Received: 2 May 2022 | Accepted: 27 December 2022

DOI: 10.1097/HC9.0000000000000082

ORIGINAL ARTICLE

OPEN

Immediate treatment for recent hepatitis C infection in people with high-risk behaviors: a systematic review and meta-analysis

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Abstract

Background and Aims: Direct-acting antivirals (DAAs) are almost exclusively approved for the treatment of chronic HCV. This poses a significant barrier to the treatment of recently acquired HCV because of the limited access to DAAs. This review seeks to address this issue by synthesizing evidence of the benefits and harms of immediate treatment after the detection of recently acquired HCV in people at higher risk of infection.

Approach and Results: A systematic review and meta-analysis were conducted reporting on populations with recently acquired HCV at higher risk of infection. Studies were included if they assessed standard duration DAA treatment regimens and reported on the benefits and harms of immediate treatment (within one year of diagnosis). Outcomes included sustained virological response at 12 weeks post-treatment (SVR12), incidence, treatment initiation and adherence, overtreatment, engagement in care, and adverse events. Eight cohort studies, 3 open-label trials, and 1 case series study were included, reporting on 2085 participants with recently acquired HCV infection. No studies included a comparison group. Eight studies assessed DAA treatment in either men who have sex with men or men who have sex with men with HIV, 2 studies assessed treatment in people who inject drugs, and 2 among people living with HIV. Immediate treatment of HCV was associated with a pooled SVR12 of 95.9% (95% CI, 92.6%–99.3%). Three studies reported on

Abbreviations: ART, antiretroviral therapy; DAA, direct-acting antiviral; IFN, interferon; IVDU, intravenous drug use; MSM, men who have sex with men; OAT, opioid agonist treatment; PLHIV, people living with HIV; PrEP, pre-exposure prophylaxis; PWID, people who inject drugs; STI, sexually transmitted infection; SVR, sustained virologic response; WHO, World Health Organization.

Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website, www.hepcommjournal.com

hepatitis C incidence, where most participants were treated in the chronic phase of infection. A treatment completion rate of 100% was reported in 2 studies, and only 1 serious adverse event was described.

Conclusions: High rates of cure were achieved with the treatment of recently acquired hepatitis C in people at higher risk of infection. Serious adverse events were rare, highlighting individual benefits consistent with the treatment of chronic hepatitis C. The impact of immediate treatment on HCV incidence requires further evaluation.

INTRODUCTION

In 2016, the World Health Organization (WHO) set targets to eliminate HCV infection as a major public health threat by 2030.[1] An integral part of achieving this goal is diagnosis and treatment: 80% of those infected need to be diagnosed and 80% of those diagnosed subsequently treated.[1] After HCV infection, approximately one quarter of individuals will spontaneously clear the virus, but this clearance is less likely in people with HIV/HCV coinfection.[2] Importantly, individuals who clear HCV infection are not immune to the virus, and those engaging in higher-risk behaviors, such as people who inject drugs (PWIDs), men who have sex with men (MSM), people in custodial settings, and other higher-risk populations, are at greater risk of reinfection. In MSM, a higher incidence of HCV infection has been observed in those living with HIV and those using HIV prophylaxis (pre-exposure prophylaxis).[3] Injecting drug use and the sharing of injecting equipment have been attributed to 43% of new HCV infections.[4] Before the advent of direct-acting antivirals (DAAs), less tolerable and longer duration interferon-based therapies were the standard of care for HCV treatment, meaning that people with recently acquired HCV were often advised to defer treatment to avoid unnecessarily treating those who may spontaneously clear the virus.

Given the significantly improved tolerability of DAAs, decreasing price, and increasing access to therapy, the opportunity costs of immediate versus delayed treatment of recently acquired infection have become increasingly important. The joint guideline of the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America recommends that HCV treatment should be initiated without waiting for possible spontaneous clearance, which generally occurs within 6 months of acute infection.[5] The rationale behind this recommendation emphasizes that immediate treatment reduces losses to follow-up and prevents transmission to others from those with HCV infection risk factors. The guideline of the European Association for the Study of Liver[6] similarly highlights the risk of onward transmission where the treatment of recently acquired hepatitis C is delayed and recommends treatment with a standard duration pangenotypic DAA regimen. In addition to the population health benefit of preventing onward transmission, individual benefits include earlier access to cure and potential psychological benefits, including those related to the stigma associated with HCV infection. This is supported by the results of the 2021 International Network of People who Use Drugs values and preferences survey, which found that the overwhelming majority of participants were supportive of being offered immediate treatment after HCV diagnosis.[7]

Despite the expert societies like American Association for the Study of Liver Diseases and European Association for the Study of the Liver recommending against delaying treatment of recently acquired HCV, DAAs are currently almost exclusively approved by regulatory bodies only for confirmed chronic HCV treatment and registration studies for HCV drugs have been limited to this population. This restriction poses a significant barrier to the treatment of recently acquired hepatitis C because of reduced access to DAAs. The question of treating recently acquired hepatitis C is of critical importance globally and is being actively considered by WHO in their updated guideline development for viral hepatitis and key populations, including PWIDs and MSM. Accordingly, our systematic review aimed to review current evidence related to the benefits and harms of immediate treatment of recently acquired hepatitis C in people at higher risk of infection and update the current body of evidence that informs the timing of HCV treatment.

METHODS

A systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for reporting systematic reviews.[8] The review protocol was registered prospectively (PROSPERO registration number 2021 CRD42021239375).

Eligibility criteria

We included studies set in populations with recently acquired hepatitis C (acquisition within 1 year of diagnosis) at higher risk of infection. People at higher risk included, but were not limited to, MSM, PWIDs, transgender people, and people in custodial settings. Studies were included if they assessed DAA treatment among people identified as recently acquiring HCV infection using licensed DAA regimens.[9] Studies using short course duration DAA therapy for recent HCV were excluded, as this review focused on currently licensed treatment regimens. Studies without a deferred treatment comparator group were eligible for inclusion. Primary articles or conference abstracts reporting on randomized controlled trials, cohort studies, and case-control studies were included. In studies where there were 2 treatment arms with different DAA treatment lengths, outcomes for the licensed duration arm were extracted. Studies published from 2015 were included to reflect the earliest availability of DAA regimens.

The case definition recommended by the European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel was used to define recently acquired hepatitis C.[10] Recently acquired hepatitis C refers to acquisition up to 1 year before diagnosis, evidenced by any of the following:

- Positive HCV RNA or antigen test in an individual that returned a negative antibody, RNA, or antigen result within the preceding year (including instances where this represents reinfection).
- Positive HCV RNA or antigen test and a current negative HCV antibody test.
- Positive antibody, RNA, or antigen test and, within the preceding year, clinical symptoms of acute hepatitis (including jaundice) OR alanine transaminase 10 times the upper limit of normal for which non-HCV causes of acute hepatitis were excluded.

The following outcomes were included as measures of the benefits and harms of treatment of recently acquired hepatitis C:

- Hepatitis C incidence
- Sustained virological response at 12 weeks post-treatment (SVR12) (intention to treat was extracted or calculated)
- Rates of treatment initiation
- Rates of overtreatment [ie, 1 minus (probability of HCV persistence in the untreated group)]
- Adverse events
- Treatment completion (proportion of participants who received at least 1 dose of treatment and went on to complete the full course of prescribed treatment)
- Treatment adherence (engagement in care)

Studies were excluded if they included children or had <15 participants in total or if they assessed the use of pegylated interferon and/or ribavirin in combination with DAAs.

Search strategy

We searched electronic journal databases, including MEDLINE, Embase, Web of Science, and Cochrane CENTRAL, on April 5, 2021. We restricted our search to articles published from 2015 onward, reflecting the earliest availability of DAAs. Search terms and syntax were modified according to each database but included combinations of medical subject headings and free text related to the following (see supplementary material, http://links.lww.com/HC9/A205, for full search details):

1. DAAs
2. Recent or acute hepatitis C infection

Reference lists of all relevant articles were reviewed for additional studies. No restrictions were made on the language of publication. Abstracts from the International Conference on Health and Hepatitis Care in Substance Users, the International Liver Congress, the Liver Meeting, the International Symposium on Viral Hepatitis and Liver Disease, the International AIDS Conference, the International AIDS Society Conference on HIV Science, and the Conference on Retroviruses and Opportunistic Infections were also reviewed.

Studies were screened and managed using Covidence (Veritas Health Innovation Ltd., Melbourne, Australia). Titles and abstracts were independently assessed by 2 reviewers (Niklas Luhmann and Lakshmi Manoharan) against the predetermined inclusion criteria. Full texts were obtained for articles appearing to meet the inclusion criteria. Where full texts could not be found or further data were required, study authors were contacted up to 2 times.

Extraction and statistical analysis

Study characteristics and outcome data were extracted and assessed independently by 2 reviewers using a prepiloted standardized form on Microsoft Excel. Authors were contacted up to 2 times to solicit missing data. The risk of bias was assessed using a quality assessment tool based on an adapted version of the Joanna Briggs Institute checklist for case series studies.[11] The main components of the assessment were the inclusion and selection of study participants, reporting of study characteristics and outcomes, and the statistical analysis method used.

Random effects meta-analysis was conducted to calculate pooled intention-to-treat SVR12 across risk

populations. Because of the difficulty in disaggregating the effects of acute versus chronic treatment on HCV incidence, a meta-analysis of incidence was not conducted. Statistical heterogeneity among studies was assessed by calculating an I^2 statistic, with an $I^2 > 50\%$ considered a moderate or high level of heterogeneity. A narrative synthesis of study characteristics and other review outcomes was conducted. All statistical analyses were performed using STATA 17 (StataCorp, College Station, TX). We assessed the certainty of evidence using the GRADE methodology.[12,13]

RESULTS

We identified 6013 studies; after discarding duplicates (2177) and studies that did not meet our selection criteria on abstract screening (3753), 83 full-text studies were retrieved, of which a further 71 were excluded (Figure 1). The 12 studies meeting our eligibility criteria included studies published between 2018 and 2020. No further eligible studies were detected from screening reference lists.

Study characteristics

The 12 included studies reported on a total of 2085 individuals with recently acquired HCV infection and comprised 8 cohort studies,[14–21] 3 open-label trials,[22–24] and 1 case series study.[25] Nine studies (66.7%) assessed immediate HCV treatment in either MSM or MSM living with HIV, 2 studies included PWID (16.7%), and 1 (8.3%) included a nonspecific sample of people living with HIV (PLHIV). No studies were undertaken in custodial settings, and none involved participants that identified as sex workers or among trans and gender-diverse people. No studies with a deferred treatment comparator group were identified. All studies were set in high-income countries. Study and cohort characteristics are presented in Table 1.

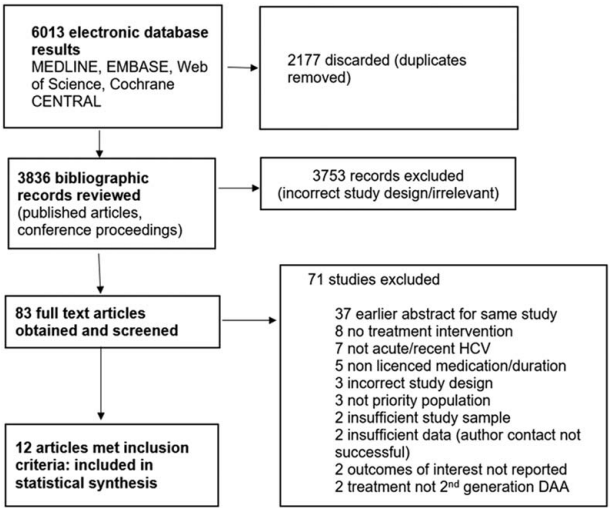

FIGURE 1 Schematic diagram of search results and screening process. Abbreviation: DAA, direct-acting antiviral.

Incidence

Three studies reported HCV incidence, assessing treatment in MSM with HIV.[17,18,23] Two of these studies reported a decrease in HCV incidence at the end of the study period; a study nested in a Swiss cohort study, which reported a decrease in incidence from 0.53/100 person years in 2014 to 0.12/100 person years in 2019[23] and a study set in the UK, which reported a decrease from 11.28/1000 person years in 2016 to 4.63/1000 person years in 2018.[18] In contrast, a study nested in a French cohort study found an increase in incidence from 0.73/100 person years in 2015 to 1.25/100 person years in 2018.[17] In all the 3 studies, a minority of participants in each cohort (0.5–0.7%) were treated in the acute HCV infection phase.

SVR12

Eight studies that included a total of 595 participants with recently acquired hepatitis C reported SVR12 in MSM, PLHIV, and PWID.[15,16,19–22,24,25] Pooled SVR12 across all risk groups was 95.9% (95% CI, 92.6%–99.3%; $I^2 = 61.3\%$) (Figure 2). Within 7 MSM studies (n = 271), the pooled SVR12 was 96.9% (95% CI, 93.1%–100%), within 3 studies, including PLHIV (n = 124), the pooled SVR12 was 97.0% (95% CI, 90.7%–100%), and within 1 study including PWID (n = 46), the pooled SVR12 was 80.4% (95% CI, 66.1%–90.6%).

Treatment initiation, completion, and adherence

One study reported treatment initiation among MSM living with HIV.[14] In this study, 13.6% (6/44) of patients with recently acquired HCV infection-initiated treatment within 6 months of diagnosis. However, it was not reported whether treatment was made available to all participants. Treatment completion was an outcome in 2 studies, both reporting 100% completion rates among 27 PLHIV[24] and 25 MSM.[25] Two studies reported on adherence. One study found 81% (22/26) adherence among PLHIV,[24] where nonadherence was classified as one or more missed doses in the 4 days preceding the end-of-treatment study visit. In the second study,[22] adherence was reported by the risk group: 79% (36/46) in PWID, 85% (55/65) in MSM, and 81% (48/59) in

TABLE 1 Study characteristics

References	Country	Study type	Risk group	Sample size (n with recent HCV infection)	No. treated infections	DAA regimen(s)	Cohort characteristics (%)			
							IVDU	OAT	ART	PrEP
Boesecke et al[14]	Austria, Denmark, France, Germany, Great Britain, Spain	Prospective cohort	MSM w/HIV	464	47	Not specified	1.1	NR	NR	NA
Braun et al[24]	Switzerland	Open-label trial	MSM w/HIV	30	23	Not specified	13.6	NR	99.4[a]	N/A
Cannon et al[16]	UK	Retrospective cohort	MSM, PWID	57	56	Not specified	55.5	NR	NR	NR
Chromy et al[17]	Austria	Prospective cohort	MSM w/HIV	62	38	SOF/LDV, 2D/3D, GRZ/ELB, SOF/VEL, G/P	8.0	NR	NR	N/A
Cotte et al[18]	France	Retrospective cohort	MSM w/HIV	619	141	Not specified	8.3	NR	97.5	N/A
Garvey et al[19]	UK	Retrospective cohort	MSM w/HIV	378	51	Not specified	NR	NR	89	N/A
Girometti et al[20]	UK	Retrospective cohort	MSM	60	28	SOF/LDV, SOF/VEL, SOF/DCV	30	NR	NR	70[b]
Gómez- Ayerbe et al[22]	Spain	Prospective cohort	MSM w/HIV	40	40	SOF/VEL, SOF/LDV, GRZ/ELB, GLE/PIB	NR	NR	100	N/A
Huang et al[21]	Taiwan	Retrospective cohort	MSM w/HIV	225	57	SOF/VEL, GRZ/ELB, SOF/LDV, SOF/DCV,	NR	NR	NR	N/A
Matthews et al[23]	Australia, Canada, New Zealand, Germany, Netherlands, Switzerland, UK, USA	Open-label trial	MSM, PWID, PLHIV	99	95	SOF/VEL	22	6	100	48[b]
Naggie et al[25]	USA	Open-label trial	PLHIV	27	27	SOF/LDV	4	NR	100	N/A
Palaniswami et al [26]	USA	Case series	MSM w/HIV	25	25	SOF/LDV	48	NR	96	N/A

[a]Ever on antiretroviral therapy.
[b]Of HCV negative participants.
Abbreviations: ART, antiretroviral therapy; DAA, direct-acting antiviral; DCV, daclatasvir; ELB, elbasvir; GLE, glecaprevir; GRZ, grazoprevir; IVDU, i.v. drug use; LDV, ledipasvir; MSM, men who have sex with men; OAT, opioid agonist treatment; PIB, pibrentasvir; PLHIV, people living with HIV; PrEP, pre-exposure prophylaxis; PWID, people who inject drugs; SOF, sofosbuvir; VEL, velpatasvir.

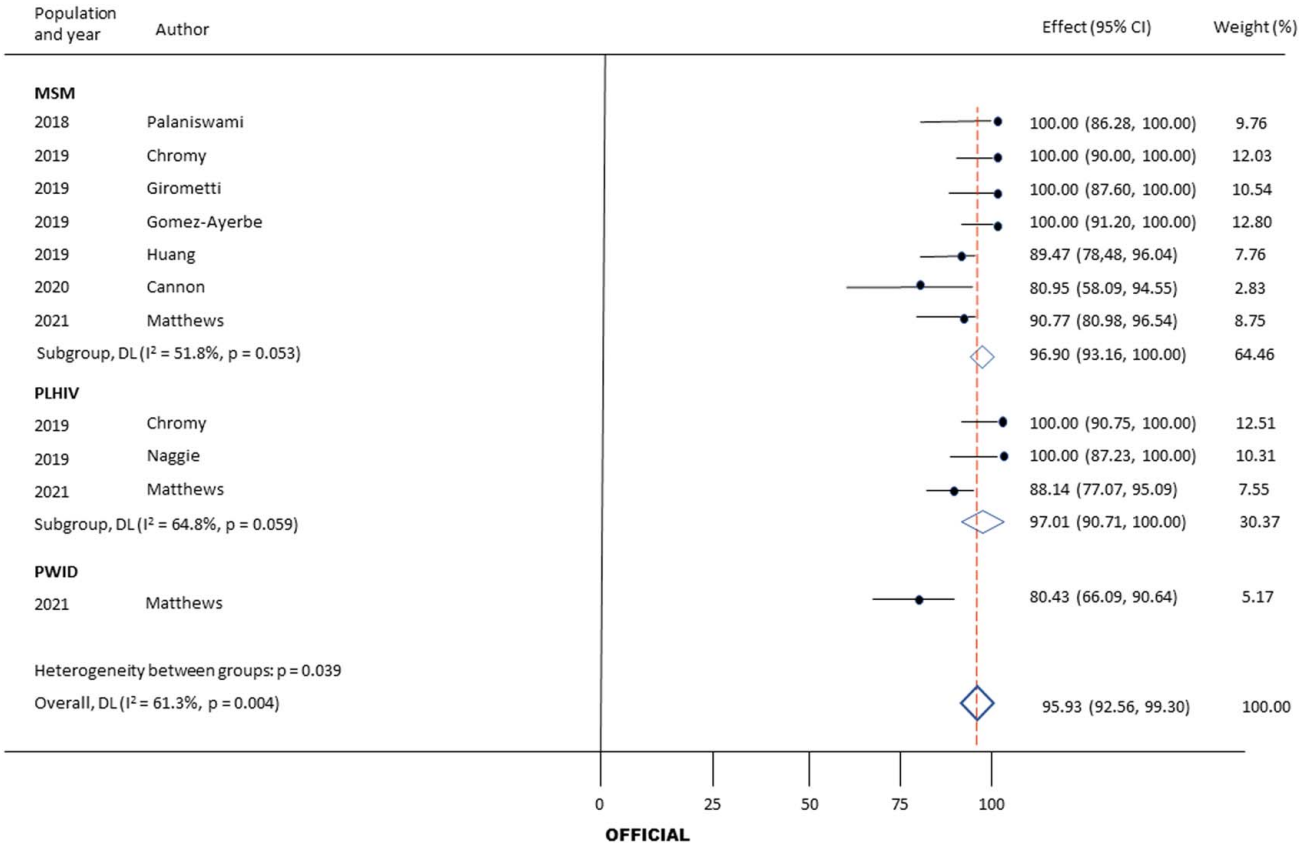

FIGURE 2 Meta-analysis of SVR12 by population risk group. Abbreviations: DL, Dersimonian-Laird; MSM, men who have sex with men; PLHIV, people living with HIV; PrEP, pre-exposure prophylaxis.

PLHIV. In this study, adherence was measured by questionnaire and pill count and defined as the completion of $\geq$95% of scheduled doses.

Adverse events and overtreatment

Adverse events were reported in 4 studies[16,22,24,25]1 only 1 serious adverse event was described (rhabdomyolysis), [22] whereas all other adverse events were classified as grade 3 or less or considered minor. Adverse event rates ranged from 22% (21/95) to 36% (9/25). No studies included a comparator group, so overtreatment was unable to be calculated.

Risk of bias and certainty of evidence assessment

The risk of bias was classified as low across the studies, whereas the GRADE certainty of the evidence was very low across all study outcomes (Supplemental material, http://links.lww.com/HC9/A205). All studies reported clear inclusion criteria; however, only half of the studies reported consecutive enrollment of participants. All studies used reliable and valid methods for measuring recent HCV infection. There was a limited characterization of participant risk behavior in some studies; however, most studies reported study-specific outcomes clearly, and statistical analysis was appropriate across all studies.

DISCUSSION

This systematic review found that standard duration DAA treatment initiated without delay in recently acquired HCV infection was associated with high rates of cure, consistent with those seen for treatment of chronic hepatitis C in similar risk groups.[26] This high rate of cure was evident across key risk populations of MSM, PWID, and PLHIV. No studies were set in populations in custodial settings, those identifying as sex workers, or among trans or gender-diverse people. There were a low number of treatment-related adverse events reported, and these events were overwhelmingly minor. There is still little population-level data to draw inferences on changes in HCV incidence as a direct result of the treatment of recently acquired HCV infection; no studies directly compared immediate to delayed treatment. Our review findings suggest significant individual-level and potential population-level benefits that support the use of DAAs for recent HCV infection and argue for a change in global guidelines

and regulatory conditions that currently restrict hepatitis C treatment among people with recently acquired HCV infection.

Improved identification and treatment of recently acquired HCV infection may bring benefits to the individual by facilitating cure as soon as possible after diagnosis and reducing the risk of loss to follow-up before treatment, as well as reducing morbidity associated with progression to chronic infection. There is also a broader population-level treatment-as-prevention benefit from curing an individual as soon as possible by reducing the period of time for which an individual is infectious and, in turn, reducing the risk of onward HCV transmission. The 3 studies that reported on incidence were nested in large cohorts of MSM in which treated acute infections made up a minority of treated patients, and most patients were treated in the chronic phase of infection. Two studies demonstrated a reduction in HCV incidence, and 1 reported an increase in incidence. As treating chronic HCV infection can also reduce incidence,[26,27] it was not possible to identify the distinct effect of treating acute versus chronic infection on incidence in these cohorts. However, modeling studies support a likely reduction in HCV incidence as a result of immediate treatment.[28] This is further supported by several cost-effectiveness models set in both high-income and low-income settings, which demonstrate that the treatment of recently acquired HCV infection is cost saving.[28–31]

This review assessed the use of licensed, standard duration DAA regimens in recently acquired HCV infection. It is possible that treating people with recently acquired HCV infection immediately may allow a shortening of the duration of treatment, as has been seen using interferon-based treatments.[32–35] If shorter DAA courses for recently acquired HCV infection are shown to be effective and are approved, the reduced pill burden, greater patient acceptability, and savings on drug costs of shorter regimens may enhance the desirability of immediate treatment. Several recent studies have examined whether shorter course DAA therapy could be used in this setting with variable results.[23,36,37] Although many of the nonrandomized studies showed high levels of SVR, [36,37] the only randomized study (REACT) in this setting, comparing 6 to 12 weeks of sofosbuvir/velpatasvir, did not demonstrate that the shortened treatment was noninferior compared with the standard duration arm.[22] Nevertheless, despite a higher rate of relapse in the short 6-week arm of this study, treatment was shown to be safe and well adhered to in this patient population.

As no studies included a comparator group, overtreatment after a recent infection (ie, treating someone who might have gone on to spontaneously clear) was unable to be calculated. Nevertheless, inherent within an early treatment strategy is the possibility of overtreatment, as approximately one quarter of individuals will spontaneously clear the virus.[38] Spontaneous clearance largely occurs in the acute (initial six months) phase of HCV infection, with a median clearance of 16.5 weeks.[2] Although there are some predictors of spontaneous clearance (female gender, those with genotype 1 infection, and symptomatic hepatitis),[2] most individuals go on to chronic infection. Importantly, people living with HIV are less likely to clear the virus spontaneously.[39] HIV-positive MSM have an increased risk of HCV infection,[3] and PWID have traditionally been harder to engage in care, so the opportunity to commence treatment immediately, if available, could be critical for these populations. Furthermore, as the cost of DAA therapies decreases, particularly in low-income and middle-income countries,[9] the economic burden of overtreatment reduces and may be outweighed by the benefits of treating recently acquired HCV infection.

Several limitations must be acknowledged in this review. Firstly, a direct comparison between immediate and deferred treatment in a real-world cohort was not possible as we did not find any comparative studies. Second, we were unable to disaggregate any effect of the treatment of acute hepatitis C on incidence from the effect of treating chronic hepatitis C. Third, the reporting of study cohort characteristics varied across studies, which made accurate comparisons of study populations challenging. Fourth, there was relatively limited evidence from cohorts of PWID, and no studies involved key risk groups of incarcerated people, transgender people, and sex workers. Finally, all studies were set in high-income countries, and findings may not be directly applicable to low-income settings where drug access and testing availability are more constrained.

This is the first systematic review assessing treatment outcomes using licensed standard duration regimens for recently acquired HCV infection in higher-risk populations. Study findings suggest an individual-level benefit of early DAA treatment, including high cure rates. Although the effect on the incidence of treating recently acquired HCV infection relative to chronic infection has not been measured directly, modeling suggests early treatment would reduce HCV incidence and be cost saving. Real-world cost-effectiveness and feasibility studies would be beneficial to further strengthen the case for the treatment of recently acquired HCV infection. These results highlight the need for comparison studies assessing immediate and delayed treatment, effects on other outcomes such as incidence and reinfection, as well as studies of early DAA treatment, which include other risk groups. Treatment of recently acquired HCV may prove to be an important aspect of achieving global HCV elimination goals, and these review findings are being used as evidence toward updated WHO-consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment, and care for key populations.

ACKNOWLEDGMENTS

Michael W. Traeger, Joseph S. Doyle, Margaret E. Hellard, and Mark Stoové thank fellowship support from the National Health and Medical Research Council.

FUNDING INFORMATION

This work was supported by the World Health Organization Global Hepatitis Programme who commissioned and funded the project. Burnet Institute was supported by the Victorian Government Operational and Infrastructure Fund. Michael W. Traeger, Joseph S. Doyle, Margaret E. Hellard, and Mark Stoové were supported by the fellowship from the National Health and Medical Research Council.

CONFLICT OF INTEREST

Gail V. Matthews consults, advises, and received grants from Gilead Sciences. She consults and received grants from ViiV; she received grants from Abbvie. Joseph S. Doyle received grants from Gilead and Abbvie. Michael W. Traeger received grants from Gilead Science. The remaining authors have no conflicts to report.

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REFERENCES

1. World Health Organisation. Global Health Sector Strategy on Viral Hepatitis 2016-2021 Towards Ending Viral Hepatitis. World Health Organization; 2016. 2016.
2. Grebely J, Page K, Sacks-Davis R, van der Loeff MS, Rice TM, Bruneau J, et al. The effects of female sex, viral genotype, and IL28B genotype on spontaneous clearance of acute hepatitis C virus infection. Hepatology. 2014;59:109–20.
3. Jin F, Dore GJ, Matthews G, Luhmann N, Macdonald V, Bajis S, et al. Prevalence and incidence of hepatitis C virus infection in men who have sex with men: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2021;6:39–56.
4. Trickey A, Fraser H, Lim AG, Peacock A, Colledge S, Walker JG, et al. The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: a modelling study. Lancet Gastroenterol Hepatol. 2019;4:435–4.
5. Ghany MG, Morgan TR. AASLD-IDSA Hepatitis C Guidance Panel. Hepatitis C Guidance 2019 update: American Association for the Study of Liver Diseases–Infectious Diseases Society of America Recommendations for Testing. Hepatology. 2020;71:686–721.
6. Pawlotsky J-M, Negro F, Aghemo A, Berenguer M, Dalgard O, Dusheiko G, et al. EASL recommendations on treatment of hepatitis C: final update of the series. J Hepatol. 2020;73:1170–218.
7. International Network of People Who Use Drugs I. Key Populations' Values and Preferences for HIV, Hepatitis and STI Services: A Qualitative Study. INPUD; 2021.
8. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339:b2535.
9. World Health Organisation. Accelerating access to hepatitis C diagnostics and treatment: overcoming barriers in low- and middle-income countries. Global progress report 2020. Geneva. 2021.
10. Panel TEATNAHCIC.. Acute hepatitis C in HIV-infected individuals: recommendations from the European AIDS Treatment Network (NEAT) consensus conference. AIDS. 2011;25:399–409.
11. Munn Z, Barker T, Moola S, Tufanaru C, Stern C, McArthur A, et al. Methodological quality of case series studies. JBI Evid Synth. 2020;18:2127–33.
12. Schünemann HJ, Mustafa RA, Brozek J, Steingart KR, Leeflang M, Murad MH, et al. GRADE guidelines: 21 part 2. Test accuracy: inconsistency, imprecision, publication bias, and other domains for rating the certainty of evidence and presenting it in evidence profiles and summary of findings tables. J Clin Epidemiol. 2020;122:142–52.
13. Schünemann HJ, Mustafa RA, Brozek J, Steingart KR, Leeflang M, Murad MH, et al. GRADE guidelines: 21 part 1. Study design, risk of bias, and indirectness in rating the certainty across a body of evidence for test accuracy. J Clin Epidemiol. 2020;122:129–41.
14. Boesecke C, Nelson M, Ingiliz P, Lutz T, Scholten S, Cordes C, et al. Can't buy me love? obstacles to microelimination of acute HCV coinfection in Europe. 26th Conference on Retroviruses and Opportunistic Infections. 2019.
15. Cannon L, Dhillon R, A T, Teo S, Garner A, Ward C, et al. Hepatitis C infection and treatment outcomes in the DAA era. HIV Med. 2020;21:51.
16. Chromy D, Mandorfer M, Bucsics T, Schwabl P, Scheiner B, Schmidbauer C, et al. High efficacy of interferon-free therapy for acute hepatitis C in HIV-positive patients. United European Gastroenterol J. 2019;7:507–16.
17. Cotte L, Hocqueloux L, Lefebvre M, Pradat P, Bani-Sadr F, Huleux T, et al. Microelimination or Not? The Changing Epidemiology of Human Immunodeficiency Virus-Hepatitis C Virus Coinfection in France 2012–2018. Clin Infect Dis. 2021;73:e3266–74.
18. Garvey LJ, Cooke GS, Smith C, Stingone C, Ghosh I, Dakshina S, et al. Decline in hepatitis C virus (HCV) incidence in men who have sex with men living with human immunodeficiency virus:

progress to HCV microelimination in the United Kingdom? Clin Infect Dis. 2020;72:233–8.
19. Girometti N, Devitt E, Phillips J, Nelson M, Whitlock G. High rates of unprotected anal sex and use of generic direct-acting antivirals in a cohort of MSM with acute HCV infection. J Viral Hepat. 2019; 26:627–34.
20. Huang M-H, Chang S-Y, Liu C-H, Cheng A, Su L-H, Liu W-C, et al. HCV reinfections after viral clearance among HIV-positive patients with recent HCV infection in Taiwan. Liver Int. 2019;39: 1860–7.
21. Gómez-Ayerbe C, Palacios R, Ríos MJ, Téllez F, Sayago C, Martín-Aspas A, et al. Acute hepatitis C virus infection and direct-acting antiviral drugs: perfect combination to eliminate the epidemic? Int J STD AIDS, 32:1257–60. doi:10.1177/095646242 11033756.
22. Matthews GV, Bhagani S, Van der Valk M, Rockstroh J, Feld JJ, Rauch A, et al. Sofosbuvir/velpatasvir for 12 vs. 6 weeks for the treatment of recently acquired hepatitis C infection. J Hepatol. 2021;75:829–39.
23. Braun DL, Hampel B, Ledergerber B, Grube C, Nguyen H, Künzler-Heule P, et al. A treatment-as-prevention trial to eliminate hepatitis C among men who have sex with men living with human immunodeficiency virus (HIV) in the Swiss HIV cohort study. Clin Infect Dis. 2020. doi:10.1093/cid/ciaa1124
24. Naggie S, Fierer DS, Hughes MD, Kim AY, Luetkemeyer A, Vu V, et al. Ledipasvir/sofosbuvir for 8 weeks to treat acute hepatitis C virus infections in men with human immunodeficiency virus infections: sofosbuvir-containing regimens without interferon for treatment of acute HCV in HIV-1 infected individuals. Clin Infect Dis. 2019;69:514–22.
25. Palaniswami PM, El Sayed A, Asriel B, Carollo JR, Fierer DS. New York acute hepatitis CSN. Ledipasvir and sofosbuvir in the treatment of early hepatitis C virus infection in HIV-infected men. Open Forum Infect Dis. 2018;5:ofy238.
26. Latham NH, Doyle JS, Palmer AY, Vanhommerig JW, Agius P, Goutzamanis S, et al. Staying hepatitis C negative: a systematic review and meta-analysis of cure and reinfection in people who inject drugs. Liver Int. 2019;39:2244–60.
27. Doyle JS, van Santen DK, Iser D, Sasadeusz J, O'Reilly M, Harney B, et al. Microelimination of hepatitis C among people with human immunodeficiency virus coinfection: declining incidence and prevalence accompanying a multicenter treatment scale-up trial. Clin Infect Dis. 2020;73:e2164–72.
28. Popping S, Hullegie SJ, Boerekamps A, Rijnders BJA, de Knegt RJ, Rockstroh JK, et al. Early treatment of acute hepatitis C infection is cost-effective in HIV-infected men-who-have-sex-with-men. PLoS One. 2019;14:e0210179.
29. Liu Y, Zhang H, Zhang L, Zou X, Ling L. Economic evaluation of hepatitis C treatment extension to acute infection and early-stage fibrosis among patients who inject drugs in developing countries: a case of China. Int J Environ Res Public Health. 2020;17:800.
30. Bethea ED, Chen Q, Hur C, Chung RT, Chhatwal J. Should we treat acute hepatitis C? A decision and cost-effectiveness analysis. Hepatology. 2018;67:837–46.
31. Mukherjee S, Colby D, Ramautarsing R, Popping S, Sriplienchan S, Chinbunchorn T, et al. Expanding reimbursement of immediate treatment using direct acting antivirals to reduce hepatitis C incidence among HIV positive men who have sex with men in Bangkok, Thailand: a cost effectiveness modelling study. J Virus Erad. 2021;7:100042.
32. Martinello M, Hellard M, Shaw D, Petoumenos K, Applegate T, Grebely J, et al. Short duration response-guided treatment is effective for most individuals with recent hepatitis C infection: the ATAHC II and DARE-C I studies. Antivir Ther. 2015;21:425–34.
33. Santantonio T, Fasano M, Sagnelli E, Tundo P, Babudieri S, Fabris P, et al. Acute hepatitis C: a 24-week course of pegylated interferon alpha-2b versus a 12-week course of pegylated interferon alpha-2b alone or with ribavirin. Hepatology. 2014; 59:2101–9.
34. Calleri G, Cariti G, Gaiottino F, De Rosa FG, Bargiacchi O, Audagnotto S, et al. A short course of pegylated interferon-α in acute HCV hepatitis. J Viral Hepat. 2007;14:116–21.
35. Martinello M, Orkin C, Cooke G, Bhagani S, Gane E, Kulasegaram R, et al. Short-duration pan-genotypic therapy with glecaprevir/pibrentasvir for 6 weeks among people with recent hepatitis C viral infection. Hepatology. 2020;72:7–18.
36. Rockstroh JK, Bhagani S, Hyland RH, Yun C, Dvory-Sobol H, Zheng W, et al. Ledipasvir–sofosbuvir for 6 weeks to treat acute hepatitis C virus genotype 1 or 4 infection in patients with HIV coinfection: an open-label, single-arm trial. Lancet Gastroenterol Hepatol. 2017;2:347–53.
37. Boerekamps A, De Weggheleire A, van den Berk GE, Lauw FN, Claassen MAA, Posthouwer D, et al. Treatment of acute hepatitis C genotypes 1 and 4 with 8 weeks of grazoprevir plus elbasvir (DAHHS2): an open-label, multicentre, single-arm, phase 3b trial. Lancet Gastroenterol Hepatol. 2019;4:269–77.
38. Micallef JM, Kaldor JM, Dore GJ. Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies. J Viral Hepat. 2006;13:34–41.
39. Grebely J, Raffa JD, Lai C, Krajden M, Conway B, Tyndall MW. Factors associated with spontaneous clearance of hepatitis C virus among illicit drug users. Can J Gastroenterol. 2007;21:796325.

How to cite this article: Manoharan MPOIFAAI-TAG, Latham NH, Munari SC, Traeger MW, Menon V, Luhmann N, et al. Immediate treatment for recent hepatitis C infection in people with high-risk behaviors: a systematic review and meta-analysis. Hepatol Commun. 2023;7:e0082. https://doi.org/10.1097/HC9.0000000000000082