Sacks-Davis R et al. *Journal of the International AIDS Society* 2018, **21**(S2):e25051
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25051/full | https://doi.org/10.1002/jia2.25051

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH

Linkage and retention in HCV care for HIV-infected populations: early data from the DAA era

Rachel Sacks-Davis[1,2§], Joseph S Doyle[1,3], Andri Rauch[4], Charles Beguelin[4], Alisa E Pedrana[1,5], Gail V Matthews[6], Maria Prins[7], Marc van der Valk[8], Marina B Klein[9], Sahar Saeed[10], Karine Lacombe[11], Nikoloz Chkhartishvili[12], Frederick L Altice[13,14,15] and Margaret E Hellard[1,5]

[§]**Corresponding author:** Rachel Sacks-Davis, 85 Commercial Rd, Melbourne, 3004, Australia. Tel: +03 9282 2287. (rachel.sacks-davis@burnet.edu.au)

Abstract

Introduction: There is currently no published data on the effectiveness of DAA treatment for elimination of HCV infection in HIV-infected populations at a population level. However, a number of relevant studies and initiatives are emerging. This research aims to report cascade of care data for emerging HCV elimination initiatives and studies that are currently being evaluated in HIV/HCV co-infected populations in the context of implementation science theory.

Methods: HCV elimination initiatives and studies in HIV co-infected populations that are currently underway were identified. Context, intervention characteristics and cascade of care data were synthesized in the context of implementation science frameworks.

Results: Seven HCV elimination initiatives and studies were identified in HIV co-infected populations, mainly operating in high-income countries. Four were focused mainly on HCV elimination in HIV-infected gay and bisexual men (GBM), and three included a combination of people who inject drugs (PWID), GBM and other HIV-infected populations. None were evaluating treatment delivery in incarcerated populations. Overall, HCV RNA was detected in 4894 HIV-infected participants (range within studies: 297 to 994): 48% of these initiated HCV treatment (range: 21% to 85%; within studies from a period where DAAs were broadly available the total is 57%, range: 36% to 74%). Among studies with treatment completion data, 96% of 1109 initiating treatment completed treatment (range: 94% to 99%). Among those who could be assessed for sustained virological response at 12 weeks (SVR12), 1631 of 1757 attained SVR12 (93%, range: 86% to 98%).

Conclusions: Early results from emerging research on HCV elimination in HIV-infected populations suggest that HCV treatment uptake is higher than reported levels prior to DAA treatment availability, but approximately half of patients remain untreated. These results are among diagnosed populations and additional effort is required to increase diagnosis rates. Among those who have initiated treatment, completion and SVR rates are promising. More data are required in order to evaluate the effectiveness of these elimination programmes in the long term, assess which intervention components are effective, and whether they need to be tailored to particular population groups.

Keywords: hepatitis C virus; disease elimination; MSM; IDU; implementation science; barriers; cascade of care

Received 28 June 2017; **Accepted** 19 December 2017; **Published** 9 April 2018

1 | INTRODUCTION

Over two million people are estimated to be HIV/HCV co-infected globally [1]. Chronic viral hepatitis accounts for approximately 10% of mortality among people living with HIV [2]. Injecting drug use is the major risk factor for HCV acquisition among those living with HIV, accounting for over 60% of infections globally, whereas in many high-income countries, high-risk sexual behaviour among HIV-infected gay and bi-sexual men (GBM), including injecting and non-injecting drug use to enhance the sexual experience, is a key driver of HCV transmission [1,3,4]. Incarcerated populations are also at elevated risk of HCV and HIV infection due to incarceration of people who inject drugs (PWID) [5].

HCV treatment has been transformed through direct-acting antiviral (DAA) medications that cure >90% of individuals using tablets over 8 to 12 weeks [6]. Despite modelling studies suggesting that if HCV treatment can be adequately scaled to need, HCV prevalence and incidence can be reduced [7,8] and optimism that local elimination of HCV might be achieved [9], real-world scale-up of HCV elimination remains largely hypothetical. Though the high price of DAAs has hindered scale-up [10], treatment levels have also been hindered by ineffective strategies to adequately target key populations who would benefit most from HCV treatment as prevention [11].

The HIV co-infected population are more likely to be engaged in medical care than the HCV-mono-infected population given increasingly high levels of HIV ART uptake globally [12].

Theoretically, this provides an opportunity for broad coverage of HCV treatment in this population, particularly given that DAA treatment regimens are similar in co-infected and mono-infected populations with equivalent treatment outcomes [13,14]. However, it is important to note that despite increases in ART coverage, coverage in the key at-risk populations still lags behind in some contexts possibly due to lower levels of engagement in medical care and discriminatory prescribing practices [15,16].

Despite the advantages of DAA therapy, engaging large numbers of HIV/HCV co-infected people in HCV DAA treatment will likely require tailored strategies for each of the three key groups at risk of co-infection: PWID, GBM and prisoners. A number of key barriers will need to be addressed to achieve a comprehensive increase in HCV treatment coverage in these three key populations. Insights from implementation science suggest that the successful and widespread implementation of any innovation is complex, even one that is supported by a high level of evidence [17,18]. This is partially due to barriers at the level of the individual health professional, such as lack of knowledge or skill or negative attitudes, but also involves structural barriers, organizational barriers, peer group barriers (differences between the local standard of care and the desired practice) and professional-patient interactions [19]. In the case of HCV, stigmatization and criminalization of the major patient groups and frequent incarceration of PWID add further to the complexity [20,21].

There is currently no published real-world data on the effectiveness of DAA treatment for elimination of HCV infection in HIV-infected populations at a population level. However, a number of relevant studies and initiatives are emerging. This paper aims to describe and report cascade of care data for emerging HCV elimination initiatives and studies that are currently being trialled in HIV/HCV co-infected populations in the context of implementation science theory.

2 | METHODS

Seven HCV elimination initiatives and studies in HIV co-infected populations that are currently underway were identified in six countries. Eligibility criteria for inclusion were either (a) monitoring an HCV elimination intervention targeted to HIV-infected populations; or (b) monitoring the effects of HCV elimination interventions in HIV-infected populations. Data on context, intervention characteristics, and initiative/study-level cascade of care were synthesized using conference abstracts, published manuscripts and personal contact with the investigators. Data collection tools were informed by relevant constructs from the consolidated framework for implementation research (CFIR) [17] and the integrated Promoting Action on Research Implementation in Health Services framework (i-PARIHS; Figure 1) [18]. Cascade of care data from

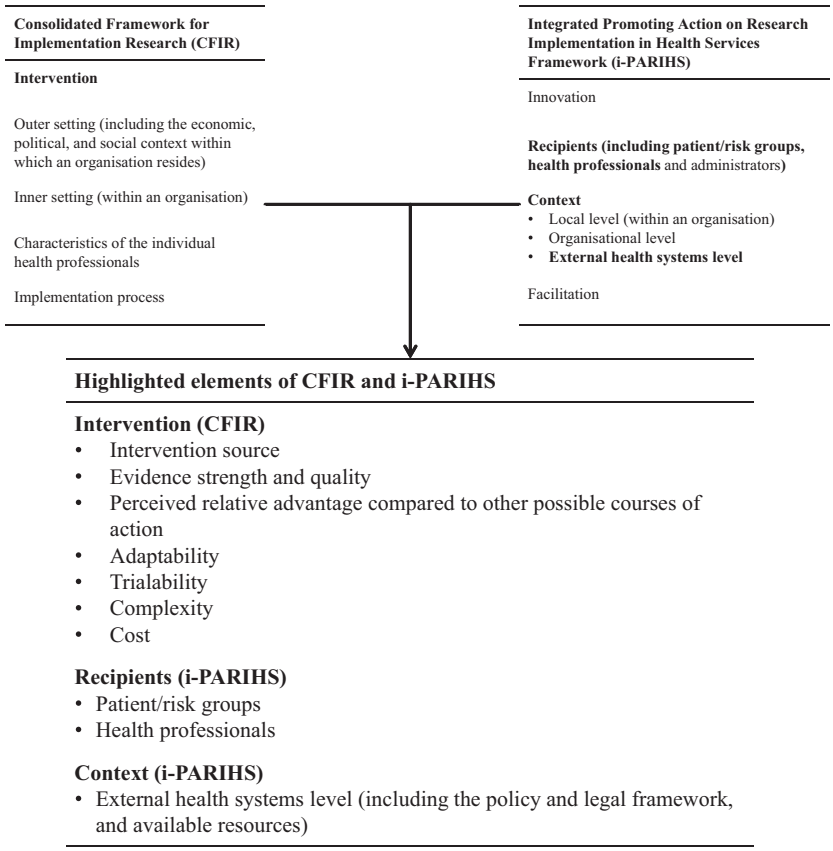

Figure 1. Overview of the CFIR and i-PARIHS implementation science frameworks with relevant constructs highlighted. While all constructs in the two implementation science frameworks are potentially relevant to HCV elimination interventions, the highlighted constructs are particularly relevant for describing and analysing progress in HCV elimination in HIV-infected populations, both in the initiatives and studies identified and in the global context.

initiatives and studies included the number of people with HCV RNA, the proportion of those with HCV RNA who initiated treatment, the proportion of those who initiated treatment that completed treatment, and the SVR rate. Where possible the SVR rate was defined as the proportion of those who were at least 12 weeks past their expected treatment completion date, who had attained SVR. Data on diagnosis rates were not generally available at the initiative/study level.

For each country in which initiatives and studies were included, model-based estimates of the numbers of people living with HIV and the proportion diagnosed with HIV were sourced from peer-reviewed journal manuscripts [22,23], surveillance reports [24-26], and conference presentations [27]. Estimates of HCV antibody prevalence among HIV-infected populations were obtained from cohort studies of people living with HIV [26,28-30], clinical databases of HIV patients [27], and country-level HIV/HCV co-infection management guidelines [31]. The number of people affected by HCV/HIV co-infection was calculated by applying the HCV antibody prevalence estimates to the estimates of the numbers of people living with HIV. An estimate of the proportion of those with HIV/HCV co-infection who were diagnosed for both HIV and HCV was only available for one country, and it was sourced from a conference presentation [27].

All contributing studies had received ethical approval from local ethics review boards in their countries.

3 | RESULTS - PROGRESS TOWARD HCV ELIMINATION IN HIV-INFECTED POPULATIONS

3.1 | Emerging research

Seven HCV elimination initiatives and/or studies in HIV-infected populations were identified, mainly in high-income countries (Australia (n=2), Canada, France, Georgia, the Netherlands and Switzerland). The broader context in which an intervention takes place is highlighted by the i-PARIHS framework (Figure 1). The six countries in which elimination initiatives or studies were identified all have harm reduction programmes for PWID, and protection against discrimination for LGBT populations. [32-33]. However, the coverage of harm reduction programmes varies substantially between countries. According to a recent systematic review, needle and syringe programme coverage was high in Australia and the Netherlands (>200 needles/syringes distributed per PWID per year), moderate in Canada, France and Switzerland (100 to 200 needles/syringes distributed per PWID per year) and low in Georgia (0 to 50 needles/syringes distributed per PWID per year). Opioid substitution therapy coverage was high in Australia, France, the Netherlands and Switzerland (>40 recipients per 100 PWID), moderate in Canada (20 to 40 recipients per 100 PWID), and low in Georgia (0 to 20 recipients per 100 PWID)

Table 1. Country-level context of the identified HCV elimination initiatives and studies in HIV-infected populations

	Australia	Canada	France	Georgia	Switzerland	The Netherlands
Main population groups affected by HIV/HCV co-infection						
PWID	N	Y	Y	Y	Y	Y[a]
GBM	Y	Y	Y	Y	Y	Y
Prisoners	N	Y	Y	Y	Y	N
Other	N	Y[b]	N	Y	N	N
National/regional HCV elimination strategy	Y	N	Y	Y	N	Y
Availability of subsidized DAAs						
Unrestricted in HIV-coinfected population (year)	Y (2016)	Y (2014/2017)[c]	Y (2017)	Y (2015)	Y (2017)	Y (2015)
Unrestricted for all chronic HCV patients (year)[d]	Y (2016)	N[e]	Y (2017)	Y (2015)	N	Y (2015)
Prescriber types						
Specialists	Y	Y	Y	Y	Y	Y
Primary care	Y	Y/N[f]	N	N[g]	N	N
Legal constraints for key populations						
Harm reduction programmes for drug use	Y	Y	Y	Y	Y	Y
Protection against discrimination for LGBT populations	Y	Y	Y	Y	Y	Y

[a]In the Netherlands, HCV/HIV coinfection is mainly observed in former PWID and GBM. Recent transmission has been observed only among GBM. Similar to the situation in other high-income countries, HCV transmission among GBM is thought to be driven partially by sexual transmission and partially by injecting and non-injecting drug use to enhance the sexual experience.
[b]Indigenous populations (mainly through injecting drug use).
[c]Simeprevir and sofosbuvir were unrestricted in Quebec for HCV mono-infected patients since 2014. Although HIV infection was a listed restriction, co-infected patients were usually granted access on a case by case basis through the "patient d'exception" process; Ledipasvir and ombitasvir/paritaprevir/ritonavir; dasabuvir were unrestricted in Quebec from 2016 and velpatasvir from 2017; and the majority of other Canadian provinces since March 2017 [34].
[d]Generally excluding those who are incarcerated.
[e]Not currently available but this is expected to change in 2018/9 in the majority of Canadian provinces.
[f]Primary care practitioners can prescribe HCV treatment in some provinces but not others [34].
[g]A pilot programme is currently underway to evaluate HCV treatment in primary care, which is expected to lead to all primary care providers being allowed to prescribe HCV treatment.

[32]. HCV elimination strategies operating at the regional or country level were in place in Australia, France, Georgia and the Netherlands (Table 1).

In addition to the broad context, another key aspect is the characteristics of the patient or target group of the intervention (Figure 1). The main population groups affected by HIV/HCV co-infection in the countries in which elimination initiatives were identified included PWID, GBM and incarcerated populations. However, the majority of the elimination efforts were targeted elimination efforts in GBM. The two Australian initiatives (CEASE and Co-EC) operate primarily in cities where GBM account for approximately 85% of HIV/HCV co-infection cases; in Amsterdam, ongoing transmission of HCV infection among HIV-infected populations is only among GBM; and in Switzerland, the Swiss HCVree Trial is a clinic trial with MSM as an eligibility criterion. Notably, the HCVree study is nested in the Swiss HIV Cohort Study which includes PWID, GBM and other HIV-infected participants, and because treatment data are not yet available for HCVree, the cascade of care data presented here are from the Swiss HIV Cohort Study. The nationwide HCV elimination programme in Georgia provides HCV treatment at harm reduction sites for PWID, HIV centres, and prisons. In Canada and France, there are no specific programmes targeting HIV-infected populations but the effects of general HCV elimination programmes are being evaluated in the HIV-infected community. France's national strategy for HCV elimination includes targeted programmes for PWID. Broad availability of DAAs is the only nation-wide elimination initiative in Canada but there are other HCV elimination initiatives in Canada that are targeted to specific subpopulations and geographic areas. The cohort studies and databases being used to evaluate the effects of HCV elimination programmes in Canada, France and Georgia include diverse HIV-infected populations including active PWID and GBM. (Table 2).

One of the characteristics highlighted in the CFIR is the complexity of the intervention (Figure 1). HCV elimination in HIV-infected populations is complex. All of the initiatives and studies include broad access to DAAs and most include additional components, including screening and testing components, treatment access components, training of health professionals, media campaigns and risk reduction components. Screening and testing interventions include nurse supported programmes to identify patients for HCV antibody testing, community-based rapid diagnostics and home-based dried blood spot testing, and study or community-based reinfection monitoring. Treatment access interventions include a case management programme for PWID and marginalized people, broadened prescriber base, treatment provision at harm reduction sites, treatment provision in prison, nurse-led primary healthcare based models of care, and community and cohort-study based test and treat models. Risk reduction components include harm reduction, healthcare-based infection control, behavioural interventions and personalized online tools for those at risk of reinfection. Of the five broad groups of intervention (screening/testing, treatment access, training of health professionals, media campaigns and risk reduction interventions), MC Free and Georgia's nationwide HCV elimination programme involve components from all five groups, Co-EC Australia involves components from four groups, CEASE Australia involves components from three groups, the National Plan for HCV Elimination and the Swiss HCVree trial include components from two groups. Although there are no targeted national elimination interventions in Canada, regional interventions such as the Targeted Disease *Elimination*^{TM} programme in British Columbia [35] and a pilot project in Big River First Nation, Saskatchewan are evaluating eliminating HCV at the community level. Some of the studies and initiatives include multiple components within a group (Table 2).

The ability to trial the intervention at a small-scale is also highlighted in CFIR (Figure 1). In the seven initiatives and studies identified, cohort studies, health information systems and surveillance systems are being used to evaluate HCV elimination interventions in people living with HIV (Table 2). None of the evaluation methods include *traditional* control groups. However the CCC (Canada) is using quasi-experimental designs to (i) evaluate treatment uptake through natural variations in DAA reimbursement policies across Canada and (ii) pilot elimination interventions at the clinic level, comparing intervention sites with matched control sites within the CCC. Similarly, several of the other studies and initiatives are using nationwide databases and/or cohorts to compare regions/sites with interventions to other regions.

The cost and available resources for implementing an intervention are highlighted in CFIR and i-PAHRIS (Figure 1). With the exception of the Swiss HCVree Trial, where drugs are provided by industry, governments and health insurance provide funding for subsidized DAAs in all of the other HCV elimination initiatives and studies. However, with the exception of the government-funded National Plan for HCV elimination in France and the nationwide HCV elimination programme in Georgia which is partially industry-funded and partially funded by the US CDC among others, additional components of the elimination interventions identified were mainly funded by industry through investigator-initiated research. These components include treatment access interventions, screening/testing, education initiatives for health professionals, media campaigns and risk reduction interventions.

3.2 | Country-level burden of HIV/HCV co-infection and diagnosis

Model-based estimates of the number of people living with HIV were available for all six countries in which the identified HCV elimination initiatives and studies were based. These ranged from 9600 in Georgia to 149,900 in France. The percent of HIV-infected participants with HCV antibodies ranged from 12% in the Netherlands to 40% in Georgia. The number of people living with HIV and HCV antibodies ranged from 2600 in Switzerland to 36,400 in France. The percent of HIV-infected individuals who were HIV diagnosed ranged from 42% in Georgia to 89% in Australia (Table 3). An estimate of the percent of co-infected individuals who were diagnosed for both HIV and HCV was reported in a conference presentation for Georgia (33%) [27], but was not available for any of the other countries. According to systematic reviews and modelling studies, the estimated proportion of people living with HCV (including those with HCV monoinfection) who were diagnosed prior to DAA availability was 37% (Switzerland), 57% (France), 61% (the Netherlands), 70% (Canada), 75% (Australia) [36-39]. However, in some countries these

Table 2. Intervention characteristics of seven key studies targeting HCV elimination in HIV/HCV co-infected populations

Name (location)	Scope of intervention	Intervention components	Who covers the cost of the intervention	Evaluation method in HIV-infected populations
(Canada)	Nation-wide	Broad access to DAAs; additional clinic-level, province-level, and community-level interventions	Government/health insurance[a]	Canadian co-infection cohort [40]
co-EC (Melbourne, Australia)	Three high HIV caseload primary healthcare clinics, the largest metropolitan sexual health centre, and the two largest hospitals for care of people living with HIV, accounting for over 75% of people living with HIV in Victoria	Broad access to DAAs and broadened prescriber base; nurse supported programmes to identify patients for HCV testing, and support for GPs to increase testing and treatment; posters displayed in participating clinics promoting HCV testing to patients; nurse-led model of care in primary healthcare to increase access to DAAs; training programmes for nurses and physicians	DAA therapy is government subsidized; practice nurses are funded by industry through investigator initiated research	An integrated HCV/HIV clinical and behavioural surveillance system monitors the impact of the programme at the local and statewide level
CEASE (predominantly Sydney, Australia)	Nation-wide observational study of HCV viraemia among HIV-infected population, with an implementation project predominantly operating in Sydney	Broad access to DAAs and broadened prescriber base; HCV Education for HIV prescribers; recurrent viraemia: monitoring of a cohort of high-risk inner city patients for reinfection	DAA therapy is government subsidized; other intervention components funded by industry through investigator initiated research	Data assessed at three cross-sectional visits; at enrolment (2014 to 2016), follow up 1 (2017 to 2018) and follow up 2 (2019 to 2020); data include HCV viraemic prevalence through DBS, behavioural risk and fibrosis assessment
MC FREE (Amsterdam MSM HCV Free, Amsterdam, the Netherlands)	City-wide	Broad access to DAAs; home-based HCV RNA dried blood spot testing service (subscription-based); online tools including information and personal advice on testing and risk reduction strategies, and test results delivered online; motivational interviewing and intensification of partner notification; online and offline media campaigns aimed at increasing HCV awareness; interventions aimed at professionals; behavioural interventions by trained HIV nurses	DAA Treatment is government subsidized; home-based testing and online/ offline strategies are supported by industry through investigator initiated research	Through the National HIV Monitoring Foundation and the MOSAIC study, the different interventions will be evaluated according to predefined criteria/ deliverables

Table 2. (*Continued*)

Name (location)	Scope of intervention	Intervention components	Who covers the cost of the intervention	Evaluation method in HIV-infected populations
National Plan for HCV Elimination (France)	Nation-wide, community-based intervention	Broad access to DAAs; community-based test and treat model involving implementation of rapid diagnostics at the community level; educators and social workers who link PWID / marginalized people to healthcare centres, through a case management (*parcours*) programme	Government/health insurance	Several cohorts of HIV-infected patients and HIV/HCV co-infected patients in addition to national surveillance systems
National HCV elimination programme (Georgia)	Nation-wide multi-component programme	Broad access to treatment and increased access to treatment through primary care, harm reduction sites, HIV centres and prisons[b]; advocacy, awareness and education; harm reduction among PWID, blood safety and infection control in traditional and non-traditional healthcare settings; national HCV screening Laboratory diagnostics capacity building; surveillance	Gilead and the CDC among others	Georgian National AIDS health information system (AIDS HIS, a secure web-based system connecting all HIV care providers countrywide)
The Swiss HCVree Trial (Switzerland)	Research study-based elimination effort among HIV/HCV co-infected MSM, operating nationwide	Cohort study based test and treat model; delivery of Elbasvir/ Grazoprevir treatment to patients infected with genotypes 1 and 4 through clinical trial (Swiss HCVree Trial); behavioural intervention delivered to patients reporting inconsistent condom use with occasional partners; the remaining patients received standard of care and written and oral information on prevention of HCV reinfection.	Investigator initiated trial nested in the Swiss HIV Cohort Study (SHCS); SHCS mainly funded by the Swiss National Science Foundation, HCVree mainly funded by industry	The Swiss HCVree Trial: all study participants tested for HCV RNA at beginning and end of the HCVree trial, change in risk behaviour is evaluated, see ClinicalTrials.gov NCT02785666; effects on HCV incidence within HIV-infected populations evaluated using the Swiss HIV Cohort Study

[a]Although all Canadian citizens and permanent residents have insurance coverage for in-hospital and physician services, medication coverage varies across the 10 provinces and 3 territories, with a mix of both public and private sources of insurance depending on individual characteristics. For example, people on social assistance receive public coverage for medications with no or minimal co-payments and Indigenous people receive medication coverage from the First Nations and Inuit Health Branch (FNIHB).
[b]Provision of HCV treatment through primary care and harm reduction sites is currently being piloted and will be implemented nationwide in the future.

Table 3. Country-level burden of HIV/HCV co-infection and diagnosis

	Australia	Canada	France	Georgia	Switzerland	The Netherlands
Estimated number of people living with HIV	26,400 [24]	65,000 [25]	149,900 [22]	9600 [27]	15,200 [23]	22,900 [26, 41]
Estimated % with HCV antibodies	13 [28]	20 to 30 [31]	24 [29]	40	17 [30]	12 [26]
Estimated number with HCV antibodies	3500	16,300	36,400	3900	2600	2700
Estimated % of those living with HIV who are HIV diagnosed	89 [24, 28]	80 [25]	81 [22]	42 [27]	81 [23]	89 [26, 41]

All numbers are rounded to the nearest 100 and percentages are rounded to the nearest percent. Estimated numbers with HCV antibodies are calculated by applying the estimated % with HCV antibodies to the estimated number of people living with HIV. Percent HIV diagnosed is among all HIV-infected people.

diagnosis rates may be quite different in the HIV-infected population.

3.3 | Initiative-level partial cascade of care

Overall, HCV RNA was detected in 4894 HIV-infected participants across the seven studies and initiatives (range within studies: 297 to 994). Of these 2338 initiated HCV treatment (48%; range: 21% to 85%). Among studies with treatment completion data, 1061 of 1109 initiating treatment (96%, range: 94% to 99%), completed treatment. Of those who were treated with DAAs and could be assessed for SVR12, 1631 of 1757 attained SVR12 (93%, range: 86% to 98%). Of the seven studies and initiatives, four reported cascade of care data from a period where DAAs were broadly available (CEASE and Co-EC - Australia, ATHENA - The Netherlands and AIDS HIS-Georgia), and three included data from prior to DAAs becoming broadly available (CCCS - Canada, SHCS - Switzerland, and HEPAVIH- France). Four initiatives/studies included a considerable proportion of PWID in addition to GBM and other patient groups (CCCS, AIDS HIS, HEPAVIH and SHCS), and three were composed mainly of GBM and former PWID (CEASE, Co-EC and ATHENA). In studies and initiatives with cascade of care data from a period where DAAs were broadly available, 1398 of 2460 (57%, range: 36% to 74%) initiated HCV treatment, 160 of 169 (95%: data from one study only) completed HCV treatment, and 1042 of 1110 (94%, range: 88% to 98%) attained SVR12. In studies and initiatives that include a considerable proportion of current PWID, 1271 of 3349 (38%, range: 21% to 85%) initiated treatment, 901 of 940 (96%: range: 94% to 99%), completed HCV treatment, and 885 of 978 (90%, range: 86% to 96%) attained SVR12; however, two of these studies and initiatives include data from prior to DAAs becoming broadly available (Table 4 and Figure 2). These data include diagnosed patients, who are in care (France, the Netherlands, Sydney), were in care previously (Melbourne, Georgia) and/or are enrolled in a cohort study (Canada, France, the Netherlands and Switzerland).

4 | DISCUSSION

Early results were synthesized from seven HCV elimination initiatives and studies in HIV-infected populations. These results demonstrate increased linkage to HCV care, successful retention in care, and high cure rates among those diagnosed with HCV/HIV co-infection. However, these are early data and the majority of initiatives and studies identified were in high-income countries with relatively low levels of criminalization of risk behaviours and discrimination and stigma of PWID and GBM. Furthermore, the majority of initiatives and studies identified were either primarily treating GBM and/or former PWID or include data from prior to broad DAA availability. None of the studies operate in incarcerated populations and treatment in this context may be more challenging. More data will be required to evaluate the effects of treatment scale-up on HCV prevalence and incidence, and confirm that these high rates of linkage and retention in care can be replicated in PWID, incarcerated populations, and in countries with greater levels of criminalization of risk behaviours and discrimination and stigma of the groups at risk. Different strategies may be required for linkage and retention in care in different populations.

Overall, approximately 50% of HCV diagnosed individuals in the seven initiatives and studies were linked to HCV treatment. This represents a substantially higher treatment uptake than prior to DAA therapies becoming available. In the Swiss HIV cohorts, treatment uptake increased fourfold after the introduction of second-generation DAAs [42]. In Georgia, approximately 100 HCV/HIV co-infected people were treated per year in the three and a half years prior to DAA availability, compared to approximately 265 treatments/year in the first 15 months of the nationwide HCV elimination programme [27]. In the CCC (Canada), treatment uptake increased from 8 per 100 person years to 28 per 100 person years after the introduction of DAA therapies. [43]. This is consistent with increases in treatment uptake following the introduction of DAA therapies in predominantly HCV-monoinfected populations [44]. However, it is not clear that these increases in treatment rates will be sustained. In the Netherlands, treatment numbers increased substantially from November 2015 when DAA therapy became available until July 2016 (on average, >150 treatments/quarter) but then returned to pre-DAA levels (<50 treatments/quarter) [45]. Moreover, although substantial increases in treatment uptake were observed after the introduction of DAA therapy, treatment uptake varied substantially between studies (21% to 91%). This is partially due to variations in when broad access to DAA therapy was attained: in Canada, France, and Switzerland, although DAA therapies were available to selected subgroups earlier, broad access to DAA therapies was only attained in 2017 and cascade of care data was either not yet available or included data

Table 4. Partial cascade of care in the HCV elimination interventions/studies identified in HIV-infected populations

	CEASE Australia	Co-EC Australia	CCC Canada	HEPAVIH France	AIDS HIS Georgia[a]	SHCS[b] Switzerland	ATHENA[c] The Netherlands
Number HCV RNA positive	297[d]	305[e]	994[f]	564	915	876	943[g]
Number initiated HCV treatment (%)[h]	196 (66)	169 (55)	278 (28)	482 (85)[i]	331 (36)	180 (21)	702 (74)
Number completed HCV treatment (%)[j]	-	160 (95)	271 (97)[k]	451 (94)	-	179 (99)	-
Number attained SVR12 (%)	15 (88)[l]	133 (89)[m]	240 (86)[n]	176 (93)[o]	296 (89)	173 (96)	598 (98)[p]

CEASE, Control and Elimination within AuStralia of HEpatitis C from people living with HIV; co-EC Study, Eliminating HCV/HIV co-infection; CCC, Canadian Co-infection Cohort; HEPAVIH, the French national prospective cohort of patients co-infected with HIV and HCV (ANRS CO13 HEPAVIH); AIDS HIS, AIDS health infection system; SHCS, Swiss HIV Cohort Study; ATHENA, AIDS Therapy Evaluation in the Netherlands (ATHENA) cohort.
[a]Data from the Georgian National AIDS health information system (a secure web-based system connecting all HIV care providers countrywide), June 2015 to August 2016. DAAs were broadly available.
[b]Cascade of care in the Swiss HIV Cohort Study because cascade of care data are not yet available for the Swiss HCVree Trial. Data are from 2014 to 2015. Second-generation DAAs were available but restricted by liver disease stage [42].
[c]Cascade of care from the ATHENA cohort of people diagnosed with HIV in the Netherlands from a period where DAAs were broadly available but prior to MC Free, Amsterdam [45]. A cascade of care at the two largest HIV clinics in Amsterdam (a subset of the ATHENA cohort) is available for the same period [46].
[d]2014 to 2016 [47].
[e]These are patients who have been tested for HCV in the past but may not currently be in HCV care. Among those who have been tested for HCV within the study period (n=194), the treatment uptake is 87%.
[f]As of 21 November 2013 (Health Canada's approval of second-generation DAAs), cohort participants who were eligible to initiate DAAs.
[g]Includes those who have tested HCV RNA positive, were treated with DAAs, have never been treated, or were treated with interferon-based therapies and failed treatment but have not yet been retreated [45].
[h]Of those HCV RNA positive.
[i]Includes initiations with interferon-based therapies during a period when DAAs were available in France but restricted [48].
[j]Of those initiating HCV treatment.
[k]Data collected up to December 2016.
[l]Up to end 2015 (17 had initiated treatment).
[m]Of those who are 12 weeks past the date of planned treatment completion. 136 of these were tested for HCV RNA at 12 weeks after treatment, and of those the SVR rate was 98%. It is likely that more participants will be tested for HCV RNA at their next HIV clinic visit.
[n]Includes DAA regimens including interferon, data collected up to July 2017 [43].
[o]Of those initiating DAA therapy prior to February (24 week therapy)/May 2015 (12 week therapy) [49].
[p]Of those who were assessed for SVR.

from before broad access was attained. Treatment rates may have increased since DAAs became broadly available.

However, even in initiatives and studies that attained broad access to DAA therapies earlier, treatment uptake ranged from 36% in Georgia to 75% in the Netherlands indicating that there are significant barriers to care other than simply access to DAA therapy, including provider-level, patient-level and structural barriers ([19-21], Table 5). Overall, more than half of diagnosed HIV/HCV co-infected individuals had not received treatment. While the data included only reflect a short timeframe after the introduction of DAAs, this suggests that substantial effort is still required to achieve HCV elimination in HIV-infected populations. In order to overcome the potential barriers to HCV elimination, it is likely that complex interventions will be required. These are likely to include interventions related to linkage and retention in care, diagnosis and screening, training of health professionals, risk reduction and identification and treatment of reinfection cases. Notably, currently the majority of intervention components in the identified studies and initiatives other than DAA therapy are funded by industry through investigator-initiated research. In order to attain HCV elimination globally, sustainable financing structures will be required to monitor the effectiveness of HCV elimination efforts and for widespread implementation of interventions that are proven to be effective.

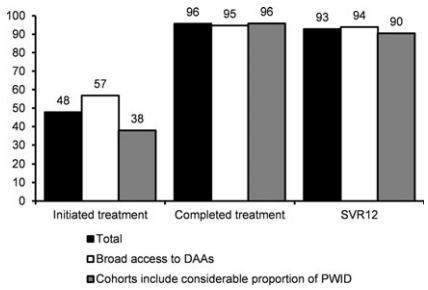

Figure 2. Partial cascade of care data from seven initiatives and studies implementing and evaluating HCV elimination interventions in HIV-infected populations. Percent of HCV RNA positive participants in care or enrolled in cohort studies initiating treatment, percent of those initiating treatment who have completed treatment, and percent of those who can be assessed for SVR12 who attained SVR12.

All treatment linkage data reflect HIV and HCV diagnosed populations. Population-wide proportions of those diagnosed with HIV/HCV co-infection who have received treatment are likely to be lower than those presented here. HCV diagnosis rates among HIV-infected populations are not currently well understood and additional research is required to estimate

Table 5. Barriers and enablers of HCV elimination in HIV-infected populations: list structure based on the CFIR and i-PARIHS frameworks

Intervention	
Strength of evidence	High level of evidence that DAAs are efficacious and tolerable in HIV-coinfected individuals [13], model-based evidence of the effectiveness of treatment as prevention [7,8].
Complexity	Complex intervention targeting populations rather than individuals, and involving case finding, engagement and retention in care, follow-up after successful treatment, and potential re-treatment following re-infection.
Adaptability	Case finding strategies and models of HCV care are adaptable [50,51].
Trialability	Small-scale trials are challenging because of the interlinked nature of the transmission networks. In many contexts HCV elimination will only be testable through before and after studies of population-wide interventions.
Cost	Initially extremely costly; however, some countries have negotiated better rates or early introduction of generics and prices of DAAs are evolving rapidly [10,52].
Source	Targets have been set by the WHO [9].
Relative advantage	In settings where resources are limited relative to the cost of DAAs, treatment of those with advanced liver disease has been prioritized over those at risk of transmission [52].
Recipients of the intervention	
Healthcare professionals	Negative attitudes of healthcare providers toward risk groups have been documented in some contexts, with consequences for quality of care [16,53]. Possible low levels of knowledge of HCV among primary care practitioners managing HIV patients [54]
Patients	Linkage to healthcare and treatment readiness in key population groups, including possible mistrust of healthcare providers among key risk groups [20] Transience of key populations, particularly PWID, including frequent short-term incarceration [20,55] Priority of HCV care in the context of comorbidities and socio-economic disadvantage [20]
Relationships between healthcare professionals and patients	Communication difficulties between patients and specialists [20]
Context	
Criminalization, discrimination and stigma of key populations	Criminalization of same-sex sexual acts in 75 countries [33]. High or medium levels of discrimination against gay and bisexual men limit access to HIV-care in low and middle-income countries in all global regions [56], limiting access to care for HCV in HIV health services. Criminalization of drugs is widespread, with decriminalization of some aspects of drug use only in relatively few countries, approximately 25 to 30 worldwide. There is some evidence that criminalization of drugs and stigma against PWID in healthcare settings negatively impact on HIV prevention and healthcare [53,57,58], and may impact negatively on HCV treatment among HIV-infected populations.
Incarceration of key populations	Incarceration of PWID and less commonly of GBM poses challenges not only for HIV and HCV-prevention, but also delivery of HCV treatment [59]. While prisons may potentially provide opportunities for HCV treatment, there are also potential challenges to providing continuity of care in the context of prison transfers and short sentences, lack of family support, high levels of stress, unpleasant healthcare context and stigmatization by other inmates and custodial staff [55]. In addition, high rates of reinfection have been observed in the prison setting, highlighting the importance of offering other harm reduction interventions such as OST alongside HCV treatment [60,61].
Health systems and regulatory frameworks	Prescriber-type restrictions for HCV treatment [62], and lack of access to transient elastography [54] may impact on access to care [20]
Resourcing	Resourcing limitations within countries are a function of drug prices (which vary substantially between countries), epidemic size and available resources. In addition to funding of drugs, screening, health-systems and risk reduction intervention costs also need to be considered.
Formal endorsement at a country or regional level	While HCV elimination is recommended by the WHO, formal endorsement at a country or regional level varies between countries.

these. Two of the initiatives and studies identified included interventions to increase HCV diagnosis in HIV diagnosed populations using community-based rapid diagnostics and home-based dried blood spot testing. Dried blood spot testing administered by professionals has previously been found to increase HCV testing uptake in populations at high risk of HCV monoinfection [63]. In Georgia, where the rate of HIV diagnosis is relatively low (approximately 40%), efforts are being made to increase diagnosis through integration of HIV, HCV and TB testing services [64].

It is likely that appropriate strategies to improve linkage to care and maintenance in care will differ by population group regardless of whether they are HIV/HCV co-infected or HCV monoinfected. For PWID, prior to the introduction of DAA therapy, a meta-analysis of determinants of HCV treatment completion and efficacy in drug users found that addiction treatment and support services during HCV therapy predicted treatment completion, and the involvement of a multidisciplinary team predicted SVR [51]. A subsequent meta-analysis that included studies of drug-using and other populations found that coordinated mental health, substance use and HCV treatment services had a modest effect on treatment completion and SVR but not on treatment uptake. The level of evidence was rated as very low on the GRADE scale although that is partially due to the difficulties of conducting blinded randomized controlled trials of these interventions. The same meta-analysis failed to find any effect of directly observed therapy on SVR [50]. Since the introduction of DAAs, conference abstracts describing a range of models of care for PWID including directly observed therapy [65,66], addiction treatment and support services during HCV therapy [67,68], support groups [65], integration of HCV treatment clinic and harm reduction services [69], community-based clinic conducting outreach at rehab clinics [70] have all reported high levels of SVR in PWID with HCV mono-infection.

Four of the HCV elimination initiatives identified in this study are implementing models of care targeting GBM. These involve integrating HCV treatment with HIV care, and targeted risk reduction strategies. Prevention of reinfection was highlighted as an important component of HCV elimination efforts in HIV-infected GBM in a mathematical model based on data from the Swiss Cohort study. In light of empirical evidence of increases in HCV-related risk behaviours in GBM being enrolled in the Swiss Cohort Study, the model suggested that if the trend toward increasing risk behaviours persist, high rates of reinfection will mean that even very high treatment rates will not result in reductions in HCV incidence unless treatment is combined with behavioural interventions to reduce risk behaviours after treatment [71]. The HCVree study includes an RCT trialling a behavioural intervention to prevent reinfection. Results are not yet available.

Prisoners are another complex population likely to require targeted approaches for HCV elimination. More research is required to understand strategies for linkage to care in this context. In addition, indigenous peoples, heterosexuals infected with HIV, and migrants from high prevalence HIV and HCV countries are other groups that may also require targeted approaches for linkage to care and maintenance in care. Further research is also required to understand the impact on HCV elimination strategies in HIV-infected populations of reinfection following successful HCV treatment [72,73], transmission of HCV between HIV infected and uninfected populations [74] and migration- and travel-related transmission of HCV between countries [75]. Furthermore, randomized controlled trials are needed to evaluate the efficacy of strategies to enhance diagnosis, linkage to care and maintenance in care, and risk reduction where feasible and ethical.

This study has a number of limitations. HCV elimination initiatives and studies in HIV-infected populations were not identified through a systematic search and the list presented here is not exhaustive. As previously indicated data on treatment linkage were all early data and represent different stages of DAA treatment availability.

Early data from the DAA era suggest that HCV treatment uptake has increased in HIV-infected populations compared to previous levels, but there is still considerable work to do on the pathway to HCV elimination in this population. This includes efforts to quantify the numbers of undiagnosed infections, and increase diagnosis rates and linkage to care. It is likely that different strategies will be required for different populations including PWID, GBM and prisoners among others. Among those who have been treated with DAAs, treatment completion and treatment success has been consistently high across a variety of settings.

AUTHORS' AFFILIATIONS

[1]Disease Elimination Program, Burnet Institute, Melbourne, Australia; [2]Department of Medicine, The University of Melbourne, Melbourne, Australia; [3]Department of Infectious Diseases, The Alfred and Monash University, Melbourne, Australia; [4]Department of Infectious Diseases, University Hospital and University of Bern, Bern, Switzerland; [5]Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia; [6]The Kirby Institute, University of New South Wales, Sydney, Australia; [7]Public Health Service Amsterdam, Amsterdam, the Netherlands; [8]International Antiviral Therapy Evaluation Center and Department of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Centre, Amsterdam, the Netherlands; [9]Division of Infectious Diseases and Chronic Viral Illness Service, McGill University Health Centre, Montreal, Canada; [10]Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Canada; [11]Infectious Diseases, AP-HP, Sorbonne Universités and Inserm UMR-S1136, Paris, France; [12]Infectious Diseases, AIDS and Clinical Immunology Research Center, Tbilisi, Georgia; [13]Section of Infectious Diseases, Yale School of Medicine, New Haven, CT, USA; [14]Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, CT, USA; [15]Centre of Excellence in Research in AIDS, University of Malaya, Kuala Lumpur, Malaysia

COMPETING INTERESTS

JSD and MEH report grants from Gilead Sciences, Abbvie and BMS to support investigator initiated research. JD and JD's institution have also received honoraria from Gilead, BMS and MSD. AR and CB report grants from MSD during the conduct of the study to support investigator initiated research. GVM reports grants from Abbvie, Gilead Sciences and BMS to support investigator initiated research. MP's institute received speaker's fees and unrestricted grants that contribute to several research projects from Gilead, Roche, MSD and Abbvie. MvdV's institute received speaker's fees and unrestricted grants that contribute to several research projects from Gilead, Roche, MSD and Abbvie. MBK has received research grants for investigator-initiated trials from Merck and ViiV Healthcare; consulting fees from ViiV Healthcare, Bristol-Meyers Squibb, Merck, Gilead and AbbVie. FLA reports grant support from the Gilead Foundation, Merck, NIDA, NIAAA, SAMHSA and HRSA, speakers bureau fees from Gilead Sciences, and advisory board/consultation fees from Gilead, Merck, and BMS. RSD, AP, SS, KL, and NC have no competing interests to declare.

AUTHORS' CONTRIBUTIONS

RSD, JSD, AR, FLA and MEH designed the data collection tool and manuscript concept; JSD, AR, CB, GVM, MP, MvdV, MBK, SS, KL, NC and MEH provided data on their HCV elimination in HIV co-infected populations initiatives and studies; RSD wrote the first draft of the manuscript; JSD, AR, CB, AEP, GVM, MP, MvdV, MBK, SS, KL, FLA, NC and MEH read and critically reviewed the manuscript draft.

ACKNOWLEDGEMENTS

We acknowledge Julia Cutts for extracting cascade of care data for the Co-EC study, and the ATHENA, Co-EC, CEASE, Canadian Co-infection Cohort, Georgian AIDSHIS, ANRS CO13 HEPAVIH, the Swiss HIV Cohort study, Swiss HCVree Trial, and MC Free participants and study teams.

FUNDING

Co-EC is funded by BMS. HCVree is funded by MSD. The Swiss HIV Cohort study is funded by the Swiss National Science Foundation (grant no. 148522), and by the SHCS Research Foundation. CEASE is funded by Gilead Sciences and BMS. MC Free is funded by Abbvie, Gilead Sciences, Johnson & Johnson,

Merck Sharp & Dohme, and Roche. The Canadian Co-infection Cohort Study is funded by the Canadian Institutes of Health Research (CIHR; FDN-143270), the CIHR Canadian HIV Trials Network (CTN-222) and the Fonds de recherche Québec- Santé, Réseau SIDA/maladies infectieuses (FRQ-S). Georgian AIDSHIS is co-funded by the Georgian national HIV/AIDS Management Program and the Global Fund to Fight AIDS, Tuberculosis and Malaria. ANRS CO13 HEPAVIH is funded by the French National Agency for Research on AIDS and Viral Hepatitis (ANRS) and also receives funding from Roche, Schering-Plough, GSK, BMS, and Merck-Serono. RSD is supported by an Early Career Fellowship from the Australian National Health and Medical Research Council. JD is supported by a Clinical Fellowship from the Australian National Health and Medical Research Council. MBK is supported by a Chercheur National career award from the FRQ-S. MH is supported by a Principal Research Fellowship from the Australian National Health and Medical Research Council. The Burnet Institute is supported by the Victorian Operational Infrastructure Support Program.

REFERENCES

1. Platt L, Easterbrook P, Gower E, McDonald B, Sabin K, McGowan C, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. Lancet Infect Dis. 2016;16(7):797–808.
2. Smith CJ, Ryom L, Weber R, Morlat P, Pradier C, Reiss P, et al. Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): a multicohort collaboration. Lancet. 2014;384(9939):241–8.
3. Mahony AA, Donnan EJ, Lester RA, Doyle JS, Knox J, Tracy SL, et al. Beyond injecting drug use: investigation of a Victorian cluster of hepatitis C among HIV-infected men who have sex with men. Med J Aust. 2013;198(4):210–4
4. Hegazi A, Lee MJ, Whittaker W, Green S, Simms R, Cutts R, et al. Chemsex and the city: sexualised substance use in gay bisexual and other men who have sex with men attending sexual health clinics. Int J STD AIDS. 2017;28(4):362–6.
5. Dolan K, Wirtz AL, Moazen B, Ndeffo-mbah M, Galvani A, Kinner SA, et al. Global burden of HIV, viral hepatitis, and tuberculosis in prisoners and detainees. Lancet. 2016; 388(10049):1089–102.
6. Doyle JS, Aspinall E, Liew D, Thompson AJ, Hellard ME. Current and emerging antiviral treatments for hepatitis C infection. Br J Clin Pharmacol. 2013;75 (4):931–43.
7. Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, Vickerman P. Combination interventions to prevent HCV transmission among people who inject drugs: modeling the impact of antiviral treatment, needle and syringe programs, and opiate substitution therapy. Clin Infect Dis. 2013;57 Suppl 2:S39–45.
8. Martin NK, Thornton A, Hickman M, Sabin C, Nelson M, Cooke GS, et al. Can hepatitis C virus (HCV) direct-acting antiviral treatment as prevention reverse the HCV epidemic among men who have sex with men in the united kingdom? epidemiological and modeling insights. Clin Infect Dis. 2016;62 (9):1072–80.
9. World Health Organization. Global Health Sector Stratgy on Viral Hepatitis 2016-2021. Towards Ending Viral Hepatitis. Geneva, Switzerland; 2016.
10. Lynch SM, Wu GY. Hepatitis C virus: a review of treatment guidelines, cost-effectiveness, and access to therapy. J Clin Transl Hepatol. 2016;4(4):310–9.
11. Hickman M, De Angelis D, Vickerman P, Hutchinson S, Martin NK. Hepatitis C virus treatment as prevention in people who inject drugs: testing the evidence. Curr Opin Infect Dis. 2015;28(6):576–82.
12. UNAIDS. Global AIDS update 2016. Geneva, Switzerland: 2016.
13. Taylor LE, Swan T, Matthews GV. Management of hepatitis C virus/HIV coinfection among people who use drugs in the era of direct-acting antiviral-based therapy. Clin Infect Dis. 2013;57 Suppl 2:S118–24.
14. Janjua NZ, Kuo M, Yu A, Alvarez M, Wong S, Cook D, et al. The population level cascade of care for hepatitis C in British Columbia, Canada: the BC Hepatitis Testers Cohort (BC-HTC). EBioMedicine. 2016;12:189–95.
15. Mathers BM, Degenhardt L, Ali H, Wiessing L, Hickman M, Mattick RP, et al. HIV prevention, treatment, and care services for people who inject drugs: a systematic review of global, regional, and national coverage. Lancet. 2010;375 (9719):1014–28.
16. Ferro EG, Culbert GJ, Wickersham JA, Marcus R, Steffen AD, Pauls HA, et al. Physician decisions to defer antiretroviral therapy in key populations: implications for reducing human immunodeficiency virus incidence and mortality in Malaysia. Open Forum Infect Dis. 2017;4(1):ofw219.
17. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4:50.
18. Harvey G, Kitson A. PARIHS revisited: from heuristic to integrated framework for the successful implementation of knowledge into practice. Implement Sci. 2016;11(1):33.
19. Grimshaw J, Eccles M, Tetroe J. Implementing clinical guidelines: current evidence and future implications. J Contin Educ Health Prof. 2004;24(S1): S31–7.
20. Harris M, Rhodes T. Hepatitis C treatment access and uptake for people who inject drugs: a review mapping the role of social factors. Harm Reduct J. 2013;10:7.
21. Bruggmann P, Grebely J. Prevention, treatment and care of hepatitis C virus infection among people who inject drugs. Int J Drug Policy. 2015;26 Suppl 1:S22–6.
22. Raymond A, Hill A, Pozniak A. Large disparities in HIV treatment cascades between eight European and high-income countries – analysis of break points. J Int AIDS Soc. 2014;17 4Suppl 3:19507.
23. Kohler P, Schmidt AJ, Cavassini M, Furrer H, Calmy A, Battegay M, et al. The HIV care cascade in Switzerland: reaching the UNAIDS/WHO targets for patients diagnosed with HIV. AIDS. 2015;29(18):2509–15.
24. Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: annual surveillance report 2017. Sydney: Kirby Institute, UNSW Sydney; 2017.
25. Public Health Agency of Canada. Summary: Measuring Canada's Progress on the 90-90-90 HIV Targets. Centre for Communicable Diseases and Infection Control: Public Health Agency of Canada; 2017.
26. van Sighem AI, Boender TS, Wit FWNM, Smit C, Matser A, Reiss P. Monitoring Report 2017. Human Immunodeficiency Virus (HIV) Infection in the Netherlands. Amsterdam: Stichting HIV Monitoring. 2017 [cited 28 November 2017]. Available from: www.hiv-monitoring.nl
27. Chkhartishvili N, Abutidze A, Bolokadze N, Chokoshvili O, Dvali N, Sharvadze L, et al. Hepatitis C Care Cascade for People Living With HIV in the Country of Georgia. IAS 2017; Paris, France; 2017.
28. Cowie B, Dore G, Sasadeusz J. Co-infection: HIV & Viral Hepatitis a guide for clinical management. Sydney: Australasian Society for HIV Medicine; 2010.
29. Larsen C, Pialoux G, Salmon D, Antona D, Le Strat Y, Piroth L, et al. Prevalence of hepatitis C and hepatitis B infection in the HIV-infected population of France, 2004. Eurosurveillance. 2008;13(22):18888.
30. Swiss HIV Cohort Study & Swiss Mother and Child HIV Cohort Study: Hepatitis C [cited 2017 14 November]. Available from: http://www.shcs.ch/281-6-hepatitis-c
31. Hull M, Shafran S, Wong A, Tseng A, Giguere P, Barrett L, et al. CIHR Canadian HIV trials network coinfection and concurrent diseases core research group: 2016 updated Canadian HIV/hepatitis C adult guidelines for management and treatment. Can J Infect Dis Med Microbiol. 2016;2016:4385643.
32. Larney S, Peacock A, Leung J, Colledge S, Hickman M, Vickerman P, et al. Global, regional, and country-level coverage of interventions to prevent and manage HIV and hepatitis C among people who inject drugs: a systematic review. Lancet Glob Health. 2017; 5(12):e1208–20.
33. International Lesbian G, Bisexual, Trans and Intersex Association: Carroll, A., Itaborahy LP. State Sponsored Homophobia 2015: A world survey of laws: criminalisation, protection and recognition of same-sex love Geneva: ILGA, 2015 May.
34. Marshall AD, Saeed S, Barrett L, Cooper CL, Treloar C, Bruneau J, et al. Restrictions for reimbursement of direct-acting antiviral treatment for hepatitis C virus infection in Canada: a descriptive study. CMAJ Open. 2016;4(4): E605.
35. British Columbia Centre for Excellence in HIV/AIDS. Targeted disease elimination [cited 27 June 2017]. Available from: http://www.cfenet.ubc.ca/research/epidemiology-population-health/hepatitis-c-research-program/targeted-disease-elimination
36. Bruggmann P, Berg T, Ovrehus AL, Moreno C, Brandao Mello CE, Roudot-Thoraval F, et al. Historical epidemiology of hepatitis C virus (HCV) in selected countries. J Viral Hepat. 2014;21 Suppl 1:5–33.
37. Wedemeyer H, Dore GJ, Ward JW. Estimates on HCV disease burden worldwide – filling the gaps. J Viral Hepat. 2015;22:1–5.
38. Pioche C, Pelat C, Larsen C, Desenclos J-C, Jauffret-Roustide M, Lot F, et al. Estimation de la prévalence de l'hépatite C en population générale, France métropolitaine, 2011. Bull Epidémiol Hebd. 2016;13–14:224–9.
39. Hajarizadeh B, Grebely J, McManus H, Estes C, Razavi H, Gray RT, et al. Chronic hepatitis C burden and care cascade in Australia in the era of interferon-based treatment. J Gastroenterol Hepatol. 2017;32(1):229–36.
40. Klein MB, Saeed S, Yang H, Cohen J, Conway B, Cooper C, et al. Cohort profile: the Canadian HIV-hepatitis C co-infection cohort study. International journal of epidemiology. 2010;39(5):1162–9.
41. Op de Coul ELM, Schreuder I, Conti S, van Sighem A, Xiridou M, Van Veen MG, et al. Changing patterns of undiagnosed HIV infection in the Netherlands: who benefits most from intensified HIV test and treat policies? PLoS One. 2015;10(7):e0133232.

42. Béguelin C, Suter A, Bernasconi E, Fehr J, Kovari H, Bucher HC, et al. Trends in HCV treatment uptake, efficacy and impact on liver fibrosis in the Swiss HIV Cohort Study. Liver Int. 2017;00:1–8.
43. Saeed S, Strumpf EC, Moodie EEM, Young J, Nitulescu R, Cox J, et al. Disparities in direct acting antivirals uptake in HIV-hepatitis C co-infected populations in Canada. J Int AIDS Soc. 2017;20(3):e25013.
44. Hill AM, Nath S, Simmons B. The road to elimination of hepatitis C: analysis of cures versus new infections in 91 countries. J Virus Erad. 2017;3(3):117–23.
45. Boerekamps A, Newsum AM, Smit C, Arends JE, Richter C, Reiss P, et al. High treatment uptake in HIV/HCV-coinfected patients after unrestricted access to direct-acting antivirals in the Netherlands. Clin Infect Dis. 2017; In press. Published online 23 November 2017.
46. Saris J, Van den Berk G, Ait Moha D, Van Der Meer J, Brinkman K, Van Der Valk M. Successful implementation of HCV treatment in two large HIV clinics in Amsterdam: HCV treatment cascade of care. AIDS. 2017;31(12):1779–80.
47. Martinello M, Dore GJ, Bopage RI, Finlayson R, Baker D, Bloch M, et al., editors. DAA treatment scale-up in HIV/HCV co-infection: characterising a population at risk for reinfection. International Liver Congree (EASL); 2017 April; Amsterdam.
48. Salmon D. Retour d'expérience, Cohorte ANRS CO13. Foie et VIH 9 Nov; Rencontres Sainte Marguerite, Marseille, France; 2017.
49. Sogni P, Gilbert C, Lacombe K, Piroth L, Rosenthal E, Miailhes P, et al. All-oral direct-acting antiviral regimens in HIV/hepatitis C virus–coinfected patients with cirrhosis are efficient and safe: real-life results from the prospective ANRS CO13–HEPAVIH cohort. Clin Infect Dis. 2016;63(6):763–70.
50. Zhou K, Fitzpatrick T, Walsh N, Kim JY, Chou R, Lackey M, et al. Interventions to optimise the care continuum for chronic viral hepatitis: a systematic review and meta-analyses. Lancet Infect Dis. 2016;16(12):1409–22.
51. Dimova RB, Zeremski M, Jacobson IM, Hagan H, Des Jarlais DC, Talal AH. Determinants of hepatitis C virus treatment completion and efficacy in drug users assessed by meta-analysis. Clin Infect Dis. 2013;56(6):806–16.
52. World Health Organization. Global hepatitis report 2017. Geneva; 2017.
53. van Boekel LC, Brouwers EPM, van Weeghel J, Garretsen HFL. Stigma among health professionals towards patients with substance use disorders and its consequences for healthcare delivery: Systematic review. Drug Alcohol Depend. 2013;131(1–2):23–35.
54. Wade A, Draper B, Doyle J, Allard N, Grinzi P, Thompson A, et al. A survey of hepatitis C management by Victorian GPs after PBS-listing of direct-acting antiviral therapy. Aust Fam Physician. 2017;46(4):235–40.
55. Yap L, Carruthers S, Thompson S, Cheng W, Jones J, Simpson P, et al. A descriptive model of patient readiness, motivators, and hepatitis C treatment uptake among Australian prisoners. PLoS One. 2014;9(2):e87564.
56. Caceres C, Pecheny M, Frasca T, Raupp Rios R. Review of Legal Frameworks and the Situation of Human Rights related to Sexual Diversity in Low and Middle Income Countries. Report commissioned by UNAIDS, 2008.
57. DeBeck K, Cheng T, Montaner JS, Beyrer C, Elliott R, Sherman S, et al. HIV and the criminalisation of drug use among people who inject drugs: a systematic review. Lancet HIV. 2017;4(8):e357–74.
58. Wolfe D, Carrieri MP, Shepard D. Treatment and care for injecting drug users with HIV infection: a review of barriers and ways forward. Lancet. 2010;376(9738):355–66.
59. Dolan K, Wirtz AL, Moazen B, Ndeffo-mbah M, Galvani A, Kinner SA, et al. Global burden of HIV, viral hepatitis, and tuberculosis in prisoners and detainees. Lancet. 2016;388(10049):1089–102.
60. Marco A, Esteban JI, Solé C, da Silva A, Ortiz J, Roget M, et al. Hepatitis C virus reinfection among prisoners with sustained virological response after treatment for chronic hepatitis C. J Hepatol. 2013;59(1):45–51.
61. Bate JP, Colman AJ, Frost PJ, Shaw DR, Harley HAJ. High prevalence of late relapse and reinfection in prisoners treated for chronic hepatitis C. J Gastroenterol Hepatol. 2010;25(7):1276–80.
62. Lazarus JV, Safreed-Harmon K, Stumo SR, Jauffret-Roustide M, Maticic M, Reic T, et al. Restrictions on access to direct-acting antivirals for people who inject drugs: The European Hep-CORE study and the role of patient groups in monitoring national HCV responses. International Journal of Drug Policy. 2017;47:47–50.
63. Coats JT, Dillon JF. The effect of introducing point-of-care or dried blood spot analysis on the uptake of hepatitis C virus testing in high-risk populations: a systematic review of the literature. Int J Drug Policy. 2015;26(11):1050–5.
64. Nasrullah M, Sergeenko D, Gamkrelidze A, Averhoff F. HCV elimination – lessons learned from a small Eurasian country, Georgia. Nat Rev Gastroenterol Hepatol. 2017;14(8):447–8.
65. Litwin AH, Agyemang L, Akiyama MJ, Norton BL, Heo M, Ning Y, et al. The PREVAIL study: intensive models of HCV care for people who inject drugs. Jersey City, USA: INHSU; 2017.
66. Boyle A, Marra F, Fox R, Fleming C, Reilly E, Heydtmann M, et al. Successful treatment of patients on opiate replacement therapy utilising partial directly observed therapy of DAAs in community pharmacies. Jersey City, USA: INHSU; 2017.
67. Valente R, Sousa M, Nunes J, Gomes C, Gouveia C, Ferreira AM. Hepatitis C treatment in people receiving opiod substitution therapy: a difficult population? Jersey City, USA: INHSU; 2017.
68. Thierfelder C, Gotthardt F, Huber C, Jochum A. High DAA-treatment uptake and success in clients with chronic HCV-infection under OST despite structural and individual challenges. Jersey City, USA: INHSU; 2017.
69. Ulstein K, Backe O, Midgard H, Vennesland K, Wusthoff L, Darlgard O. Feasability and efficacy of direct-acting antiviral hepatitis C treatment in a low threshold setting. Jersey City, USA: INHSU; 2017.
70. Robert J, Tremblay J, Bissonnet H, Zeagman T, Latour E. Linking PWUD to hepatitis C care and prevention. Jersey City, USA: INHSU; 2017.
71. Salazar-Vizcaya L, Kouyos RD, Zahnd C, Wandeler G, Battegay M, Darling KEA, et al. Hepatitis C virus transmission among human immunodeficiency virus-infected men who have sex with men: modeling the effect of behavioral and treatment interventions. Hepatology (Baltimore, MD). 2016;64(6):1856–69.
72. Lambers FA, Prins M, Thomas X, Molenkamp R, Kwa D, Brinkman K, et al. Alarming incidence of hepatitis C virus re-infection after treatment of sexually acquired acute hepatitis C virus infection in HIV-infected MSM. AIDS. 2011;25(17):F21–7.
73. Simmons B, Saleem J, Hill A, Riley RD, Cooke GS. Risk of late relapse or reinfection with hepatitis C virus after achieving a sustained virological response: a systematic review and meta-analysis. Clin Infect Dis. 2016;62(6):683–94.
74. Hoornenborg E, Achterbergh R, Schim Van Der Loeff M, Davidovich U, Hogewoning A, Vries H, et al. MSM starting pre-exposure prophylaxis are at risk of hepatitis C virus infection. AIDS. 2017;31(11):1603–1610.
75. van de Laar T, Pybus O, Bruisten S, Brown D, Nelson M, Bhagani S, et al. Evidence of a large, international network of HCV transmission in HIV-positive men who have sex with men. Gastroenterology. 2009;136(5):1609–17.