

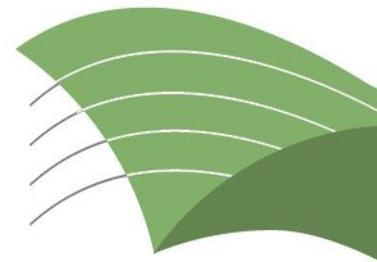


HIV and Hepatitis C coinfection

Dr Darren Russell
Director of Sexual Health
Cairns Base Hospital



Declaration of Conflicts of Interest



- Speaker's fees, Advisory Board membership, and/or travel assistance in the last 12 months from Gilead Sciences, ViiV Healthcare, and Merck



Hepatitis C prevalence in Australia

2017

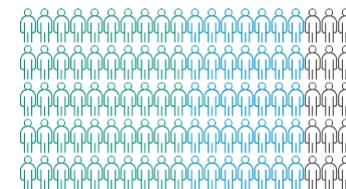


182,144

Australians living with chronic HCV infection at the end of 2017



About **80%** people infected with HCV through injecting drug use (IDU)



1 in 5 people with HCV don't know it

HCV Genotype 1
HCV Genotype 3
Other



How do we find the estimated 20% still undiagnosed?

DAA costs: The Australian response

- In late 2015, the Australian Government announced a \$1+ Billion investment in hepatitis C treatment over 5 years in exchange for an unlimited volume of DAAs for HCV from suppliers
- This approach results in lower per-patient prices

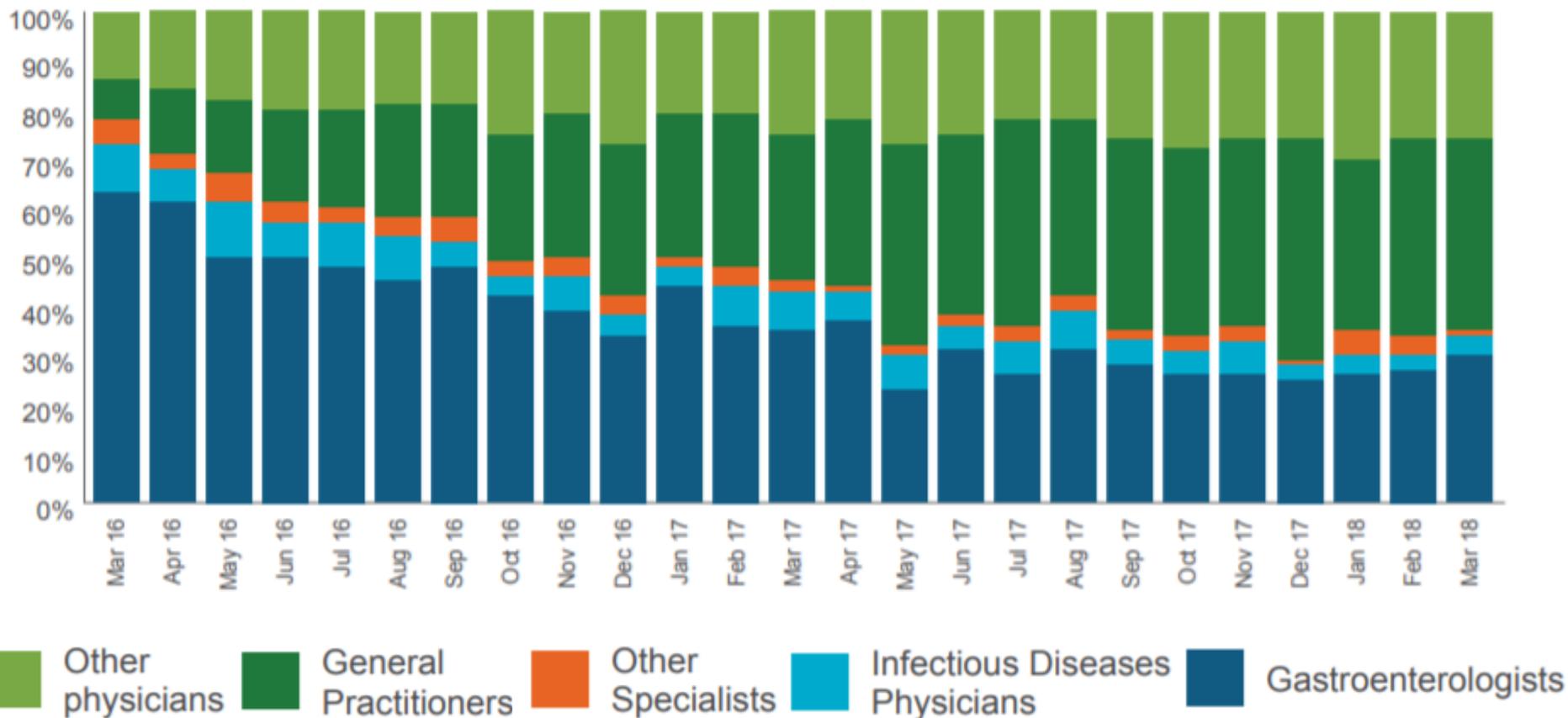
Key features -

- All people with chronic hepatitis C eligible for DAAs
- No liver disease restrictions; retreatment possible
- Current modelling suggests treatment cost at approx. AU\$9,595 per patient treatment course (far less than the ‘list price’ of up to \$94,958)

Suerie Moon, Elise Erickson. Universal Medicine Access through Lump-Sum Remuneration — Australia’s Approach to Hepatitis C, NEJM February 14, 2019.

Monitoring hepatitis C treatment uptake in Australia. Issue #9 July 2018. The Kirby Institute.

GPs are increasingly treating hepatitis C



56,968 people in total have been cured during 2015-2017

The Kirby Institute. Monitoring hepatitis C treatment uptake in Australia (Issue 9). The Kirby Institute, UNSW Sydney, Sydney, Australia, July 2018

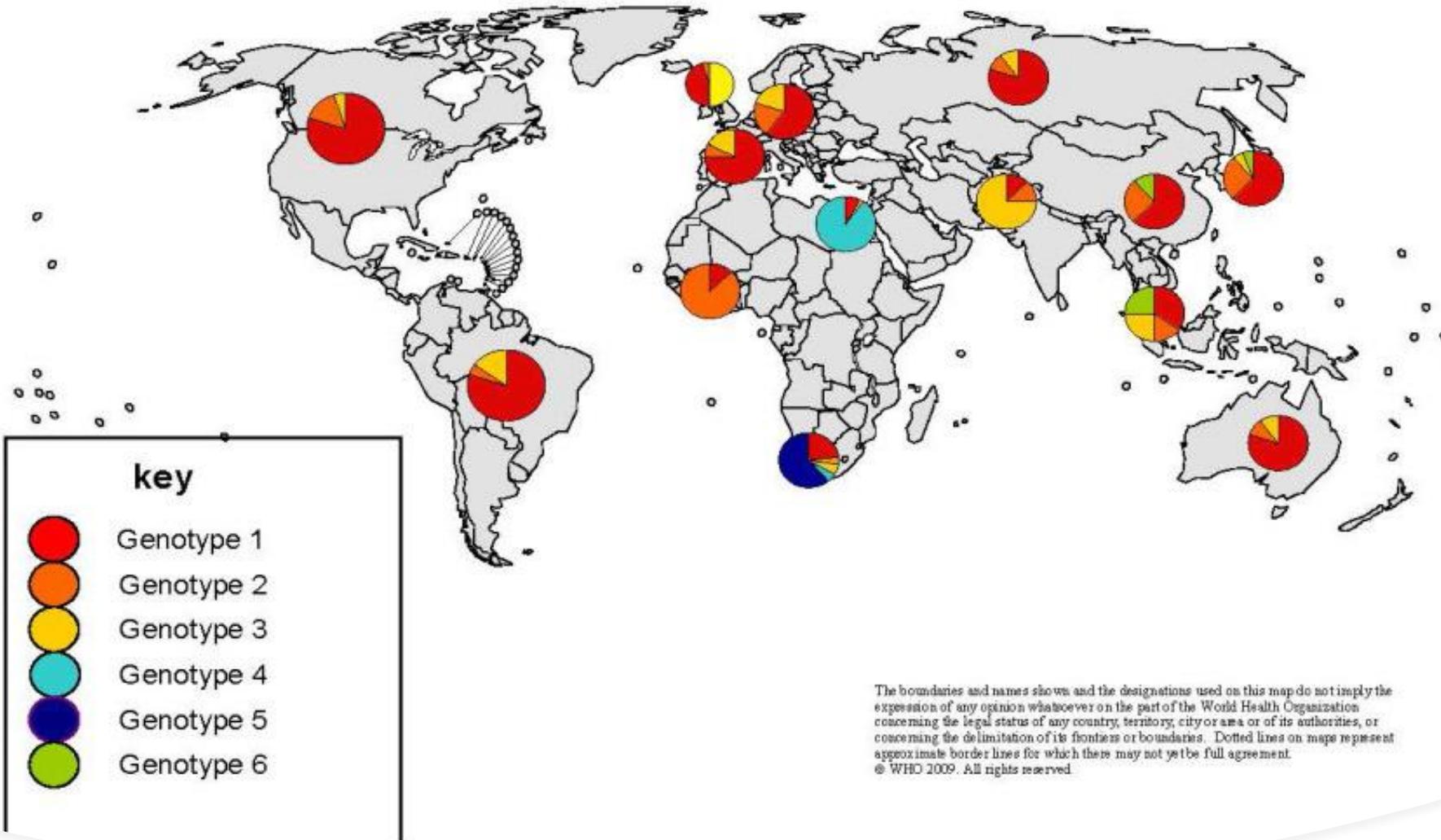
Hepatitis C virus – what is it?



- The hepatitis C virus is a small *RNA* virus
 - There are 6 main different genotypes (strains)
 - Genotypes **1** and **3** are common in Australia
 - Spread very easily via blood
 - Occasionally spread from mother to baby during pregnancy and childbirth



Global distribution of HCV genotypes



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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Hepatitis C transmission



IDU risk

70% if >3 years of use
>80% of all HCV
infections in Australia



Blood Transfusion

now very rare in Australia



Unsterile tattoos/piercing –
particularly in prison



Mother to baby ($\leq 5\%$)



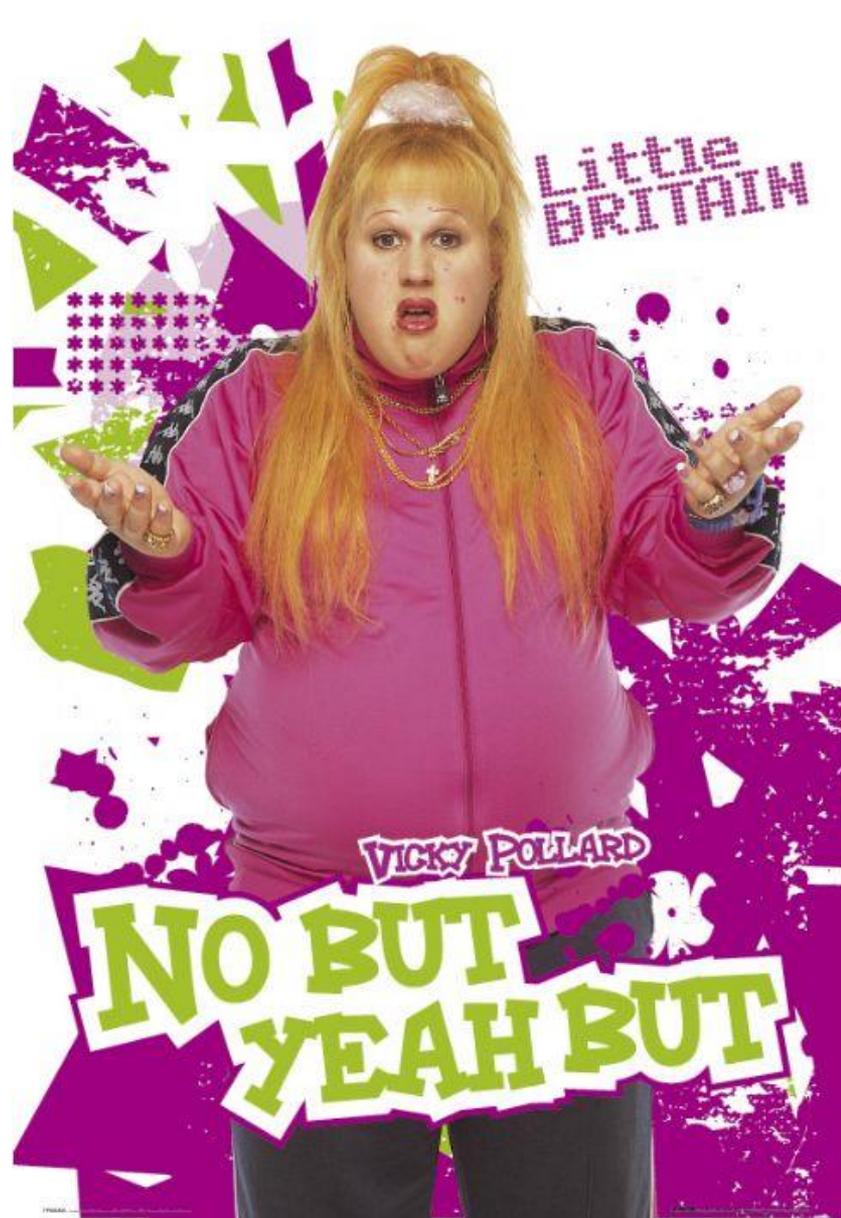
Sexual (inefficient)



Many cases are “*unknown*”



Is Hep C
sexually
transmissible
??



Sexual transmission

- The predominant risk factors for transmission of hepatitis C virus (HCV) infection are well known
 - injecting drug use (IDU)
 - contaminated blood products
- In a number of HCV-infected patients neither of these risk factors can be identified
- HCV has been occasionally isolated from saliva, semen and vaginal secretions, raising the possibility of sexual and other routes of HCV transmission



Sexual transmission

- Hepatitis C would seem to be rarely, if ever transmitted by penile-vaginal intercourse
- The risk of sexual transmission of hepatitis C virus (HCV) infection was evaluated among 895 monogamous heterosexual partners of HCV chronically infected individuals in a long-term prospective study, which provided a follow-up period of 8,060 person-years
- 776 (86.7%) spouses were followed for 10 years, corresponding to 7760 person-years of observation
- 119 (13.3%) spouses (69 whose infected partners cleared the virus following treatment and 50 who ended their relationship or were lost at follow-up) contributed an additional 300 person-years
- All couples denied practicing anal intercourse or sex during menstruation, as well as condom use
- The average weekly rate of sexual intercourse was 1.8



Sexual transmission

- 3 HCV infections were observed during follow-up corresponding to an incidence rate of 0.37 per 1,000 person-years
- However, the infecting HCV genotype in one spouse (2a) was different from that of the partner (1b), clearly excluding sexual transmission
- The remaining 2 couples had the same genotypes, but analysis showed that the corresponding partners carried different viral isolates, again excluding the possibility of intra-spousal transmission of HCV
- The authors concluded, “Our data indicate that the risk of sexual transmission of HCV within heterosexual monogamous couples is extremely low or even null. No general recommendations for condom use seem required for individuals in monogamous partnerships with HCV-infected partners.”

- *Vandelli et al. American Journal of Gastroenterology 2004;99(6): 855-859*



HIV-Infected Men Who Have Sex With Men

- Several outbreaks of sexually transmitted HCV infection among HIV-infected men who have sex with men (MSM) have been reported since 2000
- A recent systematic review reported an HCV incidence of 6.35/1000 person-years among HIV-infected MSM ([Jin, 2017](#))
- Risk factors include: group sex practices that can cause trauma to rectal mucosal tissue (e.g., receptive anal intercourse without a condom and receptive fisting), and rectal bleeding are associated with HCV transmission among HIV-infected MSM



HIV-Infected Men Who Have Sex With Men

- The recent proliferation of chemsex - use of crystal methamphetamine, mephedrone, or GHB, sometimes with PDI5 inhibitors before or during sex - has also been associated with incident HCV infection
- These HCV infections have been occurring especially in men who already have ulcerative and rectal STIs including syphilis, LGV, and genital herpes



HIV-Infected Men Who Have Sex With Men

- While it is not completely clear why higher rates of incident HCV have been reported in HIV-infected compared to uninfected MSM, behavioural factors such as serosorting and increased rates of anal sex without condoms by HIV-infected men have been implicated ([Mao, 2011](#))
- In a recent study of 33 HIV/HCV-coinfected MSM, one-third shed HCV in their semen ([Turner, 2016](#))
- In addition to being found in semen, rectal shedding of HCV has also been reported in HIV/HCV-coinfected MSM ([Foster, 2017](#))



Hep C transmission

- Investigators in Amsterdam conducted a study on the acute hepatitis C outbreak in that city
 - They retrospectively screened 1836 MSM participating in the Amsterdam Cohort Studies (1984-2003) for HCV antibodies
 - HCV incidence was 0.18 per 100 person-years (PY) (or 8 cases per 4408 PY) in HIV positive MSM, compared with 0 per 100 PY (i.e., no cases in 7807 PY) in HIV negative MSM
 - After 2000, HCV incidence among HIV positive men increased 10-fold to 0.87 per 100 PY (or 5 cases per 572 PY)
 - Based on an additional 34 hospital cases, the authors found that MSM who acquired HCV after 2000 reported high rates of ulcerative sexually transmitted infections (59%) and practice of "rough sexual techniques" (56%), but denied IDU
- *TK van de Laar et al. Journal of Infectious Diseases 196(2): 230-238. July 15, 2007*





Volume 64, Issue 3
1 February 2017

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Shedding of Hepatitis C Virus Into the Rectum of HIV-infected Men Who Have Sex With Men ^{FREE}

Andrew L. Foster, Michael M. Gaisa, Rosanne M. Hijdra, Samuel S. Turner, Tristan J. Morey, Karen B. Jacobson, Daniel S. Fierer [Author Notes](#)

Clinical Infectious Diseases, Volume 64, Issue 3, 1 February 2017, Pages 284–288,
<https://doi.org/10.1093/cid/ciw740>

Published: 24 December 2016 [Article history ▾](#)

 PDF  Split View  Cite  Permissions  Share ▾

Abstract

Background.

For over a decade we have known of an epidemic of sexually transmitted hepatitis C virus (HCV) infection among human immunodeficiency virus (HIV)-infected men who have sex with men (MSM), but there still remains significant controversy over which bodily fluid(s) are responsible for HCV transmission in these men.



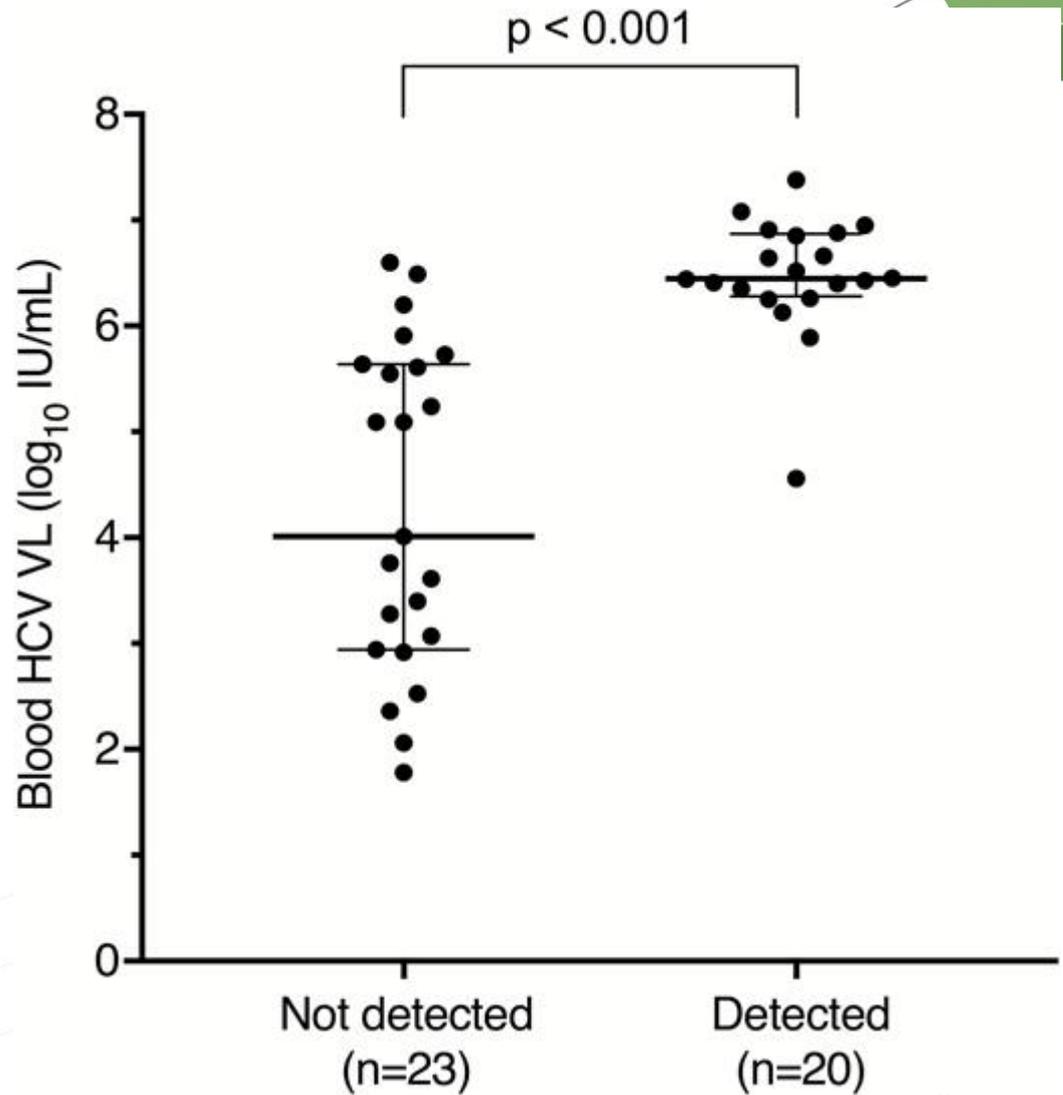
 **6** View Metrics

Email alerts

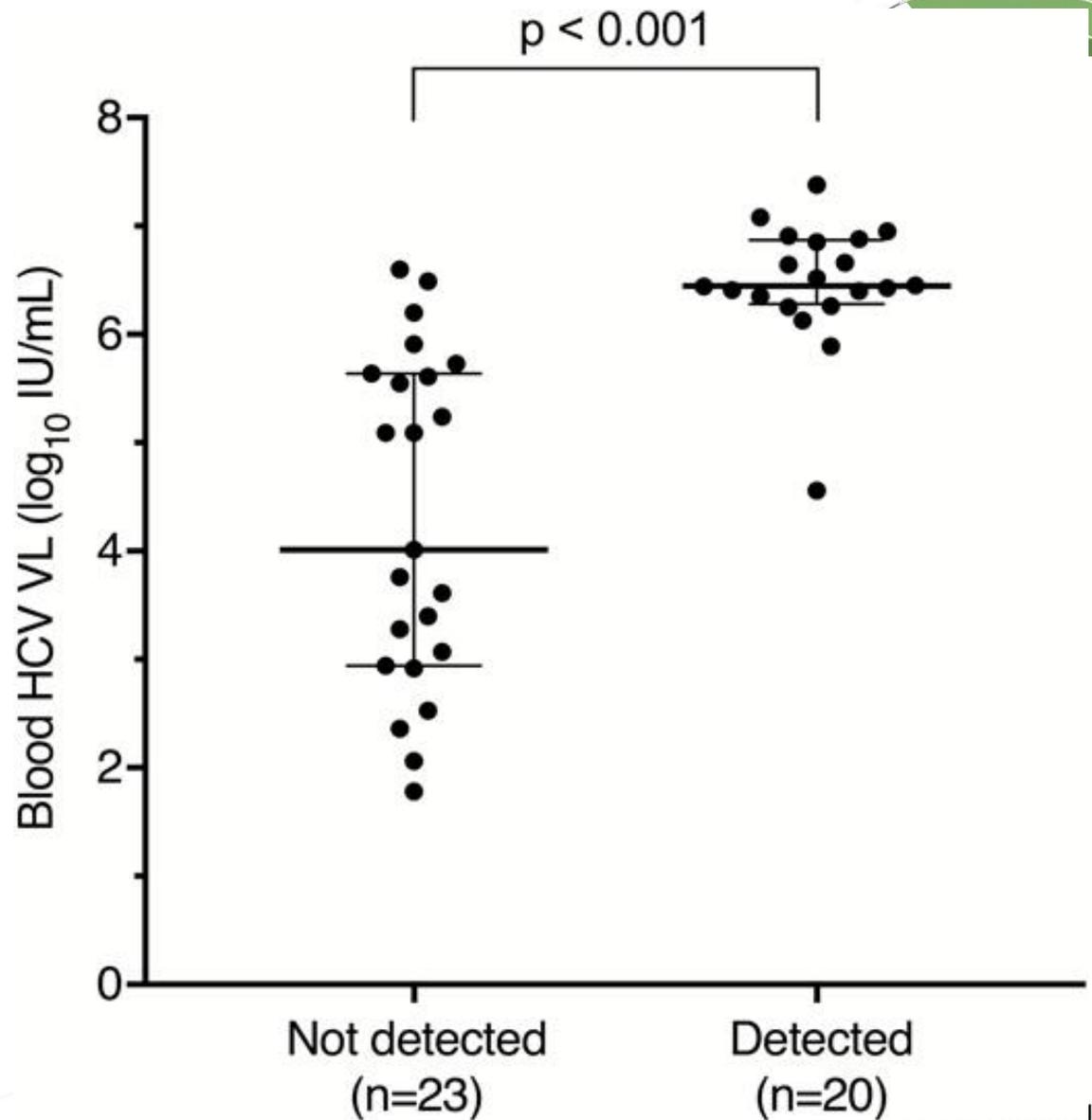
[Manage alert](#)



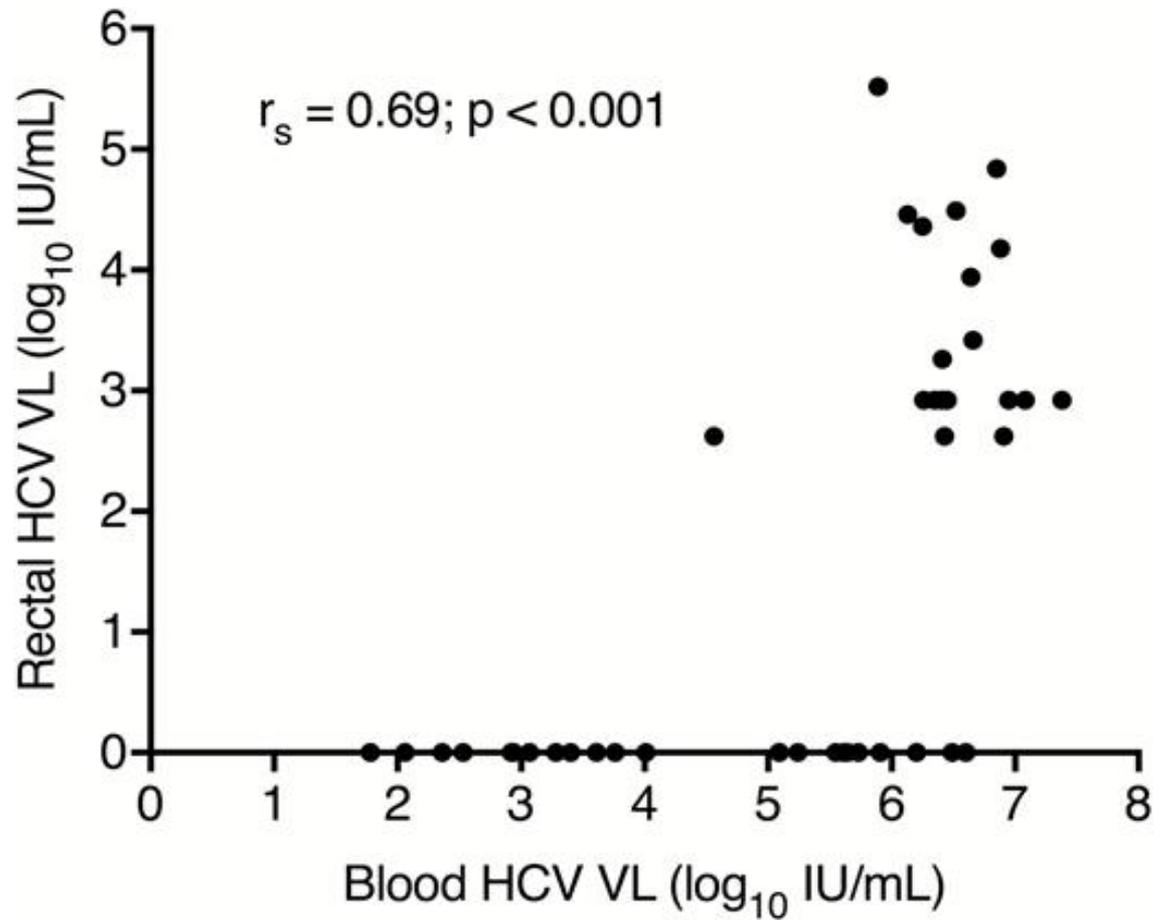
Detection of HCV in rectal fluid as a function of HCV VL in blood.

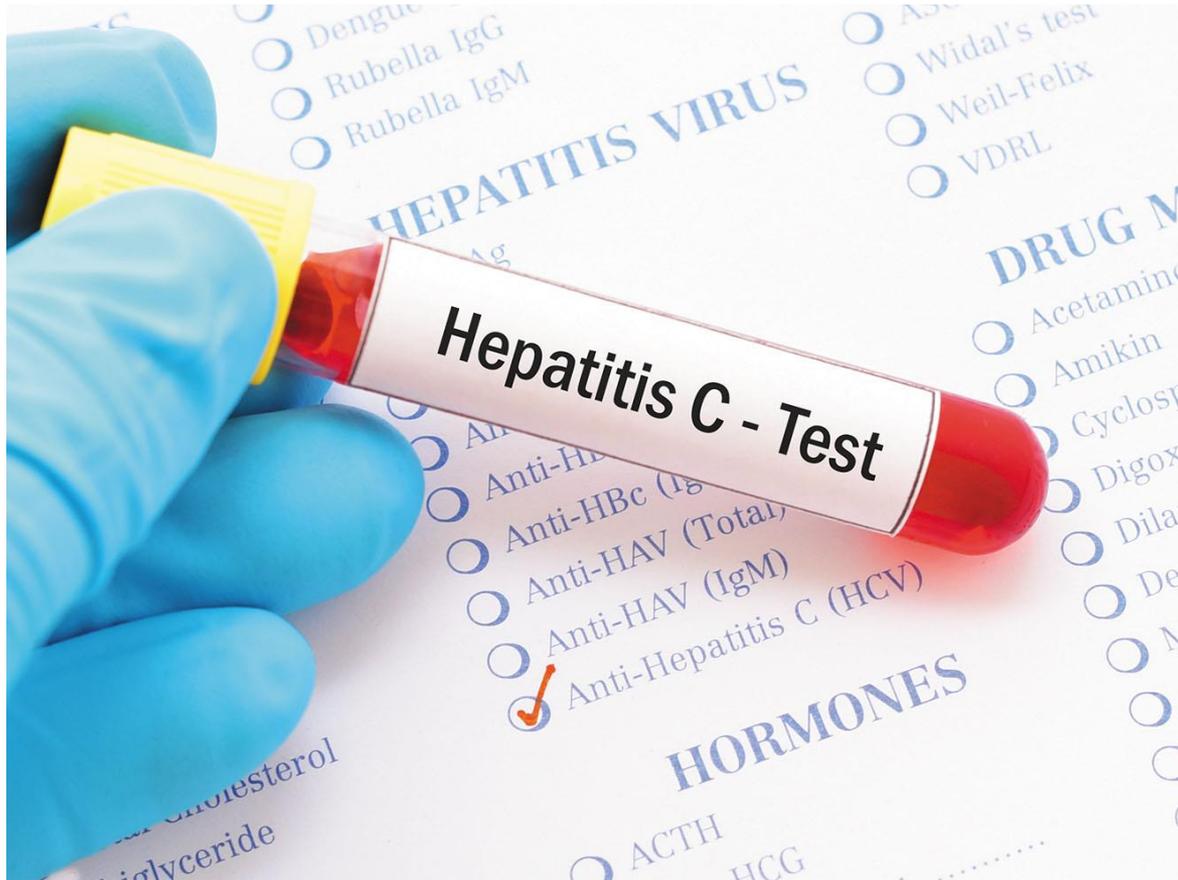


Detection of HCV in rectal fluid as a function of HCV VL in blood

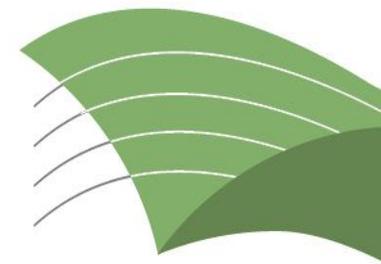


Correlation
between
HCV VL in
blood and
rectal fluid





Who should we test?



CDC Testing Recommendations

Recommendations for Testing and Prevention of HCV Infection in Men Who Have Sex With Men (MSM)	
RECOMMENDED	RATING
Annual HCV testing is recommended for sexually active HIV-infected adolescent and adult MSM. Depending on the presence of high-risk sexual or drug use practices, more frequent testing may be warranted.	IIa, C
HCV testing at HIV pre-exposure prophylaxis (PrEP) initiation and at least annually thereafter (while on PrEP) is recommended in HIV-uninfected MSM. Depending on sexual or drug use risk practices, more frequent testing may be warranted.	IIa, C
All MSM should be counseled about the risk of sexual HCV transmission with high-risk sexual and drug use practices, and educated about measures to prevent HCV infection or transmission.	IIa, C



Australian STIGMA Guidelines for asymptomatic MSM

Hepatitis C: Test
once a year in
people living with
HIV, on PrEP or
with history of
injecting drug use

https://stipu.nsw.gov.au/wp-content/uploads/STIGMA_Guidelines2019_Final-1.pdf

Screening for HCV Infection Among MSM

- Clinicians treating HIV-infected MSM should be on high alert for acute HCV infection, which is most often asymptomatic
- Screening should be performed using an HCV-antibody test in most instances. However, individuals with self-reported recent high-risk exposures and/or newly elevated alanine aminotransferase (ALT) levels should have HCV screening with both HCV-antibody and HCV-RNA tests due to concern for acute HCV infection
 - Those found to be chronically HCV infected should be offered antiviral treatment to prevent liver disease progression and transmission to others
 - These patients should also be counseled about risk factors for HCV transmission and the potential for HCV reinfection after cure



Australian Guidelines – HCV in the setting of HIV coinfection

- Simultaneous infection with HIV and HCV is associated with an increased rate of progression to liver cirrhosis, increased risk of HCC and increased mortality, even in those achieving full HIV virological suppression with ART
- Eradication of HCV can prevent these complications, and people with HCV–HIV coinfection should be prioritised for treatment of HCV
- Interferon-free DAA regimens for HCV are just as effective in the setting of HCV–HIV coinfection as they are in HCV mono-infection
- Drug–drug interactions, cumulative drug toxicities and increased pill burden are the main considerations when planning HCV treatment in people living with HIV

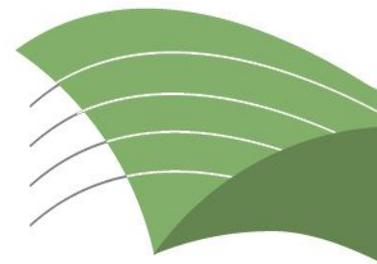


Australian Guidelines – HCV in the setting of HIV coinfection

- It is also important to note that thrombocytopaenia may occur secondary to HIV infection rather than portal hypertension; this may influence interpretation of the APRI score for liver fibrosis staging
- Serum bilirubin levels may be elevated by ARVs that inhibit biliary transporters
- *People with HIV–HCV coinfection should be cared for by a multidisciplinary team with experience in managing both viral infections*
- <http://www.hepcguidelines.org.au/special-populations/treatment-of-hcv-in-the-setting-of-hiv-coinfection/>



Drug-drug interactions



HEPATITIS C AGENTS

	INSTIs		NNRTIs		PIs	RTI	
	<ul style="list-style-type: none"> • BICTEGRAVIR (<i>Biktarvy</i>) • DOLUTEGRAVIR (<i>Tivicay, Triumeq, Juluca</i>) • RALTEGRAVIR (<i>Isentress</i>) 	<ul style="list-style-type: none"> • ELVITEGRAVIR/COBICISTAT (<i>Stribild, Genvoya</i>) 	<ul style="list-style-type: none"> • DORAVIRINE (<i>Pifeltro, Delstrigo</i>) • RILPIVIRINE (<i>Edurant, Complera, Odefsey, Juluca</i>) 	<ul style="list-style-type: none"> • EFVIRENZ (<i>Sustiva, Atripla</i>) • ETRAVIRINE (<i>Intence</i>) • NEVIRAPINE (<i>Viramune</i>) 	<ul style="list-style-type: none"> • ATAZANAVIR (<i>Reyataz/Norvir, Evotaz</i>) • DARUNAVIR (<i>Prezista/Norvir, Prezcobix, Symtuza</i>) • LOPINAVIR (<i>Kaletra</i>) 	<ul style="list-style-type: none"> • TENOFOVIR DISOPROXIL, TDF (<i>Viread, Truvada, Atripla, Complera, Delstrigo, Stribild</i>) 	<ul style="list-style-type: none"> • TENOFOVIR ALAFENAMIDE, TAF (<i>Descovy, Biktarvy, Genvoya, Odefsey, Symtuza</i>) • ABACAVIR (<i>Kivexa, Ziagen, Triumeq</i>)

DIRECT ACTING ANTIVIRALS (DAAs)

• Glecaprevir + pibrentasvir (<i>Maviret</i>)				Potential for ↓ glecaprevir, pibrentasvir	Potential for ↑ glecaprevir, pibrentasvir		
• Ledipasvir + sofosbuvir (<i>Harvoni</i>)						Potential for ↑ tenofovir	
• Velpatasvir + sofosbuvir (<i>Eplusa</i>)				Potential for ↓ velpatasvir		Potential for ↑ tenofovir	
• Velpatasvir + voxilaprevir + sofosbuvir (<i>Vosevi</i>)				Potential for ↓ velpatasvir, voxilaprevir	darunavir Atazanavir, lopinavir: potential for ↑ voxilaprevir	Potential for ↑ tenofovir	
• Elbasvir + grazoprevir (<i>Zepatier</i>)		Potential for ↑ elbasvir, grazoprevir		Potential for ↓ elbasvir, grazoprevir	Potential for ↑ elbasvir, grazoprevir		

Deciding which pangenotypic regimen to use

Glecaprevir/ Pibrentasvir

3 tablets WITH food daily

8–12 weeks of treatment

Drug interactions: some
statins, atazanavir or
rifampin

Avoid in decompensated
cirrhosis (Child-Pugh B, C)

Can be used in all renal
impairment

Similarities

Pan-genotypic

**Risk of
reactivating HBV**

**Adverse reactions:
Headache and
Fatigue**

Sofosbuvir/ Velpatasvir

1 tablet +/- food daily

12 weeks of treatment

Drug interactions: some
statins, acid suppression,
amiodarone

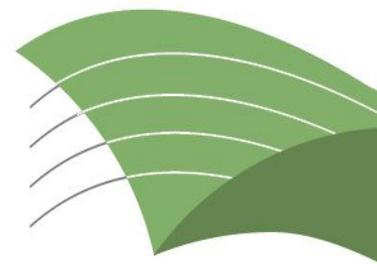
Can be used in all cirrhosis
(Child-Pugh A, B, or C)

Not recommended in
eGFR <30 mL/min

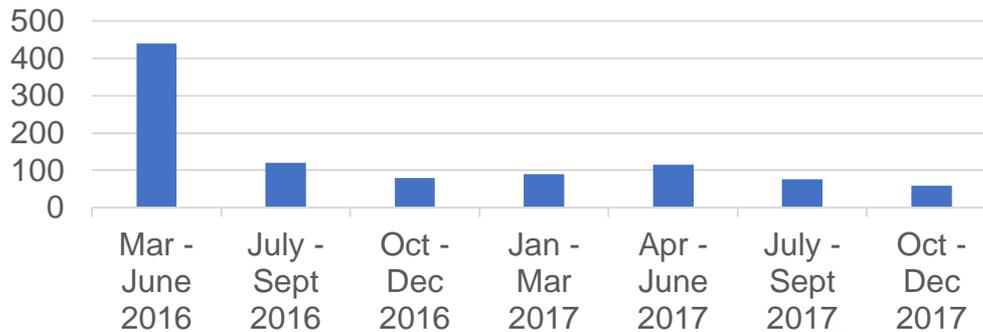


Cairns Hep C Free





People initiating DAA treatment Mar 2016 - Dec 2017 Cairns and Hinterland HHS



Source: Queensland Health Hepatitis C Treatment Progress Report March 2019

ORIGINAL RESEARCH

Journal of Virus Eradication 2018; 4: 160-164

A decentralised, multidisciplinary model of care facilitates treatment of hepatitis C in regional Australia

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³Kirby Institute, University of New South Wales, Sydney, Australia

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⁵James Cook University, Cairns, Australia

^{*}Sexual Health Service, Cairns Hospital, Cairns, Australia

Abstract

Objectives: Direct-acting antiviral (DAA) therapy for hepatitis C virus (HCV) has excellent cure rates and minimal side effects. Despite the high burden of disease, strategies to ultimately eradicate HCV are being developed. However, the delivery of care in regional settings is challenging and the efficacy of decentralised models of care is incompletely defined.

Methods: A prospective cohort study of patients whose treatment was initiated or supervised by Cairns Hospital, a tertiary hospital which provides services to a culturally diverse population across a 380,748 km² area in regional Australia. Patients' demographics, clinical features, DAA regimens and outcomes were recorded and correlated with their ensuing clinical course.

Results: Over 22 months, 734 patients were prescribed DAA therapy for HCV. No patients were prescribed interferon. Sofosbuvir/ledipasvir ($n=371$, 50.5%) and sofosbuvir/dacatasvir ($n=287$, 39.1%) were the most commonly prescribed regimens. No patients ceased treatment due to adverse effects. There were 612/734 (83.4%) patients with complete results, with 575 (94%) cured. At the end of the study period, there were 50 (6.8%) patients lost to follow-up and 72 (9.8%) awaiting SVR12 testing. The presence of cirrhosis ($n=147/612$, 24.1%) did not impact significantly on SVR12 rates, this being achieved in 136/147 (92.5%) cirrhotic patients versus 440/465 (94.6%) in non-cirrhotic patients ($p=0.34$). Treatment-experienced patients (95/612, 18.3%) were more likely to be non-responders than treatment-naïve patients (10/95 (10.5%) versus 26/517 (5%), $p=0.04$). Strategies to facilitate treatment included a dedicated clinical nurse consultant, education to primary health care providers, specialist outreach clinics to regional communities and shared care with general practitioners. SVR12 rates were similar amongst gastroenterologists (283/306, 92.5%), general practitioners (152/161, 94.4%), sexual health physicians (104/106, 98.1%) and other prescribers (37/39, 94.9%).

Conclusions: This study confirms that decentralised, multidisciplinary models of care can provide HCV treatment in regional and remote settings with excellent outcomes.

Keywords: hepatitis C, direct-acting antiviral therapy, regional Australia, model of care, service delivery

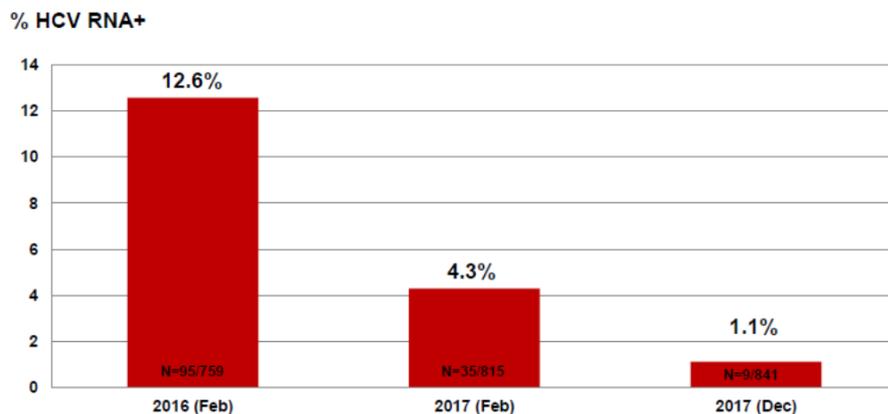


Queensland
Government

Lotus Glen Prison

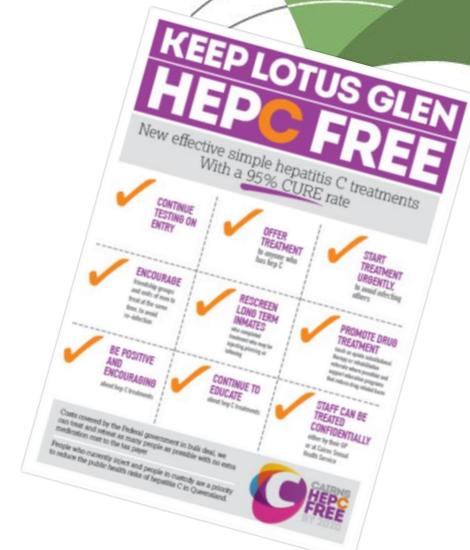
HCV elimination (near) in QLD prison: Lotus Glen

HCV burden within prison (800-850 inmates)



Bartlett S, et al. CID 2018

Bartlett SG et al. CID 2018



Clinical Infectious Diseases

BRIEF REPORT

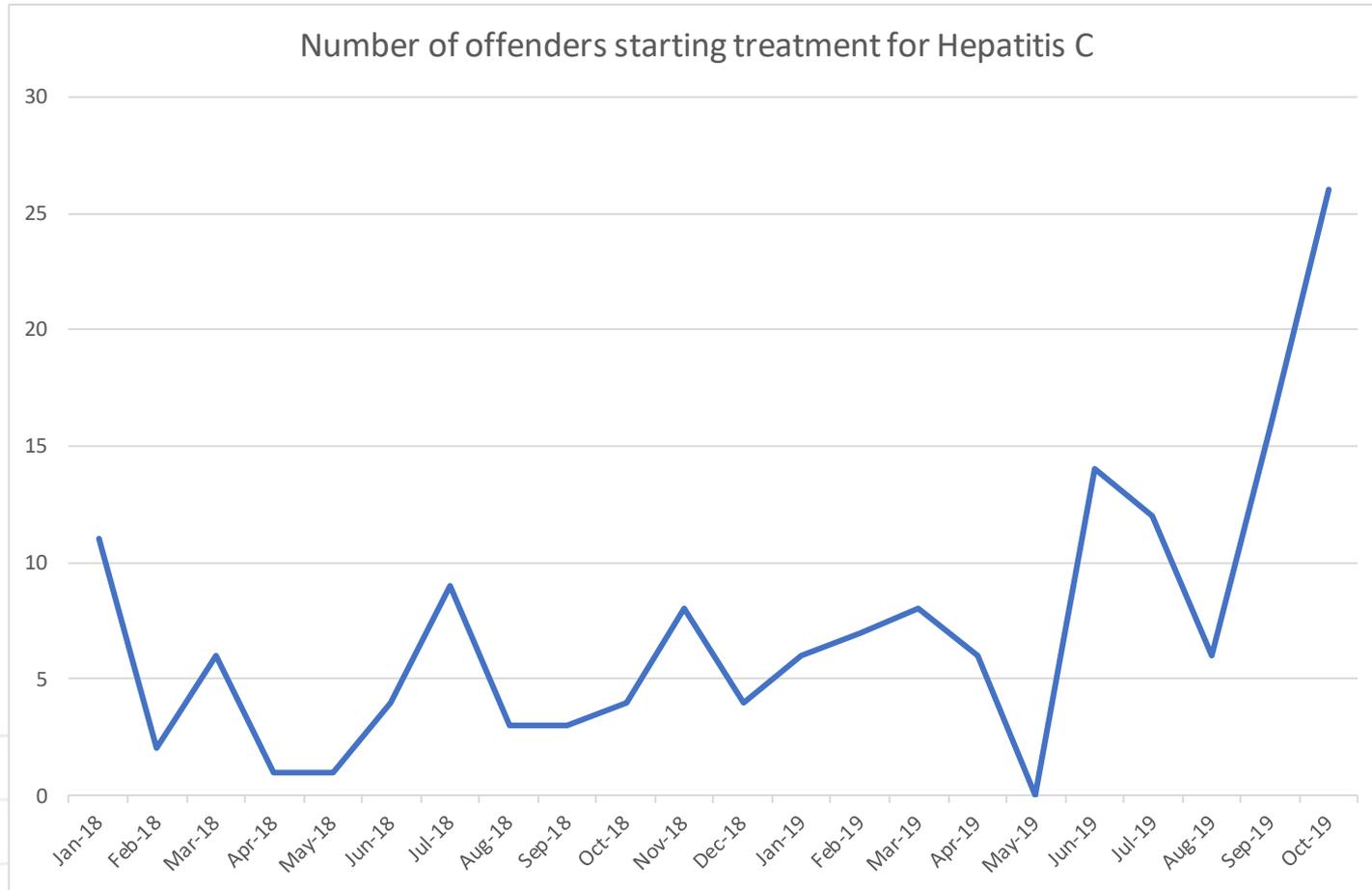
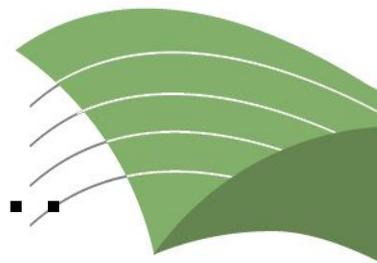
Demonstration of Near-Elimination of Hepatitis C Virus Among a Prison Population: The Lotus Glen Correctional Centre Hepatitis C Treatment Project

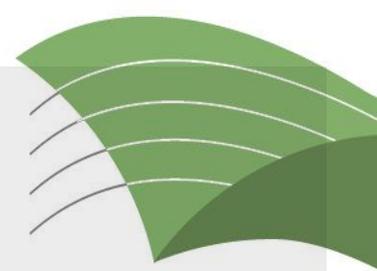
Sofia R. Bartlett,¹ Penny Fox,² Harris Cabatangan,³ Anissa Jaros,³ Carla Gorton,⁴ Rhonda Lewis,⁴ Eugene Priscott,⁴ Gregory J. Dore,^{1a} and Darren B. Russell^{1a,b,c}

¹Kirby Institute, UNSW Sydney, ²Department of Medicine, Cairns Hospital, ³Lotus Glen Correctional Centre, Mareeba, ⁴Cairns Sexual Health Service and ⁵James Cook University, Cairns, and ⁶Melbourne University, Australia.

Micro-elimination of hepatitis C virus (HCV) infection through rapid uptake of government-funded direct-acting antiviral therapy within an Australian prison setting is demonstrated. During a 22-month period, 119 patients initiated treatment for chronic HCV infection, with HCV in-prison viremic prevalence declining from 12% to 1%.

Recent prison challenge...





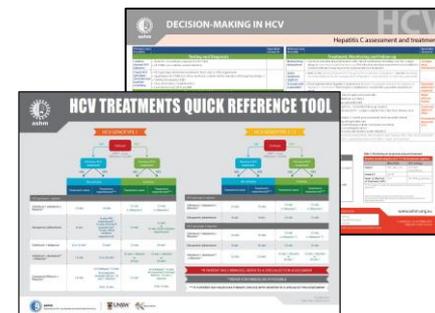
Summary of Hep C and sex...

- Hepatitis C is rarely, if ever, transmitted in heterosexual relationships
- Hep C is *occasionally* transmitted between homosexually-active men:
 - HIV coinfection
 - Fisting and “rough sex”
 - Recreational drugs
 - In the presence of other STIs
- Have a low threshold for testing
- People acquiring acute Hep C should be offered treatment if they don't clear it spontaneously after 3 months
- PLHIV with Hep C should be prioritised for treatment



Further resources and education opportunities

- ASHM resources: ashm.org.au/resources
- ASHM eLearning: lms.ashm.org.au
 - Curing hepatitis C in primary care – eLearning
 - Curing hepatitis C in primary care – Refresher Module
 - Hepatitis C in Primary Care and Drug and Alcohol Settings



For upcoming ASHM training in your area,
visit ashm.org.au/training