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ORIGINAL ARTICLE

Long-term trends in hepatitis C prevalence, treatment uptake and liver-related events in the Swiss HIV Cohort Study

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Abstract

Background and Aims: Treatment for chronic hepatitis C virus (HCV) infections changed dramatically in the last decade. We assessed changes in the prevalence of replicating HCV infection, treatment uptake and liver-related morbidity and mortality in persons with HIV (PWH) and hepatitis C in the Swiss HIV cohort study.

Methods: We included all cohort participants between 2002 and 2021. We assessed yearly prevalence of replicating HCV infection, overall and liver-related mortality, as well as the yearly incidence of liver-related events in persons with at least one documented positive HCV-RNA.

Results: Of 14 652 participants under follow-up, 2294 had at least one positive HCV-RNA measurement. Of those, 1316 (57%) ever received an HCV treatment. Treatment uptake increased from 8.1% in 2002 to a maximum of 32.6% in 2016. Overall, prevalence of replicating HCV infection declined from 16.5% in 2004 to 1.3% in 2021. HCV prevalence declined from 63.2% to 7.1% in persons who inject drugs, and from 4.1%

Abbreviations: DAA, direct acting antivirals; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LOESS, locally estimated scatter plot smoothing; MSM, men who have sex with men; PWH, persons with HIV; PY, patient-years; PWID, people who inject drugs; SHCS, Swiss HIV Cohort Study; SNF, Swiss National Science Foundation; SVR, sustained virological response.

Bernard Surial and Andri Rauch contributed equally to this study.

to 0.6% in men who have sex with men. Among the 2294 persons with replicating HCV infection, overall mortality declined from a maximum of 3.3 per 100 patient-years (PY) to 1.1 per 100 PY, and incidence of liver-related events decreased from 1.4/100 PY to 0.2/100 PY.

Conclusions: The introduction of DAA therapy was associated with a more than 10-fold reduction in prevalence of replicating HCV infection in PWH, approaching the estimates in the general population. Overall mortality and liver-related events declined substantially in persons living with HIV and hepatitis C.

KEYWORDS
DAA, HCV, hepatitis C, hepatitis C treatment outcomes, HIV, HIV coinfection

1 | INTRODUCTION

Hepatitis C virus (HCV) infection has a high impact on morbidity and mortality in people with people with HIV (PWH). Persons with HIV/hepatitis C virus (HCV) coinfection have an increased risk of dying, an accelerated development of liver cirrhosis and increased risk of decompensated liver disease compared to persons with HCV monoinfection.[1,2] Chronic HCV infection affects an estimated 58 million people worldwide, resulting in a global prevalence of 0.8%.[3] Compared to the general population, HCV infection is more common in PWH, with an estimated global prevalence of 6.2% in 2016.[4] Among PWH, the burden of HCV coinfection is greatest in people who inject drugs (PWID), in whom prevalence is estimated to be as high as 82.6%, and in men who have sex with men (MSM) with an estimated global prevalence of 6.4%.[4]

The development of second-generation direct acting antivirals (DAAs) has revolutionized HCV-care allowing for short treatment durations with very few adverse events and cure rates of >95%.[5] In real-life settings, DAAs have been shown to be highly effective and safe for people with HIV and HCV coinfection.[6] However, the availability of these drugs is limited due to their high cost and missing insurance-coverage.[7] Additionally, lack of harm reduction measures for PWID, such as needle exchange programs, might further hinder HCV elimination.[8] According to a recent analysis, the WHO's 90% screening target was achieved in PWH and HCV in Europe, but the 80% treatment target was missed in all regions.[9]

In Switzerland, low treatment uptake and high liver-related mortality was observed in people with HIV and HCV before the introduction of DAAs.[10] Second generation DAAs were approved in 2014.[11,12] Until May 2017, treatment was only reimbursed for persons with ≥F2 fibrosis or cirrhosis,[13] or within a micro-elimination program providing access to DAAs for MSM living with HIV and HCV irrespective of fibrosis stages (the Swiss HCVree Trial[14]). From May 2017 onwards, DAAs were reimbursed for all PWH and chronic HCV infection. In the Swiss HIV Cohort Study (SHCS), treatment uptake increased after the introduction of DAAs until 2016.[15] However, in this time period DAA treatment was still constrained by reimbursement limitations. The treatment uptake after lifting reimbursement limitations in 2017 remained unclear.

Key points

Hepatitis C infection poses a significant health risk to individuals living with HIV; however, thanks to advancements in treatment, most cases of hepatitis C can now be cured. This study showed that the widespread adoption of these new treatments led to a substantial decline in hepatitis C infection among people with HIV in Switzerland over the past 20 years. Furthermore, this decrease was paralleled by a decline in mortality and liver-related events.

The aim of this study was to describe the impact of the increasing availability of HCV treatment uptake in the SHCS, and to assess related changes in HCV prevalence, mortality and liver-related events over the last 20 years.

2 | METHODS

2.1 | Study design and patient selection

The SHCS (www.shcs.ch) is an ongoing prospective cohort that enrols close to 80% of all PWH currently receiving ART in Switzerland.[16] Demographic, clinical and laboratory data and medication (including HCV therapies) are recorded at enrolment and every 6 months thereafter using a standardized protocol (http://shcs.ch/292-instructions).

For the present study, we included all cohort participants with available follow-up between 01.01.2002 (date when HCV-PCR became broadly available in clinical routine) and 31.12.2021 (database closure). Participants without available information on HCV

serology or HCV-PCR were excluded. Among persons who were lost to follow-up, the observation period was censored at that time. In the SHCS, screening for HCV is performed at least yearly using HCV serology for persons who identify as MSM, and every 2 years for other cohort participants. In persons with positive serology, HCV-RNA is performed to confirm replicating infections or to detect reinfections. In addition, more frequent HCV testing is performed for persons with an increased risk for HCV transmission at the discretion of the treating physician, in line with international guidelines.[17] Reimbursement for second-generation DAAs through the general health insurance was possible after the first of August 2014 with firstly Sofosbuvir, and several others following shortly thereafter.[18,19] Until the first of May 2015, reimbursement was limited to persons with (1) ≥F3 liver fibrosis established by liver biopsy using the METAVIR-Score, (2) two consecutive liver-stiffness values above 9.5 kPa measured with transient elastography or (3) extrahepatic HCV-manifestations.[18] The fibrosis cut-off was lowered to ≥F2 between May 2015 and April 2017, and reimbursement of DAA became available for all persons with HIV and HCV coinfection irrespective of liver fibrosis thereafter.[13] Between October 2015 and February 2017, an intervention study providing systematic HCV-RNA screening and DAA treatment for MSM (the Swiss HCVree trial) was conducted in the SHCS, which provided DAA treatment for 190 patients irrespective of liver fibrosis stage.[14]

2.2 | Outcomes and definitions

The primary outcome was the yearly prevalence of replicating HCV infection between 2002 and 2021. Replicating HCV infection was defined as at least one HCV-RNA measurement >50 IU/mL in a calendar year of interest. Participants with positive HCV serology and consistently negative HCV-RNA assessments were categorized as HCV negative. Secondary outcomes included DAA uptake and treatment outcomes among all persons who ever had a positive HCV-RNA during follow-up. Changes in all-cause and liver-related mortality, as well as in liver-related events were assessed among persons with replicating HCV infection during follow-up, and compared to estimates in those without HCV infection.

HCV treatments were categorized into interferon ± ribavirin, first generation DAAs (telaprevir, boceprevir and faldaprevir), and second generation DAAs (sofosbuvir, dasabuvir, ombitasvir/paritaprevir/ritonavir, daclatasvir, velpatasvir and glecaprevir/pibrentasvir). Treatment courses that spanned across more than one calendar year were only counted in the starting year, and entries with single agents with a duration of less than 30 days were excluded as they likely represented data entry errors ($N = 5$). Treatment outcomes were categorized into untreated replicating HCV infection, spontaneous clearance, sustained virological response (SVR) and treatment without SVR (non-response or relapse). Participants were considered to have spontaneous HCV clearance if all HCV-RNA measurements were <50 IU/mL in a given calendar year following a documented replicating infection without reported treatment. As the definitions of treatment success and the respective HCV-RNA assessment time-points changed over time, SVR was defined as HCV-RNA measurements <50 IU/mL in the calendar year after HCV treatment in the previous year. Persons with treatment-induced or spontaneous HCV-RNA clearance with new detection of HCV-RNA (reinfections or relapses) were categorized as having a replicating HCV infection from the time-point of the re-emergence of HCV-RNA onwards. Liver-related events were recorded using standardized definitions (https://shcs.ch/307-shcs-code-book) and included ascites, spontaneous bacterial peritonitis, variceal bleeding, new diagnosis of liver cirrhosis or portal hypertension, hepatic encephalopathy above stage III, hepatorenal syndrome, hepatocellular carcinoma and liver transplantation. For each patient only the first liver-related event during the observation time was considered.

2.3 | Statistical analysis

The yearly prevalence of replicating HCV infection was calculated as the percentage of all persons with ongoing follow-up for a given calendar year overall and by HIV transmission risk group. Treatment uptake was reported as yearly number of treatments. If HCV-RNA measurements were missing in a calendar year of follow-up, the last known state of infection was carried forward. All-cause and liver-related mortality rates, as well as liver-related events were described as events per 100 person years (PY), stratified by calendar year in persons with and without HCV infection. For individuals with HCV coinfection, mortality and liver-related event rates were calculated from the first time-point of a positive HCV-RNA measurement. Individuals who achieved HCV-RNA clearance during follow-up remained in the HIV/HCV coinfection group. Trend lines were generated using locally estimated scatter plot smoothing (LOESS). Sensitivity analyses for mortality and liver-related events were performed among persons without hepatitis B virus (HBV) infection, defined by positive HBsAg. All analyses were performed using R version 4.2.2.

3 | RESULTS

3.1 | Patient characteristics

Of 15 164 SHCS participants with follow-up after 2002, 512 were excluded due to missing data on HCV serology or HCV-PCR. Of the remaining 14 652 participants, 2294 had at least one HCV-RNA measurement with a detectable viral load. At the end of the study period, 1103 (48%) persons with HCV infection, and 8295 (67%) without HCV infection had an active follow-up in the SHCS. The reasons for loss to follow-up in persons with and without HCV infection and viral outcomes for patients remaining under follow-up

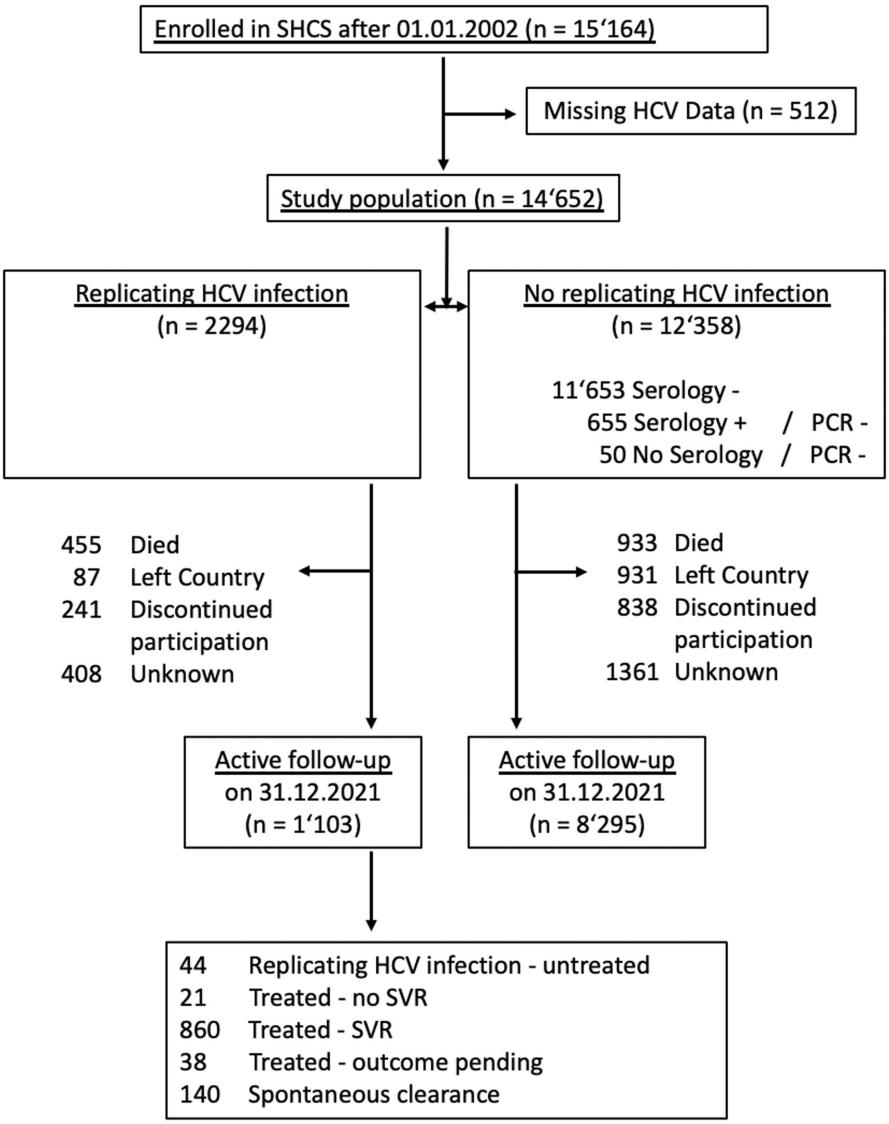

FIGURE 1 Flowchart of enrolled study participants with information on participants lost to follow-up and HCV-treatment status.

are shown in Figure 1. In participants lost to follow-up with known replicating HCV infection 748 had active infection, 141 were treated without SVR, 216 were treated with SVR and 86 had spontaneous viral clearance at last follow-up.

Compared to PWH without HCV, those who ever had a replicating HCV infection were younger, more likely to be Caucasian, and more likely to have acquired HIV through injection drug use. In addition, persons with HCV infection had a lower median CD4 cell count at the last follow-up visit (Table 1).

3.2 | Prevalence of replicating hepatitis C virus infection and treatment uptake

The prevalence of replicating HCV infection among SHCS participants was highest in 2004, reaching 16.5%. Thereafter, it steadily declined to 10.4% in 2014 and to 1.3% in 2021 (Figure 2A). The highest prevalence was found among PWID, with 63.2% of all PWID in the SHCS having a replicating HCV infection in 2005. After the introduction of second generation DAA, a rapid decline in the yearly prevalence among PWID occurred, with a prevalence of 7.1% in 2021. Among MSM, HCV prevalence increased from 2002 (1.8%) to 2016 (4.1%), before decreasing to 0.6% in 2021 (Figure S1). A yearly breakdown of cohort participants with active follow-up and replicating hepatitis C virus (HCV) infection is summarized in Table S1.

Among persons with replicating HCV infection, 1316 (57%) received at least one treatment for chronic HCV infection. The available treatment regimens for HCV changed substantially over the studied time-periods. Before 2012, interferon ± ribavirin-based HCV treatments were the only available options, and yearly treatment uptake of persons with replicating HCV infection ranged between 8.1% in 2002 and 3.8% in 2012. First generation DAAs in combination with pegylated interferon and ribavirin were only used between 2012 and 2014 with 72 treatment courses. After 2014, administered treatment regimens shifted rapidly to the almost exclusive use of second generation DAA-based treatments: second generation DAAs-based therapies comprised 75.4% all

TABLE 1 Patient characteristics, stratified by HCV coinfection.

Characteristics	No replicating HCV infection (*N* = 12 358)	Replicating[a] HCV infection (*N* = 2294)
Female	3386 (27%)	662 (29%)
Median age at registration, years (IQR)	36 (30–45)	33 (28–39)
Region of origin		
African	2100 (17%)	52 (2.3%)
Asian	539 (4.4%)	45 (2.0%)
European/USA	9104 (74%)	2133 (93%)
Latin American	550 (4.5%)	41 (1.8%)
Other/Unknown	65 (0.5%)	23 (1.0%)
HIV transmission group		
Heterosexual contacts	5121 (41%)	354 (15%)
MSM	6011 (49%)	421 (18%)
Other	705 (5.7%)	75 (3.3%)
PWID	521 (4.2%)	1444 (63%)
Median CD4 nadir, cells/μL (IQR)	221 (105–346)	151 (66–254)
CD4-cell count at last follow-up		
<200 cells/μL	646 (5.2%)	274 (12%)
200–400 cells/μL	1798 (15%)	473 (21%)
>400 cells/μL	9913 (80%)	1547 (67%)
HIV viral load <50 cp/mL at last follow-up	10 937 (89%)	1898 (83%)
ALT >2.5× ULN at any time-point	3428 (28%)	1661 (72%)
Median number of episodes with ALT >2.5× ULN (IQR)	0 (0–1)	2 (0–6)
Any platelet count <100 G/L	1564 (13%)	1009 (44%)
Any platelet count <50 G/L	582 (4.7%)	412 (18%)
HBV coinfection	554 (4.5%)	74 (3.2%)
HCV		
Genotype 1	-	1003 (44%)
Genotype 2	-	49 (2.1%)
Genotype 3	-	505 (22%)
Genotype 4	-	353 (15%)
Multiple genotypes	-	44 (1.9%)
No information	-	335 (15%)
Other/Undetermined	-	5 (0.2%)
Last HCV treatment		
No treatment	-	978 (43%)
Ribavirin/Interferon based	-	405 (18%)
Ribavirin/Interferon plus first generation DAA	-	49 (2.1%)
Ribavirin/Interferon plus second generation DAA	-	138 (6.0%)
Second generation DAA combination	-	724 (32%)

Abbreviations: ALT, alanine aminotransferase; DAA, direct-acting antivirals; HBV, hepatitis B virus; HCV, hepatitis C virus; IQR, interquartile range; MSM, men who have sex with men; PWID, persons who inject drugs; ULN, upper limit of norm (35 IU for men, 25 IU for women).

[a]At least one HCV-RNA ≥50 IU/mL.

administered treatments in 2014 and reached 100% in 2017. In parallel, HCV treatment uptake rapidly increased from 65 treatment courses in 2014 (6.7% of all patients with replicating HCV infection) to 247 treatment courses in 2016 (32.6% of all patients with replicating HCV infection, Figure 2B).

3.3 | Outcomes of replicating hepatitis C virus infection

The number of persons with ongoing replicating HCV infection, SVR, treatment without SVR, treatment with pending or unknown

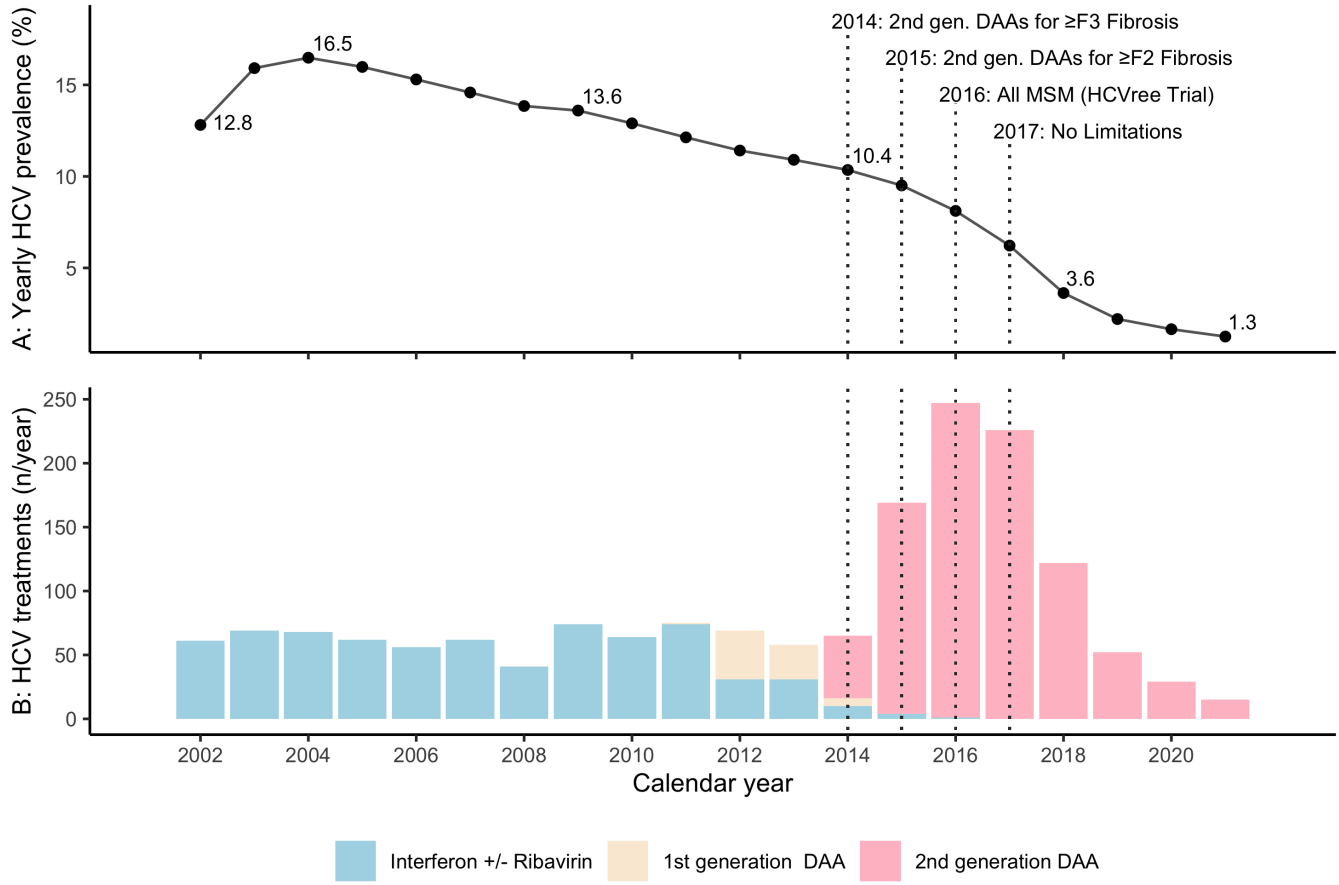

FIGURE 2 (A) Prevalence of replicating HCV coinfection as proportion of all Swiss HIV Cohort Study (SHCS) participants with follow-up in a given calendar year. (B) Yearly number of started HCV treatment courses, stratified by treatment type and year. Vertical dotted lines indicate major changes in accessibility of second generation DAA treatments. DAA, direct-acting antivirals; HCV, hepatitis C virus; MSM, men who have sex with men.

outcome and spontaneous viral clearance by year is shown for 2294 persons with at least one positive HCV-RNA measurement during follow-up in Figure 3.

Persons with HIV/HCV coinfection were followed for a median of 9.4 years (IQR 4.5–16.4). By the end of the observation period in 2021, 736 persons with HIV/HCV (32%) were lost to follow-up (mean loss to follow-up of 2.9% per year, 95% confidence interval 2.4–3.4), and 455 (20%) died. As of 2021, 860 of 1103 persons under follow-up (78%) achieved SVR with some form of HCV treatment, and 140 (13%) had spontaneous viral clearance. Sixty-five (5.9%) participants had a replicating HCV infection at the end of the study period, of whom 44 never received treatment and 21 were previously treated but did not achieve SVR. Thirty-eight participants received HCV treatment but outcome was pending or unknown (Figures 1 and 3).

3.4 | Mortality and liver-related events

Among the 2294 persons who ever had replicating HCV infection during follow-up, yearly mortality steadily declined over time from 3.3 deaths per 100 PY in 2004 to 1.1 per 100 PY in 2021. Yearly mortality in the HCV negative SHCS-population declined from 0.8 deaths per 100 person years in 2002 to 0.6 deaths per 100 person years in 2021 (Figure 4A). Liver-related mortality showed similar trends (Figure 4B), and similar trends were observed when excluding persons with HBV infection (Figure S2).

The yearly rate of first occurring liver-related events among individuals with replicating HCV infection decreased from a maximum of 1.4 per 100 PY in 2011 to 0.2 per 100 PY in 2021. In SHCS participants without HCV, the yearly number of first liver-related events per person was below 0.2 yearly events per 100 person years throughout the study period (Figure 4C). Of the 269 liver-related events in persons with HCV infection, the most frequent events included new diagnoses of liver cirrhosis (36%), hepatocellular carcinoma (19%), new-onset of portal hypertension (16%) and liver transplantation (5%).

4 | DISCUSSION

In our nationwide cohort study of persons with HIV, the prevalence of replicating HCV infection decreased substantially over the last two decades, from a maximum of 16.5% in 2004 to 1.3% in 2021. The decrease in HCV prevalence was accelerated following the increased uptake of

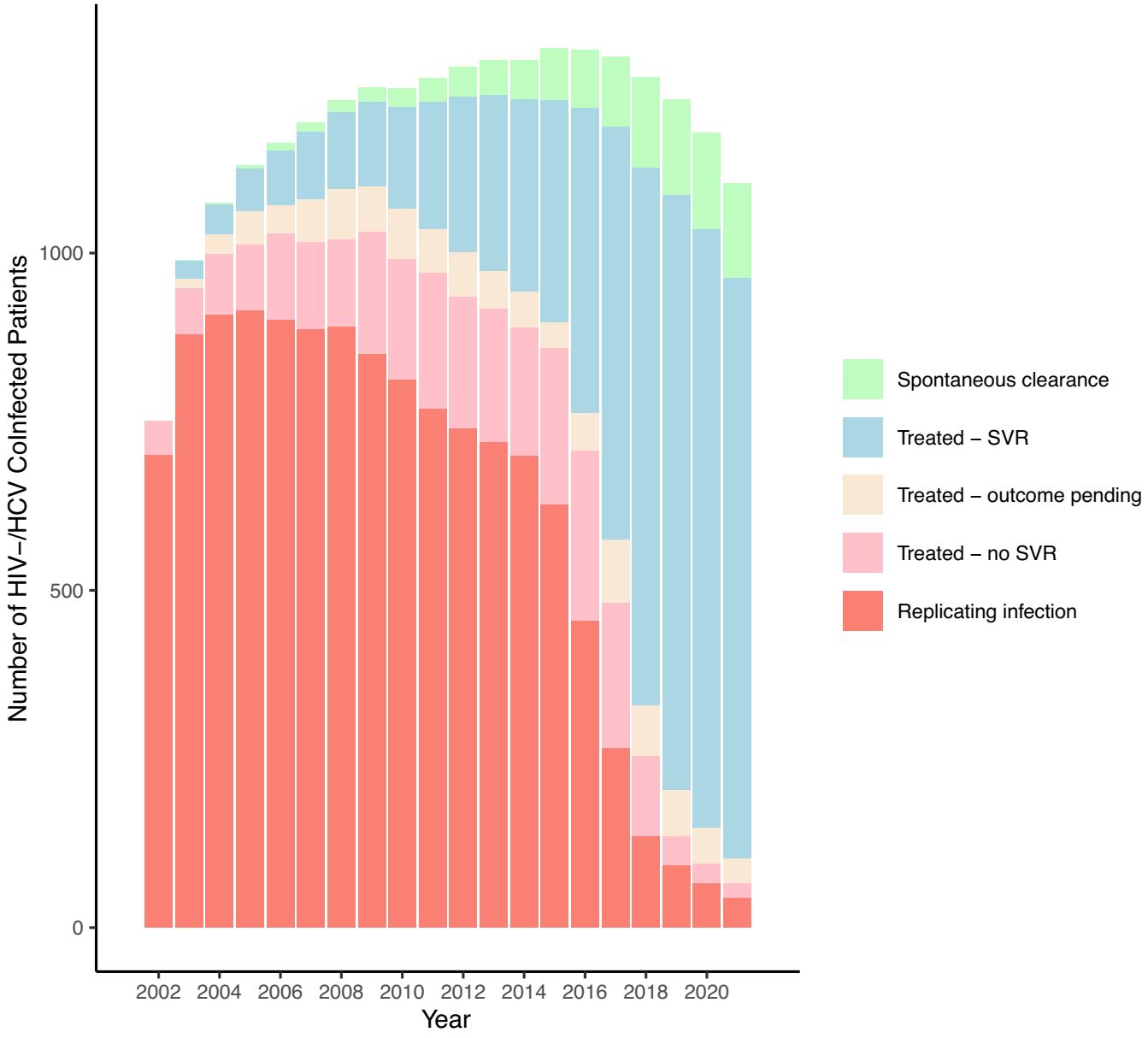

FIGURE 3 Treatment outcomes of all ongoing Swiss HIV Cohort Study (SHCS) participants with replicating hepatitis C virus (HCV) coinfection over time. SVR, sustained virological response.

second-generation DAA treatments after 2014. HCV prevalence decreased eightfold among PWID, and sevenfold among MSM and is now approaching the estimates in the general population.[20] The decreases in HCV prevalence were paralleled by declining rates of overall- and liver-related mortality in persons with HIV and HCV.

Reductions in HCV infection prevalence over time have been observed in other high-income countries among persons with HIV. A multi-cohort study in Spain reported a 90% reduction in the prevalence of replicating HCV infection from 2015 to 2019.[21] Similarly, the prevalence of HCV-viremia in the Netherlands decreased from 4%–5% between 2000 and 2004 to 0.6% in 2019. In our cohort, HCV prevalence decreased even before the upscale in HCV treatment.[22] Besides treatment uptake, harm reduction measures for PWID including provision of safe injection material and opioid substitution programmes and other preventive measures likely contributed to the reduction in the HCV burden.[15] The availability of second generation DAAs led to a substantial increase in treatment uptake in our cohort, similar to a report from the EuroSIDA cohort study.[23] The rapid increase in HCV therapies in 2015 might be partly explained by a warehousing effect in the preceding years as some treatments might have been deferred until the availability of second generation DAAs.[24] In our study, treatment uptake increased substantially after treatment eligibility was extended to persons with F2 fibrosis and higher, with a further increase observed in 2017 when treatments became available for all persons with HIV irrespective of liver fibrosis stage. Similar trends have been observed after removal of fibrosis restrictions in Canada[24] and the US,[25] underling the importance of unrestricted access to HCV treatment in order to achieve HCV elimination targets.[26,27]

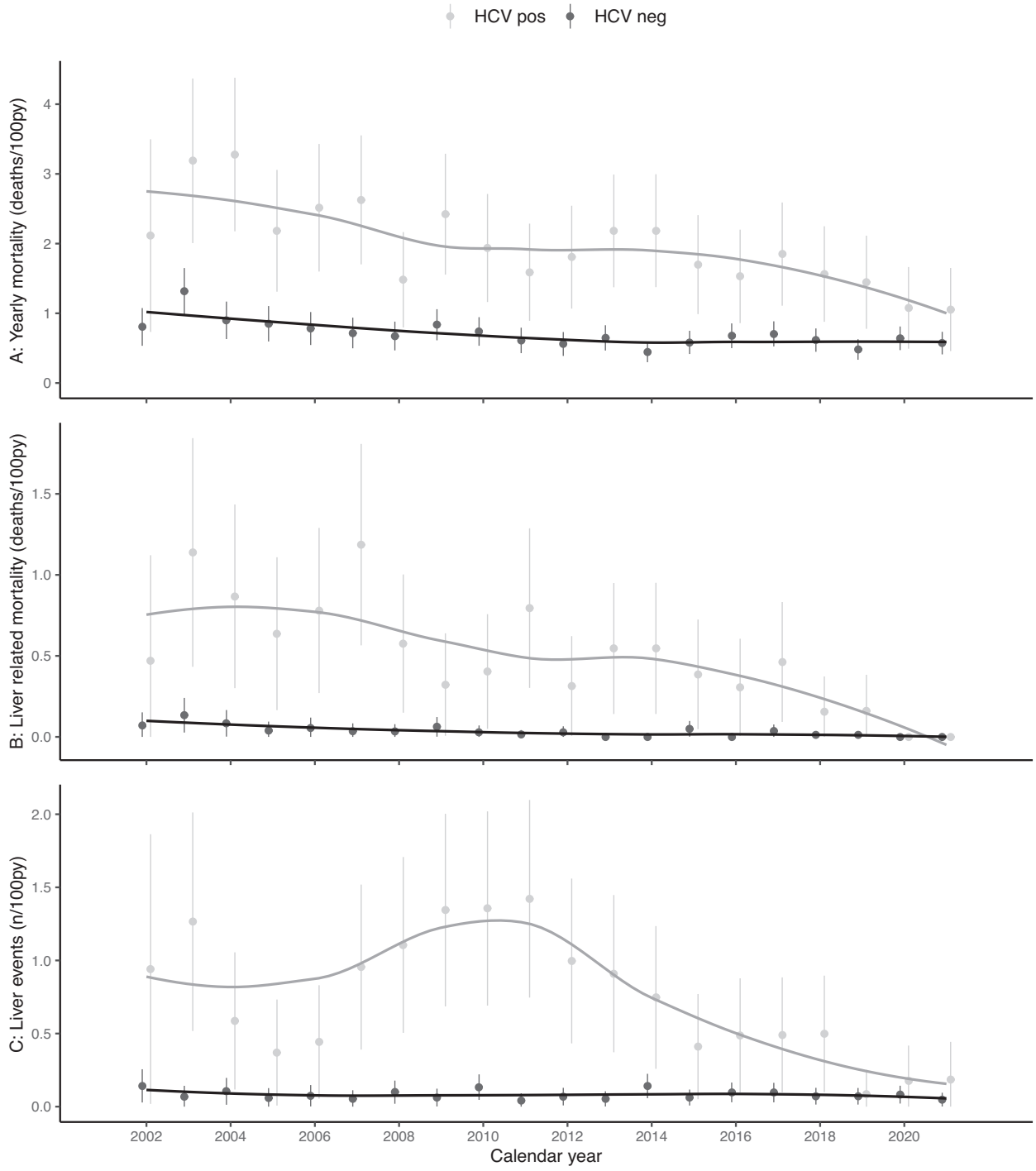

FIGURE 4 (A) Yearly rate of mortality in persons with (grey) and without (black) HCV coinfection, per 100 person years (PY). (B) Yearly rate of liver-related mortality in persons with (grey) and without (black) HCV coinfection, per 100 PY. (C) Yearly rate of liver events in persons with (grey) and without (black) HCV coinfection, per 100 PY. Solid lines represent mean values calculated using LOESS smoothers. Vertical lines correspond to 95% confidence intervals.

After the introduction of second generation DAAs, the biggest decline in HCV prevalence was observed in PWID, with a reduction from 63.2% in 2005 to 7.1% in 2021. Nevertheless, HCV prevalence remained highest in PWID despite broad access to DAAs, which might be explained by ongoing intravenous drug use, unsteady housing or disengagement from medical care.[24] Among MSM, the SwissHCVree trial had a sustained impact on prevalence and incidence of replicating HCV infection, and demonstrates the feasibility of HCV microelimination through optimized access and uptake of HCV therapies.[14,28] Our results confirm and extend the findings from previous studies reporting a marked decline in HCV incidence and a 'treatment-as-prevention' effect after DAAs became broadly available.[27,29,30]

We observed a threefold decline in all-cause mortality and a sevenfold decline in the incidence of liver-related events in persons with HIV/HCV coinfection after the introduction of DAAs. Although factors other than access to effective HCV treatment (e.g. the introduction of effective antiretroviral therapy for HIV and hepatitis B) may have contributed to our findings, they are consistent with several reports from other high-income countries that showed improved liver- and non-liver-related outcomes with second-generation DAA treatments among persons with HIV/HCV coinfection.[15,31,32] A study from the United States estimated a risk difference for mortality of −3.8% for persons treated with DAAs.[31] In the ART-CC collaboration, persons who reached SVR shortly after HCV infection were not at higher risk of overall mortality compared to PWH without HCV infection.[33] In our study, the decline in mortality and liver-related events was also observed when excluding persons with HBV coinfection. This suggests that the decline in mortality and liver-related events in the DAA era cannot be attributed solely to improved HBV treatment outcomes. Moreover, multiple reports in persons with HCV monoinfection have observed a reduced mortality and morbidity from liver disease, HCV prevalence, and overall mortality after the introduction of second-generation DAAs.[34–37] In addition to the level of treatment availability, other advances in the quality of HIV- and HCV-care, as well as the overall quality of the HCV-cascade of care, are likely to impact mortality- and morbidity-trends. In our study, persons with HCV infection before 2014 had in median a 2.8-fold higher rate in overall mortality, and a 12.9-fold higher rate in liver-related events compared to those without HCV infection. As of 2021, these differences in liver-related events and mortality between individuals who ever had replicating HCV and those without HCV markedly decreased to 1.8-fold and 3.9-fold, respectively. This decline underscores the substantial benefits of curing hepatitis C in persons with HIV.

Our study is based on high-quality, long-term data from the SHCS and provides a comprehensive update of earlier studies on treatment uptake, HCV prevalence and mortality conducted by the study group.[10,38] All SHCS participants are screened routinely every 1–2 years for HCV infection, and treatment regimens and outcomes as well as clinical events are prospectively collected which allows for reliable estimates of prevalence and outcome trends. However, there are limitations that should be considered when interpreting the results. First, differences in HCV screening intervals between MSM (yearly) and other risk groups (every 2 years) may have led to detection bias explaining parts of the differences in the HCV prevalence between risk groups. Second, some reinfections might have been missed because systematic repeated HCV-RNA screening irrespective of risk behaviour in all persons with positive HCV serology was only introduced in 2018. Third, the systematic screening and treatment of MSM during the Swiss HCVree trial likely increased the impact of DAAs on HCV prevalence estimates in this population given the intensified HCV-RNA testing in this population, which limits the generalizability to other settings with less frequent testing and treatment.

Fourth, because we used a cut-off of <50 cp/mL to indicate undetectable HCV-RNA, persons with very low HCV-RNA levels below that cut-off might have been misclassified as HCV-RNA negative. However, as HCV-RNA levels are typically higher in PWH compared to HIV-negative individuals,[39] we believe that the number of misclassified individuals is likely very low.

In conclusion, the prevalence of hepatitis C decreased more than 10-fold over the last two decades among persons living with HIV. This decrease was substantially accelerated with the introduction of DAAs, and the prevalence of replicating HCV infection is now approaching the estimates in the general population in Switzerland. HCV prevalence decreased substantially among all patient groups, including difficult-to-reach populations such as PWID. Moreover, overall and liver-related mortality substantially declined over time. These findings demonstrate the considerable success of preventive and therapeutic interventions towards eliminating the hepatitis C disease burden in PWH.

AUTHOR CONTRIBUTIONS

LB, AR and BS conceived and designed the study. LB performed the analyses, and LB, AR and BS drafted the initial manuscript. All authors contributed data to the study and to the interpretation of the results and revised the manuscript for substantial intellectual content. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

DLB reports honoraria for advisory boards paid to himself from the companies Abbvie, Gilead, MSD and ViiV outside of the submitted work. MC's institution received research grants from Gilead, MSD and Viiv outside the submitted work; MC's institution received travel

grants from Gilead. MS reports support to his institution for advisory boards and/or travel grants from MSD, Gilead Sciences, ViiV, Pfizer and Moderna. All remuneration went to his home institution and not to MS personally, and all remuneration was provided outside the submitted work. EB received travel grants and payments for participation of EB to advisory boards from Gilead Sciences, MSD, ViiV Healthcare, Pfizer AG, Abbvie, Astra Zeneca, Moderna and Ely Lilly. GW reports research grants from Gilead Sciences and Roche Diagnostics, as well as advisory board and lecture honoraria from ViiV, MSD and Gilead sciences, all outside of the submitted work and paid to his institution. BS reports support for travel grants from Gilead Sciences and ViiV healthcare, paid to his institution. AR reports support to his institution for advisory boards and/or travel grants from MSD, Gilead Sciences, Pfizer and Moderna, and an investigator initiated trial (IIT) grant from Gilead Sciences. All remuneration went to his home institution and not to AR personally, and all remuneration was provided outside the submitted work. All other authors do not have any disclosures to report.

DATA AVAILABILITY STATEMENT

The individual level datasets generated or analysed during the current study do not fulfil the requirements for open data access: (1) The SHCS informed consent states that sharing data outside the SHCS network is only permitted for specific studies on HIV infection and its complications, and to researchers who have signed an agreement detailing the use of the data and biological samples; and (2) the data is too dense and comprehensive to preserve patient privacy in persons living with HIV. According to the Swiss law, data cannot be shared if data subjects have not agreed or data is too sensitive to share. Investigators with a request for selected data should send a proposal to the respective SHCS address (www.shcs.ch/contact). The provision of data will be considered by the Scientific Board of the SHCS and the study team and is subject to Swiss legal and ethical regulations, and is outlined in a material and data transfer agreement.

ETHICS APPROVAL AND PATIENT CONSENT

Local ethical committees of all cohort centres approved this cohort study, and all patients provided written informed consent.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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