Interventions to reduce harms related to drug use among people who experience incarceration: systematic review and meta-analysis

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Summary

Background Mortality, suicide, self-harm, and substance use are elevated among people who are incarcerated. There is a wide range of heterogeneous interventions aimed at reducing these harms in this population. Previous reviews have focused on specific interventions or limited their findings to drug use and recidivism and have not explored interventions delivered after release from prison. Our aim is to examine the effect of interventions delivered to people who use drugs during incarceration or after release from incarceration, on a wide range of outcomes.

Methods In this systematic review and meta-analysis, we searched Embase, MEDLINE, and PsycINFO databases up until Sept 12, 2023 for studies published from Jan 1, 1980 onwards. All studies evaluating the effectiveness of any intervention on drug use, recidivism outcomes, sexual or injecting risk behaviours, or mortality among people who use psychoactive drugs and who were currently or recently incarcerated were included. Studies without a comparator or measuring only alcohol use were excluded. Data extracted from each study included demographic characteristics, interventions, and comparisons. Pooled odds ratios and risk ratios were calculated using random-effects meta-analyses.

Findings We identified 126 eligible studies (47 randomised controlled trials and 79 observational studies) encompassing 18 interventions; receiving opioid-agonist treatment (OAT) in prison reduced the risk of death in prison (one study; hazard ratio 0·25; 95% CI 0·13–0·48), whereas receiving OAT in the first 4 weeks following release reduced risk of death in the community (two studies; relative risk 0·24; 95% CI 0·15–0·37). Therapeutic community interventions reduced re-arrest at 6–12 months (six studies; odds ratio [OR] 0·72; 95% CI 0·55–0·95) and reincarceration at 24 months (two studies; OR 0·66; 95% CI 0·48–0·96). There was scarce evidence that OAT and syringe service provision are effective in reducing injecting risk behaviours and needle and syringe sharing.

Interpretation There are effective interventions to reduce mortality and recidivism for people who use drugs who have been incarcerated. Nonetheless, there are also substantial gaps in the research examining the effect of interventions on risk behaviours and mortality during incarceration and a need for randomised designs examining outcomes for people who use drugs after release.

Funding Australian National Health and Medical Research Council.

Lancet Public Health 2024; 9: e684–99

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Introduction

People who are incarcerated have increased risks of all-cause mortality, suicide, self-harm, and violence, compounded by comorbid substance use and mental illness.[1,2] People who use drugs and are incarcerated have an increased risk of drug-related death after release from prison,[3] as well as relapse, reincarceration, and exposure to blood-borne viruses because of risky injecting behaviours.[2,4] Studies consistently show an elevated risk of death in the few weeks immediately following release from prison,[5] particularly from drug overdose for people who are opioid dependent.[6] Drug use accounted for 59% of deaths within 3 months and 76% within 2 weeks of release.[7]

Many interventions aim to reduce substance use and associated harms, including the WHO Essential Medicines, such as maintenance on opioid-agonist treatment (OAT; eg, methadone or buprenorphine, both evidence-based treatments for opioid dependence[3] and for prevention of HIV and hepatitis C virus [HCV]). Other interventions include psychosocial interventions, therapeutic communities, needle-and-syringe programmes, and naloxone, among others.

In 2009, a review assessed the effects of interventions on HIV transmission related to drug injection in prison.[8] A summary of reviews and studies that had examined HIV-related and HCV-related outcomes delivered in prisons was published in 2016[9] and on opioids in 2020.[10,11] A review focusing on naltrexone for individuals involved in the criminal justice system was published in 2020.[12] The evidence presented in these reviews suggests that needle-and-syringe programmes and OAT provided in prisons can substantially reduce needle sharing and

Research in context

Evidence before this study

We searched for reviews published in PubMed in the past 10 years on Nov 21, 2023 using search terms "prison", "incarc*", "drugs", and "treatment". No systematic reviews examining a broad range of interventions for people who use drugs in prison or within 12 months of release were found. Several reviews examined the effectiveness of interventions for people who use drugs, but were limited to specific outcomes and interventions. For example, previous reviews have focused specifically on opioid-related treatment for people in prison and jail settings or interventions targeting injection-drug use. A review published in 2022 by Palmateer and colleagues examined the effects of opioid-agonist treatment (OAT), needle-and-syringe programmes, and psychosocial interventions. This review, however, was not focused on people who were or had been incarcerated, only examined hepatitis C virus (HCV) and HIV infection, only examined injecting risk behaviours and injection-drug use, and was limited to studies of people who inject drugs. One systematic review conducted in 2019 by Malta and colleagues focused on opioid-related interventions for people who were incarcerated or had been released from prison in the past 90 days and found that OAT was associated with reduced opioid use, non-fatal overdose, and mortality. Other reviews focused on medication-assisted treatments for opioid-use disorder for populations involved in criminal justice. Moore and colleagues found that methadone significantly reduced opioid use after release (odds ratio 0·22, 95% CI 0·15–0·32) and injection-drug use (0·26, 0·12–0·56), whereas Bahji and colleagues concluded that naltrexone reduced opioid use and reincarceration. These reviews have some overlap with the aim of the present review; however, our review is not limited to medication-assisted treatments. Other reviews have either not focused specifically on interventions for people who use drugs or have been limited to prison-based interventions. OAT has been shown to be effective in reducing drug use in a 2015 review of randomised controlled trials (RCTs) by Kouyoumdjian and colleagues and by De Andrade and colleagues in 2018. Mitchell and colleagues also reviewed interventions that were based in prison, and along with De Andrade and colleagues, found a positive effect for therapeutic communities on recidivism. In 2018, Moore and colleagues reviewed re-entry programmes and found some evidence of a reduction in recidivism and drug use. However, none of the reviews except for that of Mitchell and colleagues included meta-analyses. Two literature reviews focused on blood-borne virus prevention and found that needle and syringe provision was associated with reduced HIV prevalence and needle sharing, whereas OAT was associated with reduced opioid and injection-drug use. One systematic review of HCV treatment in prison settings, published in 2018, focused solely on sustained virological response and treatment completion. We aimed to present evidence not limited to RCTs or only to interventions delivered in prison.

Added value of this study

This global systematic review is, to our knowledge, the first to examine a broad range of interventions for people who use drugs who have been incarcerated and assess their effectiveness in reducing drug use and related harms. This review included an evaluation of commonly used interventions, such as OAT, psychosocial interventions, and therapeutic communities and a wide range of outcomes, including drug use, recidivism, and mortality. Our study provides a comprehensive assessment of the effectiveness of these interventions and identifies important gaps in the literature that should be addressed in future research.

Implications of all the available evidence

The evidence is scarce for the effect of several interventions on drug use and related harms for people who have been incarcerated. OAT, however, effectively reduces mortality, and high coverage should be ensured and maintained. There are substantial gaps in research, particularly for interventions administered and evaluated while people are incarcerated. More research should be done evaluating the implementation of interventions for people who use drugs on outcomes during incarceration, as implementation inside prison might be different than in community settings.

other HIV risk behaviours and drug use, whereas naltrexone can reduce opioid use and reincarceration. Three reviews examined the effect of interventions in prison, but were focused solely on recidivism, drug use, or both recidivism and drug use, and did not include any meta-analyses.[13–15] A review had a meta-analysis but was focused on the effect of prison-based programmes on recidivism and drug use.[16] To our knowledge, no systematic review has examined a broader range of interventions to reduce drug-related harm among people who use drugs who are also incarcerated. A 2022 review[17] did examine a broad range of interventions, but was not focused on people who had been incarcerated, and was limited to people who injected drugs. The aim of the current review is to examine the effect of a broad array of interventions to reduce harms among people who use drugs, delivered during incarceration or after release from incarceration, on a range of outcomes, including substance use, re-arrest and reincarceration, injecting and sexual risk behaviours, mortality, non-fatal overdose, and HIV and HCV treatment.

See Online for appendix

Methods

This review was conducted in adherence to PRISMA guidelines (appendix pp 6–7). The study was registered with PROSPERO (CRD42021224423).

Inclusion and exclusion criteria

Eligible studies comprised those that included people who used psychoactive drugs (excluding alcohol and nicotine)

and those that included people who were currently or had recently been incarcerated (within 12 months of release). Determination of the sample as people who use drugs was based on studies describing the sample as people who were current users of psychoactive drugs (or in the case of individuals within prison, had used psychoactive substances before entering prison) or who were described as having a drug dependence or disorder. Studies of people in closed psychiatric settings were excluded because this population was not comparable with people who had been or were currently incarcerated, as were studies with sample sizes of less than 40 individuals because of statistical power concerns and the inability to contribute any meaningful data to the meta-analyses.

We considered studies examining interventions during incarceration or after release (within 12 months), focusing on opioid agonist therapies, therapeutic communities, psychosocial interventions, HIV and HCV interventions, needle-and-syringe provision studies, naloxone, and case-management studies (table 1). Psychosocial interventions were only included when their intended outcomes were related to drug use. General psychosocial interventions for which the intended outcome was unrelated to drug use were excluded. Psychosocial interventions were defined as structured psychological or social interventions used to address substance-related problems,[18] which, in line with a Cochrane review,[19] included cognitive behavioural therapy, motivational interviewing, contingency management, screening and brief intervention, and collaborative behavioural management (for a definition of interventions included in this review, see the appendix p 281).

Randomised controlled trials (RCTs), quasi-experimental studies, before-and-after studies, prospective and retrospective cohort studies, case–control studies, analytical cross-sectional studies, and observational studies were eligible for inclusion. Commentaries, editorials, review papers, case studies, studies with no data presented, and conference abstracts were excluded. Review papers were first hand searched for any reviews not captured in database searches before being excluded at full text. Studies from Jan 1, 1980 to Sept 12, 2023 were included.

Eligible studies used any type of comparator, including placebo, waiting list controls, other interventions, and before-and-after comparisons. Studies comparing those who completed with those who did not and those with no comparators were excluded.

	Number of studies	Number of participants
Study design		
Randomised controlled trial	47	15 291
Observational	79	571 069
Intervention setting		
During incarceration	96	388 739
After release or at release	21	195 839
Both in prison and after release	9	1782
Number of centres		
Single centre	49	21 632
Multicentre	77	564 728
Intervention		
Opioid agonist therapy	30	206 701
Psychosocial interventions*	13	5439
Therapeutic communities	25	19 457
Modified therapeutic communities	9	2171
Case management	10	6201
Self-help interventions†	6	173 468
Continuity of care	4	896
Naloxone provision	2	133 148
Naltrexone	5	469
Needle or syringe provision	2	493
HIV or HCV education	3	2812
HCV treatment or testing interventions	5	1225
HIV treatment or testing interventions	4	29 528
Discharge planning	1	434
Combined interventions	3	1885
Opioid detox	1	289
Family interventions	1	274
Substance abuse treatment	2	1470
Country income status		
Low income	0	0
Lower-middle income	1	2004
Upper-middle income	4	1393
High income	121	582 963
Outcomes		
Drug use	54	26 235
HIV or HCV outcomes	18	32 768
Sexual risk behaviours	12	4088
Injecting risk behaviours	9	2776
Non-fatal overdose	6	3916
Mortality	13	332 591
Criminal activity	9	3125
Re-arrest	47	25 011
Reincarceration	49	222 137

HCV=hepatitis C virus. *We considered cognitive behavioural therapy, screening and brief interventions, contingency management, and motivational interviewing to be psychosocial interventions. †Self-help with peers and peer-based support groups were categorised as self-help interventions.

Table 1: **Summary of included studies**

Search strategy

We did initial systematic searches on Sept 14, 2020 of peer-reviewed databases (MEDLINE, Embase, and PsycInfo), using comprehensive search terms, including exploded MeSH terms and keywords for prison and other carceral settings, drug use and related harms, and interventions that target these outcomes (appendix pp 9–13). These search terms were developed with experts in systematic review methodologies. Language restrictions were not applied. Any systematic reviews with potentially relevant sources were individually reviewed for eligible papers or reports. 29 hand-searched

papers were added from these reviews. These systematic reviews are listed in the appendix (pp 101–07). We did an updated search on Sept 12, 2023, and we stopped contacting authors for additional information or data on March 22, 2024.

Study screening and selection

Two researchers independently examined titles and abstracts using the web-based systematic review programme Covidence (CM, EBC, BH, LD, JG, GM, LTT, and FLA). The full texts of relevant articles were obtained and assessed for inclusion by two independent researchers (CM, GM, MN, BH, LW, LTT, LD, FLA, and OL). Disagreement between reviewers was resolved via discussion, and in cases in which consensus was not reached, a third reviewer was consulted.

Data extraction

Data were extracted by one researcher (CM, GM, RJ, OL, LTT, AP, and WG) and double-checked by a second researcher, with discrepancies resolved through discussion and consultation with a third person. Data extracted from each reference included demographic details, interventions, and comparisons. In cases in which data were not reported in sufficient detail or when a subset of the sample was required, for example stratified data for people who use drugs or people released from prison within the past 12 months, authors were contacted via email for additional information. Authors were only contacted if the study was published within 10 years of the start of the review (2010 onwards).

Types of outcomes

The outcomes of interest were as follows: injection-drug use; patterns of drug use including opioid use and stimulant use; injecting risk (receptive needle sharing, reuse of own needle, distributive needle sharing, and sharing of other injecting equipment); sexual behaviour (eg, condom use, frequency of sexual activity, and other sexual risk behaviours); uptake of HIV and HCV testing; HIV and HCV incidence; HIV and HCV treatment uptake; non-fatal overdose; fatal overdose; non-suicidal self-harm and suicidal behaviour; suicide; overall mortality; and reoffending and reincarceration, in prison and after release (the detailed list of outcomes examined is presented in the appendix p 110).

Studies for which reoffending or reincarceration were the only outcome were included if the intervention was related to drug use. Studies evaluating only alcohol use (with no other drug use as the study outcome) were excluded. Studies were excluded if their only outcomes were knowledge, attitudes, and behaviour.

Assessment of risk of bias and grading of evidence

Six researchers completed risk of bias assessment (GM, CM, OL, LTT, RJ, and ML). Each study was independently assessed by two individuals and discrepancies were discussed and resolved between assessors. Discrepancies not resolved were discussed with a third person. Risk of bias for RCTs was assessed using the Revised Cochrane Risk-of-Bias Tool for Randomised Trials (RoB2).[20] Risk of bias for non-RCTs was assessed using Risk of Bias in Non-Randomised Studies of Interventions (ROBINS-I).[21] Both tools assess bias at the study and outcome levels. Studies were assessed on the basis of intention to treat. A list of all domains and signalling questions for the RoB2 tool and ROBINS-1 are shown in the appendix (pp 232–33).

For non-RCTs, we disregarded domain 7 (bias in selection of the reported result) because nearly all papers did not have statistical analysis plans, which would have meant that nearly all of the non-RCTs in the review would be rated as having some concerns solely on the basis of this domain.

Data analysis

The principal summary measures were odds ratios (ORs) and standardised mean differences. Mortality was measured as hazard ratios (HRs) or relative risk (RR). For binary outcomes, proportions were calculated as the number of participants in each group who did or did not experience the outcome (eg, the number of people reporting drug use at follow-up). For single studies that were not assessed for meta-analysis, adjusted ORs, HRs, and RR were used if these were provided. Otherwise, unadjusted ORs and RR were calculated. Group means and SDs were extracted for continuous outcomes.

All meta-analyses were done in Stata 17 using the meta command for meta-analysis. The Dersimonian Laird[22] random-effects method was used for data synthesis of binary outcomes for which five or more studies contributed data. When there were less than five studies contributing data, the Hartung–Knapp–Sidik–Jonkman[23] method was used. Heterogeneity was identified using the I^2 statistic.

Studies were meta-analysed only if they shared the same comparison group and when follow-up timeframes for the same outcome were within 6 months of each other (eg, 1 month and 6 months). Follow-up was recorded as occurring during incarceration or after release.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Of 36 109 identified papers, 198 met the inclusion criteria and 138 had data that could be could extracted, comprising 126 primary studies (figure; table 1) and 12 secondary studies. Secondary studies were those that used the same sample as the primary study but were reporting outcomes at longer follow-up periods (shaded

rows in the data tables in the appendix pp 166–212 denote secondary studies). Of 126 included primary studies, most were observational (n=79), delivered interventions during incarceration (n=96), and conducted in high-income countries (n=121); none were conducted in a low-income country. The most common interventions assessed were OAT (n=30), therapeutic communities (n=25), and psychosocial interventions (n=13); the most commonly examined outcomes were reincarceration (n=49), re-arrest (n=47), and drug use (n=54). Across the primary studies that provided gender information (n=108), males comprised 87% of the sample (n=352 023). Moreover, more than 25% of the 108 studies involved 100% male samples. Characteristics of included RCTs and observational studies can be found in the appendix (pp 148–165).

Our review identified only 12 studies examining the impact of an intervention on outcomes during incarceration. These studies included research on OAT (n=5),[24–28] needle and syringe provision (n=2),[29,30] HIV and HCV education (n=1),[31] HCV testing and treatment (n=3),[32–34] and supervised opioid withdrawal (n=1).[35] The most common outcomes were drug use, injecting risk behaviours, and HCV outcomes, whereas mortality was reported in only one study (tables 2, 3).[25] In cases in which several studies examined the same outcome but could not be meta-analysed, the single study with the most rigorous design (RCT) or shortest follow-up between incarceration and release was presented. Outcomes for all studies are presented in the appendix (pp 166, 198, 203, 205, 212).

Two studies examined the impact of prison-based OAT on injecting risk behaviours while incarcerated.[24,27] In one RCT (table 2) the OAT group reported significantly lower needle and syringe sharing at 4 months follow-up than the waiting list group (OR 0·21, 95% CI 0·12–0·37),[24] whereas the second OAT study found no significant difference between the intervention and control (OR 0·91, 0·33–2·57;[27] appendix p 166).

One study of needle and syringe provision demonstrated significantly fewer needle and syringe sharing events during incarceration after the introduction of needle and syringe provision than before intervention (OR 0·05, 0·10–0·26).[30]

Six studies assessed the impact of interventions on drug use during incarceration. There was evidence of the benefit of OAT in reducing the number of people reporting opioid use (OR 0·27, 95% CI 0·07–0·98),[26] heroin use (OR 0·29, 0·19–0·46),[24] and injection-drug use (OR 0·17, 0·10–0·30).[24] There was evidence of needle and syringe provision (OR 0·30, 0·16–0·59)[30] reducing injection-drug use, HIV and HCV education programmes (OR 0·17, 0·13–0·21)[31] reducing any drug use, and drug-free units (OR 0·12, 0·03–0·50)[36] reducing opioid use.

Overall, only three HCV intervention studies examined our outcomes of interest during incarceration, two of which examined the impact of point-of-care testing[33,34] and the other that of directly observed therapy.[32] No significant difference between directly observed HCV therapy and self-administered HCV therapy in the number of people with HCV cure (sustained virological response) while in prison (OR 0·79, 0·47–1·34)[32] was recorded (table 3). However, we noted a significant effect of point-of-care testing on the proportion of individuals initiating HCV treatment when compared with conventional testing methods (adjusted OR 82·35, 7·93–855·52).[34]

Only one study, specifically OAT, examined the effect on mortality during incarceration,[25] with significantly lower all-cause mortality (HR 0·25, 95% CI 0·13–0·48) and fatal suicide (HR 0·15, 0·04–0·52) in individuals receiving OAT in prison than those who did not.

Overall, 116 studies examined outcomes after release from incarceration. The outcomes most commonly reported were engagement with the criminal justice system (80 studies) followed by drug use (43 studies). The most examined interventions were OAT (24 studies), therapeutic communities (23 studies), and psychosocial interventions (13 studies; tables 4, 5). Studies that could be assessed by meta-analysis were prioritised for these tables, but in cases in which several studies examined the same outcome but could not be analysed, the single study with the most rigorous design (RCT) or shortest follow-up period between incarceration and release was

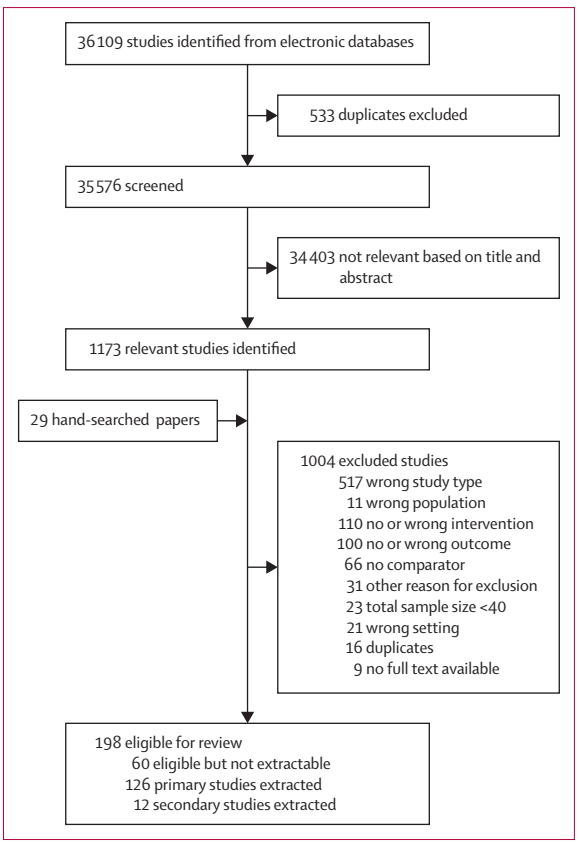

***Figure*: Study flow diagram**

	Injecting risk behaviours				Opioid use				Heroin use				Injection-drug use				Any drug use			
	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2
Opioid agonist treatment	1[24]	382	0·21 (0·12–0·37)	..	1[26]	93	0·27 (0·07–0·98)	..	1[24]	382	0·29 (0·19–0·46)	..	1[4]	382	0·17 (0·10–0·30)	..	..	..	..	..
Psychosocial interventions*	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Therapeutic communities	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Modified therapeutic communities	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Self-help interventions†	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Case management	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Continuity of care	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Naloxone	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Naltrexone	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Needle and syringe provision	1[30]	298	0·05 (0·10–0·26)	..	..	..	..	..	..	..	..	..	1[30]	298	0·30 (0·16–0·59)	..	1[29]	235	0·73 (0·44–1·23)	..
HIV treatment	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HCV treatment	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HIV testing	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HCV and HIV education programmes	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1[31]	5002	0·17 (0·13–0·21)	..
Opioid detoxification	..	..	..	..	1[35]	289	0·61 (0·20–1·77)‡	..	..	..	..	..	..	..	..	..	..	..	..	..
Discharge planning	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Drug-free programmes	..	..	..	..	1[36]	62	0·12 (0·03–0·50)	..	..	..	..	..	..	..	..	..	..	..	..	..
Family interventions	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Substance-abuse treatment programmes	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Combined interventions	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

HCV=hepatitis C virus. *We considered cognitive behavioural therapy, screening and brief interventions, contingency management, and motivational interviewing to be psychosocial interventions. †Self-help with peers and peer-based support groups were categorised as self-help interventions. ‡Odds ratio for negative opioid tests, as reported in the study.

Table 2: **Evidence for effects of interventions to address key outcomes and behaviours related to drug use during incarceration among people who are incarcerated**

	All-cause mortality				Fatal suicide				Fatal overdose				HCV cured				Initiated HCV treatment			
	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2
Opioid agonist treatment	1[25]	16715	0·25 (0·13–0·48)	..	1[25]	16715	0·15 (0·04–0·53)	..	..	..	..	..	..	..	..	..	..	..	..	..
Psychosocial interventions*	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Therapeutic communities	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Modified therapeutic communities	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Self-help interventions†	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Case management	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Continuity of care	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Naloxone	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Naltrexone	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Needle and syringe provision	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HIV treatment	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HCV treatment and testing	..	..	..	..	..	..	..	..	..	..	..	..	1[32]	303	0·79 (0·47–1·34)	..	1[34]	540	82·35 (7·93–855·52)‡	..
HIV testing	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HCV and HIV education programmes	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Opioid detoxification	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Discharge planning	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Drug-free programmes	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Family interventions	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Combined interventions	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Substance-abuse treatment programmes	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

HCV=hepatitis C virus. *We considered cognitive behavioural therapy, screening and brief interventions, contingency management, and motivational interviewing to be psychosocial interventions. †Self-help with peers and peer-based support groups were categorised as self-help interventions. ‡Adjusted odds ratio, as reported in the study.

Table 3: **Evidence for effects of interventions to address key outcomes and behaviours related to mortality and HCV status among people who are incarcerated during incarceration**

presented. The effects of all interventions on outcomes after release are shown in the appendix (pp 168–197, 199–202, 204, 206–211; forest plots for case management can be found in the appendix pp 213–214; for OAT in the appendix pp 215–223; for psychosocial interventions in the appendix pp 224–227; and for therapeutic communities in the appendix pp 229–231).

There were 43 studies examining substance use after release across all interventions. The substance use outcomes that were most commonly reported were any drug use (28 studies),[37–64] heroin use (13 studies)[53,61,65–77] and opioid use (ten studies).[37,38,53,65–67,71,72,78–82] Most of the studies reporting any drug use were either psychosocial, therapeutic community, or case-management interventions, whereas specific drug use was more commonly reported in OAT and modified therapeutic community studies.

Eight studies assessed the impact of OAT during incarceration on drug use after release (appendix pp 168–172), with only six studies that could be synthesised for opioid, heroin, injecting, and any drug use (table 4).[37,65–68,70] There was no evidence of a significant impact of OAT received during incarceration on drug use, opioid use, or heroin or injection-drug use after release from incarceration. There was also no significant impact of OAT on cannabis and cocaine use (appendix p 218).

Six studies examined the potential effect of therapeutic communities in prison on drug use after release[46–50,79,83] (appendix p 184; the studies examining any drug use, injection-drug and opioid use are summarised in table 4). There was evidence of a benefit of therapeutic communities on heroin use in one study (OR 0·33, 95% CI 0·22–0·47),[79] but no evidence from other studies examining any drug use or injection-drug use after release from incarceration, except for two studies that found a reduction in longer-term drug use[49,50] (appendix p 184). Five studies examined the impact of modified therapeutic communities in prison on drug use after release.[51–53,74,80] Four studies examining the impact of modified therapeutic communities on opioid use, heroin use, and any drug use are summarised in table 4. Evidence was scarce for a benefit of modified therapeutic communities on heroin use (OR 0·10, 0·01–0·99),[74] but not opioid use (OR 0·77, 0·19–3·19),[53] or any drug use (OR 0·71, 0·25–2·04).[51,52] One modified therapeutic study comparing drug use before and after intervention showed a reduction in opioid, cocaine, and cannabis use (appendix p 189).

Ten studies examined the effect of psychosocial interventions on drug use after release from incarceration.[40–45,73,84–86] There was no evidence of an effect of psychosocial interventions on heroin use (OR 1·19, 0·59–2·38),[73] injection-drug use at 1–6 months (OR 0·67, 0·31–1·47),[41,42] or any drug use at 3 months or 6 months (OR 1·11, 0·76–1·63).[40,42] There was, however, evidence (appendix p 224) of an effect of psychosocial interventions on any drug use at 12 months (OR 0·28, 0·17–0·44).[43,44] Results for cannabis and methamphetamine use can be found in the appendix (p 180).

Five studies of case management included four RCTs[55–58] and one cohort study.[54] There was no evidence that case management significantly reduced drug use compared with usual care (OR 1·77, 0·98–3·19). Additional analyses can be found in the appendix (pp 192–194).

There was evidence of self-help (OR 0·15, 0·05–0·50)[64] and HIV and HCV education interventions (OR 0·24, 0·09–0·58)[31,60] in reducing injection-drug use, but no evidence of an effect of naloxone (OR 1·17, 0·65–2·11)[76] or naltrexone (OR 1·15, 0·48–2·27)[81] in reducing opioid use.

Overall, there were 80 studies examining the effect of interventions on re-arrest and reincarceration outcomes. The most common interventions used to examine re-arrest or reincarceration were therapeutic community interventions, with 23 identified studies across 24 papers,[46–49,63,79,87–104] followed by OAT (18 studies across 21 papers),[37,38,65,66,69–71,78,82,105–116] psychosocial interventions (eight studies),[40,44,45,85,117–120] and case-management interventions (eight studies).[54,55,57,59,75,121–123]

Three RCTs of OAT examined re-arrest;[78,107,108] no effect of OAT received during incarceration was observed on re-arrest versus usual care at 9–12 months (OR 0·87, 0·56–1·36). Five studies examined reincarceration using data linkage, two of which were RCTs[70,107] and three cohort studies.[112,113,115] OAT received during incarceration did not affect reincarceration compared with usual care 9–12 months after release (OR 0·76, 0·46–1·26). Additional analyses can be found in the appendix (pp 176–179, 222–223).

Four cohort studies examining therapeutic communities reported re-arrest using data linkage.[79,87,92,93] Overall, therapeutic communities were associated with a reduction in re-arrests at 6–12 months (OR 0·72, 0·55–0·95). One RCT[98] and four cohort studies[92,95–97] revealed no effect of therapeutic communities on reincarceration at 12 months (OR 0·84, 0·62–1·13). Additional analyses can be found in the appendix (pp 185–187, 230, 231).

Three observational studies of psychosocial interventions delivered during incarceration reported re-arrest using data linkage.[117–119] There was no evidence of an effect of psychosocial interventions on re-arrest at 18–24 months (OR 0·82, 0·50–1·36). One observational study[44] and one RCT[42] reported reincarceration using data linkage. There was no evidence of an effect of psychosocial interventions (table 5) compared with usual care on reincarceration at 24 months (OR 0·87, 0·39–1·98).

Two studies comparing case management to usual care in self-reported reincarceration at 3–6 months follow-up are presented in table 5. One study was a cohort study[54] and the other was an RCT.[55] Overall, case management did not affect reincarceration (OR 1·50, 0·41–5·48). One cohort study[54] and one RCT[57] measured self-reported re-arrest at 3 months and, compared to usual care, there

	Injecting risk behaviours				Opioid use				Heroin use				Injection-drug use				Any drug use			
	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2
Opioid agonist treatment	..	..	..	..	2[65-67]	291	0·54 (0·10–2·86)	88·3	3[65-67]	331	0·57 (0·22–1·51)	65·4	3[66,68,70]	458	0·78 (0·42–1·42)	69·1	1[37]	223	0·56 (0·30–1·04)	..
Psychosocial interventions*	1[41]	400	0·95 (0·58–1·56)	..	..	..	..	..	1[73]	180	1·19 (0·59–2·38)	..	2[41,42]	793	0·67 (0·31–1·47)	50·0	2[40,42]	914	1·11 (0·76–1·63)	46·5
Therapeutic communities	..	..	..	..	..	..	..	..	1[79]	446	0·33 (0·22–0·47)	..	1[47]	314	1·31 (0·41–4·22)	..	2[47,48]	536	0·78 (0·50–1·23)	0·32
Modified therapeutic communities	..	..	..	..	1[53]	220	0·77 (0·19–3·19)	..	1[74]	41	0·10 (0·01–0·99)	..	..	..	..	..	2[51,52]	230	0·71 (0·25–2·04)	64·3
Self-help interventions†	..	..	..	..	..	..	..	..	..	..	..	..	1[64]	100	0·15 (0·05–0·50)	..	..	..	..	..
Case management	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	5[54-58]	2206	1·77 (0·98–3·19)	82·4
Continuity of care	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Naloxone	..	..	..	..	..	..	..	..	1[76]	205	1·17 (0·65–2·11)	..	..	..	..	..	..	..	..	..
Naltrexone	..	..	..	..	1[81]	90	1·15 (0·48–2·27)	..	..	..	..	..	..	..	..	..	..	..	..	..
Needle-and-syringe provision	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HIV treatment	..	..	..	..	..	..	..	..	..	..	..	..								
HCV treatment	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HIV testing	..	..	..	..	..	..	..	..	1[61]	106	3·51 (0·35–34·89)	..	..	..	..	..	..	..	..	..
HCV and HIV education programmes	..	..	..	..	..	..	..	..	..	..	..	..	2[31,60]	1873	0·24 (0·09–0·58)	0·62	1[60]	371	0·63 (0·42–0·97)	..
Opioid detoxification	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Discharge planning	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Drug-free programmes	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Family interventions	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Combined interventions	..	..	..	..	..	..	..	..	1[77]	209	4·82 (2·00–11·59)	..	..	..	..	..	..	..	..	..

HCV=hepatitis C virus. *We considered cognitive behavioural therapy, screening and brief interventions, contingency management, and motivational interviewing to be psychosocial interventions. †Self-help with peers and peer-based support groups were categorised as self-help interventions.

Table 4: **Evidence for effects of interventions to address key outcomes and behaviours related to drug use among people who are incarcerated following release from incarceration**

	All-cause mortality				Fatal overdose				Non-fatal overdose				Rearrest				Reincarceration			
	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2	K studies	N	Effect estimate	I^2
Opioid agonist treatment	3[6,129,130]	44 510	0·24 (0·17–0·35)	0·0	3[6,129,130]	44 510	0·20 (0·12–0·34)	0·0	2[37,66]	226	0·72 (0·12–4·31)	9·32	3[78,107,108]	364	0·87 (0·56–1·36)	7·9	5[70,107,112,113,115]	2345	0·76 (0·46–1·26)	79·4
Psychosocial interventions	..	..	..	..	..	..	..	..	..	..	..	..	4[117–119]	2604	0·82 (0·50–1·36)	63·9	2[42,44]	674	0·87 (0·39–1·98)	60·6
Therapeutic communities*	..	..	..	..	..	..	..	..	..	..	..	..	6[79,87,92,93]	2566	0·72 (0·55–0·95)	56·57	5[92,95–98]	3998	0·84 (0·62–1·13)	75·8
Modified therapeutic communities	..	..	..	..	..	..	..	..	..	..	..	..	1[52]	91	0·60 (0·21–1·73)	..	1[52]	91	0·52 (0·19–1·41)	..
Self-help interventions†	..	..	..	..	..	..	..	..	..	..	..	..	2[124,125]	1103	0·86 (0·40–1·86)	83·4	2[124,126]	239 282	1·79 (1·32–2·43)	52·2
Case management	..	..	..	..	..	..	..	..	..	..	..	..	2[54,57]	1699	0·75 (0·40–1·38)	72·0	2[54,55]	1147	1·50 (0·41–5·48)	91·3
Continuity of care	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1[147]	362	0·06 (0·02–0·18)	..
Naloxone	..	..	..	..	2[76,127]	4739	NA‡	..	1[76]	205	3·50 (0·72–16·90)	..	..	..	..	..	..	..	..	..
Naltrexone	..	..	..	..	1[128]	70	NA‡	..	..	..	..	..	1[148]	51	0·45 (0·23–0·89)	..	..	..	..	..
Needle-and-syringe provision	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HIV treatment					..	..	..	..	..	..	..	..	..	..	..	..	1[149]	1917	0·31 (0·24–0·39)	..
HCV treatment	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HIV testing	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
HCV and HIV education programmes	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Opioid detoxification	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Discharge planning	..	..	..	..	..	..	..	..	..	..	..	..	1[150]	430	0·34 (0·12–0·98)	..	..	..	..	..
Drug-free programmes	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Family interventions	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1[151]	274	1·63 (0·95–2·81	..
Combined interventions	..	..	..	..	..	..	..	..	..	..	..	..	1[152]	405	0·63 (0·39–1·00)	..	1[152]	405	0·90 (0·54–1·51)	..
Substance-abuse treatment programme	..	..	..	..	..	..	..	..	..	..	..	..	1[153]	645	1·56 (0·93–2·64)	..	..	..	..	..

HCV=hepatitis C virus. *We considered cognitive behavioural therapy, screening and brief interventions, contingency management, and motivational interviewing to be psychosocial interventions. †Self-help with peers and peer-based support groups were categorised as self-help interventions. ‡Effect size could not be calculated because only the number of deaths was reported rather than mortality.

Table 5: **Evidence for effects of interventions to address key outcomes and behaviours related to mortality, overdose, rearrest, and reincarceration among people who are incarcerated following release from incarceration**

was no effect for case management (OR 0·75, 0·40–1·38). Additional analyses can be found in the appendix (pp 193–194, 214).

Compared with usual care, self-help interventions were not shown to affect re-arrest at 24 months (OR 0·86, 0·40–1·86),[124,125] but there was evidence of increased reincarceration at 24 months (OR 1·79, 1·32–2·43).[124,126] Additional analyses can be found in the appendix (p 199) and forest plots in the appendix (p 228).

Two RCTs[37,66] measured non-fatal overdose among people who received OAT during incarceration (table 5). Compared with the control (appendix p 219), there was no evidence of an effect of OAT 1 month after release (OR 0·72, 0·12–4·31). One study of naloxone that measured non-fatal overdose at 3 months follow-up found no significant effect compared with control (OR 3·50, 0·72–16·90).[76]

The only interventions identified in the review that examined mortality as an outcome were OAT, naloxone, and naltrexone. Studies of naltrexone (K=1) and naloxone (k=2) could not be used to estimate intervention effects because these studies reported the number of deaths rather than mortality.[76,127,128]

Three studies measured all-cause mortality in the first 4 weeks since release from prison in people who had received OAT while in prison compared to those who had not received OAT while in prison.[6,129,130] OAT was associated with lower all-cause mortality in the first 4 weeks of release (RR 0·24, 95% CI 0·17–0·35), as well as drug-related deaths (RR 0·20, 0·12–0·34). Two studies measured all-cause mortality on the basis of OAT status in the community after release from incarceration.[6,114] Compared with those not receiving OAT, OAT was associated with lower all-cause mortality (RR 0·09, 0·02–0·56).[131] Forest plots for OAT mortality can be found in the appendix (pp 220–221).

Most RCTs were assessed as having some concerns, mainly because of bias in outcome measurement (relying on self-report), missing outcome data, or bias in the randomisation process. Notably, bias in the randomisation process was prevalent in case-management[56,57,59,75] and therapeutic or modified therapeutic community studies,[47,98,99,132–134] mainly because of the absence of a detailed description of the randomisation process. Studies with a high risk of bias were found across all interventions, often because of missing outcome data.

Observational studies were mostly at a moderate risk of bias, primarily because of potential confounding. Similar to RCTs, other areas commonly rating as moderate risk of bias were caused by missing data or measurement of outcomes, as many relied on self-report. Observational studies at serious risk of bias were found across all interventions, with a high frequency in OAT interventions,[26,27,68,69,106,109,112,113,135] and tended to be because studies did not control for confounding (risk of bias visualisations by outcome and intervention as shown in the appendix pp 234–279).

Discussion

To our knowledge, this is the first systematic review and meta-analysis to examine the effect of a broad range of interventions targeting people who use drugs who were incarcerated or recently released from incarceration. We synthesised the results of 126 studies assessing outcomes including drug use, mortality, and recidivism. Our findings suggest that receiving OAT in prison or in the community reduces the risk of death both in prison and after release, particularly in the first 4 weeks after release. There is some evidence of therapeutic communities in reducing re-arrest and reincarceration in studies that measured these outcomes using data-linkage methods. Studies examining injecting risk behaviours in prison suggest that OAT and needle and syringe provision can be effective in reducing needle sharing and drug injection.

There was no evidence of a benefit of OAT, psychosocial interventions, therapeutic communities, or case management on recidivism outcomes or drug use. In the case of OAT, it may have reduced opioid use, but there would be no expected benefit on use of non-opioid drugs. It is important to note that some of these studies, particularly OAT interventions, were at a moderate-to-high risk of bias because of missing data or confounding. High attrition rates could have affected the ability of these studies to detect a significant difference between experimental and treatment groups. Additionally, the majority of studies relied on self-reported data for measuring drug use, which past research has shown can be vulnerable to biases such as social desirability bias,[136–138] and could result in under-reporting of drug use. Only a small number of studies used urinalysis to validate self-reported data. A recent systematic review, however, found that overall, agreement between self-reported drug use and biological samples ranged from good to excellent, including in criminal justice settings and those with perceived consequences for reporting drug use.[139]

It is also important to consider the heterogeneity within psychosocial and therapeutic community interventions, which might have affected the ability to draw conclusive results. For example, psychosocial interventions might differ from one another in their theoretical basis (eg, cognitive behaviour therapy or motivational interviewing) or programme duration. Specific features might also differ from one therapeutic community to another, for example incorporating work release programmes or having drug testing requirements. It is not possible to discern whether specific features of these heterogenous interventions contribute to better drug use or recidivism outcomes.

This review highlighted important gaps in the literature, suggesting the need for better data. Firstly, there was a general scarcity of data. It is important to note that although this review examined a broad range of outcomes, many were underexamined in the literature, such as specific drug use, sexual and injecting risk

behaviours, and non-fatal overdose and self-harm. This review explored interventions delivered during prison and after release from incarceration, yet we only identified 12 studies examining outcomes while individuals were incarcerated. Less than half of the included studies used randomised designs. Finally, we found no evidence of studies done in low-to-middle-income countries. Each of these research gaps is important to target in future research.

The scarce available evidence suggests that OAT and needle-and-syringe interventions can reduce drug use, injecting risk behaviours, and mortality during incarceration. The few studies that did examine injecting risk behaviours during incarceration, however, did not specify whether needle sharing was distributive or receptive and only provided information regarding needle sharing in general. Only one study, specifically one investigating OAT, examined mortality in prison and found that OAT significantly reduced deaths in custody. We only identified two HIV and HCV studies fitting our inclusion criteria that measured outcomes during incarceration and three after incarceration. A review of the available evidence on prison-based interventions for people who use drugs by the European Monitoring Centre for Drugs and Drug Addiction similarly concluded that although there is robust evidence of many interventions in the community, more prison-based research is needed on the effects of interventions such as needle-and-syringe programmes and take-home naloxone.[140] Given that HCV incidence is elevated in prison settings and is particularly high among people with a history of IDU,[141] it is important that more studies examining the effect of HCV interventions on drug use and HCV-related outcomes such as testing uptake, treatment completion, successful viral eradication, and reinfection are conducted.

A systematic review of global coverage for interventions to manage and prevent drug-related harms found that although around 90 countries had OAT or needle-and-syringe programmes programmes, there were no data on their implementation and only five of them provided high coverage.[142] Thus, it is not only important that interventions such as OAT and needle-and-syringe programmes are better implemented, but also that high coverage is reached and maintained, particularly in carceral settings, where the risk of drug-related harms is elevated. It is also important to consider the dosage of OAT provided at release, as two large studies identified this as having a significant effect on its benefits.[143,144] The evidence base for psychosocial and therapeutic community interventions could be strengthened by standardising programmes and further experimental study using randomised designs, yet these strategies have limited effectiveness in community settings. It is crucial that more research evaluates interventions within prisons and measures outcomes while individuals are still incarcerated.

We identified clear limitations in the evidence on this issue, the first related to a scarcity of studies examining outcomes both during and after incarceration. Second, many studies had moderate-to-high risk of bias because of either missing outcome data or the lack of controlling for confounders. The issue of confounding was particularly evident for OAT observational studies measuring drug use and recidivism outcomes. Most psychosocial and therapeutic community studies were observational studies, and although many controlled for confounding variables, they remain at substantial risk for residual confounding.

Although our review included studies published in other languages, most of them originated from English-speaking countries and thus present a geographically limited perspective of prison research. The majority of the evidence relates to interventions for opioid-use disorder, which might be less relevant to other regions of the world such as South America, in which opioid-use disorder is less prevalent but exerts the highest disease burden.[145]

There were also many studies that we could not use in the review because they used dissimilar measures, and as such could not be harmonised with other studies, or they did not stratify results by the target group (ie, people who use drugs that were recently or currently incarcerated). To maximise the number of studies, every effort was made to contact authors to obtain the required data. It is also important to consider the effect of serious mental illness on the outcomes we measured, particularly mortality. We were unable to examine the effect of comorbid mental illness and drug use, namely because in many studies, this information was not reported, but also because serious mental illness was often an exclusion criterion. Finally, we were unable to stratify results by sex or ethnicity, which might have had an effect on the findings.

Our findings have important implications for individual and public health as well as policy because they demonstrate the impact of interventions in reducing harms for people who use drugs and indicate a need for more evidence-based interventions at reducing harms within carceral settings. Populations within prison may include people that are difficult to identify and treat within the community, and thus incarceration represents an important opportunity to improve the health of individuals before they return to the community. Moreover, reducing drug use has important public health implications including reducing drug-related harms and reoffending. Although there is ongoing support for efforts to reduce incarceration,[146] there are evidence-based interventions such as OAT that significantly reduce mortality for people incarcerated and recently released from prison. Coverage of OAT should be increased in carceral settings, including achieving optimal dosing, and should be continued after release. Therapeutic communities might reduce recidivism, but more experimental data are needed as most studies were

observational. Similarly, OAT and needle-and-syringe programmes appear to reduce drug use and injecting risk behaviours while people are still incarcerated, but more data are required that incorporate coverage and delivery strategies. As prison-based services are often outside public scrutiny, further assessment of these interventions is imperative in providing a stronger evidence base for the provision of such services both within prison and after release.

Contributors

LD, FLA, JG, BH, EBC, and LTT contributed to conceptualisation and data curation. CM, GM, OL, and LTT conducted the screening, extraction, and risk of bias. CM, GM, and OL conducted the statistical analysis. LD, JG, BH, and EBC completed screening, double checked the extractions, and oversaw the statistical analysis including verifying the data. CM led the writing of the manuscript. LD, FLA, JG, BH, EBC, LTT, GM, OL, and MF contributed to reviewing and editing. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

In the past 3 years, LD and MF have received investigator-initiated untied educational grants for studies of opioid medications in Australia from Indivior and Seqirus. FLA has had grants from the US National Institutes of Health, Gilead Sciences, and MSD over the past 3 years. JG is a consultant or advisor and has received research grants from AbbVie, bioLytical, Camurus, Cepheid, Gilead Sciences, Hologic, Indivior, and Merck or MSD. These companies and organisations had no knowledge of or role in the design, conduct, interpretation, or publication of these findings. All other authors declare no competing interests.

Data sharing

Researchers wishing to undertake additional analyses of the data are invited to contact the corresponding author.

Acknowledgments

This review was supported by an Australian National Health and Medical Research Council (NHMRC) ASCEND Programme grant (1150078), an NHMRC Investigator Grant (2016825), and the National Drug and Alcohol Research Centre (NDARC). NDARC is supported by funding from the Australian Government Department of Health under the Drug and Alcohol Programme. The views expressed in this publication do not necessarily represent the position of the Australian Government. LD is supported by an Australian NHMRC Senior Principal Research Fellowship (APP1135991). FLA has research funding from the National Institute on Drug Abuse (R01DA029910, R01DA041271, R01DA033679, and R01DA043125), National Institute on Allergy and Infectious Diseases (R01AI177082), and the Fogarty International Centre (R01TW012674, D43TW012492, and D43TW011324). We thank Daisy Gibbs, Brodie Clark, Rachel Jenkins, Michelle Lynch, Aidan Pillard, Sophie Ottaviano, Jeremy Ireland, Xin Zhou, Madeline News, Michael Bennetts, and Mary Tate for their assistance in data screening, data extracting, or risk of bias. We thank Thomas Santo Jr for provision of calculated effects for OAT mortality data. We also thank Angela Robertson, Kimberly Page, Jennifer Evans, Thana Khawcharoenporn, Lynda Stein, and Suzanne Sales for providing additional data to inform this review.

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