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Integration of care for HIV and opioid use disorder: a systematic review of interventions in clinical and community-based settings

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Abstract

Objective: We sought to identify optimal strategies for integrating HIV- and opioid use disorder-(OUD) screening and treatment in diverse settings.

Design: Systematic review.

Methods: We searched Ovid MEDLINE, PubMed, Embase, and PsycINFO and pre-identified websites. Studies were included if they were published in English on or after 2002 through May 2017, and evaluated interventions that integrated, at an organizational level, screening and/or treatment for HIV and OUD in any care setting in any country.

Results: Twenty-nine articles met criteria for inclusion, including 23 unique studies: six took place in HIV care settings, 12 in opioid treatment settings, and five elsewhere. Eight involved screening strategies, 22 involved treatment strategies, and seven involved strategies that encompassed screening and treatment. Randomized controlled studies demonstrated low to moderate risk of bias and observational studies demonstrated fair to good quality. Studies in HIV care settings (n=6) identified HIV- and OUD-related clinical benefits with the use of buprenorphine/naloxone for OUD. No studies in HIV care settings focused on screening for OUD. Studies in opioid treatment settings (n=12) identified improving HIV screening uptake and clinical

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Authors' contributions

All authors contributed to the writing of the manuscript. B.J.O. and E.J.E. conceived the idea. B.J.O. wrote all major drafts of the manuscript. B.J.O., N.M., and M.F. contributed to collecting the data. B.J.O., N.M., J.M.T., and E.J.E. analyzed the data and interpreted the results. N.M., M.F., M.V., M.P.M., J.M.T., and E.J.E. contributed to the critical review of the manuscript.

Conflicts of interest

There are no conflicts of interest.

benefits with antiretroviral therapy when provided on-site. Counseling intensity for OUD medication adherence or HIV-related risk reduction was not associated with clinical benefits.

Conclusion: Screening for HIV can be effectively delivered in opioid treatment settings, yet there is a need to identify optimal OUD screening strategies in HIV care settings. Strategies integrating the provision of medications for HIV and for OUD should be expanded and should not be contingent on resources available for behavioral interventions.

Registration: A protocol for record eligibility was developed a priori and was registered in the PROSPERO database of systematic reviews (registration number CRD42017069314).

Keywords

HIV; opioid-related disorders; integrated delivery system; systematic review

Introduction

HIV and opioid use disorder (OUD) are substantial global risk factors for disability and mortality, and they manifest as intersecting epidemics worldwide [1, 2]. Particularly prevalent among persons living with HIV (PLWH) [3, 4], OUD is associated with worse clinical outcomes, ongoing HIV risk behaviors [5], and ongoing HIV transmission [6, 7]. The growing burden of OUD and related HIV outbreaks highlight a need for novel strategies for screening and treatment of both disorders [8, 9]. These public health trends have garnered unprecedented motivation for the adoption of unified models for OUD management and primary care, including HIV primary care [10].

Although care for people with or at risk for HIV and OUD can be complex [11], integrating HIV- and OUD-related care is feasible in HIV care settings, opioid treatment settings, and other care sites like primary care or public health clinics [12–21]. Integrated care is valued by PLWH with OUD [22, 23], a patient population that has demonstrated limited engagement with routine health services [24] and that is subject to overlapping forms of stigma that may obstruct care and worsen biologic and/or social outcomes [25–27]. International organizations, including the Joint United Nations Programme on HIV/AIDS and the World Health Organization [28, 29] as well as US health reform laws [30] support the integration of substance use disorder services with primary care (including HIV primary care). Yet integration often does not occur [31, 32], how to integrate effectively in different care settings remains poorly understood, and quality metrics for integrated care are lacking [33].

Previous systematic reviews have demonstrated the feasibility and impact of integrating HIV care with other chronic conditions, including cardiovascular disease, diabetes [34], and mental health disorders [35]. One systematic review examined strategies for integrating HIV- with substance use-related care including 51 articles published through October 2015, but it did not use opioid-derived search terms nor compare between integrated and non-integrated models or between different integration strategies [36]. Therefore, we performed a systematic review to identify interventions wherein HIV and OUD-related care are integrated, across the spectrum of care from screening to treatment and across diverse care

settings. This review will generate a comprehensive understanding of the evidence for integrated care to inform practice and policy for a large and vulnerable population.

Materials and methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards of quality for reporting systematic reviews [37]. This is part of a larger systematic review on the integration of OUD care with the care of infectious complications including hepatitis C and HIV. We developed a protocol for study eligibility *a priori* and registered it in the PROSPERO database of systematic reviews (registration number CRD42017069314) [38]. Our data synthesis process drew from realist synthesis, an analytic approach that considers the interaction between context, mechanism, and outcome in evaluating an intervention [39–41]. This study was not considered human subjects research by the Yale School of Medicine Human Investigation Committee.

Search strategy

Guided by the PICOS framework, we defined the populations, interventions, comparisons, outcomes, and study designs of interest *a priori* [42] (see Text Box). We defined integrated interventions as screening and/or treatment (including medications—such as antiretroviral therapy [ART], methadone, buprenorphine/naloxone, or naltrexone—or behavioral interventions) for HIV and OUD, employed at an organizational level [43].

We searched Ovid MEDLINE, PubMed, Embase, and PsycINFO on May 24, 2017. We identified additional studies by scanning other systematic reviews and bibliographies. We also searched the websites of the following pre-identified organizations: Society for General Internal Medicine, Substance Abuse and Mental Health Services Organization, the Association for Medical Education and Research in Substance Abuse, and the U.S. Health and Human Services' HIV.gov website. We limited our search to studies with human subjects and those published in the English language. We also limited our search to those studies published in or after 2002 for three reasons. First, buprenorphine/naloxone was approved by the US Food and Drug Administration as the first schedule III medication for the treatment of OUD in 2002, heralding a new era for the outpatient management of OUD [44], including in PLWH [45]. Second, in late 2001 the US Centers for Disease Control and Prevention published new recommendations for screening for HIV that focused on the expansion of screening in all medical settings, including those that provide services related to substance use disorders [46]. Third, this time point corresponds approximately with the advent of the late ART era (2000 and later), during which HIV treatments were associated with greater efficacy than previous eras [47].

To produce relevant vocabulary terms, we analyzed five previously identified key articles using the Yale MeSH Analyzer (http://mesh.med.yale.edu/). In each database, we ran scoping searches and used an iterative process to translate and refine the search strategies. We used the previously identified articles to validate the success of our searches (eSearch 1 in Supplement).

Study selection

Two authors (BO and NM) independently screened titles to remove clearly irrelevant citations, then these two authors independently screened abstracts using an algorithm developed *a priori*, resolving conflicts by consensus. We used Covidence, a systematic review software, to facilitate screeners' independent organization, retrieval, and assessment of articles [48].

Quality assessment

Two reviewers independently completed the quality assessment of each study using the Cochrane Risk of Bias Tool for randomized trials [49] and the Newcastle-Ottawa Scales for observational studies [50] (BO reviewed all articles; NM, JT, and EJE shared the role of second reviewer).

Data extraction

For each screened article, two authors independently abstracted information about the context (HIV care settings, opioid treatment settings, or other), participants, intervention type (screening or treatment), and outcomes (including uptake of services, behavioral or biochemical outcomes, and general health outcomes along the care continuum [51]) in a standardized form. Extraction occurred concurrently with quality assessment by the same two authors (BO and either NM, JT, or EJE).

Intervention and outcome heterogeneity precluded meta-analyses. Instead, because we were interested in how integration strategies differed in different care settings, we drew from a realist synthesis strategy in which reviewers delineated the contextual influences that contributed to the outcomes of interest [40, 41] based on the following typology.

Intervention typology

Similar to previous systematic reviews on the integration of HIV care with the management of other disorders [35, 36], we classified interventions according to the entry point at which patients receive care: HIV care settings, opioid treatment settings, and other settings. HIV care settings included Infectious Disease clinics, specialized HIV clinics, and community-based HIV or AIDS services organizations (which focus on case management and other supportive services, and may provide clinical services). Opioid treatment settings included opioid treatment programs or settings licensed to provide medications for OUD. Other clinical and community-based settings included those that could not be classified into the previous categories. In addition to corresponding with other reviews, this typology may facilitate the development of best-practices in different care settings.

Results

Our search yielded 7,178 articles and 3,188 remained after the removal of duplicates (Figure 1). After screening titles, we screened 594 abstracts and identified 29 articles that met criteria for inclusion [12, 15, 17–20, 52–74]. On three occasions, multiple articles presented data from one study ([12, 17–19, 57, 62], [65, 66], and [69, 75]) yielding a total of 23 unique studies. These included eight randomized trials [20, 55, 58, 61, 63, 64, 69, 73, 75], 13 cohort

studies [12, 15, 17–19, 52, 53, 56, 57, 59, 60, 62, 65–68, 70–72], and two cross-sectional studies [54, 74].

Description of studies

We identified six studies that occurred in HIV care settings [12, 17–20, 57, 58, 61–63, 67, 73], 12 studies that occurred in opioid treatment settings [52–56, 60, 64–66, 68–70, 74, 75], and five studies that occurred in other settings, including correctional settings [71, 72], primary care clinics [58], mobile syringe-exchange units [15] or public health clinics [59]. The added element that defined interventions as integrated care was most often either OUD care or HIV care alone to a facility already providing care for the other disorder; in two studies both OUD and HIV care were introduced simultaneously and correctional facilities were the points-of-entry for both [71, 72]. With respect to outcomes measured, 19 studies examined clinical and laboratory outcomes, four examined health-related quality of life [54, 58, 62, 72], two examined quality of care indicators [18, 54], one examined cost [19], and one examined patient satisfaction [74].

While most studies took place in North America (n=15 in the United States and n=1 in Canada), four took place in Europe [53, 54, 60, 68] and three took place in Asia [52, 59, 74]. Half of studies had a follow-up period of 12 months or longer (Table 1).

Quality assessment

The risk of bias among randomized studies was low to moderate (eTable 1 in Supplement), although no randomized studies blinded participants and personnel of the treatment phase and few described blinding of outcome assessment [55, 73]. Cohort studies were of fair to good quality (eTable 2 in Supplement). The most common reason for low quality assessment was the low quality of the non-exposed cohort (9 of 13), which was either drawn from a different source as the exposed cohort or no comparator cohort was generated other than a pre-intervention baseline [12, 15, 17–19, 52, 56, 57, 59, 60, 62, 68, 70, 71].

Interventions in HIV care settings

Among studies in HIV care settings (n=6), five examined interventions involving medications for OUD [12, 17–20, 57, 61–63, 73] and one in which motivational interviewing, social work, and peer groups were offered [67] (Table 2). Four of the five medication-based interventions included buprenorphine/naloxone and recruited an aggregate of 414 patients [12, 17–20, 57, 62, 63, 73], while one offered injectable naltrexone [61] and assigned 25 patients to the intervention and 26 to treatment-as-usual. Studies that centered on the provision of buprenorphine/naloxone demonstrated that administering these medications in HIV clinics correlates with clinical benefits such as initiation ART [12], decreased needle sharing [57], decreased opioid use [17],; operational sequelae included increased labor, overhead, and urine toxicology costs [19] as well as more primary care visits to the HIV specialist [63]. Health-related quality of life and HIV quality of care indicators were favorably associated with buprenorphine/naloxone administration if it was continued for one year [62]. Injectable naltrexone offered in HIV care settings demonstrated feasibility and safety and suggested that those offered injectable naltrexone were more likely to initiate and be retained on treatment than those offered treatment-as-usual, but the study

was not powered to detect clinical HIV or OUD outcomes [61]. The study whose intervention did not provide on-site treatment with medications for OUD, but instead on-site motivational interviewing with referral for medications, did not show improvements in HIV clinical outcomes [67].

Two randomized controlled trials examined different intensities of adjunctive counseling in addition to buprenorphine/naloxone [20, 73].Neither the addition of nurse-led counseling and adherence management [73], nor nurse-led enhanced medical management improved HIV- or OUD-related outcomes [20] compared favorably to physician-delivered medical management of buprenorphine/naloxone.

Interventions in opioid treatment settings

Among studies in opioid treatment settings (n=12), all occurred in outpatient settings and one included hospital-based detoxification programs [55], two examined HIV testing and counseling [55, 69, 75], six examined HIV medication management with antiretroviral therapy (ART) [53, 56, 60, 64–66, 68, 70], and three examined interventions that involved both HIV testing and counseling as well as ART management [52, 54, 74] (Table 3). In two randomized trials, HIV testing and counseling alone in opioid treatment settings led to increased HIV testing performed and feedback of results [55, 75], but the addition of sexual risk-reduction counseling did not lead to significant changes in sexual risk behaviors [69]. ART management in opioid treatment settings involved the prescription of ART in methadone clinics [68] or directly-administered ART (DAART) [53, 56, 60, 64–66, 70]. DAART in residential opioid treatment settings [53] and methadone clinics was safe and feasible [56, 60, 64–66, 70], but a randomized trial demonstrated that DAART compared with self-administered ART in methadone clinics did not lead to significant differences in clinical outcomes [63].

Interventions in opioid treatment settings that involved both HIV counseling and testing as well as ART management demonstrated high patient satisfaction [74], achievement of HIV and addiction quality indicators and higher likelihood of ART receipt [54], but no significant differences in clinical outcomes or health-related quality of life [52, 54].

Interventions in other settings

Other interventions (n=5) occurred in primary care clinics [58], mobile syringe-exchange units [15], government-run public health clinics [59], or used the criminal justice system as a point-of-entry [71, 72]. An intervention in primary care settings demonstrated that those receiving buprenorphine/naloxone, when randomized to brief sexual risk management or enhanced sexual risk management, exhibited similar process (retention in OUD treatment) and clinical outcomes (health-related quality of life or sexual risk) [58]. When methadone and HIV testing and treatment were integrated into public health clinics, more clients seek testing and start ART [59].

One small cohort (n=13 patients) demonstrated that HIV medication management in a syringe-exchange mobile unit led to improvements in HIV-1 RNA levels and CD4 cell counts in a pre-post design [15].

Two studies enrolled participants upon release from the criminal justice system. These demonstrated that, compared to those who did not opt for buprenorphine/naloxone, those who did along with ART provided in a community-based setting demonstrated improved viral suppression [72] and fewer opioid cravings [71].

Implementing integrated care

Many studies did not explicitly describe specifics of program implementation, such as the additional staff or training needed [12, 15, 17, 18, 52–55, 57–60, 69, 74, 76]. When a need for additional staff was described in the studies, these involved study personnel such as study clinicians [61] or research assistants [64, 70], nurses [19, 20, 63], peers or counselors [67, 71, 72], addiction clinicians [19, 73] or HIV clinicians [56, 68].

Discussion

Summary of the evidence

This systematic review identified 23 studies that investigated the integration of care for HIV and OUD across a range of clinical settings, including HIV care settings, opioid treatment settings, primary care or public health clinics, mobile syringe-exchange units, and the US criminal justice system. These data suggest three principles to guide further research, clinical practice, and policy. First, HIV testing can be successfully integrated into a range of settings where OUD care occurs, including primary care clinics, hospital-based detoxification programs, mobile syringe-exchange vans, and methadone clinics. However, there is a lack of studies focused on OUD screening in HIV care settings. Second, medications for the treatment of HIV and OUD can be integrated into a range of HIV, opioid treatment, and other settings, but it is unclear which clinicians should be optimally involved (infectious diseases specialists, addiction specialists, primary care physicians or other providers). Third, while high-quality, randomized trials support the integration of HIV- and OUD-related care in specialty settings (HIV clinics and methadone clinics), high-quality evidence is needed to identify integration strategies in other settings such as primary care clinics, mobile syringe-exchange units, and community-based AIDS services organizations.

While previous systematic reviews have demonstrated that HIV care can be integrated with care for other disorders [34, 35] including substance use disorders [36], this is the first systematic review to focus on OUD specifically and draw comparisons between integration strategies. By focusing specifically on OUD and not all substance use disorders, this review facilitates comparison across models and strategies (for example, medications versus behavioral interventions). This review is timely given the evolving burden of OUD in the US, the interplay between the OUD epidemic and HIV transmission globally [8, 9, 77, 78], and the need for integrated care for these two disorders [10, 23, 33].

Medications are the cornerstone of treatment for HIV [79] and for OUD [80]. Integrated care strategies identified in this review focused on administering medications for both disorders in single organizations. While behavioral interventions may be important adjunctive treatments for PLWH who have OUD, the strategies identified in our review did not demonstrate added benefit to nurse-led adherence management nor to sexual risk-reduction

counseling. Therefore, a lack of ability to provide psychosocial and behavioral interventions should not be a barrier to the development of integrated care strategies. This is concordant with other systematic reviews that have not demonstrated benefit of behavioral interventions when combined with medications in the management of OUD [81].

Of the FDA-approved medications for the management of OUD, buprenorphine/naloxone and naltrexone are two practical options for HIV and/or primary care providers in the US given the regulatory restrictions on methadone dispensing [80, 82]. The evidence appraised here supports the use of buprenorphine/naloxone in HIV care settings. When enough prescribers are available to ensure sufficient coverage and a buprenorphine/naloxone coordinator (such as a nurse or counselor) is available, this integrated practice is feasible and can be highly satisfying to providers [83]. Only one study examined the use of naltrexone in HIV care settings and demonstrated feasibility and safety only [61]. This identifies a need for clinicians who care for PLWH to be proficient and certified to prescribe buprenorphine/naloxone given a low prevalence of certified providers [84] and as prioritization among HIV providers often localizes OUD treatment lower than other health domains [85]. Furthermore, in countries where there are regulations on the prescription of buprenorphine/naloxone or methadone by primary care providers, such as in the United States, policies that decrease these barriers should be considered [86, 87] to increase access.

However, no studies directly compared methadone and buprenorphine/naloxone in integration strategies that were otherwise identical. Methadone remains an integral and effective treatment for OUD and is associated with HIV risk reduction [88].

The evidence appraised here supports the expansion of HIV medication management in opioid treatment settings, including methadone clinics, settings that provide buprenorphine/naloxone, and other settings that offer evidence-based strategies for harm reduction among people with OUD such as mobile needle-exchange vans. Directly-observed ART therapy is feasible in these settings but not necessary, as data to date do not suggest that DAART is superior to self-administration [64]. As HIV medical management has become simpler [89], it is feasible that primary care clinicians including advanced practice nurses and non-specialists can provide this care in opioid treatment settings [90].

Gaps in the literature persist regarding optimal strategies for screening for OUD in HIV treatment settings as well as the optimal arrangements of providers who should be involved in integrated care provision. Minimizing barriers that primary care providers face in providing evidence-based treatments for OUD and/or HIV is needed. The development of best practices will depend upon filling these gaps, as well as ongoing feedback from front-line providers and patients who are engaging in novel integrated models [91]. Effectiveness-implementation hybrid study designs—which evaluate clinical interventions while collecting data on implementation [92]—may allow researchers to identify ideal models regarding staffing, training, and infrastructure, and such efforts are currently underway to address implementation of addiction treatment in HIV care settings [93]. Implementing co-located services may be a non-trivial investment in many settings and so future research should identify those implementation strategies that are associated with improved outcomes, cost-effectiveness, and feasibility.

Limitations

This systematic review was limited to only English-language publications, so studies from low- and middle-income countries may have not been included. However, a recent systematic review of articles that focus on integration of HIV with substance use disorder care included studies from other languages and only identified one, and this was published before our time period of interest [36]. By including only studies published in or after 2002, we may have missed articles from earlier periods. However, treatment for OUD and screening recommendations for HIV changed considerably in 2001 and 2002 [45–47], suggesting opportunities for integrated care not applicable to previous time periods. The varying nature of the clinical sites and interventions prohibited meta-analyses, and so we employed a narrative synthesis based on a realist framework to identify strategies that work in different clinical contexts [41]. Because we focused on interventions wherein care was integrated within one organization, we may have missed effective strategies that promote coordinated care across organizations [94]. Finally, because we included only quantitative studies, we did not include qualitative studies that may offer valuable insights into complex care processes and patient experiences [95].

Conclusion

Integrating HIV and OUD-related care can be effective across a range of settings and can be associated with improved provision of evidence-based treatments and better patient outcomes. Moderate to high-quality evidence supports the use of medications for HIV and OUD when integrated in single sites, including methadone clinics, HIV clinics, other opioid treatment settings, primary care clinics, or sites that offer evidence-based harm reduction strategies such as mobile syringe-exchange units. A lack of ability to provide behavioral interventions should not prohibit organizations from offering buprenorphine/naloxone to PLWH with OUD, and a lack of infrastructure for DAART should not prohibit organizations from offering HIV medication management. Policies that reduce the barriers for primary care providers to offer buprenorphine/naloxone or methadone to PLWH with OUD should be considered so that access to evidence-based medications can increase and strategies for care integration in primary care sites can be evaluated.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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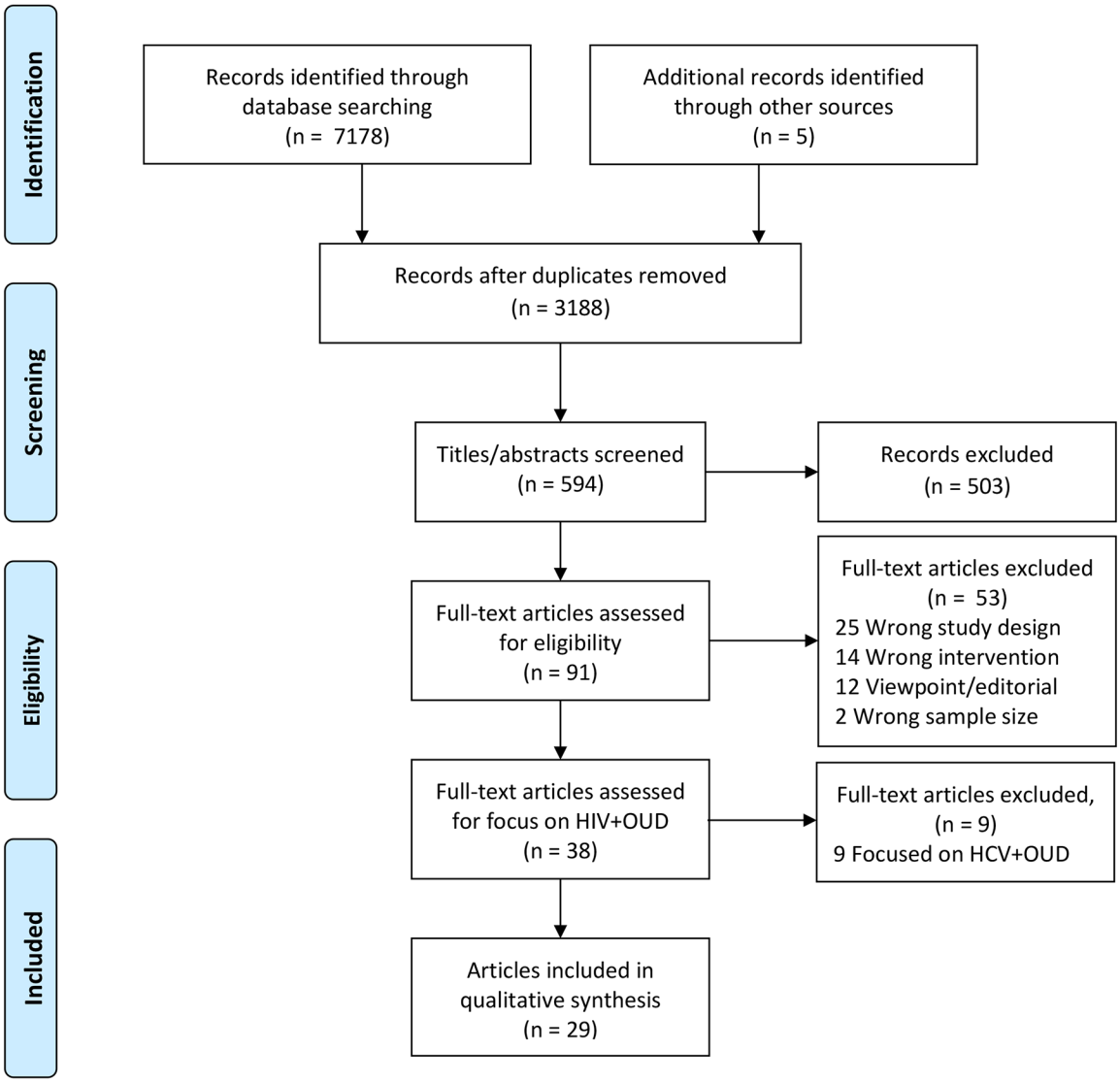

Figure 1.
PRISMA flow chart of study selection.(OUD: opioid use disorder; HCV: hepatitis C virus)

Table 1.

Characteristics of studies (n=23).

Characteristic	n (%)
Study design	8 (35)
Randomized trial	13 (57)
Cohort study	2 (7)
Cross-sectional study	
Point of entry into care	6 (26)
HIV care setting	12 (52)
OUD care setting	5 (22)
Other facility	
Added intervention	0 (0)
OUD screening only	5 (22)
OUD treatment only	1 (4)
OUD screening and treatment	1 (4)
HIV screening only	8 (35)
HIV treatment only	6 (26)
HIV screening and treatment	2 (9)
Both HIV care and OUD care	
Length of follow-up	2 (9)
0 months (cross-sectional)	6 (26)
<6 months	4 (17)
6–12 months	11 (48)
>12 months	
Location of study	16 (70)
North America	4 (17)
Europe	3 (13)
Asia	

Table 2.

Characteristics of interventions based in HIV care settings (n=6).

Added intervention	First author(s) (or study name) and country	Study design	Intervention description	Number of patients in intervention	Key findings
OUD[1] care	BHIVES[2] Collaborative 2011 USA [13, 18–20, 55, 60]	Cohort	PLWH[3] with OUD initiated buprenorphine/naloxone in HIV clinics	303	Initiating buprenorphine/naloxone in HIV clinical settings correlates with: • initiation of antiretroviral therapy and improved CD4 lymphocyte counts [13] • decreased needle-sharing but no change in sexual risk behaviors [55] • decreased opioid use [18] • improved health-related quality of life (if buprenorphine/naloxone continued for one year) [19] • improved HIV quality of care indicators (if buprenorphine/naloxone continued for one year) [60] • increased labor, overhead, and urine toxicology costs [20]
	Korthuis 2017 USA [59]	Randomized trial	PLWH with OUD initiated extended-release naltrexone in HIV clinics	25 (26 control: treatment as usual)	Compared with treatment as usual, extended-release naltrexone is feasible and safe for treatment of OUD in HIV clinics; study not powered to detect secondary HIV or OUD outcomes
	Lucas 2010 USA [61]	Randomized trial	PLWH with OUD initiated buprenorphine/naloxone in an HIV clinic	48 (48 control: referral to OUD treatment	Compared with referred treatment, HIV clinic-based buprenorphine/naloxone led to: • quicker initiation of buprenorphine/naloxone • greater use of buprenorphine/naloxone over 12 months • fewer urine drug tests positive for opioids and cocaine • more visits with HIV providers • no significant change in HIV-1 RNA levels
	Sullivan 2006 USA [71]	Randomized trial	PLWH with OUD initiated buprenorphine/naloxone in an HIV clinic and brief physician management with or without nurse-led counseling and adherence management	16	No significant differences based on counseling intervention were detected in CD4 cell count, HIV-1 RNA levels, or opioid-positive weekly urine tests.

Added intervention	First author(s) (or study name) and country	Study design	Intervention description	Number of patients in intervention	Key findings
	Tetrault 2012 USA [21]	Randomized trial	PLWH with OUD initiated buprenorphine/naloxone in an HIV clinic with 15-min physician management with or without 45-min nurse-led enhanced medical management	25 physician management only; 22 physician management with enhanced medical management	No significant differences based on counseling intervention were detected in percentage of opioid-negative urine tests, duration of abstinence, HIV-1 RNA levels or CD4 cell counts.
OUD screening and OUD care	Pisu 2010 USA [65]	Cohort	PLWH received OUD-targeted weekly motivational interviewing, social work, peer groups in HIV clinics, and referrals to psychiatry for medications and psychology for psychotherapy	128	Compared to those who declined the program, the intervention was associated with • no significant differences in HIV-1 RNA levels nor CD4 cell counts

[1] OUD = opioid use disorder

[2] BHIVES = Buprenorphine-HIV Evaluation and Support

[3] PLWH = persons living with HIV

Table 3.

Characteristics of interventions based in opioid treatment settings (n=12).

Added intervention	First author(s) (or study name) and country	Study design	Intervention description	Number of patients in intervention	Key findings
HIV screening	Bartholow 2005 USA [53]	Randomized trial	People who inject drugs randomized to receive home HIV testing kits or traditional counseling and testing in three settings: methadone clinics, hospital-based detox, and syringe exchange	239 home testing; 249 traditional counseling and testing	Compared with traditional counseling and testing, home testing led to: • increased HIV testing performed • no significant difference in HIV test results received.
	Metsch 2012 & Schwartz 2013 USA [67, 73]	Randomized trial	People already enrolled in drug treatment programs cluster-randomized to referral for off-site HIV testing, on-site testing, or on-site testing with counseling	1,281	Compared with off-site referral for HIV testing, on-site HIV testing led to: • significantly higher rates of HIV testing and feedback of results [73]. Compared with no sexual risk-reduction counseling, sexual risk-reduction counseling led to: • no significant changes in sexual risk behaviors [67].
HIV Care	Babudieri 2011 Italy [51]	Cohort	PLWH with OUD offered directly-administered medications for HIV in residential drug treatment facilities	106 directly-observed; 106 self-administered	Compared with self-administering medications, directly-observed HIV medication management was associated with: • higher likelihood of adherence • higher likelihood of increased CD4 cell count • no statistically significant difference in achieving undetectable HIV-1 RNA
	Conway 2004 Canada [54]	Cohort	PLWH with OUD offered directly-observed medications for HIV in methadone clinics	54	Directly-observed medications for HIV can be administered in a methadone clinic: • regardless of ongoing cocaine use • regardless of hepatitis C status
	Lucas 2004 & 2006 USA [63, 64]	Cohort	PLWH with OUD offered directly-observed medications for HIV in methadone clinics	38 [64] + 82 [63]	Compared with self-administered medications for HIV, directly-observed medications were associated with: • likelihood of HIV-1 viral suppression • likelihood of increased CD4 cell count
	Kinahan 2016 Ireland [58]	Cohort	PLWH with OUD offered medication management and directly-observed	19	After engaging with HIV care in the methadone clinic, there was:

Added intervention	First author(s) (or study name) and country	Study design	Intervention description	Number of patients in intervention	Key findings
			medications for HIV in a methadone clinic		• no significant change in percentage of urine tests positive for opioids • no significant change in other drug use • no significant change in attendance to methadone clinic • a significant increase in participants who received directly-observed medications of HIV • no significant change in HIV-1 RNA levels • a significant mean increase in CD4 cell count
	Lucas 2013 USA [62]	Randomized trial	PLWH with OUD randomized to directly-observed medications for HIV in methadone clinics or self-administered medications	55 directly-observed, 52 self-administered	Compared with self-administered therapy, directly-observed therapy led to: • no significant differences in adherence, average CD4 cell counts, change in HIV-1 RNA levels, opportunistic conditions, hospitalizations, mortality, or drug resistance
	Sánchez 2012 Spain [66]	Cohort	PLWH with OUD offered HIV medication management with psychosocial support in a methadone clinic	71	Compared to PLWH presumed to have acquired HIV through sexual transmission, those with OUD participating in this study: • had similar rates of HIV-1 RNA suppression
	Sorensen 2012 USA [68]	Cohort	PLWH with OUD offered directly-observed medications for HIV in a methadone clinic	24	Directly-observed medications were associated with: • high rates of retention • improvement in HIV-1 RNA levels • difficult transition to self-administration of HIV medications
HIV screening and HIV care	Achmad 2009 Indonesia [50]	Cohort	People who inject drugs offered HIV testing and HIV medication management in methadone clinics	35 patients starting HIV medication management in methadone clinics compared with 175 starting elsewhere	Compared with those starting HIV medications elsewhere, patients starting HIV medications in methadone clinics: • Had no significant differences in mortality, non-adherence, loss to follow-up, or CD4 cell counts.
	Bachireddy 2014 Ukraine [52]	Cross-sectional	PLWH with OUD receive either co-located (OUD and HIV care at the same location), non-co-located (OUD and HIV care at different locations) or harm	97 (co-located) 104 (non-co-located) 95 (harm reduction only)	Compared with non-co-located care and harm reduction-only care, co-located care was associated with • Higher quality healthcare indicators • Higher likelihood of HIV medication receipt

Added intervention	First author(s) (or study name) and country	Study design	Intervention description	Number of patients in intervention	Key findings
			reduction only (syringe exchange and case management but no medications)		• Higher likelihood of tuberculosis preventive care • No significant different in health-related quality of life
	Tran 2015 Vietnam [72]	Cross-sectional	Patients with OUD received methadone at clinics with and without HIV medication management	1,016	Compared with patients receiving methadone at clinics without HIV health care services availably on-site, those at sites with HIV care on-site were more likely to report patient satisfaction

Table 4.

Characteristics of interventions based in other settings (n=5).

Added intervention	First author(s) (or study name) and country	Study design	Intervention description	Number of patients in intervention	Key findings
HIV screening	Edelman 2013 USA [56]	Randomized trial	People with OUD already receiving buprenorphine/naloxone randomized to HIV testing with brief sexual risk management (2 sessions) or enhanced sexual risk management (4 sessions) in a primary care clinic	15 brief sexual risk management; 15 enhanced sexual risk management	Compared with brief sexual risk management, enhanced sexual risk management did not lead to differences in process (retention in OUD treatment) or clinical outcomes (health-related quality of life, sexual risk)
HIV care	Altice 2003 USA [16]	Cohort	PLWH with OUD offered HIV medication management in a syringe exchange van	13	From before intervention to 12-months after: • 54% of participants had an undetectable HIV-1 RNA level • net increase in CD4 cell count was 150 cells/mm^3.
OUD care	Springer 2010 USA [69]	Cohort	PLWH with OUD were offered medications for OUD following release from prison out of a group already engaging in directly-observed medications for HIV	30	Compared with baseline, participants: • had reduced opioid cravings • high satisfaction • no changes in non-detectable HIV-1 RNA level or CD4 cell count
	Springer 2012 USA [70]	Cohort	PLWH with OUD offered medications or OUD after prison release out of a group already receiving directly-observed medications for HIV	50	Retention on buprenorphine/naloxone for 24 months correlated with maximum viral suppression, while the receipt of directly-observed medications for HIV or methadone did not.
HIV care and OUD care	Hung 2016 Vietnam [57]	Cohort	PLWH with OUD offered HIV testing, HIV treatment, and methadone maintenance at outpatient clinics	7,395	In sites that integrated methadone, HIV testing, and HIV treatment: • More clients sought testing • More clients initiated medications for HIV • No change in mortality was observed

Text box.

Inclusion criteria (PICOS[1] framework).

Population	Adults with or at risk for (as deemed by study authors) HIV and/or opioid use disorder; n ≥ 10
Intervention	Screening or treatment for both HIV and opioid use disorder occurring within the same treatment setting or across settings that are integrated at the organizational level
Comparison	Screening or treatment for HIV and opioid use disorder occurring not in integrated settings, which may include a historical control, or a comparison between two integrated care strategies
Outcome	HIV or opioid use disorder screening uptake, HIV or opioid use disorder quality of care measures, HIV or opioid use disorder biochemical outcomes, or general health outcomes
Study design	Randomized trials, prospective cohort studies with controls, historically controlled trials

[1]PICOS = Population, Intervention, Comparison, Outcome, Study Design