*, 681*, 682*, 7071*, 7078*, 7079*, 7098*, 7236*, 72886, 7293, 72930, 72939, 7854* | I80*, L97*, L988, M793*, A480, G06*, G09, K630, K650, K750, L02*, L03*, M5402, M726*, N10, R02 | Janjua NZ, Islam N, Kuo M, et al. Identifying injection drug use and estimating population size of people who inject drugs using healthcare administrative datasets. *The International journal on drug policy* 2018; **55**: 31-9. |

## eTable 5: Variables

| **Demographic and study details** | |
|---|---|
| Author; PubYear; LitType | Publication details |
| Country; Area; Area_Spec | Geographical details |
| Studytype; RCT | Study design e.g. RCT, retrospective cohort |
| Subpopulation | If the study was restricted to a particular group among people with OUD e.g. HIV+ |
| Recruitment_setting; Recruitment_other | How were participants recruited? |
| OAT_avail; OAT_availspecify | OAT drug used in the study |
| OATsites | Whether the study was single or multi-site |
| OUD_define | How opioid use disorder was defined |
| Linkage | Was this a linkage study? |
| Data_sources | What data sources were used? |
| Deathverify; Deathverify_other | How were deaths verified? |
| RCT_groups | For RCTs – what were the comparison groups? |
| Elig_notes | Eligibility criteria |
| Datestart; Dateend | Study years |
| Subgroups; Subgroups_select; Subgroups_specify | Indicates whether relevant data is available stratified by subgroups |
| FU_dur; FU_durM; FU_durMed; FU_durSD; FU_durRange | Details reported for follow up duration for group involved in OAT |
| FU_loss; FU_loss% | n/% lost to follow up for group involved in OAT |
| FU_dur_overall; FU_durM_overall; FU_durMed_overall; FU_durSD_overall; FU_durRange_overall | Details reported for follow up duration for whole sample if not all were involved in OAT |
| FU_loss_overall; FU_loss%_overall | n/% lost to follow up for whole sample if not all were involved in OAT |
| FU_dur_comp; FU_durM_comp; FU_durMed_comp; FU_durSD_comp; FU_durRange_comp | Details reported for follow up duration for comparator group |
| FU_loss_comp; FU_loss%_comp | n/% lost to follow up for comparator group |
| N; N_overall; N_comp | Total N in OAT group, total cohort and comparator group |
| M; M_overall; M_comp | Number of males in OAT group, total cohort and comparator group |
| M%; M%_overall; M%_comp | % males in OAT group, total cohort and comparator group |
| F; F_overall; F_comp | Number of females in OAT group, total cohort and comparator group |
| F%; F%_overall; F%_comp | % females in OAT group, total cohort and comparator group |
| age; age_unit; age_SD; age_min; age_max | Age details as reported for sample engaged in OAT |
| age_overall; age_unit_overall; age_SD_overall; age_min_overall; age_max_overall | Age details as reported for total cohort if not all were involved in OAT |
| age_comp; age_unit_comp; age_SD_comp; age_min_comp; age_max_comp | Age details as reported for comparator group |
| homestable_n; homestable_%; homeunstab_n; homeunstab_% | n/% with stable/unstable housing situations as reported |
| primOp; primOp_n; primOp_% | Primary opioid used |
| OUage_unit; OU_age; OUage_SD; OUage_IQR | Age commenced opioid use |
| Inj_n; Inj_%; Inj_curr | n/% reporting current injection drug use & definition of current |
| od_define; odhxLT_n; odhxLT_%; odhxRec_n; odhxRec_%; odhx_recency | n/% with recent or lifetime history of overdose – with definitions of overdose and recency |
| DxHIV; DxHIV_n; DxHIV_%; DxHIV_test | Whether whole sample is HIV+ or n/% diagnosed HIV+ and verification test if specified |
| DxHCV; DxHCV_n; DxHCV_%; DxHCV_test | Whether whole sample is HCV+ or n/% diagnosed HCV+ and verification test if specified |
| DxSUD; DxSUD_n; DxSUD_% | Whether whole sample has co-morbid substance use disorder or n/% with co-morbid substance use disorder |
| DxPsy | Whether sample all has a psychiatric co-morbidity |
| DxPsy1; DxPsy1_n; DxPsy1_% | n/%/specification for first psychiatric co-morbidity reported on |

| | |
|---|---|
| DxPsy2; DxPsy2_n; DxPsy2_% | n/%/specification for second psychiatric co-morbidity reported on |
| DxMed | Whether sample all has a medical co-morbidity |
| DxMed1; DxMed1_n; DxMed1_% | n/%/specification for first medical co-morbidity reported on |
| DxMed2; DxMed2_n; DxMed2_% | n/%/specification for second medical co-morbidity reported on |
| Prison; Prison_n; Prison_% | Whether the whole cohort was in prison or n/% who were |
| Sexwk; Sexwk_n; Sexwk_% | Whether the whole cohort was engaged in sex work or the n/% who were |
| MMT_dose; BMT_dose | Average dose of methadone and/or buprenorphine |
| MMT_prov; BMT_prov; OAT_prov | Treatment provider for methadone, buprenorphine and/or overall OAT |
| MMT_inge; BMT_inge | Ingestion/intake details for methadone and/or buprenorphine |
| MMT_naivecoh; BMT_naivecoh; OAT_naivecoh | Whether sample engaged in methadone, buprenorphine and/or OAT overall was previously treatment naive |
| MMT_takeaway; BMT_takeaway; OAT_takeaway | Whether takeaway doses were available for methadone, buprenorphine and/or OAT overall |
| MMT_dur; BMT_dur; OAT_dur; MMT_durIQR; BMT_durIQR; OAT_durIQR | Median treatment duration (and interquartile range) for methadone, buprenorphine and/or OAT overall |
| MMT_OutTx; BMT_OutTx; OAT_Outtx | Definition of in and out of treatment for methadone, buprenorphine and/or OAT overall |
| ConcurTx; ConcurTx_specify | Whether another treatment was provided concurrently and if so which |
| TxLocate_Community; TxLocate_Prison; TxLocate_PostPris; TxLocate_Hospital | Location/circumstance of treatment – community, prison, post-release or hospital |
| **In and out of treatment mortality data** | |
| inTx_py | person years in treatment |
| inTx_deaths | number of deaths in treatment |
| inTx_allCMR; inout_unit; inout_unitother | Crude Mortality Rate in treatment (all-cause); & associated unit |
| inTx_allSMR | Standardized Mortality Rate in treatment |
| inTx_missing_n; inTx_missing_notes | number for whom in treatment data is missing |
| outTx_py | person years out of treatment |
| outTx_deaths | number of deaths out of treatment |
| outTx_allCMR | Crude Mortality Rate out of treatment |
| outTx_allSMR | Standardised Mortality Rate out of treatment |
| outTx_missing_n; outTx_missing_notes | number for whom out of treatment data is missing |
| InjPois_define | definition of 'All injury and poisoning' deaths |
| Drug_define | definition of 'Drug-induced deaths' |
| AccDrug_define | definition of 'Accidental drug-induced deaths' |
| AccOp_define | definition of 'Accidental opioid deaths' |
| Suic_define | definition of 'Suicide' |
| Viol_define | definition of 'Violence' deaths |
| Cardio_define | definition of 'Cardiovascular disease' deaths |
| Liver_define | definition of 'All-liver-related' deaths |
| VirHep_define | definition of 'Viral hepatitis' deaths |
| Alc_define | definition of 'All alcohol-related' deaths |
| Canc_define | definition of 'Cancer' deaths |
| HIV_define | definition of 'HIV-related' deaths |
| CRD_define | definition of 'Chronic respiratory disease' deaths |
| Digest_define | definition of 'Digestive disorders' deaths |
| Flu_define | definition of 'Influenza and pneumonia' deaths |
| Inject_define | definition of 'Injection-related injuries and diseases' deaths |
| Endo_define | definition of 'Endocarditis' deaths |
| Seps_define | definition of 'Bacteraemia or sepsis' deaths |
| Skin_define | definition of 'Skin or soft tissue infections' deaths |
| MVA_define | definition of 'Motor vehicle and transport accidents' deaths |
| Fall_define | definition of 'Falls/Fires/Burns/Drownings' deaths |
| inTx_*XXXX*_n | number of deaths in treatment for each CoD |
| outTx_*XXXX*_n | number of deaths out of treatment for each CoD |
| G1_inTx_py | person years in treatment on methadone |
| G1_inTx_deaths | number of deaths in treatment on methadone |
| G1_inTx_allCMR | Crude Mortality Rate in treatment (all-cause) & associated unit |
| G1_inTx_allSMR | Standardised Mortality Rate in treatment on methadone |

| | |
|---|---|
| G1_inTx_missing_n; G1_inTx_missing_notes | number for whom in treatment (methadone) data is missing |
| G1_outTx_py | person years in treatment on methadone |
| G1_outTx_deaths | number of deaths in treatment on methadone |
| G1_outTx_allCMR | Crude Mortality Rate out of methadone treatment |
| G1_outTx_allSMR | Standardised Mortality Rate out of methadone treatment |
| G1_outTx_missing_n;<br>G1_outTx_missing_notes | number for whom out of treatment data is missing |
| G1_inTx_*XXXX*_n | number of deaths in methadone treatment for each CoD |
| G1_outTx_*XXXX*_n | number of deaths out of methadone treatment for each CoD |
| G2_inTx_py | person years in treatment on buprenorphine |
| G2_inTx_deaths | number of deaths in treatment on buprenorphine |
| G2_inTx_allCMR | Crude Mortality Rate in treatment with buprenorphine |
| G2_inTx_allSMR | Standardised Mortality Rate in treatment with buprenorphine |
| G2_inTx_missing_n; G2_inTx_missing_notes | number for whom in treatment (buprenorphine) data is missing |
| G2_outTx_py | person years out of buprenorphine treatment |
| G2_outTx_deaths | number of deaths out of buprenorphine treatment |
| G2_outTx_allCMR | Crude Mortality Rate out of buprenorphine treatment |
| G2_outTx_allSMR | Standardised Mortality Rate out of buprenorphine treatment |
| G2_outTx_missing_n;<br>G2_outTx_missing_notes | number for whom out of treatment (buprenorphine) data is missing |
| G2_inTx_*XXXX*_n | number of deaths in buprenorphine treatment for each CoD |
| G2_outTx_*XXXX*_n | number of deaths out of buprenorphine treatment for each CoD |
| G3_specify | specification of 'other' OAT type for which in/out data is available |
| G3_inTx_py | person years in 'other' treatment |
| G3_inTx_deaths | number of deaths in 'other' treatment |
| G3_inTx_allCMR | Crude Mortality Rate in 'other' treatment |
| G3_inTx_allSMR | Standardised Mortality Rate in 'other' treatment |
| G3_inTx_missing_n; G3_inTx_missing_notes | number for whom in 'other' treatment data is missing |
| G3_outTx_py | person years out of 'other' treatment |
| G3_outTx_deaths | number of deaths out of 'other' treatment |
| G3_outTx_allCMR | Crude Mortality Rate out of 'other' treatment |
| G3_outTx_allSMR | Standardised Mortality Rate out of 'other' treatment |
| G3_outTx_missing_n;<br>G3_outTx_missing_notes | number for whom out of 'other' treatment is missing |
| G3_inTx_*XXXX*_n | number of deaths in 'other' treatment for each CoD category |
| G3_outTx_*XXXX*_n | number of deaths out of 'other' treatment for each CoD category |
| **In and out of treatment mortality data by time period (4 week/remainder) – each variable collected for overall/any OAT, methadone only, buprenorphine only and other specified OAT type** | |
| inTxstart4_py | person years in first four weeks of treatment |
| inTxstart4_deaths | number of deaths in first four weeks of treatment |
| start4_unit; start4_unitother | unit if CMRs/SMRs are reported |
| inTxstart4_allCMR | Crude Mortality Rate for first four weeks in treatment |
| inTxstart4_allSMR | Standardised Mortality Rate for first four weeks in treatment |
| inTxremainder4_py | person years in remainder of time in treatment |
| inTxremainder4_deaths | number of deaths in remainder of time in treatment |
| inTxremainder4_allCMR | Crude Mortality Rate for remainder of time in treatment |
| inTxremainder4_allSMR | Standardised Mortality Rate for remainder of time in treatment |
| outTxstart4_py | person years in first four weeks out of treatment |
| outTxstart4_deaths | number of deaths in first four weeks out of treatment |
| outTxstart4_allCMR | Crude Mortality Rate for first four weeks out of treatment |
| outTxstart4_allSMR | Standardised Mortality Rate for first four weeks out of treatment |
| outTxremainder4_py | person years in first four weeks out of treatment |
| outTxremainder4_deaths | number of deaths in first four weeks out of treatment |
| outTxremainder4_allCMR | Crude Mortality Rate for first four weeks out of treatment |
| outTxremainder4_allSMR | Standardised Mortality Rate for first four weeks out of treatment |
| inTxstart4_*XXXX*_n | number of deaths during first four weeks of treatment for each CoD category |
| inTxremainder4_*XXXX*_n | number of deaths during remainder of time in treatment for each CoD category |

| | |
|---|---|
| outTxstart4_*XXXX*_n | number of deaths during first four weeks out of treatment for each CoD category |
| outTxremainder4_*XXXX*_n | number of deaths during remainder of time out of treatment for each CoD category |
| **In and out of treatment mortality data by time period (other) – each variable collected for overall/any OAT, methadone only and buprenorphine only** | |
| startother_define | definition of start/remainder periods |
| inTxstartother_py | person years in 'start' period in treatment |
| inTxstartother_deaths | number of deaths in 'start' period in treatment |
| inTxremainderother_py | person years in 'remainder' period in treatment |
| inTxremainderother_deaths | number of deaths in 'remainder' period in treatment |
| outTxstartother_py | person years in 'start' period out of treatment |
| outTxstartother_deaths | number of deaths in 'start' period out of treatment |
| outTxremainderother_py | person years in 'remainder' period out of treatment |
| outTxremainderother_deaths | number of deaths in 'remainder' period out of treatment |
| inTxstartother_*XXXX*_n | number of deaths during 'start' period in treatment for each CoD category |
| inTxremainderother_*XXXX*_n | number of deaths during 'remainder' period in treatment for each CoD category |
| outTxstartother_*XXXX*_n | number of deaths during 'start' period out of treatment for each CoD category |
| outTxremainderother_*XXXX*_n | number of deaths during 'remainder' period out of treatment for each CoD category |
| **In and out of treatment mortality stratified by client and treatment features** | |
| male_inTx_py | person years in treatment for males |
| male_inTx_deaths | number of deaths in treatment for males |
| male_outTx_py | person years out of treatment for males |
| male_outTx_deaths | number of deaths out of treatment for males |
| female_inTx_py | person years in treatment for females |
| female_inTx_deaths | number of deaths in treatment for females |
| female_outTx_py | person years out of treatment for females |
| female_outTx_deaths | number of deaths out of treatment for females |
| und35_inTx_py | person years in treatment for those under 35 at baseline |
| und35_inTx_deaths | number of deaths in treatment for those under 35 at baseline |
| und35_outTx_py | person years out of treatment for those under 35 at baseline |
| und35_outTx_deaths | number of deaths out of treatment for those under 35 at baseline |
| 35over_inTx_py | person years in treatment for those 35 and over at baseline |
| 35over_inTx_deaths | number of deaths in treatment for those 35 and over at baseline |
| 35over_outTx_py | person years out of treatment for those 35 and over at baseline |
| 35over_outTx_deaths | number of deaths out of treatment for those 35 and over at baseline |
| PWID_inTx_py | person years in treatment for people who inject drugs |
| PWID_inTx_deaths | number of deaths in treatment for people who inject drugs |
| PWID_outTx_py | person years out of treatment for people who inject drugs |
| PWID_outTx_deaths | number of deaths out of treatment for people who inject drugs |
| nonPWID_inTx_py | person years in treatment for people who do not inject drugs |
| nonPWID_inTx_deaths | number of deaths in treatment for people who do not inject drugs |
| nonPWID_outTx_py | person years out of treatment for people who do not inject drugs |
| nonPWID_outTx_deaths | number of deaths out of treatment for people who do not inject drugs |
| HIVpos_inTx_py | person years in treatment for people who are HIV-positive |
| HIVpos_inTx_deaths | number of deaths in treatment for people who are HIV-positive |
| HIVpos_outTx_py | person years out of treatment for people who are HIV-positive |
| HIVpos_outTx_deaths | number of deaths out of treatment for people who are HIV-positive |
| HCVpos_inTx_py | person years in treatment for people who are HCV-positive |
| HCVpos_inTx_deaths | number of deaths in treatment for people who are HCV-positive |
| HCVpos_outTx_py | person years out of treatment for people who are HCV-positive |
| HCVpos_outTx_deaths | number of deaths out of treatment for people who are HCV-positive |
| spec_inTx_py | person years in treatment with a specialist |
| spec_inTx_deaths | number of deaths in treatment with a specialist |
| spec_outTx_py | person years out of treatment with a specialist |
| spec_outTx_deaths | number of deaths out of treatment with a specialist |

| | |
|---|---|
| nonspec_inTx_py | person years in treatment with a GP/mixed/other provider |
| nonspec_inTx_deaths | number of deaths in treatment with a GP/mixed/other provider |
| nonspec_outTx_py | person years out of treatment with a GP/mixed/other provider |
| nonspec_outTx_deaths | number of deaths out of treatment with a GP/mixed/other provider |
| **Mortality data for randomised controlled trials** | |
| ComparType; ComparType_Other; ComparType_Notes | Details about comparator to OAT |
| Cmp_inTx_py | person years of follow-up in OAT group |
| Cmp_inTx_deaths | deaths in OAT group |
| Cmp_inTx_allCMR; Cmp_unit; Cmp_unitother | Crude Mortality Rate for OAT group including specification of unit for CMRs and SMRs |
| Cmp_inTx_allSMR | Standardised Mortality Rate for OAT group |
| Cmp_inTx_missingn; Cmp_inTx_missingNotes | n for whom outcome data is missing in OAT group |
| Cmp_outTx_py | person years of follow-up in comparator group |
| Cmp_outTx_deaths | deaths in comparator group |
| Cmp_outTx_allCMR | Crude Mortality Rate for comparator group |
| Cmp_outTx_allSMR | Standardised Mortality Rate for comparator group |
| Cmp_outTx_missingn; Cmp_outTx_missingNotes | n for whom outcome data is missing in the comparator group |
| Cmp_inTx_*XXXX*_n | number of deaths in OAT group for each CoD category |
| Cmp_outTx_*XXXX*_n | number of deaths in comparator group for each CoD category |
| Cmp_start_define | definition of start and remainder time periods e.g. first four weeks & remainder |
| Cmp_inTxStart_py | person years in 'start' period for OAT group |
| Cmp_inTxStart_deaths | number of deaths in 'start' period for OAT group |
| Cmp_inTxStart_*XXXX*_n | number of deaths during 'start' period for each CoD category in the OAT group |
| Cmp_inTxRem_py | person years in 'remainder' period for OAT group |
| Cmp_inTxRem_deaths | number of deaths during 'remainder' period for OAT group |
| Cmp_inTxRem_*XXXX*_n | number of deaths during 'remainder' period for each CoD category in the OAT group |
| Cmp_outTxStart_py | person years in 'start' period for comparator group |
| Cmp_outTxStart_deaths | number of deaths in 'start' period for comparator group |
| Cmp_outTxStart_*XXXX*_n | number of deaths during 'start' period for each CoD category in the comparator group |
| Cmp_outTxRem_py | person years in 'remainder' period for comparator group |
| Cmp_outTxRem_deaths | number of deaths during 'remainder' period for comparator group |
| Cmp_outTxRem_*XXXX*_n | number of deaths during 'remainder' period for each CoD category in the comparator group |

**eTable 6: Key extracted and used data**

| Study (Author, ref) | Years of cohort observation | Country | N | All-Cause Deaths | | | | Drug-Induced Deaths | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | N deaths in treatment | N person-years in treatment | N deaths out of treatment | N person-years out of treatment | N deaths in treatment | N person-years in treatment | N deaths out of treatment | N person-years out of treatment |
| **Abrahamsson 2017** | 2005-2012 | Sweden | 4501 | 194 | 14550 | 163 | 6888 | 83 | 14550 | 110 | 6888 |
| **Appel 2000** | 1966-1976 | United States | 1544 | 93 | 6130 | 83 | 2355 | 37 | 6130 | 56 | 2355 |
| **Bakker 2017** | 1994-2015 | England | 278 | 15 | 1289 | 26 | 892 | | | | |
| **Bazazi 2018** | 2010-2014 | Malaysia | 214 | 42 | 606.3 | 19 | 259.4 | | | | |
| **Bukten 2019** | 1997-2009 | Norway | 7843 | 378 | 29172 | 319 | 11345 | 160 | 29172 | 227 | 11345 |
| **Buster 2002** | 1986-1998 | Netherlands | 5200 | | | | | 42 | 18747 | 26 | 10983 |
| **Chang 2015** [A] | 2006-2011 | Taiwan | 983 | 16 | 2861 | 52 | 1535 | | | | |
| **Cousins 2011** [A] | 1993-2004 | Scotland | 3162 | 61 | 4067.99 | 79 | 4313.24 | 31 | 4067.99 | 24 | 4313.24 |
| **Cousins 2016** [A] | 2004-2010 | Ireland | 6983 | 115 | 22647.9 | 98 | 6247.4 | 54 | 22347.6 | 24 | 6195.2 |
| **Davoli 2007** | 1998-2001 | Italy | 10258 | | | | | 7 | 5751.28 | 34 | 7370.27 |
| **Degenhardt 2009** [A] | 1985-2006 | Australia | 42676 | 1223 | 202337.09 | 2580 | 223660.69 | 434 | 186542 | 1411 | 201073 |
| **Digiusto 2004** | - | Australia | 1244 | 0 | 267.6 | 2 | 19.7 | 0 | 267.6 | 0 | 19.7 |
| **Dupouy 2017** [A] | 2007-2013 | France | 713 | 4 | 1401.97 | 25 | 1817.56 | | | | |
| **Durand 2020** [A] | 2010-2015 | Ireland | 2899 | 107 | 11874.75 | 45 | 1426.01 | 48 | 11874.75 | 7 | 1426.01 |
| **Evans 2015** | 2006-2010 | United States | 32322 | 163 | 25277 | 868 | 51380 | | | | |
| **Fellows-Smith 2011** | 1998-2000 | Australia | 2520[#] | 14 | 1922 | 23 | 3096 | | | | |
| **Fugelstad 2007** | 1988-2000 | Sweden | 848 | 77 | 3353.9 | 108 | 2170.6 | 0 | 3353.9 | 67 | 2170.6 |
| **Gearing 1974** | 1964-1971 | United States | 801 | 110 | 14473.68 | 33 | 1170.21 | 33 | 14473.68 | 21 | 1170.21 |
| **Gronbladh 1990** | 1967-1988 | Sweden | 281 | 16 | 1085.4767 | 80 | 1407.1 | 7 | 1085.4767 | 70 | 1407.1 |
| **Hickman 2018** [A] | 1998-2014 | UK | 11033 | 132 | 14384.548 | 384 | 25713.947 | 35 | 14384.548 | 125 | 25713.947 |
| **Huang 2011** | 2007-2008 | Taiwan | 1982 | 3 | 1244.6 | 28 | 719.2 | | | | |
| **Huang 2013** [A] | 2006-2008 | Taiwan | 1616 | 13 | 550.62 | 13 | 208.84 | 1 | 550.62 | 0 | 208.84 |
| **Kelty 2019** [A] | 2001-2010 | Australia | 5116 | 87 | 14989.8 | 177 | 19187.6 | 35 | 14989.8 | 73 | 19187.6 |
| **Kimber 2015** [A] | 2001-2010* | Australia | 46531 | 481 | 83485.8 | 1211 | 119691.12 | 162 | 83485.8 | 464 | 119691.12 |
| **Degenhardt 2014** [A] | 2000-2012 | Australia | 16453 | By OAT post-release: 63 | 15438.57 | 355 | 18504.67 | 15 | 15438.57 | 101 | 18504.67 |

| Study (Author, ref) | Years of cohort observation | Country | N | All-Cause Deaths | | | | Drug-Induced Deaths | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | N deaths in treatment | N person-years in treatment | N deaths out of treatment | N person-years out of treatment | N deaths in treatment | N person-years in treatment | N deaths out of treatment | N person-years out of treatment |
| | | | | By OAT in prison: 156 | 17405.68 | 262 | 16537.55 | 29 | 17405.68 | 87 | 16537.55 |
| **Larney 2014** | 2000-2012 | Australia | 16453 | 11 | 16440 | 40 | 14548 | 0 | 16440 | 6 | 14548 |
| **Larochelle 2018** | 2012-2015 | United States | 17568 | 43 | 2255.83 | 764 | 15025.83 | | | | |
| **Liu 2013** | 2004-2011 | China | 306786 | 1527 | 190646.4 | 4046 | 282058.7 | | | | |
| **Marsden 2017** [A] | 2010-2016 | England | 12260 | 81 | 7263 | 79 | 5869 | 47 | 7263 | 55 | 5869 |
| **Morozova 2013** [A] | 2011-2012 | Ukraine | 110 | 6 | 13.35 | 3 | 12.208 | | | | |
| **Muga 2014** [A] | 1992-2010 | Spain | 1678 | 299 | 9685.1 | 142 | 5439.2 | | | | |
| **Pavarin 2017** [A] | 2001-2013** | Italy | 2232 | 36 | 5080.84 | 77 | 11242.21 | 7 | 5080.84 | 24 | 11242.21 |
| **Pearce 2020** [A] | 1996-2018 | Canada | 55347 | 2197 | 202315.36 | 4833 | 198501.82 | 460 | 202315.36 | 1837 | 198501.82 |
| **Pierce 2016** | 2005-2009 | England | 151983 | | | | | 712 | 272280 | 787 | 170666 |
| **Reece 2010** | 2000-2007 | Australia | 2518[#] | 3 | 1118.54 | 40 | 6911.48 | 3 | 1118.54 | 13 | 6911.48 |
| **Scherbaum 2002** | 1988-1996 | Germany | 244 | 18 | 1114 | 14 | 172 | | | | |
| **Weber 1990** | 1984- | Switzerland | 297 | 7 | 168.67 | 33 | 371.225 | 0 | 168.67 | 12 | 371.225 |

**eTable 7: Characteristics of eligible randomised controlled trials and observational studies that reported on the impact of opioid agonist treatment (OAT) on mortality**

| Randomised controlled trials | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Study** | **Years** | **Country** | **Geographic area** | **Recruitment setting** | **Type of OAT (comparator)** | **Treatment provider** | **Follow Up Length (planned)** | **% LTFU** | **N OAT** | **N Comparator** | **% women** | **Mean age at baseline** | **% PWID** |
| **Gordon 2014**[43] | 2008-2012 | USA | Prison clinics | Maryland prisons | Buprenorphine (counselling) | Mixed | 3–6 months | B: 39; C: 29 | 104 | 107 | B: 31; C: 29 | 39 | NR |
| **Gruber 2008**[44] [A] | 1995-1997 | USA | Single clinic | Hospital (outpatient clinic) | Methadone (detoxification) | NR | 6 months | M: 50; C: 62 | 72 | 39 | M: 46; C: 26 | M: 41; C: 43 | NR |
| **Gunne 1981**[26] | 1973-1979 | Sweden | National | OAT clinic | Methadone (waitlist) | Psychiatrist | 2 years [B] | Me: 0; C: 12 | 17 | 17 | M: 35; C: 12 | M: 23; C: 23 | 100 |
| **Kakko 2003**[45] | 2000-2001 | Sweden | Single clinic | Drug treatment clinic | Buprenorphine (detoxification, placebo) | NR | 1 year | B: 25; C: 100 | 20 | 20 | B: 25; C: 70 | B: 29; C: 32 | 98 |
| **Kinlock 2009**[46] | 2003-2006 | USA | Single clinic | Prison | Methadone (counselling) | NR | 12 months | M: 0; C: 7 | 71 | 140 | 0 | M: 34; C: 41 | NR |
| **Krook 2002**[47] | 2000 | Norway | Single clinic | Waitlist for OAT clinic | Buprenorphine (placebo) | Mixed | 3 months | B: 7; C: 6 | 55 | 51 | B: 35; C: 33 | B: 38; C: 38 | NR |
| **Lee 2018**[48] | 2014-2017 | USA | 8 community sites | Inpatient detox, community | Buprenorphine (injectable naltrexone) | Mixed | 9 months | B: 14; C: 19 | 287 | 283 | B: 72; C: 31 | B: 34; C: 34 | 63 |
| **Ling 2010**[49] | 2007-2008 | USA | 18 community sites | Community treatment centres | Buprenorphine (placebo) | Physician | 6 months | B: 34; C: 69 | 108 | 55 | B: 33; C: 27 | B: 36; C: 39 | NR |
| **Metzger 2015**[50] | 2007-2011 | China, Thailand | City/Jurisdictional | Drug and HIV treatment, community | Buprenorphine (detoxification) | NR | 2 years | B: 5; C: 6 | 623 | 627 | B: 8; C: 8 | B: 33; C:34 (median) | 100 |
| **Newman 1979**[51] | 1972-1975 | Hong Kong | Single clinic | OAT clinic | Methadone (detoxification) | Mixed | 3 years | OAT: 44; C: 98 | 50 | 50 | 0 | OAT: 38; C: 38 | 38 |
| **Rich 2015**[52] | 2011-2015 | USA | Prison clinic | Prison (Rhode Island) | Methadone (forced withdrawal) | NR | 1-26 weeks | M: 4; C: 20 | 114 | 109 | M: 24; C: 21 | M: 33; C: 36 | NR |
| **Schottenfeld 2008**[53] | 2003-2005 | Malaysia | Single clinic | Community | Buprenorphine (detox, placebo/naltrexone) | NR | 6 months | B: 18; C: 37 | 44 | 82 | NR | B: 36; C: 38 | 41 |
| **Strain 1993**[54] [A] | 1988-1990 | USA | Single clinic | OAT Clinic | Methadone (detoxification) | NR | 6 months | NR | 166 | 81 | M: 31; C: 28 | M (20mg): 33; M (50mg): 35; C: 33 | 100 |
| **Tanum 2017**[55] | 2012-2015 | Norway | 5 addiction clinics | Outpatient clinics and detox units | Buprenorphine (injectable naltrexone) | NR | 3 months | B: 19; C: 29 | 79 | 80 | B: 32; C: 24 | B: 36; C: 36 | 86 |
| **Yancovitz 1991**[56] | 1989 | USA | Single Clinic (NYC) | Waitlist for OAT clinic | Methadone (waitlist) | Mixed | 1 month | M: 28; C: 43 | 149 | 152 | M: 19; C: 22 | M: 35; C: 34 | NR |

| Observational studies | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Study** | **Years** | **Country** | **Geographic area** | **Recruitment setting** | **Type of OAT** | **Treatment provider** | **Mean follow up years** | **N** | **% women** | **Mean age at baseline** | **% PWID** |
| **Abrahamsson 2017**[57] | 2005-2012 | Sweden | National | National Registry | Unspecified OAT | Psychiatrist | 5 | 4501 | 26 | 34 (median) | NR |
| **Ledberg 2017**[58] [A] | 2006-2013 | Sweden | State: Stockholm County | Registry | Methadone | NR | 5 (median) | 441 | 24 | 41 | NR |
| **Appel 2000**[59] | 1966-1976 | USA | City: Greater New York City | OAT Clinic | Methadone | NR | NR | 1544 | NR | NR | NR |
| **Bakker 2017**[60] | 1994-2015 | England | Single clinic (inner London) | General practice | Unspecified OAT | GP | NR | 278 | 31 | NR | NR |
| **Bazazi 2018**[20] | 2010-2014 | Malaysia | City: Kajang Prison | Prison | Methadone | NR | 12 months | 291 | 0 | 39 | 95 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Bukten 2019**[61] | 1997-2009 | Norway | National | National registry | Unspecified OAT | Addiction medicine specialist | NR | 7843 | 29 | 36 | NR |
| **Buster 2002**[62] | 1986-1998 | Netherlands | City: Amsterdam | Registry | Methadone | NR | NR | 5200 | 23 | 30 | NR |
| **Chang 2015**[63] [A] | 2006-2011 | Taiwan | National | OAT clinic | Methadone | Psychiatrist | NR | 983 | 12 | 38 | 91 |
| **Cousins 2011**[64] [A] | 1993-2004 | Scotland | City: Tayside | Registry | Methadone | GP | 4 (median) | 3162 | 35 | 31 | NR |
| **Cousins 2016**[40] [A] | 2004-2010 | Ireland | National | Registry | Methadone | Mixed | 1577 days (median) | 6983 | 31 | 29 | NR |
| **Davoli 2007**[65] | 1998-2001 | Italy | National | Public Treatment Centres | Methadone | NR | NR | 10258 | 20 | 32 | 72 |
| **Degenhardt 2009**[66] [A] | 1985-2006 | Australia | State: NSW | Registry | Methadone, Buprenorphine | Mixed | 9 (median) | 42676 | NR | NR | NR |
| **Digiusto 2004**[67] | - | Australia | National | OAT and GP clinics, hospitals | Methadone, Buprenorphine, LAAM | Mixed | - | 1244 | 35 | 31 | NR |
| **Dupouy 2017**[68] [A] | 2007-2013 | France | National | Registry | Buprenorphine | Mixed | 5 | 713 | 25 | 33 | NR |
| **Durand 2020**[69] [A] | 2010-2015 | Ireland | City: Dublin | Registry | Methadone | Mixed | 6 (median) | 2899 | 32 | 34 | NR |
| **Evans 2015**[70] | 2006-2010 | USA | State: California | Registry | Methadone | NR | 3 (median) | 32322 | 36 | 35 | 55 |
| **Fellows-Smith 2011**[71] | 1998-2000 | Australia | State: Western Australia | Single clinic and community OAT | Methadone | Mixed | NR | 2520 [C] | NR | 31 | NR |
| **Fugelstad 2007**[72] | 1988-2000 | Sweden | City: Stockholm | OAT clinic | Methadone | Specialist | NR | 848 | NR | 35 | NR |
| **Gearing 1974**[73] | 1964-1971 | USA | State: New York | OAT clinic | Methadone | Specialist | Cohort 1 62mths; Cohort 2 18mths | 3850 | 15 | 27 | NR |
| **Gronbladh 1990**[74] | 1967-1988 | Sweden | Single clinic | OAT clinic | Methadone | Specialist | NR | 281 | 29 | NR | NR |
| **Hickman 2018**[75] [A] | 1998-2014 | UK | National | Registry | Methadone, Buprenorphine | GP | NR | 11033 | 32 | NR | NR |
| **Huang 2011**[21] | 2007-2008 | Taiwan | National | Prison | Methadone | Mixed | NR | 1982 | 10 | 37 (median) | NR |
| **Huang 2013**[76] [A] | 2006-2008 | Taiwan | City: Yunlin | MMT programs at hospitals | Methadone | Addiction medicine specialist | 15 weeks (median) | 1616 | 15 | 36 | 100 |
| **Kelty 2019**[77] [A] | 2001-2010 | Australia | State: Western Australia | Registry | Methadone, Buprenorphine | NR | M: 6; Be: 5 | 8226 | 34 | 32 | NR |
| **Kimber 2015**[78] [A] | 2001-2010 [D] | Australia | State: NSW | Registry | Methadone, Buprenorphine | Mixed | 8 | 46531 | 33 | 29 | NR |
| **Degenhardt 2014**[18] [A] | 2000-2012 | Australia | State: NSW | Registry | Methadone, Buprenorphine | Mixed | 6 | 16453 | 21 | 30 (median) | NR |
| **Larney 2014**[17] | 2000-2012 | Australia | State: NSW | Registry | Methadone, Buprenorphine | Mixed | NR | 16715 | 21 | 30 (median) | NR |
| **Langendam 2001**[79] [E] | 1985-1996 | Netherlands | City: Amsterdam | OAT and other clinics | Methadone | Mixed | NR | 827 | 40 | 31 | NR |
| **Larochelle 2018**[80] | 2012-2015 | USA | State: Massachusetts | Registry | Unspecified OAT | Mixed | 12 months | 17568 | 38 | NR | NR |
| **Liu 2013**[81] | 2004-2011 | China | National | OAT clinic | Methadone | Clinic staff (unspecified) | NR | 306786 | 16 | NR | 64 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Marsden 2017**[19 A] | 2010-2016 | England | National | Prison | Unspecified OAT | NR | 12 months (study period) | OAT: 6662; C: 5598 | OAT: 24; C: 19 | OAT: 35; C: 35 | 65 |
| **Morozova 2013**[82 A] | 2011-2012 | Ukraine | National: Two sites * 3 hospitals | Hospital (outpatient clinic) | Methadone | NR | 90 days (study period) | M: 57; C: 53 | M: 18; C: 21 | 36 (median) | NR |
| **Muga 2014**[83 A] | 1992-2010 | Spain | Single clinic | OAT clinic | Methadone | Addiction medicine specialist | 9 | 1678 | 17 | 32 | NR |
| **Pavarin 2017**[84 A] | 2001-2013 | Italy | State: Emilia Romagna | Registry | Unspecified OAT | NR | 7 | 2232 | 23 | 30 | NR |
| **Pearce 2020**[25 A] | 1996-2018 | Canada | State: British Columbia | Registry | Methadone, Buprenorphine | Mixed | NR | 55347 | 34 | 36 | 41 |
| **Pierce 2016**[85] | 2005-2009 | England | National | Registry | Unspecified OAT | Mixed | 3 | 151983 | 31 | 33 (median) | NR |
| **Reece 2010**[86] | 2000-2007 | Australia | Single clinic | OAT clinic | Buprenorphine | GP | 3 | 2518[C] | 27 | 33 | NR |
| **Scherbaum 2002**[87] | 1988-1996 | Germany | State: North Rhine-Westphalia | OAT clinic | Methadone | Mixed | NR | 244 | 22 | 32 | NR |
| **Weber 1990**[88] | 1984-1990 | Switzerland | Single clinic | Hospital (outpatient clinic) | Methadone | Mixed | 16 months | 297 | 36 | OAT: 36; C: 36 | 46 |

**Table Notes** Shaded rows indicate secondary paper(s) from which some data has been used in sub-analyses. Secondary papers are listed directly below the corresponding primary paper. [A] Authors sent additional information. [B] Using two-year follow-up data. [C] Methadone or Buprenorphine patients only (i.e., only OAT data used). [D] Used 2006-2010 data to avoid overlap with Degenhardt 2009. [E] Although eligible, no data from this study could be used in pooled quantitative syntheses. **PWID**: people who inject drugs. **NR** – not reported. **LFTU** – lost to follow-up. **OAT** – opioid agonist treatment. **Rx** – treatment. **M** – methadone; **B** – buprenorphine; **C** – comparator group

**eTable 8: List of all eligible observational studies (shading indicates a secondary publication)**

| Study (Author, ref) | Years of cohort observation | Country | Sample description | N | N deaths | N person-years | Inclusion Status |
|---|---|---|---|---|---|---|---|
| **Abrahamsson 2017** | 2005-2012 | Sweden | Swedish residents with opiate dependence prescribed and dispensed methadone or buprenorphine for OMT between 2005-2012. | 4501 | 356 | 21438 | Primary – observational |
| **Ledberg 2017** [A] | 2006-2013 | Sweden | Methadone maintenance therapy initiators in Stockholm county between 2006-2011 as identified using Lakemedelsregistret (nation-wide official registry of prescription drugs sold in pharmacies). | 441 | 67 | 2419 | Secondary – some data used |
| **Appel 2000** | 1966-1976 | United States | Methadone maintenance treatment patients in New York City admitted in 1966-7 (population) or 1972 (random sample). | 1544 | 176 | 8485 | Primary – observational |
| **Joseph 1985** | 1975-1977 | United States | Patients who entered methadone treatment in the New York area in either 1966-7 or 1972. | 1545 | 176 | - | Secondary – no data used |
| **Bakker 2017** | 1994-2015 | England | Patients treated for opiate dependence at Lisson Grove Health Centre in central London between 1994-2014 as identified through EMIS database | 278 | 41 | 2181 | Primary - observational |
| **Bazazi 2018** | 2010-2014 | Malaysia | HIV+ males allocated to receive methadone maintenance treatment or not in prison and followed post-release. | 214 | 61 | 8656 | Primary – observational |
| **Bukten 2019** | 1997-2009 | Norway | All patients included in OMT in Norway in the period 01.01.1997–31.12.2009 linked to data from the Norwegian Cause of death registry in the same period. | 7843 | 697 | 40520 | Primary - observational |
| **Clausen 2008** | 1997-2003 | Norway | People who were opioid dependent who applied and were accepted for OMT in Norway between 1997-2003. | 3789 | 213 | 10934 | Secondary – no data used |
| **Clausen 2009** | 1997-2003 | Norway | People who were opioid dependent who applied and were accepted for OMT in Norway between 1997-2003. | 3789 | 213 | 10934 | Secondary – no data used |
| **Haarr 2007** | 1997-2006 | Norway | Patients of the first author's general practice prescribed OAT for abuse of opioids (via injection) from 1/8/1997 - 1/8/2006, commencing treatment by 1/5/2006. | 146 | 11 | 574 | Secondary – no data used |
| **Buster 2002** | 1986-1998 | Netherlands | Clients currently receiving or recently left methadone treatment who were born and residing in Amsterdam. | 5200 | 68 (overdose) | 29600 | Primary - observational |
| **Chang 2015** [A] | 2006-2011 | Taiwan | Opioid dependent patients receiving OST in the Jianan Psychiatric Centre with either methadone or buprenorphine between 2006-2008. | 983 | 68 | 4396 | Primary - observational |
| **Cousins 2011** [A] | 1993-2004 | Scotland | People residing in Tayside, Scotland, who were registered with a GP and were prescribed and dispensed liquid methadone. | 3162 | 184 | 14597 | Primary - observational |
| **Cousins 2016** [A] | 2004-2010 | Ireland | People aged 16-65 registered on the Central Treatment List (CTL) who were prescribed and dispensed at least one prescription for methadone in primary care during the study period. | 6983 | 213 | 28895 | Primary - observational |
| **Davoli 2007** | 1998-2001 | Italy | Heroin users entering treatment, including MMT, at public treatment centres within the National Health Service. | 10258 | 41 | 13122 | Primary - observational |
| **Degenhardt 2009** [A] | 1985-2006 | Australia | Clients administered methadone or buprenorphine as opioid replacement therapy between 1985-2006 as identified using NSW PHDAS | 42676 | 3803 | 425998 | Primary - observational |

| Study (Author, ref) | Years of cohort observation | Country | Sample description | N | N deaths | N person-years | Inclusion Status |
|---|---|---|---|---|---|---|---|
| **Bell 1992** | 1988-1989 | Australia | Individuals seeking entry to methadone maintenance treatment whose applications were assessed at Westmead hospital who were either admitted to or rejected from the program in 1986-7 and were later followed up. | 321 | 6 | 463 | Secondary – no data used |
| **Caplehorn 1994** | 1987-1991 | Australia | Patients with a history of opioid addiction admitted into methadone maintenance in the Parramatta programme prior to July 1 1979. | 307 | 47 | 4254 | Secondary – no data used |
| **Caplehorn 1996** | Pre-1979 - 1991 | Australia | Opiate addicted patients aged 20-40 and admitted to methadone maintenance in the Parramatta programme prior to July 1 1979. | 296 | 42 | 3797 | Secondary – no data used |
| **Degenhardt 2015** | 1998-2000 | Australia | Patients in WA being treated with oral naltrexone and all patients of methadone programs in WA and NSW | 14791 | 219 | 25545 | Secondary – no data used |
| **Digiusto 2004** | - | Australia | Participants in trials of pharmacotherapies for opioid dependence conducted under the Australian National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD) project. | 1244 | 2 | 287 | Primary - observational |
| **Dupouy 2017** [A] | 2007-2013 | France | Subjects, in a representative sample of those covered by the French Health Insurance System, with a dispensation of buprenorphine or buprenorphine-naloxone 2007-2011 and no OAT exposure in the year prior. | 713 | 29 | 3220 | Primary - observational |
| **Durand 2020** [A] | 2010-2015 | Ireland | Patients who were registered on the national register (Central Treatment List) and prescribed and dispensed at least one prescription for methadone in specialist addiction services in Dublin Southwest and Kildare during the study period. | 2899 | 152 | 13301 | Primary – observational |
| **Evans 2015** | 2006-2010 | United States | All individuals first enrolled in publicly funded pharmacological treatment for opioid dependence in California 2006-2010. | 32322 | 1031 | 76657 | Primary - observational |
| **Fellows-Smith 2011** | 1998-2000 | Australia | Patients who were dependent on opioids and received either RODS-naltrexone treatment or methadone treatment in Western Australia. | 2520[D] | 17 | 1573 | Primary - observational |
| **Fugelstad 2007** | 1988-2000 | Sweden | All individuals who had applied for or had participated in the methadone programme in Stockholm in 1988-2000. | 848 | 185 | 5525 | Primary – observational |
| **Fugelstad 1995** | 1986-1990 | Sweden | All known HIV-positive injection drug users in the Stockholm area during 1986-1990. | 472 | 69 | 1793 | Secondary – no data used |
| **Fugelstad 1998** | 1986-1993 | Sweden | Patients treated at Serafens (a compulsory care centre) 1986-88 who reported their main drug of abuse as being intravenous heroin. | 101 | 40 | 505 | Secondary – no data used |
| **Gearing 1974** | 1964-1971 | United States | Patients admitted to Methadone Maintenance Treatment Program (up to 200 separate Tx programs through NY – data from Tx agencies as well as official sources i.e. registries) in New York City. | 801 | 143 | 15644 | Primary - observational |
| **Concool 1979** | 1969-1976 | United States | Persons admitted for the first time to Mount Sinai Methadone Maintenance and Aftercare Treatment Program 1969-1976. | 1156 | 45 | 2308 | Secondary – no data used |
| **Cushman 1977** | 1966-1976 | United States | All patients with a history of opioid dependence admitted to St Luke's Clinic in New York City from 1966 to 1976 and administered at least one dose of methadone. | 547 | 39 | 1952 | Secondary – no data used |

| Study (Author, ref) | Years of cohort observation | Country | Sample description | N | N deaths | N person-years | Inclusion Status |
|---|---|---|---|---|---|---|---|
| **Gronbladh 1990** | 1967-1988 | Sweden | Heroin users in Sweden, some of whom spent time in a methadone treatment program whilst others remained untreated. | 281 | 96 | 2493 | Primary - observational |
| **Hickman 2018** [A] | 1998-2014 | UK | GP practices in the UK reporting to the CPRD. 49,279 patients who received 1+ prescriptions of methadone or buprenorphine Jan 1 1998 – Nov 20 2017 (additional data received). | 11033 | 587 | 30410 | Primary - observational |
| **Cornish 2010** | 1990-2005 | England | Primary care patients diagnosed with substance misuse and prescribed methadone or buprenorphine between 1990-2005. | 5577 | 178 | 17732 | Secondary – no data used |
| **Macleod 2019** | 1998-2014 | UK | Primary care patients within the CPRD receiving methadone or buprenorphine interpreted as being OAT, during the study period. | 12118 | 657 | 36126 | Secondary – no data used |
| **Huang 2011** | 2007-2008 | Taiwan | Prisoners granted amnesty and released from prison on 16 July 2007 with a history of drug use. We have restricted to those who entered MMT at some point in the study. | 1982 | 31 | 1964 | Primary – observational |
| **Huang 2013** [A] | 2006-2008 | Taiwan | People who use inject heroin voluntarily seeking methadone treatment in the Yunlin catchment area. | 1616 | 26 | 760 | Primary – observational |
| **Kelty 2019** [A] | 2001-2010 | Australia | Patients treated with implant naltrexone, methadone, or buprenorphine for the first time between 2001 and 2010 in Western Australia. | 5116 | 264 | 34177 | Primary - observational |
| **Kimber 2015** [A] | 2001-2010[B] | Australia | People with opioid dependence who started a treatment episode of opioid substitution in NSW 1985-2010. | 46531 | 1600 | 190233 | Primary – observational |
| **Degenhardt 2014** [A] | 2000-2012 | Australia | Prisoners who are opioid dependent released at least once between 2000-2012 entering OST between 1985-2010 as identified through PHDAS and NSW Department of Corrective Services. | 16453 | 1050 | 33943 | Secondary – data used in prison sub-analysis |
| **Dolan 2005** | 1997-2002 | Australia | Male heroin users that participated in the RCT of NSW prison-based MMT in 1997-1998 and were followed-up between 1998 and 2002. | 382 | 17 | 1573 | Secondary – no data used |
| **Larney 2014** | 2000-2012 | Australia | Opioid dependent people who had been incarcerated at least once 2000-2012 followed during periods of incarceration in NSW across this time. | 16715 | 51 | 30988 | Secondary – data used in prison sub-analysis |
| **Gibson 2008** | 1996-2006 | Australia | Opioid dependent individuals recruited to randomised trials of buprenorphine and methadone who were then followed up after the trials. | 405 | 30 | 3394 | Secondary – no data used |
| **Langendam 2001**[E] | 1985-1996 | Netherlands | People who use heroin within Amsterdam Cohort Study | 827 | 150 | 4961 | Primary – no data used |
| **Larochelle 2018** | 2012-2015 | United States | Massachusetts adults without cancer who survived an opioid overdose between 2012 and 2014 | 17568 | 807 | 17282 | Primary - observational |
| **Liu 2013** | 2004-2011 | China | Clients enrolled in China's MMT program between 2004-2011 | 306786 | 5573 | 472705 | Primary - observational |
| **Marsden 2017** [A] | 2010-2016 | England | Prisoners diagnosed with opioid use disorder in 39 adult prisons in England | 12260 | 160 | 13115 | Primary - observational |
| **Morozova 2013** [A] | 2011-2012 | Ukraine | Patients with pulmonary tuberculosis being treated in hospitals, some of whom received MMT. | 110 | 9 | 26 | Primary - observational |

| Study (Author, ref) | Years of cohort observation | Country | Sample description | N | N deaths | N person-years | Inclusion Status |
|---|---|---|---|---|---|---|---|
| **Muga 2014** [A] | 1992-2010 | Spain | Opioid dependent patients admitted to a methadone treatment program in the North of Spain between 1992 and 2010. | 1678 | 441 | 15124 | Primary - observational |
| **Pavarin 2017** [A] | 2001-2013[C] | Italy | Residents of the Local Health Unit of Forlì (Emilia Romagna region), who engaged with a drug abuse treatment service run by the National Health Service for problems caused primarily by heroin abuse | 2232 | 113 | 16323 | Primary – observational |
| **Pearce 2020** [A] | 1996-2018 | Canada | All OAT recipients with at least one OAT dispensation in PharmaNet during the study period. | 55347 | 7030 | 400817 | Primary - observational |
| **Nosyk 2015** | 1996-2010 | Canada | HIV positive people in British Columbia with either a history of opioid substitution therapy prior to initial HAART receipt or an indication of injection drug use before HIV infection. | 1727 | 493 | 9913 | Secondary – no data used |
| **Russolillo 2018** | 1998-2015 | Canada | Individuals in British Columbia with a history of conviction who filled a methadone prescription between 1998 and 2015 | 14530 | 1275 | 114244 | Secondary – no data used |
| **Pierce 2016** | 2005-2009 | England | Adults treated for opioid dependence during April 2005 to March 2009 based on the English National Drug Treatment Monitoring System | 151983 | 1499 | 442950 | Primary - observational |
| **Reece 2010** | 2000-2007 | Australia | Patients treated at a clinic with buprenorphine between 2000-2007 identified through Dangerous Drugs Unit of Queensland Health | 2518[#] | 43 | 8030 | Primary - observational |
| **Scherbaum 2002** | 1988-1996 | Germany | Patients enrolled in a multicentre trial for methadone maintenance therapy in North Rhine-Westphalia with a history of being addicted to opioids and at least two previous failures with abstinence-oriented treatments | 244 | 32 | 1286 | Primary - observational |
| **Weber 1990** | 1984- | Switzerland | HIV-positive former or current injection drug misusers, some of whom were enrolled in a methadone maintenance treatment program. | 297 | 40 | 540 | Primary - observational |

[A] Additional data supplied by authors. [B]Restricted to 2006-2010 for overall main analyses to avoid overlap with Degenhardt 2009. [C]Additional data received restricted to March 2001 to avoid any potential overlap with Davoli 2007. [D]Methadone or Buprenorphine data used from this cohort (i.e., OAT data only). [E] Met inclusion criteria but no data eligible for analysis. In and out of treatment outcomes report causes of death as natural only. Author no longer able to access archived data to provide specific causes.

**eTable 9: List of included RCTs**

| Study | Years | Country | OAT group | Comparator group | Sample | N OAT | N comp | N deaths OAT | N deaths comp |
|---|---|---|---|---|---|---|---|---|---|
| **Gordon 2014** | 2008-2012 | USA | Buprenorphine-naloxone | Counselling | Opioid dependent individuals in Maryland prisons with a minimum of 3-6 months left incarcerated. | 104 | 107 | 0 | 0 |
| **Gruber 2008** [A] | 1995-1997 | USA | Methadone (minimal counselling, standard counselling) | Detoxification (21-day) | Heroin dependent patients recruited from a public hospital's 21-day outpatient methadone detoxification program. Part of a clinical trial investigating tuberculosis prevention in injection drug users. | 72 | 39 | 0 | 0 |
| **Gunne 1981** | 1973-1979 | Sweden | Methadone | Waitlist control | Opioid dependent adults (20-24 years old) who inject drugs who were referred to the national Swedish MMT programme. | 17 | 17 | 0 | 2 |
| **Kakko 2003** | 2000-2001 | Sweden | Buprenorphine | Detoxification followed by placebo | Individuals seeking medically assisted heroin withdrawal who met criteria for opiate dependence but not for methadone maintenance treatment. | 20 | 20 | 0 | 4 |
| **Kinlock 2009** | 2003-2006 | USA | Methadone | Counselling (Counselling only, and Counselling + Transfer) | Male prisoners with pre-incarceration heroin dependence. Methadone and counselling group were offered MMT within prison and continued into community upon release. Individuals in the counselling and transfer group were only transferred into MMT in the community upon their release. | 71 | 140 | 1 | 8 |
| **Krook 2002** | 2000 | Norway | Buprenorphine | Placebo | Opioid dependent patients on a waiting list for medication assisted rehabilitation in Oslo who were recruited to a randomised trial comparing Subutex and placebo as an interim therapy. | 55 | 51 | 0 | 0 |
| **Lee 2018** | 2014-2017 | USA | Buprenorphine-naloxone | Extended-release naltrexone | Patients with opioid use disorder recruited through community treatment centres, where they mainly presented for inpatient detoxification. | 287 | 283 | 4 | 3 |
| **Ling 2010** | 2007-2008 | USA | Buprenorphine (implant) | Placebo (implant) | Opioid dependent adults recruited from community addiction clinics that were willing to be randomised in to 2:1 trial for either buprenorphine or placebo implant. | 108 | 55 | 0 | 0 |
| **Metzger 2015** | 2007-2011 | China & Thailand | Buprenorphine-naloxone | Detoxification (assisted by buprenorphine-naloxone) | Opioid dependent adults who inject drugs who were HIV-negative and recruited to an RCT. | 623 | 627 | 8 | 9 |
| **Newman 1979** | 1972-1975 | Hong Kong | Methadone | Detoxification followed by placebo | Heroin addicts in a double-blind study that were admitted into hospital for stabilisation on 60mg on methadone for two weeks prior to randomisation. | 50 | 50 | 3 | 0 |

| Study | Years | Country | OAT group | Comparator group | Sample | N OAT | N comp | N deaths OAT | N deaths comp |
|---|---|---|---|---|---|---|---|---|---|
| **Rich 2015** | 2011-2015 | USA | Methadone | Withdrawal | Prisoners who were enrolled in community methadone maintenance treatment at time of incarceration and had one week to 6 months left. | 114 | 109 | 0 | 1 |
| **Schottenfeld 2008** | 2003-2005 | Malaysia | Buprenorphine | Detoxification followed by naltrexone or placebo with counselling | Opioid dependent individuals recruited from the community. | 44 | 82 | 0 | 0 |
| **Strain 1993** [A] | 1988-1990 | USA | Methadone (20mg, 50mg) | Detox (0mg) | Opioid dependents patients in a methadone treatment research clinic treated one for at least 5 weeks prior to randomisation to a stable dose. | 166 | 81 | 0 | 0 |
| **Tanum 2017** | 2012-2015 | Norway | Buprenorphine-naloxone | Extended-release naltrexone | Newly detoxified opioid dependent individuals from urban addiction clinics. | 79 | 80 | 0 | 0 |
| **Yancovitz 1991** | 1989 | USA | Methadone (interim clinic) | Control (waitlist) | Heroin dependent individuals on the waitlist to the Beth Israel Methadone maintenance program were recruited to the interim clinic. | 149 | 152 | 0 | 2 |

[A] Additional data supplied by authors.

**eTable 10: Features of OAT in included primary observational studies**

| Study (Author, ref) | Treatment setting | Type of OAT provided (M, B, O) | Comparator (no Rx, detox, TAU, antagonist) | M methadone dose | M buprenorphine dose | Other treatments provided? (yes/no) |
|---|---|---|---|---|---|---|
| **Abrahamsson 2017** | Community | Unspecified OAT | - | - | - | No |
| **Ledberg 2017** [A, B] | Community | Methadone | - | - | - | No |
| **Appel 2000** | Community, Hospital | Methadone | - | - | N/A | No |
| **Bakker 2017** | Community | Unspecified OAT | - | - | - | No |
| **Bazazi 2018** | Prison, Post-release | Methadone | - | 61mg | N/A | Yes |
| **Bukten 2019** | Community | Unspecified OAT | - | 100mg | 18mg | Yes |
| **Buster 2002** | Community | Methadone | - | - | N/A | No |
| **Chang 2015** [A] | Community | Methadone | - | - | - | No |
| **Cousins 2011** [A] | Community | Methadone | - | - | N/A | No |
| **Cousins 2016** [A] | Community | Methadone | - | - | N/A | No |
| **Davoli 2007** | Community | Methadone | No MMT (detox, therapeutic community, psychosocial) | - | N/A | Yes |
| **Degenhardt 2009** [A] | Community | Unspecified OAT | - | - | - | No |
| **Digiusto 2004** | Community | Methadone, Buprenorphine, LAAM | Naltrexone | - | - | No |
| **Dupouy 2017** [A] | Community | Buprenorphine | - | N/A | - | Yes |
| **Durand 2020** [A] | Community, Prison, Post-release | Methadone | - | - | N/A | No |
| **Evans 2015** | Community | Methadone | Detox | - | N/A | No |
| **Fellows-Smith 2011** | Community | Methadone | Naltrexone (oral)[D] | 60-80mg recommended daily dose | N/A | No |
| **Fugelstad 2007** | Community | Methadone | - | - | N/A | Yes |
| **Gearing 1974** | Community | Methadone | - | - | N/A | Yes |
| **Gronbladh 1990** | Community | Methadone | - | - | N/A | No |
| **Hickman 2018** [A] | Community | Methadone, Buprenorphine | - | 65mg | 8mg | No |
| **Huang 2011** | Post-release | Methadone | - | - | N/A | No |
| **Huang 2013** [A] | Community | Methadone | - | 48mg | N/A | No |
| **Kelty 2019** [A] | Community | Methadone, Buprenorphine | Naltrexone (implant) | - | - | No |
| **Kimber 2015** [A] | Community | Methadone, | - | - | - | No |

| Study (Author, ref) | Treatment setting | Type of OAT provided (M, B, O) | Comparator (no Rx, detox, TAU, antagonist) | M methadone dose | M buprenorphine dose | Other treatments provided? (yes/no) |
|---|---|---|---|---|---|---|
| | | Buprenorphine | | | | |
| **Degenhardt 2014** [A, B] | Post-release | Unspecified OAT | - | - | - | No |
| **Larney 2014** [B] | Prison | Unspecified OAT | - | - | - | No |
| **Langendam 2001** | Community & prison | Methadone | - | - | - | No |
| **Larochelle 2018** | Community | Unspecified OAT | Naltrexone | - | - | No |
| **Liu 2013** | Community | Methadone | - | <50mg[C] | N/A | No |
| **Marsden 2017** [A] | Prison, post-release | Unspecified OAT | - | 40mg[C] | - | No |
| **Morozova 2013** [A] | Hospital | Methadone | TAU (detox if prescribed by drug addiction specialist) | 81mg | N/A | Yes |
| **Muga 2014** [A] | Community | Methadone | - | - | N/A | Yes |
| **Pavarin 2017** [A] | Community | Unspecified OAT | No OAT (no treatment, detox, therapeutic community, psychosocial) | - | - | No |
| **Pearce 2020** [A] | Community | Methadone, Buprenorphine | - | - | - | No |
| **Pierce 2016** | Community | Unspecified OAT | - | - | - | Yes |
| **Reece 2010** | Community | Buprenorphine | - | N/A | - | No |
| **Scherbaum 2002** | Community | Methadone | - | 47mg | N/A | Yes |
| **Weber 1990** | Hospital | Methadone | No MMT (former and persisting injecting drug misusers) | - | N/A | Yes |

[A] Additional data supplied by authors.[B]Secondary (overlap in data) but some data used in sub-analyses. [C] Median. [D]Methadone patient data only included in analyses.

**eTable 11: Features of OAT in included RCTs**

| Study (Author, ref) | Treatment setting | Type of OAT provided | Comparator (no Rx, detox, TAU, antagonist) | Mean methadone dose | Mean buprenorphine dose | Other treatments provided? |
|---|---|---|---|---|---|---|
| **Gordon 2014** | Prison | Buprenorphine | Counselling | N/A | - | Yes |
| **Gruber 2008** [A] | Hospital | Methadone | Detoxification | 60-90mg | N/A | Yes |
| **Gunne 1981** | Community | Methadone | Waitlist | - | N/A | No |
| **Kakko 2003** | Community, Hospital | Buprenorphine | Detox followed by placebo | N/A | 16 mg | Yes |
| **Kinlock 2009** | Prison | Methadone | Counselling | 60mg | N/A | Yes |
| **Krook 2002** | Community | Buprenorphine | Placebo | - | 16mg | No |
| **Lee 2018** | Community | Buprenorphine | Naltrexone (injectable) | N/A | 16mg[C] | No |
| **Ling 2010** | Community | Buprenorphine[B] | Placebo[B] | N/A | 80mg | Yes |
| **Metzger 2015** | Community | Buprenorphine | Detoxification | N/A | - | Yes |
| **Newman 1979** | Community | Methadone | Detoxification | 97mg | N/A | No |
| **Rich 2015** | Prison | Methadone | Withdrawal | 98mg | N/A | No |
| **Schottenfeld 2008** | Community | Buprenorphine | Naltrexone (oral) | N/A | 8mg[D] | Yes |
| **Strain 1993** [A] | Community | Methadone | Detoxification | Group 1:20mg<br>Group 2: 50mg | N/A | Yes |
| **Tanum 2017** | Hospital | Buprenorphine | Naltrexone | N/A | 16mg | Yes |
| **Yancovitz 1991** | Community | Methadone | Waitlist | 80mg | N/A | No |

[A] Additional data supplied by authors [B]Implants. [C]Median..[D]Patients received two 8mg of buprenorphine every Monday and Wednesday, and three 8mg every Friday. If withdrawal symptoms were present, dosage was increased.

**eTable 12: Characteristics of included primary observational studies**

| Study (Author, ref) | Years | Country | Opioid dependence definition | Treatment naïve? | Subpopulation | Method of assessing mortality | Method of assessing time in and out of treatment |
|---|---|---|---|---|---|---|---|
| **Abrahamsson 2017** | 2005-2012 | Sweden | Documented opioid dependence for at least one year, and prescribed/dispensed methadone and buprenorphine by licensed psychiatrists | NR | None | National/state death registry | OAT discontinuation defined as a case of more than 90-day prescription-free period following the most recent prescription. |
| ***Ledberg 2017** [A] | 2006-2013 | Sweden | NR | NR | None | National/state death registry | Prescription histories were used to track time in and out of treatment. Discrepancies between the number of doses collected and the time point of next methadone purchase were flagged for further investigation if the period was greater than 14 days. |
| **Appel 2000** | 1966-1976 | United States | NR | NR | None | National/state death registry | NR |
| **Bakker 2017** | 1994-2015 | England | Patients on OST at a general practice | NR | None | National/state death registry | OAT duration calculated in months from date of first consultation until last day that GP prescribed for or until 10th June 2014. |
| **Bazazi 2018** | 2010-2014 | Malaysia | Opioid dependence in 12 months prior to incarceration by Rapid Opioid Dependence Screen and confirmation with clinician-administered assessment of DSM-IV criteria in the MINI | NR | HIV+, Prison | National/state death registry | NR (NB: person-time calculated according study groups: methadone, no methadone) |
| **Bukten 2019** | 1997-2009 | Norway | Opioid dependence | NR | None | National/state death registry | National opioid maintenance registry that includes treatment start and stop dates. These dates used to define pre-treatment, in-treatment and post-treatment periods where patients can contribute to multiple observation periods. |
| **Buster 2002** | 1986-1998 | Netherlands | NR | No | None | Coroner's reports for unnatural deaths | Out of treatment time classified in full calendar weeks with no methadone prescription registered. Observations censored one year after leaving treatment. Overdose fatalities occurring during treatment or within 3 days after last prescription were considered cases within treatment. |
| **Chang 2015** [A] | 2006-2011 | Taiwan | Diagnosed opioid dependence by qualified psychiatrists according to DSM-IV criteria | NR | None | National/state death registry | OAT duration calculated from national system, where out of treatment time was consecutive periods of 2 weeks without any treatment or 1 month without receiving any prescription. Some cases are defined as immediate out of treatment if incarcerated. |
| **Cousins 2011** [A] | 1993-2004 | Scotland | NR | NR | None | National/state death registry | If patient did not receive a new prescription within 3 days after the end of previous prescription, this patient is then considered to have ceased treatment. Cases occurring within 3 days of final days of coverage were considered in treatment events. |
| **Cousins 2016** [A] | 2004-2010 | Ireland | NR | NR | None | National/state death registry | OAT duration based on coverage of prescriptions. If a new prescription was received within 3 days of the end of the previous prescription's coverage, considered as continuous treatment. If a new prescription was not received within 3 days, this was considered off treatment. |
| **Davoli 2007** | 1998-2001 | Italy | Dependent heroin users | NR | None | National/state death registry | Out of treatment defined from the second day of absence of pharmacological treatment |
| **Degenhardt 2009** [A] | 1985-2006 | Australia | NR | NR | None | National/state death registry | New treatment episodes defined as one commencing 7 or more days after the end of a previous episode. A change in medication type did not of itself, constitute a new episode. Deaths occurring in the 6 days following treatment were classified as in treatment. |
| **Digiusto 2004** | - | Australia | Majority are assessed opioid dependent (DSM-IV) at entry | No (23% on MMT already) | None | Reporting of serious and adverse events within clinical trials | End of treatment period taken to be the last date on which medication was administered, including one takeaway dose where applicable. |
| **Dupouy 2017** [A] | 2007-2013 | France | NR | NR | None | National/state death registry | A period of more than 35 days between two reimbursements was considered as treatment interruption (prescription maximum is 28 days) |
| **Durand 2020** [A] | 2010-2015 | Ireland | NR | NR | None | National/state death registry | OAT duration defined as continuous daily supply with tolerance for up to 7 days of interrupted supply. Out of treatment was classified when the patients left the treatment on a voluntary and permanent basis or after 7 days after the end of coverage of a prescription. |
| **Evans 2015** | 2006-2010 | United States | Opioid dependence | NR | None | National/state death registry | Discharge records are filed when appointments are missed without notification for >/=14 consecutive days for MMT. Successive OAT episodes less than 14 days were merged. |
| **Fellows-Smith 2011** | 1998-2000 | Australia | Opioid dependence | No | None | National/state death registry | Out of treatment includes discharges from treatment (includes voluntary and involuntary, wherein the latter from breaking treatment rules) |
| **Fugelstad 2007** | 1988-2000 | Sweden | NR | NR | None | Medical Examiner's Office | NR |
| **Gearing 1974** | 1964-1971 | United States | 'Hard-core' heroin addict | NR | None | National/state death registry | NR |
| **Gronbladh 1990** | 1967-1988 | Sweden | NR | NR | None | National/state death registry | NR |

| Study (Author, ref) | Years | Country | Opioid dependence definition | Treatment naïve? | Subpopulation | Method of assessing mortality | Method of assessing time in and out of treatment |
|---|---|---|---|---|---|---|---|
| **Hickman 2018** [A] | 1998-2014 | UK | Patients who received one or more prescriptions of methadone or buprenorphine (excluding those for pain relief) | NR | None | GP Clinics | Time on treatment was calculated from periods of continuous prescription. New treatment episodes were categorised when there were gaps of at least 28 days from the expected date of completion of one prescription to the start of the next. |
| **Huang 2011** | 2007-2008 | Taiwan | History of drug use and injecting heroin | NR | Amnestied Prisoners | National/state death registry | Dropouts are patients who were absent and stopped taking the medication for at least 14 days (not due to re-incarceration). Individuals in this study could re-enrol in MMT on multiple occasions if they dropped out. |
| **Huang 2013** [A] | 2006-2008 | Taiwan | DSM-IV opioid dependence | NR | None | National/state death registry | Treatment status measured at the end of follow up where patients were counted as on treatment if their last methadone prescription was within 14 days of death or end of study. |
| **Kelty 2019** [A] | 2001-2010 | Australia | Opioid use disorder | NR | None | National/state death registry | On treatment time commenced on day 29 (after the induction period of first 28 days of treatment as this is considered a time of high risk) and continued until ceased treatment, death, or 31st Dec 2012. |
| **Kimber 2015** [A] | 2001-2010 | Australia | Individuals recorded in the Pharmaceutical Drugs of Addiction System (database) as having received opioid substitution treatment from 2001-2010. | NR | None | National/state death registry | First 6 days following a treatment episode as classified as part of that treatment episode. Accordingly, to qualify as an out of treatment period, there must be at least 7 consecutive days on which treatment was not received. |
| **Degenhardt 2014*** [A] | 2000-2012 | Australia | Receipt of first recorded and eligible opioid substitution treatment episode | No | Post-release | National/state death registry | New episodes commence after 7 days or more following a discharge from a previous treatment episode. If there are less than 7 days between changes in medication (methadone to buprenorphine or vice versa), this was considered as a continuous treatment episode. |
| **Larney 2014*** | 2000-2012 | Australia | Individuals recorded in the Pharmaceutical Drugs of Addiction System as having received opioid substitution at some point in 1986-2010 | No | Prison | National/state death registry | New episodes commence after 7 days or more following a discharge from a previous treatment episode. If there are less than 7 days between changes in medication (methadone to buprenorphine or vice versa), this was considered as a continuous treatment episode. |
| **Langedam 2001** | 1985-1996 | Netherlands | NR | NR | None | National/state death registry | Data from the Central Methadone Register in Amsterdam which includes methadone prescription and dispensation records. This was available on a weekly or daily basis through the follow up period. |
| **Larochelle 2018** | 2012-2015 | United States | Opioid use disorder | NR | None | National/state death registry | Medical claim for, or record of treatment with, methadone. Monitored at monthly intervals. |
| **Liu 2013** | 2004-2011 | China | Heroin users | NR | None | Active follow-up by local CDC and methadone clinic staff | Discontinuation of methadone treatment for more than 30 days was defined as a treatment break. |
| **Marsden 2017** [A] | 2010-2016 | England | Diagnosis of opioid use disorder | NR | Prison | National/state death registry | OST exposure at release was determined by whether prisoners met threshold of >20 mg for methadone and >2mg for buprenorphine at release. |
| **Morozova 2013** [A] | 2011-2012 | Ukraine | ICD-10 opioid dependence | NR | Tuberculosis | Hospital (where treatment takes place) | NR |
| **Muga 2014** [A] | 1992-2010 | Spain | DSM-IV opioid dependence | NR | None | National/state death registry | Patients are considered out of treatment after 30 days without picking up their medication. Typically, patients would collect their medication every week at the municipal centre. |
| **Pavarin 2017** [A] | 2000-2013 | Italy | Individuals seeking treatment for problems caused primarily by heroin abuse | NR | None | National/state death registry | In treatment duration was calculated from admission and discharge dates. Periods of less than 7 days between treatment episodes were combined to form an overall treatment episode. |
| **Pearce 2020** [A] | 1996-2018 | Canada | Opioid use disorder | NR | None | National/state death registry | On treatment time is any continuous period of dispensed medication with no interruptions in doses lasting at least 5 days for methadone and slow-release oral morphine, and 3 days for injectable OAT. Deaths occurring at least one day after OAT prescribed/dispensed were classified as off treatment. |
| **Pierce 2016** | 2005-2009 | England | Individuals in the national system that records treatment delivery of psychoactive substance-related problems. Details include self-report illicit drug injecting status and self-report of additional problematic psychoactive substances. | NR | None | National/state death registry | Treatment time for each episode calculated from dates of admission and discharge. Out of treatment started the day after a treatment episode ends and continues until the day before the next episode begins or the end of follow-up. In treatment period was extended to death date if death occurred within 14 days of a treatment episode. |
| **Reece 2010** | 2000-2007 | Australia | NR | NR | None | National/state death registry | Treatment time calculated from dates of admission, discharge, or censorship. Multiple treatment episodes were totalled. |
| **Scherbaum 2002** | 1988-1996 | Germany | Long history of opioid dependency with at least two failed abstinence-oriented treatment | NR | None | NR | NR |
| **Weber 1990** | 1984-1986 | Switzerland | People who inject drugs | NR | None | NR | NR |

**eTable 13: Characteristics of included RCTs**

| Study (Author, ref) | Years | Country | Comparator | Opioid dependence definition | OAT treatment naïve? | Subpopulation (HIV, HCV, Prison, None) | Method of assessing mortality |
|---|---|---|---|---|---|---|---|
| **Gordon 2014** | 2008-2012 | United States | Counselling | DSM-IV opioid dependence, physiological dependence or enrolled in OAT the year before incarceration | No | Prison | Serious and adverse events recorded in clinical trials. |
| **Gruber 2008** [A] | 1995-1997 | United States | Detoxification | DSM-III-R diagnosis of opioid dependence | NR | Latent TB Infection | Serious and adverse events recorded in clinical trials. |
| **Gunne 1981** | 1973-1979 | Sweden | Waitlist control | Minimum 4 years compulsive intravenous misuse of opiates as documented by hospital records, and withdrawal signs and urinary opioid excretion measurable on admission to the clinic | NR | None | Tracing treatment clinics, social workers, criminality registers, social security information, etc. |
| **Kakko 2003** | 2000-2001 | Sweden | Detox followed by placebo | DSM-IV opioid dependence | NR | None | Serious and adverse events recorded in clinical trials. |
| **Kinlock 2009** | 2003-2006 | United States | Counselling | DSM-IV criteria of heroin dependence at time of incarceration and physiologically dependent during year prior to incarceration | No | Prison | Serious and adverse events recorded in clinical trials. |
| **Krook 2002** | 2000 | Norway | Placebo | DSM-IV opioid dependence | No (previous OAT – 14) | None | Serious and adverse events recorded in clinical trials. |
| **Lee 2018** | 2014-2017 | United States | Naltrexone (injectable) | DSM-5 opioid use disorder | NR | None | Serious and adverse events recorded in clinical trials. |
| **Ling 2010** | 2007-2008 | United States | Placebo (implant) | DSM-IV opioid dependence | No | None | Serious and adverse events recorded in clinical trials. |
| **Metzger 2015** | 2007-2011 | China, Thailand | Detoxification | DSM-IV opioid dependence | NR | None | Serious and adverse events recorded in clinical trials. |
| **Newman 1979** | 1972-1975 | Hong Kong | Detoxification | Documented history of addiction and current addiction as determined by 3 consecutive positive urine tests for morphine | NR | None | Serious and adverse events recorded in clinical trials. |
| **Rich 2015** | 2011-2015 | United States | Withdrawal | Enrolment in Rhode Island MMT programme at time of incarceration | No | Prison | Serious and adverse events recorded in clinical trials. |
| **Schottenfeld 2008** | 2003-2005? | Malaysia | Naltrexone (oral) | DSM-IV opioid dependence | NR | None | Serious and adverse events recorded in clinical trials. |
| **Strain 1993** [A] | 1988-1990 | United States | Detoxification | History of intravenous opioid dependence, urine sample positive for opioids, and physical examination consistent with acute and chronic needle use | No | None | Serious and adverse events recorded in clinical trials. |
| **Tanum 2017** | 2012-2015 | Norway | Naltrexone | DSM-IV opioid dependence | NR | None | Serious and adverse events recorded in clinical trials. |
| **Yancovitz 1991** | 1989 | United States | Waitlist | NR | NR | None | Serious and adverse events recorded in clinical trials. |

[A] Additional data supplied by authors.

**eTable 14: Characteristics of participants in included primary observational studies**

| Study (Author, ref) | N | % HIV+ | % HCV+ | % SUD | % mental disorders | % other physical health problems | % homeless or unstable housing | % prison history | % sex work history |
|---|---|---|---|---|---|---|---|---|---|
| **Abrahamsson 2017** | 4501 | NR | NR | NR | Received inpatient psychiatric treatment – 8 | NR | NR | NR | NR |
| **Ledberg 2017* [A]** | 441 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Appel 2000** | 1544 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Bakker 2017** | 278 | 3 | 57 | NR | Psychiatric illness – 25 | NR | NR | Criminal records – 72 | Women – 40 |
| **Bazazi 2018** | 291 | 100 | NR | NR | NR | NR | NR | 100 | NR |
| **Bukten 2019** | 7843 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Buster 2002** | 5200 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Chang 2015 [A]** | 983 | 18 | 91 | 23 | NR | HBV antigen positive – 18<br>Syphilis antibody positive – 4 | NR | NR | NR |
| **Cousins 2011 [A]** | 3162 | NR | NR | NR | Psychiatric admissions – 33 | NR | NR | NR | NR |
| **Cousins 2016 [A]** | 6983 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Davoli 2007** | 10258 | 8 | NR | NR | Psychiatric comorbidity – 13 | NR | NR | NR | NR |
| **Degenhardt 2009 [A]** | 42676 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Digiusto 2004** | 1244 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Dupouy 2017 [A]** | 713 | 1 | NR | 10 | Hospitalisation for psychiatric disorder – 4 | NR | NR | NR | NR |
| **Durand 2020 [A]** | 2899 | NR | NR | NR | Mental/behavioural disorder – 66 | Digestive system diseases – 34<br>Respiratory diseases – 24 | NR | NR | NR |
| **Evans 2015** | 32322 | NR | 13 | NR | Mental illness – 23 | Disability – 16 | NR | NR | NR |
| **Fellows-Smith 2011** | 2520 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Fugelstad 2007** | 848 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Gearing 1974** | 3850 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Gronbladh 1990** | 281 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Hickman 2018 [A]** | 11033 | NR | NR | 19 | Self-harm history – 2 | NR | 2 | 6 | NR |
| **Huang 2011** | 1982 | 15 | NR | NR | NR | NR | NR | 100 | NR |
| **Huang 2013 [A]** | 1616 | 18 | 77 | Alcohol use disorder – 20 | Psychiatric Rx history – 11 | Cardiovascular disease – 6<br>Respiratory – 2 | NR | NR | NR |
| **Kelty 2019 [A]** | 8226 | NR | 53 | NR | NR | NR | NR | NR | NR |
| **Kimber 2015 [A]** | 46531 | NR | NR | NR | NR | NR | NR | 37 | NR |
| **Degenhardt 2014* [A]** | 16453 | NR | NR | NR | NR | NR | NR | 100 | NR |
| **Larney 2014*** | 16715 | NR | NR | NR | NR | NR | NR | 100 | NR |
| **Langendam 2001** | 827 | 27 | NR | NR | NR | NR | NR | NR | NR |
| **Larochelle 2018** | 17568 | NR | NR | NR | Anxiety – 17<br>Depression – 21 | NR | NR | NR | NR |
| **Liu 2013** | 306786 | 6 | NR | NR | NR | NR | NR | NR | NR |
| **Marsden 2017 [A]** | 12260 | NR | NR | Problematic alcohol use – 31 | NR | NR | NR | NR | NR |
| **Morozova 2013 [A]** | 110 | 68 | NR | NR | NR | Pulmonary tuberculosis – 100 | NR | NR | NR |
| **Muga 2014 [A]** | 1678 | 54 | 74 | NR | Mood disorders – 46 | NR | NR | NR | NR |
| **Pavarin 2017 [A]** | 2234 | 5 | 35 | NR | NR | NR | NR | NR | NR |
| **Pearce 2020 [A]** | 55347 | 2 | 3 | Concurrent SUD – 64 | MH disorder – 64 | Chronic pain – 54 | NR | NR | NR |
| **Pierce 2016** | 151983 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Reece 2010** | 2518 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Scherbaum 2002** | 244 | NR | NR | NR | Unspecified – 70 | NR | NR | NR | NR |
| **Weber 1990** | 297 | 100 | NR | NR | NR | NR | NR | NR | NR |

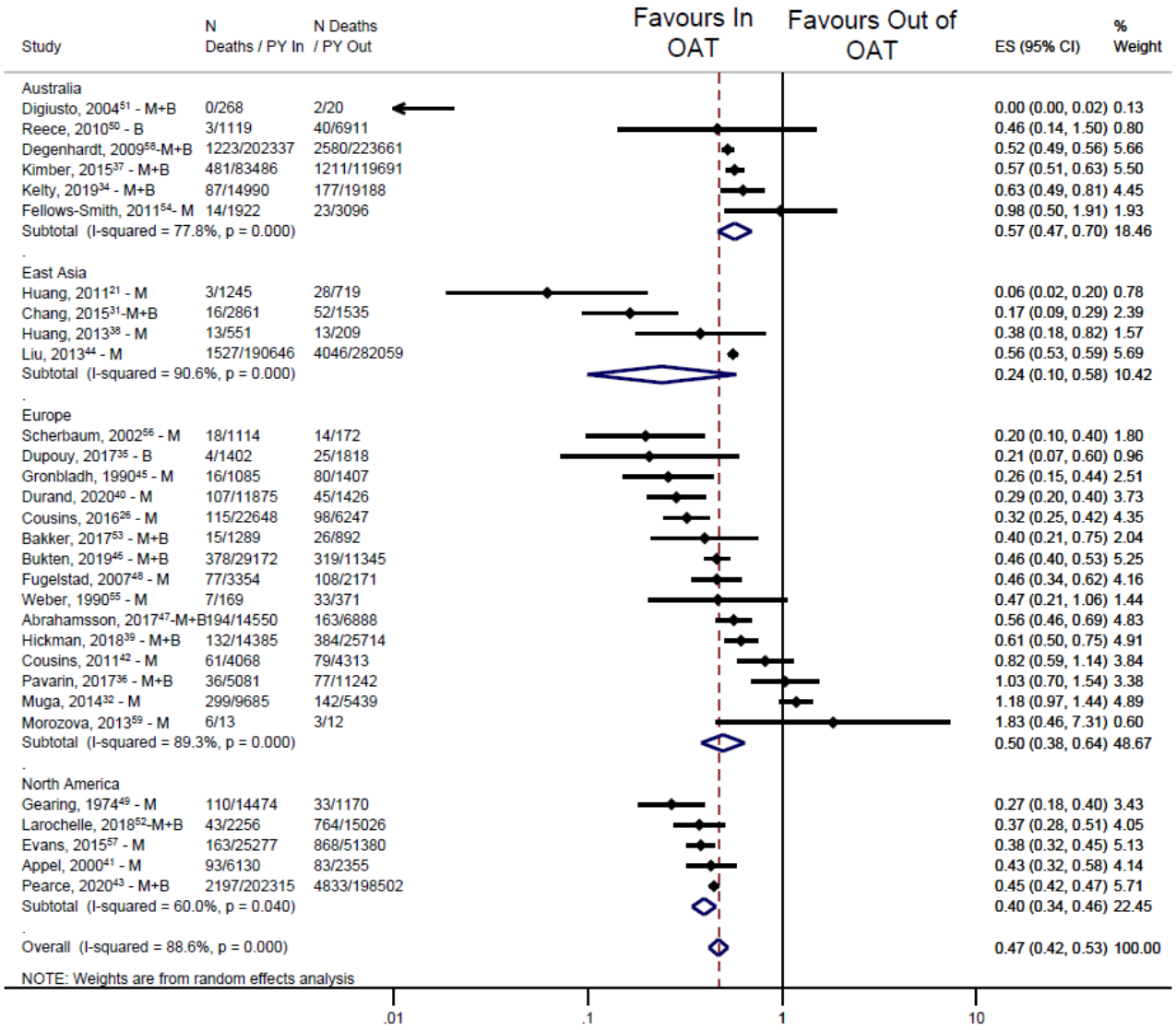
[A] Additional data supplied by authors.

**eTable 15: Characteristics of participants in included RCTs**

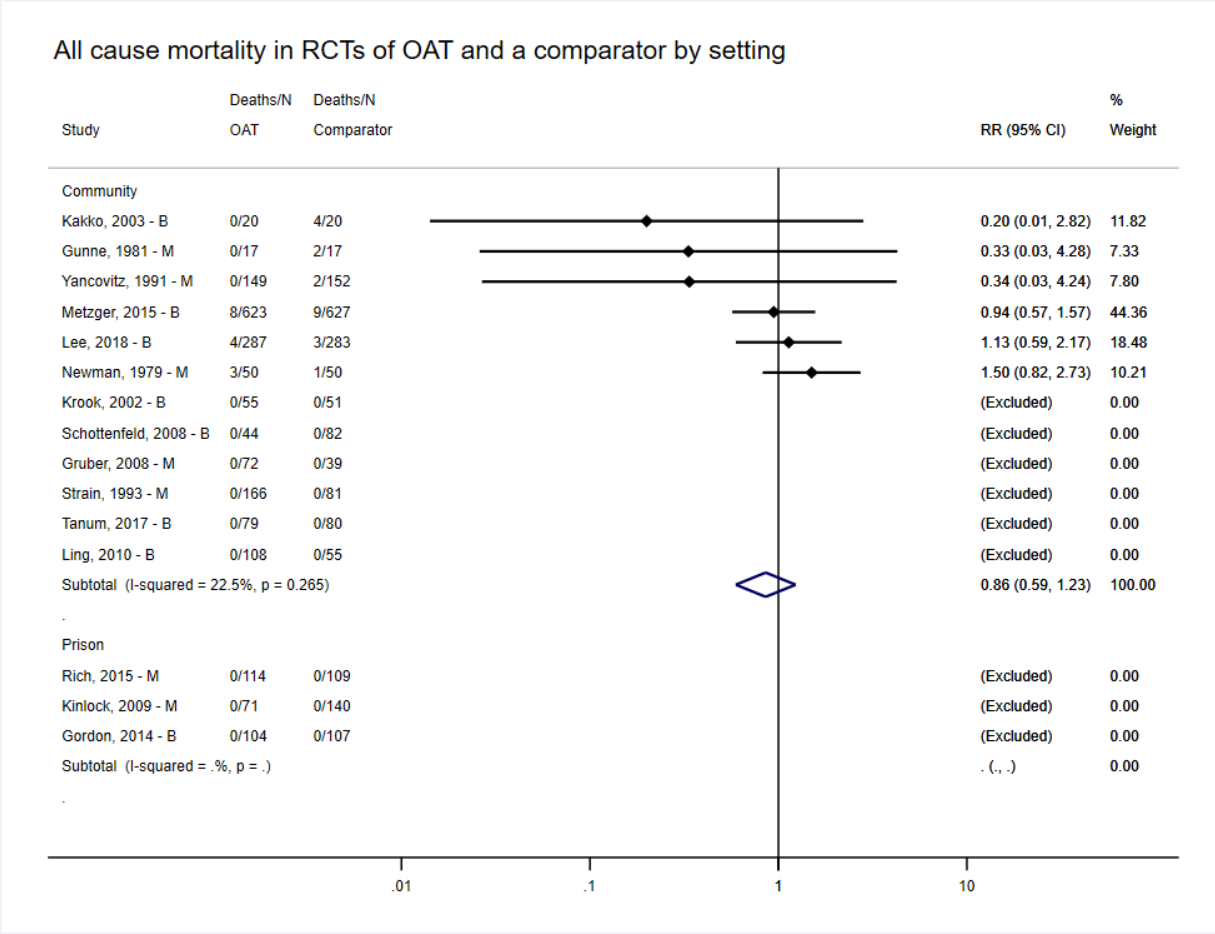
| Study (Author, ref) | N | % HIV+ | % HCV+ | %SUD | % with mental disorders | % with other physical health problems | % homeless or unstable housing | % prison history | % sex work history |
|---|---|---|---|---|---|---|---|---|---|
| **Gordon 2014** | 211 | NR | NR | NR | NR | NR | NR | 100 | NR |
| **Gruber 2008** [A] | 111 | NR | NR | 12 | Major depression – 31 | Latent TB infection – 100 | NR | NR | NR |
| **Gunne 1981** | 34 | NR | NR | NR | NR | NR | NR | NR | NR |
| **Kakko 2003** | 40 | 3 | 75 | 0 | Psychosis/any major psychiatric condition – 0 | Hepatitis B – 35 | NR | NR | NR |
| **Kinlock 2009** | 211 | NR | NR | NR | NR | NR | NR | 100 | NR |
| **Krook 2002** | 106 | NR | NR | 100 | NR | NR | NR | NR | NR |
| **Lee 2018** | 570 | NR | NR | 0 | History of psychiatric disorders – 67 | Any serious medical condition – 0 | NR | NR | NR |
| **Ling 2010** | 163 | 0 | NR | 0 | History of psychosis – 0 | NR | NR | NR | NR |
| **Metzger 2015** | 1251 | 0 | NR | NR | NR | NR | NR | NR | NR |
| **Newman 1979** | 100 | NR | NR | NR | Psychosis/major psychiatric illness – 0 | TB and peptic ulcer – 100 | NR | NR | NR |
| **Rich 2015** | 87 | 26 | 38 | 0 | NR | Hepatitis B – 2<br>Pulmonary tuberculosis – 17 | NR | 100 | NR |
| **Schottenfeld 2008** | 247 | NR | NR | NR | Any major mental illness - 0 | Any chronic illness – 0 | NR | NR | NR |
| **Strain 1993** [A] | 159 | 3 | 54 | 0 | Any serious psychiatric condition – 0 | Any serious somatic illness – 0 | NR | NR | NR |
| **Tanum 2017** | 301 | 3 | 53 | NR | NR | NR | NR | NR | NR |
| **Yancovitz 1991** | 111 | NR | NR | 12 | Major depression – 31 | Latent TB infection – 100 | NR | NR | NR |

[A] Additional data supplied by authors.

**eFigure 2: All-Cause Mortality in OAT Compared to Out of OAT**



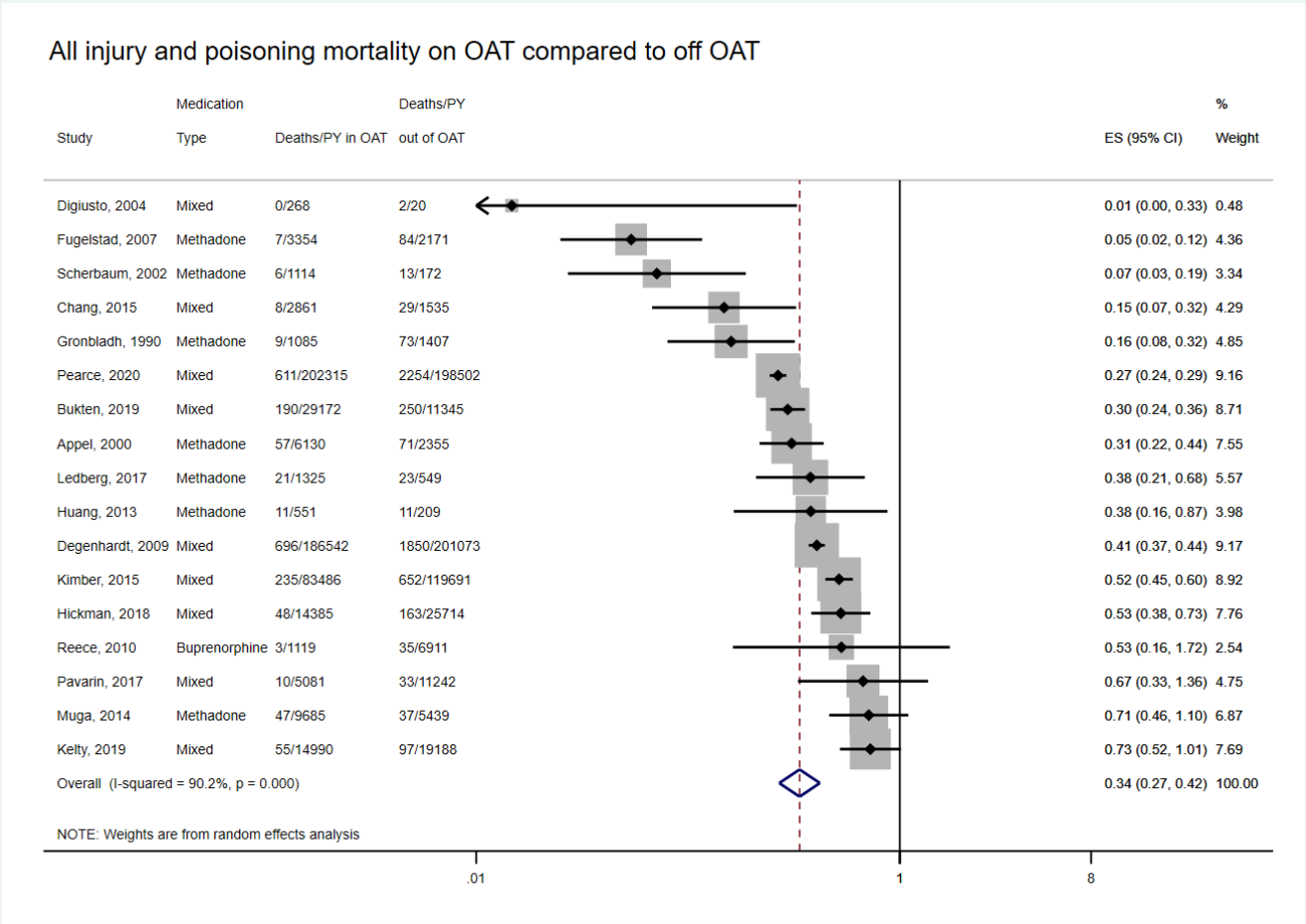
**eFigure 3: All Cause Mortality in and out of OAT in RCTs**



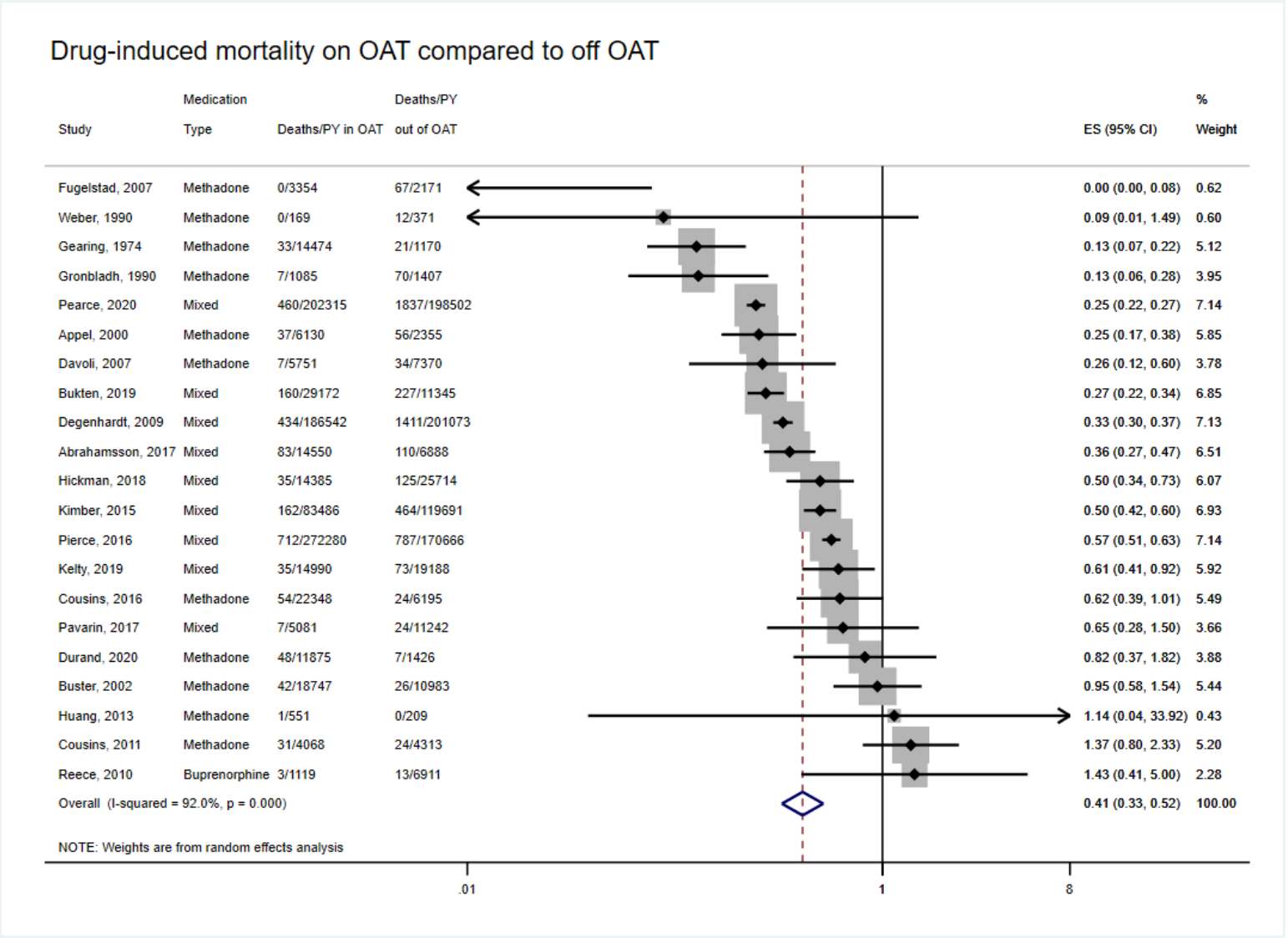
**eTable 16: Meta-regression of potential sources of heterogeneity in the pooled all-cause crude mortality rate ratio (in vs. out of OAT)**

| | N studies | Coefficient (SE) | Adj. $R^2$ | *P* |
|---|---|---|---|---|
| **Cohort characteristics at baseline** | | | | |
| % injecting | 6 | .9882901(.0121986) | -4.26% | 0.394 |
| % women | 25 | 1.008945(.0199953) | -7.34% | 0.657 |
| Mean/median age | 24 | .9594928(.0535743) | 1.07% | 0.467 |
| % HIV positive | 11 | 1.009127(.0087951) | -2.66% | 0.324 |
| % HCV Positive | 8 | .9969695(.0079878) | -19.12% | 0.718 |
| **Study characteristics** | | | | |
| Year of follow-up completion | 27 | 1.009268(.0095595) | 1.02% | 0.339 |
| Sample size | 30 | 1.000001(2.02e-06) | -6.52% | 0.634 |
| Person-years of follow-up | 30 | 1.000001(8.74e-07) | -5.79% | 0.537 |
| Length of follow-up (years) | 19 | 1.028529(.0354897) | 1.39% | 0.426 |

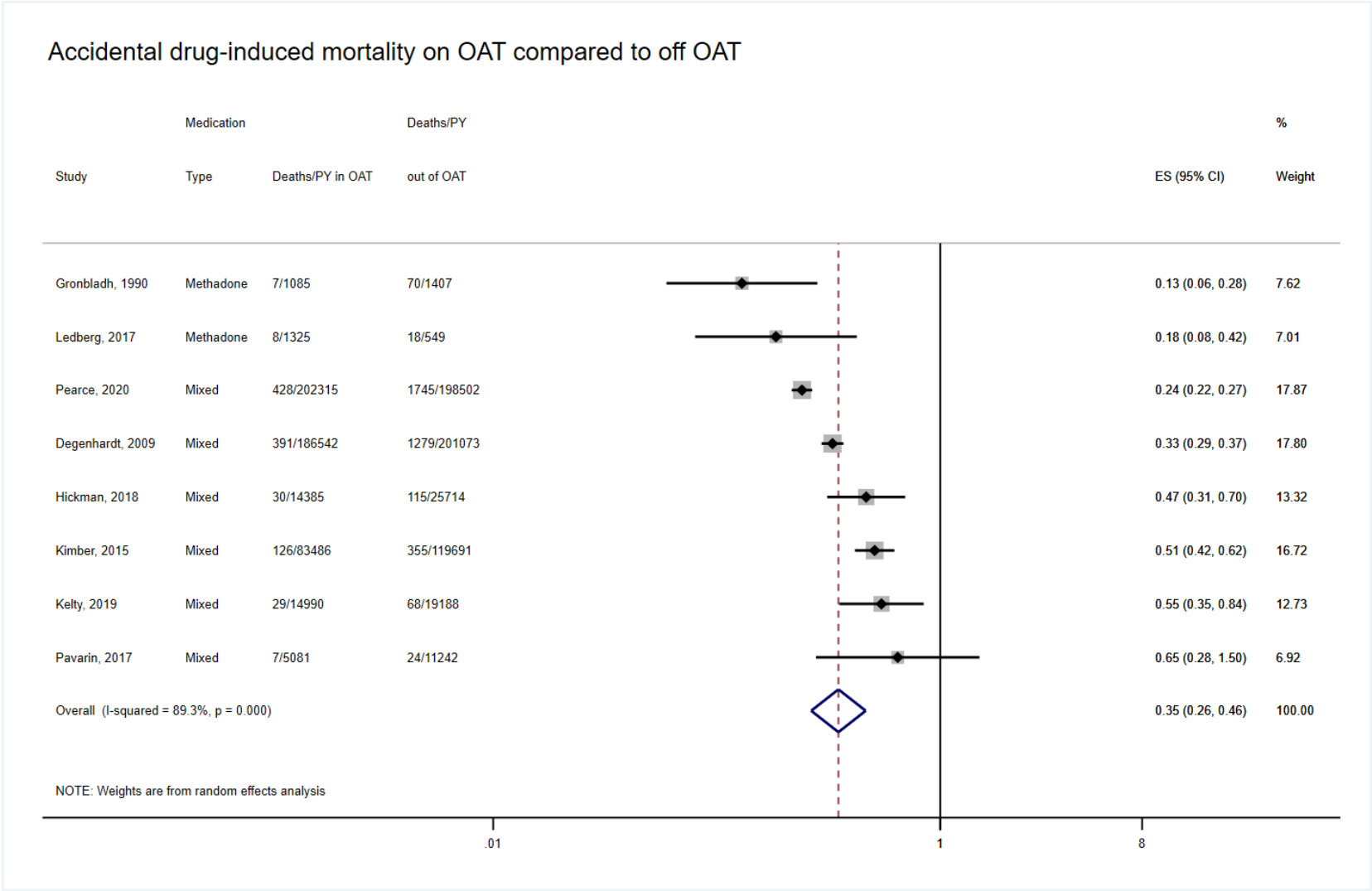
**eFigure 4: Cause-specific mortality: all injury and poisoning**



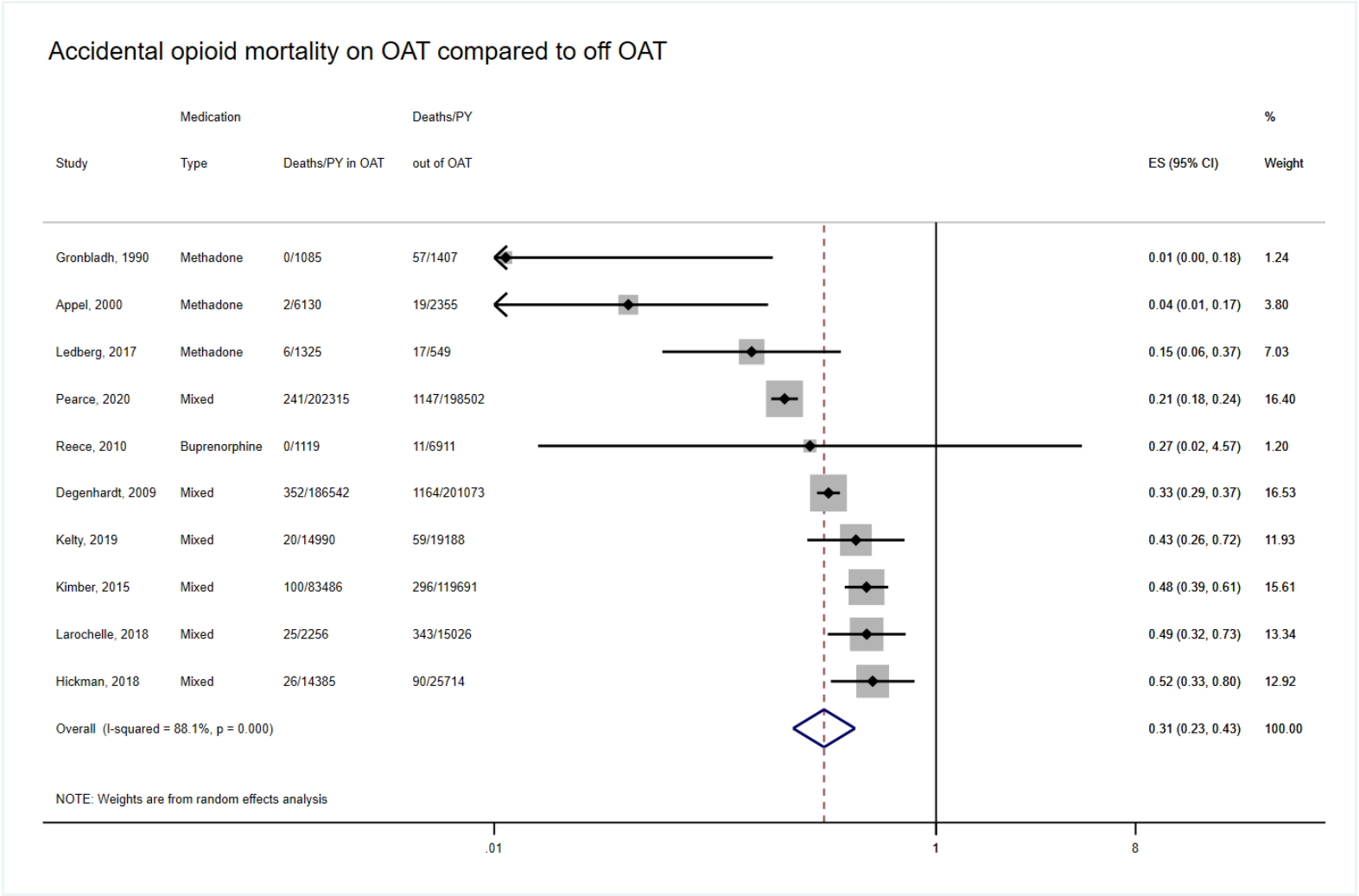
**eFigure 5: Cause-specific mortality: drug-induced**



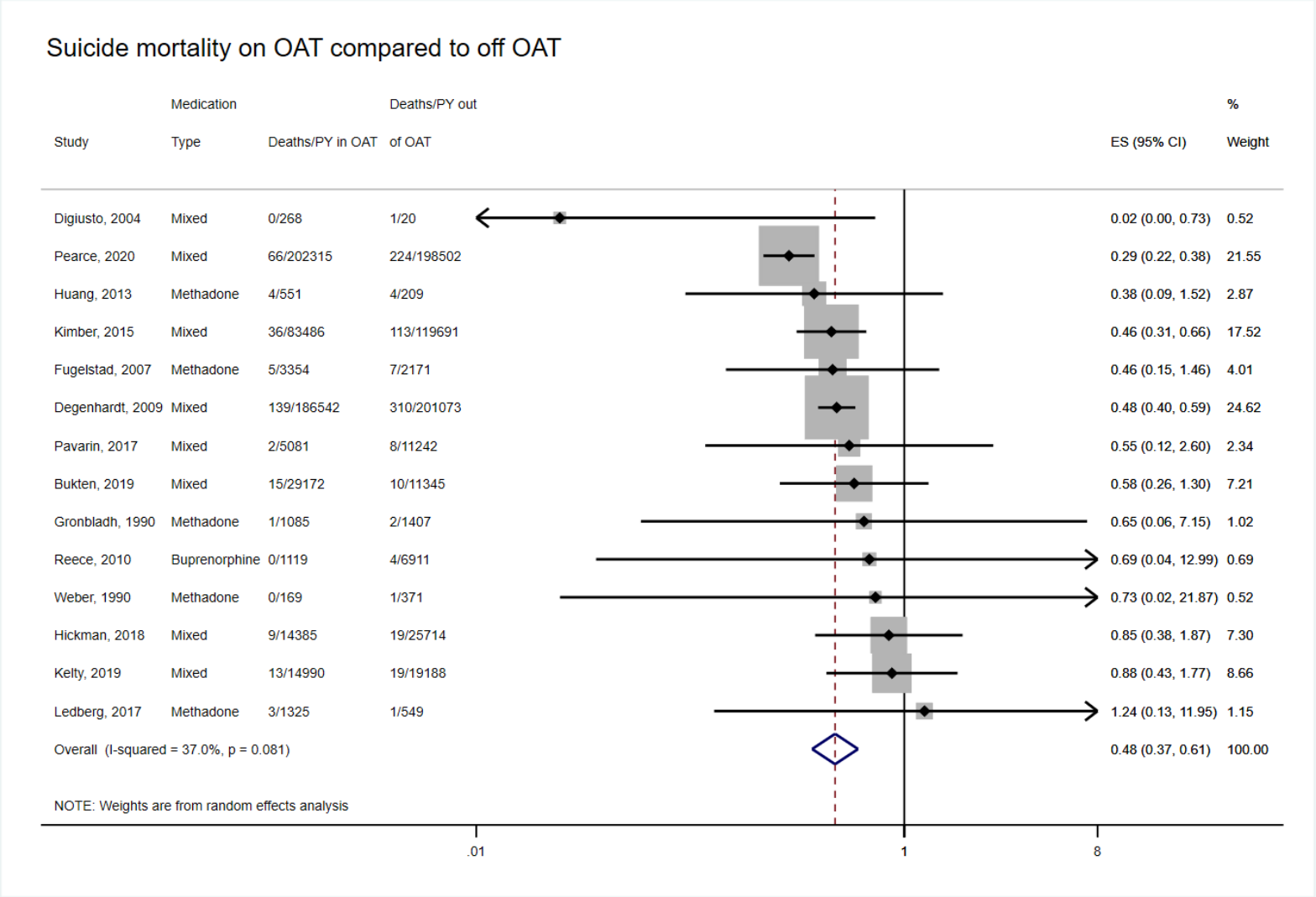
**eFigure 6: Cause-specific mortality: accidental drug-induced**



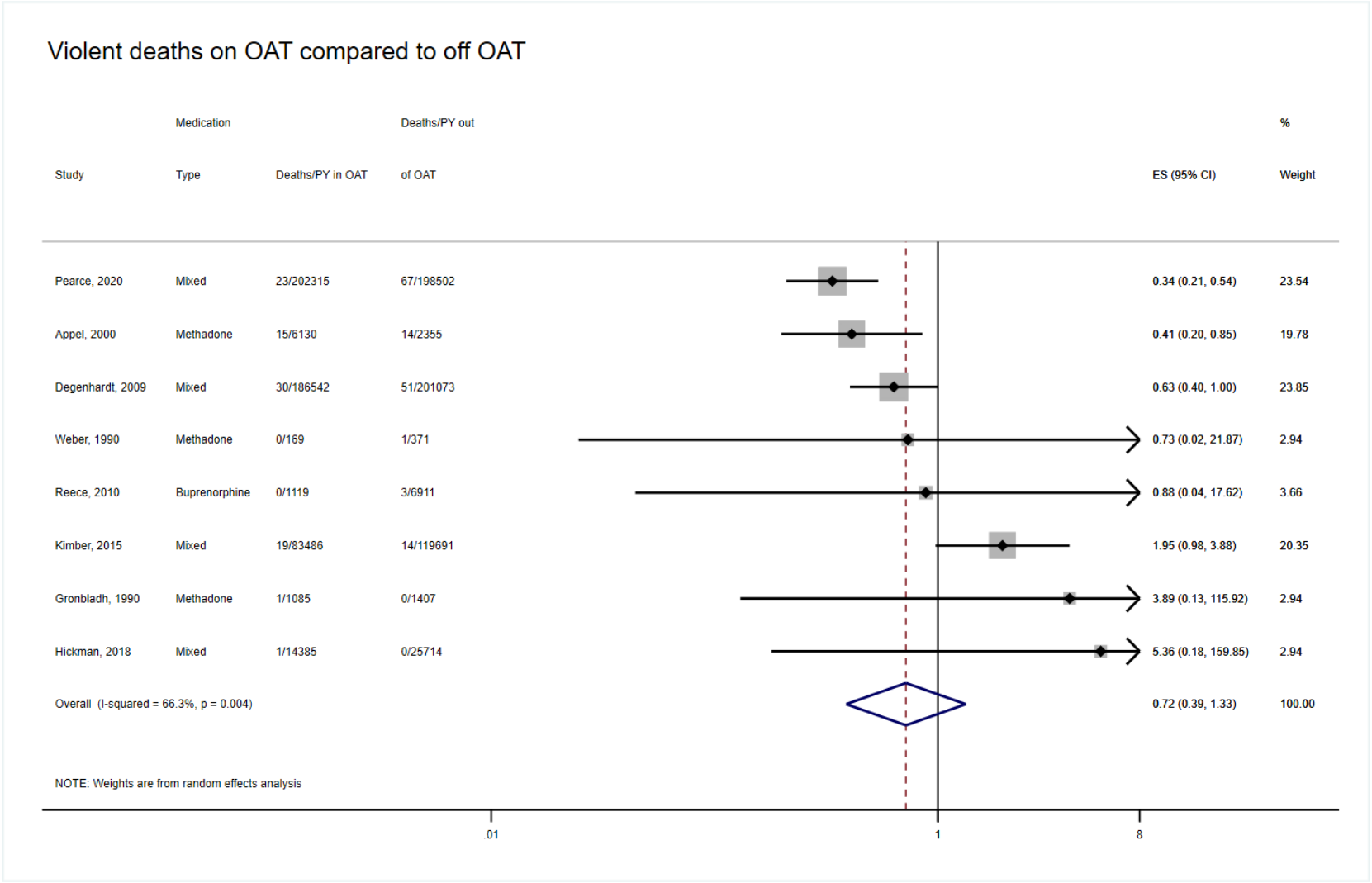
**eFigure 7: Cause-specific mortality: accidental opioid**



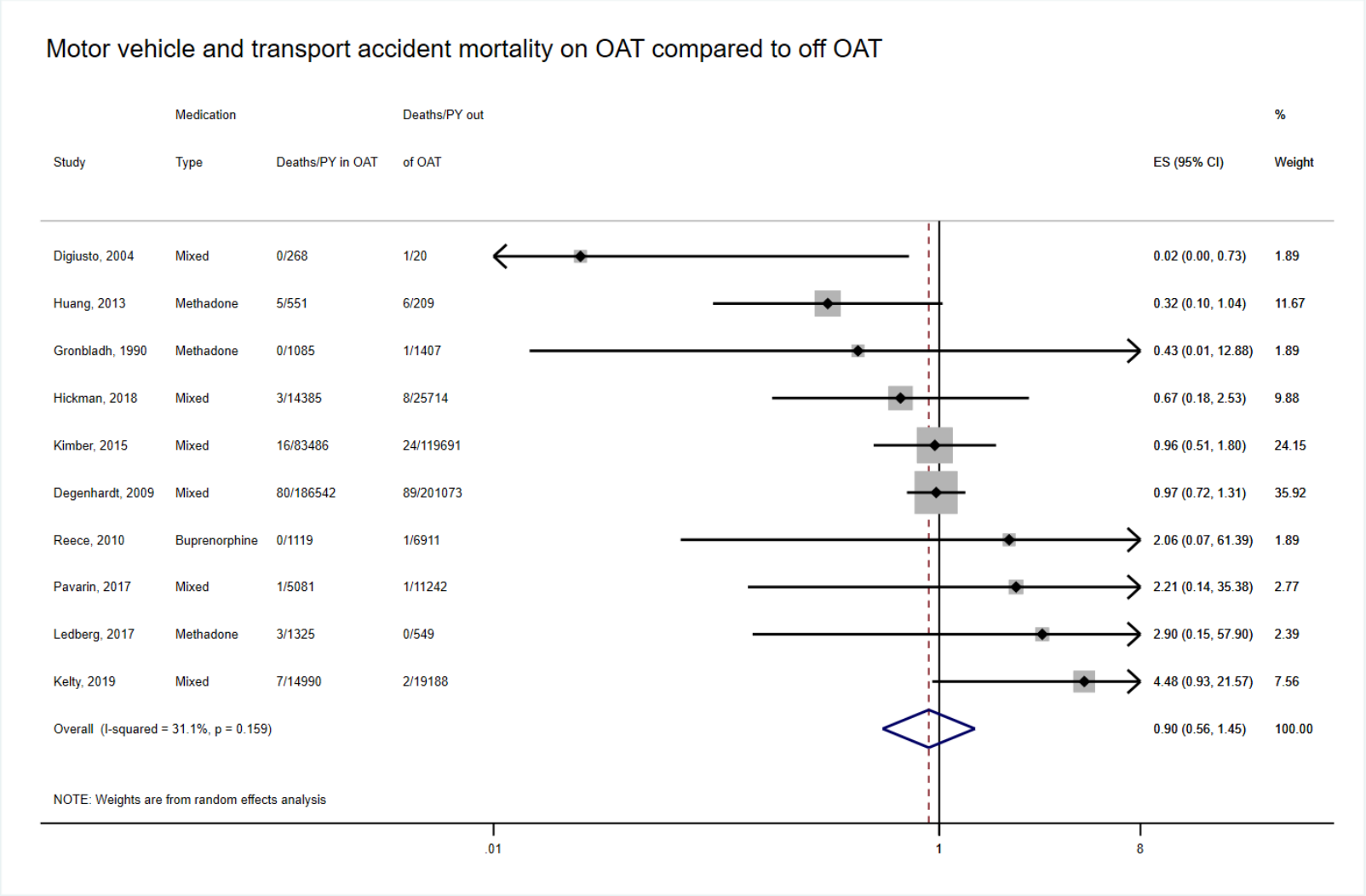
**eFigure 8: Cause-specific mortality: suicide**



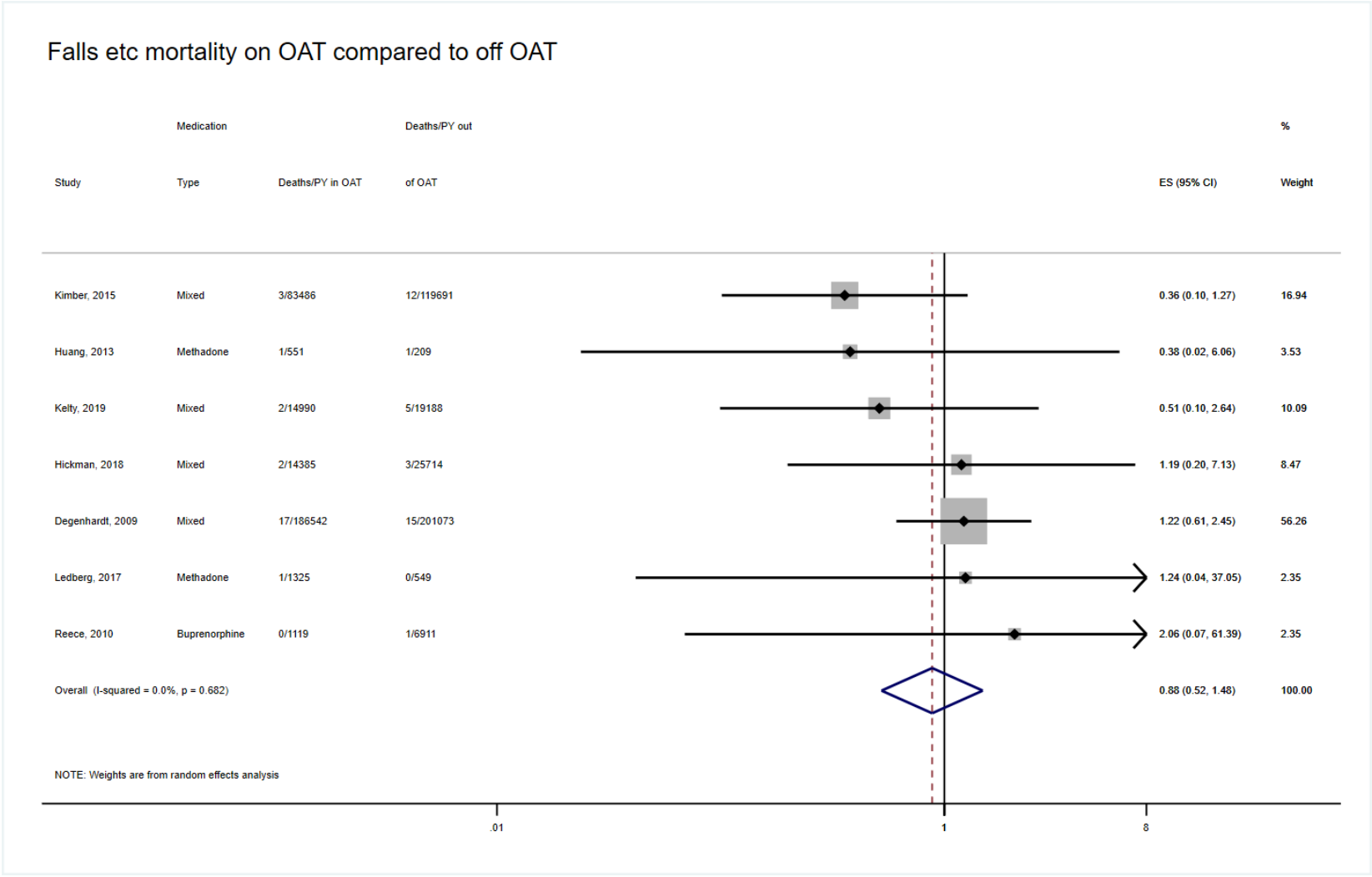
**eFigure 9: Cause-specific mortality: violence**



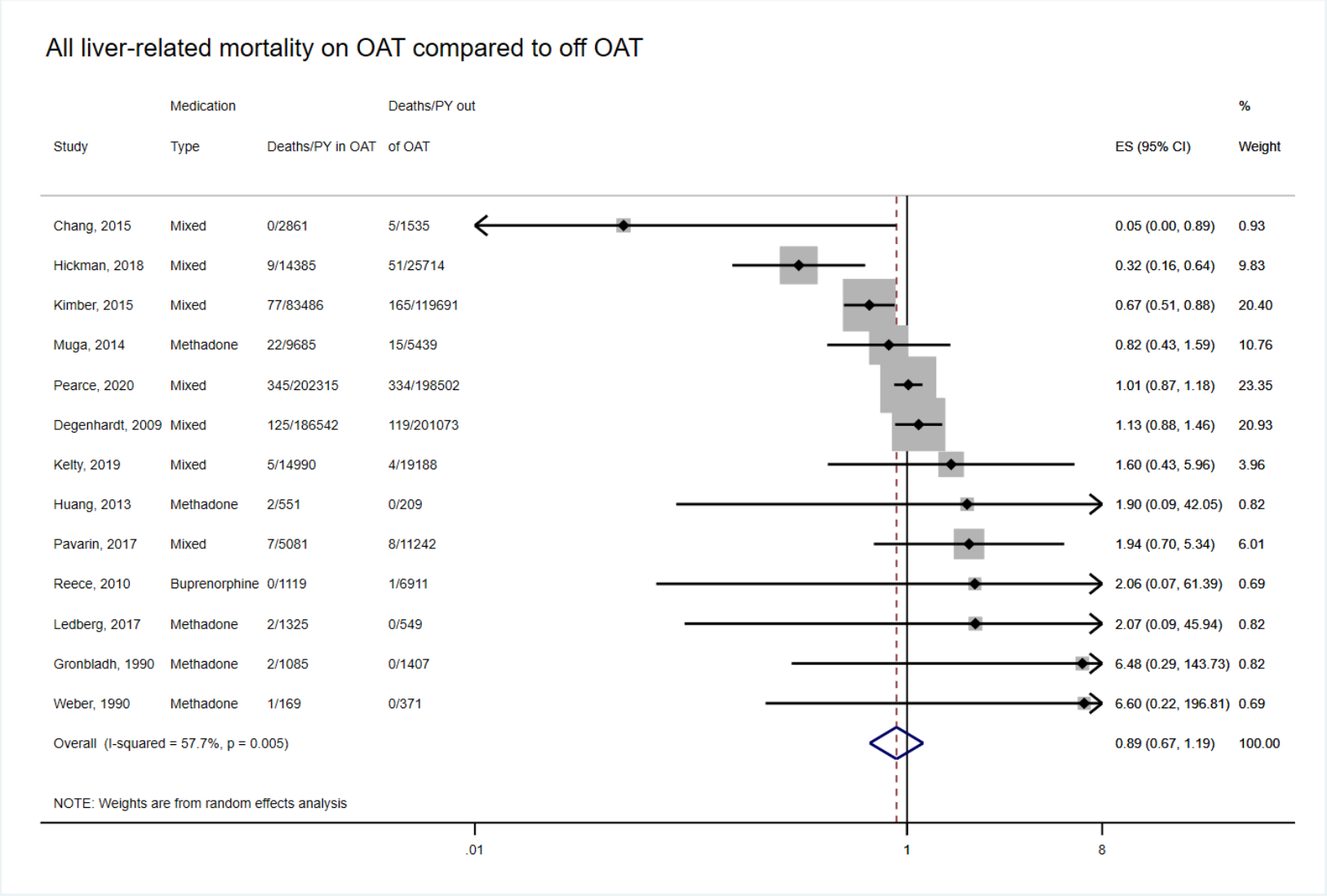
**eFigure 10: Cause-specific mortality: motor vehicle and transport accidents**



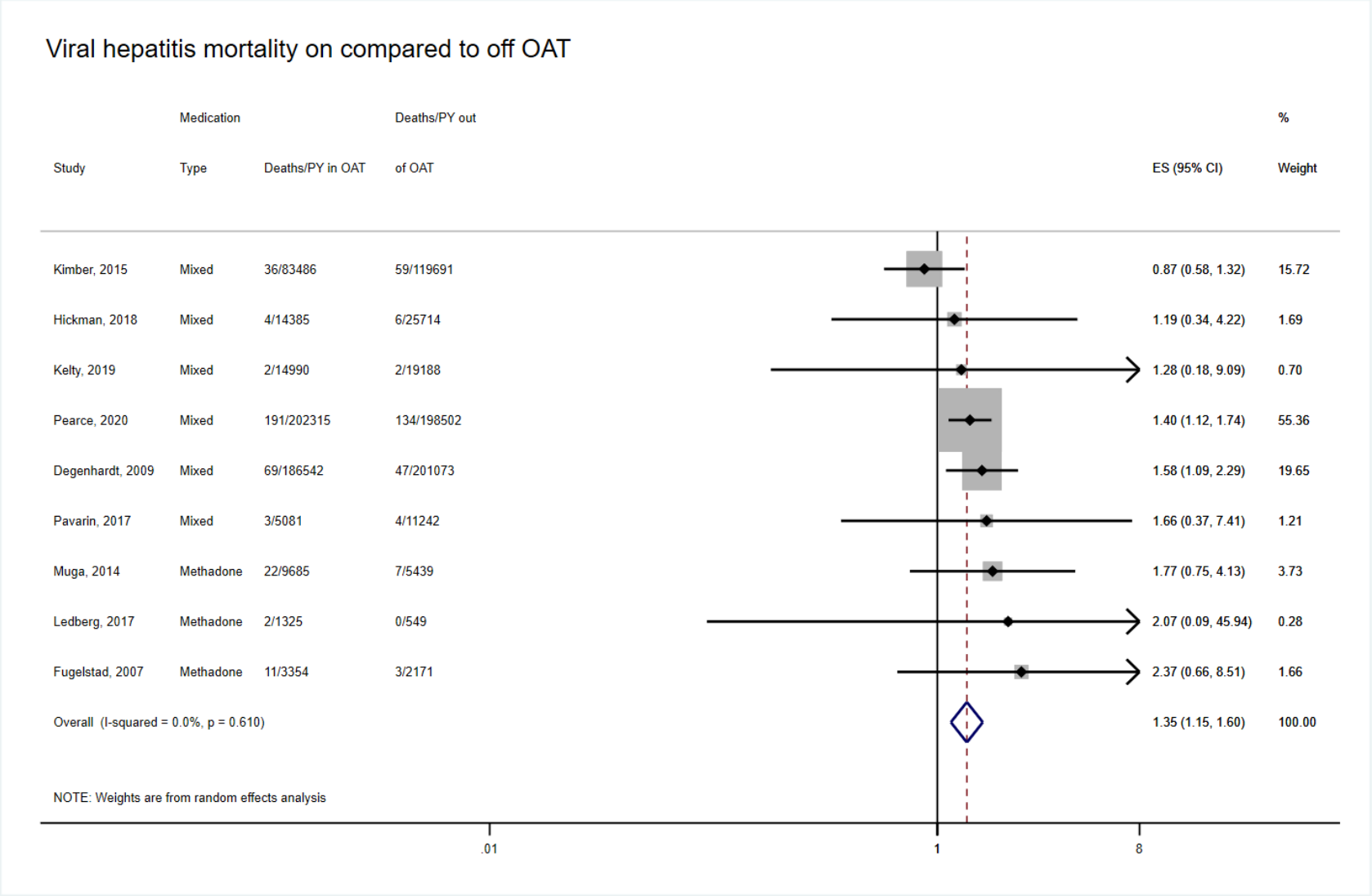
**eFigure 11: Cause-specific mortality: falls, fires, burns drownings**



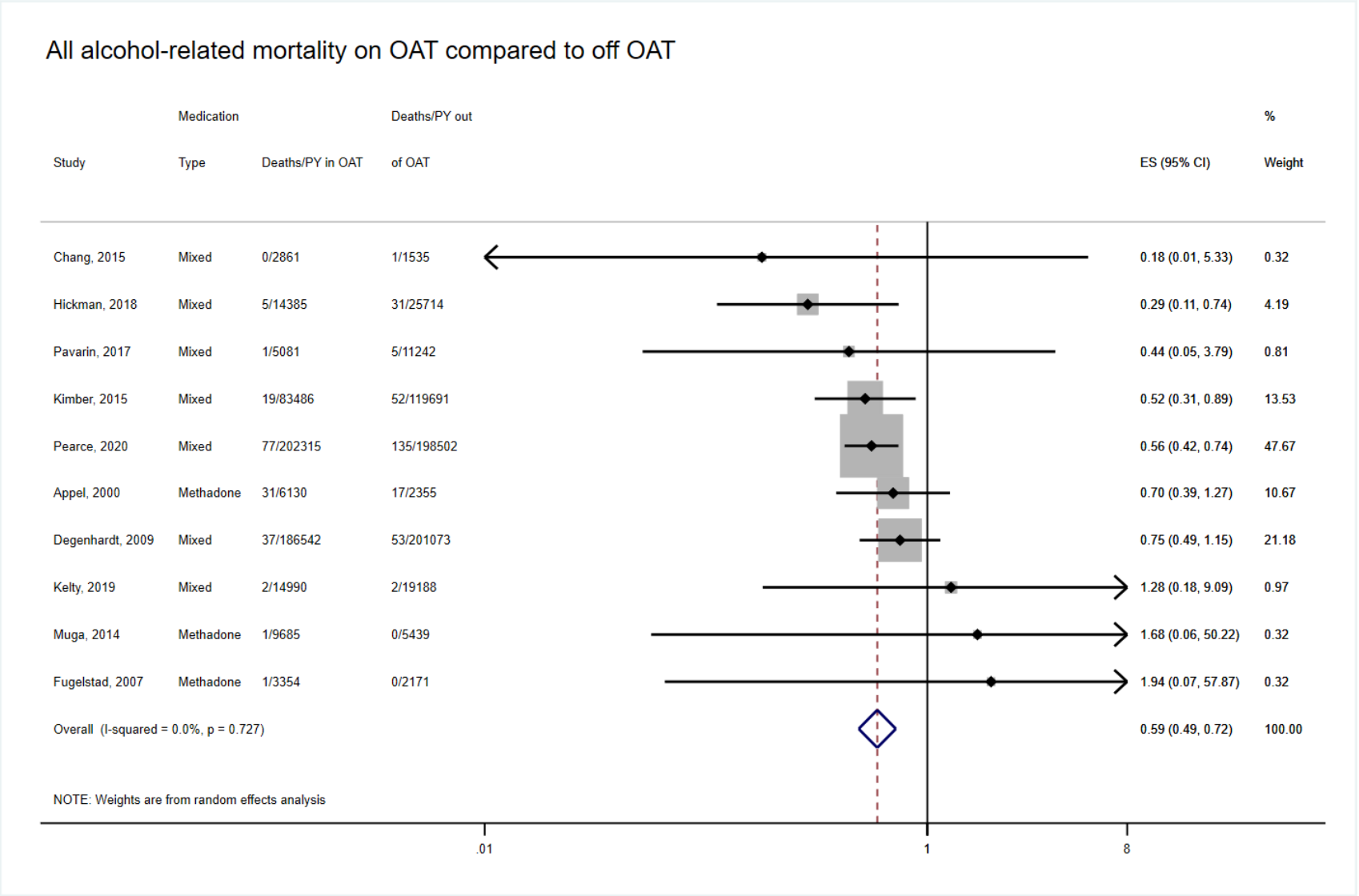
**eFigure 12: Cause-specific mortality: all liver-related**



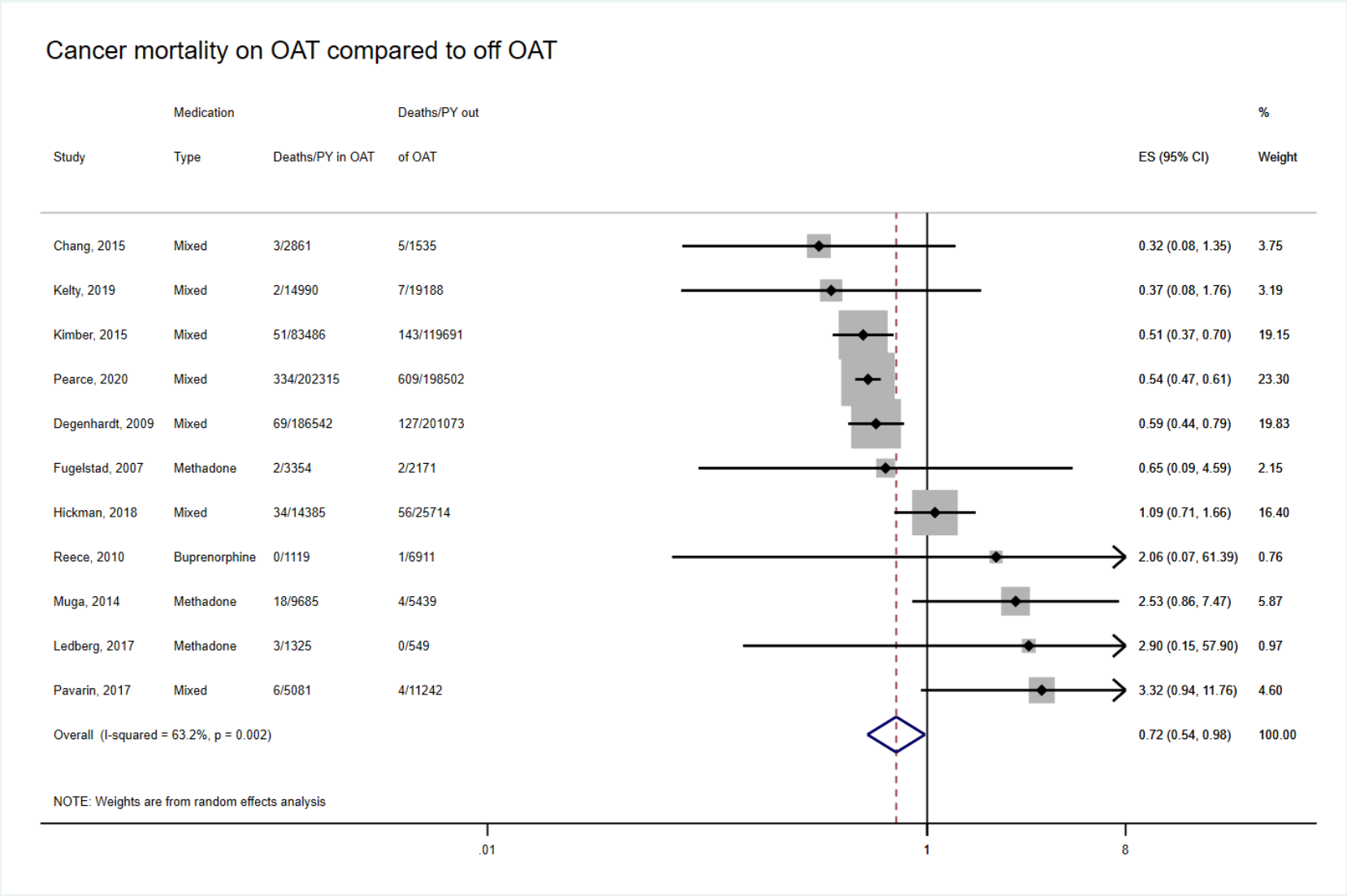
**eFigure 13: Cause-specific mortality: viral hepatitis**



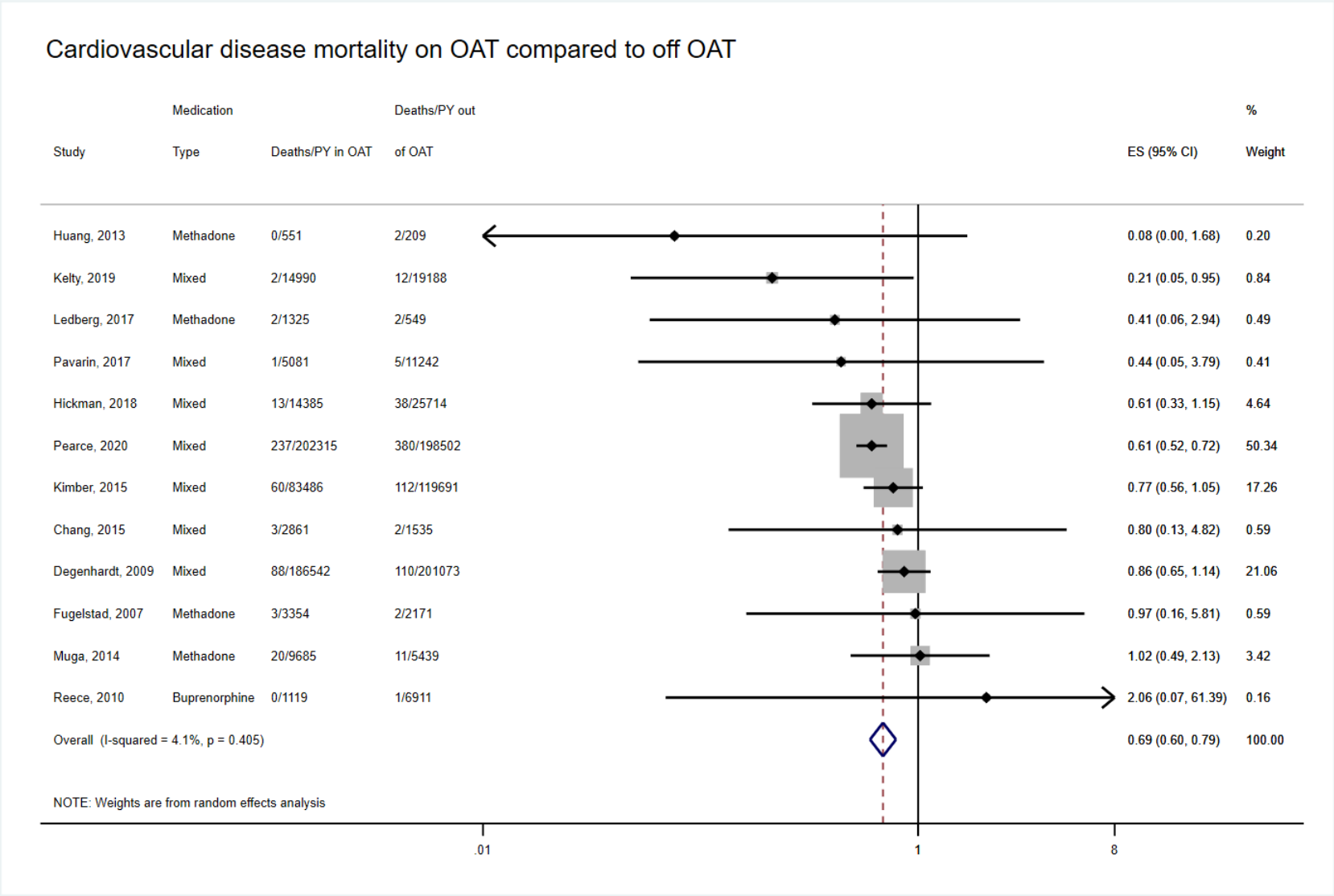
**eFigure 14: Cause-specific mortality: all alcohol related**



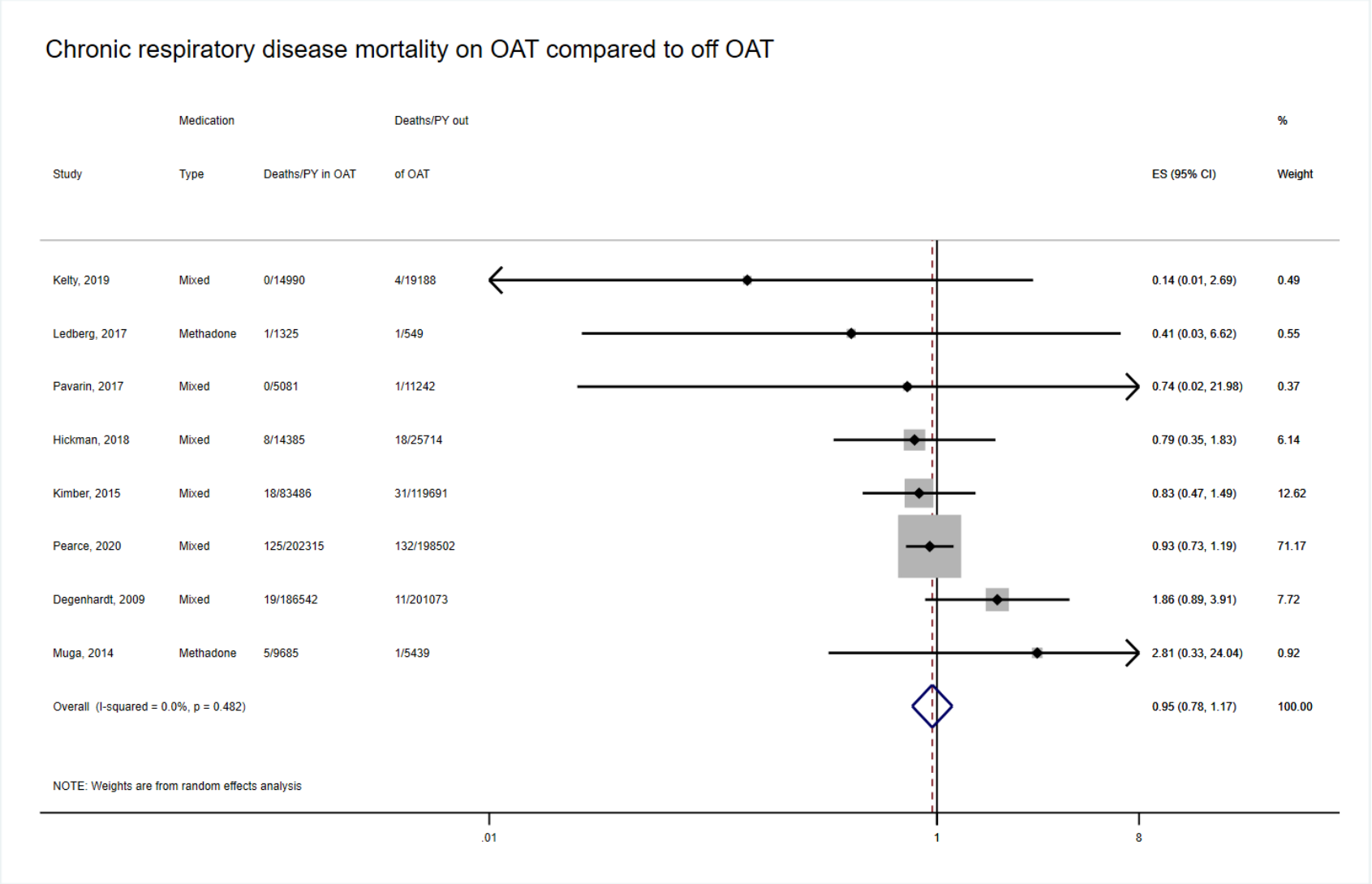
**eFigure 15: Cause-specific mortality: cancer**



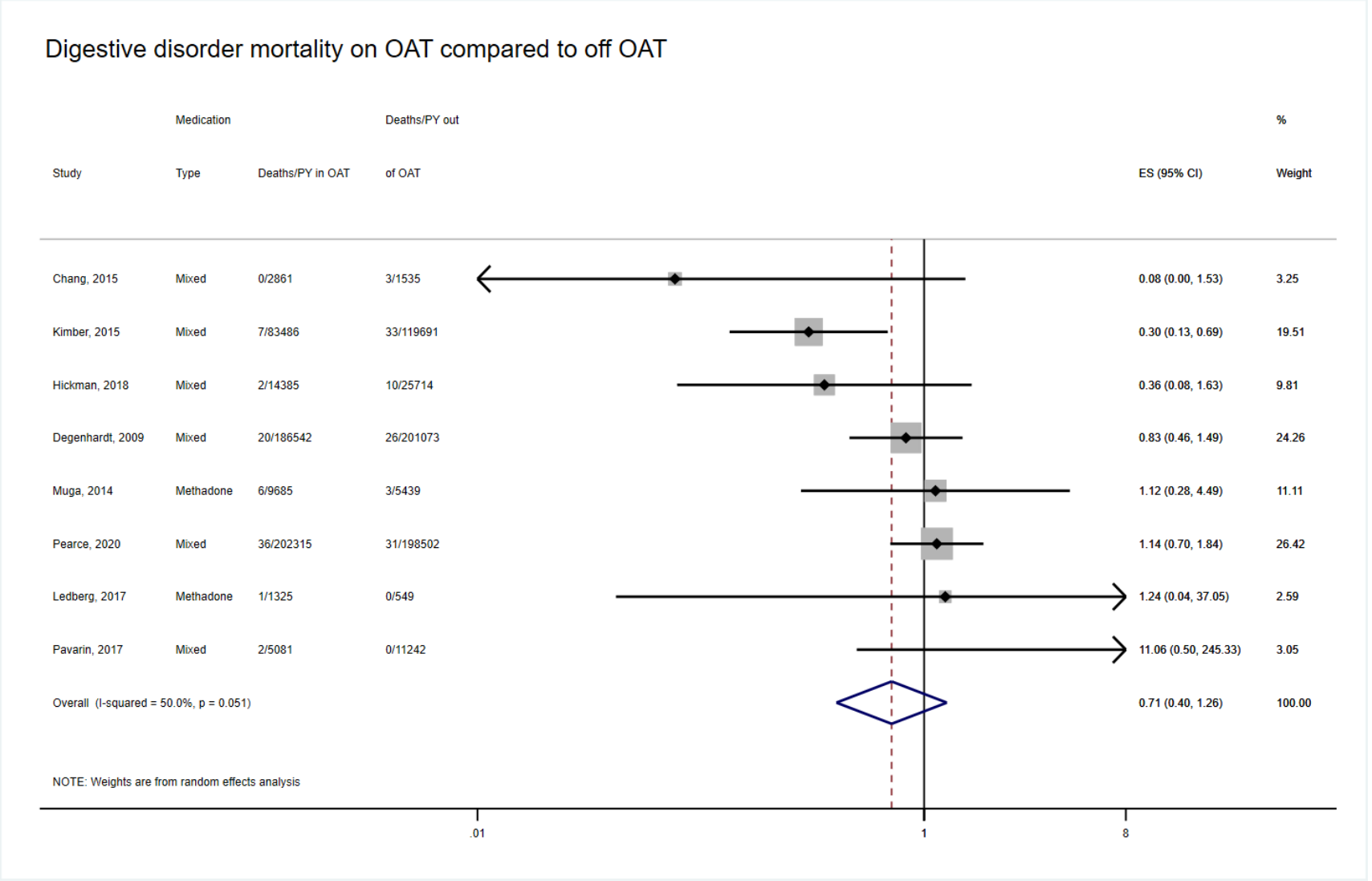
**eFigure 16: Cause-specific mortality: cardiovascular disease**



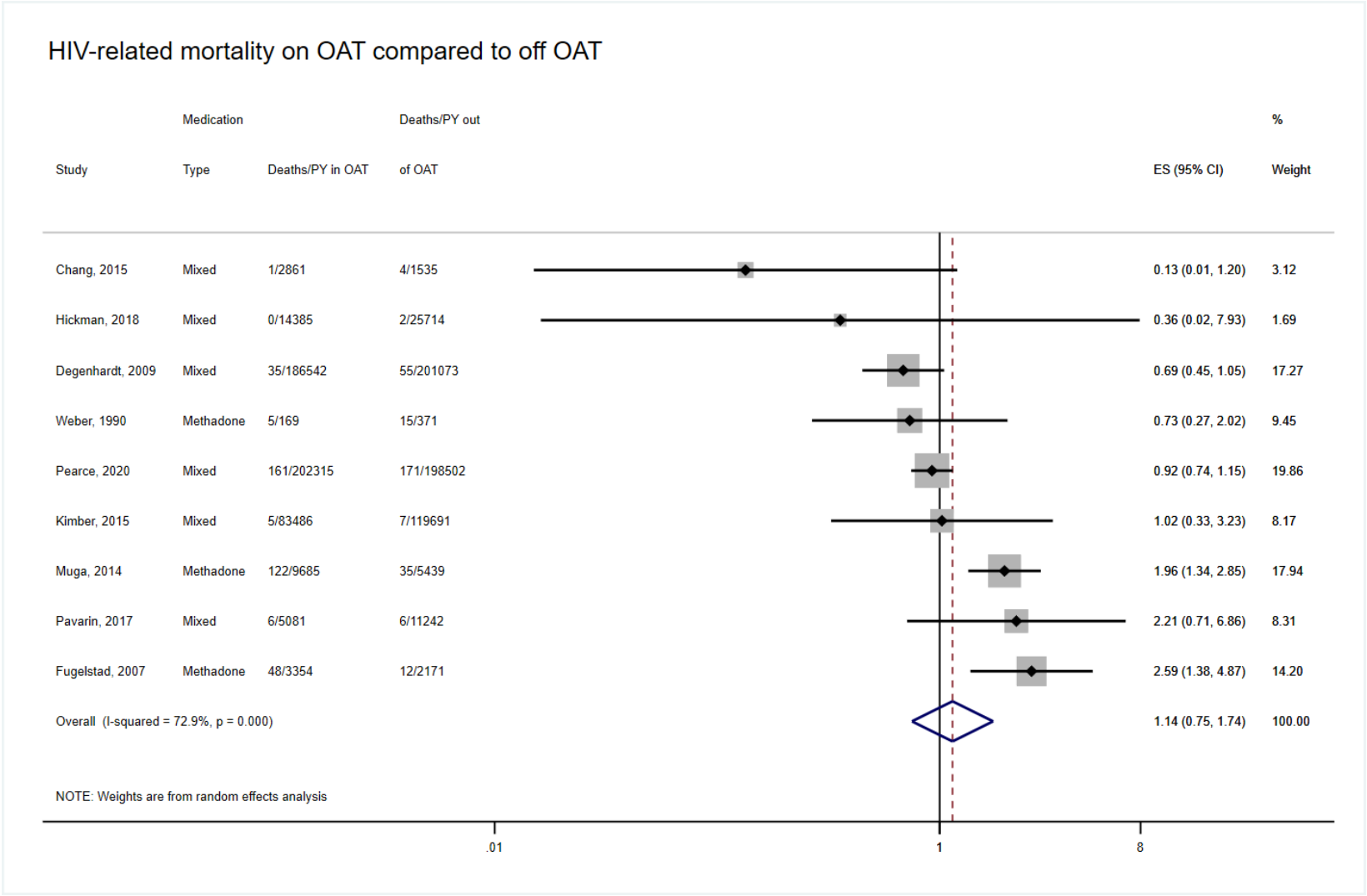
**eFigure 17: Cause-specific mortality: chronic respiratory disease**



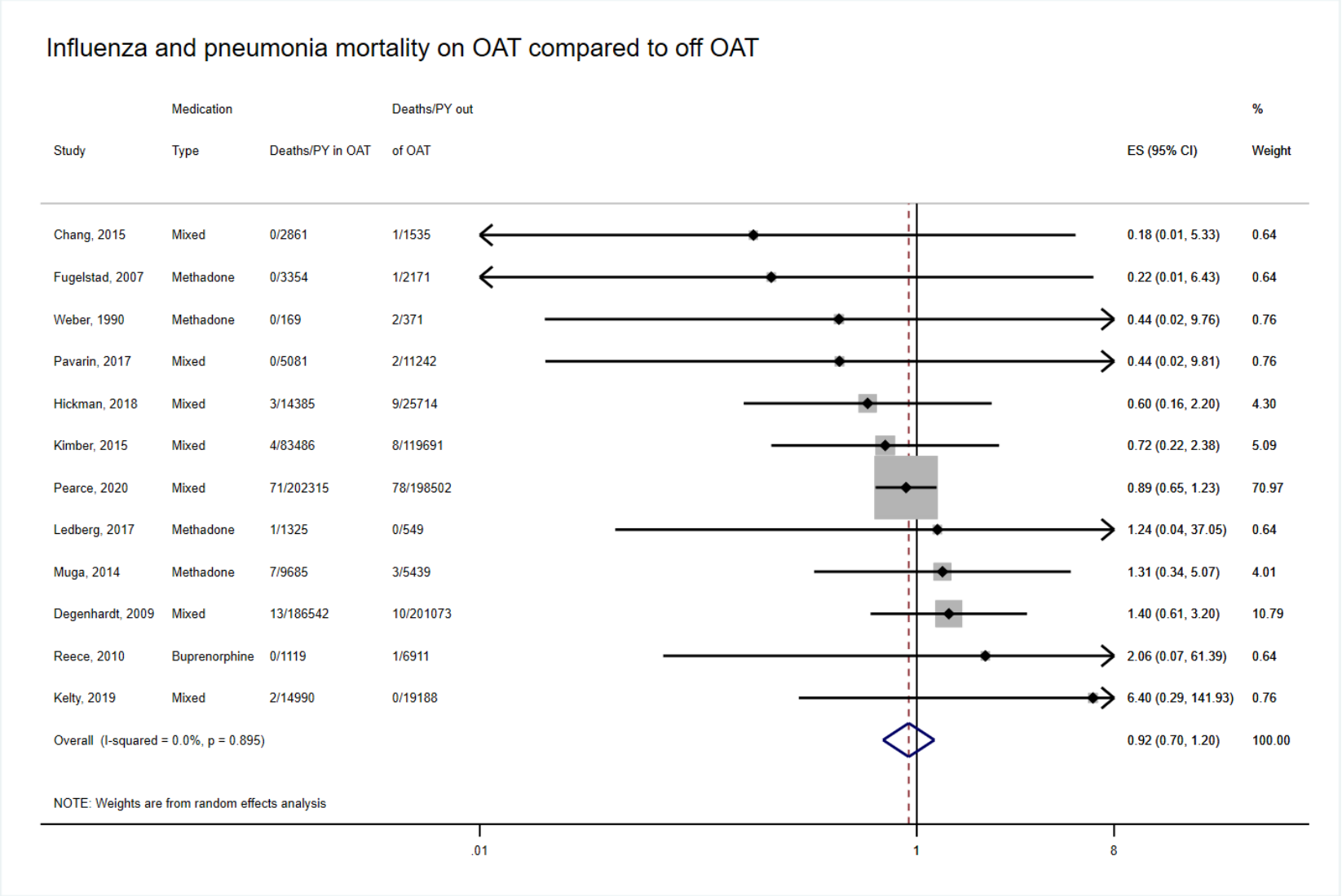
**eFigure 18: Cause-specific mortality: digestive disorders**



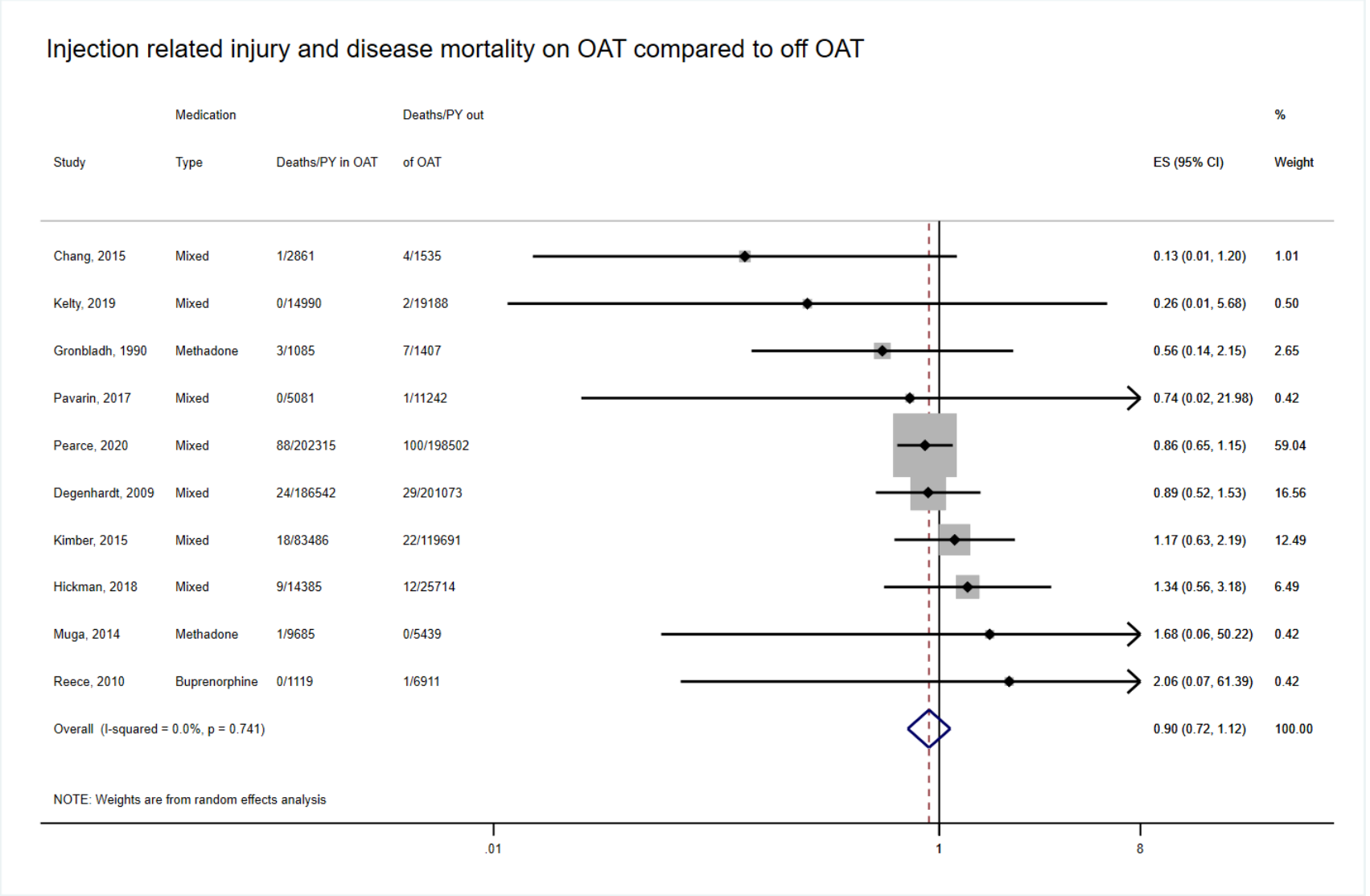
**eFigure 19: Cause-specific mortality: HIV-related**



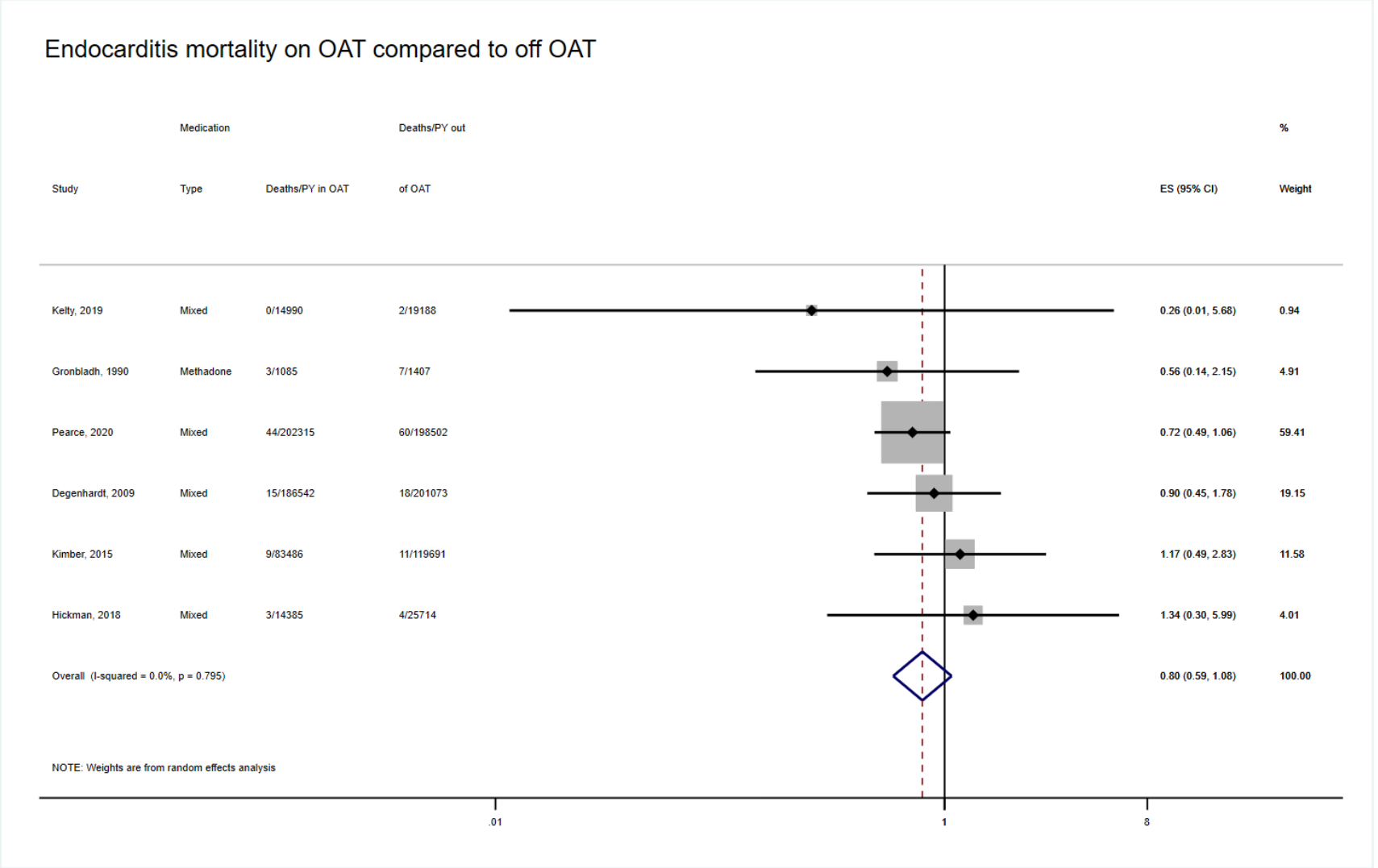
**eFigure 20: Cause-specific mortality: influenza and pneumonia**



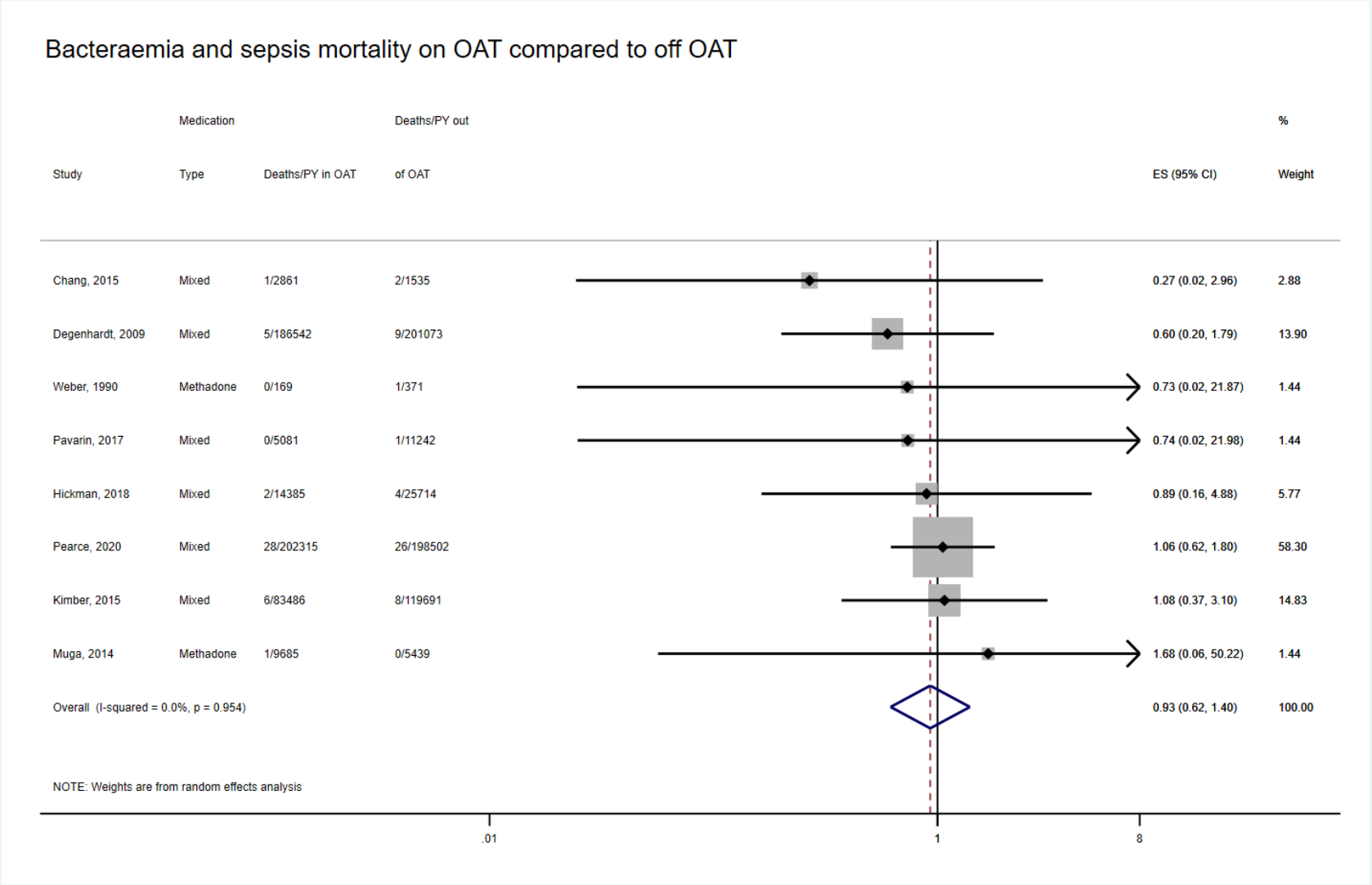
**eFigure 21: Cause-specific mortality: injection related injury and disease**



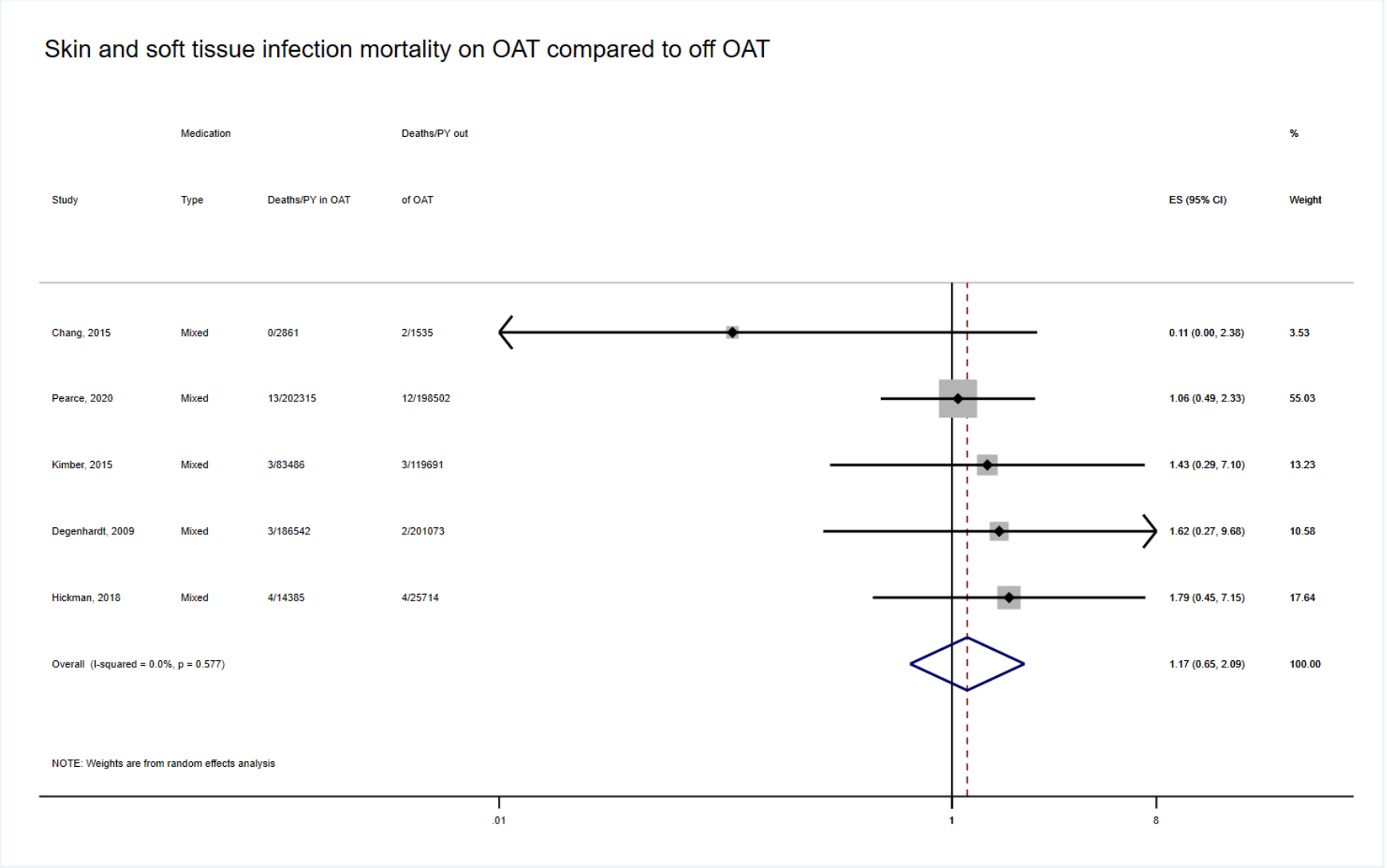
**eFigure 22: Cause-specific mortality: endocarditis**



**eFigure 23: Cause-specific mortality: bacteraemia and sepsis**



**eFigure 24: Cause-specific mortality: skin and soft tissue infections**

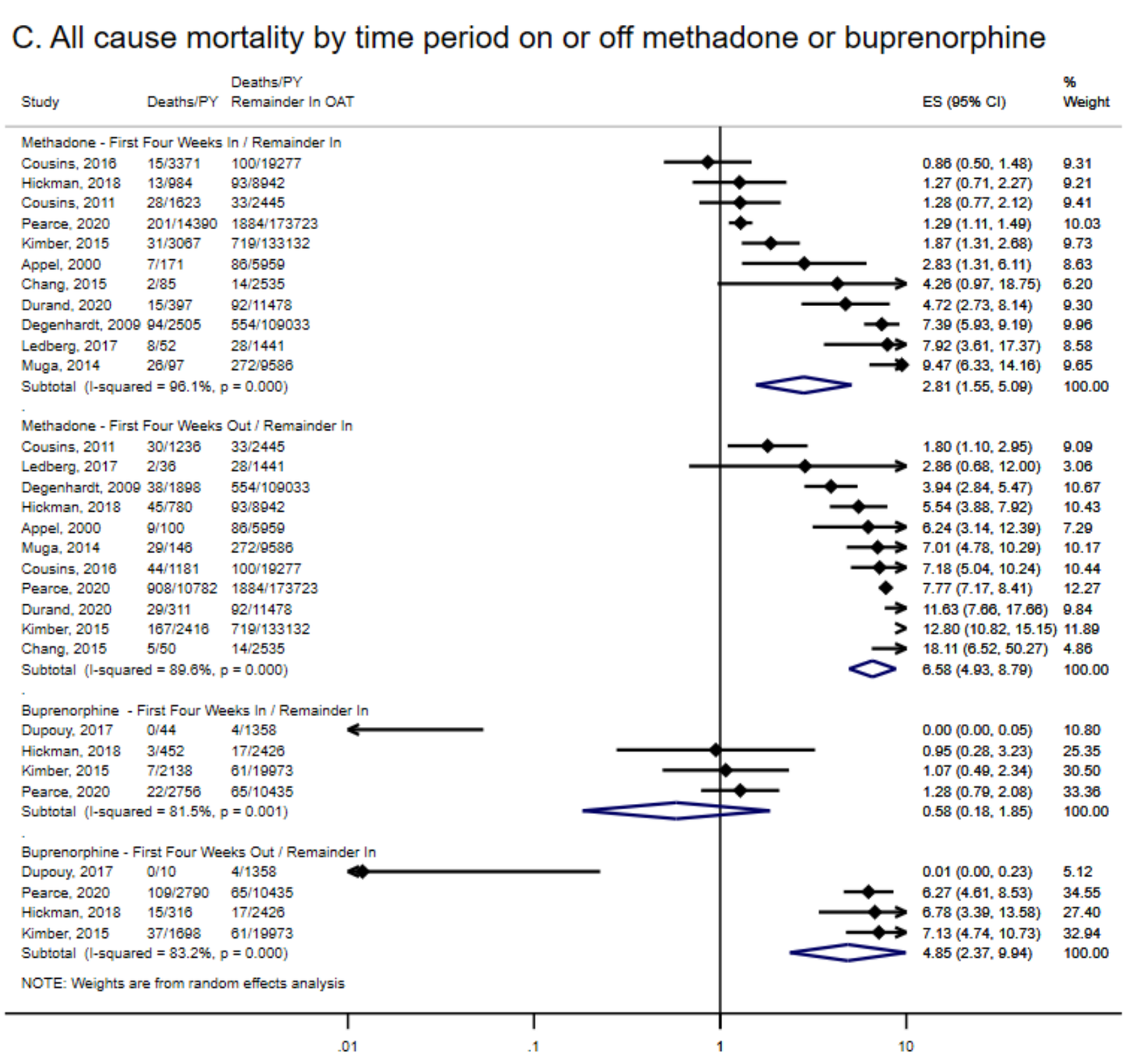


## eTable 17: Findings from observational studies on the pooled cause-specific mortality rates, and mortality rate ratios in people receiving OAT, by specific time periods in and out of treatment

| | | | | In treatment | | | | | | | | Out of treatment | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | First four weeks in OAT | | | | Remainder in OAT | | | | First four weeks out of OAT | | | | Remainder out of OAT | | | | | | | | |
| | References | N cohorts | N people | Deaths | PY | Pooled CMR per 1,000PY (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR per 1,000PY (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR per 1,000PY (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR per 1,000PY (95%CI) | $I^2$ % | Rate ratio first 4 weeks in/ remainder in | $I^2$ % | Rate ratio first 4 weeks out/remainder in | $I^2$ % | Rate ratio remainder out/ remainder in | $I^2$ % |
| **All-cause** | 21,25,40,58,59,63,64,66,68,69,75,78,83,84 | 14 | 175,213 | 497 | 34,390 | 23.98(13.80, 41.67) | 96.4 | 4,305 | 533,327 | 8.99 (6.68. 12.09 | 98.6 | 1,486 | 26,453 | 54.19 (37.65, 78.01) | 95.9 | 8,162 | 576,841 | 16.85 (13.30, 21.35) | 98.7 | 1.92 (1.10, 3.35) | 95.2 | 6.01 (4.32, 8.36) | 92.0 | 1.81 (1.50, 2.18) | 92.3 |
| **All injury and poisoning** | 25,58,63,66,75,78,83,84 | 8 | 157,930 | 219 | 28,552 | 13.48 (6.27, 28.89) | 95.5 | 1,457 | 492,811 | 3.31 (2.82, 3.88) | 81.3 | 651 | 23,461 | 23.11 (14.49, 36.86) | 91.9 | 4,390 | 562,954 | 8.05 (6.39, 10.13) | 97.5 | 1.24 (0.53, 2.92) | 95.0 | 6.95 (4.31, 11.20) | 89.8 | 2.36 (1.87, 2.97) | 88.2 |
| Drug-induced deaths | 25,40,58,61,63,64,66,69,75,78,84 | 11[A] | 177,139 | 212 | 32,434 | 7.03 (3.61, 13.69) | 93.9 | 1,193 | 542,509 | 2.99 (2.19, 4.07) | 95.7 | 508 | 25,074 | 19.27 (11.66, 31.87) | 92.5 | 3,658 | 571,918 | 7.74 (5.54, 10.82) | 98.6 | 1.41 (0.61, 3.23) | 95.0 | 6.72 (3.92, 11.53) | 91.3 | 2.78 (2.10, 3.69) | 90.7 |
| Accidental drug-induced deaths | 25,58,63,66,75,78,84 | 7[A] | 156,252 | 172 | 26,431 | 8.74 (3.42, 22.35) | 96.2 | 818 | 481,051 | 1.70 (1.45, 1.99) | 66.7 | 448 | 23,256 | 14.26 (8.36, 24.31) | 91.4 | 3,088 | 556,103 | 5.46 (3.81, 7.84) | 98.6 | 1.96 (0.63, 6.08) | 96.4 | 8.46 (5.60, 12.77) | 79.5 | 2.89 (2.11, 3.94) | 89.7 |
| Accidental opioid deaths | 25,58,63,66,75,78,84 | 7[B] | 156,252 | 139 | 26,431 | 6.64 (2.20, 20.04) | 96.3 | 586 | 476,153 | 1.27 (1.07, 1.50) | 64.9 | 317 | 23,024 | 11.78 (7.96, 17.42) | 82.0 | 2,397 | 545,093 | 5.15 (3.66, 7.24) | 98.1 | 4.34 (1.65, 11.43) | 93.7 | 8.95 (5.23, 15.31) | 86.9 | 3.26 (2.23, 4.77) | 91.5 |
| Suicide | 58,63,66,75,78,84 | 6[A] | 100,905 | 17 | 8,096 | 2.81 (0.57, 13.90) | 72.1 | 172 | 296,038 | 0.58 (0.44, 0.76) | 38.5 | 25 | 9,284 | 2.72 (1.84, 4.03) | 0.0 | 426 | 371,308 | 0.97 (0.71, 1.34) | 78.7 | * | | * | | 2.03 (1.70, 2.43) | 0.0 |
| Violence | 25,58,63,66,75,78,84 | 7[C] | 156,252 | 1 | 5,871 | 0.17 (0.02, 1.21) | | 72 | 474,879 | 0.16 (0.11, 0.22) | 38.7 | 34 | 21,840 | 0.72 (0.13, 4.11) | 77.4 | 98 | 520,014 | 0.18 (0.13, 0.26) | 64.3 | * | | * | | * | |
| Motor vehicle and transport accidents | 58,59,66,75,78,84 | 6[D] | 101,466 | 4 | 6,904 | 0.60 (0.23, 1.60) | 0.0 | 99 | 296,038 | 0.36 (0.18, 0.74) | 78.9 | 10 | 9,284 | 1.08 (0.58, 2.01) | 0.0 | 112 | 370,791 | 0.26 (0.16, 0.43) | 70.8 | * | | * | | 0.43 (0.13, 1.44) | 85.9 |
| Falls/fires/burns/drownings | 58,59,66,75,78,84 | 6[E] | 101,466 | 0 | - | - | - | 23 | 291,140 | 0.11 (0.04, 0.26) | 60.6 | | - | - | - | 30 | 359,781 | 0.09 (0.06, 0.12) | 0.0 | * | | * | | * | |
| **Injection-related injuries and diseases** | 58,63,66,75,78,83,84 | 7[F] | 102,583 | 2 | 5,963 | 1.36 (0.02, 79.90) | 88.4 | 51 | 299,452 | 0.23 (0.10, 0.52) | 85.2 | 11 | 9,284 | 1.44 (0.57, 3.63) | 56.6 | 57 | 372,270 | 0.29 (0.11, 0.75) | 90.5 | * | | * | | 3.49 (0.43, 28.40) | 95.2 |
| Endocarditis | 58,63,66,75,78,84 | 6[G] | 100,905 | 0 | - | - | - | 27 | 289,866 | 0.10 (0.06, 0.17) | 35.2 | 6 | 9,284 | 0.80 (0.28, 2.26) | 35.8 | 27 | 359,781 | 0.08 (0.05, 0.11) | 0.0 | * | | * | | * | |
| Bacteraemia or sepsis | 25,58,63,66,75,78,84 | 7[H] | 156,252 | 2 | 5,963 | 1.36 (0.02, 79.90) | 88.4 | 12 | 289,866 | 0.06 (0.02, 0.17) | 68.9 | 4 | 9,284 | 0.47 (0.18, 1.24) | 0.0 | 20 | 372,270 | 0.11 (0.04, 0.35) | 82.5 | * | | * | | * | |
| Skin or soft tissue infections | 25,58,63,66,75,78,84 | 7[I] | 156,252 | 0 | - | - | - | 10 | 289,866 | 0.06 (0.01, 0.34) | 87.9 | 1 | 1,874 | 0.53 (0.08, 3.79) | 0.0 | 10 | 361,260 | 0.08 (0.01, 0.61) | 90.6 | * | | * | | * | |

**Table Notes**: *Rate ratios are suppressed where at least half of the studies reported 0 deaths for one of the time periods involved; **The following studies recorded 0 deaths for the given category and so were only included in N cohorts and N people but did not contribute to the pooled analysis** – [A] Chang 2015; [B] Chang 2015, Pavarin 2017; [C] Chang 2015, Ledberg 2017, Pavarin 2017; [D] Appel 2000; [E] Pavarin 2017, Appel 2000; [F] Ledberg 2017; [G] Chang 2015, Ledberg 2017, Pavarin 2017; [H] Ledberg 2017, Pearce 2020; [I] Ledberg 2017, Pavarin 2017, Pearce 2020. **OAT** – opioid agonist treatment. **CMR** – crude mortality rate.

eFigure 25. Studies on the Association of Opioid Agonist Treatment (OAT) With All-Cause Mortality by specific time periods in and out of treatment from observational studies, stratified by buprenorphine (B) or methadone (M)

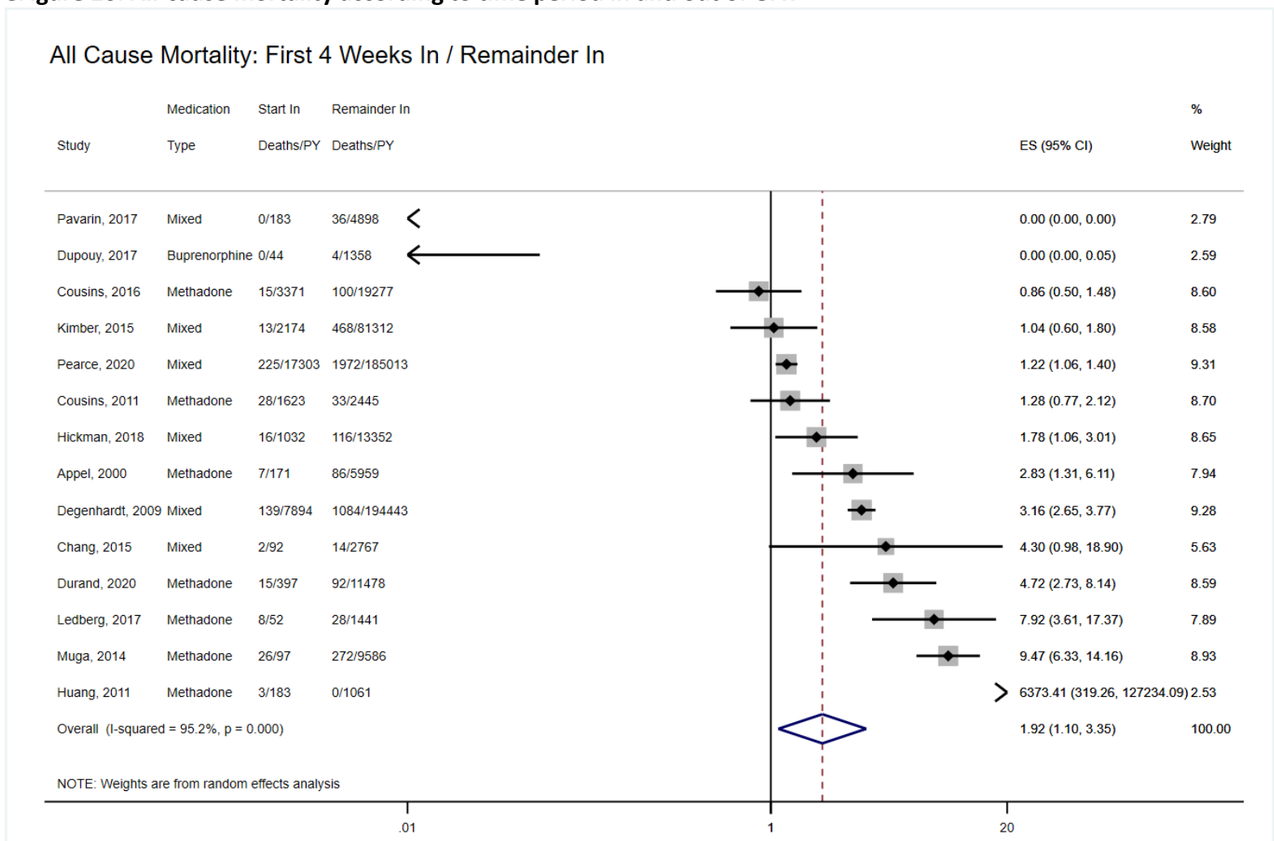


**eTable 18: Additional causes of death by time period in or out of OAT**

| | | | | In treatment | | | | | | | | Out of treatment | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | First four weeks | | | | Remainder | | | | First four weeks | | | | Remainder | | | | | | | |
| | Refs | N cohorts | N people | Deaths | PY | Pooled CMR (95%CI) | $I^2$ | Deaths | PY | Pooled CMR (95%CI) | $I^2$ | Deaths | PY | Pooled CMR (95%CI) | $I^2$ | Deaths | PY | Pooled CMR (95%CI) | $I^2$ | Rate ratio first 4 weeks in/ remainder in | $I^2$ | Rate ratio first 4 weeks out/remainder in | $I^2$ | Rate ratio remainder out/ remainder in | $I^2$ |
| **All liver-related** | [1-7] | 7 | 102,583 | 8 | 9,128 | 1.67 (0.43, 6.49) | 70.5% | 234 | 305,624 | 1.00 (0.64, 1.56) | 86.1% | 58 | 9,430 | 9.14 (2.61, 32.06) | 94.5% | 303 | 377,533 | 1.14 (0.70, 1.88) | 92.7% | 0.15 (0.01, 2.29) | 92.4% | 1.32 (0.25, 6.98) | 94.8% | 1.32 (0.57, 3.03) | 91.9% |
| Viral Hepatitis | [1-7] | 7[a] | 102,583 | 6 | 9,128 | 1.42 (0.29, 6.97) | 73.3% | 130 | 305,624 | 0.58 (0.27, 1.24) | 92.2% | 25 | 9,430 | 3.50 (0.73, 16.76) | 89.4% | 98 | 376,054 | 0.30 (0.20, 0.45) | 65.1% | 0.22 (0.01, 4.27) | 91.9% | 0.78 (0.08, 7.17) | 93.1% | 0.49 (0.25, 0.95) | 70.5% |
| All alcohol-related | [1-8] | 8[b] | 157,930 | 0 | - | - | - | 63 | 304,350 | 0.21 (0.17, 0.27) | 0.0% | 40 | 22,992 | 1.86 (0.88, 3.92) | 69.2% | 237 | 557,065 | 0.49 (0.31, 0.78) | 89.4% | 0.00 (0.00, 0.00) | 77.7% | 5.44 (0.12, 257.11) | 96.6% | 13.76 (1.51, 125.60) | 97.0% |
| Cancer | [1-8] | 8 | 157,930 | 65 | 24,353 | 3.79 (1.48, 9.72) | 78.6% | 453 | 493,403 | 1.08 (0.62, 1.90) | 95.3% | 184 | 23,137 | 8.73 (4.63, 16.44) | 90.9% | 764 | 562,328 | 1.06 (0.54, 2.06) | 98.0% | 0.12 (0.02, 0.88) | 95.1% | 1.42 (0.50, 4.07) | 94.0% | 0.93 (0.58, 1.51) | 86.5% |
| Cardiovascular disease | [1-8] | 8 | 157,930 | 27 | 25,537 | 2.42 (0.51, 11.44) | 89.5% | 397 | 493,403 | 0.87 (0.56, 1.34) | 90.6% | 89 | 23,370 | 4.05 (2.03, 8.08) | 78.3% | 570 | 562,845 | 1.05 (0.64, 1.71) | 95.0% | 0.19 (0.03, 1.38) | 92.9% | 2.18 (0.85, 5.55) | 84.2% | 1.31 (1.15, 1.49) | 0.0% |
| Chronic respiratory disease | [1-8] | 8[A] | 157,930 | 17 | 24,256 | 1.25 (0.33, 4.81) | 74.7% | 159 | 484,464 | 0.31 (0.14, 0.71) | 93.8% | 33 | 16,733 | 2.01 (1.43, 2.82) | 0.0% | 162 | 561,366 | 0.28 (0.13, 0.59) | 91.9% | 0.27 (0.01, 7.23) | 95.4% | 0.07 (0.00, 1.86) | 96.6% | 2.35 (0.88, 6.32) | 88.5% |
| Digestive disorders | [1-7] | 7 | 102,583 | 1 | 5,871 | 0.17 (0.02, 1.21) | 0.0% | 37 | 305,624 | 0.22 (0.10, 0.49) | 78.0% | 10 | 9,485 | 2.63 (0.62, 11.11) | 79.4% | 65 | 366,523 | 0.27 (0.14, 0.52) | 80.3% | 0.00 (0.00, 0.10) | 90.0% | 2.98 (0.24, 37.13) | 90.8% | 0.43 (0.04, 4.03) | 94.2% |
| HIV-related | [1-8] | 8[B] | 157,930 | 22 | 23,271 | 2.37 (0.05, 114.16) | 98.5% | 307 | 478,777 | 0.62 (0.12, 3.08) | 99.3% | 42 | 20,167 | 5.40 (0.91, 32.13) | 94.7% | 238 | 562,328 | 0.49 (0.18, 1.34) | 97.5% | 0.05 (0.00, 0.57) | 95.7% | 0.29 (0.04, 2.15) | 94.7% | 1.58 (0.71, 3.52) | 90.8% |
| Influenza and pneumonia | [1-7] | 7 | 102,583 | 5 | 5,968 | 3.30 (0.04, 257.30) | 95.9% | 23 | 300,726 | 0.16 (0.06, 0.43) | 80.0% | 4 | 7,556 | 1.26 (0.18, 8.81) | 72.7% | 29 | 377,533 | 0.15 (0.06, 0.37) | 78.9% | 0.04 (0.00, 7.94) | 96.6% | 0.24 (0.00, 13.38) | 93.2% | 4.41 (0.45, 43.32) | 92.4% |

The following studies recorded 0 deaths for the given category and so were only included in N cohorts and N people but did not contribute to the analysis: [A]Chang 2015; [B]Ledberg 2017.

**eFigure 26: All-cause mortality according to time period in and out of OAT**



## All Cause Mortality: First 4 Weeks Out / Remainder In

| Study | Medication Type | Start Out Deaths/PY | Remainder In Deaths/PY | ES (95% CI) | % Weight |
|---|---|---|---|---|---|
| Dupouy, 2017 | Buprenorphine | 0/10 | 4/1358 | 0.01 (0.00, 0.23) | 1.12 |
| Pavarin, 2017 | Mixed | 3/232 | 36/4898 | 1.76 (0.54, 5.70) | 4.51 |
| Cousins, 2011 | Methadone | 30/1236 | 33/2445 | 1.80 (1.10, 2.95) | 8.58 |
| Ledberg, 2017 | Methadone | 2/36 | 28/1441 | 2.86 (0.68, 12.00) | 3.53 |
| Degenhardt, 2009 | Mixed | 132/6259 | 1084/194443 | 3.78 (3.16, 4.53) | 10.31 |
| Hickman, 2018 | Mixed | 45/1152 | 116/13352 | 4.50 (3.19, 6.34) | 9.53 |
| Appel, 2000 | Methadone | 9/100 | 86/5959 | 6.24 (3.14, 12.39) | 7.28 |
| Muga, 2014 | Methadone | 29/146 | 272/9586 | 7.01 (4.78, 10.29) | 9.30 |
| Pearce, 2020 | Mixed | 1027/13707 | 1972/185013 | 7.03 (6.52, 7.58) | 10.58 |
| Cousins, 2016 | Methadone | 44/1181 | 100/19277 | 7.18 (5.04, 10.24) | 9.47 |
| Kimber, 2015 | Mixed | 120/1874 | 468/81312 | 11.13 (9.10, 13.60) | 10.23 |
| Durand, 2020 | Methadone | 29/311 | 92/11478 | 11.63 (7.66, 17.66) | 9.09 |
| Chang, 2015 | Mixed | 5/55 | 14/2767 | 17.97 (6.47, 49.88) | 5.26 |
| Huang, 2011 | Methadone | 11/164 | 0/1061 | 23354.39 (1372.57, 397378.13) | 1.20 |
| Overall (I-squared = 92.0%, p = 0.000) | | | | 6.01 (4.32, 8.36) | 100.00 |

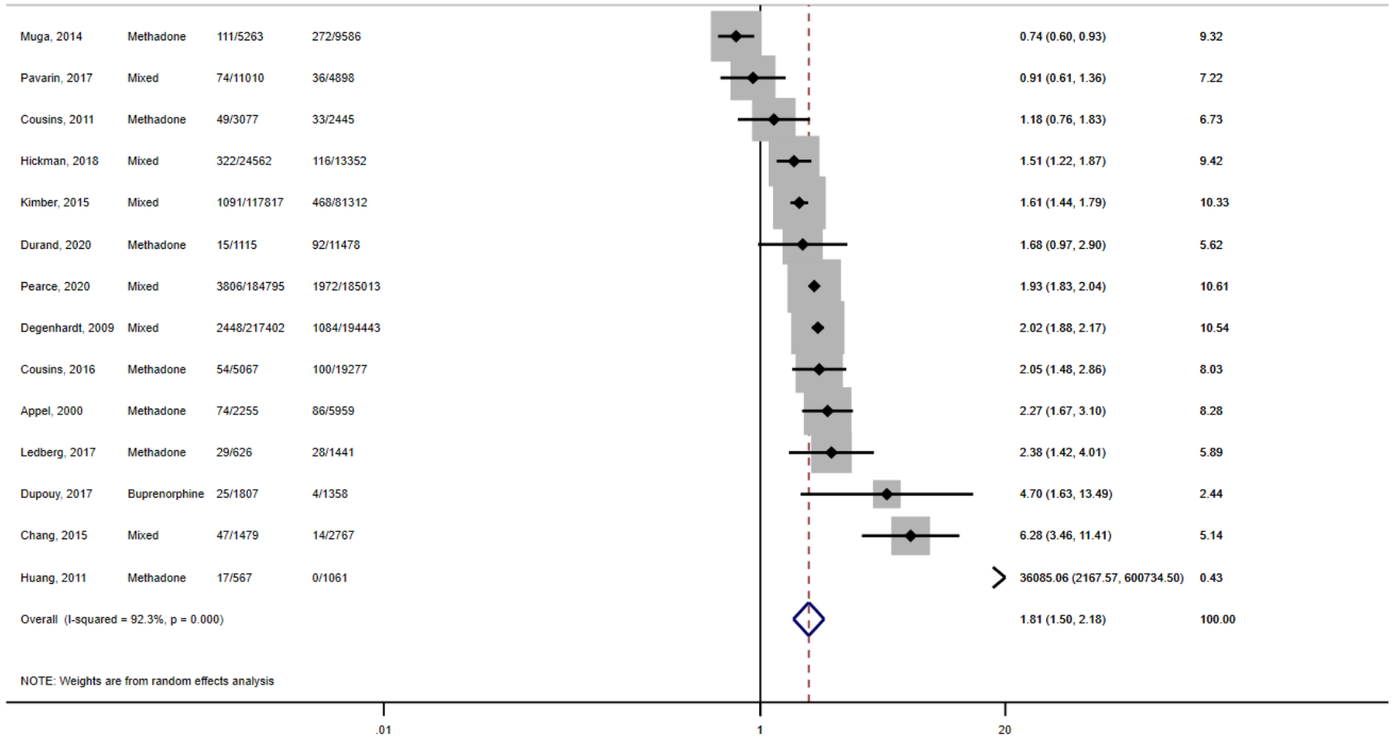
NOTE: Weights are from random effects analysis

.01 1 20

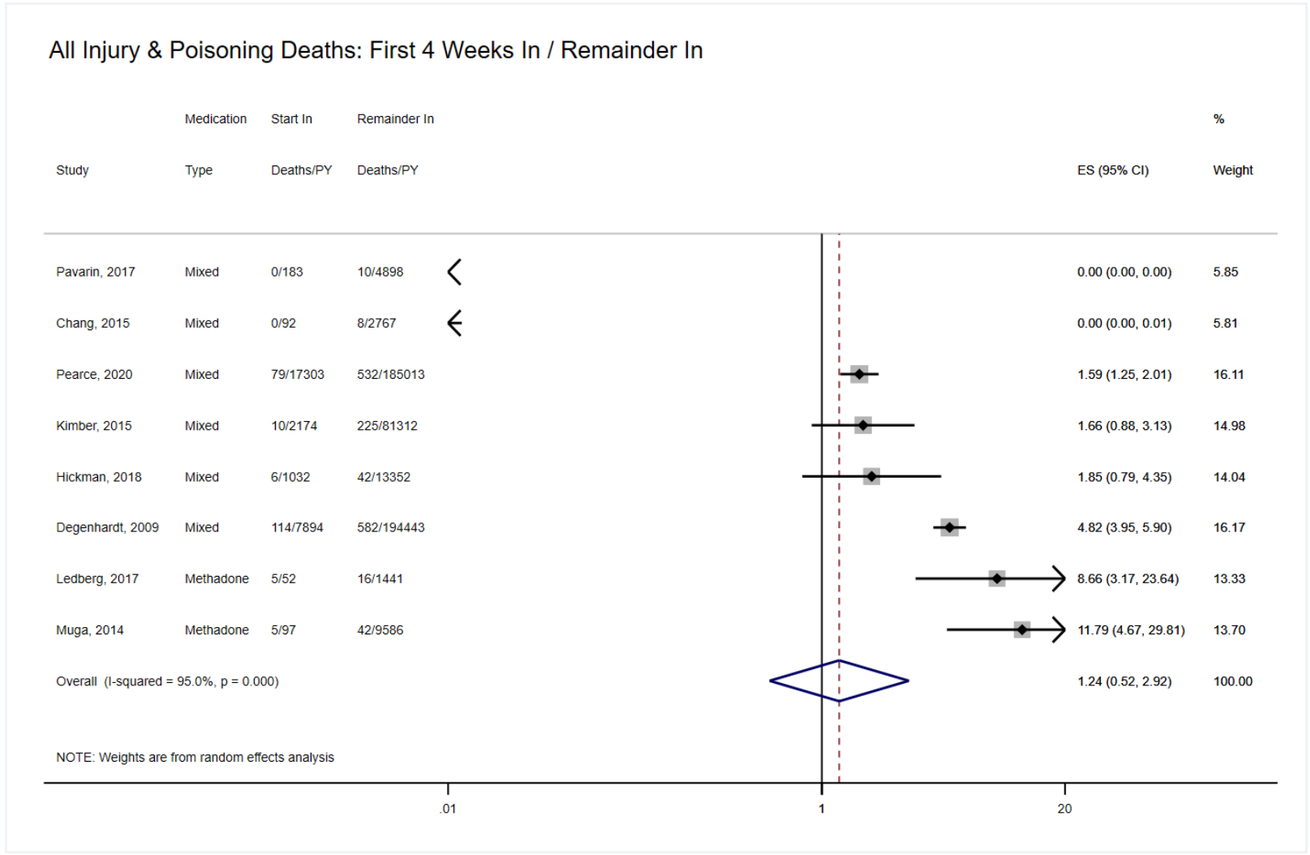
## All Cause Mortality: Remainder Out / Remainder In

| Study | Medication Type | Remainder Out Deaths/PY | Remainder In Deaths/PY | ES (95% CI) | % Weight |
|---|---|---|---|---|---|
| Muga, 2014 | Methadone | 111/5263 | 272/9586 | 0.74 (0.60, 0.93) | 9.32 |
| Pavarin, 2017 | Mixed | 74/11010 | 36/4898 | 0.91 (0.61, 1.36) | 7.22 |
| Cousins, 2011 | Methadone | 49/3077 | 33/2445 | 1.18 (0.76, 1.83) | 6.73 |
| Hickman, 2018 | Mixed | 322/24562 | 116/13352 | 1.51 (1.22, 1.87) | 9.42 |
| Kimber, 2015 | Mixed | 1091/117817 | 468/81312 | 1.61 (1.44, 1.79) | 10.33 |
| Durand, 2020 | Methadone | 15/1115 | 92/11478 | 1.68 (0.97, 2.90) | 5.62 |
| Pearce, 2020 | Mixed | 3806/184795 | 1972/185013 | 1.93 (1.83, 2.04) | 10.61 |
| Degenhardt, 2009 | Mixed | 2448/217402 | 1084/194443 | 2.02 (1.88, 2.17) | 10.54 |
| Cousins, 2016 | Methadone | 54/5067 | 100/19277 | 2.05 (1.48, 2.86) | 8.03 |
| Appel, 2000 | Methadone | 74/2255 | 86/5959 | 2.27 (1.67, 3.10) | 8.28 |
| Ledberg, 2017 | Methadone | 29/626 | 28/1441 | 2.38 (1.42, 4.01) | 5.89 |
| Dupouy, 2017 | Buprenorphine | 25/1807 | 4/1358 | 4.70 (1.63, 13.49) | 2.44 |
| Chang, 2015 | Mixed | 47/1479 | 14/2767 | 6.28 (3.46, 11.41) | 5.14 |
| Huang, 2011 | Methadone | 17/567 | 0/1061 | 36085.06 (2167.57, 600734.50) | 0.43 |
| Overall (I-squared = 92.3%, p = 0.000) | | | | 1.81 (1.50, 2.18) | 100.00 |

NOTE: Weights are from random effects analysis



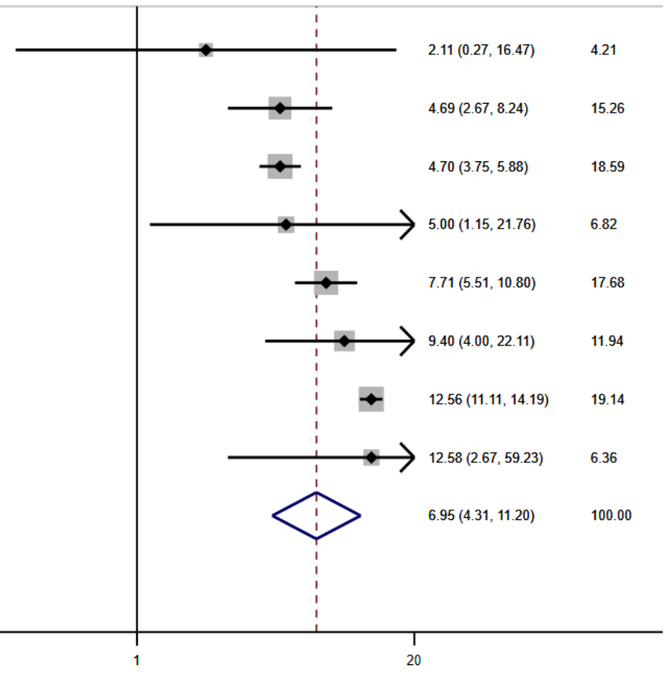
**eFigure 27: All injury and poisoning mortality according to time period in and out of OAT**



## All Injury & Poisoning Deaths: First 4 Weeks Out / Remainder In

| Study | Medication Type | Start Out Deaths/PY | Remainder In Deaths/PY | ES (95% CI) | % Weight |
|---|---|---|---|---|---|
| Pavarin, 2017 | Mixed | 1/232 | 10/4898 | 2.11 (0.27, 16.47) | 4.21 |
| Hickman, 2018 | Mixed | 17/1152 | 42/13352 | 4.69 (2.67, 8.24) | 15.26 |
| Degenhardt, 2009 | Mixed | 88/6259 | 582/194443 | 4.70 (3.75, 5.88) | 18.59 |
| Ledberg, 2017 | Methadone | 2/36 | 16/1441 | 5.00 (1.15, 21.76) | 6.82 |
| Kimber, 2015 | Mixed | 40/1874 | 225/81312 | 7.71 (5.51, 10.80) | 17.68 |
| Muga, 2014 | Methadone | 6/146 | 42/9586 | 9.40 (4.00, 22.11) | 11.94 |
| Pearce, 2020 | Mixed | 495/13707 | 532/185013 | 12.56 (11.11, 14.19) | 19.14 |
| Chang, 2015 | Mixed | 2/55 | 8/2767 | 12.58 (2.67, 59.23) | 6.36 |
| Overall (I-squared = 89.8%, p = 0.000) | | | | 6.95 (4.31, 11.20) | 100.00 |

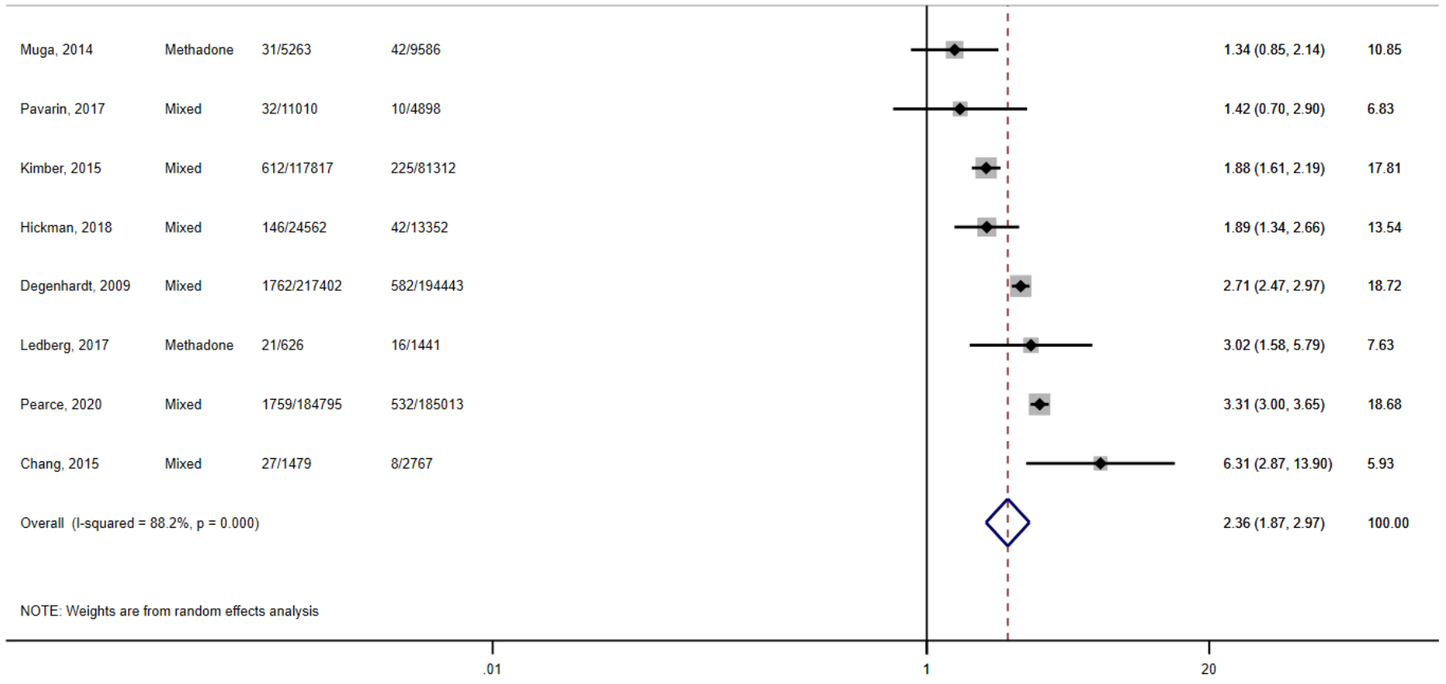
NOTE: Weights are from random effects analysis



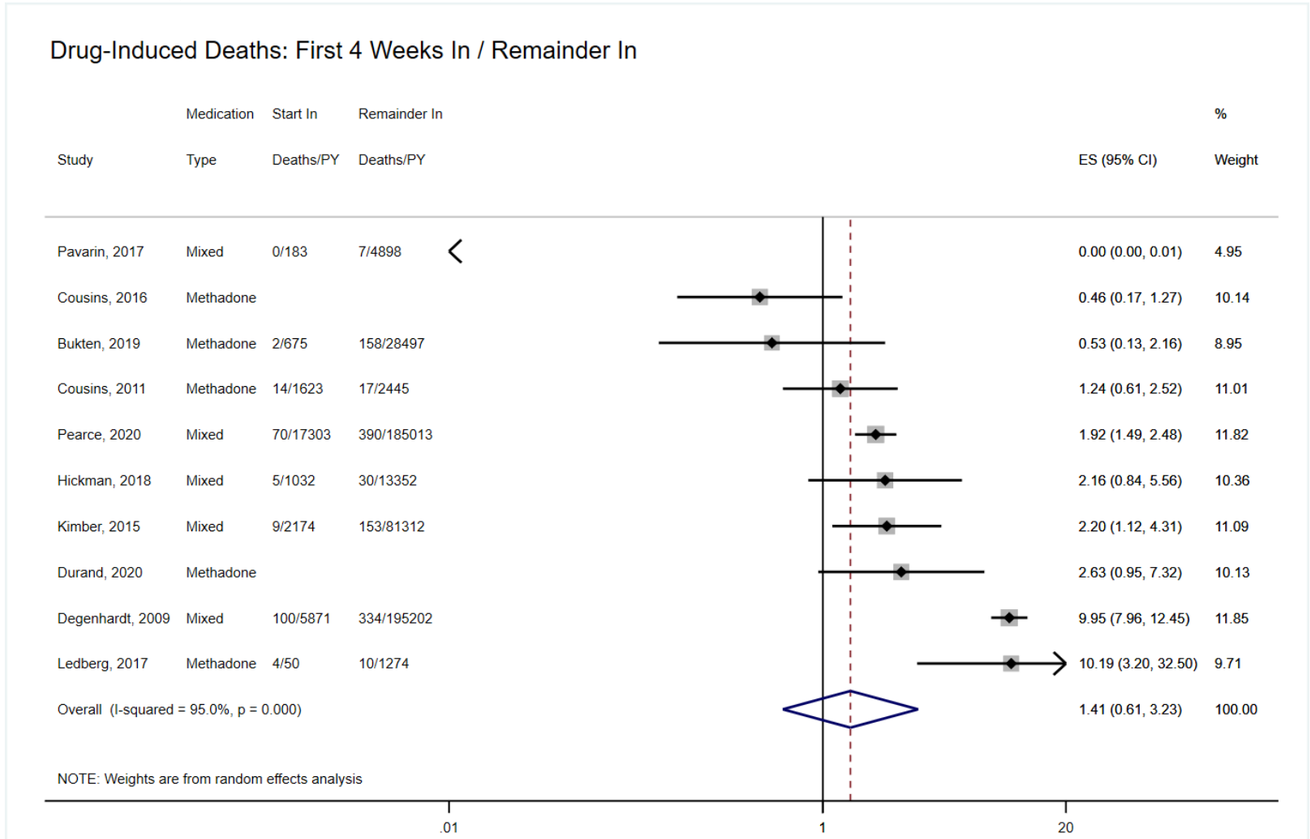
## All Injury & Poisoning Deaths: Remainder Out / Remainder In

| Study | Medication Type | Remainder Out Deaths/PY | Remainder In Deaths/PY | ES (95% CI) | % Weight |
|---|---|---|---|---|---|
| Muga, 2014 | Methadone | 31/5263 | 42/9586 | 1.34 (0.85, 2.14) | 10.85 |
| Pavarin, 2017 | Mixed | 32/11010 | 10/4898 | 1.42 (0.70, 2.90) | 6.83 |
| Kimber, 2015 | Mixed | 612/117817 | 225/81312 | 1.88 (1.61, 2.19) | 17.81 |
| Hickman, 2018 | Mixed | 146/24562 | 42/13352 | 1.89 (1.34, 2.66) | 13.54 |
| Degenhardt, 2009 | Mixed | 1762/217402 | 582/194443 | 2.71 (2.47, 2.97) | 18.72 |
| Ledberg, 2017 | Methadone | 21/626 | 16/1441 | 3.02 (1.58, 5.79) | 7.63 |
| Pearce, 2020 | Mixed | 1759/184795 | 532/185013 | 3.31 (3.00, 3.65) | 18.68 |
| Chang, 2015 | Mixed | 27/1479 | 8/2767 | 6.31 (2.87, 13.90) | 5.93 |
| Overall (I-squared = 88.2%, p = 0.000) | | | | 2.36 (1.87, 2.97) | 100.00 |

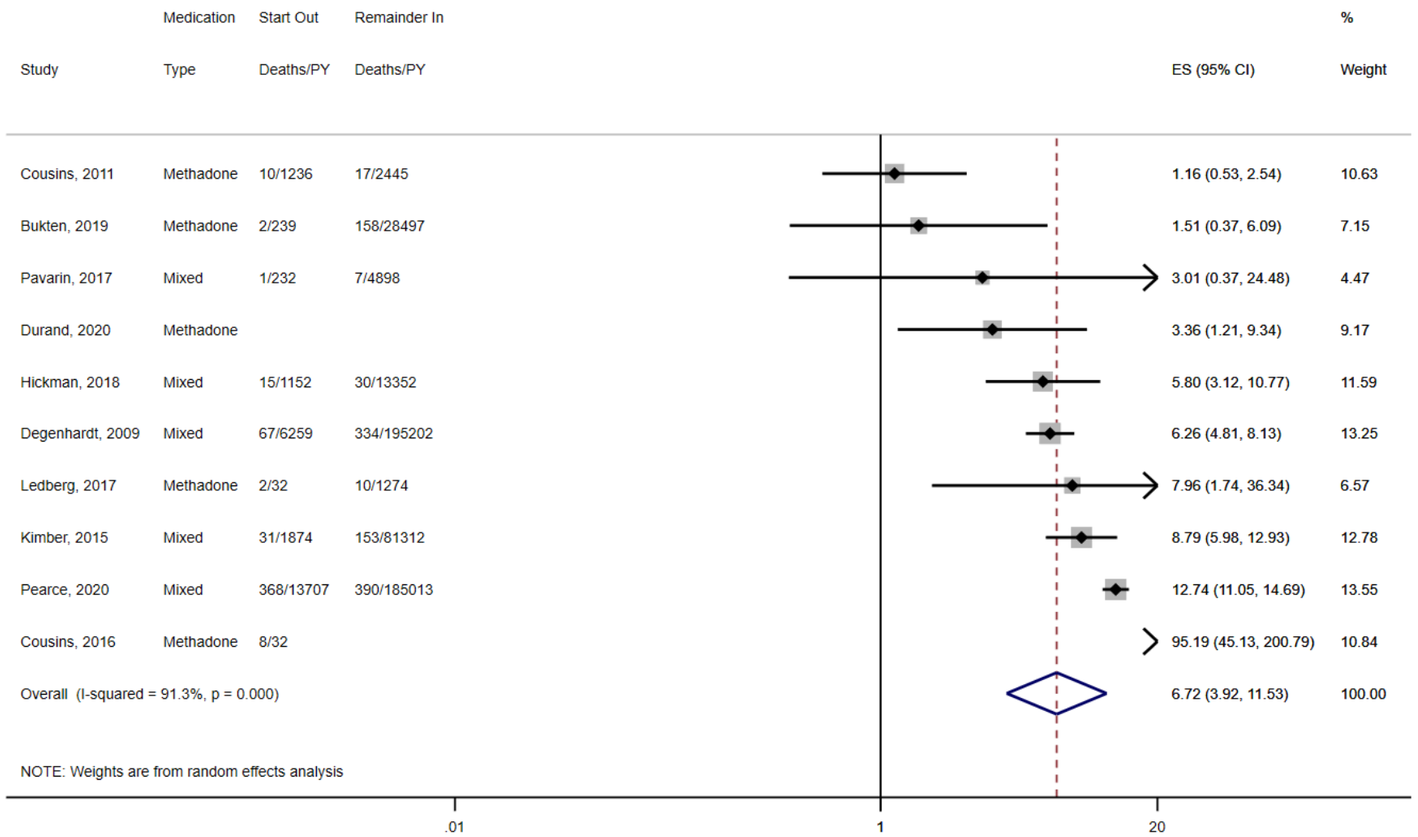
NOTE: Weights are from random effects analysis



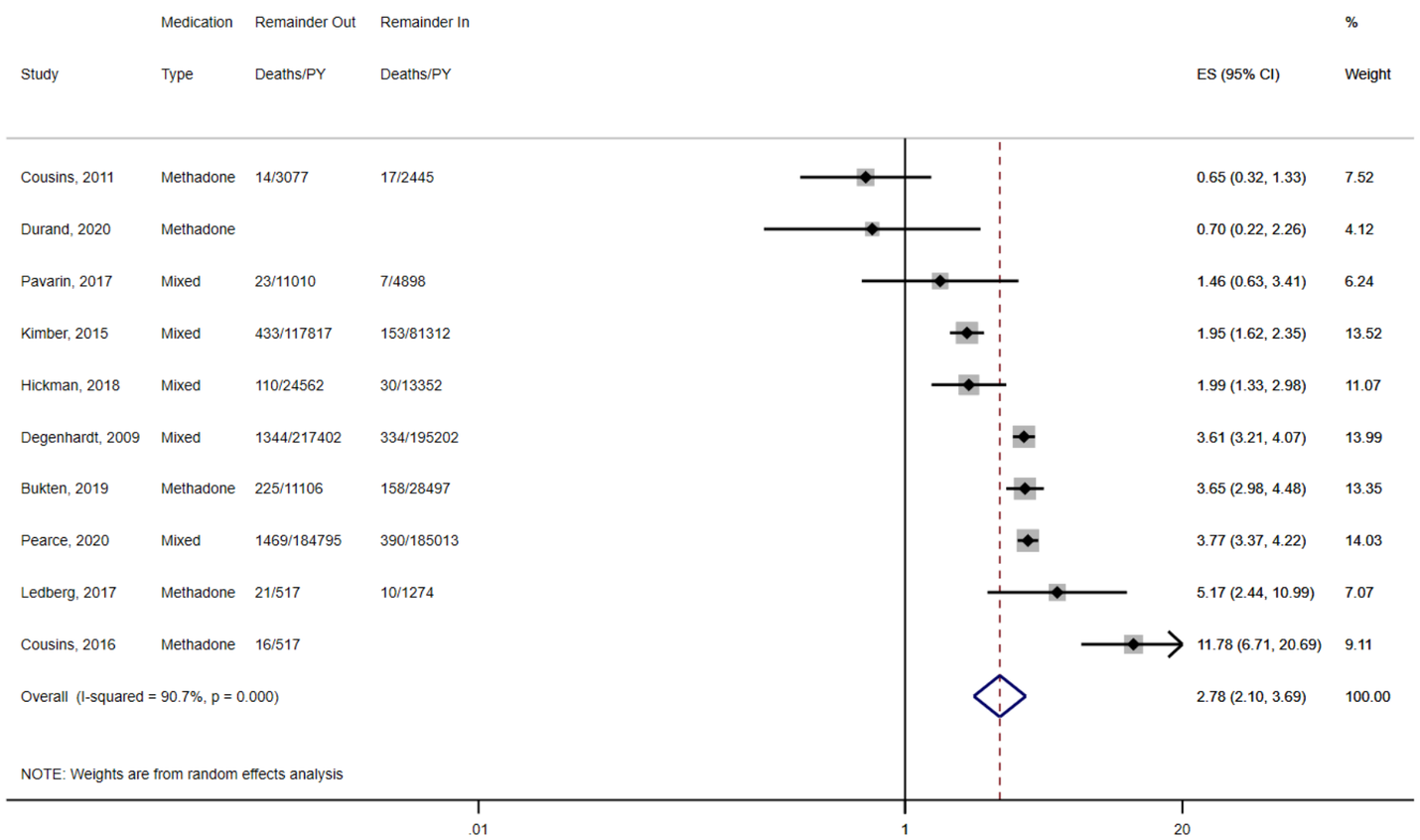
**eFigure 28: Drug-induced mortality according to time period in and out of OAT**



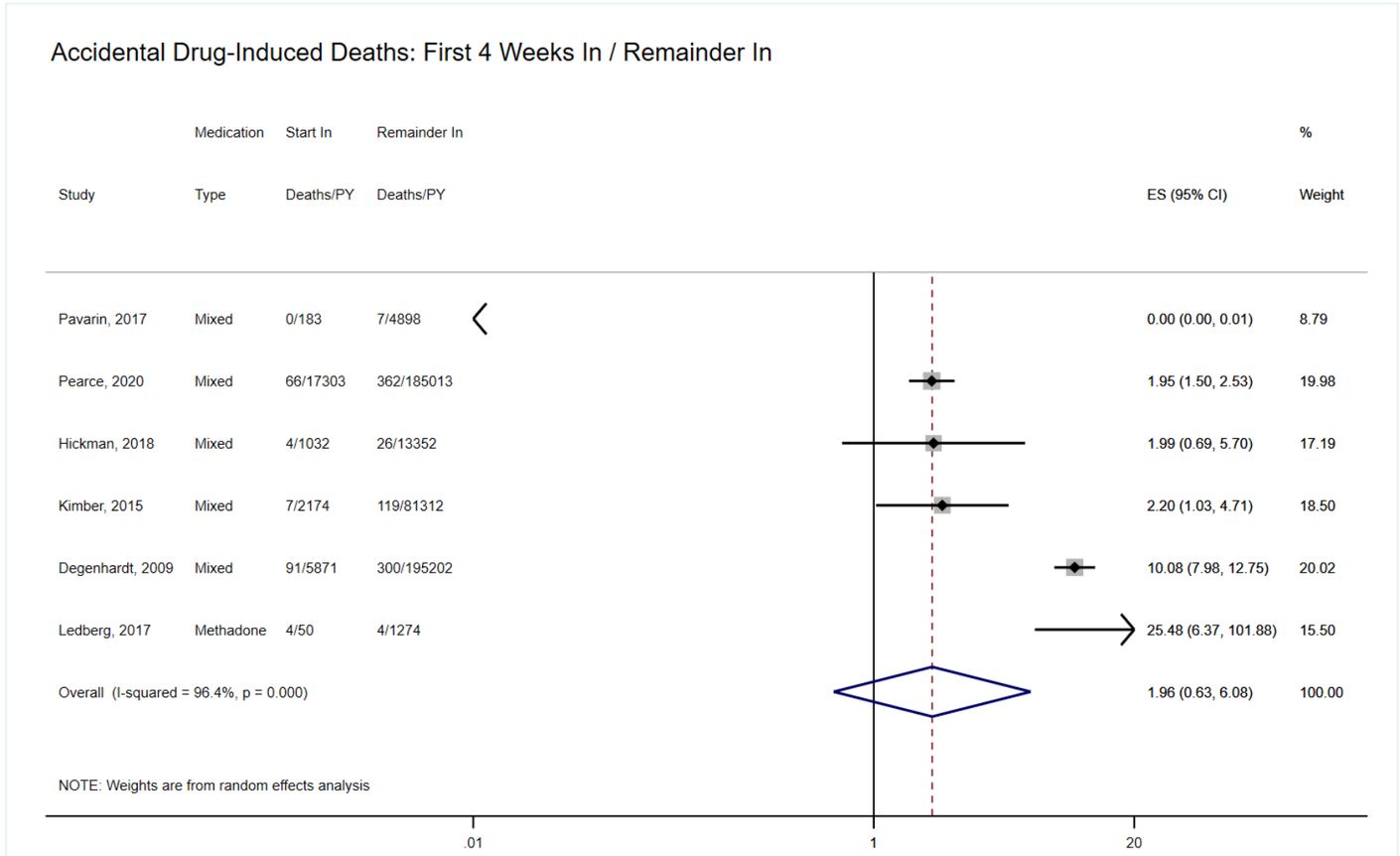
## Drug-Induced Deaths: First 4 Weeks Out / Remainder In



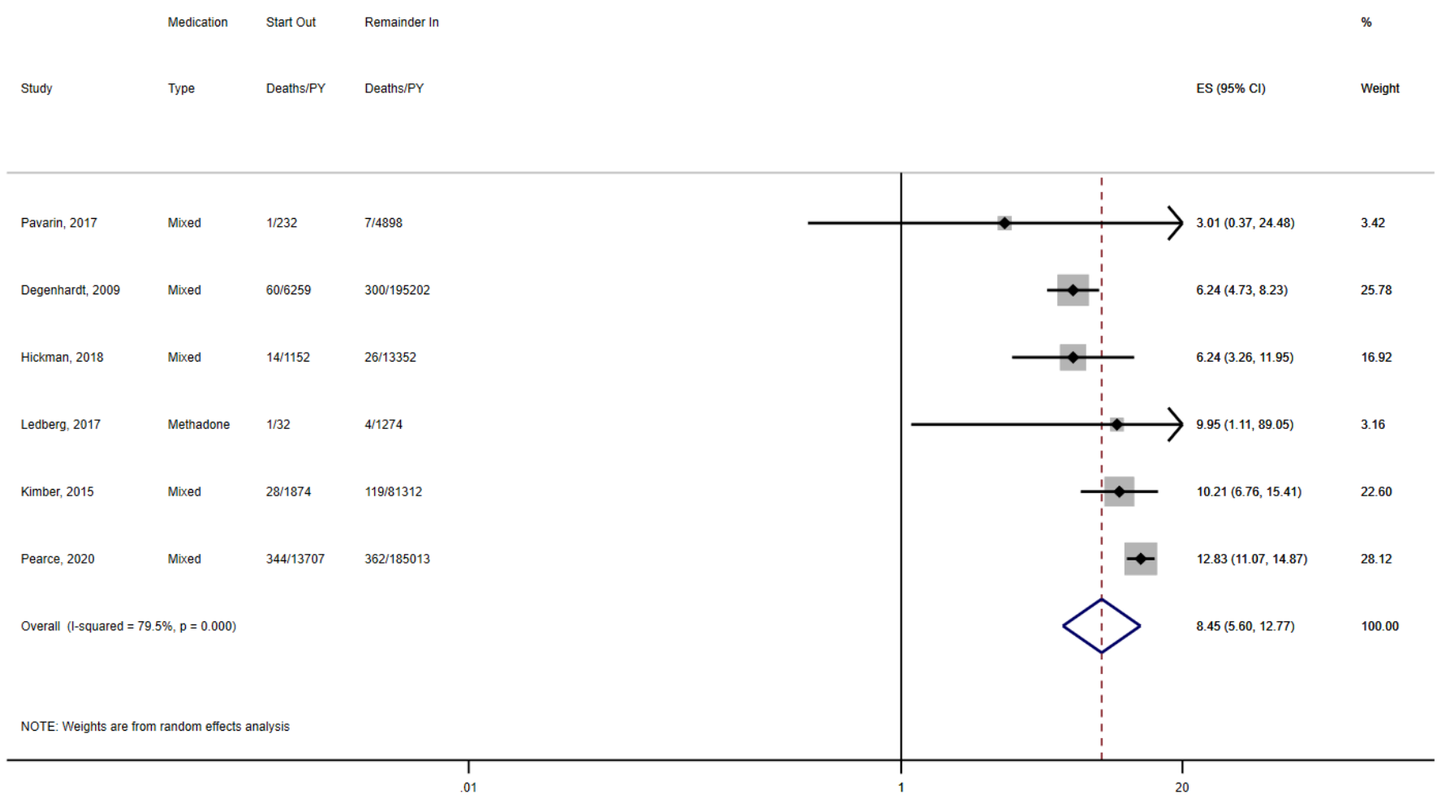
## Drug-Induced Deaths: Remainder Out / Remainder In



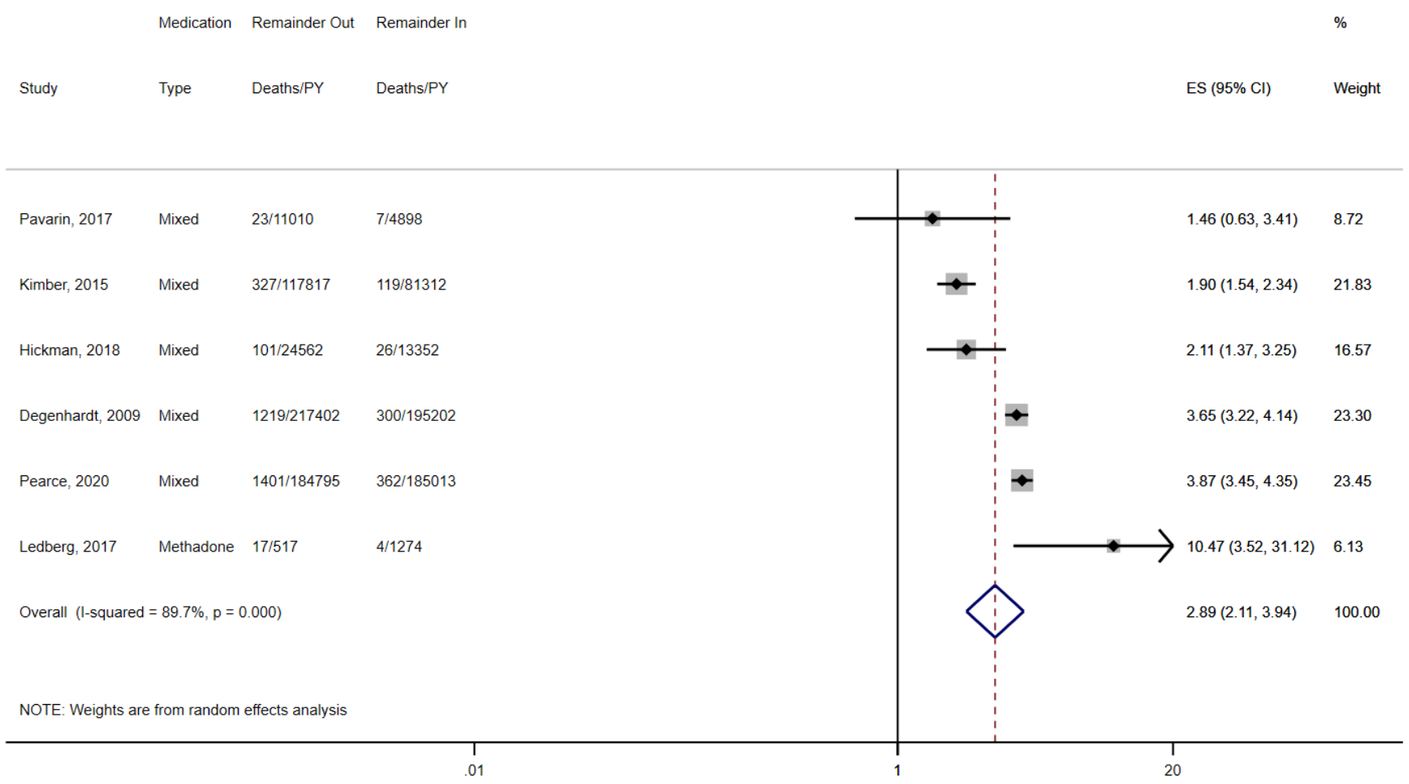
**eFigure 29: Accidental drug-induced mortality according to time period in and out of OAT**



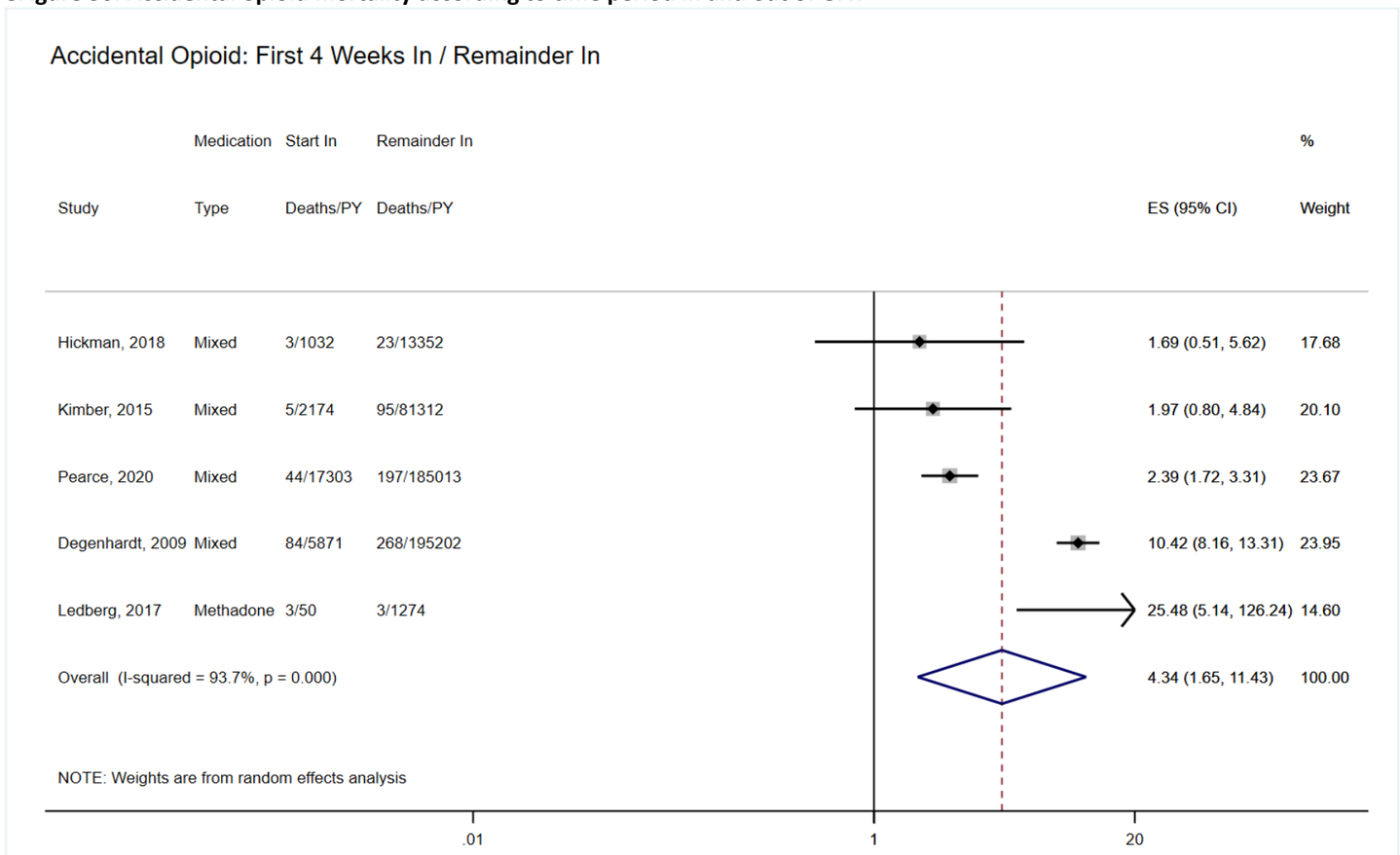
## Accidental Drug-Induced Deaths: First 4 Weeks Out / Remainder In



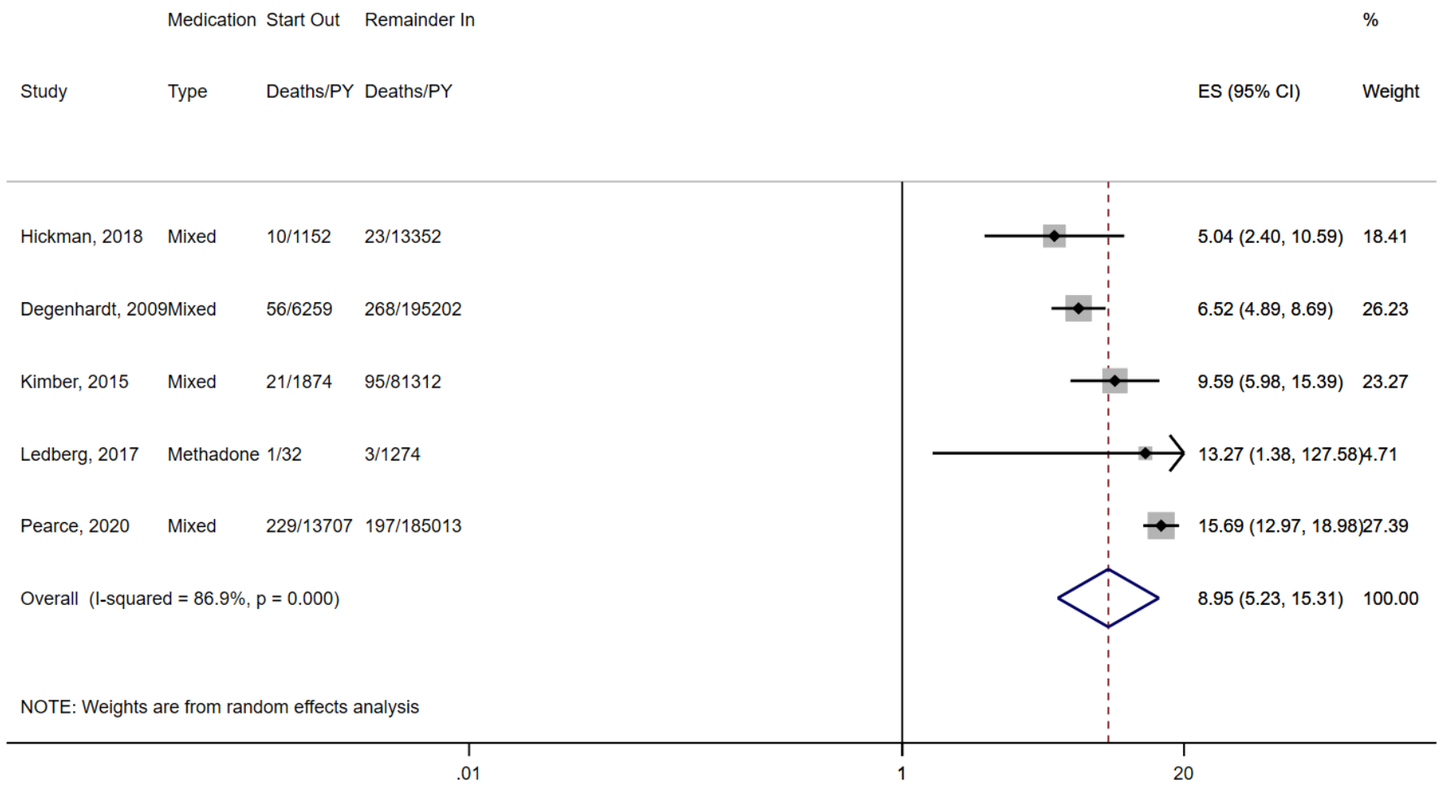
## Accidental Drug-Induced Deaths: Remainder Out / Remainder In



**eFigure 30: Accidental opioid mortality according to time period in and out of OAT**

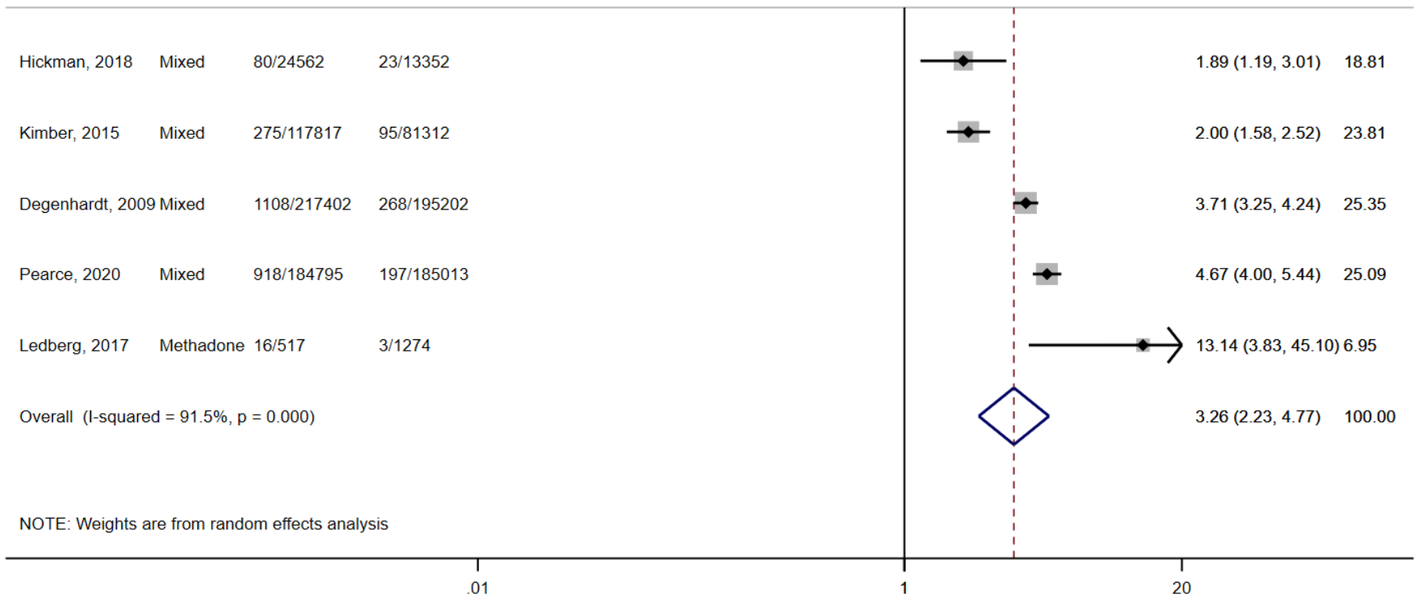


## Accidental Opioid: First 4 Weeks Out / Remainder In

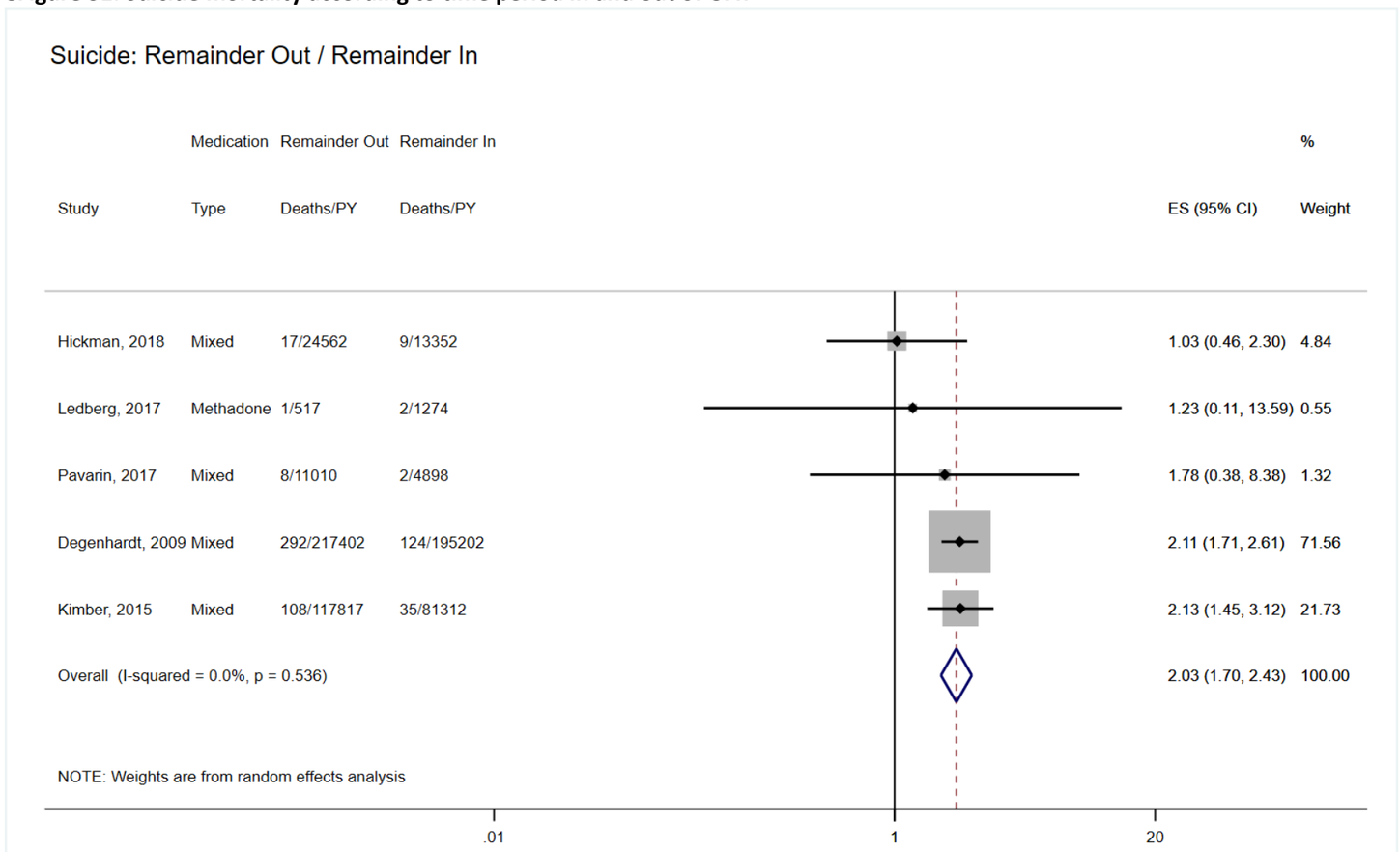


## Accidental Opioid: Remainder Out / Remainder In

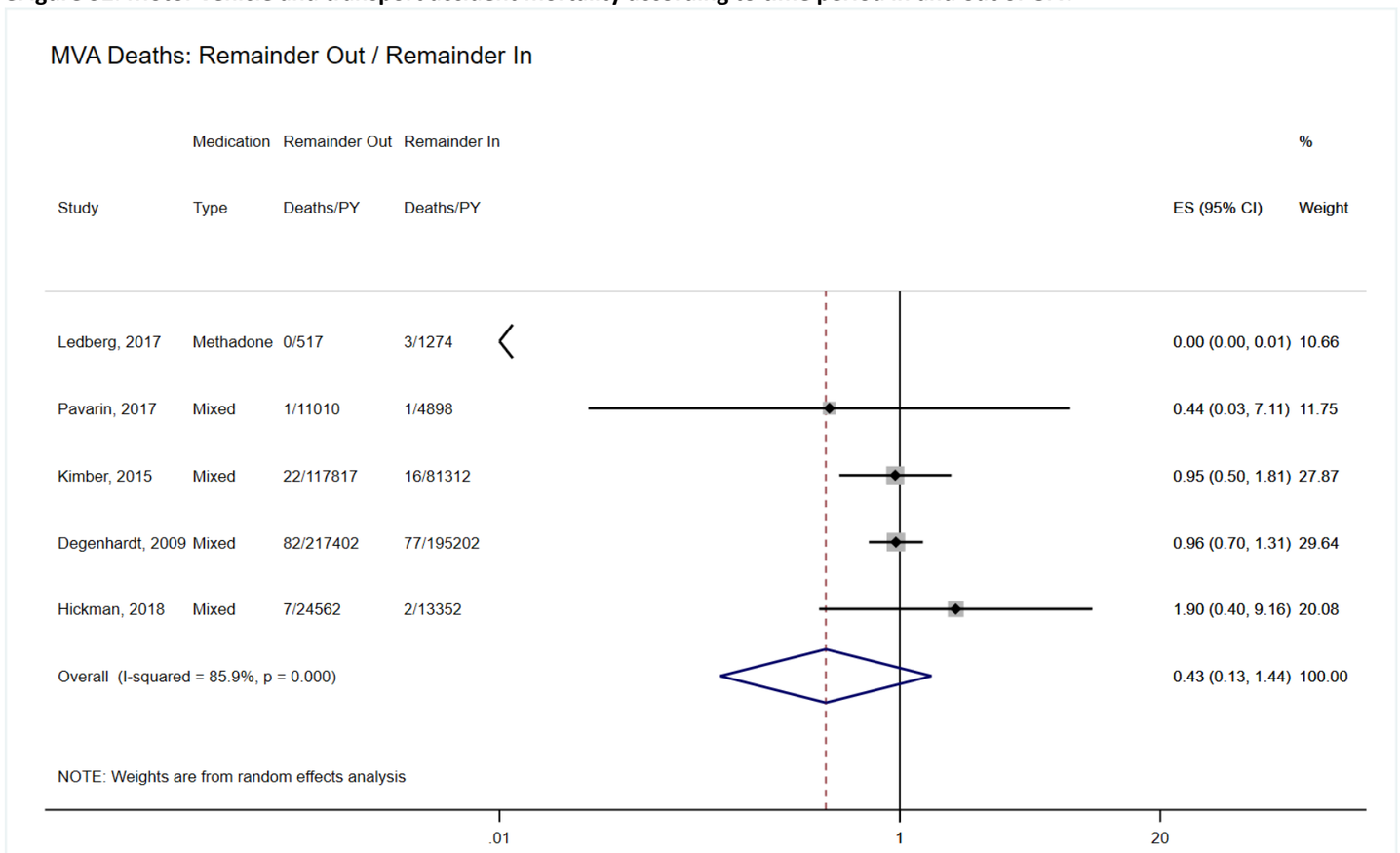
| Study | Medication Type | Remainder Out Deaths/PY | Remainder In Deaths/PY | ES (95% CI) | % Weight |
|---|---|---|---|---|---|
| Hickman, 2018 | Mixed | 80/24562 | 23/13352 | 1.89 (1.19, 3.01) | 18.81 |
| Kimber, 2015 | Mixed | 275/117817 | 95/81312 | 2.00 (1.58, 2.52) | 23.81 |
| Degenhardt, 2009 | Mixed | 1108/217402 | 268/195202 | 3.71 (3.25, 4.24) | 25.35 |
| Pearce, 2020 | Mixed | 918/184795 | 197/185013 | 4.67 (4.00, 5.44) | 25.09 |
| Ledberg, 2017 | Methadone | 16/517 | 3/1274 | 13.14 (3.83, 45.10) | 6.95 |
| Overall (I-squared = 91.5%, p = 0.000) | | | | 3.26 (2.23, 4.77) | 100.00 |



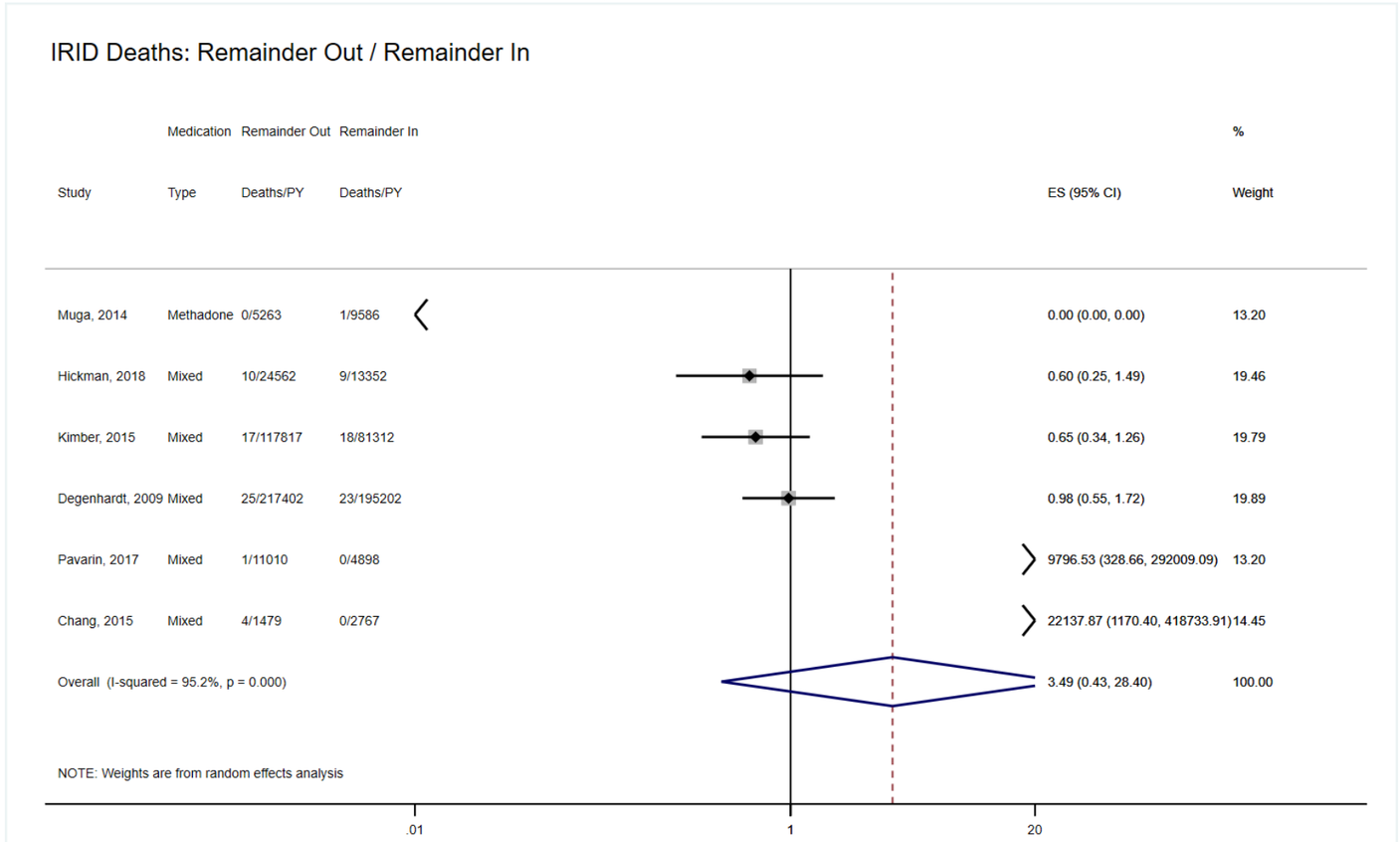
**eFigure 31: Suicide mortality according to time period in and out of OAT**



**eFigure 32: Motor vehicle and transport accident mortality according to time period in and out of OAT**



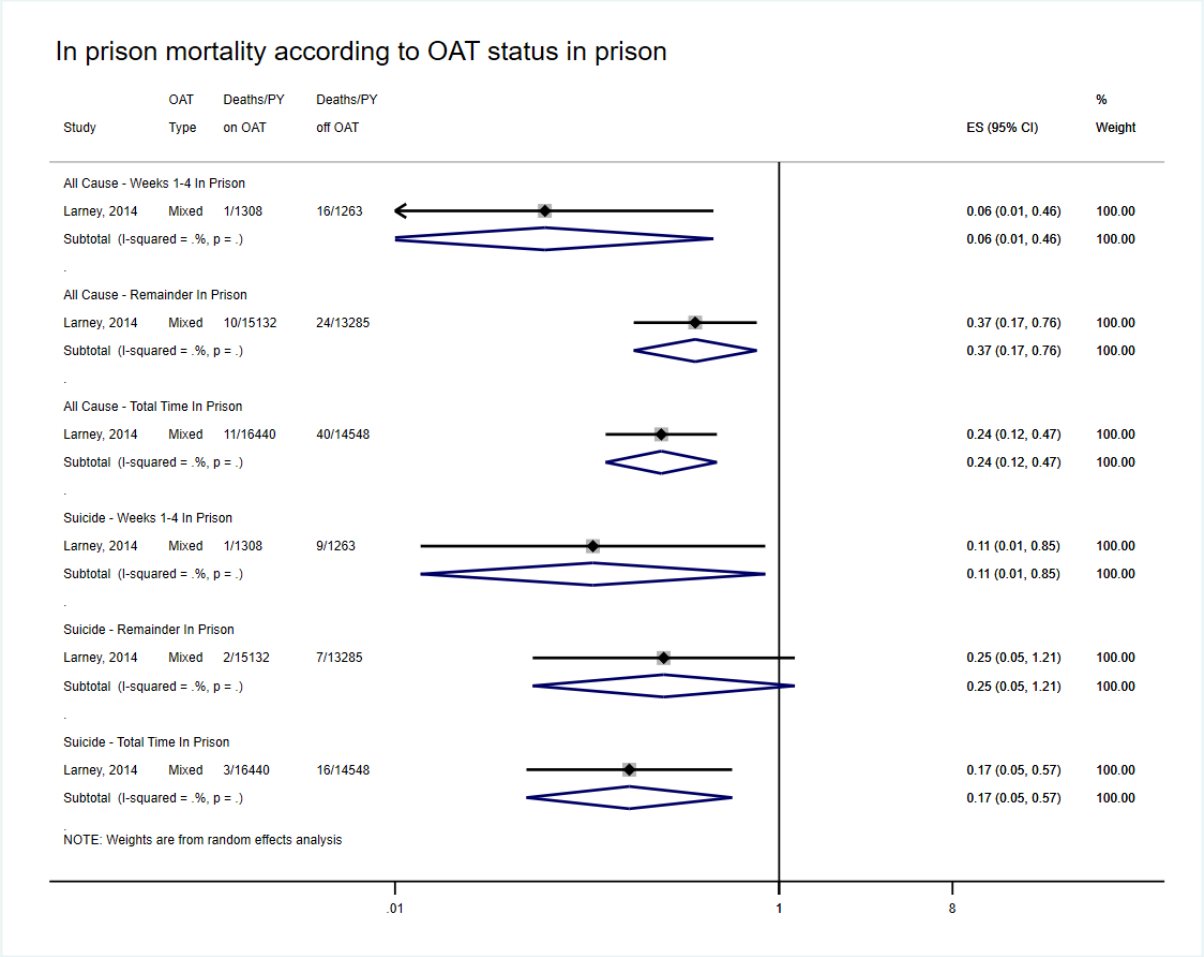
**eFigure 33: Injection-related injury and disease mortality according to time period in and out of OAT**



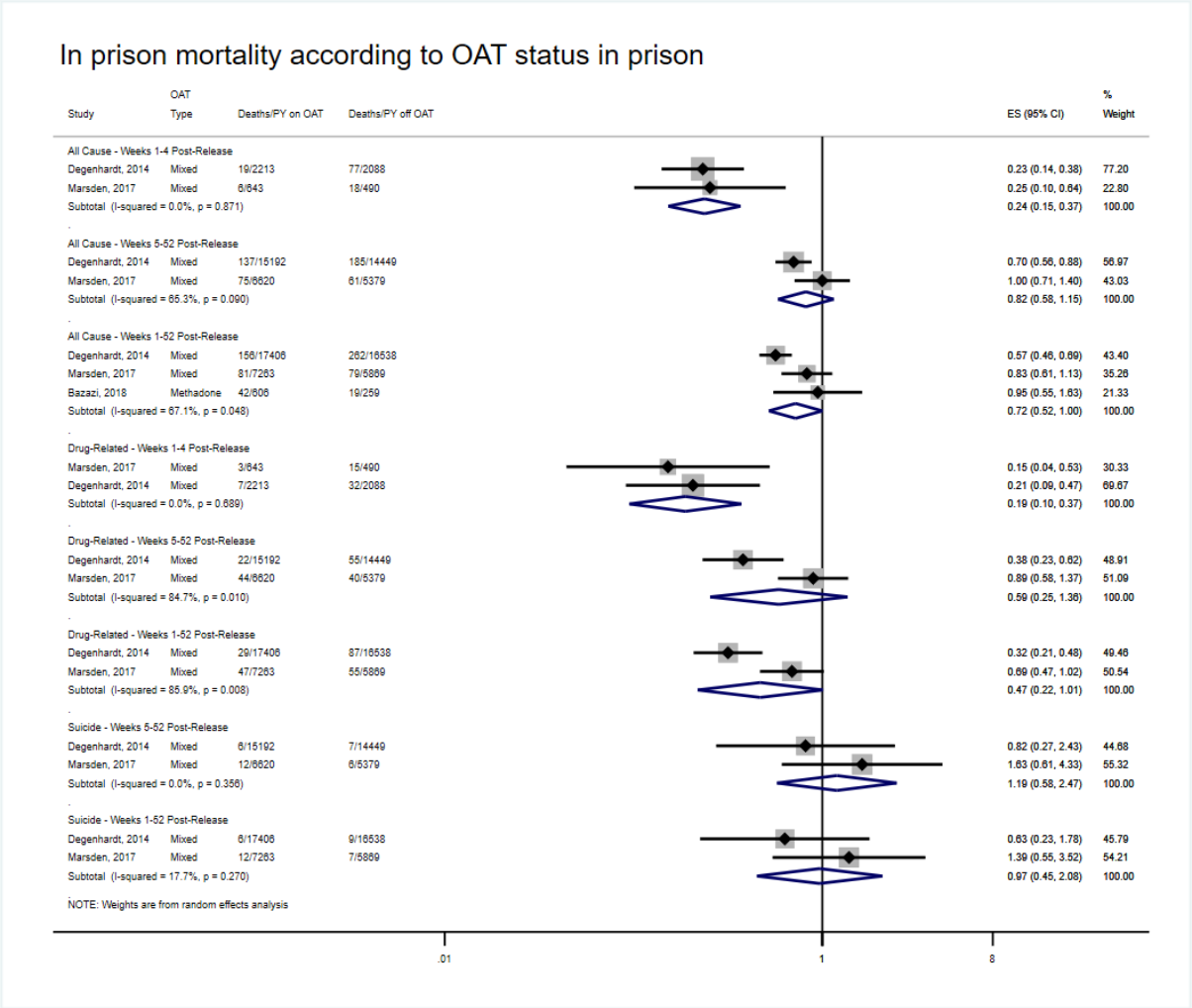
**eTable 19: Pooled all-cause and drug-induced mortality rates in people receiving OAT, by time in and out of treatment (first two weeks in and out of OAT)**

| | | | | In treatment | | | | | | | | Out of treatment | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | First two weeks in | | | | Remainder in | | | | First two weeks out | | | | Remainder out | | | | | | | | |
| | References | N cohorts | N people | Deaths | PY | Pooled CMR per 1,000PY (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR per 1,000PY (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR per 1,000PY(95% CI) | $I^2$ % | Deaths | PY | Pooled CMR per 1,000PY (95%CI) | $I^2$ % | Rate ratio first 4 weeks in/ remainder in | $I^2$ % | Rate ratio first 4 weeks out/remainder in | $I^2$ % | Rate ratio remainder out/ remainder in | $I^2$ % |
| **All-cause** | [6,9-12] | 4 | 89,824 | 147 | 7,434 | 13.43 (5.54, 32.54) | 91.8 | 1,732 | 272,000 | 6.95 (4.40, 10.98) | 98.5 | 94 | 4,223 | 25.98 (15.86, 42.58) | 74.3 | 2,903 | 237,031 | 16.02 (8.32, 30.84) | 99.1 | 1.95 (0.77, 4.94) | 92.1 | 4.12 (2.33, 7.30) | 77.8 | 2.10 (1.97, 2.23) | 0.0 |
| Drug-induced deaths | [9,11,12] | 3 | 20,026 | 18 | 3,673 | 3.75 (1.37, 10.28) | 59.2 | 475 | 66,847 | 3.01 (1.52, 5.95) | 95.6 | 29 | 2,139 | 3.03 (1.02, 8.97) | 41.4 | 384 | 26,227 | 5.77 (1.28, 26.06) | 98.5 | 1.28 (0.38, 4.32) | 69.4 | 0.04 (0.00, 4.85) | 96.4 | 1.98 (0.93, 4.24) | 90.4 |

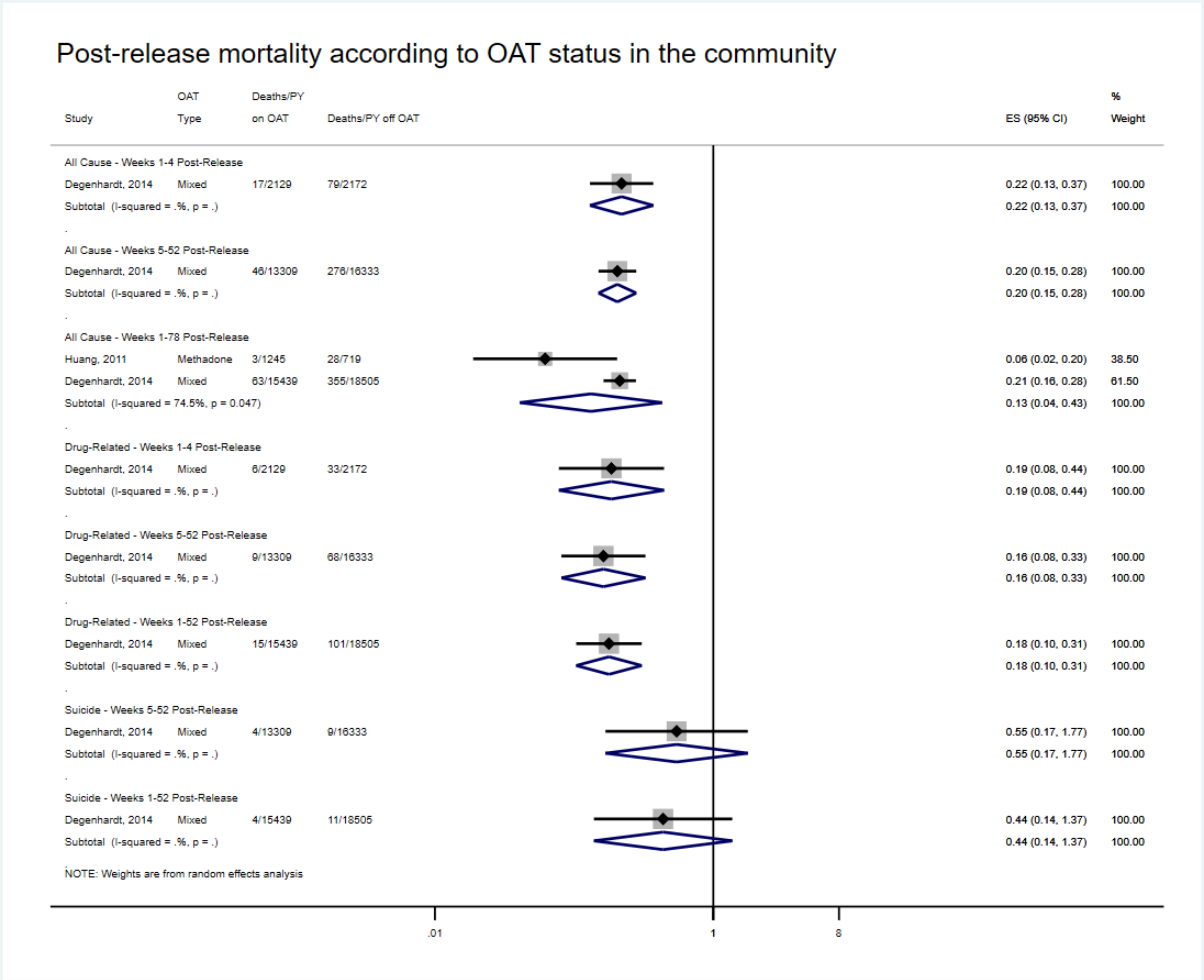
**eFigure 34: All-cause and cause-specific mortality during incarceration according to OAT status, stratified by the first four weeks and remainder of time in incarceration**



**eFigure 35: All-cause and cause-specific mortality post-release according to OAT status in incarceration, stratified by the first four weeks and remainder of time (up to 1 year) post-release from incarceration**



**eFigure 36: All-cause and cause-specific mortality post-release from incarceration according to OAT status post-release, stratified by the first four weeks and remainder of time (up to 18 months) post-release from incarceration**



## eTable 20: Additional pooled cause-specific rates in people receiving OAT, by time during incarceration and post-release from incarceration

| | Refs | N cohorts | N people | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Rate Ratio (in OAT/out of OAT) | $I^2$ % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mortality during incarceration** | | | | **Time spent in OAT during incarceration** | | | | **Time spent out of OAT during incarceration** | | | | **Rate Ratio** | |
| Unnatural causes - First 4 weeks of incarceration | [13] | 1 | 16,715 | 1 | 1,279 | 0.78 (0.11, 5.55) | - | 12 | 1,094 | 10.97 (6.23, 19.32) | - | 0.07 (0.01, 0.55) | - |
| Violence - First 4 weeks of incarceration | [13] | 1 | 16,715 | 0 | 1,279 | - | - | 0 | 1,094 | - | - | - | - |
| Natural causes – First 4 weeks of incarceration | [13] | 1 | 16,715 | 0 | 1,279 | - | - | 2 | 1,094 | 1.83 (0.46, 7.31) | - | * | - |
| Unnatural causes - Remainder of incarceration | [13] | 1 | 16,715 | 4 | 14,098 | 0.28 (0.11, 0.76) | - | 15 | 11.368 | 1.32 (0.80, 2.19) | - | 0.07 (0.02, 0.21) | - |
| Violence - Remainder of incarceration | [13] | 1 | 16,715 | 2 | 14,098 | 0.14 (0.04, 0.57) | - | 0 | 11.368 | - | - | * | - |
| Natural causes - Remainder of incarceration | [13] | 1 | 16,715 | 5 | 14,098 | 0.35 (0.15, 0.85) | - | 4 | 11.368 | 0.35 (0.13, 0.94) | - | 0.00 (0.00, 0.00) | - |
| Unnatural causes - Total incarceration | [13] | 1 | 16,715 | 5 | 15,377 | 0.33 (0.14, 0.78) | - | 27 | 12,462 | 2.17 (1.49, 3.16) | - | 0.15 (0.06, 0.39) | - |
| Violence - Total incarceration | [13] | 1 | 16,715 | 2 | 15,377 | 0.13 (0.03, 0.52) | - | 0 | 12,462 | - | - | * | - |
| Natural causes – Total incarceration | [13] | 1 | 16,715 | 5 | 15,377 | 0.33 (0.14, 0.78) | - | 6 | 12,462 | 0.48 (0.22, 1.07) | - | 0.68 (0.21, 2.21) | - |
| **Mortality post-release from incarceration** | | | | **Left incarceration on OAT** | | | | **Left incarceration not on OAT** | | | | **Rate Ratio** | |
| All injury and poisoning - First 4 weeks post-release | [14] | 1 | 16,453 | 11 | 2,213 | 4.97 (2.75, 8.97) | - | 37 | 2,088 | 17.72 (12.84, 24.46) | - | 0.28 (0.14, 0.55) | - |
| Accidental drug-induced - First 4 weeks post-release | [14] | 1 | 16,453 | 7 | 2,213 | 3.16 (1.51, 6.64) | - | 31 | 2,088 | 14.85 (10.44, 21.11) | - | 0.21 (0.09, 0.48) | - |
| Accidental opioid - First 4 weeks post-release | [14] | 1 | 16,453 | 7 | 2,213 | 3.16 (1.51, 6.63) | - | 31 | 2,088 | 14.85 (10.44, 21.11) | - | 0.21 (0.09, 0.48) | - |
| Violence - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,213 | - | - | 0 | 2,088 | - | - | - | - |
| Motor vehicle and transport accidents - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,213 | 0.45 (0.06, 3.21) | - | 1 | 2,088 | 0.48 (0.07, 3.40) | - | 0.94 (0.06, 15.08) | - |
| Falls, fires, burns & drownings - First 4 weeks post-release | [14] | 1 | 16,453 | 2 | 2,213 | 0.90 (0.23, 3.61) | - | 1 | 2,088 | 0.48 (0.07, 3.40) | - | 1.89 (0.17, 20.81) | - |
| All liver-related - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,213 | 0.45 (0.06, 3.21) | - | 1 | 2,088 | 0.48 (0.07, 3.40) | - | 0.94 (0.06, 15.08) | - |
| Viral hepatitis - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,213 | 0.45 (0.06, 3.21) | - | 1 | 2,088 | 0.48 (0.07, 3.40) | - | 0.94 (0.06, 15.08) | - |
| All alcohol related - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,213 | 0.45 (0.06, 3.21) | - | 1 | 2,088 | 0.48 (0.07, 3.40) | - | 0.94 (0.06, 15.08) | - |
| Cancer - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,213 | 0.45 (0.06, 3.21) | - | 0 | 2,088 | - | - | * | - |
| Cardiovascular disease - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,213 | - | - | 0 | 2,088 | - | - | - | - |
| Chronic respiratory disease - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,213 | - | - | 0 | 2,088 | - | - | - | - |

| | Refs | N cohorts | N people | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Rate Ratio (in OAT/out of OAT) | $I^2$ % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Digestive disorders - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,213 | - | - | 0 | 2,088 | - | - | - | - |
| HIV-related - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,213 | 0.45 (0.06, 3.21) | - | 1 | 2,088 | 0.48 (0.07, 3.40) | - | 0.94 (0.06, 15.08) | - |
| Influenza & pneumonia - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,213 | - | - | 0 | 2,088 | - | - | - | - |
| Injection related injuries and diseases - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,213 | - | - | 0 | 2,088 | - | - | - | - |
| Endocarditis - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,213 | - | - | 0 | 2,088 | - | - | - | - |
| Bacteraemia and sepsis - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,213 | - | - | 0 | 2,088 | - | - | - | - |
| Skin or soft tissue infections - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,213 | - | - | 0 | 2,088 | - | - | | - |
| All injury and poisoning - Remainder post-release | [14] | 1 | 16,453 | 38 | 15,192 | 2.50 (1.82, 3.44) | - | 76 | 14,449 | 5.26 (4.20, 6.59) | - | 0.48 (0.32, 0.70) | - |
| Accidental drug-induced - Remainder post-release | [14] | 1 | 16,453 | 19 | 15,192 | 1.25 (0.80, 1.96) | - | 53 | 14,449 | 3.67 (2.80, 4.80) | - | 0.34 (0.20, 0.58) | - |
| Accidental opioid - Remainder post-release | [14] | 1 | 16,453 | 16 | 15,192 | 1.05 (0.65, 1.72) | - | 43 | 14,449 | 2.98 (2.21, 4.01) | - | 0.35 (0.20, 0.63) | - |
| Violence - Remainder post-release | [14] | 1 | 16,453 | 5 | 15,192 | 0.33 (0.14, 0.79) | - | 4 | 14,449 | 0.28 (0.10, 0.74) | - | 1.19 (0.32, 4.43) | - |
| Motor vehicle and transport accidents - Remainder post-release | [14] | 1 | 16,453 | 5 | 15,192 | 0.33 (0.14, 0.79) | - | 5 | 14,449 | 0.34 (0.14, 0.83) | - | 0.95 (0.28, 3.29) | - |
| Falls, fires, burns & drownings - Remainder post-release | [14] | 1 | 16,453 | 0 | | - | - | 2 | 14,449 | 0.14 (0.03, 0.55) | - | * | - |
| All liver-related - Remainder post-release | [14] | 1 | 16,453 | 3 | 15,192 | 0.20 (0.06, 0.61) | - | 2 | 14,449 | 0.14 (0.03, 0.55) | - | 1.43 (0.24, 8.54) | - |
| Viral hepatitis - Remainder post-release | [14] | 1 | 16,453 | 1 | 15,192 | 0.07 (0.01, 0.47) | - | 0 | | - | - | * | - |
| All alcohol related - Remainder post-release | [14] | 1 | 16,453 | 1 | 15,192 | 0.07 (0.01, 0.47) | - | 1 | 14,449 | 0.07 (0.01, 0.49) | - | 0.95 (0.06, 15.21) | - |
| Cancer - Remainder post-release | [14] | 1 | 16,453 | 7 | 15,192 | 0.46 (0.22, 0.97) | - | 5 | 14,449 | 0.35 (0.14, 0.83) | - | 1.33 (0.42, 4.20) | - |
| Cardiovascular disease - Remainder post-release | [14] | 1 | 16,453 | 5 | 15,192 | 0.33 (0.14, 0.79) | - | 4 | 14,449 | 0.28 (0.10, 0.74) | - | 1.19 (0.32, 4.43) | - |
| Chronic respiratory disease - Remainder post-release | [14] | 1 | 16,453 | 1 | 15,192 | 0.07 (0.01, 0.47) | - | 1 | 14,449 | 0.07 (0.01, 0.49) | - | 0.95 (0.06, 15.21) | - |
| Digestive disorders - Remainder post-release | [14] | 1 | 16,453 | 1 | 15,192 | 0.07 (0.01, 0.47) | - | 1 | 14,449 | 0.07 (0.01, 0.49) | - | 0.95 (0.06, 15.21) | - |
| HIV-related - Remainder post-release | [14] | 1 | 16,453 | 1 | 15,192 | 0.07 (0.01, 0.47) | - | 0 | | - | - | * | - |
| Influenza & pneumonia - Remainder post-release | [14] | 1 | 16,453 | 0 | | - | - | 1 | 14,449 | 0.07 (0.01, 0.49) | - | 0.00 (0.00, 0.00) | - |

| | Refs | N cohorts | N people | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Rate Ratio (in OAT/out of OAT) | $I^2$ % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Injection related injuries and diseases - Remainder post-release | [14] | 1 | 16,453 | 2 | 15,192 | 0.13 (0.03, 0.53) | - | 2 | 14,449 | 0.14 (0.03, 0.55) | - | 0.95 (0.13, 6.75) | - |
| Endocarditis - Remainder post-release | [14] | 1 | 16,453 | 2 | 15,192 | 0.13 (0.03, 0.53) | - | 2 | 14,449 | 0.14 (0.03, 0.55) | - | 0.95 (0.13, 6.75) | - |
| Bacteraemia and sepsis - Remainder post-release | [14] | 1 | 16,453 | 0 | | - | - | 0 | | - | - | - | - |
| Skin or soft tissue infections - Remainder post-release | [14] | 1 | 16,453 | 0 | | - | - | 0 | | - | - | - | - |
| All injury and poisoning – Total-time post-release | [14] | 1 | 16,453 | 49 | 17,406 | 2.82 (2.12, 3.72) | - | 113 | 16,538 | 6.83 (5.68, 8.22) | - | 0.41 (0.29, 0.58) | - |
| Accidental drug-induced - Total-time post-release | [14] | 1 | 16,453 | 26 | 17,406 | 1.49 (1.02, 2.19) | - | 84 | 16,538 | 5.08 (4.10, 6.29) | - | 0.29 (0.19, 0.46) | - |
| Accidental opioid - Total-time post-release | [14] | 1 | 16,453 | 23 | 17,406 | 1.32 (0.88, 1.99) | - | 74 | 16,538 | 4.47 (3.56, 5.62) | - | 0.30 (0.18, 0.47) | - |
| Violence - Total-time post-release | [14] | 1 | 16,453 | 5 | 17,406 | 0.29 (0.12, 0.69) | - | 4 | 16,538 | 0.24 (0.09, 0.64) | - | 1.19 (0.32, 4.42) | - |
| Motor vehicle and transport accidents - Total-time post-release | [14] | 1 | 16,453 | 6 | 17,406 | 0.34 (0.15, 0.77) | - | 6 | 16,538 | 0.36 (0.16, 0.81) | - | 0.95 (0.31, 2.95) | - |
| Falls, fires, burns & drownings - Total-time post-release | [14] | 1 | 16,453 | 2 | 17,406 | 0.11 (0.03, 0.46) | - | 3 | 16,538 | 0.18 (0.06, 0.56) | - | 0.63 (0.11, 3.79) | - |
| All liver-related - Total-time post-release | [14] | 1 | 16,453 | 4 | 17,406 | 0.23 (0.09, 0.61) | - | 3 | 16,538 | 0.18 (0.06, 0.56) | - | 1.27 (0.28, 5.66) | - |
| Viral hepatitis - Total-time post-release | [14] | 1 | 16,453 | 2 | 17,406 | 0.11 (0.03, 0.46) | - | 1 | 16,538 | 0.06 (0.01, 0.43) | - | 1.90 (0.17, 20.96) | - |
| All alcohol related - Total-time post-release | [14] | 1 | 16,453 | 2 | 17,406 | 0.11 (0.03, 0.46) | - | 2 | 16,538 | 0.12 (0.03, 0.48) | - | 0.95 (0.13, 6.74) | - |
| Cancer - Total-time post-release | [14] | 1 | 16,453 | 8 | 17,406 | 0.46 (0.23, 0.92) | - | 5 | 16,538 | 0.30 (0.13, 0.73) | - | 1.52 (0.50, 4.65) | - |
| Cardiovascular disease - Total-time post-release | [14] | 1 | 16,453 | 5 | 17,406 | 0.29 (0.12, 0.69) | - | 4 | 16,538 | 0.24 (0.09, 0.64) | - | 1.19 (0.32, 4.42) | - |
| Chronic respiratory disease - Total-time post-release | [14] | 1 | 16,453 | 1 | 17,406 | 0.06 (0.01, 0.41) | - | 1 | 16,538 | 0.06 (0.01, 0.43) | - | 0.95 (0.06, 15.19) | - |
| Digestive disorders - Total-time post-release | [14] | 1 | 16,453 | 1 | 17,406 | 0.06 (0.01, 0.41) | - | 1 | 16,538 | 0.06 (0.01, 0.43) | - | 0.95 (0.06, 15.19) | - |
| HIV-related - Total-time post-release | [14] | 1 | 16,453 | 2 | 17,406 | 0.11 (0.03, 0.46) | - | 1 | 16,538 | 0.06 (0.01, 0.43) | - | 1.90 (0.17, 20.96) | - |
| Influenza & pneumonia - Total-time post-release | [14] | 1 | 16,453 | 0 | 17,406 | - | - | 1 | 16,538 | 0.06 (0.01, 0.43) | - | * | - |

| | Refs | N cohorts | N people | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Rate Ratio (in OAT/out of OAT) | $I^2$ % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Injection related injuries and diseases - Total-time post-release | [14] | 1 | 16,453 | 2 | 17,406 | 0.11 (0.03, 0.46) | - | 2 | 16,538 | 0.12 (0.03, 0.48) | - | 0.95 (0.13, 6.74) | - |
| Endocarditis - Total-time post-release | [14] | 1 | 16,453 | 2 | 17,406 | 0.11 (0.03, 0.46) | - | 2 | 16,538 | 0.12 (0.03, 0.48) | - | 0.95 (0.13, 6.74) | - |
| Bacteraemia and sepsis - Total-time post-release | [14] | 1 | 16,453 | 0 | 17,406 | - | - | 0 | 16,538 | - | - | - | - |
| Skin or soft tissue infections - Total-time post-release | [14] | 1 | 16,453 | 0 | 17,406 | - | - | 0 | 16,538 | - | - | - | - |
| **Mortality post-release from incarceration** | | | | **Time spent in OAT post-release** | | | | **Time spent out of OAT post-release** | | | | **Rate Ratio** | |
| All injury and poisoning - First 4 weeks post-release | [14] | 1 | 16,453 | 9 | 2,129 | 4.23 (2.19, 8.12) | - | 39 | 2,172 | 17.96 (13.11, 24.58) | - | 0.24 (0.11, 0.49) | - |
| Accidental drug-induced - First 4 weeks post-release | [14] | 1 | 16,453 | 6 | 2,129 | 2.82 (1.27, 6.27) | - | 32 | 2,172 | 14.73 (10.42, 20.83) | - | 0.19 (0.08, 0.46) | - |
| Accidental opioid - First 4 weeks post-release | [14] | 1 | 16,453 | 6 | 2,129 | 2.82 (1.27, 6.27) | - | 32 | 2,172 | 14.73 (10.42, 20.83) | - | 0.19 (0.08, 0.46) | - |
| Violence - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 0 | 2,172 | - | - | - | - |
| Motor vehicle and transport accidents - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,129 | 0.47 (0.07, 3.33) | - | 1 | 2,172 | 0.46 (0.06, 3.27) | - | 1.02 (0.06, 16.31) | - |
| Falls, fires, burns & drownings - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,129 | 0.47 (0.07, 3.33) | - | 2 | 2,172 | 0.92 (0.23, 3.68) | - | 0.51 (0.05, 5.63) | - |
| All liver-related - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 2 | 2,172 | 0.92 (0.23, 3.68) | - | * | - |
| Viral hepatitis - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 2 | 2,172 | 0.92 (0.23, 3.68) | - | * | - |
| All alcohol related - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,129 | 0.47 (0.07, 3.33) | - | 1 | 2,172 | 0.46 (0.06, 3.27) | - | 1.02 (0.06, 16.31) | - |
| Cancer - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,129 | 0.47 (0.07, 3.33) | - | 0 | 2,172 | - | - | * | - |
| Cardiovascular disease - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 0 | 2,172 | - | - | - | - |
| Chronic respiratory disease - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 0 | 2,172 | - | - | - | - |
| Digestive disorders - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 0 | 2,172 | - | - | - | - |
| HIV-related - First 4 weeks post-release | [14] | 1 | 16,453 | 1 | 2,129 | 0.47 (0.06, 3.33) | - | 1 | 2,172 | 0.46 (0.06, 3.27) | - | 1.02 (0.06, 16.31) | - |
| Influenza & pneumonia - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 0 | 2,172 | - | - | - | - |
| Injection related injuries and diseases - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 0 | 2,172 | - | - | - | - |
| Endocarditis - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 0 | 2,172 | - | - | - | - |
| Bacteraemia and sepsis - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 0 | 2,172 | - | - | - | - |
| Skin or soft tissue infections - First 4 weeks post-release | [14] | 1 | 16,453 | 0 | 2,129 | - | - | 0 | 2,172 | - | - | - | - |
| All injury and poisoning - Remainder post-release | [14] | 1 | 16,453 | 19 | 13,309 | 1.43 (0.91, 2.24) | - | 95 | 16,333 | 5.82 (4.76, 7.11) | - | 0.25 (0.15, 0.40) | - |

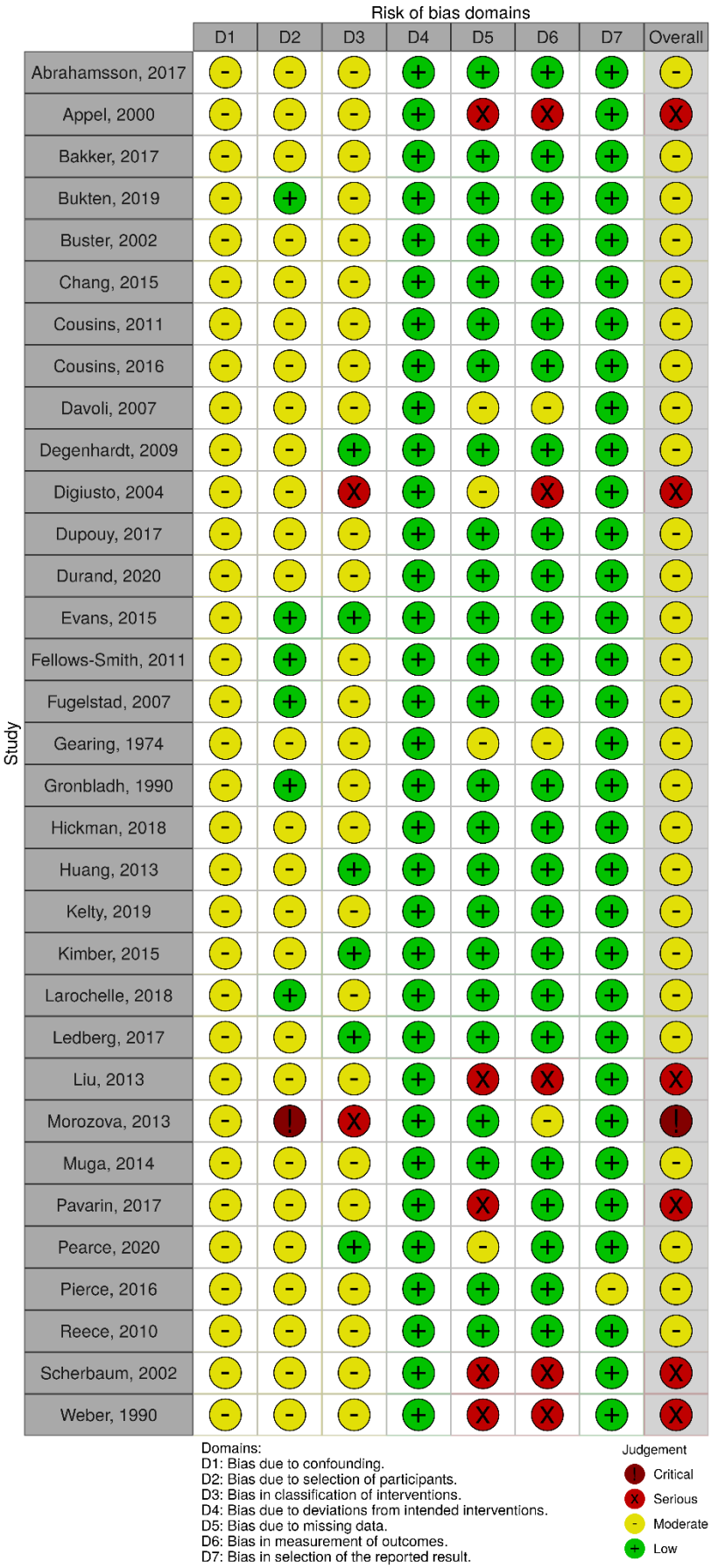
| | Refs | N cohorts | N people | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Rate Ratio (in OAT/out of OAT) | $I^2$ % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Accidental drug-induced - Remainder post-release | [14] | 1 | 16,453 | 7 | 13,309 | 0.53 (0.25, 1.10) | - | 65 | 16,333 | 3.98 (3.12, 5.08) | - | 0.13 (0.06, 0.29) | - |
| Accidental opioid - Remainder post-release | [14] | 1 | 16,453 | 6 | 13,309 | 0.45 (0.20, 1.00) | - | 53 | 16,333 | 3.25 (2.48, 4.25) | - | 0.14 (0.06, 0.32) | - |
| Violence - Remainder post-release | [14] | 1 | 16,453 | 3 | 13,309 | 0.23 (0.07, 0.70) | - | 6 | 16,333 | 0.37 (0.17, 0.82) | - | 0.61 (0.15, 2.45) | - |
| Motor vehicle and transport accidents - Remainder post-release | [14] | 1 | 16,453 | 3 | 13,309 | 0.23 (0.07, 0.70) | - | 7 | 16,333 | 0.43 (0.20, 0.90) | - | 0.53 (0.14, 2.03) | - |
| Falls, fires, burns & drownings - Remainder post-release | [14] | 1 | 16,453 | 0 | 13,309 | - | - | 2 | 16,333 | 0.12 (0.03, 0.49) | - | * | - |
| All liver-related - Remainder post-release | [14] | 1 | 16,453 | 0 | 13,309 | - | - | 5 | 16,333 | 0.31 (0.13, 0.74) | - | * | - |
| Viral hepatitis - Remainder post-release | [14] | 1 | 16,453 | 0 | 13,309 | - | - | 1 | 16,333 | 0.06 (0.01, 0.43) | - | * | - |
| All alcohol related - Remainder post-release | [14] | 1 | 16,453 | 0 | 13,309 | - | - | 2 | 16,333 | 0.12 (0.03, 0.49) | - | 0.00 (0.00, 0.00) | - |
| Cancer - Remainder post-release | [14] | 1 | 16,453 | 3 | 13,309 | 0.23 (0.07, 0.70) | - | 9 | 16,333 | 0.55 (0.29, 1.06) | - | 0.41 (0.11, 1.51) | - |
| Cardiovascular disease - Remainder post-release | [14] | 1 | 16,453 | 2 | 13,309 | 0.15 (0.04, 0.60) | - | 7 | 16,333 | 0.43 (0.20, 0.90) | - | 0.35 (0.07, 1.69) | - |
| Chronic respiratory disease - Remainder post-release | [14] | 1 | 16,453 | 1 | 13,309 | 0.08 (0.01, 0.53) | - | 1 | 16,333 | 0.06 (0.01, 0.43) | - | 1.23 (0.08, 19.62) | - |
| Digestive disorders - Remainder post-release | [14] | 1 | 16,453 | 0 | 13,309 | - | - | 2 | 16,333 | 0.12 (0.03, 0.49) | - | * | - |
| HIV-related - Remainder post-release | [14] | 1 | 16,453 | 0 | 13,309 | - | - | 1 | 16,333 | 0.06 (0.01, 0.43) | - | * | - |
| Influenza & pneumonia - Remainder post-release | [14] | 1 | 16,453 | 0 | 13,309 | - | - | 1 | 16,333 | 0.06 (0.01, 0.43) | - | * | - |
| Injection related injuries and diseases - Remainder post-release | [14] | 1 | 16,453 | 1 | 13,309 | 0.08 (0.01, 0.53) | - | 3 | 16,333 | 0.18 (0.06, 0.57) | - | 0.41 (0.04, 3.93) | - |
| Endocarditis - Remainder post-release | [14] | 1 | 16,453 | 1 | 13,309 | 0.08 (0.01, 0.53) | - | 3 | 16,333 | 0.18 (0.06, 0.57) | - | 0.41 (0.04, 3.93) | - |
| Bacteraemia and sepsis - Remainder post-release | [14] | 1 | 16,453 | 0 | 13,309 | - | - | 0 | 16,333 | - | - | - | - |
| Skin or soft tissue infections - Remainder post-release | [14] | 1 | 16,453 | 0 | 13,309 | - | - | 0 | 16,333 | - | - | - | - |

| | Refs | N cohorts | N people | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Rate Ratio (in OAT/out of OAT) | $I^2$ % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| All injury and poisoning – Total-time post-release | [14] | 1 | 16,453 | 28 | 15,439 | 1.81 (1.25, 2.63) | - | 134 | 18,505 | 7.24 (6.11, 8.58) | - | 0.25 (0.17, 0.38) | - |
| Accidental drug-induced - Total-time post-release | [14] | 1 | 16,453 | 13 | 15,439 | 0.84 (0.49, 1.45) | - | 97 | 18,505 | 5.24 (4.29, 6.40) | - | 0.16 (0.09, 0.29) | - |
| Accidental opioid - Total-time post-release | [14] | 1 | 16,453 | 12 | 15,439 | 0.78 (0.44, 1.37) | - | 85 | 18,505 | 4.59 (3.71, 5.68) | - | 0.17 (0.09, 0.31) | - |
| Violence - Total-time post-release | [14] | 1 | 16,453 | 3 | 15,439 | 0.19 (0.06, 0.60) | - | 6 | 18,505 | 0.32 (0.15, 0.72) | - | 0.60 (0.15, 2.40) | - |
| Motor vehicle and transport accidents - Total-time post-release | [14] | 1 | 16,453 | 4 | 15,439 | 0.26 (0.10, 0.69) | - | 8 | 18,505 | 0.43 (0.22, 0.86) | - | 0.60 (0.18, 1.99) | - |
| Falls, fires, burns & drownings - Total-time post-release | [14] | 1 | 16,453 | 1 | 15,439 | 0.06 (0.01, 0.46) | - | 4 | 18,505 | 0.22 (0.08, 0.58) | - | 0.30 (0.03, 2.68) | - |
| All liver-related - Total-time post-release | [14] | 1 | 16,453 | 0 | 15,439 | - | - | 7 | 18,505 | 0.38 (0.18, 0.79) | - | * | - |
| Viral hepatitis - Total-time post-release | [14] | 1 | 16,453 | 0 | 15,439 | - | - | 3 | 18,505 | 0.16 (0.05, 0.50) | - | * | - |
| All alcohol related - Total-time post-release | [14] | 1 | 16,453 | 1 | 15,439 | 0.06 (0.01, 0.46) | - | 3 | 18,505 | 0.16 (0.05, 0.50) | - | 0.40 (0.04, 3.84) | - |
| Cancer - Total-time post-release | [14] | 1 | 16,453 | 4 | 15,439 | 0.26 (0.10, 0.69) | - | 9 | 18,505 | 0.49 (0.25, 0.93) | - | 0.53 (0.16, 1.73) | - |
| Cardiovascular disease - Total-time post-release | [14] | 1 | 16,453 | 2 | 15,439 | 0.13 (0.03, 0.52) | - | 7 | 18,505 | 0.38 (0.18, 0.79) | - | 0.34 (0.07, 1.65) | - |
| Chronic respiratory disease - Total-time post-release | [14] | 1 | 16,453 | 1 | 15,439 | 0.06 (0.01, 0.46) | - | 1 | 18,505 | 0.05 (0.01, 0.38) | - | 1.20 (0.07, 19.16) | - |
| Digestive disorders - Total-time post-release | [14] | 1 | 16,453 | 0 | 15,439 | - | - | 2 | 18,505 | 0.11 (0.03, 0.43) | - | * | - |
| HIV-related - Total-time post-release | [14] | 1 | 16,453 | 1 | 15,439 | 0.06 (0.01, 0.46) | - | 2 | 18,505 | 0.11 (0.03, 0.43) | - | 0.60 (0.05, 6.61) | - |
| Influenza & pneumonia - Total-time post-release | [14] | 1 | 16,453 | 0 | 15,439 | - | - | 1 | 18,505 | 0.05 (0.01, 0.38) | - | * | - |
| Injection related injuries and diseases - Total-time post-release | [14] | 1 | 16,453 | 1 | 15,439 | 0.06 (0.01, 0.46) | - | 3 | 18,505 | 0.16 (0.05, 0.50) | - | 0.40 (0.04, 3.84) | - |
| Endocarditis - Total-time post-release | [14] | 1 | 16,453 | 1 | 15,439 | 0.06 (0.01, 0.46) | - | 3 | 18,505 | 0.16 (0.05, 0.50) | - | 0.40 (0.04, 3.84) | - |
| Bacteraemia and sepsis - Total-time post-release | [14] | 1 | 16,453 | 0 | 15,439 | - | - | 0 | 18,505 | - | - | - | - |

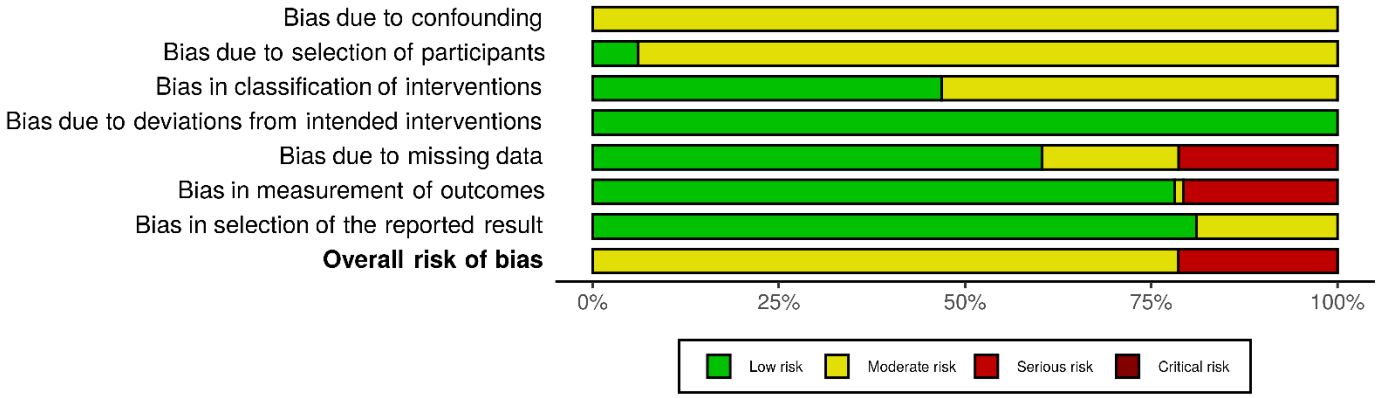
| | Refs | N cohorts | N people | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Deaths | PY | Pooled CMR (95%CI) | $I^2$ % | Rate Ratio (in OAT/out of OAT) | $I^2$ % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Skin or soft tissue infections - Total-time post-release | [14] | 1 | 16,453 | 0 | 15,439 | - | - | 0 | 18,505 | | - | - | - |

**Table Notes:** "First 4 weeks" refers to the first 4 weeks in or out of incarceration; "remainder" refers to remainder of time in incarceration or post-release; "Total time" refers to total time spent in incarceration, or total time post-release up to 12 months post-release from incarceration. * Rate ratios are suppressed where at least half of the studies reported 0 deaths for one of the time periods involved.

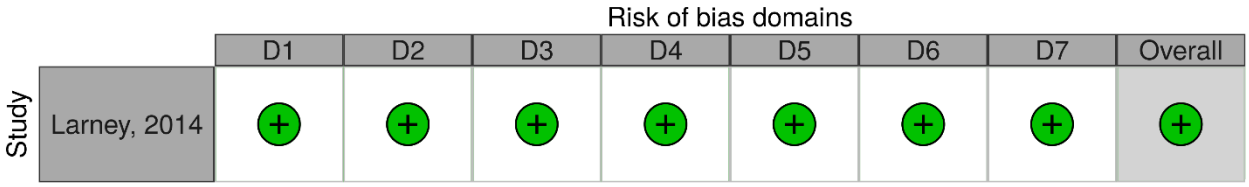
**eFigure 37: ROBINS-I for community-based observational studies used in analyses**



**eFigure 38: ROBINS-I for community-based observational studies – pooled domain scores weighted by person years contributed by each study**




**eFigure 39: ROBINS-I for studies used in analyses of the impact of OAT provided during incarceration on mortality during incarceration**




Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

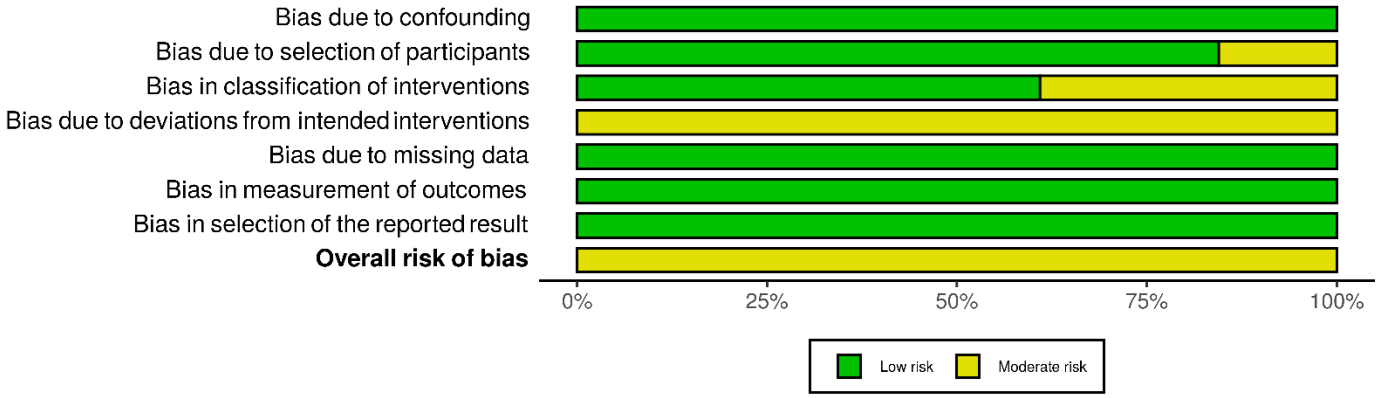
Judgement
Low

**eFigure 40: ROBINS-I for studies used in analyses of the impact of OAT provided during incarceration upon post-release mortality**

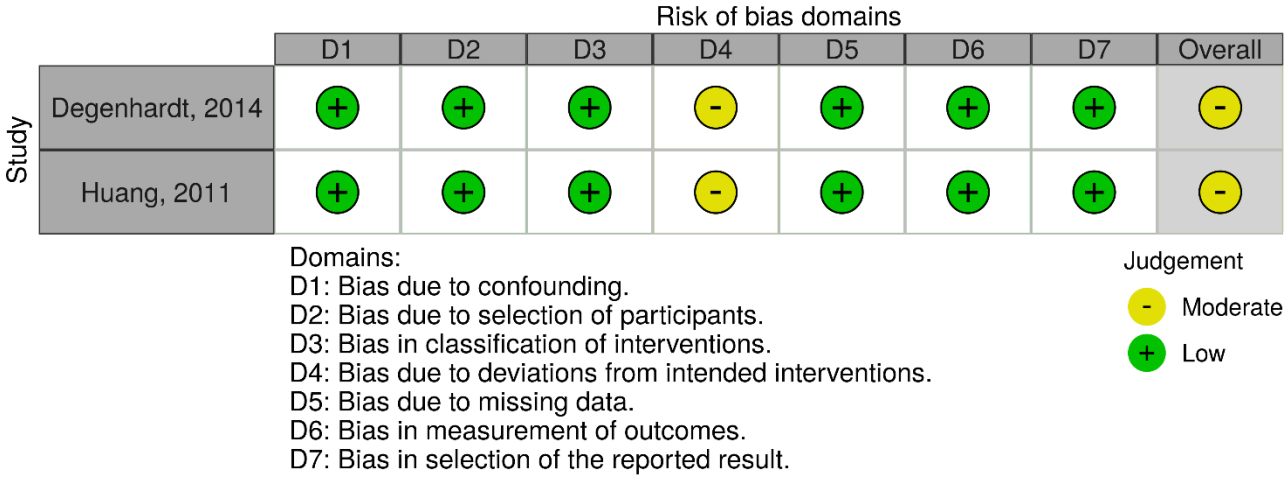

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
Moderate
Low

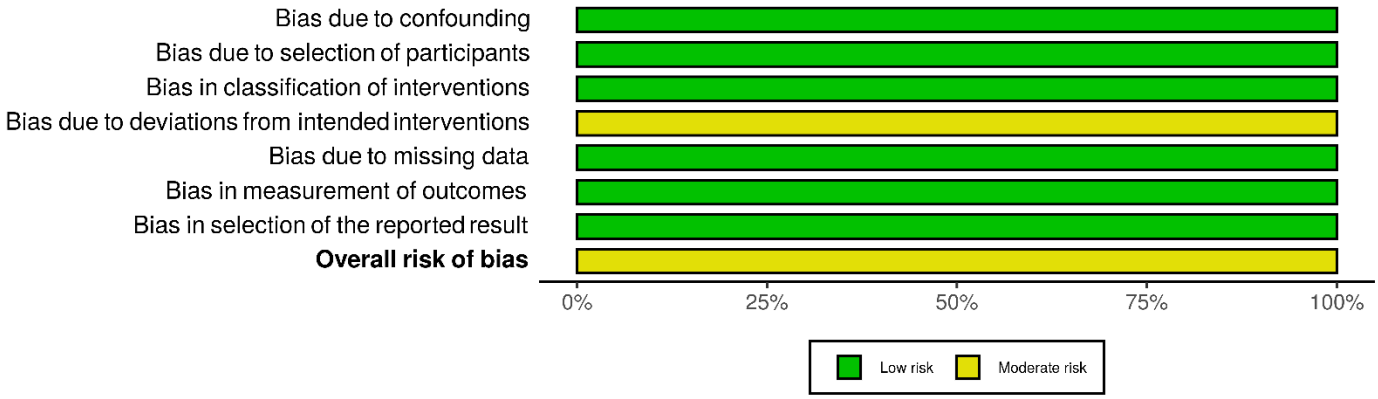
**eFigure 41: ROBINS-I for studies of OAT impact during incarceration – pooled domain scores weighted by person years contributed by each study**




**eFigure 42: ROBINS-I for studies used in analyses of the effect of post-release OAT on mortality**




**eFigure 43: ROBINS-I for of OAT impact post-release – pooled domain scores weighted by person years contributed by each study**



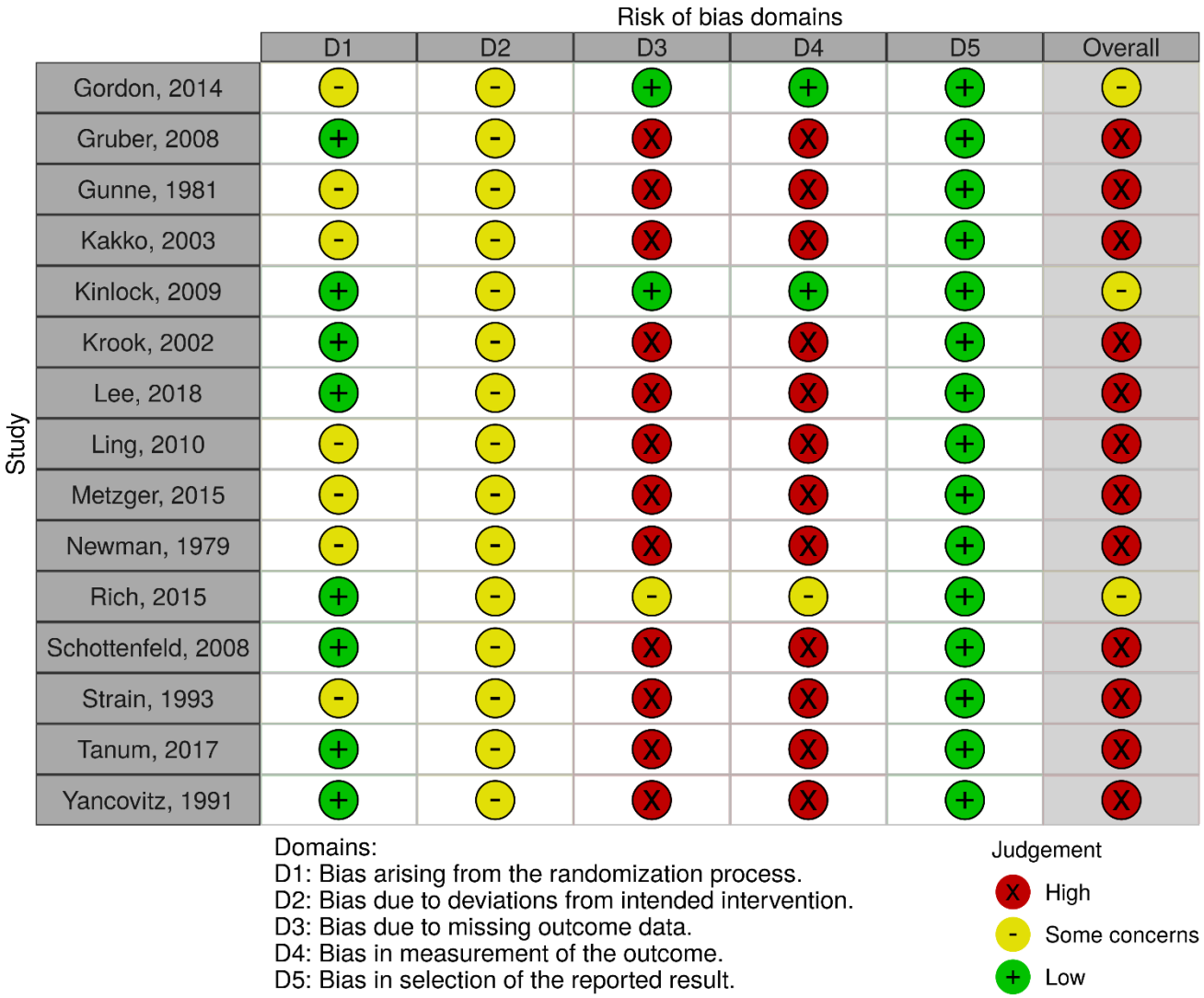
## eTable 21: Summary of studies that adjusted for confounding in observational studies of the impact of OAT on mortality

| Study | N people | OAT setting | Adjusted for confounding? | Variables included | Bivariate association of OAT with all-cause mortality | Adjusted association of OAT with all-cause mortality |
|---|---|---|---|---|---|---|
| **Abrahamsson 2017**[15] | 4,501 | Community OAT | Yes | Gender, age, inpatient treatment for a) non-fatal overdose, b) psychiatric disorders, and c) suicide attempt, benzodiazepine treatment, Z-drug treatment, pregabalin treatment. | HR 0.56 (0.45, 0.69) | AHR 0.55 (0.44, 0.68) |
| **Ledberg 2017**[3 A, B] | 441 | Community OAT | Yes | Gender, age, year of treatment entry. | NR | AHR 0.47 (0.29, 0.77) |
| **Appel 2000**[16] | 1,544 | Community OAT | No | -- | -- | -- |
| **Bakker 2017**[17] | 278 | Community OAT | No | -- | -- | -- |
| **Bazazi 2018**[18] | 291 | Released from incarceration on OAT | Yes | Age, marital status, ethnicity, employment, education, prison sentence, dependence severity, injecting history, HIV symptoms, study randomisation phase. | HR 1.32 (0.58, 3.03) | AHR 1.07 (0.44, 2.61) |
| **Bukten 2019**[12] | 7,843 | Community OAT | No | -- | -- | -- |
| **Buster 2002**[9] | 5,200 | Community OAT | No | -- | -- | -- |
| **Chang 2015**[1 A] | 983 | Community OAT | No | -- | -- | -- |
| **Cousins 2011**[19 A] | 3,162 | Community OAT | Yes | Gender, age, social class, comorbidity, methadone dose, no. MMT episodes, psychiatric admission, benzodiazepine prescription, urine drug tests, "overuse" of methadone. | HR 1.19 (0.70, 2.04) (*drug-related only*) | NA (*drug-related only*) |
| **Cousins 2016**[11 A] | 6,983 | Community OAT | Yes | Time period of treatment, sex, age, no. of treatment episodes, methadone dose, supervised consumption, median comorbidity score, co-prescriptions. | RR 0.32 (0.18, 0.57) | ARR 0.27 (0.16, 0.47) |
| **Davoli 2007**[20] | 10,258 | Community OAT | Yes | Age, gender, psychiatric comorbidity, HIV status, previous non-fatal overdose, route of administration, length of use. | HR 0.09 (0.04, 0.19) *(overdose only)* | AHR 0.09 (0.04, 0.19) *(overdose only)* |
| **Degenhardt 2009**[6 A] | 42,676 | Community OAT | No | -- | -- | -- |
| **Digiusto 2004**[21] | 1,244 | Community OAT | No | -- | -- | -- |
| **Dupouy 2017**[22 A] | 713 | Community OAT | Yes | Age, sex, Charlson co-morbidity index, psychiatric diagnoses recorded as chronic diseases or during a hospitalisation, dispensed psychoactive medications, socio-economic covariates (ecologic estimator of social deprivation, the status of the beneficiary, and universal insurance coverage). | HR 0.03 (0.01, 0.09) | AHR 0.03 (0.01, 0.09) |
| **Durand 2020**[23 A] | 2,899 | Community OAT | Yes | Gender, age, incarceration history, methadone dose, mental disorders, disease categories. | RR 0.57 (0.38, 0.97) | ARR 0.49 (0.29, 0.83) |
| **Evans 2015**[10] | 32,322 | Community OAT | Yes | Primary drug, age, gender, race/ethnicity, disability, labour force status, Med-Cal beneficiary, mentally ill, hepatitis C status, tuberculosis status, hospitalisation in past 30 days, HIV testing status, educational attainment, years from first primary drug use to first treatment episode, criminal justice system involvement, secondary drug type. | -- | AHR 0.27 (0.23, 0.32) |
| **Fellows-Smith 2011**[24] | 2,520 | Community OAT | No | -- | -- | -- |
| **Fugelstad 2007**[25] | 848 | Community OAT | No | -- | -- | -- |
| **Gearing 1974**[26] | 3,850 | Community OAT | No | -- | -- | -- |
| **Gronbladh 1990**[27] | 281 | Community OAT | No | -- | -- | -- |
| **Hickman 2018**[7 A] | 11,033 | Community OAT | Yes | Sex, age, calendar year, comorbidity score, geographical region, benzodiazepine co-prescription, gabapentinoid co-prescription, number of OAT patients per GP practice, number of GPs prescribing per practice, history of recorded self-harm, overdose poisoning, alcohol problems, imprisonment or homelessness. Propensity scores based on the probability of being prescribed buprenorphine were incorporated into models as inverse probability weights. | IRR 0.45 (0.37, 0.55) | AIRR 0.36 (0.31, 0.41) |
| **Huang 2011**[28] | 1,982 | OAT post-release | Yes | Age, gender, area of residence, HIV status prior to release. | -- | AHR 0.07 (0.02, 0.21) |
| **Huang 2013**[29 A] | 1,616 | Community OAT | Yes | Sex, age, living with a partner, education, cardiovascular disease, pneumonia/bronchitis/asthma, diabetes, HBV antigen, HCV antibody, HIV antibody, syphilis antibody, psychiatric treatment, multiple illicit substance use, alcohol disorder, previous drug overdose, previous suicide attempts, methadone dose, duration of heroin use | HR 0.32 (0.14, 0.72) | AHR 0.32 (0.13, 0.80) |
| **Kelty 2019**[30 A] | 8,226 | Community OAT | No | -- | -- | -- |
| **Kimber 2015**[5 A, C] | 46,531 | Community OAT | No | -- | -- | -- |

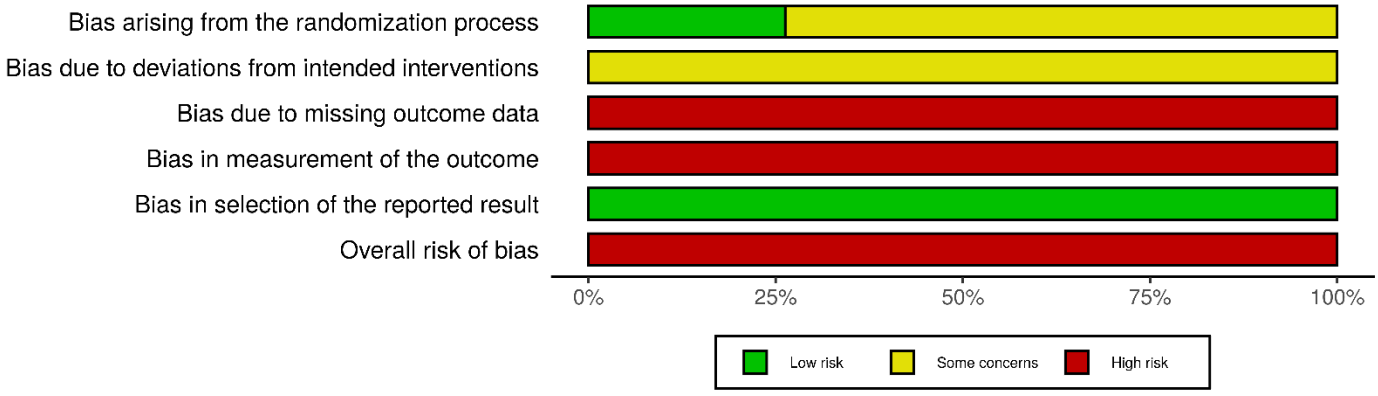
| Study | N people | OAT setting | Adjusted for confounding? | Variables included | Bivariate association of OAT with all-cause mortality | Adjusted association of OAT with all-cause mortality |
|---|---|---|---|---|---|---|
| **Degenhardt 2014**[14] [A, B] | 16,453 | Released from incarceration on OAT OAT post-release | Yes | Gender; Age; Indigenous status; juvenile offending history; length of prison episode; no. prior prison episodes; prior property offence; prior drug offence; prior violent offence | **First 4 weeks post-release:** HR 0.32 (0.21, 0.50) **Total time post-release:** HR 0.22 (0.13, 0.37) | **First 4 weeks post-release:** AHR 0.06 (0.01, 0.30)[E] **Total time post-release:** AHR 0.25 (0.12, 0.53) |
| **Larney 2014**[13] [B] | 16,715 | OAT during incarceration | Yes | Gender, Indigenous status, age, incarceration history (number & duration), offending history (drug, property and violent offences) | HR 0.25 (0.13, 0.48) | AHR 0.26 (0.13, 0.5) |
| **Langendam 2001**[31] [D] | 827 | Community OAT | No | -- | -- | -- |
| **Larochelle 2018**[32] | 17,568 | Community OAT | Yes | Age, sex, anxiety diagnosis, depression diagnosis, receipt of methadone, buprenorphine, opioid and benzodiazepine prescriptions in the 12 months before index nonfatal opioid overdose, benzodiazepine prescriptions, detoxification episode and short- and long-term residential treatments. | -- | M-AHR 0.37 (0.24, 0.59) B-AHR 0.35 (0.23, 0.53) |
| **Liu 2013**[33] | 306,786 | Community OAT | Yes | Age, gender, marital status, education, ethnicity, route of administration, needle sharing, methadone dose, HIV status. | HR 0.53 (0.50, 0.56) | AHR 0.56 (0.53, 0.59) |
| **Marsden 2017**[34] [A] | 12,260 | Released from incarceration on OAT | Yes | Age, injection drug use, self-reported problem alcohol use, non-medical benzodiazepine use, cocaine use, demographic and clinical co-variates, prison transfer, community treatment. | HR 0.25 (0.10, 0.60) | AHR 0.25 (0.09, 0.64) |
| **Morozova 2013**[35] [A] | 110 | Hospital | No | -- | -- | -- |
| **Muga 2014**[2] [A] | 1,678 | Community OAT | No | -- | -- | -- |
| **Pavarin 2017**[4] [A] | 2,232 | Community OAT | No | -- | -- | -- |
| **Pearce 2020**[8] [A] | 55,347 | Community OAT | Yes | Age, sex, medication type (buprenorphine/naloxone only, methadone only), OAT period | HR 0.45 (0.43, 0.49) | AHR 0.40 (0.34, 0.46) |
| **Pierce 2016**[36] | 151,983 | Community OAT | Yes | Age, gender, patient-reported injecting status, patient-reported problematic use of alcohol, benzodiazepines, crack cocaine, cocaine powder, amphetamines; referred from the criminal justice system. | HR 0.64 (0.58, 0.71) *(drug-related only)* | AHR 0.58 (0.52, 0.64) *(drug-related only)* |
| **Reece 2010**[37] | 2,518 | Community OAT | No | -- | -- | -- |
| **Scherbaum 2002**[38] | 244 | Community OAT | No | -- | -- | -- |
| **Weber 1990**[39] | 297 | Community OAT | No | -- | -- | -- |

**Table notes:** [A] Authors sent additional information.). [B] Secondary paper (overlap in data) but data used in sub-analyses. Shaded rows indicate secondary paper(s) to the one directly above them. [C] Used 2006-2010 data to avoid overlap with Degenhardt 2009. [D] Although eligible, no data from this study could be used in pooled quantitative syntheses. [E] There was an interaction with time since release with the protective effect extremely marked in first few days and then decaying to no impact**. HR:** hazard ratio. **AHR:** adjusted hazard ratio. **NR:** not reported. **NA:** not reported as not significant in univariate analyses. **RR:** relative risk. **ARR:** adjusted relative risk. **IRR:** Hickman. **AIRR:** Hickman. **M:** methadone. **B:** buprenorphine. **PWID:** people who inject drugs. **LFTU**: lost to follow-up. **OAT:** opioid agonist treatment. **Rx:** treatment.

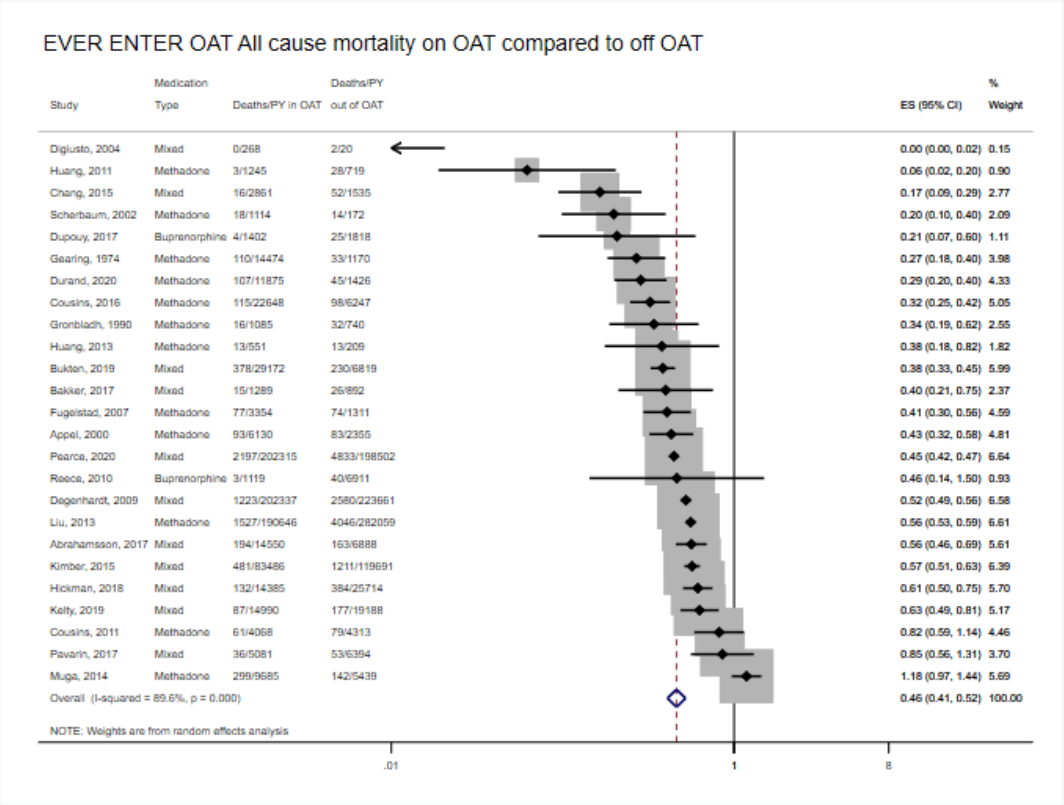
**eFigure 44: ROB-2 for RCTs**

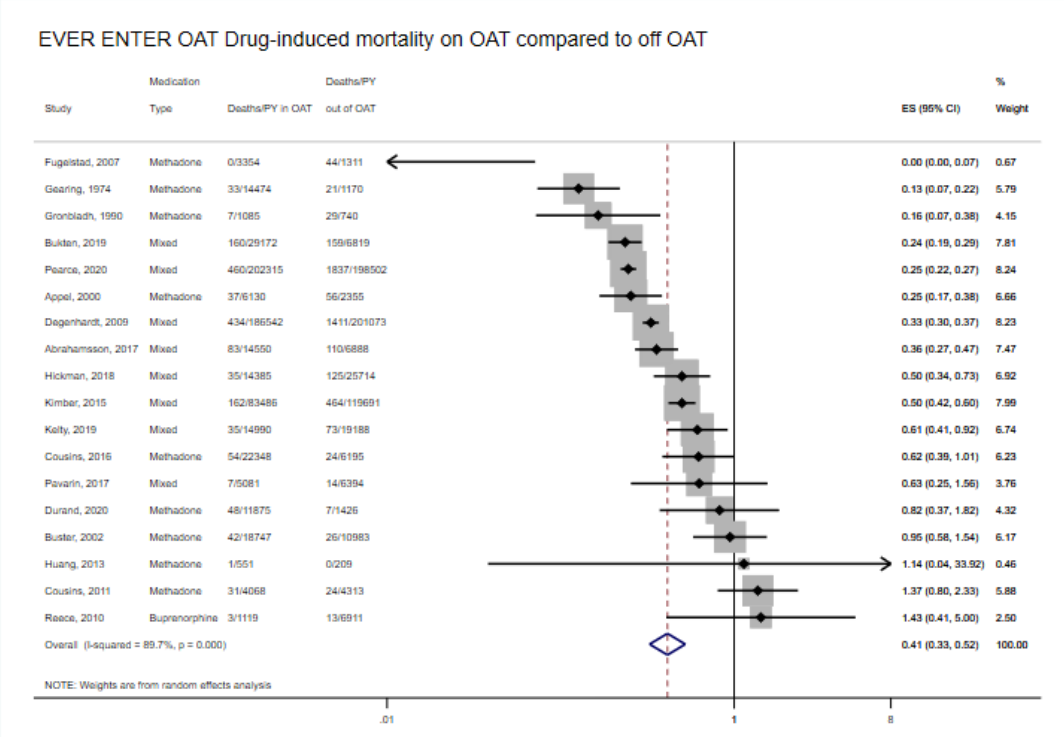



**eFigure 45: ROB-2 RCTs – pooled domain scores weighted by contribution of each study to pooled mortality estimate**

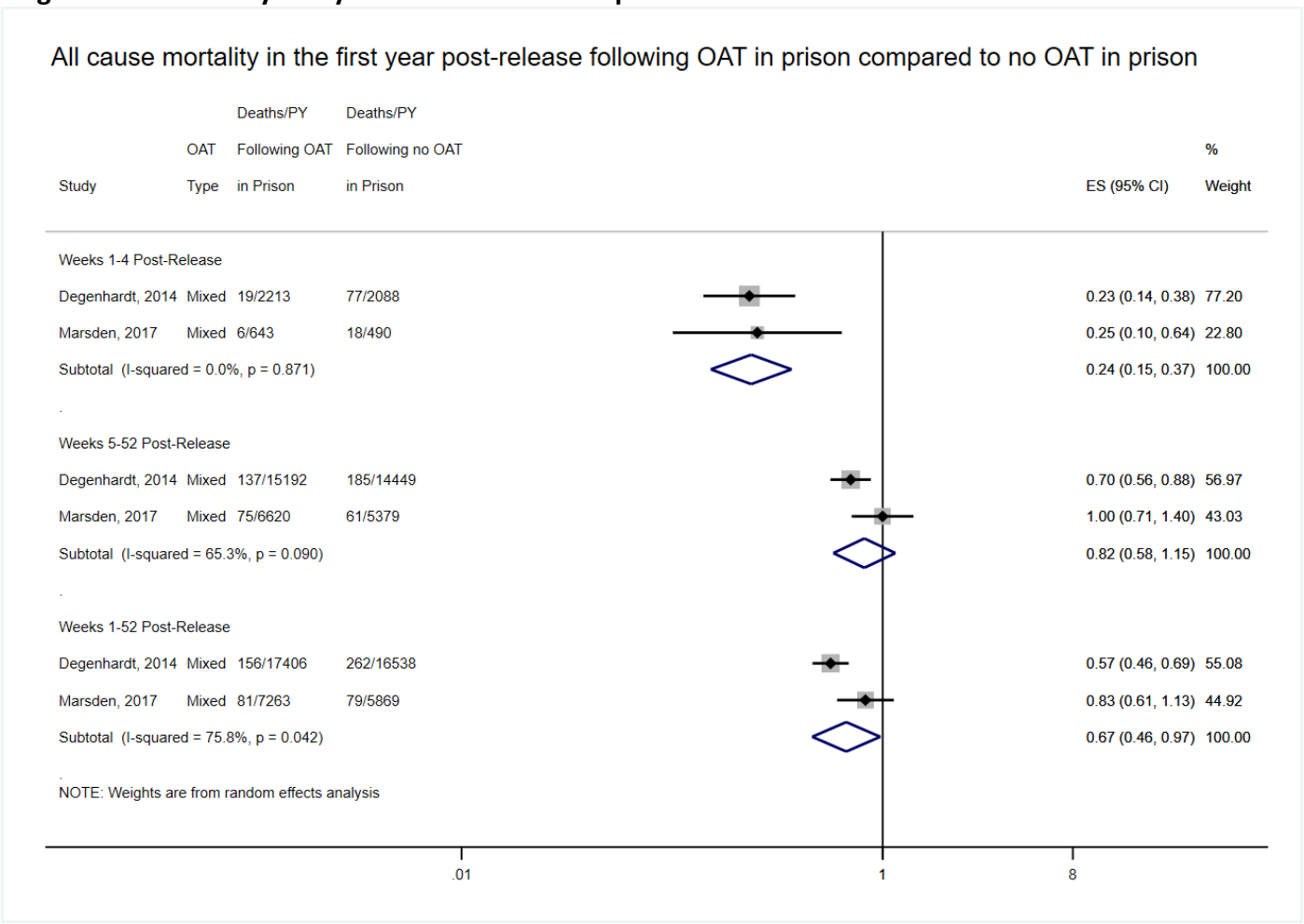


**eFigure 46: Sensitivity analysis restricted to those who ever enter OAT**

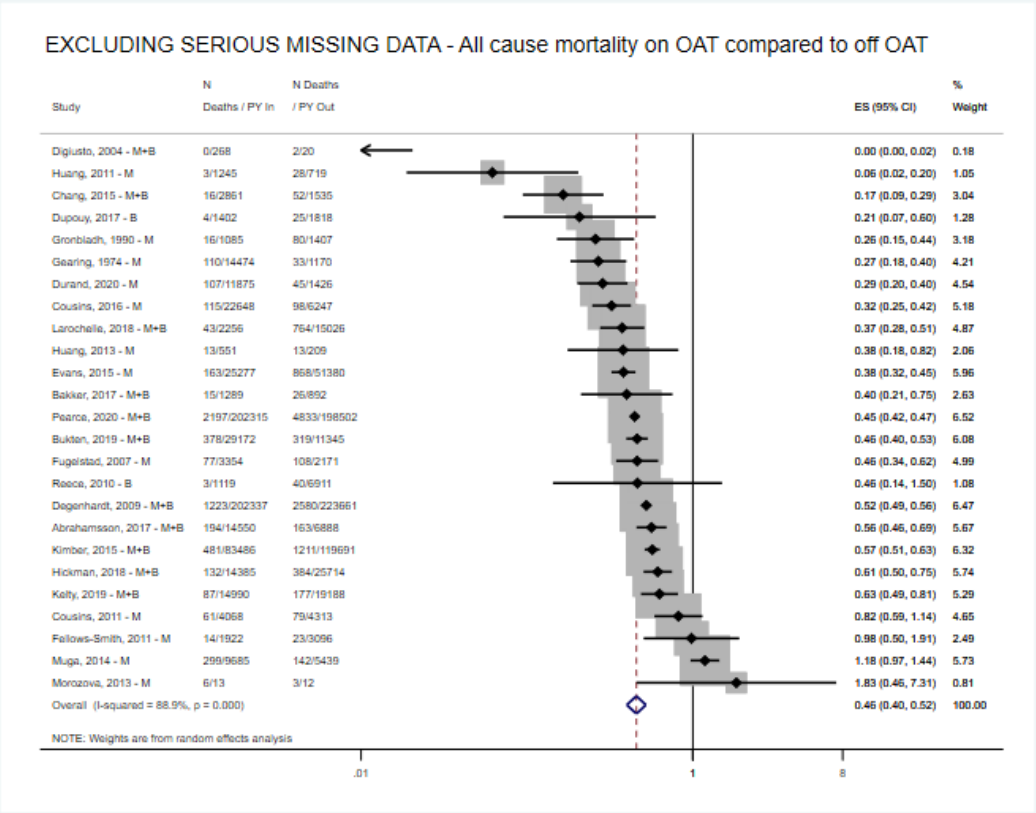


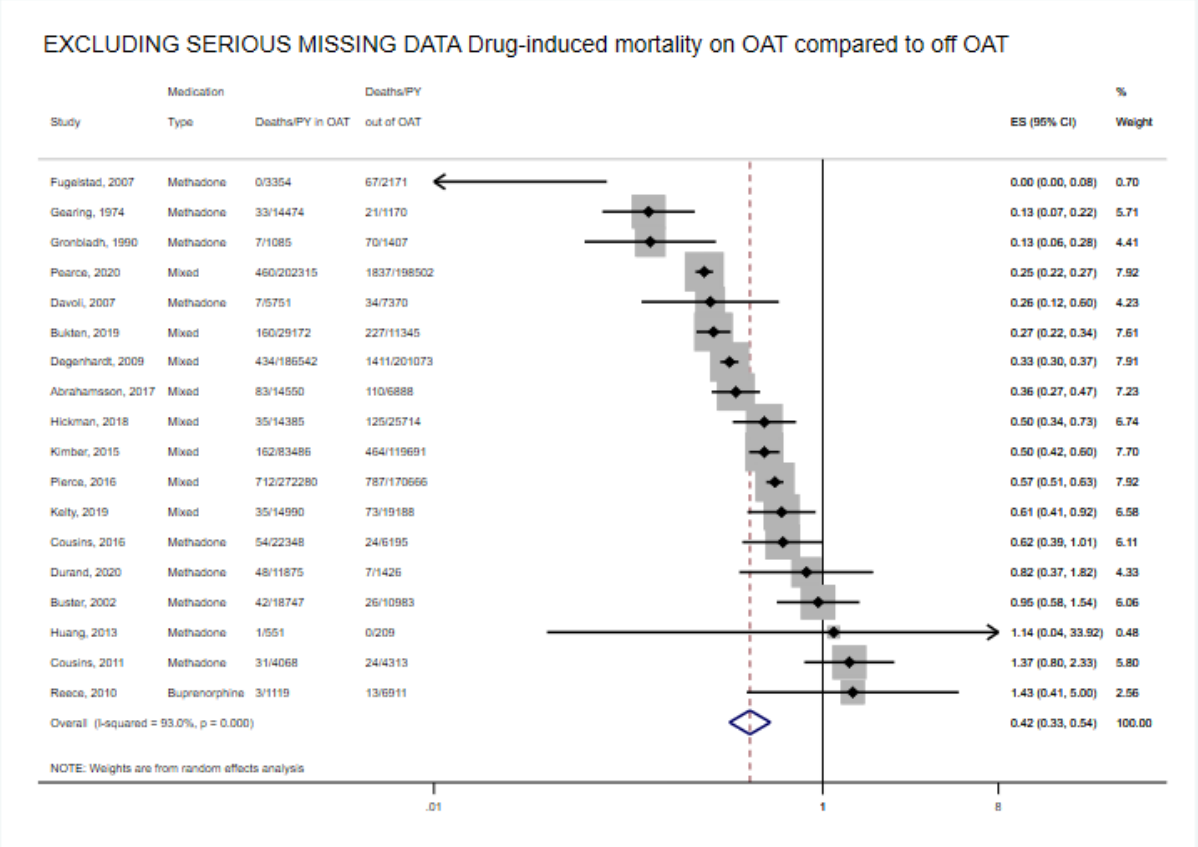



**eFigure 47: Sensitivity analysis for studies of OAT post-release from incarceration**

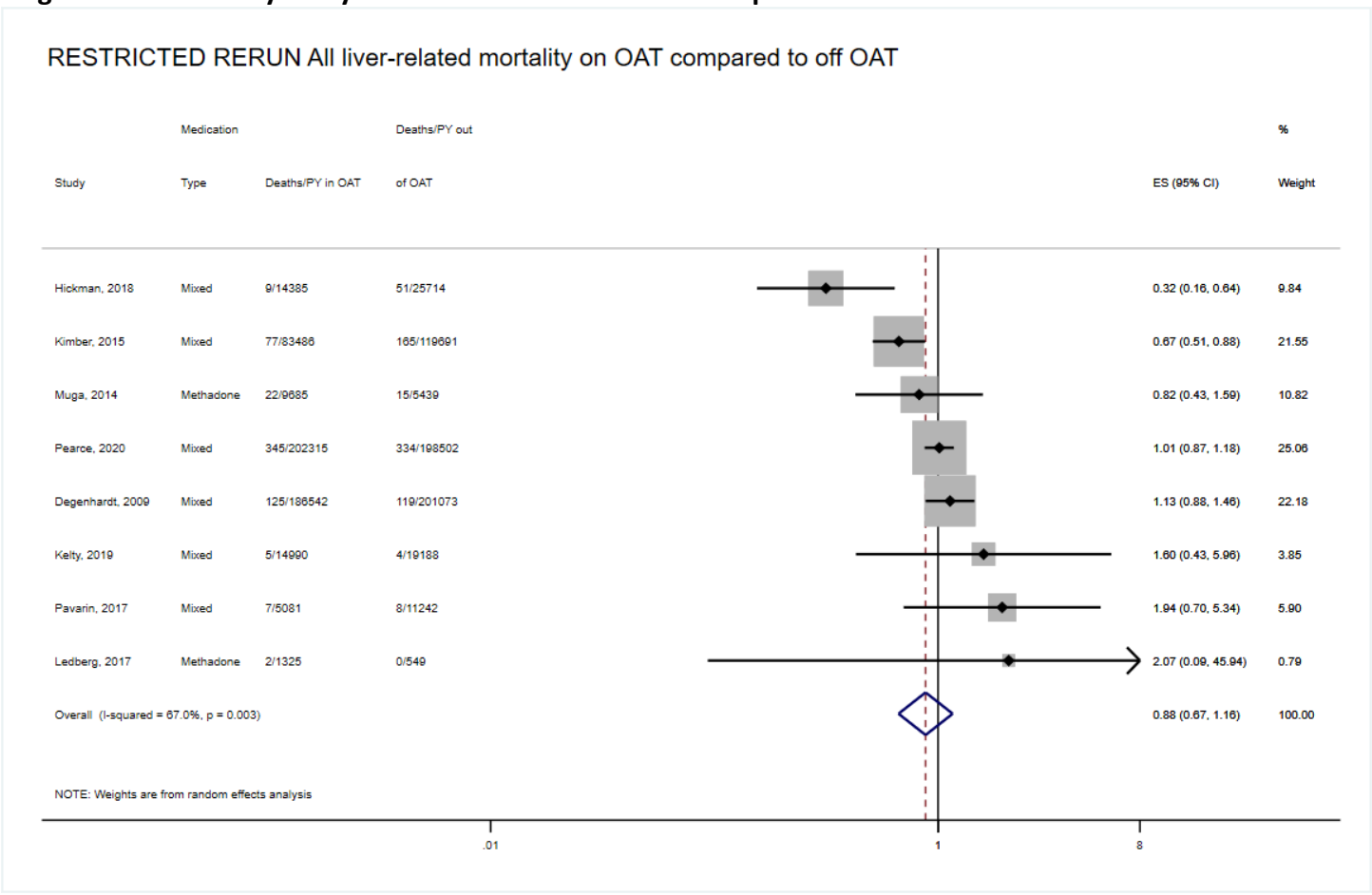


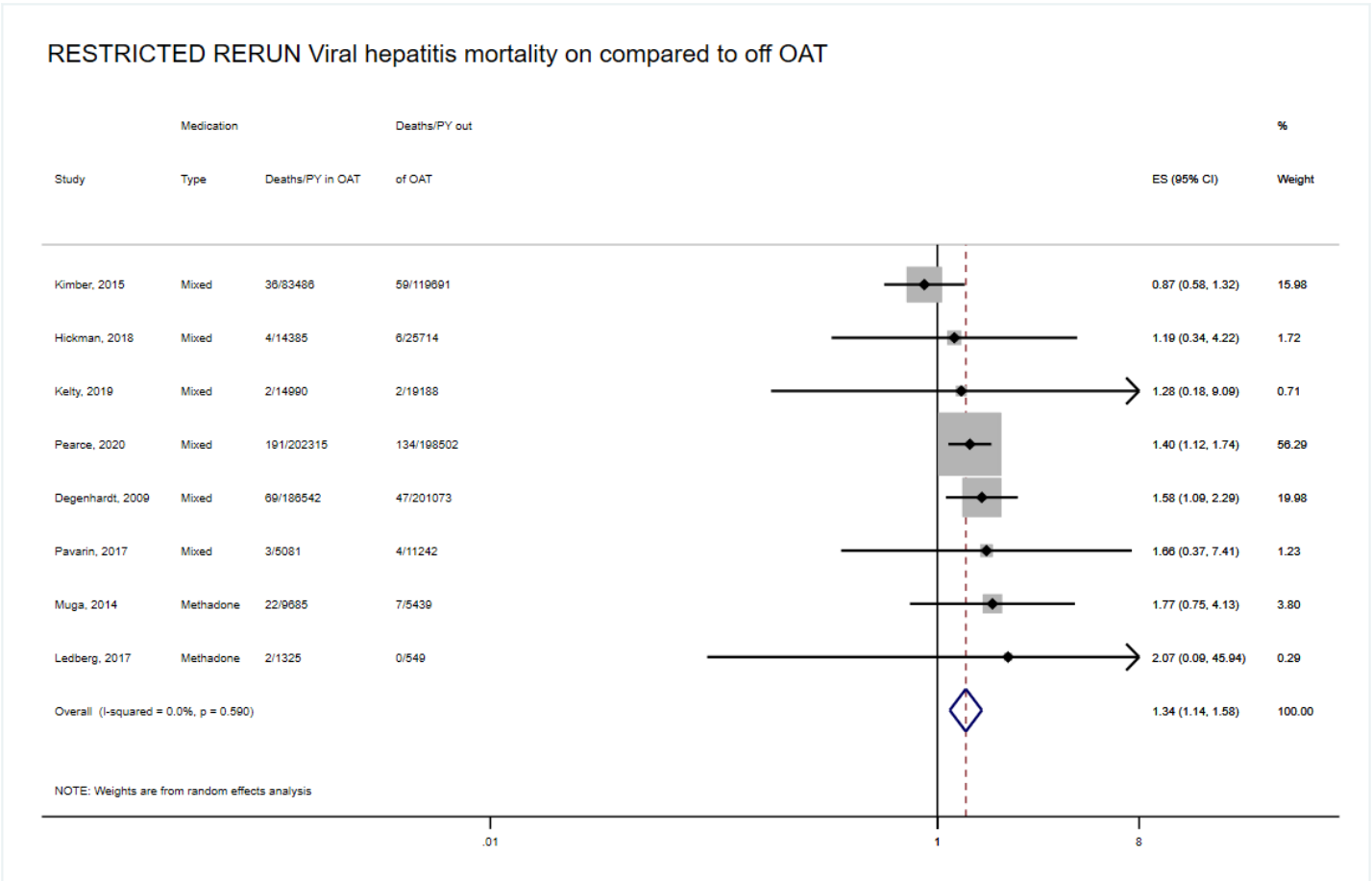
**eFigure 48: Sensitivity analysis excluding studies with serious risk of bias due to missing data**



**eFigure 49: Sensitivity analysis- All liver-related and viral hepatitis RRs restricted to the same cohorts**



## eReferences


1. Chang KC, Lu TH, Lee KY, Hwang JS, Cheng CM, Wang JD. Estimation of life expectancy and the expected years of life lost among heroin users in the era of opioid substitution treatment (OST) in Taiwan. *Drug & Alcohol Dependence* 2015; **153**: 152-8.
2. Muga R, Rivas I, Faure E, et al. Sex-specific disease outcomes of HIV-positive and HIV-negative drug users admitted to an opioid substitution therapy program in Spain: a cohort study. *BMC Infectious Diseases* 2014; **14**: 504.
3. Ledberg A. Mortality related to methadone maintenance treatment in Stockholm, Sweden, during 2006-2013. *Journal of Substance Abuse Treatment* 2017; **74**: 35-41.
4. Pavarin RM, Fioritti A, Sanchini S. Mortality trends among heroin users treated between 1975 and 2013 in Northern Italy: Results of a longitudinal study. *Journal of Substance Abuse Treatment* 2017; **77**: 166-73.
5. Kimber J, Larney S, Hickman M, Randall D, Degenhardt L. Mortality risk of opioid substitution therapy with methadone versus buprenorphine: A retrospective cohort study. *The Lancet Psychiatry* 2015; **2**(10): 901-8.
6. Degenhardt L, Randall D, Hall W, Law M, Butler T, Burns L. Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: Risk factors and lives saved. *Drug and Alcohol Dependence* 2009; **105**(1-2): 9-15.
7. Hickman M, Steer C, Tilling K, et al. The impact of buprenorphine and methadone on mortality: a primary care cohort study in the United Kingdom. *Addiction (Abingdon, England)* 2018; **113**(8): 1461-76.
8. Pearce LA, Min JE, Piske M, et al. Opioid agonist treatment and risk of mortality during opioid overdose public health emergency: population based retrospective cohort study. *Bmj* 2020; **368**: m772.
9. Buster MC, van Brussel GH, van den Brink W. An increase in overdose mortality during the first 2 weeks after entering or re-entering methadone treatment in Amsterdam. *Addiction* 2002; **97**(8): 993-1001.
10. Evans E, Li L, Min J, et al. Mortality among individuals accessing pharmacological treatment for opioid dependence in California, 2006-10. *Addiction* 2015; **110**(6): 996-1005.
11. Cousins G, Boland F, Courtney B, Barry J, Lyons S, Fahey T. Risk of mortality on and off methadone substitution treatment in primary care: A national cohort study. *Addiction* 2016; **111**(1): 73-82.
12. Bukten A, Stavseth MR, Clasuen T. From restrictive to more liberal: variations in moratlity among patients in opioid maintenance treament over a 12-year period. *BMC health services research* 2019; **19**(1): 553.
13. Larney S, Gisev N, Farrell M, et al. Opioid substitution therapy as a strategy to reduce deaths in prison: retrospective cohort study. *BMJ Open* 2014; **4**(4): e004666.
14. Degenhardt L, Larney S, Kimber J, et al. The impact of opioid substitution therapy on mortality post-release from prison: retrospective data linkage study. *Addiction* 2014; **109**(8): 1306-17.
15. Abrahamsson T, Berge J, Ojehagen A, Hakansson A. Benzodiazepine, z-drug and pregabalin prescriptions and mortality among patients in opioid maintenance treatment-A nation-wide register-based open cohort study. *Drug and Alcohol Dependence* 2017; **174**: 58-64.
16. Appel PW, Joseph H, Richman BL. Causes and rates of death among methadone maintenance patients before and after the onset of the HIV/AIDS epidemic. *Mount Sinai Journal of Medicine* 2000; **67**(5-6): 444-51.
17. Bakker A, Streel E. Benzodiazepine maintenance in opiate substitution treatment: Good or bad? A retrospective primary care case-note review. *Journal of Psychopharmacology* 2017; **31**(1): 62-6.

18. Bazazi AR. Characterizing and responding to the epidemics of HIV and injection drug use in Malaysia. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2018; **78**(7-B(E)): No Pagination Specified.
19. Cousins G, Teljeur C, Motterlini N, McCowan C, Dimitrov BD, Fahey T. Risk of drug-related mortality during periods of transition in methadone maintenance treatment: A cohort study. *Journal of Substance Abuse Treatment* 2011; **41**(3): 252-60.
20. Davoli M, Bargagli AM, Perucci CA, et al. Risk of fatal overdose during and after specialist drug treatment: The VEdeTTE study, a national multi-site prospective cohort study. *Addiction* 2007; **102**(12): 1954-9.
21. Digiusto E, Shakeshaft A, Ritter A, O'Brien S, Mattick R. Serious adverse events in the Australian National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD). *Addiction* 2004; **99**(4): 450-60.
22. Dupouy J, Palmaro A, Fatseas M, et al. Mortality Associated With Time in and Out of Buprenorphine Treatment in French Office-Based General Practice: A 7-Year Cohort Study. *Annals of family medicine* 2017; **15**(4): 355-8.
23. Durand L, O'Driscoll D, Boland F, et al. Do interruptions to the continuity of methadone maintenance treatment in specialist addiction settings increase the risk of drug-related poisoning deaths? A retrospective-cohort study. *Addiction* 2020; **07**.
24. Fellows-Smith J. Opioid-dependent error processing. *Journal of Opioid Management* 2011; **7**(6): 443-9.
25. Fugelstad A, Stenbacka M, Leifman A, Nylander M, Thiblin I. Methadone maintenance treatment: the balance between life-saving treatment and fatal poisonings. *Addiction* 2007; **102**(3): 406-12.
26. GEARING FR, SCHWEITZER MD. An epidemiologic evaluation of long-term methadone maintenance treatment for heroin addiction. *American Journal of Epidemiology* 1974; **100**(2): 101-12.
27. Gronbladh L, Ohlund LS, Gunne LM. Mortality in heroin addiction: impact of methadone treatment. *Acta Psychiatrica Scandinavica* 1990; **82**(3): 223-7.
28. Huang YF, Kuo HS, Lew-Ting CY, et al. Mortality among a cohort of drug users after their release from prison: an evaluation of the effectiveness of a harm reduction program in Taiwan. *Addiction* 2011; **106**(8): 1437-45.
29. Huang CL, Lee CW. Factors associated with mortality among heroin users after seeking treatment with methadone: a population-based cohort study in Taiwan. *Journal of Substance Abuse Treatment* 2013; **44**(3): 295-300.
30. Kelty E, Joyce D, Hulse G. A retrospective cohort study of mortality rates in patients with an opioid use disorder treated with implant naltrexone, oral methadone or sublingual buprenorphine. *American Journal of Drug & Alcohol Abuse* 2019; **45**(3): 285-91.
31. Langendam MW, van Brussel GH, Coutinho RA, van Ameijden EJ. The impact of harm-reduction-based methadone treatment on mortality among heroin users. *American journal of public health* 2001; **91**(5): 774-80.
32. Larochelle MR, Bernson D, Land T, et al. Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality: A Cohort Study. *Annals of Internal Medicine* 2018; **169**(3): 137-45.
33. Liu E, Rou K, McGoogan JM, et al. Factors associated with mortality of HIV-positive clients receiving methadone maintenance treatment in China. *Journal of Infectious Diseases* 2013; **208**(3): 442-53.
34. Marsden J, Stillwell G, Jones H, et al. Does exposure to opioid substitution treatment in prison reduce the risk of death after release? A national prospective observational study in England. *Addiction* 2017; **112**(8): 1408-18.

35. Morozova O, Dvoryak S, Altice FL. Methadone treatment improves tuberculosis treatment among hospitalized opioid dependent patients in Ukraine. *International Journal of Drug Policy* 2013; **24**(6): e91-8.
36. Pierce M, Bird SM, Hickman M, et al. Impact of treatment for opioid dependence on fatal drug-related poisoning: a national cohort study in England. *Addiction* 2016; **111**(2): 298-308.
37. Reece AS. Favorable mortality profile of naltrexone implants for opiate addiction. *Journal of Addictive Diseases* 2010; **29**(1): 30-50.
38. Scherbaum N, Specka M, Hauptmann G, Gastpar M. Does maintenance treatment reduce the mortality rate of opioid addicts? *Fortschritte der Neurologie, Psychiatrie* 2002; **70**(9): 455-61.
39. Weber R, Ledergerber B, Opravil M, Siegenthaler W, Luthy R. Progression of HIV infection in misusers of injected drugs who stop injecting or follow a programme of maintenance treatment with methadone. *Bmj* 1990; **301**(6765): 1362-5.