AIDS and Behavior
https://doi.org/10.1007/s10461-024-04436-6

SUBSTANTIVE REVIEW

Disengagement from Care Among People Co-Infected with HIV and HCV: A Scoping Review

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Accepted: 27 June 2024

Abstract

Disengagement from care among people with HIV (PWH) and hepatitis C (HCV) increases the risks of adverse health outcomes and poses significant barriers to achieving global HIV and HCV elimination goals. In accordance with the Joanna Briggs Institute framework, a scoping review was conducted to synthesize and highlight existing gaps in the literature on (dis)engagement in care among PWH and HCV. We searched for original studies on (dis)engagement in care among PWH and HCV in high-income countries using eight electronic databases from inception to May 2023. Our search yielded 4462 non-duplicated records, which were scoped to 27 studies. Definitions of (dis)engagement in care were diverse, with considerable heterogeneity in how retention was operationalized and temporally measured. Studies identified predictors of (dis)engagement to be related to drug and substance use ($n=5$ articles), clinical factors ($n=5$), social and welfare ($n=4$), and demographic characteristics ($n=2$). When engagement in care was treated as an exposure, it was associated with HCV treatment initiation ($n=3$), achieving sustained virological response ($n=2$), and maintaining HIV viral suppression ($n=1$). Interventions to improve care engagement among PWH and HCV were limited to five studies using cash incentives ($n=1$) and individual case management ($n=4$). (Dis)engagement in care is a dynamic process influenced by shifting priorities that may 'tip the balance' towards or away from regularly interacting with healthcare professionals. However, inconsistent definitions render cross-study comparisons and meta-analyses virtually impossible. Further research needs to establish a standardized definition to identify patients at high risk of disengagement and develop interventions that leverage the nested HIV/HCV care cascades to retain and recover patients lost from care.

Keywords HIV-hepatitis C co-infection · HIV · Hepatitis C · Retention · Disengagement · Lost-to-follow-up · Scoping review

Introduction

Human immunodeficiency virus (HIV) and hepatitis C (HCV) co-infection is a global public health challenge. It is estimated that 2.3 million individuals are living with HIV/HCV—80% of whom are people who previously injected drugs (PWID) [1]. HIV/HCV co-infection exacerbates the natural history of both infections [2], accelerating the progression of HCV-related liver disease [3] and mortality risks [4, 5]. Significant advancements in HIV and HCV treatments underscore the capacity to address HIV/HCV co-infection effectively [6–9]. Following the advent of highly efficacious and safe direct-acting antiviral agents (DAAs) in 2013 [10, 11], the WHO announced an ambitious yet feasible goal towards eliminating viral hepatitis: reduce new viral hepatitis infections by 90% and mortality by 65% by 2030 [12]. Simultaneously, combined HIV antiretroviral therapy (cART) allows individuals to achieve undetectable HIV viral loads and become untransmissible (U=U) [13]. This progress is instrumental in realizing the UNAIDS 95-95-95 targets, which aim for 95% of people with HIV (PWH) to know their HIV status, 95% of those diagnosed to be on ART, and 95% of those on treatment to

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Published online: 11 July 2024

achieve viral suppression [14]. However, these international targets rely on people accessing and sustaining clinical care and treatment.

The cascade of care also referred to as care continuums, captures cross-sectional snapshots that describe clinical care milestones. PWH and HCV follow two nested care cascades that present unique healthcare challenges [2, 15]. The HIV care cascade is marked by five key stages—diagnosis, linkage to care, receipt of antiretroviral therapy, retention in care, and achievement of viral suppression—where the final stage requires continuous and consistent engagement in clinical care [16]. The International Antiviral Society-USA Panel (IAS-USA) recommends HIV virology tests every six months following viral suppression [17, 18], whereas the European AIDS Clinical Society (EACS) recommends HIV virology tests every 3–6 months [19]. Although the HCV care cascade follows similar sequential steps to the HIV care cascade [20, 21], it rarely includes steps following sustained virological response (SVR) [22], defined as undetectable HCV RNA 12–24 weeks after treatment completion [23].

In high-income settings, the majority of PWH and HCV are diagnosed and engaged in care, making them an ideal "micro-population" to target for HCV care and achieving WHO targets [24, 25]. However, the cascade of care PWH and HCV follow is dynamic, marked by changing clinical and social factors influencing patient engagement in different steps [26, 27]. For instance, dual HIV/HCV stigma, unmet mental health needs, and socio-structural complexities can function as pervasive barriers to care [28–30]. Thus, disengagement from care, or loss to follow-up (LTFU), can occur at any step of the care cascades, contributing to increased risks of HIV- [31–33] and HCV- [22] related morbidity and mortality.

Disengagement from care among PWH and HCV needs to be better understood. Varying definitions of disengagement/LTFU and retention in care exist across the literature [22, 34–37]. This ambiguity hinders the development of patient-centred interventions that ensure retention in care and optimal health outcomes. The paucity of synthesized information covering the topic necessitated a scoping review. Our primary objective was to examine the scope of literature on (dis)engagement from care among PWH and HCV in high-income countries, highlighting existing gaps in the literature and clarifying concepts regarding the research topic. Our research sub-questions were:

- How was (dis)engagement in care defined in the context of care cascade for PWH and HCV?
- What key factors influence (dis)engagement in care among PWH and HCV?
- What are the health outcomes associated with (dis)engagement in care?
- What are the existing interventions aimed at addressing (dis)engagement/LTFU among HIV/HCV co-infected individuals?

Methods

The scoping review was conducted in accordance with the Joanna Briggs Institute framework [38], originally described by Arksey and O' Malley [39]. The scoping review included the following stages: (i) identifying the research questions; (ii) information sources and search strategy; (iii) study selection; (iv) data extraction and synthesis; and (v) collating, summarizing, and reporting the results [38]. The protocol was registered in the Open Science Framework [40]. Modifications to the protocol included (i) the consolidation of the data extraction tools, (ii) data extraction simplifications, and (iii) the omission of grey literature from the summary of factors, outcomes, and interventions.

Eligibility Criteria

Eligible studies provided insight into retention in clinical care and disengagement/LTFU among PWH and HCV [41]. Due to the variations in health services between high and low- and middle-income countries, particularly concerning HIV [42] and HCV [43] infections, the review focused solely on high-income countries. This scoping review considered peer-reviewed journal articles and grey literature sources (e.g., conference abstracts, preprints, and graduate theses), contributing primary empirical data. To prevent data duplication, secondary sources of information, including systematic reviews, opinion papers and grey literature that were subsequently peer-reviewed/published, were not considered.

Guided by a conceptualization proposed by the WHO [44] for HIV care, we adopted a pragmatic definition of retention as continuous engagement (i.e., no documented interruptions) in the care cascade(s) following linkage to care. Conversely, disengagement from care was conceptualized as discontinuing care (i.e., ceasing to interact with healthcare professionals or access care) for any reason following linkage to care.

Search Strategy

A health sciences librarian assisted in conducting the search strategy, which involved locating published and unpublished studies on the topic.

This scoping review searched eight online databases (MEDLINE (Ovid), Embase (Ovid), Cochrane CENTRAL

(Ovid EBM Reviews), Global Health (Ovid), Web of Science Core Collection, CINAHL, ProQuest Dissertation and Theses Global, and the Preprint Citation Index) from database inception through May 2023. Relevant keywords and database-specific subject headings (MeSH) for HIV, HCV, co-infection, and LTFU [45–48] were used to develop a comprehensive search strategy (see Supplemental File #S1).

Following the database searches, the reference lists of all included articles were screened for additional studies. Cited reference searching was also performed for all included studies using Google Scholar.

Study/Source of Evidence Selection

All identified citations were collated and uploaded into the systematic review software Covidence (Veritas Health Innovation, Melbourne, Australia), and duplicates were removed. Prior to screening, the research team conducted meetings and pilot testing [38] to ensure consistency and reliability in the screening process. Pilot testing involved an initial screening of a random sample of 25 titles/abstracts, assessed by two reviewers (DAD, YT) against the inclusion criteria. Interrater reliability was measured, and conflicts were discussed with another reviewer (SS) to achieve consensus. The described pilot testing was repeated until an interrater reliability metric of ≥ 75% was achieved. Following pilot testing, the reviewers began the independent title/abstract screening process.

Two reviewers (DAD, YT) then assessed the full text of selected citations in detail against the inclusion criteria. Conflicts were resolved by the third reviewer (SS).

Data Extraction

One independent reviewer (DAD) extracted data from the included studies and verified it by another reviewer (SS). Conflicts were resolved through discussion until consensus was achieved.

We classified papers as defining (dis)engagement as the outcome, the exposure, and/or interventions related to (dis)engagement. Initially, the protocol included three separate extraction sheets for each category. However, recognizing the potential overlap among articles in these categories (e.g., an intervention article that describes factors of (dis)engagement), we utilized a single consolidated extraction sheet (see Supplemental File #S2).

Data extracted included study characteristics, such as author(s), year, study timeframe (i.e., during the interferon-era (January 2002 - December 2013), DAA-era (January 2014-Present), or both) [49], primary objectives, country/study setting, study population characteristics (e.g., relevant demographic characteristics and sample size), and the focal care cascade (i.e., HIV, HCV, or both); conceptualizations of key terms; and reported outcomes pertaining to the research question (i.e., factors and outcomes associated with (dis)engagement). To facilitate the synthesis and comparison of data, a protocol modification was made to simplify factors associated with (dis)engagement into categories based on studies that have identified patient-, provider-, and system factors that influence retention in care [28, 30, 50]. These categories included the following: demographics (e.g., age, race, gender), substance use (i.e., any substance misuse or illicit drug use), social/welfare (i.e., psychosocial influences such as employment status, housing stability, incarceration, discrimination), clinical (e.g., HIV/HCV disease progression, treatments, and physical comorbidities), mental health (i.e., diagnoses of any mental health disorders), and other factors that do not fit into the pre-specified categories. For studies focused on describing an intervention or care programme, additional data was abstracted on the engagement method, facilitators involved in the intervention, and relevant outcomes.

Data Analysis and Presentation

Quantitative descriptive analyses involving frequency counts and proportions of study characteristics were conducted. A narrative summary of results was produced to describe and summarize the extracted data. Given the lack of specificity in definitions of (dis)engagement and description of statistical methodologies in included grey literature, only peer-reviewed articles were included to summarize factors, outcomes, and interventions. Data extracted from the grey literature articles are detailed in a supplementary file for readers (See Supplement #S3). Consistent with best-practice scoping review methodology [39], the scope of the data was mapped descriptively without assessing the source's quality. The results of this scoping review are reported following the PRISMA-ScR guidelines (see Supplemental File #S4) [51, 52].

Results

Characteristics of Included Studies

The database search yielded a total of 6682 records, with 4462 titles and abstracts screened for after removal of duplicates. 152 database-searched articles were identified for full-text screening. Of these, 25 met the inclusion criteria. An additional two sources were identified through citation searching. In total, 27 studies were identified for final review [20, 25, 53–77]. The PRISMA flow diagram (Fig. 1) depicts

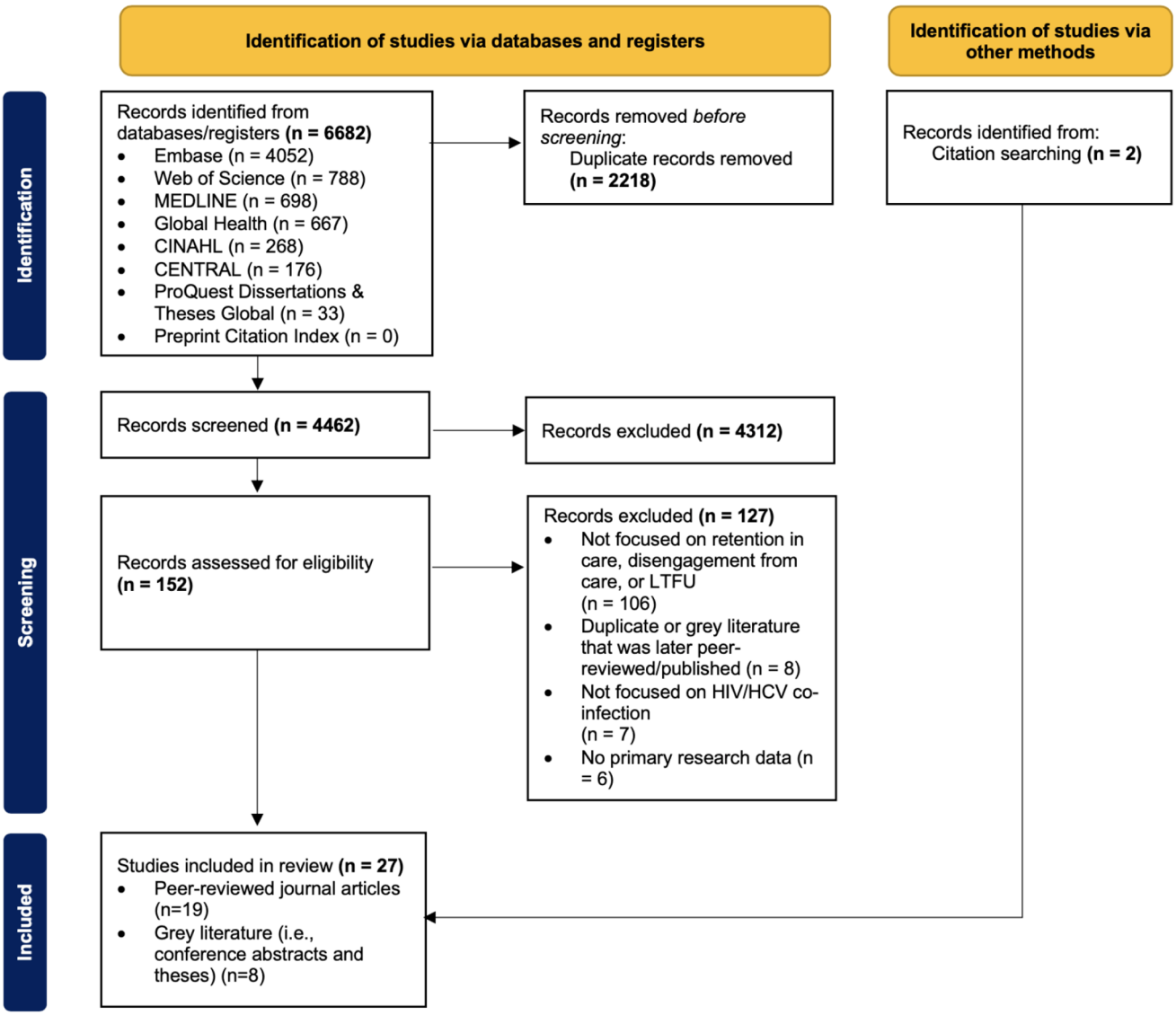

Fig. 1 PRISMA flow diagram of study selection and results

the process of identifying records that meet the inclusion criteria.

Table 1 summarizes the demographic information and characteristics of included studies. Among the 27 studies included, 19 (70.4%) were peer-reviewed articles, and eight (29.6%) were grey literature. Sample sizes ranged from $n=46$ to $n=5114$, with a majority of included studies ($n=23$, 85.2%) consisting entirely of PWH and HCV [25, 53–63, 65–69, 71, 72, 74–77]. 16 studies were retrospective observational studies [20, 53, 55–61, 63–65, 67, 72–74], five were prospective observational [25, 54, 62, 66, 69], four experimental (e.g., randomized controlled trials) [68, 75–77], and two were cross-sectional surveys [70, 71]. 16 studies were conducted in the United States [20, 53, 55, 57, 60, 62, 63, 67, 68, 70, 72–77], five in Canada [25, 59, 61, 64, 69], one each in the UK [71], Austria [58], Taiwan [65], and the Netherlands [66]; and two in multiple countries [54, 56] (i.e., HCV-Tren and EuroSIDA cohort studies).

Four studies examined (dis)engagement in clinical care during the interferon-era (January 2002 - December 2013) [20, 61, 70, 74], 14 during the DAA-era (January 2014-Present) [53, 55–57, 60, 62, 63, 66–68, 71, 72, 75, 76], and six during both [25, 54, 58, 65, 69, 73]; three studies did not specify their study period [59, 64, 77]. Based on the primary objective of the studies, 22 were focused on the HCV care cascade [20, 25, 53–60, 62, 63, 65–67, 70–73, 75–77], two on the HIV care cascade [61, 64], and three on both [68, 69, 74]. 16 sources (12 peer-reviewed [20, 56–58, 61, 62, 65, 69, 70, 72, 73, 75] and 4 grey literature [54, 60, 74, 77]) identified factors associated with retention or disengagement in care; 10 (6 peer-reviewed [25, 55, 62, 63, 66, 71] and 4 grey literature [53, 59, 64, 67]) measured (dis)

Table 1 Characteristics of included studies ($n = 27$)

Citation	Study Design	Type of Article	Study Time frame	Population and Sample Size	Country/ Setting	Study Objective	Care Cascade	Conceptualization of key terms	Identified Factor(s)?	Identified Outcome(s)?	Identified an Intervention?
Ajose et al., 2019	Observational (Retrospective)	Conference Abstract	January 2012 - December 2017; DAA era	HIV/HCV co-infected individuals at the hospital ($n = 819$)	USA/Hospital in Atlanta	To determine barriers to DAA treatment uptake	HCV	No clear definition of "loss to follow up"		X	
Amele et al., 2021	Observational (Prospective: EuroSIDA)	Thesis	January 2011 - January 2017; DAA & IFN Eras	Chapter 4.2; PWH with anti-HCV antibodies enrolled in the EuroSIDA study ($n = 4418$); of whom 54.5% had a history of IDU	Europe, Israel, and Argentina/ EuroSIDA study	Chapter 4.2; To apply the longitudinal HIV/HCV care cascade to the EuroSIDA study and explore factors associated with HCV-treated and HCV-RNA negative	HCV	**LTFU**: "not having a CD4 count, HIV-RNA, or visit data for 15 months"	X		
Cachay et al., 2014	Observational (Retrospective)	Peer Reviewed	January 2008 - December 2012; IFN era	PWH receiving care at the clinic ($n = 4725$); of whom, 11.9% had an active HCV infection($n = 562$)	USA/HCV coinfection clinic co-located in an HIV clinic in San Diego	To investigate the HCV care cascade, and identify barriers to HCV treatment non-referral and non-initiation following linkage to care	HCV	**Engagement in care**: "having 2 or more visits with a primary care physician in our system separated by 3 or more months in each calendar year for the entire defined study period or until date of referral for HCV therapy, unless patient transferred care or was incarcerated."	X		
Cachay et al., 2018	Observational (Retrospective)	Peer Reviewed	January 2014 - December 2017; DAA era	PWH with active HCV new to the clinic ($n = 202$)	USA/HCV coinfection clinic co-located in an HIV clinic in San Diego	To evaluate characteristics of PWH with HCV who failed to attend an initial HCV intake visit and who failed to establish HCV care (i.e., treatment initiation)	HCV	**(Lack of) Engagement in HIV care**: (Not) "having 2 or more visits with an HIV primary care provider in our clinic separated by ≥ 3 months in each calendar year for the entire defined study period or until the date of HCV intake referral appointment, unless the patient transferred care or was incarcerated"		X	

Table 1 (continued)

Citation	Study Design	Type of Article	Study Time frame	Population and Sample Size	Country/ Setting	Study Objective	Care Cascade	Conceptualization of key terms	Identified Factor(s)?	Identified Outcome(s)?	Identified an Intervention?
Cachay et al., 2019	Observational (Retrospective)	Peer Reviewed	January 2014 - December 2017; DAA era	PWH with active HCV infection and initiated DAA ($n=784$)	USA, Spain, and Italy/ HCV-TREN study	To investigate predictors of HCV clinical and virological treatment failure	HCV	No clear definition of "loss to follow-up" ***HCV clinical failure***: *the proportion of patients who discontinued DAA therapy prematurely due to any cause including death or loss to follow-up. Patients who were lost to follow-up were considered to have ongoing HCV viremia.*	X		
Cachay et al., 2020	Observational (Retrospective)	Peer Reviewed	2018; DAA era	PWH with active HCV ($n=143$); of whom, 64% identified as MSM and 62% had a history of IDU	USA/University hospital in San Diego	To investigate factors of HCV treatment non-referral	HCV	**(Non-)Engagement in HIV care**: (Not) "Having ≥ 2 visits with an HIV provider separated by three or more months per calendar year during the study period"	X		
Chromy et al., 2023	Observational (Retrospective)	Peer Reviewed	2002 - December 2020; IFN & DAA era	HIV/HCV co-infected individuals who initiated HCV ($n=461$); of whom 61% had a history of IDU	Austria/viral hepatitis clinic in Vienna	To compare patient characteristics, transmission risks, HCV treatment initiation, and HCV treatment success rates between different HCV treatment eras	HCV	**LTFU**: "All patients without any visits and/or HCV-PCR test results at 24/12 weeks after the end of treatment or afterward"	X		
Conway et al., 2015	Observational (Retrospective)	Conference Abstract	Not specified	PWH who received HCV care from the program ($n=245$), of whom 70.2% were active PWID	Canada/multidisciplinary outreach program in Vancouver	To analyse factors associated with achieving HCV sustained virological response	HCV	No clear definition of "active engagement"		X	
Elion et al., 2019	Observational (Retrospective)	Conference Abstract	January 2013 - October 2018; DAA era	HIV/HCV co-infected individuals with no history of HCV treatment ($n=3896$)	USA/HIV treatment centres	To investigate factors associated with HCV non-treatment during the DAA era	HCV	**LTFU**: "no evidence of treatment or cure and no longer in care at practice"	X		

Table 1 (continued)

Citation	Study Design	Type of Article	Study Time frame	Population and Sample Size	Country/ Setting	Study Objective	Care Cascade	Conceptualization of key terms	Identified Factor(s)?	Identified Outcome(s)?	Identified an Intervention?
Emery et al., 2010	Observational (Retrospective)	Peer Reviewed	January 1996 - June 2008; IFN era	HIV/HCV co-infected individuals treated with HAART ($n=183$); of whom ~78% had a history of IDU	Canada/Immunodeficiency clinic in Ottawa	To assess clinical outcomes associated with ART initiation	HIV	No clear definition of "lost to follow-up"	X		
Falade-Nwulia et al., 2019	Observational (Prospective)	Peer Reviewed	2013 - December 2018; DAA era	PWH with active HCV ($n=593$); of whom 73% had a history of IDU	USA/Hospital in Baltimore	To characterize barriers and facilitators to HCV care in the DAA era	HCV	**Poorly engaged in care**: "Two or more missed [HIV care] visits in the year before study baseline"	X	X	
Hanna et al., 2022	Observational (Retrospective)	Peer Reviewed	January 2015 - June 2018; DAA era	PWH with active HCV ($n=46$)	USA/HIV Clinic in an underserved community	To evaluate a pharmacist-led campaign to reduce proportions of PWH with HCV	HCV	**Poor engagement in care**: "failing to have at least two visits with a clinic provider separated by at least 3 months during a 12-month period"		X	X
Holeska et al., 2019	Observational (Retrospective)	Conference Abstract	Not specified	HCV-infected people who inject drugs ($n=486$); of whom 19% were co-infected with HIV	Canada/Infectious disease centre in Vancouver	To assess the impact of long-term engagement in multidisciplinary care on HIV treatment success among PWH with HCV who inject drugs	HIV	**Long-term engagement in care**: continuing [care] after HCV treatment		X	
Huang et al., 2021	Observational (Retrospective)	Peer Reviewed	2011–2018; IFN & DAA eras	PWH with anti-HCV antibodies ($n=287$); of whom, 92.3% identified as MSM	Taiwan/Hospital in Taipei	To examine the HCV care cascade among PWH with HCV in a Taiwanese hospital	HCV	No clear definition of "engagement in care"	X		
Jain et al., 2018	Observational (Retrospective)	Conference Abstract	November 2015 - October 2017; DAA era	PWH with anti-HCV antibodies ($n=914$)	USA/Hospital in Dallas	To examine the factors (e.g., lost to care, missed visits) associated with being HCV-RNA positive	HCV	**Lost to care**: "No visits for > 1 year"		X	

Table 1 (continued)

Citation	Study Design	Type of Article	Study Time frame	Population and Sample Size	Country/ Setting	Study Objective	Care Cascade	Conceptualization of key terms	Identified Factor(s)?	Identified Outcome(s)?	Identified an Intervention?
Isfordink et al., 2022	Observational (Prospective: ATHENA)	Peer Reviewed	October 2015 - November 2020; DAA era	PWH with active HCV infection ($n=1031$); of whom 65% identified as MSM	Netherlands/ ATHENA study	To investigate the prevalence of HCV-viremia and barriers to DAA treatment during unrestricted DAA access	HCV	**LTFU: "**no contact for over 1 year, and no new appointment planned"; does not include participants deceased or moved abroad		X	
Metsch et al., 2021	Experimental (Randomized Control Trial)	Peer Reviewed	February 2017 - January 2018; DAA era	PWH who have a history of opioid, stimulant or heavy alcohol use and are HCV antibody positive ($n=113$)	USA/Study sites in Atlanta, Baltimore, Boston, Chicago, Dallas, Miami, New York, and Philadelphia	To evaluate the efficacy of a 6-month care facilitation intervention (CTN-0064) on the HCV care cascade	HIV/HCV	No clear definition of a key term; measured steps along the HIV/ HCV care continuum			X
Palayew et al., 2021	Observational (Prospective: Canadian Co-infection Cohort study)	Peer Reviewed	2003–2018; IFN & DAA eras	PWH with anti-HCV antibodies ($n=1842$); of whom, 82% report a history of IDU	Canada/ Canadian Co-infection Cohort	To develop and estimate an individual-level model-based deprivation index for PWH with HCV using an item response theory model	HIV/HCV	**Disengagement in care**: "Attending a second cohort visit (scheduled every 6 months)"	X		
Pundhir et al., 2016	Cross-sectional survey	Peer Reviewed	November 2009 - February 2011; IFN era	People infected with HCV ($n=292$); of whom, 51% are co-infected with HIV and 53% report a history of IDU	USA/County health and hospital system in Dallas	To examine factors associated with appointment-keeping behaviour and non-engagement in care	HCV	No clear definition of a key term; measured appointment-keeping behaviour	X		
Raya et al., 2023	Clinic survey and retrospective case-note review	Peer Reviewed	May 2021 - July 2021; DAA era	People co-infected with HIV and HCV who attended one of these services; case-note reviews included PWH with active HCV infection ($n=283$)	UK/95 regional specialist centres and HIV services	To describe and assess UK clinical policies for managing HIV/HCV co-infection	HCV	No clear definition of "lack of engagement in care"		X	

Table 1 (continued)

Citation	Study Design	Type of Article	Study Time frame	Population and Sample Size	Country/ Setting	Study Objective	Care Cascade	Conceptualization of key terms	Identified Factor(s)?	Identified Outcome(s)?	Identified an Intervention?
Rizk et al., 2019	Observational (Retrospective)	Peer Reviewed	January 2014–March 2017; DAA era	PWH with active HCV infection ($n=173$); of whom 54.3% reported active drug use	USA/Hospital in New Haven	To evaluate the impacts of an HCV/HIV co-located clinic on the HCV care cascade, with particular focus on linkage to care and treatment initiation	HCV	**Not engaged in HCV care**: "patients who were not prescribed DAA treatment"; separate from death, relocation, and incarceration)	X		X
Roberson et al., 2018	Observational (Retrospective)	Peer Reviewed	January 2008 - December 2015; IFN & DAA eras	People infected with HCV ($n=5114$); of whom, 8.3% are co-infected with HIV	USA/Veterans affairs medical center in Washington, D.C.	To describe the HCV care continua across different HCV treatment eras	HCV	**Engagement in care**: "at least one visit to any primary care clinic"	X		
Saeed et al., 2020	Observational (Prospective: Canadian Co-infection Cohort)	Peer Reviewed	2010–2018; IFN & DAA eras	PWH with active HCV infection ($n=1843$);	Canada/CCC study	To evaluate the impacts of unrestricted HCV treatment access on HCV treatment initiation rates	HCV	**Disengagement in care: "**not having a cohort visit within 18 months of our administrative censoring date (excluding those who had formally withdrawn from the study and those who died)."		X	
Schnee et al., 2016	Observational (Retrospective)	Conference Abstract	2006–2012; IFN era	HIV/HCV coinfected individuals ($n=49$); of whom, 55% had a history of IDU	USA/Clinic in South Carolina	To evaluate factors associated with poor retention among PWH with HCV	HIV/HCV	**Retention**: "at least 2 visits, divided by 90 days within a 1 year period"	X		
Starbird et al., 2020	Experimental (Randomized Control Trial)	Peer Reviewed	January 2016 - February 2018; DAA era	PWH with active HCV infection ($n=68$)	USA/infectious disease outpatient practice in Baltimore	To investigate the impact of a nurse care management intervention on engagement in HCV care continuum	HCV	**Engagement in HCV care**: at least one visit to the viral hepatitis practice in the past 12 months	X		X

Table 1 (continued)

Citation	Study Design	Type of Article	Study Time frame	Population and Sample Size	Country/ Setting	Study Objective	Care Cascade	Conceptualization of key terms	Identified Factor(s)?	Identified Outcome(s)?	Identified an Intervention?
Ward et al., 2019	Experimental (Randomized Control Trial)	Peer Reviewed	August 2015 - October 2016; DAA era	PWH with active HCV infection who have not engaged in HCV care within 8 months ($n = 194$)	USA/infectious disease outpatient practice in Baltimore	To test the impacts of cash incentives and peer mentors on HCV treatment initiation and cure rates	HCV	No clear definition of a key term; analysed steps along care continuum			X
Wegener et al., 2020	Experimental	Conference Abstract	Not specified	HIV/HCV co-infected individual out of care for > 12 months ($n = 196$)	USA/Surveillance databases (CTEDSS and eHARS); New Haven	To evaluate the efficacy of using a disease intervention specialist to re-engage individuals back into HCV care	HCV	**Disengagement (Out of care)**: no HIV lab within a specified time frame (12 months or 18 months)	X		X

Note DAA, direct-acting antiretrovirals; IDU, injection drug use; HCV, hepatitis C; IFN, interferon; LTFU, lost to follow-up; MSM, men who have sex with men; PWH, people with HIV

engagement as an exposure and identified outcomes; and 6 identified an intervention (5 peer-reviewed [63, 68, 72, 75, 76] and one grey literature [77]) to improve engagement across the care cascade.

Conceptualization of Key Terms

Of the 27 included studies, 18 conceptualized retention or disengagement in care (Table 1). Definitions of (dis)engagement in care were diverse, with considerable heterogeneity in how retention was operationalized and temporally measured (Fig. 2).

The most common definition of (dis)engagement in care was based on scheduling and attending appointments over a six-month period [20, 55, 57, 62, 63, 74, 75] (e.g., "Having two or more visits with an HIV primary care provider in our clinic separated by ≥ 3 months in each calendar year" [55]). Other conceptualizations of engagement in care were operationalized based on records of blood biomarker testing [54, 58, 77] (e.g., LTFU defined as being "without any visits and/or HCV-PCR test result at 24/12 weeks after the end of treatment or afterward" [58]) or treatment access [60, 72] (e.g., LTFU defined as "no evidence of treatment or cure and no longer in care at practice" [60]). Five studies clearly distinguished between disengagement and other clinical events such as death [25, 66, 72], clinic transfers or study withdrawals [20, 25, 55, 66, 72], and incarceration [20, 55]. Furthermore, five studies [54, 55, 57, 62, 63] conceptualized (dis)engagement in care based on HIV care guidelines, such as by the EACS [19], Infectious Diseases Society of America (IDSA) [78], and US Department of Health and Human Services (DHHS) [79, 80], whereas the others did not specify their basis. One definition based on EACS guidelines (version 10.1) defined lost to follow-up as "Not having a CD4 count, HIV-RNA, or visit data for 15 months" to account for any deferrals in blood biomarker testing or visits [54].

Factors Associated with Retention in Care or Disengagement in Care

Twelve peer-reviewed studies identified factors associated with retention in care or disengagement from care **(**Table 2**).**

Demographics

Demographic characteristics affect retention in the HCV/HIV care cascades [61, 72]. Factors associated with poor retention in care included male sex [61], female sex [72], and younger age [72]. The underlying reasons for gender-based differences in HIV/HCV care retention are not well understood [61], with speculations including women

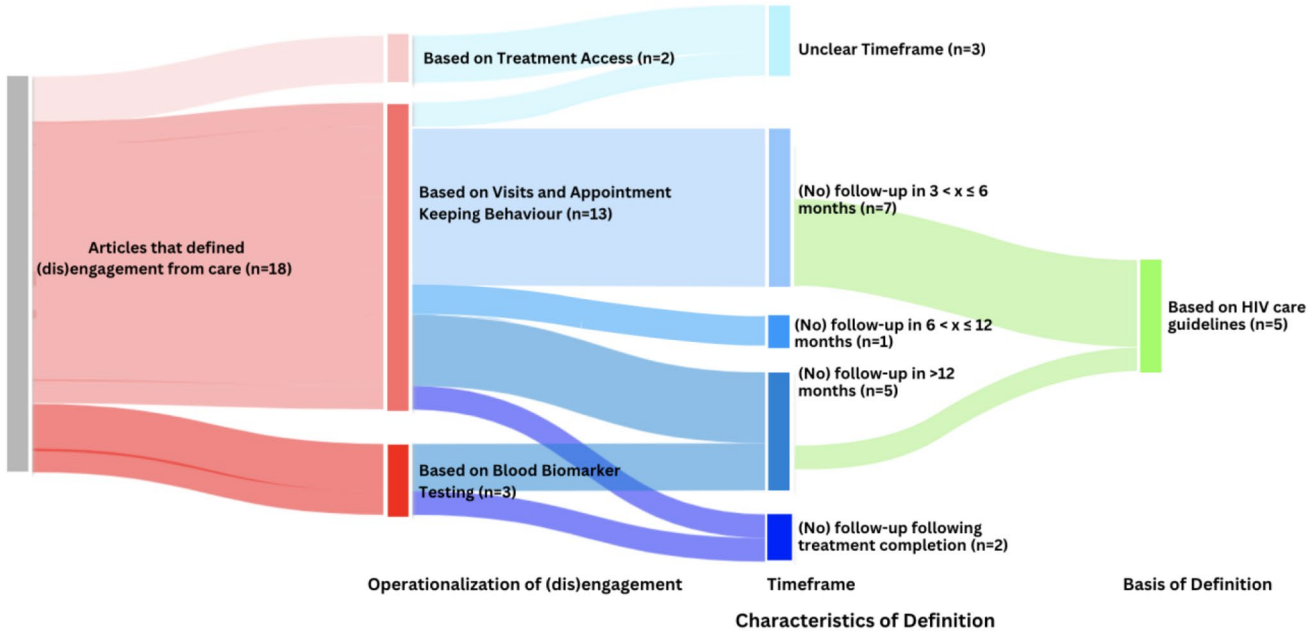

Fig. 2 Sankey diagram showcasing heterogeneity in the definitions of (dis)engagement from care ($n = 18$). Note Of the 27 included studies, 18 defined (dis)engagement in care based on how it was operationalized (records of scheduling and attending appointments, blood biomarker testing, and/or treatment access) and their timeframes. Five of these 18 studies specified definitions were based on HIV clinical care guidelines, such as by the European AIDS Clinical Society (EACS) [19], Infectious Diseases Society of America (IDSA) [78], and US Department of Health and Human Services (DHHS) [79, 80]

Table 2 Summary of factors and outcomes associated with retention in/disengagement from the HCV and HIV cascades

First Author	Year	Factors						Outcomes		
		Drug and Substance Use	Social/ Welfare Factors	Clinical Related Factors	Demographic	Mental Health	Treatment Location	HCV Treatment Initiation	HCV Treatment Success	HIV Treatment Success
Cachay	2014	(-)								
Cachay	2018							(=)		
Cachay	2019	(-)	(-)	(-)		(-)				
Cachay	2020	(-)	(-)							
Chromy	2023			(+)			(+)			
Emery	2010				(-)					
Falade-Nwulia	2019	(-)						(+)		(+)
Hanna	2022								(+)	
Huang	2021			(+)						
Isfordink	2022							(+)		
Palayew	2021		(-)							
Pundhir	2016		(-)							
Raya	2023							(+)		
Rizk	2019				(-)					
Roberson	2018			(+)						
Saeed	2020								(+)	
Starbird	2020	(+)		(+)						

Note + represents items associated with retention/engagement in care, – represents items associated with disengagement from care, while = represents a non-significant association

deferring treatment due to family obligations or other traditionally gendered domestic responsibilities [72]. Three peer-reviewed studies evaluated the role of race on (dis) engagement in care [62, 69, 72], but none found a statistically significant association.

Substance Use

Substance use emerged as a significant factor affecting retention in care among PWH and HCV in five studies [20, 56, 57, 62, 75]. Generally, injection drug use [56, 57, 62] and alcohol misuse [56, 57] were associated with poor retention in care. In a bivariate analysis from an HCV-TREN cohort study, ongoing injection drug use and alcohol misuse were key predictors of HCV treatment challenges, manifesting as premature treatment discontinuation due to any cause, including losses to follow-up [56]. However, a counterintuitive positive association between alcohol use and engagement in HCV care (OR = 3.79, 95% CI [1.14–12.61]) was observed in one study, suggesting motivation among some to achieve HCV cure to reduce the synergistic effects of alcohol use [75].

Social/Welfare

Social and welfare factors also affect disengagement from care. Experiences of unstable housing have been linked to non-engagement in HIV care [57] and HCV clinical failures [56]. Moreover, social isolation—reflective of experiences of stigma —can negatively influence maintaining liver clinic appointments among both HCV and HIV/HCV co-infected patients [70]. To further explore these individual experiences, the Canadian Co-infection Cohort study developed a deprivation index with social/lifestyle variables (income >$1500/month, education > high school, employment, identifying as gay or bisexual, Indigenous status, injection drug use in last 6 months, injection drug use ever, past incarceration, and past psychiatric hospitalization) and found that higher deprivation scores were linked to increased odds of failing to attend a second care appointment (OR = 1.17, 95% CI [1.02–1.34]), suggestive of greater propensity for disengagement from care [69].

Clinical-Related Factors

The introduction of DAAs has had a transformative effect on retention in HCV care [58, 65, 73]. A study conducted at a viral hepatitis clinic in Austria indicated reduced odds of LTFU during the restricted DAA era (January 2014-September 2017; OR = 0.11, 95% CI [0.03–0.46]) and unrestricted DAA era (October 2017-December 2020; OR = 0.47, 95% CI [0.24–0.92]), compared to the interferon era (before December 2013) [58]. Disease progression in PWH and HCV, along with co-morbidities, can also influence retention in HCV care [56, 58, 75]. Clinical indicators such as advanced liver fibrosis [58] and higher CD4 cell count [75] have been associated with improved retention in care, suggesting that advanced disease may facilitate shifts in individual risk behaviour [58]. In direct contrast, another study indicated that advanced liver fibrosis was associated with HCV treatment failures [56], but the reason for the discrepancy remains elusive.

Other

Other factors, including treatment location, mental illness, and peer influence, have also been recognized for their role in HCV care retention [56, 58, 75]. Having personal connections to individuals who have been cured of HCV infection [75] and participation in dedicated treatment programs [58] are associated with greater odds of engagement in care (OR = 5.25, 95% CI [1.40-19.55]) and reduced risk of loss to follow-up (OR = 0.26, 95% CI [0.13–0.52]), respectively. In contrast, mental illness has been associated with any clinical HCV failure (OR = 2.78, 95% CI [1.71–4.52]) [56].

Outcomes

Six peer-reviewed studies identified outcomes associated with disengagement (Table 2).

HCV Treatment Initiation

Three studies cited treatment initiation as an outcome associated with retention in care [62, 66, 71]. A prospective observational study from Baltimore reported a negative association between missing a majority of HIV primary care appointments and HCV treatment initiation (HR = 0.39, 95% CI [0.25–0.60]) [62].

HIV- and HCV-Treatment Success

Three studies also drew a connection between successful HIV and HCV treatment outcomes and retention in care [25, 62, 63]. In line with existing research [25], a retrospective chart review of a hospital-based clinic in an underserved community indicated that patients who had a lapse in care for > 12 months were at reduced odds of achieving SVR (OR = 0.069, 95% CI [0.014–0.337]) [63]. Likewise, individuals poorly engaged in HIV care were less likely to achieve HIV viral suppression [62].

Interventions Addressing Engagement in Care

Five peer-reviewed articles detailed interventions to increase engagement among PWH and HCV in HCV care (Table 3) [63, 68, 72, 75, 76]. Interventions included contingency measures [76] ($n=1$), such as peer support and contingent financial incentives, and individual case management [63, 68, 72, 75] ($n=4$). The case management approach—facilitated by various healthcare professionals, including pharmacists [63], nurses [75], care facilitators with a social work background [68], or a multidisciplinary team of health professionals [72]—focused on providing HCV treatment education and assistance in appointment scheduling and attendance.

Integrated HCV and HIV care services with a multidisciplinary team can improve the care cascades via sustained patient engagement and decreased barriers to care [72, 76]. However, the efficacy of specific interventions to increase HCV care engagement among PWH was considered modest. Individual case management by an individual healthcare professional improved rates of linkage to HCV care [75], reduced clinic prevalence of HCV infection [63], and overall progress along the HCV care cascade [68], but did not improve rates of achieving HCV SVR [68, 75]. Further, there were no significant differences in engagement in care in the intervention based on peer support and contingent cash incentives [76].

Discussion

The present scoping review examined 27 sources, shedding light on the complexity of disengagement from care among PWH and HCV in high-income countries. While several reviews exist in the context of HIV and HCV mono-infection [22, 37, 46, 47, 50, 81], to our knowledge, this is the first review to synthesize literature on disengagement from HIV and HCV co-infection care.

Our scoping review highlights heterogeneity in the conceptualization of (dis)engagement in care among PWH and HCV. Most included studies characterize engagement through patients' adherence to appointment schedules within a specific timeframe, ranging from three to over 12 months, while others encompass aspects such as accessing treatment and reports of laboratory blood work. Five studies adopted conceptualizations of (dis)engagement in care based on national HIV guidelines (e.g., the EACS and DHHS guidelines); however, the remaining 22 failed to explicitly state or justify the specific definitions employed. Furthermore, a minority of studies differentiated LTFU from other clinical events, such as death, incarceration, and clinic transfers.

This lack of uniformity in definitions renders cross-study comparisons and meta-analyses virtually impossible. Similar challenges were described in existing systematic reviews on retention in care and LTFU among HIV and HCV mono-infected populations [22, 36, 50]. Moreover, this variability in defining engagement in care distorts measures of SVR success rates, complicating our ability to track progress towards the WHO goals. Failures to appropriately identify and account for individuals' LTFU in the HCV care cascade may lead to inaccurate and incomparable SVR success rates. Definitions of disengagement from care should be standardized to HIV and HCV clinical care guidelines, with specific operationalizations and timeframes. Disengagement from care should also be clearly distinguished from permanent clinical events, such as mortality and clinic transfers. To account for variations in engagement timeframes and ensure the robustness of findings, sensitivity analyses with varying definitions of disengagement from care (e.g., with varying timeframes) should be provided whenever possible [82].

While disengagement from care does not necessarily imply medication non-adherence, health outcomes associated with disengagement are conspicuous. In the context of HIV and HCV co-infection, poor engagement in care impedes rates of HCV treatment initiation [62, 66, 71] and achieving both HCV SVR [25, 63] and HIV viral suppression [62]. However, the link between disengagement from care and risks of adverse long-term health outcomes, such as HCV reinfection and mortality, among PWH and HCV were not identified.

Furthermore, a majority of included studies ($n=18$ (66.7%)) were cross-sectional in design (i.e., retrospective cohort studies or cross-sectional surveys), failing to capture patients' actual experiences in care [83]. Retention is a multi-factorial concept [26, 27], influenced by shifting priorities that may 'tip the balance' towards or away from regularly interacting with healthcare professionals [84]. PWH and HCV may exit and re-enter care at various points along the care continuum, exhibiting dynamic transition patterns that significantly impact mortality and treatment outcomes [82]. Thus, this reliance on cross-sectional studies limits our ability to track and accurately understand (dis)engagement in care.

In the present scoping review, several factors of (dis)engagement in care among PWH and HCV were identified, including substance use-, social/welfare-, clinical-, and demographic-related factors. Congruent with findings from a systematic review on retention in HIV care [50], injection drug use [56, 57, 62] emerged as a primary factor influencing poor retention in care among PWH and HCV in high-income countries. PWID face substantial socio-structural barriers to care [2], including fractured social networks, competing priorities such as attaining stable housing, and experiences

Table 3 Summary of interventions aimed at improving engagement in care among PWH and HCV ($n=5$)

Citation	Study Design	Study Time frame	Country/ Setting	Population and Sample Size	Objective	Intervention	Intervention Category	Facilitator	Reported Outcomes
Hanna et al., 2022	Observational (Retrospective)	January 2015 - June 2018	USA/HIV Clinic in an underserved community	PWH and active HCV ($n=46$)	To evaluate a pharmacist-led campaign to reduce proportions of PWH with HCV	An initial effort to treat and manage PWH and HCV for HCV infection via a multidisciplinary team, including physicians, nurse practitioner, and clinic staff. Remaining untreated patients were approached by a pharmacy team (clinical pharmacist and ambulatory care pharmacy resident) to initiate HCV treatment. Case-management was then carried out by the pharmacy team, included patient education on DAA-based therapies during routine clinic visits or phone call and medication coordination.	Individual Case Management	Pharmacist	There was a statistically significant difference in HCV prevalence in the clinic from baseline to the end of the pharmacy-led initiative (46 patients with active HCV infections vs. 6 patients; $p<.0001$).

Table 3 (continued)

Citation	Study Design	Study Time frame	Country/ Setting	Population and Sample Size	Objective	Intervention	Intervention Category	Facilitator	Reported Outcomes
Metsch et al., 2021	Experimental (Randomized Control Trial)	February 2017 - January 2018	USA/Study sites in Atlanta, Baltimore, Boston, Chicago, Dallas, Miami, New York, and Philadelphia	PWH who have a history of opioid, stimulant or heavy alcohol use and are HCV antibody positive ($n=113$)	To evaluate the efficacy of a 6-month care facilitation intervention (CTN-0064) on the HCV care cascade	Participants were randomized into one of two groups: (i) control group ($n=61$) and (ii) care facilitation group ($n=52$). The control group was referred for HCV treatment and were assisted in scheduling the first appointment; the care facilitation group received motivation and strength-based case management (e.g., assistance with scheduling and attending appointments, regular meetings with care facilitator, and motivational interviewing) to ensure engagement in HCV/ HIV care.	Individual Case Management	Care facilitator with a background in social work	There was a statistically significant improvement in advancement along the HIV/ HCV care cascade among the intervention group, compared to the control group (2.44 steps vs. 1.68 steps; $\chi2\ (1)=7.36$, $p=.0067$). Across both groups, there were no statistically significant differences between rates of HIV viral suppression ($P=.244$) and achieving HCV SVR.

Table 3 (continued)

Citation	Study Design	Study Time frame	Country/ Setting	Population and Sample Size	Objective	Intervention	Intervention Category	Facilitator	Reported Outcomes
Rizk et al., 2019	Observational (Retrospective)	January 2014–March 2017	USA/Hospital in New Haven	PWH and active HCV infection ($n=173$); of whom 54.3% reported active drug use	To evaluate the impacts of a HCV/HIV co-located clinic on the HCV care cascade, with particular focus on linkage to care and treatment initiation	HCV/HIV co-infected clinic included a multidisciplinary team, consisting of physicians, a nurse, a physician assistant, pharmacists, and data managers. Individual patient plans were regularly managed by the multidisciplinary team. Patients not referred, linked, or treated were contacted via phone calls.	Individual Case Management	Multidisciplinary healthcare team	HCV care cascade in this clinic compares favourably to national HCV treatment cascades, with 93%, 85%, 71%, and 56% of co-infected individuals having been referred, linked, DAA treatment-initiated, and achieved SVR12, respectively. EMR data suggests that the multidisciplinary team sustained continuous cycles of engagement among PWH and HCV.

Table 3 (continued)

Citation	Study Design	Study Time frame	Country/ Setting	Population and Sample Size	Objective	Intervention	Intervention Category	Facilitator	Reported Outcomes
Starbird et al., 2020	Experimental (Randomized Control Trial)	January 2016 - February 2018	USA/ infectious disease outpatient practice in Baltimore	PWH and active HCV infection ($n=68$)	To investigate the impact of a nurse care management intervention on engagement in HCV care continuum	Participants randomized to one of two groups: (i) usual care ($n=33$) or (ii) nurse care management ($n=35$). Usual care involved normal outpatient clinical processes at the Baltimore practice; nurse care management involved HCV referral, face-to-face HCV education, social support, patient navigation, appointment reminders via personalized messages, and medication coordination.	Individual Case Management	Nurse	A higher proportion of participants in the nurse care management group, compared to the usual care group, were linked into HCV care within 60 days of enrolment (47% vs. 25%; $p=.031$). There were no statistically significant differences in DAA-prescription ($p=.670$), DAA-treatment initiation ($p=.164$), and achieving HCV SVR ($p=.651$) within 180 days between both treatment groups.

Table 3 (continued)

Citation	Study Design	Study Time frame	Country/ Setting	Population and Sample Size	Objective	Intervention	Intervention Category	Facilitator	Reported Outcomes
Ward et al., 2019	Experimental (Randomized Control Trial)	August 2015 - October 2016	USA/ HCV clinic co-located in an HIV clinic in Baltimore	PWH and active HCV infection who have not engaged in HCV care within 8 months ($n=194$)	To test the impacts of cash incentives and peer mentors on HCV treatment initiation and cure rates	Participants randomized to one of three groups: (i) usual care ($n=36$), (ii) usual care and cash incentive ($n=54$), and usual care and peer mentor support ($n=54$). Usual care involved a clinician-managed treatment regimen of HIV antiretroviral therapy and ledipasvir/ sofosbuvir, alongside case management led by a nurse. Cash incentives (a total maximum of $220) were contingent on attendance, and peer mentor support involved face-to-face or mobile phone calls before, during, and after HCV treatment, with another PWH engaged in care who has been successfully treated for HCV.	Peer Support and Cash Incentives	N/A	76% ($n=110/144$) and 69% ($n=100/144$) of participants successfully initiated HCV treatment and achieved SVR, respectively. There were no statistically significant differences between treatment groups i, ii, and iii in HCV treatment initiation (67% vs. 76% vs. 83%, $p=.11$) and HCV SVR (90% vs. 91% vs. 92%). Enhanced usual care in the clinic may account for lack of statistically significant differences in outcomes between treatment groups.

of stigma in healthcare settings [85, 86]. These barriers contribute to institutional mistrust [87] among PWID and may lead to poor engagement in clinical care. Even following HCV treatment success, mortality rates among PWID remain disproportionately high [88], underscoring the need for tailored and continued care for this group. Interestingly, our search highlighted a significant gap in the literature on the associations of race/ethnicity, socioeconomic status, and supervised consumption services (SCS) with (dis)engagement in care. Understanding the impact of race/ethnicity and socioeconomic status is crucial, given the profound effects of systemic inequities and discrimination on healthcare access and outcomes [28, 89, 90]. Furthermore, SCS often employ multidisciplinary teams that can facilitate testing, linkage to care, and referrals to other harm reduction services [91–94], making them a promising avenue for future interventions to enhance engagement in care for PWH and HCV. Further research should continue to elucidate factors associated with (dis)engagement in care, including the role of race/ethnicity, socioeconomic status, and SCS.

While limited engagement interventions were identified, the findings from this scoping review corroborate existing research on the effectiveness and practicality of HIV/ HCV co-located clinics [72, 76]. Given the complex needs

of PWH and HCV, employing multidisciplinary teams of healthcare professionals may be fruitful in engaging patients, particularly in earlier stages of care. Considering overlaps in the HIV and HCV care cascades, integrating HCV care into established HIV clinics has the potential to reduce accessibility barriers, extend the reach of resources, and streamline patient-centred care [95].

The continuous nature of the HIV care continuum can help healthcare professionals retain individuals with HCV post-SVR [95]. However, this scoping review reveals a lack of studies that include post-SVR care as part of the HCV care continuum. Unlike HIV care, in which life-long engagement is required to achieve viral suppression [16], HCV care often concludes upon achieving SVR [22]. While SVR is a cure, concluding engagement in care at this point is suboptimal, overlooking the need for ongoing health monitoring for PWH and HCV [22]. HCV reinfection following SVR is a substantial concern, particularly among high-risk persons, including PWH, men who have sex with men, and PWID [96, 97]. Despite achieving SVR, competing co-morbidities may put people at high mortality risk [98], underscoring the need for ongoing support. The interconnected nature of the HIV and HCV care cascade provides an opportunity for continual engagement in care and intervention. Future research should focus not only on engaging PWH and HCV in care until treatment success but also beyond—especially those with advanced liver fibrosis, who may still face long-term liver outcomes after achieving SVR [22], and those considered at high-risk of reinfection.

Findings from this scoping review should be interpreted within several limitations. Firstly, terminology and conceptualizations used to describe (dis)engagement varied markedly, restricting comparisons between studies and complicating the inclusion/exclusion criteria. Secondly, the present scoping review is not intended to assess the validity of study results or the efficacy of interventions; instead, it serves as a synthesis of existing literature. Interpretations of factors and outcomes should be cautiously approached, as they do not encompass an exhaustive list of all possible variables associated with (dis)engagement in care. Furthermore, the findings discussed in this scoping review are specific to high-income settings, where access to HIV and HCV care and sociocultural beliefs are not generalizable to low- or middle-income settings [42, 43]. Nonetheless, this scoping review is a comprehensive literature synthesis, providing valuable insights to inform future research and interventions for PWH and HCV.

Conclusion

Despite recent breakthroughs in HIV and HCV treatments, disengagement from care remains a pressing public health concern. Our scoping review highlights significant gaps in the literature on disengagement from care among PWH and HCV. Future research should address (i) a standardized definition of disengagement from care, (ii) interventions that capitalize on the nested HIV and HCV care continuums, and (iii) longitudinal study designs to analyze diverse factors and outcomes associated with disengagement. Eliminating HIV and HCV infections extends beyond medicine. It demands a holistic and coordinated approach to ensuring retention in care—vital to moving global efforts of HIV and HCV eradication toward success.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10461-024-04436-6.

Acknowledgements We thank Sandra McKeown (Bracken Health Sciences Library, Queen's University) for her assistance in developing the literature search strategy.

Author Contributions Conceptualization: DAD, YT & SS; Methodology: DAD & SS; Formal analysis and investigation: DAD, YT & SS; Visualization: DAD; Writing - original draft preparation: DAD; Writing - review and editing: DAD, YT, & SS; Supervision: SS. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Funding DAD was supported by a summer student fellowship from the Canadian Network on Hepatitis C (CanHepC) and the CIHR; CanHepC is funded by a joint initiative of the CIHR [NPC-178912] and the Public Health Agency of Canada. The funders had no role in the production of this manuscript.

Declarations

Financial Interests DAD reports a stipend from the Canadian Network on Hepatitis C (CanHepC) as part of a summer student fellowship. SS reports consulting fees from Novo Nordisk (unrelated to this study). YT declares they no financial interests.

Non-Financial Interests Not applicable.

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