Research Article
Viral Hepatitis

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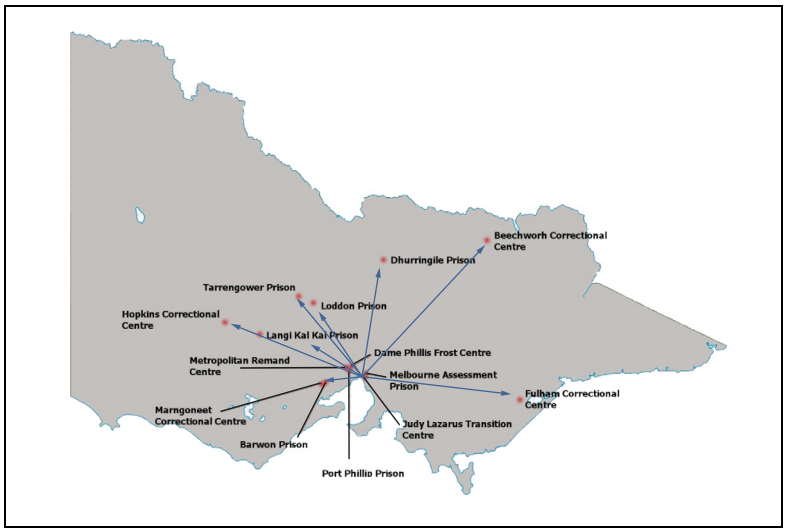
Graphical abstract



Highlights

- Nurse-led care was associated with SVR12 rates of >95% in large numbers of prisoners.
- <20% of prisoners required specialist input.
- >80% of prisoner had never pursued specialist hepatitis C care in the community.

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Lay summary

There is a high burden of hepatitis C infection among prisoners worldwide. Prisoners who continue to inject drugs are also at risk of developing new infections. For this reason, the prison setting provides an opportunity to treat those people at greatest risk of infection and to stop transmission to others. We developed a new method of providing hepatitis C treatment to prisoners, in which nurses rather than doctors assessed prisoners locally at each prison site. Treatment was safe and most prisoners were cured. Such programs will contribute greatly to achieving the World Health Organization's hepatitis C elimination goals.

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Outcomes of treatment for hepatitis C in prisoners using a nurse-led, statewide model of care

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Background & Aims: Treatment programs for people who inject drugs (PWID), including prisoners, are important for achieving hepatitis C elimination targets. There are multiple barriers to treatment of hepatitis C in prisons, including access to specialist physicians, testing and antiviral therapy, short prison sentences, and frequent inter-prison transfer. We aimed to assess the effectiveness of a nurse-led model of care for the treatment of prisoners with hepatitis C.

Methods: A statewide program for assessment and management of hepatitis C was developed in Victoria, Australia to improve access to care for prisoners. This nurse-led model of care is supported by telemedicine to provide decentralized care within all prisons in the state. We prospectively evaluated the feasibility and efficacy of this nurse-led model of care for hepatitis C within the 14 adult prisons over a 13-month period. The primary endpoint was sustained virological response at post-treatment week 12 (SVR12) using per protocol analysis.

Results: There were 416 prisoners included in the analysis. The median age was 41 years, 90% were male, 50% had genotype 3 and 44% genotype 1 hepatitis C and 21% had cirrhosis. Injecting drug use was reported by 68% in the month prior to prison entry, 54% were receiving opioid substitution therapy, and 86% reported never previously engaging with specialist HCV care. Treatment duration was 8 weeks in 24%, 12 weeks in 59%, and 24 weeks in 17% of treatment courses. The SVR12 rate was 96% (301/313) per protocol. Inter-prison transfer occurred during 26% of treatment courses but was not associated with lower SVR12 rates. No treatment-related serious adverse events occurred.

Conclusion: Hepatitis C treatment using a decentralized, nurse-led model of care is highly effective and can reach large numbers of prisoners. Large scale prison treatment programs should be considered to support hepatitis C elimination efforts.

Lay summary: There is a high burden of hepatitis C infection among prisoners worldwide. Prisoners who continue to inject drugs are also at risk of developing new infections. For this reason, the prison setting provides an opportunity to treat those people at greatest risk of infection and to stop transmission to others. We developed a new method of providing hepatitis C treatment to prisoners, in which nurses rather than doctors assessed prisoners locally at each prison site. Treatment was safe and most prisoners were cured. Such programs will contribute greatly to achieving the World Health Organization's hepatitis C elimination goals.

Introduction

The World Health Organization (WHO) has set global targets for the elimination of viral hepatitis as a public health threat.[1] For hepatitis C, the goals are to reduce incidence by 80% and mortality by 65% by 2030. In Western countries where injecting drug use is the dominant risk factor for hepatitis C transmission,[2] eliminating incident infection will require coordinated efforts using harm reduction strategies as well as "treatment as prevention" to interrupt transmission among people who inject drugs (PWID). This population has not typically been well engaged with specialist care, highlighting the need to develop new models of care for hepatitis C among marginalized, high transmitting populations.

Prison systems provide a unique opportunity to scale-up hepatitis C treatment.[3] The prevalence of hepatitis C is higher in prisoners than in the general population, reflecting the criminalization of drug use and the frequent detention of PWIDs.[4,5] In Australia, 46% of prisoners self-report a lifetime history of injecting drug use, and the hepatitis C seroprevalence among incarcerated PWID is greater than 50%.[6] Harm reduction strategies currently available in Australian prisons include bleach for cleansing of injection devices and opioid substitution therapy (OST). Despite this, ongoing incident hepatitis C infection has been reported among PWID in Australian prisons.[7] The median sentence length in Australia is less than 6 months and there are high rates of recidivism, meaning that prisoners frequently cycle between incarceration and freedom, creating new networks for hepatitis C transmission.[8] Mathematical modelling studies have demonstrated that the global elimination of HCV will require widespread treatment of key risk populations, in particular PWID.[9,10] Treatment programs in prisons, where a

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large numbers of PWID can be screened and treated, could therefore significantly contribute to the HCV elimination agenda.[9]

Despite WHO recommending universal screening of all prisoners for hepatitis C,[3] rates remain low in many regions worldwide and treatment programs have been limited by multiple barriers.[11–14] Historical barriers have included the nature of interferon-based therapy (parenteral, long duration, significant toxicity and poor efficacy) as well as systemic barriers (limited local access to clinicians, need for hospital-based specialist review, frequent transfer between prisons interrupting care, and budgetary policy requiring that funding for testing and treatment come from local prison budgets rather than national health schemes). The recent introduction of direct-acting antivirals (DAAs) for the treatment of hepatitis C has provided highly effective therapy that is simple and safe, with short treatment durations – ideal for the prison environment. However, DAAs are expensive, which has limited the implementation of prison treatment programs worldwide;[15] less than 20% of surveyed European countries provided access to hepatitis C treatment in all prisons.[14] Where treatment is available to people in custody, it has often been restricted to prisoners with advanced liver disease.[16,17] Such a policy will withhold effective treatment from most people living with hepatitis C in prison, including those at risk of transmission.

In March 2016, the Australian Government approved universal access to DAAs for all Australians living with chronic hepatitis C, including prisoners. A decentralized nurse-led model of care was therefore developed to make viral hepatitis assessment and treatment available to all prisoners across all 14 prisons in the state of Victoria, Australia. We present the first evaluation of the feasibility and efficacy of this novel model of care for hepatitis C.

Patients and methods

Model of care

Australia has a policy of state-sponsored universal health care for all members of the general community, managed by the federal government. However, prisoners are not eligible for this scheme, and medical care during the period of incarceration becomes the budgetary responsibility of the local correctional service under the state government. Such a funding silo challenges the feasibility of DAA therapy given the high list price of these medications. The Australian Government, recognizing the importance of providing DAAs to prisoners if hepatitis C elimination is to be achieved, classified DAA treatment for hepatitis C under both the general drug schedule for the community, as well as a highly specialized schedule, which allows drugs to be provided to prisoners with the requirement that they are prescribed by a specialist and dispensed to prisons from a hospital pharmacy.

In this context, the Victorian Statewide Hepatitis Program was developed by St Vincent's Hospital, Melbourne under contract to the Department of Justice and Regulation, State Government of Victoria, Australia. At the time of evaluation, there were 14 prisons for adults (12 male, 2 female) in the state of Victoria, with capacity for 7,441 prisoners (Fig. 1). In the 12 month period from November 2015, more than 10,500 prisoners were received into the Victorian prison system.[18] Each of the 14 Victorian prison sites was serviced by the program, as described below. The program staff included 2 full-time hepatitis program

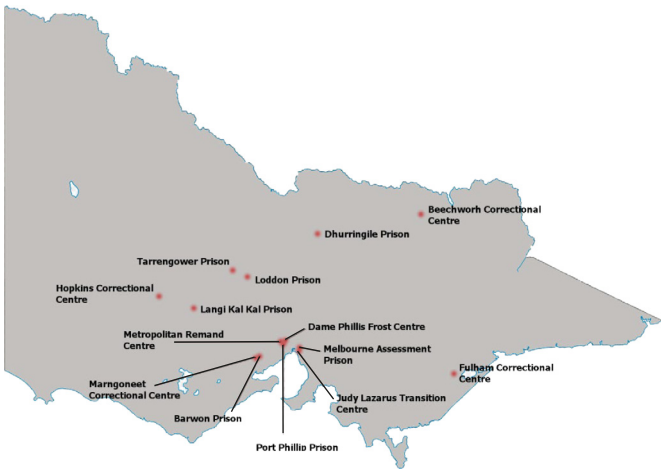

Fig. 1. Distribution of Victoria Prisons, Australia. (This figure appears in colour on the web.)

nurses, 3 part-time hepatologists (0.25 equivalent full-time (EFT) staffing in total), and a central pharmacist and pharmacy technician (time commitment increased from 0.2 to 0.6 EFT during the period of evaluation). A centralized electronic medical record was accessible at each prison as well as from St Vincent's Hospital. The medical record could be accessed by nursing, medical, and pharmacy staff to review and coordinate relevant investigations and track prisoner movements across the system to minimize interruptions of care from referral to the sustained virological response at post-treatment week 12 (SVR12) timepoint.

Victorian prison healthcare policy is that all prisoners are offered opt-in screening for viral hepatitis at first prison reception and at each transfer between prison sites. This is the responsibility of the primary healthcare service at each prison. If a prisoner was seropositive for hepatitis C, or self-reported a previous diagnosis of hepatitis C, they were referred to the Statewide Hepatitis Program for protocol-driven face-to-face assessment by a program nurse at their residing prison. A program nurse visited each prison on a weekly, fortnightly or monthly basis. Assessment involved a detailed clinical questionnaire including evaluation of risk behavior, liver stiffness measurement using transient elastography (portable FibroScan™), and blood-based investigations, including general biochemistry, hepatitis C viral load and genotype, HBV and HIV serology. The presence of comorbid medical conditions was assessed, including psychiatric illness (self-reported). The evaluation of risk behavior included assessment of active injecting drug use, defined as injecting in the month prior to incarceration. Injecting drug use in prison was defined as the use of drugs requiring needles and/or other injecting apparatus in either the current or a previous incarceration. Significant alcohol intake included pre-imprisonment or historically significant daily drinking (more than 2 standard drinks, most days, for both men and women)[19] or binge drinking (heavy intermittent alcohol intake).

Prisoners identified as having chronic hepatitis C infection were then triaged as either 'low risk' or 'higher risk'. 'Low risk' prisoners were either non-cirrhotic or had compensated cirrhosis without significant comorbidities, for whom the hepatologist prescribed DAA therapy after a paper-based consultation with a program nurse, without the physician having direct interaction with the prisoner. 'Higher risk' prisoners had evidence of cirrhosis (clinical/FibroScan), including all prisoners who had

decompensated cirrhosis and/or significant comorbid conditions potentially complicating hepatitis C treatment such as renal failure or HBV coinfection. 'Higher risk' prisoners were referred for either a telemedicine consult (conducted from their local prison) or face-to-face assessment by a hepatologist. Face-to-face consultation for prisoners located at one of the 13 peripheral prisons required prisoner transfer to the central prison. At clinical review, it was decided whether 'higher risk' prisoners were to commence DAA therapy immediately or required further assessment prior to treatment initiation.

Prisoners with hepatitis C and cirrhosis were enrolled in surveillance programs for hepatocellular carcinoma (HCC) and esophageal varices as recommended by consensus guidelines.[20,21] A viral hepatitis education program for prisoners and prison staff, including primary care staff, drug and alcohol service providers and correctional officers, was provided at all 14 correctional facilities to support the clinical service.

Harm reduction

An OST program is available in Victorian prisons, which 11% of prisoners utilized in 2016.[22] Bleach is available which can be used to clean injecting equipment. There is no provision of clean needles or syringes.

Treatment eligibility

To be eligible for treatment prisoners had to be 18 years of age or older, have evidence of chronic hepatitis C with detectable serum HCV RNA, and have an adequate sentence duration to facilitate complete hepatitis C treatment while incarcerated (between 8 to 24 weeks depending on the selected treatment regimen). It was not a requirement however, that prisoners remained in prison to complete blood tests at week 12 post-treatment. Prisoners commenced on DAA therapy who were released early (early parole) were provided with their remaining medication to complete treatment in the community. Prisoners for whom a short sentence duration made them ineligible for treatment whilst incarcerated were referred to a healthcare service for treatment upon release to the community.

Standard correctional pharmacy procedures required that medications be repackaged into blister packs at the central hospital pharmacy before being couriered to the prisons. Initial packs were prepared to include 28 days of therapy, and subsequent packs were distributed to each prison monthly thereafter, until therapy was completed. Two of the 14 prisons provided medications to prisoners in weekly packets while the remaining 12 prisons dispensed medications to the prisoners daily. Medications moved with patients at time of inter-prison transfer to minimize treatment interruption and prisoner location was confirmed in real time using the electronic medical record. When DAAs first became available on 1 March 2016, the program had capacity to initiate 6 prisoners per week. This subsequently increased to 16 prisoners per week in June 2016 with increased pharmacy staff resources.

Analysis

This analysis evaluated hepatitis C treatment outcomes among all prisoners who commenced therapy over the 13-month period between 1 November 2015, when the program started, and 1 December 2016.

All prisoners had serum HCV RNA tested at baseline, at the end-of-treatment (EOT), and at week 12 post-treatment. The pre-specified period of follow-up was to week 12 post-treatment. The primary endpoint was SVR12, which was defined as undetectable serum HCV RNA 12 weeks after the EOT. Secondary endpoints included EOT response (defined as undetectable serum HCV RNA at EOT), confirmed HCV reinfection (defined as detectable serum HCV RNA with HCV genotype switch between EOT and SVR12) and treatment-associated adverse events. Relapse was defined as prisoners who achieved an EOT response, but in whom serum HCV RNA was detectable at week 12 post-treatment, without HCV genotype switch.

We considered 2 analyses for virological outcome – the primary outcome was rate of SVR12 per protocol, including those prisoners with a serum HCV RNA result at 12 weeks post-treatment (complete follow-up). This analysis was performed to account for the high number of prisoners 'lost to freedom'; that is prisoners released to freedom after the EOT but prior to SVR12, as well as a small number of prisoners who were granted parole during their treatment course. We also considered overall SVR12 rate by intention to treat.

Data were described using median and interquartile ranges (IQR). Categorical data were described as number and percentage. Comparisons between groups were made using appropriate statistical tests after considering distribution of data.

Ethical considerations

This study was approved by the St Vincent's Hospital Melbourne Human Research Ethics Committee.

Results

Prisoner characteristics

During the 13-month period of evaluation, 949 prisoners were assessed by the Statewide Hepatitis Program, of whom 562 (59%) prisoners were eligible for treatment, and 416 (44%) were commenced on therapy during the period of evaluation. Reasons for treatment ineligibility are detailed (Table S2). Baseline characteristics are described in detail in Table 1. In brief, the cohort was predominately male (90%), the median age was 41 [34–46] years, 80% were Caucasian, 12% were Indigenous, and 4% were Asian. Cirrhosis was present in 21%. HIV and HBV coinfection were uncommon, but past HBV infection (anti-HBc positivity) was present in 24%. The majority of prisoners responded to detailed questions about their past and/or current injecting practices. Injecting drug use was reported by 68% (n = 262/386) in the month prior to incarceration and the most common drug of choice was heroin (60%, n = 120/200). Mental health comorbidities were reported by 70%. Only 14% of prisoners had previously seen a specialist to discuss their hepatitis C; 94% were treatment naïve (Table 1).

HCV DAA therapy and virological response

The DAA regimens prescribed are listed (Table 2). The rate of SVR12 was 96% (n = 301/313) per protocol (Table 3). SVR12 rates exceeded 95% for all genotypes, including genotype 1a (96%, n = 137/143), genotype 1b (100%, n = 11/11), genotype 2 (100%, n = 5/5), genotype 3a (96%, n = 147/153) and genotype 6 (100%, n = 1/1). There was no difference in SVR12 between cirrhotic and non-cirrhotic prisoners (97% *vs.* 94%, $p = 0.51$). SVR12 rates by ITT analysis were lower (SVR12 72%, n = 301/416), Table 3); the most common reason for not achieving SVR12 was loss to follow-up due to being released to freedom (90%, n = 103/115).

Table 1. Prisoner characteristics.

Characteristics	N = 416
Age, yr, median [IQR]	41 [34–46]
Male sex, n (%)	376 (90)
Ethnicity, n (%)	
Caucasian	332 (80)
Indigenous	51 (12)
Asian	15 (4)
Other	18 (4)
Body mass index, kg/m^2, mean [IQR]	31 [27–34]
HCV genotype, n (%)	
Genotype 1a	184 (44)
Genotype 1b	14 (3)
Genotype 2	8 (2)
Genotype 3	208 (50)
Genotype 6	2 (1)
HCV viral load, IU/ml, median [IQR]	685,000 [192,000–2,630,000]
ALT, U/ml, median [IQR]	88 [55–145]
Platelet count, median [IQR]	218 [176–256]
HBV serology, n (%)	
HBsAg[+]	6 (2)
Anti-HBs[+]	310 (75)
Anti-HBc[+]	98 (24)
HIV serology, n (%)	8 (2)
Liver stiffness measurement[~], n (%)	
<9.5 kPa	278 (71)
9.5–12.5 kPa	40 (10)
>12.5 kPa	71 (19)
Cirrhosis, n (%)	86 (21)
Compensated	77 (19)
Decompensated	9 (2)
Opiate substitution therapy	228 (54)
Comorbid psychiatric illness[*]	291 (70)
Psychotropic medication	208 (50)
Significant alcohol history[#], n (%)	243 (58)
Injecting drug use, n (%)	
PWID, current/previous	389 (94)
Injecting prior to incarceration[+]	262/386 (68)
Injecting in prison, current/previous[^]	130/228 (57)
Previous specialist care for HCV, n (%)	59 (14)
Treatment experienced, n (%)	25 (6)

ALT, alanine aminotransferase; HBsAg, HBV surface antigen; PWID, people who inject drugs.
[~] Valid liver stiffness measurements using transient elastography were obtained in 94% (n = 389). The remaining 6% (n = 27) of prisoners were either cirrhotic (n = 10) (evidenced by clinical decompensation and/or radiological evidence of portal hypertension) or had unsuccessful elastography due to body habitus (n = 17).
[*] Self-reported or recorded from medical record at initial assessment.
[#] Recent (pre-imprisonment) or historically significant daily (more than 2 standard drinks, most days, for men and women) or binge drinking (significant intermittent alcohol intake).
[+] Injecting drug use within 1 month of incarceration ^injecting drug use in the current or previous incarceration.

Table 2. Treatment regimens and durations.

Treatment regimen	(N = 416)
Sofosbuvir 400 mg/ledipasvir 90 mg, n (%)	
8 weeks	100 (24)
12 weeks	77 (18)
24 weeks	4 (1)
Sofosbuvir 400 mg/daclatasvir 90 mg ± RBV, n (%)	
12 weeks	147 (35)
24 weeks	65 (16)
Sofosbuvir 400 mg/RBV 1,000–1,200 mg, n (%)	5 (1)
Paritaprevir 150 mg/ritonavir 100 mg/ombitasvir 25 mg/dasabuvir 250 mg, n (%)	16 (4)
Sofosbuvir 400 mg/PegIFN ± RBV, n (%)	2 (1)

RBV, ribavirin.

Treatment failure was due to virological relapse in 11 prisoners (Table S1) and confirmed hepatitis C reinfection in one prisoner. Three of the 11 prisoners who relapsed had treatment interruptions of greater than 1-week duration, including 2 prisoners prescribed sofosbuvir plus daclatasvir for 24 weeks who received only 6 and 7 weeks respectively due to being released on parole; both were HCV PCR positive on re-incarceration within the follow-up period. The one prisoner with confirmed reinfection, who had risk factors for reinfection, was diagnosed by recurrent HCV viremia between EOT and SVR12, with a switch from genotype 1a to genotype 3 between EOT and SVR12 time points.

Treatment-related adverse events were infrequent (7.9%, 37 events in 33 participants, Table 4). One prisoner (0.2%) discontinued treatment at week 8 of 12 due to insomnia (SVR12 achieved). There were no treatment-related deaths. Nine prisoners had decompensated liver disease at treatment initiation (Child Pugh B, n = 4 and Child Pugh C, n = 5). The SVR12 rate was 71% (n = 5/7) amongst this group. Two prisoners experienced virological relapse and 2 prisoners were released to freedom prior to SVR12. One Child Pugh C prisoner achieved SVR12 and was referred to a liver transplantation service and waitlisted for transplantation while incarcerated. This patient underwent successful orthotropic liver transplantation following release from prison. No *de novo* HCCs were diagnosed during the period of evaluation.

There were 6 prisoners who were HCV-HBV co-infected. All were non-cirrhotic. One prisoner who was HBeAg-positive with a high serum HBV DNA level was initially commenced on antiviral therapy for hepatitis B (tenofovir 300 mg daily), and then subsequently hepatitis C, 4 weeks later. Five prisoners were HBeAg-negative and had serum HBV DNA levels <2,000 IU/ml at baseline. These prisoners were monitored with liver function tests and serial measurements of HBV DNA levels. Two prisoners experienced on-treatment increases in serum HBV DNA levels without biochemical flare and antiviral therapy for HBV was not commenced. Past HBV infection was present in 24% of the cohort. There were no cases of on-treatment or post-treatment hepatitis flare to suggest HBV reactivation.

Nurse-led care was delivered effectively across the statewide network

Most prisoners (82%, n = 340) were suitable for treatment based on nurse-led evaluation only and did not require a formal hepatologist assessment ('low risk'). The remaining 76 prisoners (18%) were categorized as 'higher risk' and required either face-to-face (13%, n = 55), telemedicine hepatologist consultation (3%, n = 13), or both (2%, n = 8) (Fig. 2). Rates of SVR12 were comparable in 'low risk' and 'higher risk' prisoners, both per protocol (96% *vs.* 93%, $p = 0.27$), and by ITT (74% *vs.* 67%, $p = 0.26$) analysis (Fig. 2).

The decentralized, nurse-led model of care removed the requirement for most prisoners to attend a central prison or hospital for hepatitis C assessment and treatment. However, 26% of prisoners still had at least one prison transfer while receiving DAA therapy (n = 110, range 0–6). The frequency of prison transfers while receiving hepatitis C treatment was not associated with diminished SVR12 outcomes (SVR12 96–100%, Fisher's exact test $p = 0.89$) (Fig. 3).

The cascade of care from referral is presented in detail for each prison in Table S2. Assessing the cascade of care following referral to the program, 562 (59%) were eligible for treatment

Table 3. Virological response.

Virological response EOT, n (%)	Overall (N = 416)	Per protocol (n = 364)
HCV PCR negative	364 (88)	364 (100)
Lost to freedom*	52 (12)	–
Virological breakthrough	0 (0)	0 (0)
Treatment-related death	0 (0)	–
SVR12, n (%)	**(N = 416)**	**(n = 313)**
HCV PCR negative	301 (72)	301 (96)
Genotype 1a	137/184 (74)	137/143 (96)
Genotype 1b	11/14 (79)	11/11 (100)
Genotype 2	5/8 (63)	5/5 (100)
Genotype 3	147/208 (71)	147/153 (96)
Genotype 4/5	–	–
Genotype 6	1/2 (50)	1/1 (100)
Cirrhosis		
Yes	59/86 (69)	59/63 (94)
No	242/330 (73)	242/250 (97)
Lost to freedom	103 (25)	–
Virological relapse	11 (2.8)	11 (3.5)
Reinfection	1 (0.2)	1 (0.5)
Treatment-related death	0 (0)	–

EOT, end-of-treatment; SVR12, sustained virological response at post-treatment week 12.
* Lost to freedom; prisoners either released on-treatment or after end-of-treatment but prior to week 12 post-treatment.

Table 4. Adverse events.

Adverse events, n (%)	N = 416
Treatment-related	
Headache	12 (2.9)
Gastrointestinal symptoms	9 (2.2)
Lethargy	8 (1.9)
Rash	4 (1.0)
Myalgia	3 (0.7)
Serious adverse events	0 (0)
Treatment-related deaths	0 (0)
Leading to discontinuation of treatment	
Treatment-related	
Insomnia	1 (0.2)

and 416 (44%) were started on therapy. The majority of those ineligible had an insufficient remaining period of incarceration to complete treatment (61%, n = 235/387). During the period of evaluation, the average time from assessment to treatment was 4.6 months, reflecting in large part the fact that assessments commenced in November 2015, 4 months prior to reimbursement of DAAs in March 2016. The period between assessment and initiating treatment has since fallen to an average of 3 weeks.

Discussion

This is the first large scale hepatitis C prison management program to be implemented across an entire jurisdiction. The

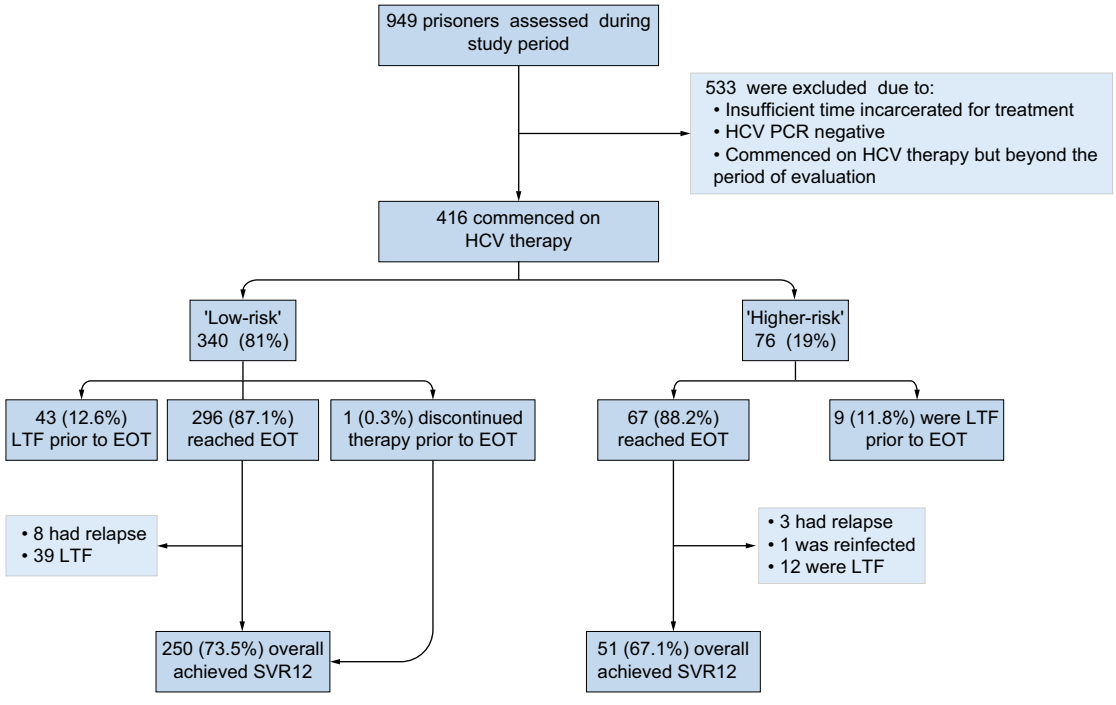

Fig. 2. Decentralized, nurse-led model of care. EOT, end-of-treatment; LFT, loss to freedom; SVR, sustained virological response at post-treatment week 12.

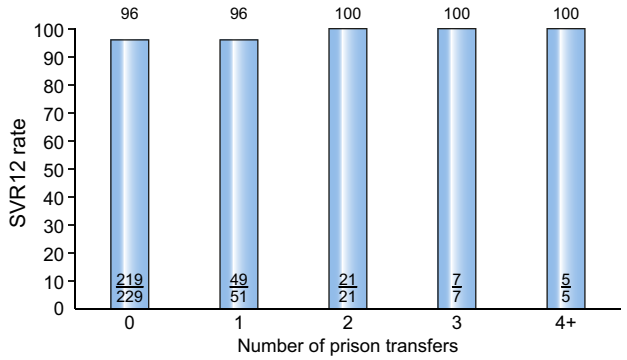

Fig. 3. Treatment outcome (SVR12 rate) by number of inter-prison transfers while receiving HCV DAA therapy. DAA, direct-acting antiviral; SVR12, sustained virological response at post-treatment week 12.

decentralized, nurse-led model of care implemented across 14 prisons has overcome many of the traditional systemic barriers to providing effective and efficient hepatitis C treatment to large numbers of prisoners, including the need for specialist consultation and hospital transfer, and treatment interruption from prisoner transfer between correctional facilities with partitioned clinical services. Importantly hepatitis C cure rates achieved by this new model were high.

Although many countries continue to mandate specialist physician management for hepatitis C therapy initiation,[23] our data demonstrate that nurse-led treatment is safe and effective in the correctional setting, with only 18% of assessed prisoners requiring specialist consultation. Whilst inter-prison transfer was frequent (driven by movement in the justice system rather than related to prisoners need to access hepatitis C services), it did not lead to treatment interruption or diminished efficacy. The model of care allows high treatment numbers with existing resources now permitting 16 new treatment starts per week. The key features of the program that likely support its success include the nurse-led model delivering DAA therapy locally, the statewide coverage across all correctional facilities, the use of information technology including telemedicine and a central electronic medical record, a centralized pharmacy distribution with real-time prisoner tracking, and federal government policy supporting prisoner access to DAAs.

An important benefit of the program it is that it engages a marginalized population in hepatitis C treatment and primary healthcare more broadly. Many prisoners had a history of current or recent injecting prior to incarceration, and most had psychiatric comorbidities. As expected, a high proportion (86%) had never previously consulted a clinician about hepatitis C treatment. PWID are the group at greatest risk of hepatitis C infection in many developed countries and are traditionally difficult to engage in health care. Prison-based hepatitis C treatment programs can therefore play a vital role in increasing care and treatment in this group.

There is now a global focus on how to best utilize public health platforms to eliminate hepatitis C as a public health threat. Mathematical modelling has estimated that for Victoria to achieve the WHO elimination targets by 2030,[1] treatment rates among current PWID will need to be scaled up to approximately 59/1,000, or around 1,300 active PWID per year.[9,24] Sustaining this level of treatment uptake in the community will require increased testing and retention of PWID in care,[9] including the treatment of prisoners, many of whom have a history of current or recent injecting.

The success of our program has been recognized by a recent increase in resourcing to increment treatment start numbers to 20 per week (1,040/year). This treatment rate means the program would potentially contribute >50% of the overall yearly elimination target for treatment scale-up among PWID in Victoria, based on our data that 68% of prisoners with hepatitis C were considered current PWID. This highlights the vital contribution that prison treatment programs can make as part of a broader elimination agenda.

Limitations of this study include the large proportion of prisoners 'lost to freedom', most of whom were released from prison between EOT and SVR12. The study, however, evaluates a proposed model of care to increase treatment scale-up amongst a priority population, rather than to assess DAA effectiveness, which is already established.[25,26] Despite a high proportion of prisoners who were 'lost to freedom', approximately 90% did complete DAA therapy while incarcerated and most are anticipated to have achieved cure. Previous Australian studies have demonstrated a hepatitis C incidence of >10% annually amongst incarcerated PWID.[7] In our study there was only one confirmed case of hepatitis C reinfection identified, although the duration of follow-up was only 12 weeks post-treatment; with a longer duration of follow-up a higher number of reinfections is anticipated. It is possible that a number of the cases of relapse were in fact reinfections with the same hepatitis C genotype; regardless, the number of relapses was also low. The program supports retreatment of those reinfected to engage prisoners at highest risk of transmission, key for reducing prison hepatitis C prevalence and achieving community elimination targets. Finally, detailed data concerning the rate of opt-in screening at reception, overseen by the prison medical staff, was not available, this step in the cascade of care preceding referral to the program. The estimate of the percentage of viremic prisoners treated was informed by Australian data estimating hepatitis C seroprevalence within prisons, the proportion therefore anticipated to be hepatitis C RNA positive and the short average duration of imprisonment (Table S2). Although the average time between assessment and treatment was 4.6 months at the time of evaluation, there was a 4-month disparity between commencement of clinical assessments in November 2015 and hepatitis C treatment availability in March 2016. The period between assessment and initiating treatment has since fallen to an average of 3 weeks, with 75% of prisoners assessed now starting DAA therapy.

Future work will explore refinements to prison-based models of care. This will include evaluating the role for peer workers to increase prisoner engagement and the role for point-of-care testing to increase screening uptake and reduce time from assessment to treatment start. This will also examine the success of linkage to community care for prisoners released to freedom, including treatment completion rates for those who are released on-treatment, as well as treatment uptake in those referred to community treatment centers for DAA therapy post-release. In addition, long-term follow-up studies monitoring HCV reinfection are underway.

In conclusion, DAA therapy for hepatitis C using a decentralized, nurse-led model of care was highly effective in increasing hepatitis C treatment access to a large population of prisoners, with high rates of hepatitis C cure. Given the high prevalence of hepatitis C among prisoners, with many reporting current

or recent injecting drug use, large scale prison treatment programs should be promoted to benefit both the individual prisoner and also hepatitis C elimination efforts in the broader community.

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Conflict of interest

TP: honoraria from Merck. LM: honoraria from Gilead, Merck and AbbVie. JH: investigator initial research funding to institution from Gilead. JD: investigator initiated research funding to institution from Gilead, Merck, AbbVie and BMS. Honoraria to institution from Gilead, Merck, and BMS. AP: no disclosures. ARL: investigator initiated research funding to institution from Gilead and Merck. MS: no disclosures. MH: investigator initiated research funding to institution from Gilead, Merck, AbbVie and BMS. DI: honoraria from AbbVie, BMS, Gilead and Merck. AJT: investigator initiated research funding to institution from Gilead, Merck, AbbVie and BMS; advisory board – Gilead, AbbVie, BMS, Merck, Eisai. All other authors declare no conflicts of interest.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

TP was responsible for study design, analysis, acquisition and interpretation of data, and drafting and revision of the manuscript. LM, AC and LG were responsible for acquisition of the data and revision of the manuscript content. PD was responsible for substational contribution to the study conception and design and revision of the manuscript content. DW, RW and NS were responsible for analysis and interpretation of the data and revision of the manuscript content. JH was responsible for substantial contribution to the conception and design of the study and for revision of the manuscript content. JD and AP were responsible for substantial contribution of study design and data interpretation and revision of the manuscript content. AL was responsible for substantial contribution to the conception and design of the study and revision of the manuscript. MS and MH were responsible for analysis and interpretation of the data and revision of the manuscript. DI was responsible for study design, analysis, acquisition and interpretation of the data and revision of the manuscript. AT was responsible for a substantial contribution to the conception and design, acquisition, analysis, or interpretation of the data and drafting and revision of the manuscript content. All authors were responsible for giving final approval of the version to be published, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the article are appropriately investigated and resolved.

Supplementary data

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