Evaluation of hepatitis C treatment-as-prevention within Australian prisons (SToP-C): a prospective cohort study

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Summary

Background Limited empirical evidence exists for the effectiveness of hepatitis C virus (HCV) treatment-as-prevention. The Surveillance and Treatment of Prisoners with hepatitis C (SToP-C) study aimed to assess the effect of HCV treatment-as-prevention in the prison setting.

Methods SToP-C was a prospective study, including a before-and-after analysis, within a cohort of people incarcerated in two maximum-security prisons (male) and two medium-security prisons (one male, one female) in New South Wales, Australia. All prison inmates aged at least 18 years were eligible for enrolment. After HCV testing, participants were monitored for risk behaviours and HCV infection, among three sub-populations: uninfected (HCV antibody-negative); previously infected (HCV antibody-positive, HCV RNA-negative); and infected (HCV antibody and HCV RNA-positive). Uninfected participants were followed up every 3–6 months to detect HCV primary infection and previously infected participants were followed up every 3–6 months to detect re-infection. Participants with HCV infection were assessed for treatment, initially standard-of-care treatment (administered by prison health services) from 2014 to mid-2017, then direct-acting antiviral (DAA) treatment scale-up from mid-2017 onwards (12 weeks of sofosbuvir plus velpatasvir, administered through SToP-C). Participants were followed up until study closure in November, 2019. The primary study outcome was HCV incidence before and after DAA treatment scale-up among participants at risk of HCV primary infection or re-infection. This study is registered with ClinicalTrials.gov, NCT02064049.

Findings Between Oct 30, 2014, and Sept 30, 2019, 3691 participants were enrolled in the SToP-C study. 719 (19%) participants had detectable HCV RNA, 2240 (61%) were at risk of primary HCV infection, and 725 (20%) were at risk of re-infection at baseline. DAA treatment was initiated in 349 (70%) of 499 eligible participants during the treatment scale-up period. The HCV incidence analysis comprised 1643 participants at risk of HCV infection or re-infection during longitudinal follow-up (median age 33 years [IQR 27–42]; 1350 [82%] male). 487 (30%) of 1643 participants reported injecting drugs in prison. HCV incidence decreased from 8·31 per 100 person-years in the pre-treatment scale-up period to 4·35 per 100 person-years in the post-treatment scale-up period (incidence rate ratio [IRR] 0·52 [95% CI 0·36–0·78]; p=0·0007). The incidence of primary infection decreased from 6·64 per 100 person-years in the pre-treatment scale-up period to 2·85 per 100 person-years in the post-treatment scale-up period (IRR 0·43 [95% CI 0·25–0·74]; p=0·0019), whereas the incidence of re-infection decreased from 12·36 per 100 person-years to 7·27 per 100 person-years (0·59 [0·35–1·00]; p=0·050). Among participants reporting injecting drugs during their current imprisonment, the incidence of primary infection decreased from 39·08 per 100 person-years in the pre-treatment scale-up period to 14·03 per 100 person-years in the post-treatment scale-up period (IRR 0·36 [95% CI 0·16–0·80]; p=0·0091), and the incidence of re-infection decreased from 15·26 per 100 person-years to 9·34 per 100 person-years (0·61 [0·34–1·09]; p=0·093). The adjusted analysis (adjusted for age, Indigenous Australian ethnicity, duration of stay in prison, previous imprisonment, injecting drug use status, and prison site) indicated a significant reduction in the risk of HCV infection between the pre-DAA treatment scale-up and post-DAA treatment scale-up periods (adjusted hazard ratio 0·50 [95% CI 0·33–0·76]; p=0·0014).

Interpretation DAA treatment scale-up was associated with reduced HCV incidence in prison, indicative of a beneficial effect of HCV treatment-as-prevention in this setting. These findings support broad DAA treatment scale-up within incarcerated populations.

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See Online for appendix

Introduction

Globally, an estimated 71 million people have chronic hepatitis C virus (HCV) infection.[1] The advent of direct-acting antiviral (DAA) regimens has led to a revolution in HCV therapy,[2] with simple (once-daily dosing oral regimens), well tolerated, short duration

Research in context

Evidence before this study

We searched MEDLINE and Scopus for papers published from inception to Sept 10, 2020, using a combination of search terms: ("hepatitis C" OR HCV) AND treatment* AND (prevent* OR incidence) AND ("direct acting antiviral*" OR DAA) AND (prison* OR jail* OR correction* OR convict*). We found no interventional studies investigating the effectiveness of hepatitis C virus (HCV) treatment-as-prevention in prison settings. Some repeated surveys showed decreased HCV prevalence following increased uptake of HCV treatment in prisons. However, these studies did not include systematic surveillance and did not evaluate risk status or HCV incidence. Some modelling studies have suggested that increasing HCV treatment uptake in prisons and improved harm reduction strategies could control HCV transmission and decrease HCV incidence. However, there is limited empirical evidence to support these findings in a real-world setting.

Added value of this study

To our knowledge, SToP-C is the first HCV treatment-as-prevention study to be done in the prison setting, and the largest interventional HCV treatment-as-prevention study done in any setting. This study provides empirical evidence of HCV treatment-as-prevention in a cohort of participants enrolled from four prisons (two maximum-security and two medium-security prisons), with HCV incidence almost halved (from 8·31 per 100 person-years to 4·35 per 100 person-years) following rapid scale-up of direct-acting antiviral (DAA) treatment (sofosbuvir plus velpatasvir). The magnitude of the HCV treatment-as-prevention effect was larger against primary HCV infection than against HCV re-infection, and in participants who reported injecting drugs during their current imprisonment compared with those who did not report injecting drugs.

Implications of all the available evidence

WHO has set a goal to eliminate HCV as a major global public health threat by 2030, including reducing the number of new HCV infections by 90%. In most countries, prisons are a priority setting for HCV elimination efforts, given the high prevalence and incidence of HCV infection in most prisons. The findings of the SToP-C study highlight both the feasibility and the positive effect of scaling up DAA treatment in reducing the incidence of HCV infection in the prison setting. This demonstration of the effectiveness of HCV treatment-as-prevention should encourage enhanced access to DAA treatment, including rapid scale-up of treatment uptake among incarcerated populations.

(8–12 weeks), pangenotypic treatment leading to cure rates greater than 95%. The broad implementation of DAA therapy has considerable public health potential, with WHO setting ambitious HCV elimination targets, including a 90% reduction in HCV incidence, treatment of 80% of HCV infections, and a 65% reduction in HCV mortality by 2030.[3]

The capacity to achieve HCV elimination targets depends on many factors, but provision of DAA therapy to marginalised populations with HCV infection is crucial. People who inject drugs (PWID) are incarcerated at high rates for drug-related crimes.[4] Thus, in many countries, PWID and people who are incarcerated are priority populations, given their high burden of HCV infection and their role in ongoing HCV transmission.[5,6] Delivery of effective HCV prevention and treatment interventions to these two populations is central to elimination efforts. Improving HCV prevention measures in prisons is also important for controlling HCV infections in the community, given high rates of transitioning between prison and the community.

Treatment-as-prevention, initially used in the context of HIV therapy,[7] incorporates treatment as a tool for limiting the spread of an infection in epidemics in a particular setting.[8] Although mathematical modelling has shown that HCV treatment-as-prevention is a potentially effective strategy among PWID and in prison settings,[5,6,9] very little empirical data exist to confirm these modelling-based impact projections in a real-world setting. The adoption of HIV treatment-as-prevention has been pivotal to the global HIV response and elimination efforts.[7,10] Similarly, well conducted, large-scale clinical trials are now required to evaluate the effectiveness of HCV treatment-as-prevention.

We hypothesised that rapid scale-up of DAA-based treatment in prisons would reduce HCV transmission, defined by the incidence of primary HCV infection and HCV re-infection. The Surveillance and Treatment of Prisoners with hepatitis C (SToP-C) study aimed to evaluate the effect of DAA treatment scale-up on HCV incidence in four Australian prisons.

Methods

Study setting and design

SToP-C was a prospective study, including a before-and-after analysis, that was designed to evaluate the effect of HCV treatment-as-prevention, by comparing HCV incidence before and after rapid scale-up of DAA treatment within a cohort of participants from four prisons in New South Wales, Australia. Two of the prisons (Goulburn and Lithgow) are predominantly maximum-security male prisons, and the other two are predominantly medium-security prisons, one male (Outer Metropolitan Multi-Purpose Correctional Centre; OMMPCC) and one female (Dillwynia). In 2016, these prisons had a combined population of 1452 incarcerated individuals (appendix p 2),[11] of whom approximately a third were unsentenced (ie, on remand). All prisons offered harm reduction services, including opioid agonist therapy and access to the quaternary ammonium disinfectant Fincol (Jasol, North Ryde, NSW, Australia) to cleanse injecting equipment, but not needle and

syringe programmes. Participant enrolment started in October, 2014, at Goulburn; in July, 2015, at Lithgow; and in April, 2016, at OMMPCC and Dillwynia.

The SToP-C study consisted of two major phases: a pre-DAA treatment scale-up phase (or surveillance phase) and a DAA treatment scale-up phase. In the initial phase of the study (pre-DAA treatment scale-up) from October, 2014, to mid-2017, standard-of-care HCV treatment was available in prisons through a nurse-led model of care,[12,13] including interferon-based treatment until March, 2016, when DAA treatment became available following the Australian Government subsidised listing,[14] which included access to DAAs for those in custody.[13] In the second phase of the study, rapid scale-up of DAA treatment was initiated in all four SToP-C prisons from mid-2017 onwards (in June, 2017, in Goulburn and Lithgow; in September, 2017, in Dillwynia; and in October, 2017, in OMMPCC), and ran until study closure in November, 2019. The SToP-C study was therefore designed to evaluate the effect of DAA treatment scale-up (provided by SToP-C), compared with interferon therapy as standard of care, with an expectation that DAAs would become the standard of care within the duration of the study. We anticipated low HCV treatment uptake in the the pre-DAA scale-up phase, even with DAA as standard of care once DAA treatment became available in prisons in Australia, given the limited capacity of prison health services to deliver treatment.

Study participants, intervention, and assessments

All prison inmates who were at least 18 years of age were eligible for enrolment, irrespective of HCV infection status, HCV treatment history, risk behaviours, or sentence or remand status. Exclusion criteria were lack of adequate English to provide written informed consent, and individuals with a security designation making clinic attendance for study visits logistically difficult. Participants who were transferred to a non-SToP-C prison, or released from prison (ie, returned to the community) after enrolment, could re-enter the study if they were subsequently re-incarcerated into any SToP-C prison.

For the DAA intervention, participants with detectable HCV RNA underwent standard clinical and laboratory assessments. Participants with all HCV genotypes and liver disease stages (F0 to F4 [compensated cirrhosis]) were eligible for treatment. Exclusion criteria for treatment included clinical evidence of hepatic decompensation, ongoing severe psychiatric disease, or pregnancy. Laboratory exclusion criteria included alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentrations more than ten times the upper limit of normal or platelet counts less than 50 000 per µL. Current PWID were eligible for treatment. Full eligibility criteria are provided in the study protocol, which is available online. A detailed SToP-C implementation toolkit for health and corrections administrators is also available online.

After providing written informed consent to participate in the study, participants were tested for HCV exposure and infection (HCV antibody and RNA) at enrolment. Thus, from the enrolment visit, participants were categorised into three subpopulations: uninfected (HCV antibody-negative); previously infected (HCV antibody-positive and HCV RNA-negative); and infected (HCV antibody-positive and HCV RNA-positive). Uninfected and previously infected (ie, at-risk) participants were followed up for HCV primary infection and re-infection. Infected participants underwent pre-treatment clinical and laboratory assessments, transient fibro-elastography (FibroScan; Echosens, Paris, France), and evaluation of potential drug–drug interactions. During the initial phase of the study, infected participants were referred for standard-of-care HCV treatment through the prison health service. During the rapid DAA treatment scale-up phase, from mid-2017, participants who were eligible for HCV treatment were offered sofosbuvir plus velpatasvir for 12 weeks, a pangenotypic DAA regimen. Sofosbuvir plus velpatasvir was administered orally once daily as a fixed-dose combination tablet (400 mg sofosbuvir and 100 mg velpatasvir). Participants who became re-infected after treatment were offered re-treatment. All initial clinical assessments were done by specifically trained nurses, and each case was then discussed with an infectious diseases specialist before the appropriate treatment was prescribed.[13]

Across the 5-year study period, scheduled visits were done at enrolment, and then every 3–6 months in all participants. At enrolment, a demographic, clinical, and risk behaviour interview was administered to all participants by the research nurses. Risk behaviour questions included those about the use, type, and frequency of injecting and non-injecting drugs, sharing of injecting equipment, HCV risks not related to drug use (eg, tattooing, fights), receiving opioid agonist therapy, and using disinfectant to cleanse injecting equipment. The risk behaviour interview was repeated at all follow-up visits. At each visit, participants were also assessed for HCV infection or re-infection by HCV antibody or RNA testing, or both. The study was promoted through awareness campaigns for correction officers, incarcerated people, and prison health-care staff. Participants received a payment (AUD$10) following each visit for study participation. The value of this remuneration was approved by the ethics committees as an undue incentive versus compensation for time and inconvenience. Enrolment continued from October, 2014, through to September 2019, with final follow-up in November, 2019.

In the subpopulation receiving treatment through SToP-C, additional study visits were done at baseline (treatment initiation), week 4 of treatment, week 12 of treatment (end of treatment), and week 12 after treatment. Assessments at these visits included

For the **study protocol** see https://kirby.unsw.edu.au/project/stop-c

For the **SToP-C implementation toolkit** see https://stopc.org

	Total (n=3691)	Year of enrolment				
		2014–15 (n=376)	2016 (n=703)	2017 (n=901)	2018 (n=1009)	2019 (n=702)
Prison site						
Goulburn	1162 (31%)	304 (81%)	188 (27%)	270 (30%)	268 (27%)	132 (19%)
Lithgow	957 (26%)	72 (19%)	241 (34%)	289 (32%)	218 (22%)	137 (20%)
OMMPCC	891 (24%)	0	161 (23%)	210 (23%)	308 (31%)	212 (30%)
Dillwynia	681 (18%)	0	113 (16%)	132 (15%)	215 (21%)	221 (31%)
Sex						
Female	679 (18%)	0	113 (16%)	132 (15%)	215 (21%)	219 (31%)
Male	3010 (82%)	376 (100%)	590 (84%)	769 (85%)	794 (79%)	481 (69%)
Transgender	2 (<1%)	0	0	0	0	2 (<1%)
Age, years	33 (26–41)	34 (26–44)	34 (27–41)	32 (26–39)	33 (27–40)	32 (26–40)
Aborigines and Torres Strait Islanders						
No	2563 (69%)	275 (73%)	477 (68%)	631 (70%)	728 (72%)	452 (64%)
Yes	1005 (27%)	95 (25%)	174 (25%)	236 (26%)	279 (28%)	221 (31%)
Data not available	123 (3%)	6 (2%)	52 (7%)	34 (4%)	2 (<1%)	29 (4%)
Country of birth						
Australia	2905 (79%)	309 (82%)	530 (75%)	703 (78%)	802 (80%)	561 (80%)
Other countries	668 (18%)	62 (17%)	123 (18%)	164 (18%)	206 (20%)	113 (16%)
Data not available	118 (3%)	5 (1%)	50 (7%)	34 (4%)	1 (<1%)	28 (4%)
Formal education level						
No formal education or completed primary school	1238 (34%)	127 (34%)	244 (35%)	335 (37%)	285 (28%)	247 (35%)
Completed high school	1709 (46%)	162 (43%)	312 (44%)	430 (48%)	517 (51%)	288 (41%)
Tertiary education	613 (17%)	80 (21%)	97 (14%)	98 (11%)	203 (20%)	135 (19%)
Data not available	131 (4%)	7 (2%)	50 (7%)	38 (4%)	4 (<1%)	32 (5%)
Duration of stay in current prison, months	9 (3–29)	29 (10–58)	13 (5–36)	9 (3–29)	7 (2–23)	5 (2–17)
Previous imprisonment						
No	967 (26%)	112 (30%)	171 (24%)	224 (25%)	291 (29%)	169 (24%)
Yes	2607 (71%)	259 (69%)	482 (69%)	643 (71%)	718 (71%)	505 (72%)
Data not available	117 (3%)	5 (1%)	50 (7%)	34 (4%)	0	28 (4%)
Tattoo or piercing in prison (current imprisonment)						
No	3152 (85%)	343 (91%)	567 (81%)	758 (84%)	879 (87%)	605 (86%)
Yes	419 (11%)	30 (8%)	77 (11%)	103 (11%)	130 (13%)	79 (11%)
Data not available	120 (3%)	3 (1%)	59 (8%)	40 (4%)	0	18 (3%)
Injecting drug use status						
Never injected	1654 (45%)	170 (45%)	271 (39%)	395 (44%)	496 (49%)	322 (46%)
Had history of injecting, but not in current imprisonment	792 (21%)	63 (17%)	126 (18%)	206 (23%)	229 (23%)	168 (24%)
Injected more than 6 months ago (current imprisonment)	139 (4%)	39 (10%)	37 (5%)	22 (2%)	19 (2%)	22 (3%)
Injected in previous 2–6 months (current imprisonment)	198 (5%)	24 (6%)	48 (7%)	51 (6%)	48 (5%)	27 (4%)
Injected in previous month (current imprisonment)	797 (22%)	76 (20%)	176 (25%)	191 (21%)	217 (22%)	137 (20%)
Data not available	111 (3%)	4 (1%)	45 (6%)	36 (4%)	0	26 (4%)
Opioid agonist therapy*						
Never	591/1134 (52%)	46/139 (33%)	114/265 (43%)	143/269 (53%)	177/284 (62%)	111/186 (60%)
Yes, previously	237/1134 (21%)	34/139 (24%)	80/265 (30%)	81/269 (30%)	72/284 (25%)	48/186 (26%)
Yes, currently	315/1134 (28%)	59/139 (42%)	71/265 (27%)	45/269 (17%)	35/284 (12%)	27/186 (15%)
Frequency of injecting†						
Less than once a week	189/797 (24%)	23/76 (30%)	46/176 (26%)	50/191 (26%)	44/217 (20%)	26/137 (19%)
1–6 days per week, not daily	209/797 (26%)	17/76 (22%)	54/176 (31%)	43/191 (23%)	57/217 (26%)	38/137 (28%)
Once a day or more	389/797 (49%)	36/76 (47%)	72/176 (41%)	92/191 (48%)	116/217 (53%)	73/137 (53%)
Data not available	10/797 (1%)	0	4/176 (2%)	6/191 (3%)	0	0

(Table 1 continues on next page)

	Total (n=3691)	Year of enrolment				
		2014–15 (n=376)	2016 (n=703)	2017 (n=901)	2018 (n=1009)	2019 (n=702)
(Continued from previous page)						
Re-used a needle or syringe after someone else had used it†						
No	76/797 (10%)	12/76 (16%)	13/176 (7%)	16/191 (8%)	22/217 (10%)	13/137 (10%)
Yes	709/797 (89%)	63/76 (83%)	159/176 (90%)	168/191 (88%)	195/217 (90%)	124/137 (91%)
Data not available	12/797 (2%)	1/76 (1%)	4/176 (2%)	7/191 (4%)	0	0
Re-used any injecting equipment after someone else had used it†						
No	63/797 (8%)	9/76 (12%)	13/176 (7%)	14/191 (7%)	19/217 (9%)	8/137 (6%)
Yes	722/797 (91%)	66/76 (87%)	159/176 (90%)	170/191 (89%)	198/217 (91%)	129/137 (94%)
Data not available	12/797 (2%)	1/76 (1%)	4/176 (2%)	7/191 (4%)	0	0

Data are n (%), n/N (%), or median (IQR). OMMPCC=Outer Metropolitan Multi-Purpose Correctional Centre. *Among participants who injected at any time in current imprisonment. †Among participants who injected in the previous month during current imprisonment.

Table 1: **Background and behavioural characteristics of SToP-C study participants at enrolment, overall, and by year of enrolment**

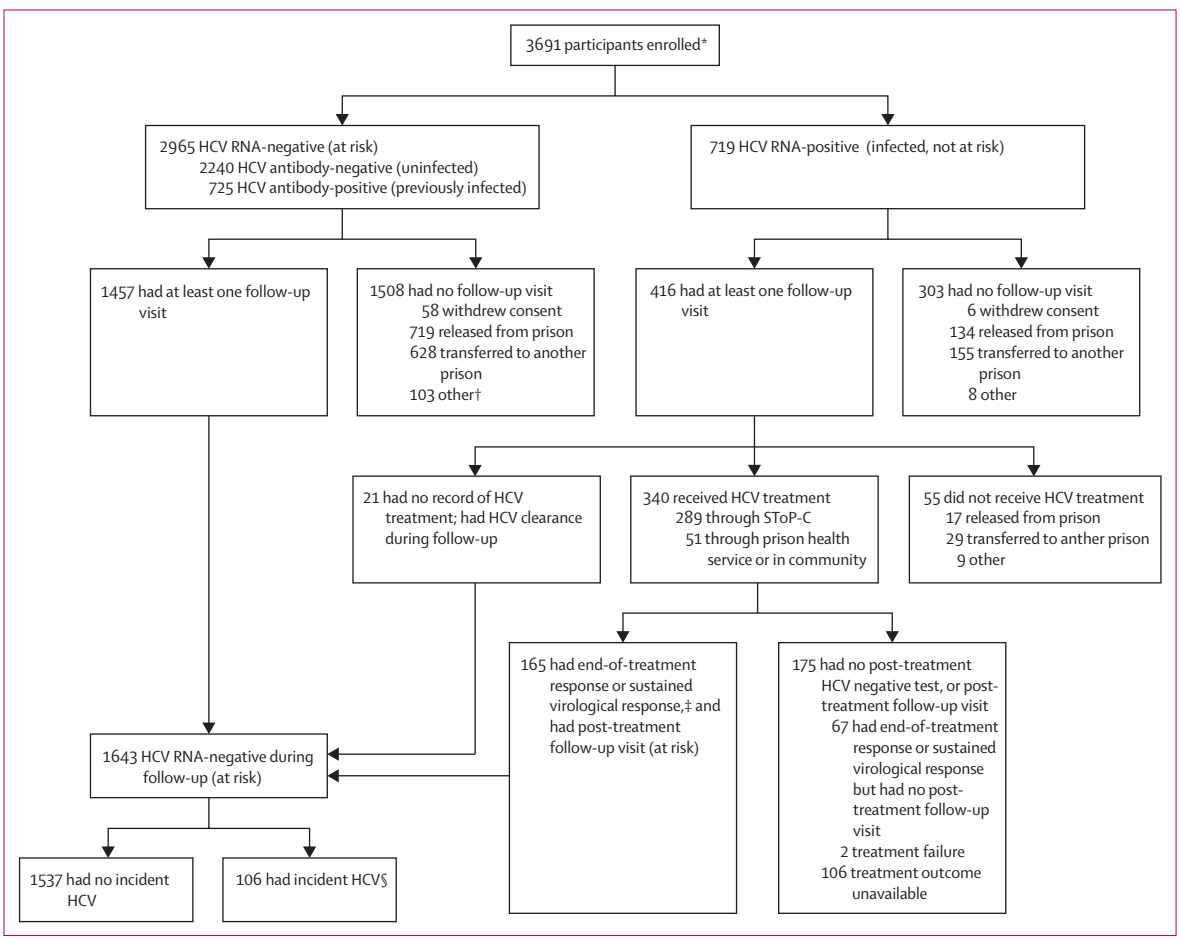

Figure 1: **Overview of SToP-C study participants**
HCV=hepatitis C virus. *HCV test results at enrolment were not available for seven participants. †96 participants were enrolled during late 2019 and were not due for follow-up or there was no access to the participant by the end of the study. Seven participants were not followed up due to a variety of reasons (not listed). ‡For participants receiving treatment through SToP-C, end-of-treatment response was considered since phylogenetic analysis was used to distinguish post-treatment re-infection from relapse. For other participants, sustained virological response was considered. §Five participants had the second incident HCV infection after clearance of the first infection (111 HCV incident events).

symptom-directed physical examinations, assessment of HCV RNA, and standard laboratory testing. Study medication was dispensed every 4 weeks (for the majority of participants) or on a daily observed basis, based on a standardised risk assessment for likely non-adherence. Participants transferred to a non-SToP-C prison continued DAA treatment, but not SToP-C study follow-up. Participants released from prison were provided their remaining therapy and a referral to a community primary care practitioner for follow-up.

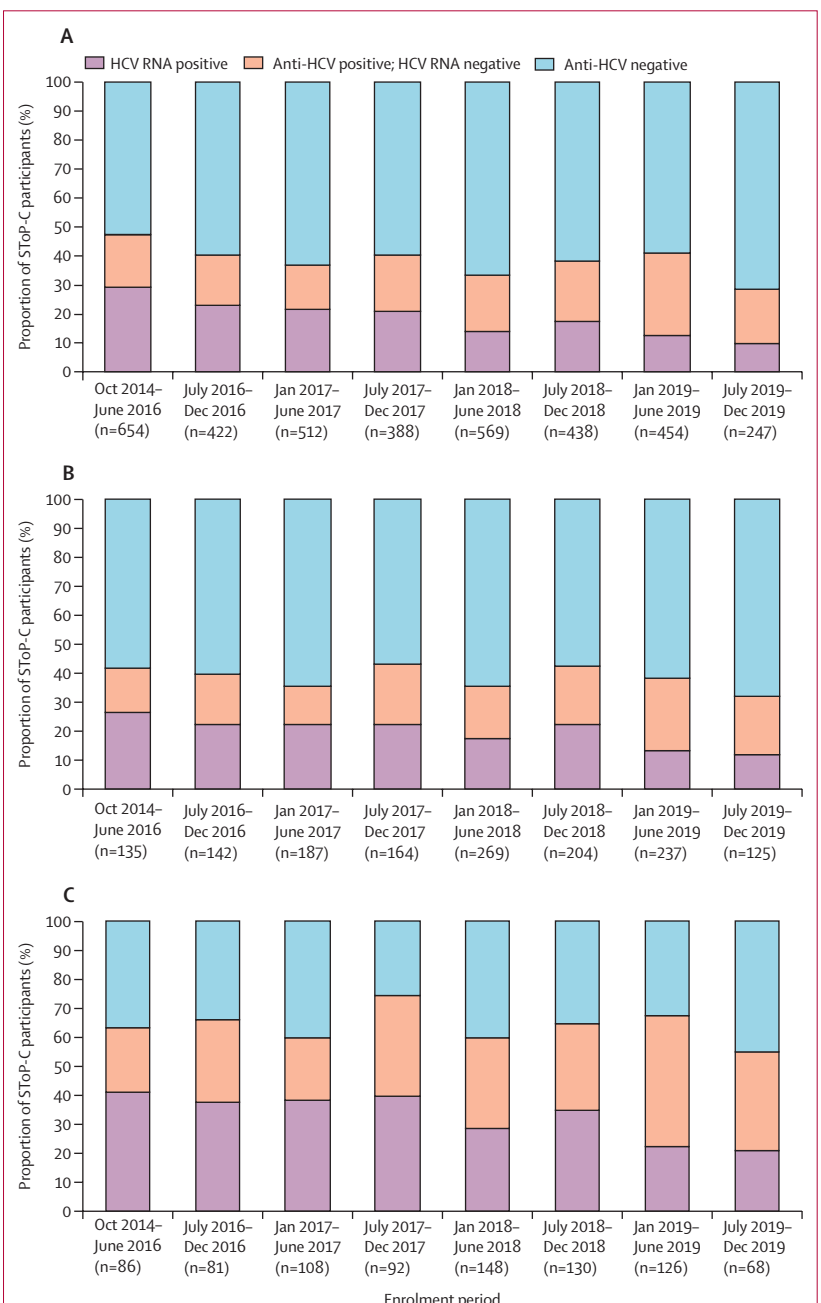

Figure 2: **HCV status at enrolment, by year of enrolment**
(A) Among total SToP-C participants. (B) Among all new prison entrants enrolled into SToP-C within 6 months of entering prison. (C) Among new prison entrants who had ever injected drugs at enrolment. HCV=hepatitis C virus.

Laboratory assessments

All samples were tested for HCV antibody and RNA in a central laboratory (Prince of Wales Hospital, Sydney, NSW, Australia). Samples were tested for HCV antibody with ARCHITECT Anti-HCV (Abbott; Chicago, IL, USA) and Murex anti-HCV (DiaSorin; Saluggia, Italy); for HCV RNA with COBAS TaqMan (Roche; Basel, Switzerland; lower limit of detection 15 IU/mL); for hepatitis B surface antigen with ARCHITECT HBsAg (Abbott; Chicago, IL, USA); and for HIV antibody with ARCHITECT HIV Ag/Ab Combo (Abbott; Chicago, IL, USA). HCV genotype was determined with COBAS HCV GT (Roche; Basel, Switzerland). Among participants with a positive HCV RNA test after treatment, Sanger sequencing of the NS5A, NS5B, and Core-E2 regions of pre-treatment and post-treatment samples was done to ascertain whether recurrent HCV viraemia was due to virological failure (homologous strains) or re-infection (heterologous strains).

Study definitions

Incident HCV primary infection was defined as a positive HCV antibody test in participants with a negative HCV antibody test result at the previous visit. Incident HCV re-infection was defined as a positive HCV RNA test in participants with a negative HCV RNA test result at the previous visit. Among participants receiving HCV treatment as part of the SToP-C study, post-treatment HCV re-infection was defined as a recurrent positive HCV RNA test after the end of treatment with an HCV strain that was confirmed as heterologous from the primary infecting strain.

Participants with detectable HCV RNA, no exclusion criteria for treatment, and at least one follow-up assessment after enrolment were defined as being eligible for treatment.

Among participants who received HCV treatment, an end-of-treatment response was defined as non-quantifiable HCV RNA at the end of treatment. HCV treatment outcomes were classified as: sustained virological response (defined as non-quantifiable HCV RNA at or after 12 weeks following the end of treatment), virological failure (defined as quantifiable HCV RNA at 12 weeks after the end of treatment with re-infection excluded on sequencing), or non-virological failure (including re-infection, death, premature treatment discontinuation, or loss to follow-up).

The date of incident HCV infection was estimated on the basis of a hierarchical algorithm with serological, virological, and treatment data. In participants with no HCV treatment following the previous visit, the date of incident infection was estimated as the mid-point between the last HCV negative and the first HCV positive test (HCV antibody or HCV RNA).

In participants who received HCV treatment through SToP-C, the date of incident infection was estimated as the mid-point between the end-of-treatment response and the first HCV RNA positive test. And in participants who received HCV treatment outside of SToP-C (eg, through the prison health service or in the community) and achieved a sustained virological response, the date of incident infection was estimated as the mid-point between a documented sustained virological response and the first HCV RNA-positive test.

Liver fibrosis stage was assessed by measurement of liver stiffness (transient fibro-elastography). Significant liver fibrosis was defined as liver stiffness greater than 7·1 kPa and cirrhosis as liver stiffness greater than 12·5 kPa.[15] Compensated liver disease was defined as an international normalised ratio (INR) less than 1·8, serum albumin greater than 30 g/L, and total serum bilirubin less than 35 µmol/L.

Outcomes

The primary outcome of the SToP-C study was the HCV incidence rate ratio (IRR), which compared HCV incidence before and after DAA treatment scale-up among participants at risk of primary infection or re-infection. Although DAA treatment scale-up commenced in mid-2017, it was staggered across the four prisons and high treatment coverage was not achieved until the end of 2017. Thus, the post-treatment scale-up period (in the context of the primary outcome evaluation) was designated as January, 2018, to November, 2019, and the pre-treatment scale-up period was designated as October, 2014, to the end of 2017. Changes in HCV incidence, including primary infection and re-infection, were reported. The secondary outcome of the SToP-C study was HCV treatment outcome, as defined above.

Statistical analysis

The study sample size was calculated to have 80% and 90% statistical power in different scenarios, assuming various levels of HCV incidence before treatment scale-up and expected reduction in HCV incidence rate after treatment scale-up (appendix p 2). Assuming a baseline HCV incidence of ten per 100 person-years, 1500 person-years of follow-up were needed to have 90% power to detect a 25% reduction in incidence, 310 person-years of follow-up were needed to have 90% power to detect a 50% reduction in incidence, and 106 person-years of follow-up were needed to have 90% power to detect a 75% reduction in incidence.

The incidence of HCV infection (primary infection, re-infection, and both primary infection and re-infection) and corresponding 95% CIs were calculated as rates per 100 person-years by use of Poisson distribution, with follow-up censored at the estimated date of incident HCV infection, last follow-up visit before prison transfer or release (for which no return to prison was documented), or last study follow-up visit.

HCV incidence rates were calculated for the pre-DAA treatment scale-up phase (October, 2014, to December, 2017) and the DAA treatment scale-up phase (January, 2018, to November, 2019). HCV incidence rates before and after treatment scale-up were compared by calculating IRRs and corresponding 95% CIs, and by doing Mantel-Haenszel significance tests. HCV incidence rates were also calculated in 6-month intervals across the whole study period. Given the slow enrolment of participants before 2016, in the early stages of recruitment the first interval was considered to be October, 2014, to June, 2016. Interrupted time series regression analysis[16] was then done to evaluate changes in HCV incidence before and after DAA treatment scale-up. The model was adjusted for calendar time (6-month intervals) and HCV prevalence among new prison entrants, as a surrogate of the HCV reservoir transferring from the community to the prison over time. The prevalence of HCV infection among participants who were enrolled in the study within 6 months of entering prison was used for this adjustment.

In the stratified analysis, HCV incidence rates were compared before and after DAA treatment scale-up in three risk groups defined on the basis of injecting drug use at enrolment: participants who had never injected; those who had a history of injecting but not in their current imprisonment; and those who were injecting in their current imprisonment.

The risk of HCV infection before and after treatment scale-up was also assessed by use of unadjusted and adjusted Cox proportional hazards regression analyses, with the following a-priori covariates: sex, age, Indigenous ethnicity (Aborigines and Torres Strait Islanders), duration of stay in prison at enrolment, previous imprisonment, injecting drug use status at each visit, and prison site. Since prison sites were sex-specific (three men-only prisons and one women-only prison), sex was not included in the adjusted model due to collinearity with prison site.

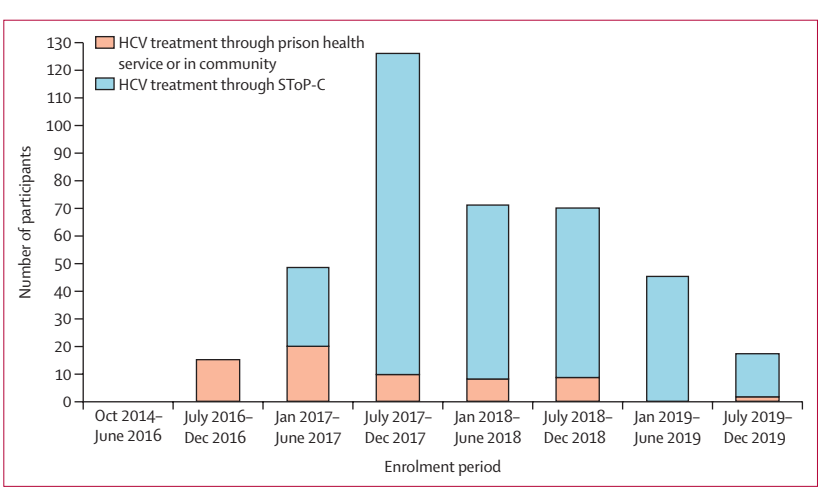

Figure 3: **Number of participants receiving HCV treatment through the SToP-C study or outside of the study, by year of enrolment**
HCV=hepatitis C virus.

Injecting drug use status was included as a time-varying covariate in the models. Other potential covariates (eg, tattooing, having sex, and being in a fight in prison) were not included in the model.

Given earlier commencement of participant enrolment in two maximum-security prison sites, a sensitivity analysis was done, restricting the analysis to participants from these two prisons. People stay in prison for transient periods, with many SToP-C study participants exiting prison and re-entering during follow-up, in some of whom the estimated date of HCV incident infection fell during the time they were out of prison. Thus, another sensitivity analysis was done to exclude participants who were out of prison at their estimated date of HCV incident infection.

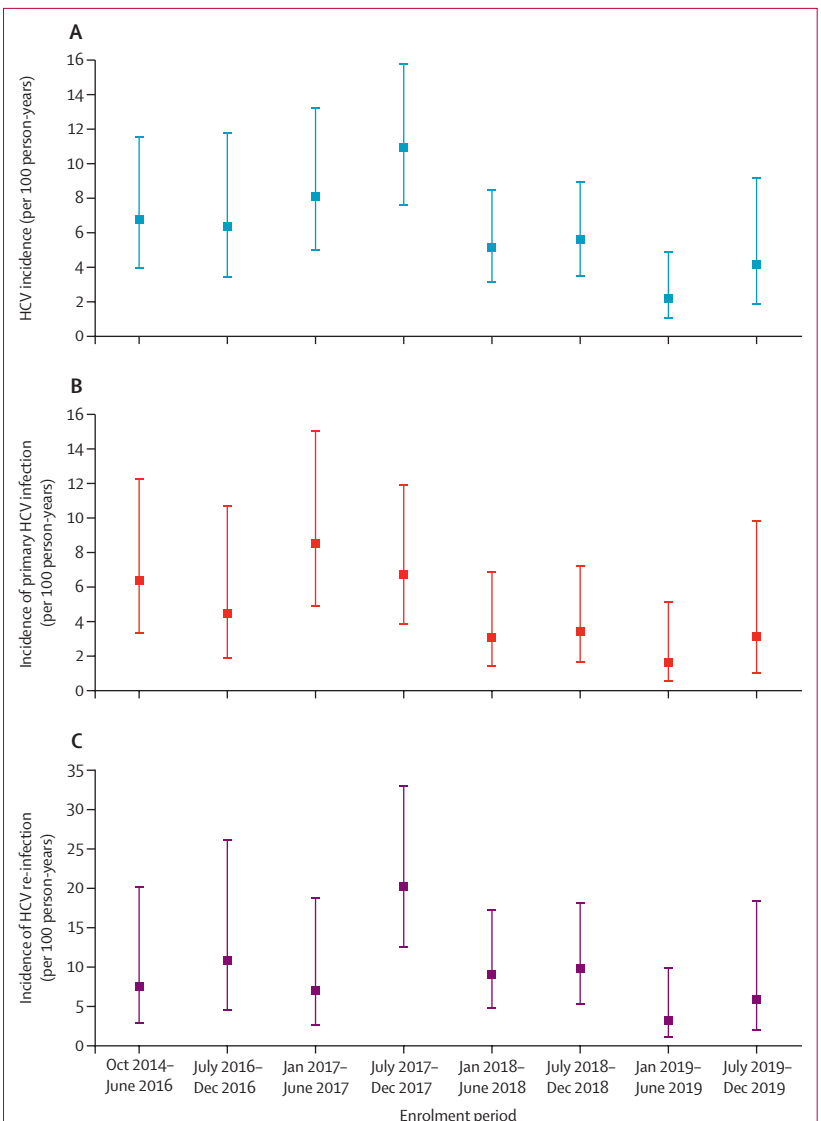

Figure 4: **Incidence of HCV infection in the SToP-C study**
(A) All HCV infection. (B) Primary HCV infection. (C) HCV re-infection. The time period between October, 2014, and June, 2016, was merged to increase person-years of follow-up. HCV=hepatitis C virus.

Statistical significance was assessed at $p<0·05$ (two-sided p values). Data analysis was done with Stata, version 14.2.

The study protocol was approved by the New South Wales Justice Health and Forensic Mental Health Network Human Research Ethics Committee (HREC/14/JH/7), Aboriginal Health and Medical Research Council Human Research Ethics Committee (1047/14 and 1253/17), and New South Wales Corrective Services Ethics Committee. The study was done according to the Declaration of Helsinki and International Conference on Harmonization Good Clinical Practice (ICH/GCP) guidelines, and is registered with ClinicalTrials.gov, NCT02064049.

Role of the funding source

This study was funded jointly by the Australian National Health and Medical Research Council (NHMRC) and Gilead Sciences through a NMHRC Partnership Project grant. Gilead Sciences provided the study medication. The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The sponsor (The Kirby Institute, UNSW Sydney, Sydney, NSW, Australia) collected the data, managed study samples, and monitored study conduct.

Results

Between Oct 30, 2014, and Sept 30, 2019, 3691 participants were enrolled, representing a range of 53% to 89% of all people incarcerated in the four SToP-C prisons up to September, 2019. Most participants were male (3010 [82%] of 3691) with a median age of 33 (IQR 26–41) years. The median duration of current imprisonment was 9 months (IQR 3–29), while 1029 (28%) of 3691 participants were on remand. More than half of participants (1926 [52%] of 3691) reported a history of injecting drugs, while 1134 (31%) reported injecting drugs during their current imprisonment, and 797 (22%) of 3691 reported injecting in the past month in prison. Among participants who reported injecting drugs during their current imprisonment, 315 (28%) of 1134 were receiving opioid agonist therapy at enrolment. Among those reporting injecting drugs in the past month, 722 (91%) of 797 reported sharing injecting equipment while in prison (table 1).

At enrolment, 2240 (61%) of 3691 participants had a negative HCV antibody test (ie, were at risk of primary HCV infection), 725 (20%) had a positive HCV antibody test and negative HCV RNA test (ie, were at risk of HCV re-infection), and 719 (19%) had a positive HCV RNA test (had HCV infection; figure 1). The prevalence of HCV infection at enrolment decreased from 29% among participants enrolled before June, 2016, to 10% among those enrolled after July, 2019 (figure 2A).

1873 participants had at least one follow-up visit after enrolment. Baseline characteristics were similar between participants with and without follow-up. As the only exception, those who were followed up had a longer time in prison at enrolment than those without (median 14 months [IQR 5–39] *vs* 6 months [2–17]), and were less

likely to be on remand (429 [23%] of 1875 *vs* 600 [33%] of 1816; appendix pp 3–4).

Among 719 participants who were HCV RNA-positive at baseline, 315 (44%) had HCV genotype 1 infection, 308 (43%) had genotype 3 infection, and 26 (4%) had other or mixed genotype infections. In the other 70 participants, genotype results were not available (in 67 due to low viral load, and in three for other reasons). 20 (3%) participants had severe liver fibrosis (F3) and 14 (2%) had cirrhosis (F4). No participant had HIV infection, while six (1%) had chronic hepatitis B virus infection.

499 HCV RNA-positive participants had follow-up assessments after baseline: 416 who were HCV RNA-positive at baseline and 83 who had incident HCV infection and no spontaneous clearance during follow-up. In the initial phase (October, 2014, to mid-2017, before DAA treatment scale-up), 39 participants received HCV treatment though the prison health service or in the community during the time after release from prison (three participants received interferon-based therapy). In the second phase (after DAA treatment scale-up), 349 (70%) of 499 participants received DAA treatment, among whom 324 participants received treatment through SToP-C and 25 received treatment through the prison health service or in the community (figure 3).

Among 324 participants receiving treatment through SToP-C, 211 (65%) stayed in prison until the end of treatment (ie, completed treatment), while 113 (35%) exited before treatment completion due to prison transfer (n=63), release (n=48), or withdrawal of consent (n=2). Among 143 participants who completed treatment and had a sustained virological response assessment, two had virological failure (relapse).

1643 participants were at risk of HCV infection or re-infection during follow-up and contributed to the HCV incidence analysis (figure 1). 82% of the at-risk population was male (1350 of 1643 participants), with a median age of 33 years (IQR 27–42), and 487 (30%) reported injecting drugs in their current period of imprisonment at enrolment (appendix pp 3–4). Median follow-up was 10 months (IQR 5–18) in the overall analysis population, including 10 months (5–19) among participants who were sentenced and 8 months (5–14) among those on remand. With 1818 person-years of follow-up, 111 incident HCV infections were detected: consisting of 57 primary infections and 54 re-infections. Five participants had two incident infection episodes (the second episode occurred following spontaneous or treatment-induced clearance of the first incident infection). During the entire study follow-up period the incidence of HCV infection was 6·11 per 100 person-years (95% CI 5·07–7·35), while that of primary infection was 4·60 per 100 person-years (3·56–5·96), and that of re-infection was 9·34 per 100 person-years (7·15–12·19). HCV incidence was 5·48 per 100 person-years (95% CI 4·40–6·83) among imprisoned participants and 9·07 per 100 person-years (6·34–12·98) among those on remand.

HCV incidence increased before DAA treatment scale-up, from 6·73 per 100 person-years (95% CI 3·91–11·60) to 10·93 per 100 person-years (7·54–15·82) through December, 2017. Following treatment scale-up, HCV incidence decreased to 5·13 per 100 person-years (95% CI 3·10–8·52) in January, 2018, to June, 2018, and was between 2·20 per 100 person-years and 5·60 per 100 person-years until November, 2019 (figures 4, 5).

When comparing the overall incidence rate before treatment scale-up (2014–17) with that after treatment scale-up (2018–19), there was a reduction in incidence, from 8·31 per 100 person-years to 4·35 per 100 person-years (IRR 0·52 [95% CI 0·36–0·78]; p=0·0007; table 2).

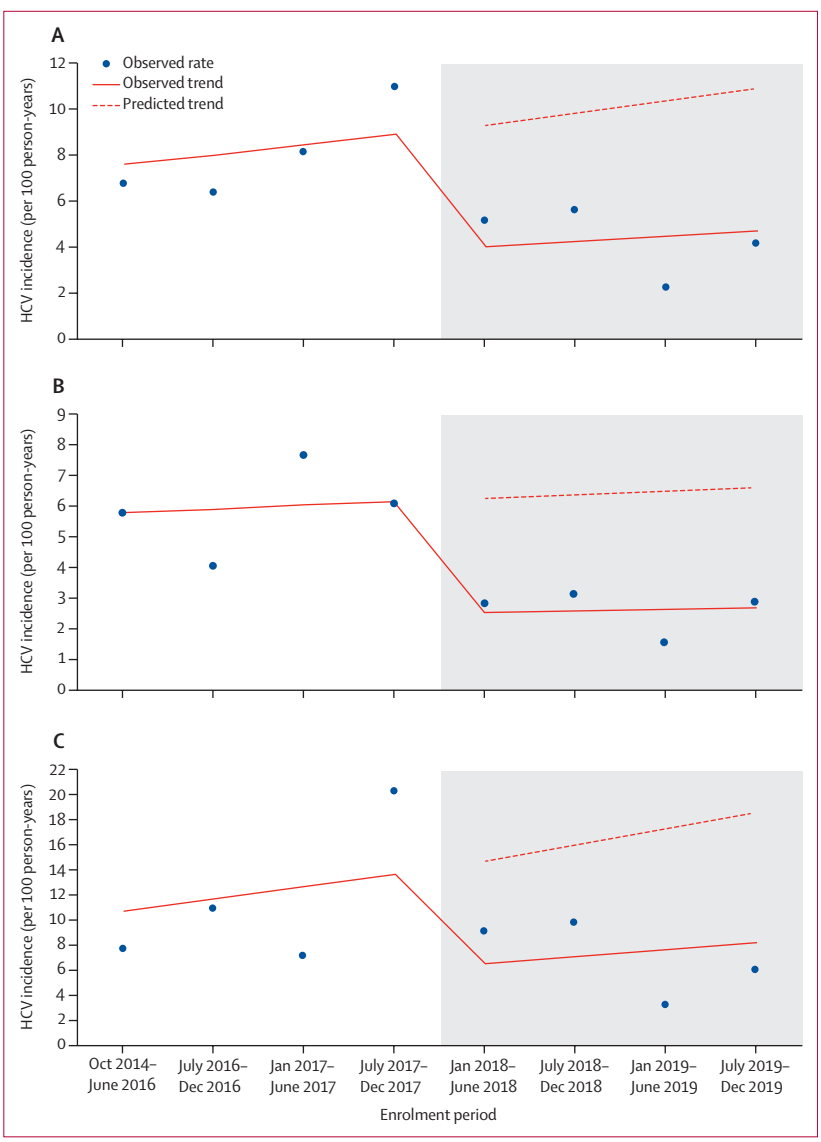

Figure 5: **HCV incidence trends in the SToP-C study**
(A) HCV infection. (B) Primary HCV infection. (C) HCV re-infection. The red solid line represents the observed trend and the red dashed line represents the predicted counterfactual by removing the effect of the intervention for the period after 2017. The grey shaded area represents the period of rapid scale-up of direct-acting antiviral treatment. HCV=hepatitis C virus.

	Person-years of follow-up	Incident infections (n)	Incidence rate per 100 person-years (95% CI)	Incidence rate ratio (95% CI)	p value
HCV primary infection and re-infection					
All participants					
2014–17	807	67	8·31 (6·54–10·55)	1 (ref)	..
2018–19	1011	44	4·35 (3·24–5·85)	0·52 (0·36–0·78)	0·0007
Participants who never injected					
2014–17	458	7	1·53 (0·73–3·20)	1 (ref)	..
2018–19	541	7	1·29 (0·62–2·72)	0·84 (0·30–2·42)	0·76
Participants with a history of injecting, but not in current imprisonment					
2014–17	126	13	10·30 (5·98–17·73)	1 (ref)	..
2018–19	171	7	4·10 (1·95–8·60)	0·40 (0·16–0·98)	0·041
Participants who injected in current imprisonment					
2014–17	216	47	21·74 (16·34–28·94)	1 (ref)	..
2018–19	293	30	10·25 (7·17–14·67)	0·47 (0·30–0·75)	0·0010
HCV primary infection					
All participants					
2014–17	572	38	6·64 (4·83–9·13)	1 (ref)	..
2018–19	667	19	2·85 (1·82–4·46)	0·43 (0·25–0·74)	0·0019
Participants who never injected					
2014–17	447	5	1·12 (0·47–2·69)	1 (ref)	..
2018–19	524	7	1·34 (0·64–2·80)	1·19 (0·38–3·76)	0·76
Participants with a history of injecting, but not in current imprisonment					
2014–17	61	10	16·34 (8·79–30·38)	1 (ref)	..
2018–19	80	4	5·00 (1·88–13·32)	0·31 (0·10–0·98)	0·034
Participants who injected in current imprisonment					
2014–17	59	23	39·08 (25·97–58·82)	1 (ref)	..
2018–19	57	8	14·03 (7·02–28·5)	0·36 (0·16–0·80)	0·0091
HCV re-infection					
All participants					
2014–17	235	29	12·36 (8·59–17·79)	1 (ref)	..
2018–19	344	25	7·27 (4·92–10·76)	0·59 (0·35–1·00)	0·050
Participants who never injected					
2014–17	12	2	17·02 (4·26–68·07)	..	..
2018–19	17	0	0·00 (0·00–17·65)*	..	..
Participants with a history of injecting, but not in current imprisonment					
2014–17	65	3	4·61 (1·49–14·30)	1 (ref)	..
2018–19	91	3	3·31 (1·07–10·25)	0·72 (0·15–3·55)	0·68
Participants who injected in current imprisonment					
2014–17	157	24	15·26 (10·23–22·76)	1 (ref)	..
2018–19	236	22	9·34 (6·15–14·19)	0·61 (0·34–1·09)	0·093

HCV=hepatitis C virus. *Given the zero event, 95% CIs were calculated on the basis of the "rule of three".[37]

Table 2: **Comparison of the incidence rates of HCV infection before and after direct-acting antiviral treatment scale-up, overall, and by injecting drug use status at enrolment**

There was a reduction in HCV incidence from 6·64 per 100 person-years to 2·85 per 100 person-years for primary infection (IRR 0·43 [95% CI 0·25–0·74]; p=0·0019) and from 12·36 per 100 person-years to 7·27 per 100 person-years for re-infection (0·59 [0·35–1·00]; p=0·050; table 2).

The prevalence of HCV infection among participants enrolled into SToP-C within 6 months of entering prison decreased from 27% (36 of 135) among those enrolled before June, 2016, to 12% (15 of 125) among those enrolled after July, 2019 (figure 2B). The interrupted time-series regression analysis was adjusted for calendar time (underlying trend) and HCV prevalence among new prison entrants; the change in HCV incidence following DAA treatment scale-up remained significant (adjusted IRR 0·43 [95% CI 0·21–0·88]; p=0·021). This analysis also indicated reductions in HCV primary infection (0·41 [95% CI 0·15–1·11]; p=0·078) and HCV re-infection (0·44 [0·16–1·20]; p=0·11), although neither reduction was significant.

In the stratified analysis by injecting drug use status at enrolment, in participants who reported a history of injecting but not in their current imprisonment, there was a reduction in HCV incidence from 10·30 per 100 person-years in the pre-treatment scale-up period to 4·10 per 100 person-years in the post-treatment scale-up period (IRR 0·40 [95% CI 0·16–0·98]; p=0·041). Among participants who reported injecting drug use in their current imprisonment, HCV incidence decreased from 21·74 per 100 person-years to 10·25 per 100 person-years (IRR 0·47 [95% CI 0·30–0·75]; p=0·0010). Among these participants, the incidence of primary infection decreased from 39·08 per 100 person-years to 14·03 per 100 person-years (IRR 0·36 [95% CI 0·16–0·80]; p=0·0091), and the incidence of re-infection decreased from 15·26 per 100 person-years to 9·34 per 100 person-years (0·61 [0·34–1·09]; p=0·093). HCV incidence among participants who reported never injecting drugs was low throughout the study (table 2).

The Cox proportional hazards regression analysis indicated a significant reduction in the risk of HCV infection during 2018–19 compared with 2014–17, after adjustment for participants' age, Indigenous Australian ethnicity, duration of stay in prison, previous imprisonment, injecting drug use status, and prison site (table 3). Independent of study period, the risk of HCV infection was significantly lower in older participants, and significantly higher among participants with previous imprisonments (table 3). Compared with participants reporting no injecting in their current imprisonment, the risk of HCV infection was three times higher among participants who injected more than 6 months ago, and six times higher among those who injected during the previous 6 months (table 3).

In a sensitivity analysis, restricting the study population to participants enrolled from two maximum-security prisons, similar results were observed (appendix pp 5, 7). In another sensitivity analysis, excluding 33 participants whose estimated date of HCV incident infection occurred in the time when they were out of prison, the results were again similar (appendix p 6).

Discussion

The SToP-C study provides empirical evidence for the effectiveness of HCV treatment-as-prevention in the prison setting, showing a significant reduction in

	Unadjusted hazard ratio (95% CI)	p value	Adjusted hazard ratio (95% CI)*	p value
Study period				
2014–17	1 (ref)	..	1 (ref)	..
2018–19	0·55 (0·37–0·82)	0·0028	0·50 (0·33–0·76)	0·0014
Sex†				
Female	1 (ref)	..	..	..
Male	0·62 (0·39–0·98)	0·041	..	..
Age at enrolment, years‡	0·92 (0·89–0·94)	<0·0001	0·92 (0·89–0·95)	<0·0001
Age at enrolment				
≤25 years	1 (ref)	..	..	..
25–35 years	0·67 (0·44–1·01)	0·058	..	..
35–45 years	0·30 (0·17–0·53)	<0·0001	..	..
>45 years	0·04 (0·01–0·18)	<0·0001	..	..
Aborigines and Torres Strait Islanders				
No	1 (ref)	..	1 (ref)	..
Yes	2·01 (1·37–2·96)	0·0004	1·02 (0·66–1·57)	0·93
Duration of stay in current prison at enrolment				
Up to 12 months	1 (ref)	..	1 (ref)	..
13–24 months	0·69 (0·40–1·18)	0·17	0·92 (0·51–1·67)	0·79
25–36 months	0·54 (0·28–1·03)	0·060	0·89 (0·44–1·82)	0·76
>36 months	0·39 (0·25–0·63)	0·0001	0·82 (0·46–1·44)	0·48
Previous imprisonment				
No	1 (ref)	..	1 (ref)	..
Yes	3·02 (1·78–5·14)	<0·0001	2·27 (1·21–4·26)	0·011
Injecting drug use status				
Not injected in current imprisonment	1 (ref)	..	1 (ref)	..
Injected more than 6 months ago (current imprisonment)	4·52 (1·61–12·73)	0·0043	3·32 (1·04–10·59)	0·043
Injected in the previous 6 months (current imprisonment)	10·32 (5·27–20·20)	<0·0001	6·14 (3·16–11·92)	<0·0001
Prison site at the last visit				
Lithgow	1 (ref)	..	1 (ref)	..
Dillwynia	2·05 (1·16–3·62)	0·014	2·10 (1·06–4·15)	0·034
Goulburn	2·02 (1·26–3·25)	0·0036	1·97 (1·18–3·29)	0·0094
OMMPCC	0·53 (0·25–1·14)	0·10	1·18 (0·53–2·63)	0·69

HCV=hepatitis C virus. OMMPCC=Outer Metropolitan Multi-Purpose Correctional Centre. *1785 person years of follow-up with 110 incident events included in the model. †Sex was not included in the adjusted model given high collinearity with prison site. ‡HR indicates increased hazard for each year increase in age.

Table 3: **Unadjusted and adjusted Cox proportional hazards models evaluating factors associated with the risk of HCV infection**

HCV incidence following rapid scale-up of DAA therapy in four prisons in New South Wales, Australia. These findings support enhanced HCV treatment access and coverage among incarcerated people, including unrestricted access to DAA treatment and rapid treatment scale-up, to improve individual health outcomes and boost HCV elimination efforts within the prison and broader community settings.

The observed incidence of HCV infection before DAA treatment scale-up in SToP-C was 8·31 per 100 person-years, consistent with a previous study from New South Wales prisons, which only included PWID and documented an HCV incidence of 11·4 per 100 person-years.[18] Notably, HIV prevalence in Australian prisons is very low[19] (with zero cases detected in SToP-C), contrasting with many other prison settings worldwide.[20]

The SToP-C study showed a reduction in HCV incidence, from 8·31 per 100 person-years to 4·35 per 100 person-years, following DAA treatment scale-up. Although a decrease in HCV prevalence among new prison entrants was also observed during the study period, suggesting reductions in transfer of the HCV reservoir from the community to the prison setting during the study period, after adjustment for HCV prevalence the analysis still showed a significant reduction in HCV incidence. This finding provides evidence of the effect of HCV treatment-as-prevention—which is particularly notable since harm reduction measures might not be optimal in the prison setting.

As expected, HCV incidence was higher among participants with a previous history of injecting drug use than in those without, and highest among those reporting injecting in their current imprisonment. Furthermore, the greatest reduction in HCV incidence after DAA treatment scale-up was observed among people

who injected drugs, with DAA treatment reducing HCV risk by more than half among participants who reported injecting drugs in their current imprisonment. HCV incidence was consistently very low among the 45% of STоP-C study participants without a history of injecting drug use at enrolment. This finding also suggests good validity of self-reported HCV risk behaviour, and a low risk of HCV transmission through non-injecting means.

There are several possible reasons for the non-significant effect of DAA treatment scale-up on HCV re-infection. First, the statistical power for this analysis was more limited than for the overall evaluation of HCV incidence or for primary infection. Second, detection of HCV re-infection is partly related to the frequency of HCV RNA testing.[21,22] Primary infection is determined on the basis of HCV antibody seroconversion, which is sustained. By contrast, cases of re-infection can undergo spontaneous clearance and avoid detection, particularly in a setting in which HCV RNA testing is done every 6 months.[23] Finally, HCV treatment of high-risk individuals initially expands the susceptible population for HCV re-infection and thereby increases the risk level in this population. Irrespective of these potential explanations, further strategies are required to reduce rates of HCV re-infection in the prison setting (eg, enhanced harm reduction interventions).

The number of DAA treatment initiations through STоP-C was several times higher than that by the prison health services following access to government-subsidised DAA treatment, highlighting the feasibility of a rapid scale-up approach. The rapid transition from diagnosis to treatment initiation is likely to boost the effect of a treatment-as-prevention strategy by reducing loss to follow-up and restricting the possibility of further transmissions. In the STоP-C study, the care cascade was used with venepuncture sampling and HCV testing in a central laboratory, necessitating a delay of several weeks in treatment initiation. By contrast, point-of-care HCV testing in prison has been shown to result in a shorter time to treatment and increased treatment uptake.[24,25]

28% of STоP-C participants were receiving opioid agonist therapy at enrolment. A previous analysis of risk behaviours in a prospective cohort of people in Australian prisons who inject drugs revealed increased risk behaviour after incarceration, with increased rates of sharing injecting equipment and increased use of opioids, including heroin and diverted methadone or buprenorphine.[26] Mathematical modelling of HCV transmission trends in New South Wales prisons has shown that DAA treatment scale-up to 40% of all people with HCV infection in prisons would provide an effect size on HCV incidence reduction comparable to that reported in the STоP-C study.[5] Furthermore, the modelling revealed that the combination of DAA treatment scale-up with enhanced access to opioid agonist therapy enabled greater reductions in HCV incidence. Accordingly, expansion of opioid agonist therapy, including access to depot-buprenorphine preparations, in the prison setting should further reduce HCV risk behaviour. Although there are clear barriers to their implementation,[27] evaluation of prison-based needle and syringe programmes in Australia and the feasibility of broad access to these programmes should be considered to match community-based access. Continued HCV elimination efforts, particularly among PWID in the community, should also reduce HCV prevalence among people entering prison, as was observed in the STоP-C study.

Interferon-based treatment was previously a major barrier against treatment uptake, given the considerable side-effects and long treatment duration. By contrast, DAA treatment has shifted the notion of HCV therapy, with its once daily oral dosing, minimal side-effects, short duration, and high efficacy. However, HCV treatment programmes in prison settings worldwide have been relatively limited, often with small numbers of individuals with HCV infection being treated.[28,29] In Australia, specific arrangements were put in place to ensure prison-based access to the DAA treatment programme, which has led to a steady increase in treatment uptake in correctional centres in the country. Although prison-based initiation of DAA treatment constituted approximately 6% of the national DAA treatment uptake in 2016,[30] this figure increased to 31% in 2019,[31] which is a promising observation and crucial for national elimination efforts. DAA treatment scale-up in prisons is also important for elimination efforts outside prison, given the high rates of transitioning between prisons and the community. We could not assess the effect of DAA treatment scale-up in prisons on HCV transmission in the community since this was beyond the scope of this study. Incarceration, however, is often a missed opportunity to provide HCV care to a highly marginalised population.[32] An HCV testing and treatment programme in prisons in Italy reported that 81% of people diagnosed with HCV through screening in prison had never received HCV care before incarceration.[33] Surveillance of DAA treatment uptake in prison settings is therefore a key element of national elimination efforts.

Once the DAA treatment scale-up commenced in STоP-C, the uptake of DAA therapy among individuals with HCV infection was encouraging, with most individuals who were available for post-screening follow-up initiating therapy. The reasons for non-initiation of treatment were primarily related to the dynamic population in prison, including frequent transfers to other prisons and return to the community. High DAA uptake was seen, despite earlier qualitative research (done as a part of a feasibility assessment of the STоP-C study)[34] before DAA scale-up identifying concerns around HCV re-infection as a potential barrier to treatment initiation. Further studies are required to evaluate the effectiveness of interventions to maintain the continuum

of care for people who are diagnosed with HCV in prison but transitioning, including initiatives for referral to community services for those released from prison or to other prison health services for those transferred.

The SToP-C study had a number of limitations. First, the study was designed as a before-and-after evaluation, rather than a larger cluster-randomised controlled trial across the 40 prisons in New South Wales. However, adequate resources for such a large undertaking were not available. Second, although enrolment coverage (ie, the proportion of all individuals incarcerated in the four prisons who were enrolled in the SToP-C study) was higher than 80%, we were unable to assess HCV risk status and transmission through people not enrolled in the study. Third, the rate of transitioning of enrolled individuals between prisons, and the rate of release from prison was higher than anticipated, even among those incarcerated in maximum-security prisons. Describing incarcerated people as a captive population in the context of HCV elimination efforts is, therefore, inappropriate both in terms of the associated stigma and the epidemiological reality. Almost half of participants had no follow-up visit; among those who were followed up, only 41% had follow-up extending beyond 12 months, demonstrating the highly dynamic nature of this population. However, background and behavioural characteristics of participants with and without follow-up were comparable, suggesting minimal chances of selection bias. Finally, although the study included one female prison, this centre had the lowest relative enrolment and person-years of follow-up, making a stratified analysis by sex problematic.

In conclusion, the findings of the SToP-C study indicate that HCV treatment-as-prevention, through DAA treatment scale-up, is an effective strategy in prison settings. The findings support enhanced delivery of DAA therapy for incarcerated populations, and suggest further consideration of HCV treatment-as-prevention strategies among the broader population at risk of HCV infection. The combination of rapid DAA treatment scale-up with efficient HCV diagnosis and enhanced primary HCV prevention strategies is likely to have even greater effect on HCV transmission, given the high HCV transmission risk associated with injecting drug use in the prison setting.

Contributors

GJD and ARL designed and proposed the study. JG, TB, NKM, GMC, CT, JGMc, DMB, and JA contributed to study design and drafting the grant. GJD, BH, JG, MB, PM, and ARL were involved in coordination and supervision of the study. GJD, JG, TB, CT, PV, NKM, GMC, LG, CM, and ARL provided study governance through the protocol steering committee. BH did the statistical analyses, with assistance from EBC and HMc and with oversight from JA and GJD. BH, ARL, and GJD verified the data and drafted the manuscript, with input from all authors. All authors have seen and approved the final version of the manuscript. All authors had access to all the data in the study, all authors had final responsibility for the decision to submit for publication.

Declaration of interests

GJD is a consultant and adviser for, and has received research grants from, Gilead, AbbVie, Merck, Bristol-Myers Squibb, and Cepheid. ARL is a consultant and adviser for, and has received investigator-initiated research grants from, Gilead, Merck, and Bristol-Myers Squibb. JG is a consultant and adviser for, and has received research grants from, Gilead, AbbVie, Merck, and Cepheid. PV has received investigator-initiated untied grants from Gilead and honorarium from Gilead and Merck. NKM has received unrestricted research grants from Gilead and Merck. JGMc is a stockholder and ex-employee of Gilead Sciences. DMB is a stockholder and employee of Gilead Sciences. All other authors declare no competing interests.

Data sharing

Individual participant data that underlie the results reported in this Article, and a data dictionary, will be available, after de-identification (text, tables, figures, and appendices), beginning 9 months and ending 36 months following publication of the Article. Data requests, including a methodologically sound proposal, may be submitted to the Kirby Institute. The study steering committee will review data request applications. Following approval, data will be shared to achieve the aims in the approved proposal. Data requesters will need to sign a data access agreement before having access to the data.

For **data requests** contact recpt@kirby.unsw.edu.au

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