

## Interventions to increase testing, linkage to care and treatment of hepatitis C virus (HCV) infection among people in prisons: A systematic review

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### ABSTRACT

**Background:** While the burden of chronic hepatitis C virus (HCV) infection is significantly higher among people in prisons compared to the general population, testing and treatment uptake remain suboptimal. The aim of this systematic review was to synthesize evidence on the effectiveness of interventions to increase HCV testing, linkage to care and treatment uptake among people in prisons.

**Methods:** We searched Medline (Ovid 1996–present), Embase (Ovid 1996–present), and the Cochrane Central Register of Controlled Trials for English language articles published between January 2007 and November 2017. Studies evaluating interventions to enhance HCV testing, linkage to care and treatment uptake for people in prison were included. Two independent reviewers evaluated articles selected for full-text review. Disagreements were resolved by consensus.

**Results:** A total of 475 unique articles were identified, 29 were eligible for full text review, and six studies were included. All but one study was conducted in the pre-direct-acting antiviral (DAA) era; no studies were conducted in low- or middle-income countries. Of the six studies, all but one focused on testing. Only two were randomised controlled trials; the remaining were single arm studies. Interventions to enhance HCV testing in prison settings included combination risk-based and birth-cohort screening strategies, on-site nurse-led opt-in screening clinics with pre-test counselling and education, and systematic dried blood spot testing. All interventions increased HCV testing, but risk of study bias was high in all studies. Interventions to enhance linkage to care included facilitated referral for HCV assessment and scheduling of specialist appointments; however, risk of study bias was critical.

**Conclusions:** There is a lack of recent data on interventions to improve the HCV care cascade in people in prisons. With the introduction of short-course, well-tolerated DAAs, rigorous controlled studies evaluating interventions to improve testing, linkage and treatment uptake for people in prison are necessary.

### Introduction

More than 11 million people are imprisoned worldwide at any given time (Walmsley, 2016). It is estimated that 3%–38% of people in prison have been previously exposed to hepatitis C virus (HCV), with differences in estimates related primarily to geography and prevalence of injection drug use (Zampino, Coppola, Sagnelli, Di Caprio, & Sagnelli, 2015). Modelling studies have confirmed the negative impact of incarceration on perpetuating the HCV epidemic (Altice et al., 2016) and

estimates of HCV incidence among people in prison with a history of injection drug use are as high as 16.4 per 100 person-years (Larney et al., 2013). Despite this, routine HCV testing in correctional facilities remains largely limited (Kronfli & Cox, 2018; Beckwith et al., 2015).

Addressing the HCV epidemic among people in prison is an essential component of the global response (Kouyoumdjian & McIsaac, 2015). Experts are encouraging the “micro-elimination” of HCV – a pragmatic approach to pursue elimination goals for individual sub-populations, for which treatment interventions can be delivered more quickly and

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efficiently using targeted methods (Lazarus, Wiktor, Colombo, & Thursz, 2017). With the advent of all oral short-course and highly effective direct-acting antiviral (DAA) therapy, the goal of reducing global HCV infections by 90% as of 2030 among people in prison may be feasible (WHO, 2017), particularly if combined with prison-based opioid substitution therapy (Stone et al., 2017).

The HCV cascade of care describes successive health care steps specific to chronic HCV infection that result in optimal health outcomes (Linás et al., 2014). Screening, the first step of the HCV care continuum, lays the foundation for subsequent linkage to care, initiation of treatment, and achievement of HCV cure. Despite recommendations from the World Health Organization (WHO) that “all prisoners be tested for hepatitis C” (WHO, 2014) and from the United Nations Basic Principles for the Treatment of Prisoners that people in prison “have access to the health services available in the country without discrimination of the grounds of their legal situation” (United Nations, 1990), practice is inconsistent worldwide. Access to DAA treatment has not been prioritized in most prison settings for various reasons including high turnover rates due to short incarcerations, frequent prison transfers, and the high cost of DAA therapy (Kronfli & Cox, 2018). However, modeling studies have shown that in some settings, scaling-up prison-based HCV treatment to 80% of chronically-infected people who inject drugs (PWID) with sentences greater than 16 weeks could reduce HCV incidence and prevalence among all PWID by at least 45%, suggesting both an individual and population-level impact (Stone et al., 2017). Prior to the expansion of treatment, systematic screening for HCV in prison should become routine practice – a standard of care that is not currently in place in many developed countries including Canada and the United States (Morris, Brown, & Allen, 2017). The result is that a limited number of people with chronic HCV infection are aware of their potential need for treatment and progress along the cascade of care towards cure.

A systematic review of evidence-based interventions aimed at people in prison along the HCV care cascade has not yet been published. We sought to synthesize evidence on the effectiveness of interventions to increase HCV testing, linkage to care, and treatment uptake among people in prison.

## Methods

This systematic review was performed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009). A research protocol was developed *a priori* (available from authors on request).

### Eligibility criteria

Studies were included if they met all of the following criteria:

1. **Population:** Participants of any age who were in prison or where at least a portion of the study sample was people in prison.
2. **Intervention:** Interventions aimed at increasing engagement at any (or combination) of the following stages of HCV care:
  - a) Testing for HCV antibodies and/or HCV RNA; and/or
  - b) Linkage to HCV care, defined as clinical assessment of chronic HCV infection; and/or
  - c) Treatment uptake, defined as the dispensation of either interferon-based or interferon-free regimens.
3. **Comparison:** The comparison group was composed of participants receiving either no intervention or standard of care.
4. **Outcomes:** The primary outcomes were:
  - a) Proportion of the study population tested for HCV;
  - b) Proportion of the study population with chronic HCV who are linked to care; and
  - c) Proportion with chronic HCV initiating treatment.

Exclusion criteria were studies that were not peer-reviewed scientific articles, review articles including systematic reviews, and non-comparative studies. Public health interventions targeting health care providers were excluded.

### Information sources

Studies were identified by searching the following electronic databases for English-language full-text and abstract entries published between January 2007 and November 2017: Medline (Ovid 1996–present), Embase (Ovid 1996–present), and the Cochrane Central Register of Controlled Trials. Reference lists of selected articles retrieved during the initial search were hand-searched and forward citation checks were performed to further identify studies.

### Search strategy

A comprehensive list of search terms, related to each of the HCV care cascade components, was used to develop search strategies for each electronic database. Keywords and phrases within groups of hepatitis C; prison population and hepatitis C outcome terms were combined using the ‘OR’ operator; and each group was combined using the ‘AND’ operator. The detailed list of search terms; as well as full search strategies used for all electronic databases; are included in the Supplementary material. Abstracts from selected scientific conferences (International Liver Congress 2016 and American Association for the Study of Liver 2016) were screened for review eligibility.

### Study selection

Data retrieved through the search strategy were imported into EndNote X7 (Thomson Reuters, New York, NY, USA) and duplicates were removed. Titles obtained from the initial search strategy were screened by one reviewer (N.K.) and irrelevant citations removed. Abstracts were reviewed for eligibility by two reviewers (N.K. and B.L.). Full-texts for all identified abstracts were then assessed independently by two reviewers (N.K. and B.L.) for inclusion. Disagreements between reviewers were resolved by consensus. Reasons for exclusion were reported.

### Data collection process and data items collected

Data from studies included for analysis were extracted by one reviewer (B.L.) using a standardized data extraction form. A second reviewer (N.K.) verified extracted data, and disagreements were resolved by discussion and consensus. The following variables were collected: title, first author, publication year, study design, study location, setting, population characteristics, sample size (in both intervention and control arms where applicable), intervention description, comparator description, duration of intervention, outcome description, number of participants achieving the outcome of interest (and proportions if applicable) in each of the intervention and control arms.

### Risk of bias assessment in individual studies

Risk of bias in individual studies was assessed independently by two reviewers (N.K. and B.L.) using the Cochrane Collaboration’s risk of bias tool for randomised studies (Higgins, 2013) and the ROBINS-I tool (Risk Of Bias In Non-randomised Studies – of Interventions) (Sterne et al., 2016) for non-randomised studies. Disagreements were then resolved by discussion between the two reviewers until consensus was reached. For randomised studies, outcomes were evaluated along the following six domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. The overall risk of bias for each outcome was classified into three categories: low risk of bias, high risk of bias or unclear risk of bias. The number of ‘high risk’ domains for

each randomised study per outcome was identified. Outcomes of non-randomised studies were evaluated along the following seven domains: bias due to confounding, bias in selection of participants into study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported result. The overall risk of bias for each outcome was classified into five categories: low risk of bias, moderate risk of bias, serious risk of bias, critical risk of bias or no information. The overall risk of bias for each non-randomised study was determined based on the highest level of bias achieved in at least one domain. No studies were excluded from the review on the basis of the risk of bias.

### Data analysis

As the study designs, participants, interventions, and reported outcomes varied significantly, a decision to not perform meta-analyses was made post-hoc. Tables were used to summarize the characteristics and results of the included studies.

## Results

### Study selection

The numbers of studies identified, reviewed and chosen and the reasons for exclusion are summarized in Fig. 1. The initial search retrieved 749 records. After removing duplicates, 475 records remained, of which 395 were excluded due to non-relevant titles. An additional 51 records were excluded for reasons depicted in Fig. 1. The remaining 29

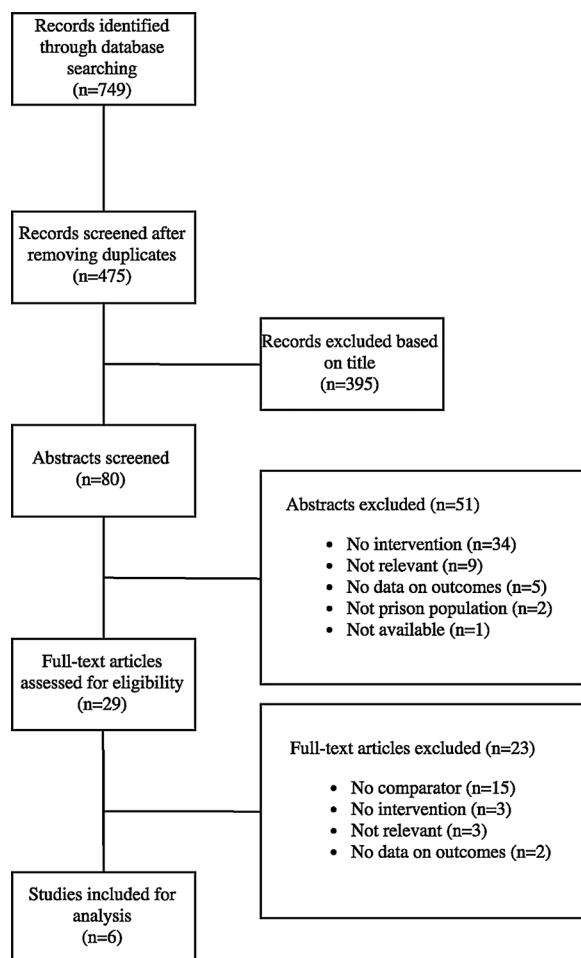


Fig. 1. Study selection process.

studies were retained for full-text review. No additional studies were added through backward/forward citation checks. Following the full-text review, 23 studies were excluded for the following reasons: no comparator group ( $n = 15$ ), no intervention ( $n = 3$ ), non-relevant studies ( $n = 3$ ), and no data on outcomes ( $n = 2$ ). A total of six studies were identified for inclusion in the review.

### Study characteristics and results of individual studies by outcome

The characteristics and results of included studies for HCV testing and linkage to care are summarized in Tables 1 and 2; there were no studies involving interventions to enhance HCV treatment uptake in prison settings.

Of the six studies included in the review, five focused on increasing HCV testing while one aimed to increase linkage to HCV care. All included studies were conducted in high-income countries. All but one study was conducted in the pre-DAA era.

### HCV testing

Five studies evaluated interventions to enhance HCV testing uptake (Table 1) (Craine et al., 2015; Hickman et al., 2008; McLeod et al., 2014; Stockman et al., 2016; Winter et al., 2016). Two (40%) of the included studies were cluster RCTs and three were non-randomised studies. There were three distinct intervention types: on-site testing with education and counselling, combination birth-cohort and risk-based testing, and dried blood spot (DBS) testing.

On-site testing was evaluated in one non-randomised study (Winter et al., 2016). This prison-based intervention, consisting of opt-in blood-borne virus and sexually transmitted infection (BBV/STI) testing through a once-weekly clinic operated by specialist public health nurses (versus standard of care), was evaluated in three state prisons in Australia. Their convenience sample consisted of 100 consecutive new inmates in each of the prisons. The proportion of people in prison tested for HCV increased from 13% (95% confidence interval (CI): 9.1–16.9%) to 25% (95% CI: 20.3–30.5%) despite similar proportions of tests offered (75%) in the pre- and post-intervention periods.

A combination of birth-cohort (1945–1965) and risk-based testing was evaluated in one non-randomised study in two adult state prisons in Wisconsin, United States (Stockman et al., 2016). While the proportion of people in prison tested for HCV increased from 28% to 37%, the addition of birth-cohort to risk-based screening alone did not significantly increase HCV testing sensitivity (which increased from 88% (95% CI: 83–93%) to 92% (95% CI: 88–96%)), and decreased specificity from 80% (95% CI: 78–83%) to 71% (95% CI: 68–74%).

On-site DBS testing was evaluated in three studies (Craine et al., 2015; McLeod et al., 2014; Hickman et al., 2008). One cluster RCT evaluated DBS testing exclusively in correctional facilities (Craine et al., 2015), while the other cluster RCT evaluated DBS in both drug specialty clinics and prisons in the United Kingdom (Hickman et al., 2008). The non-randomised study (McLeod et al., 2014) evaluated DBS testing in multiple settings including prisons in the United Kingdom. All three studies compared opt-in DBS testing with pre- and post-test counselling to standard of care testing via on-demand venipuncture. The sample sizes for the intervention arms of the three studies ranged from 1830 to 2237 participants.

The results for DBS testing were mixed. In particular, the two cluster RCTs showed conflicting results; the study by Craine et al. demonstrated that DBS testing was not sufficient to increase HCV testing (odds ratio (OR) 0.84; 95% CI: 0.68–1.03) while the Hickman et al. study showed that, overall, DBS testing provided in specialty clinics and prisons (i.e. to all participants) increased the proportion tested for HCV by 14.5% (95% CI: 1.3–28%). When restricted to the three prison sites only, a difference-in-difference analysis revealed that DBS non-significantly increased the proportion of individuals tested by 24.8% (95% CI: –10.9 to 60.5%).

The McLeod et al. study analysed a package of prison-based

**Table 1**  
Characteristics and results of included studies of interventions to increase HCV testing.

Author (year)	Study Design	Location	Setting	Population	Sample size (Intervention; Comparator)	Intervention description	Comparator description	Outcome description	Outcome in intervention arm	Outcome in comparator arm
<b>On-site HCV testing with education and counselling</b>										
Winter et al. (2016)	Two-arm, (pre-post) controlled	Australia	3 adult prisons (2 male, 1 female)	100% prisoners; 67% male	565 (280; 285)	Opt-in blood-borne virus and sexually transmitted infection (BBV/STI) testing through a once-weekly clinic operated by specialist public health nurses	Standard of care	HCV testing uptake	25.4% tested (95% CI: 20.3–30.5%)	13.0% tested (95% CI: 9.1–16.9%)
<b>Combination birth-cohort and risk-based testing</b>										
Stockman et al. (2016)	Single arm	USA	2 adult state prisons (1 male, 1 female)	100% prisoners; 85% male	1239	Risk-based HCV testing with universal testing for 1945–1965 cohort	Risk-based HCV testing. (Any one of: history of injection drug use; elevated liver enzymes; anti-HCV Ab+; HIV+; or history of liver disease)	HCV testing uptake	36.9% tested	28.3% tested
<b>Dried blood spot (DBS) testing</b>										
Crane et al. (2015)	Step-wedged RCT	United Kingdom	5 prisons (4 male, 1 female)	100% prisoners	15345 (2237; 13108)	Opt-in DBS testing	Standard of care: on-demand venipuncture	HCV testing uptake	OR = 0.84 (95% CI: 0.68–1.03)	
Hickman et al. (2008)	Cluster RCT	United Kingdom	14 sites (3 prisons; 11 drug specialty clinics)	100% male	3490 (1830; 1660)	Opt-in DBS testing	Standard of care: on-demand venipuncture	HCV testing uptake	348 tested*	122 tested*
McLeod et al. (2014)	Two-arm, (pre-post) controlled	United Kingdom	Multiple settings (GP, hospital, GUM clinic, drug service, prison and other/unknown)	No demographic information provided	4200	A package of prison-based interventions: improved accessibility of HCV testing, targeted activities to promote HCV testing, and DBS testing	Standard of care: on-demand venipuncture	HCV testing uptake	429 tested*	257 tested*

Ab+ : Antibody positive; CI: Confidence interval; GP: General practitioner; GUM: Genitourinary medicine; RCT: Randomised-controlled trial; \*Rates for all participants and not restricted to prison settings alone.

**Table 2**  
Characteristics and results of included studies of interventions to increase linkage to HCV care.

Author (year)	Study Design	Location	Setting	Population	Intervention description	Comparator description	Outcome description	Outcome in intervention arm	Outcome in comparator arm
<b>Facilitated referral and scheduling of appointment with specialist</b>									
Tait et al. (2010)	Cohort study (pre-post)	United Kingdom	Multiple settings including prison	No prison-specific demographic information provided	Non-medical and outreach nurse-led facilitated referral to hepatitis specialist	Medical-led referral only (usual care)	Hepatitis specialist appointment attendance	75 linked	4 linked

interventions including improved accessibility of HCV testing, targeted activities to promote HCV testing, and DBS testing. Their model demonstrated an increase in HCV testing in prison settings at the time that this combination of services was introduced (relative risk (RR) 1.32; 95% CI: 1.00–1.74) and a modest but statistically significant increase in the trend in total yearly HCV tests compared to pre-intervention (RR 1.19; 95% CI: 1.15–1.24). The effect of DBS testing alone was not analysed within prisons. As such, while there was increased HCV testing in prison settings, it was attributable to a package of services and not solely to DBS testing.

#### HCV linkage to care

There was only one study that evaluated whether facilitated referral for HCV assessment and scheduling of specialist appointments enhanced linkage to HCV care (Tait, McIntyre, McLeod, Nathwani, & Dillon, 2010). This large retrospective cohort study was conducted in multiple settings including prisons. Facilitated referrals of HCV antibody positive individuals by non-medical and outreach nurse officers increased hepatologist appointment attendance for all participants from 66% to 82% (RR 1.26; 95% CI: 1.17–1.35) (Bajis et al., 2017). Restricting the results to prison participants only, facilitated referrals increased hepatologist appointment attendance from four to 75 people; however, given missing data regarding the number qualifying for referral, it is unclear whether this represents an increase in the proportion of participants referred.

#### Risk of bias assessment in individual studies

Risk of bias assessment for the studies is summarized in Table 3. Among the non-randomised studies focused on enhancing HCV testing, the risk of bias ranged between moderate to serious. The study by McLeod et al. was deemed to be of serious risk of bias due to confounding and deviations from the intended intervention. Given the pre-post study design spanning 12 years, time-varying confounding was likely. The two RCTs each had at least two domains at high risk of bias. These domains were performance and attrition biases. There were also several domains where bias was unclear as no information was provided by the study authors.

The one study that assessed linkage to care was evaluated as being of critical bias. Similarly to the McLeod study, the critical nature of bias was related to confounding. The Tait et al. study employed a pre-post study design over 14 years that also likely introduced time-varying confounding. Furthermore, the bias due to deviations from the intended intervention was also deemed to be serious as a result of the long study period.

#### Discussion

This systematic literature review summarizes interventions in prison settings that aim to enhance engagement along the HCV care cascade from screening to treatment uptake. All but one study assessed an intervention to increase HCV testing among people in prison. Interventions to increase HCV testing included on-site testing with education and counselling, combination birth-cohort and risk-based

testing, and DBS testing. One intervention to increase linkage to HCV care included facilitated referral for HCV assessment and scheduling of specialist appointments. Overall, the results of this review demonstrate that there has been little effort to increase engagement beyond screening with no studies evaluating interventions to enhance treatment uptake for people in prison, and that there is a dearth of rigorous controlled studies conducted in prison settings to date.

We found that HCV testing increased almost two-fold when on-site opt-in HCV testing with pre-test counselling and education was available in prisons (Winter et al., 2016). This is consistent with two recent systematic reviews of interventions in PWID (Bajis et al., 2017) and in the general population (Zhou et al., 2016) that found similar results. Despite the improvement in HCV screening, testing increased to only 25% of people in prison, implying that the overall effect is modest and that other strategies are needed to reach universal screening rates.

The addition of birth-cohort (1945–1965) to risk-based screening did not improve the proportion of individuals with chronic HCV identified through testing (Stockman et al., 2016). However, risk-based screening alone may not be sufficient in high HCV-prevalence settings such as prisons (Kuncio et al., 2015). While this is the only study which assessed birth-cohort screening in correctional facilities, several recent studies evaluating this screening method in the United States have demonstrated increased identification of previously undiagnosed HCV infections (Yartel et al., 2017; Flanagan et al., 2017), in addition to an increased proportion of individuals tested, corroborating the recommendations made by the Centre for Disease Control and Prevention (CDC) and the U.S. Preventative Services Task Force for one-time HCV testing for persons born between 1945 and 1965 in the United States (CDC, 2012). Although the cost-effectiveness of birth-cohort testing has not been specifically evaluated in prison settings, birth-cohort testing was found to be cost-effective in countries with well-established HCV birth cohort profiles (Morgan, Servidone, Easterbrook, & Linas, 2017). There are key advantages to screening using this approach in that it avoids the need to distinguish individuals with stigmatized behaviours as the basis for testing as well as the need to categorize individuals as being “high risk”. However, it is likely that birth cohort screening will be less useful over time given the aging prison demographics (Akiyama et al., 2016; Larney et al., 2014).

DBS testing provided on-site was associated with mixed results compared to traditional HCV testing. While DBS testing offered in conjunction with other services was associated with increased HCV testing (McLeod et al., 2014), DBS testing offered alone was not (Craine et al., 2015). These findings imply that the success of DBS testing in prison settings may be dependent on a package of interventions that enhance accessibility to HCV testing. The success of DBS testing has been previously demonstrated in two systematic reviews evaluating this technique in PWID (Bajis et al., 2017) and in high-risk populations (Coats & Dillon, 2015). HCV point-of-care testing, via finger prick or salivary, was recently found to be a feasible and acceptable screening method among people in prison (Beckwith et al., 2016; Candfield et al., 2017; Courtemanche, Poulin, Serhir, & Alary, 2016), and could increase testing and diagnosis among vulnerable populations (Bottero et al., 2015). Either finger prick or salivary testing may also be a more feasible option for the prison population given the relatively high likelihood of



**Table 3**  
Risk of bias assessment of included studies.

A. HCV testing								
Risk of bias assessment for included randomised studies using the Cochrane Collaboration's risk of bias tool								
Author (year)	Selection bias (random sequence)	Selection bias (allocation concealment)	Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias	Number of domains of high risk of bias
Craine et al. (2015)	Unclear	Low	High	Unclear	High	Low	Unclear	2
Hickman et al. (2008)	Low	High	High	Unclear	High	Unclear	High	4
Risk of bias assessment for included non-randomised studies using the ROBINS-I assessment tool								
Author (year)	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Risk of bias judgement
Stockman et al. (2016)	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
McLeod et al. (2014)	Serious	Moderate	Moderate	Serious	Moderate	Moderate	Moderate	Serious
Winter et al. (2016)	Moderate	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
B. Linkage to HCV Care								
Risk of bias assessment for included non-randomised studies using the ROBINS-I assessment tool								
Author (year)	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Risk of bias judgement
Tait et al. (2010)	Critical	Moderate	Moderate	Serious	Moderate	Moderate	Moderate	Critical

poor venous access due to injection drug use. DBS testing was also found to be cost-effective in prison settings, but only if continuity of care was assured for at least 40% of those who tested positive (Martin et al., 2013). Given that the median time in custody can be as little as weeks to a few months (Fazel & Baillargeon, 2011; Spaulding et al., 2011), linkage to HCV care at the time of release becomes of utmost importance if screening is to be integrated routinely in correctional facilities, or if treatment is to be initiated prior to release.

Facilitated referral for HCV assessment and scheduling of specialist appointments may improve linkage to care for people in prison. The major limitation of the Tait et al. study was that there was no statistical evaluation of facilitated referral for the subsample of people in prison. Facilitated referral and appointment scheduling was associated with improved linkage in two recent systematic reviews of interventions in PWID (Bajis et al., 2017) and in the general population (Zhou et al., 2016), implying that it may have potential to enhance linkage for people in prison as well.

Interventions to support linkage to care following release are important if care is to continue along the cascade of HCV care. In addition to facilitated referrals, the provision of post-release transportation to medical appointments has been associated with increased linkage to HIV care (Althoff et al., 2013), an intervention that may be applicable to HCV care. This is in line with a recent qualitative study that outlined that transportation to health care facilities was a major barrier to HCV care for people in prison (Yap et al., 2014). Linkage to care at the time of release may be particularly challenging due to multiple competing priorities (Binswanger et al., 2007; Wang et al., 2013). While standard procedures to facilitate linkage with care post-release do not exist in many correctional facilities, several recent studies have demonstrated the feasibility of HCV linkage-to-care post-release programs (Akiyama et al., 2017; Schoenbachler et al., 2016). Linkage to care strategies could be provided by an onsite multidisciplinary care team involving nurses, social workers and patient navigators; multidisciplinary care

has been shown to be associated with improved engagement along the HCV care cascade and patient-reported outcomes (Tait et al., 2010). In the context of a population with multimorbidity, strengthening linkages with primary care, rather than disease-specific specialty care following release, may be the ideal long-term solution (Kronfli & Cox, 2018).

Ensuring ongoing continuity of care through linkage to care following release is particularly important for people who were initiated on HCV treatment in prisons. A recent study comparing HCV cure rates in people in prison, as indicated by sustained virologic response (SVR) at week 12, found that the proportion who were cured was highest for those who completed treatment in prison (74%) compared to those who were transferred (59%) or released during treatment (45%) (Aspinall et al., 2016). These findings highlight the risk of treatment interruption (with subsequent failure) when initiating HCV treatment for individuals who may be transferred or released during therapy. Conversely, a Canadian study demonstrated that if appropriate follow-up was organized at the time of release, a higher proportion of individuals achieved SVR (65%) (Farley, Truong, Nguyen, & Shum, 2012).

Despite demonstrated feasibility (MacDonald et al., 2017), we failed to find a single intervention that focused on increasing HCV treatment uptake for people in prisons. In a recent systematic review, nurse-facilitated referral to a hepatology clinic (Cullen et al., 2006), integrated mental health, substance use disorders and hepatitis services (Ho et al., 2015), and on-site non-invasive liver disease assessments with motivational education (Moussalli et al., 2010) were all associated with increased treatment uptake among PWID. As a starting point, these interventions could be tested in prison settings. One provider-centric intervention, known as the Extension for Community Healthcare Outcomes (ECHO) model, connects primary care providers in prisons with specialist clinicians via teleconferencing, videoconferencing, and e-mail communications (Arora et al., 2011). The success of this model demonstrated that the relative lack of specialist clinicians in settings such as prisons could be overcome with telemedicine. Similarly, nurse-led

models of care in Australian prisons have shown increased HCV treatment uptake (Lloyd et al., 2013), and, given recent data suggesting similar cure rates irrespective of the prescriber (Kattakuzhy et al., 2017), may be a cost-effective way forward. In fact, an Australian needs assessment found that the provision of specialist hepatitis nurses was the most frequently recommended approach to improving prison hepatitis services (Mina, Herawati, Butler, & Lloyd, 2016).

The provision of HCV treatment in prisons should ideally be provided concurrently with harm reduction services (Webster, 2012). Opioid substitution therapy reduces the risk of HCV acquisition and has a stronger protective effect when combined with needle and syringe programs (Platt et al., 2018). It is thus no surprise that the WHO recommends that harm reduction strategies including sterile syringes and opioid substitution therapies should be available in all prisons (WHO, 2007). Given the high prevalence of past and current injection drug use, and sharing of drug paraphernalia among people in prisons, the risks of primary HCV infection and HCV re-infection are high (Farley, Truong, Horvath, Nguyen, & Shum, 2012). Regular HCV testing for those at ongoing risk should be offered to all people in custody as part of comprehensive HCV prevention and care (Kronfli & Cox, 2018). There is substantial evidence for the use of opioid substitution therapy in prison settings as a means of reducing risky behaviours, initiating treatments such as for HCV, and minimizing overdose risks upon release (Degenhardt et al., 2014; Hedrich et al., 2012; Marsden et al., 2017). Advocacy for access to harm reduction programs within and outside prisons to limit both new and recurrent HCV infections remains important, as does collaboration with correctional officials to ensure long-term sustainability of these services.

Our systematic literature review has several limitations. First, a limited number of databases were searched, and restrictions were made to English-language studies. Search strings were developed independently without the consultation of a librarian. We chose 2007 as the starting date for the systematic literature review as this coincides with the year that interferon-based therapies were available in most countries, and we wanted to capture recent data. As a result of these reasons, our systematic literature review may have excluded relevant studies, and we were unable to perform meta-analyses due to the diversity of the interventions.

There are also limitations of the literature that are worth noting. First, all interventions but one were evaluated in the pre-DAA era and no studies were identified in low- and middle-income countries (LMICs). In addition, the quality of studies was limited; the majority were single arm trials and the two cluster RCTs were susceptible to bias in multiple domains. All studies had at least a moderate to serious risk of bias.

Our study highlights several implications with the conduct of research in correctional facilities. While it is evident that there is an increased need for more rigorous studies in prison settings, several unique ethical, regulatory, and environmental challenges exist. Given the disproportionate number of people in prison with chronic HCV, correctional settings have considerable potential for contributing to epidemiological, prevention and treatment research. However, in light of the research environment, it is not surprising that correctional researchers report significantly more obstacles than those in non-correctional settings (Johnson, Kondo, Brems, & Eldridge, 2015). While the obstacles cited emerge from HIV/AIDS research, they are likely applicable to HCV given identical system-, provider-, and patient-level barriers. Some of these barriers include gaining access to the research setting, obtaining research review and approval, navigating the research settings' policies and procedures, and managing interruptions and delays due to the research setting (Johnson et al., 2015). Other commonly cited barriers include securing or maintaining informed consent and ensuring compensation was available to participants, while ensuring appropriate follow-up in the post-implementation phase (Johnson et al., 2015). These findings support those reported by others on the complex environment that correctional settings present to researchers (Applebaum,

2008; Wakai, Shelton, Trestman, & Kesten, 2009), and confirm and expand on the qualitative findings reported by Eldridge et al. where confidentiality, privacy and autonomy were cited as key ethical challenges vis-à-vis HIV/AIDS research in correctional facilities (Eldridge, Robinson, Corey, Brems, & Johnson, 2012). These challenges have likely contributed to the modest number and quality of HCV studies conducted in prison settings to date. In order to improve the transparency and processes associated with health research and research ethics in prisons, disclosures should be made, particularly for refusals of studies (Silva, Matheson, & Lavery, 2017). Dialogue among correctional researchers should be promoted to facilitate the process, manage the challenges encountered in a timely fashion, and to ensure the maintenance of a high ethical code for health research in prison settings. Finally, bolstering training opportunities for correctional researchers will be an important step towards increasing research conducted (Kondo, Johnson, Ironside, Brems, & Eldridge, 2014).

Further, efforts should be made to address the barriers in access and uptake of HCV screening among prisoners. A qualitative study in the United Kingdom described a lack of proactive approaches to offering testing, prisoner fears, lack of knowledge about HCV infection, and concerns about confidentiality and stigma as significant barriers to HCV screening (Khaw, Stobbary, & Murtagh, 2007). These findings suggest that pre- and post-test counselling should be routinely integrated to help ensure higher screening uptake in prison settings. With the advent of simpler and pan-genotypic DAA regimens, a “test and treat” model may be a more feasible approach to HCV care in prison settings, recognizing that expediting care for this population has tremendous individual- and community-level benefits. However, while some LMICs have made agreements that provide for discounted DAA therapies, for others, the costs of these regimens may prohibit this approach and preclude wider treatment expansion.

Finally, a great deal can be learned and applied from the successes of HIV screening in correctional facilities. First, universal or systematic HIV screening has proven to be successful; opt-out testing results in higher testing rates when compared to opt-in or on-demand testing (CDC, 2011; Rumble, Pevalin, & O'Moore, 2015). Despite the increased number of tests that are performed with opt-out testing, opt-out HCV screening has been shown to be highly cost-effective (He et al., 2016). Second, the timing of opt-out testing has also been shown to be instrumental. A study offering opt-out HIV testing to inmates at the time of incarceration found that testing rates were highest when offered within 24 h of incarceration (53% tested) when compared to being offered immediately upon entry (45% tested) or when delayed for a week (33% tested) (Kavasery, Maru, Sylla, Smith, & Altice, 2009). This study indicates that offering testing within the first 24 h after incarceration may be the most opportune time for people in prison. The entire cascade of HCV care is dependent on screening; until universal screening becomes commonplace in correctional facilities, we will continue to miss a substantial number of people chronically infected with HCV (Morris et al., 2017; He et al., 2016).

### Conclusions

To achieve the WHO hepatitis elimination targets by 2030 (WHO, 2017), “micro-elimination” strategies must prioritize people in prison. This review highlights the dearth of studies focused on enhancing engagement along the HCV care cascade for people in prison, and emphasizes the need for rigorous controlled studies evaluating interventions to improve testing, linkage and treatment uptake in prison settings.

### Declarations of interest

NK has received consulting fees from ViiV Healthcare, Merck and Gilead; research funding from ViiV Healthcare and Gilead; and payment for lectures from Gilead. MK has received consulting fees from ViiV

Healthcare, BMS, Merck, Gilead and AbbVie; and research funding from Merck, Gilead and ViiV Healthcare. BL has received consulting fees from ViiV Healthcare and Gilead; research funding from Merck, Gilead and AbbVie; and payment for lectures from Merck and Gilead. GS has received consulting fees from Merck and BMS; research funding from Merck; and payment for lectures from Merck, BMS, Gilead and AbbVie. JC has received consulting fees from ViiV Healthcare and Gilead; research funding from ViiV Healthcare, Merck and Gilead; and payment for lectures from Gilead.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.drugpo.2018.04.003>.

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