Bridging the Prescriber Divide: Treatment Made Easy

Professor Alex Thompson
St Vincent's Hospital Melbourne
11th August 2017

ST VINCENT'S HEALTH AUSTRALIA

THE UNIVERSITY OF MELBOURNE

GESA Gastroenterological Society of Australia
ala Australian Liver Association

Acknowledgement to Country

- We recognise the traditional custodians of the land and sea on which we live and work

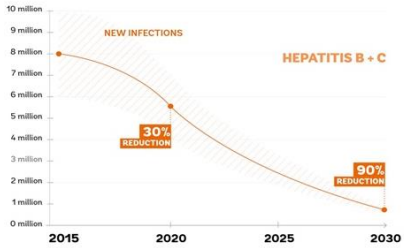
Disclosures

- Advisory board member - Gilead, Abbvie, Bristol-Myers Squibb (BMS), Merck/MSD, and Roche Diagnostics
- Speaker - Gilead, Janssen, Merck, BMS, Abbvie
- PI - Gilead, Merck, BMS, Janssen, Spring Bank, GenFit, Sillajen
- Research / grant support – Gilead, Merck, BMS, Abbvie
- My presentation includes discussion of drugs which are not approved for clinical use

WHO global hepatitis strategy

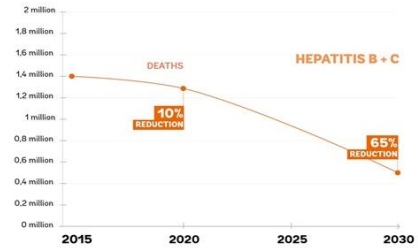
Elimination – a reduction in HCV incidence and HCV-related mortality to a level that are no longer a public health concern

90% reduction in new cases of of chronic HBV and HCV infection



6-10 million infections (in 2015) to 900,000 infections (by 2030)

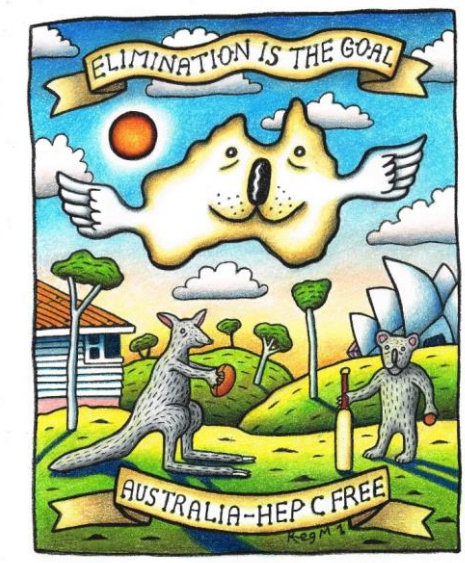
65% reduction in deaths from chronic HBV and HCV



1.4 million deaths (in 2015) to under 500,000 deaths (by 2030)

Hirnschall G, et al ILC 2016

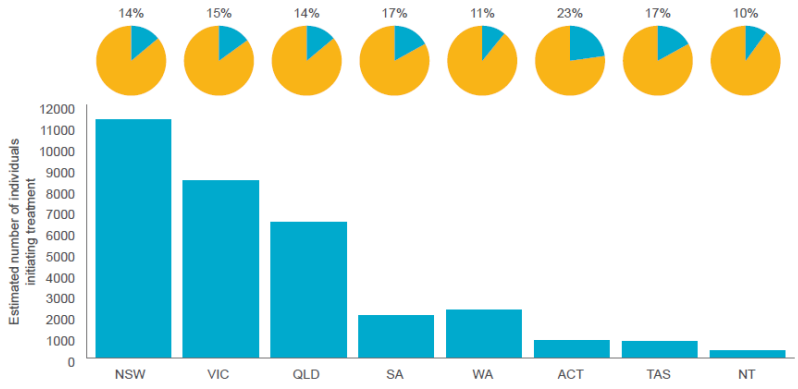
Australia is aiming to achieve the WHO targets



Key features of Australian DAA Access

- Multiple DAA regimens subsidised
  - SOF/VEL, SOF/LDV, SOF/DCV, PrOD, EBR/GZR ± RBV
- Risk-sharing arrangement between government and industry
  - capped annual government expenditure
  - no cap on number of patients treated per year
    - no restrictions based on liver disease stage or drug and alcohol use
    - retreatment (including for reinfections) allowed
  - patient co-payment: $AUD 7-38/month
- Broad practitioner base: specialists AND GPs / NPs
- Hospital AND community pharmacy dispensing

32,400 Australians were treated with DAAs (Mar – Dec 2016)

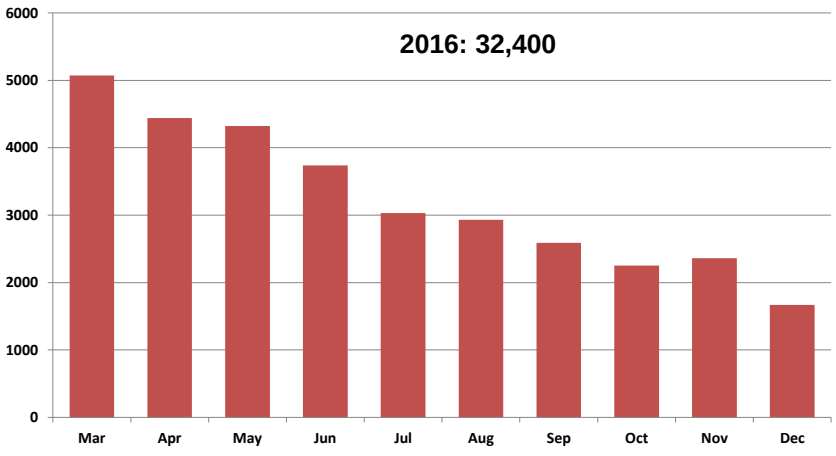


NSW: New South Wales; VIC: Victoria; QLD: Queensland; SA: South Australia; WA: Western Australia; ATC: Australian Capital Territory; TAS: Tasmania; NT: Northern Territory

Monitoring hepatitis C treatment uptake in Australia. Issue #7, July 2017.
Available at: https://kirby.unsw.edu.au/sites/default/files/kirby/report/Monitoring-hep-C-treatment-uptake-in-Australia_Iss7-JUL17.pdf

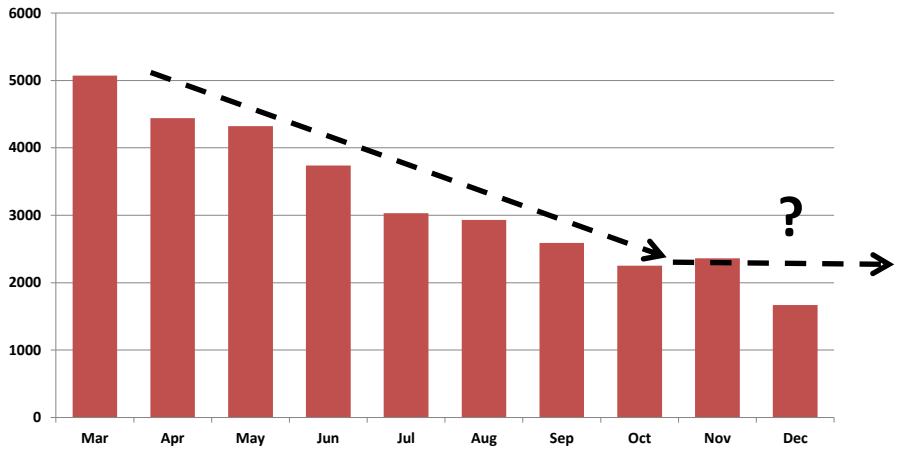
Clearing the specialist warehouse:

HCV treatment in Australia: March-December 2016



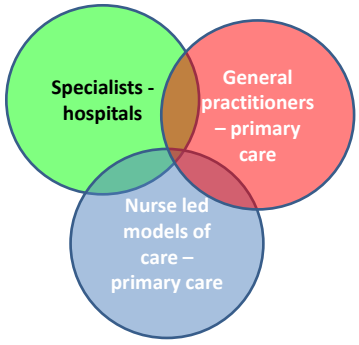
Slide courtesy of Greg Dore

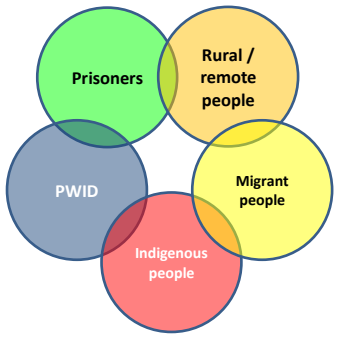
Moving beyond the specialist warehouse



Slide courtesy of Greg Dore

New models of care for Hep C are needed





Prescribing Hep C treatment

Population criteria: Patient must be aged 18 years or older. **N = 10**
Treatment criteria: Must be treated by a medical practitioner or an authorised nurse practitioner* experienced in the treatment of chronic hepatitis C infection; or in consultation with a gastroenterologist, hepatologist or infectious diseases physician experienced in the treatment of chronic hepatitis C infection.
The following information must be provided at the time of application: a) the hepatitis C virus genotype; and b) the patient's cirrhotic status (non-cirrhotic or cirrhotic) The following information must be documented in the patient's medical records: a) evidence of chronic hepatitis C infection (repeatedly antibody to hepatitis C virus (anti-HCV) positive and hepatitis C virus ribonucleic acid (HCV RNA) positive); and b) evidence of the hepatitis C virus genotype

* PBS authority approval from the Department of Human Services (Medicare) — via written or telephone channels — will be required for each prescription; the medicines will not be available under streamlined authority.

GPs cannot treat Hep C overseas!

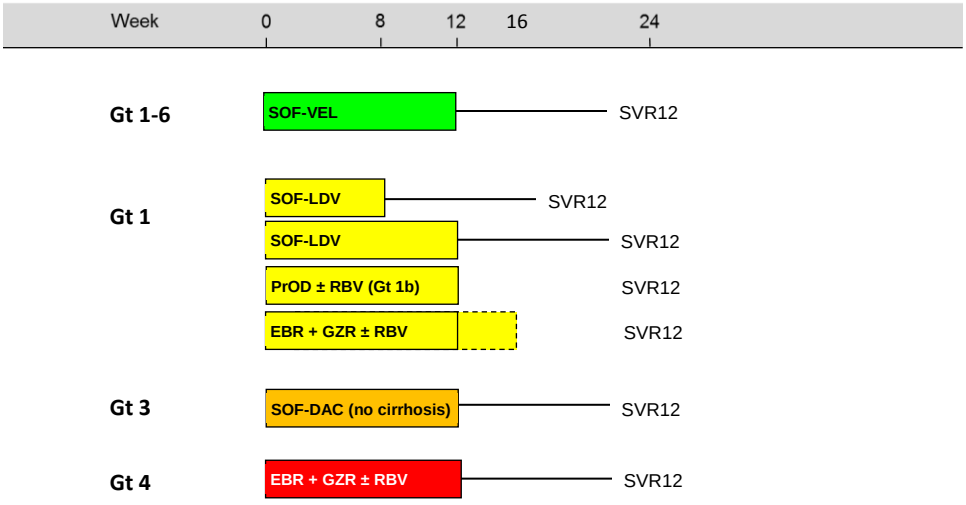
94% (n=32) of European countries require specialists to prescribe DAA therapy

Marshall A, LB-505, EASL, 2017

Barriers to community-based treatment

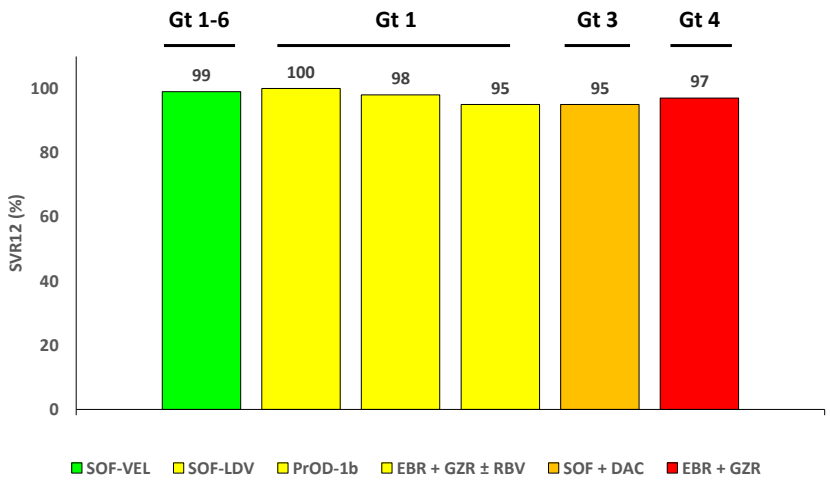
- "I don't have any hep C patients"
- "Is there treatment for hep C?" - "can hep C be cured?"
- "Don't specialists treat hep C?"
- "It's all too hard – I don't know how to treat hep C"
- "It's all too hard – I don't have time to treat hep C"
- "The drugs are very expensive – what if I stuff it up?"
- "I don't have a FibroScan"

Hep C treatment ≤12 Weeks



Cure > 95%

Patients with no cirrhosis



Hep C treatments are well tolerated

Adverse Effects with Sofosbuvir + Ledipasvir Reported in ≥5% of Subjects			
	Ledipasvir-Sofosbuvir		
	8 Weeks	12 Weeks	24 Weeks
	N=215	N=539	N=326
Fatigue	16%	13%	18%
Headache	11%	14%	17%
Nausea	6%	7%	9%
Diarrhea	4%	3%	7%
Insomnia	3%	5%	6%

Note. Mild, moderate or severe hepatic impairment (Child-Pugh Class A, B or C).
- No dose adjustment of HARVONI is required

Note. Sofosbuvir is renally excreted
- **not recommended in patients with eGFR <30 mL/min/1.73m^2**

FDA Label

www.gesa.org.au
Thompson AJ, Med J Aust 2016; 204 (7): 268-272

The KISS principle…

- 5 key questions:
  - What is the HCV genotype?
    - What is the viral load?
    - Is the patient treatment experienced?
  - Is cirrhosis present?
    - FibroScan, APRI, other
  - Is HBV-HCV or HIV-HCV coinfection present?
  - Are there potential drug-drug interactions?
    - www.**hep-druginteractions**.org
  - What is the renal function (eGFR)?

Is cirrhosis present?

NON-INVASIVE methods for excluding cirrhosis		
Method	**Formula**	**Key threshold for excluding cirrhosis**
Transient elastography	**FibroScan**	LSM < 12.5
APRI	= (AST [IU/L] / AST upper normal limit [IU/L] * 100) / platelet count (x 10^9/L) http://www.hepatitisc.uw.edu/page/clinical-calculators/apri	APRI < 1.0
Hepascore	Patented formula combining bilirubin, GGT, hyaluronate, α-2-macroglobulin, age and gender	HS < 0.80
FibroGENE	Patented formula based on age, platelet count, AST, GGT and IFNL3 (rs12979860) genotype http://www.fibrogene.com/viral_hepatitis.html	Threshold not published but online calculator available
ELF test	Patented formula combining age, hyaluronate, MMP-3 and TIMP-1	ELF < 9.8
Note - these thresholds have good performance characteristics for excluding the presence of cirrhosis. Patients in whom results exceed these thresholds should be referred for further assessment for the presence of cirrhosis by a with experience in assessing liver disease severity and managing patients with advanced liver disease. These thresholds alone should not be used to diagnose cirrhosis. **Note – the performance of Hepascore and APRI for predicting the presence of cirrhosis may be less accurate in people with HIV coinfection than in people with HCV mono-infection (be aware of false positive results due to HIV-induced thrombocytopaenia – APRI or ART-related hyperbilirubinaemia – Hepascore).**		

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Is cirrhosis present?

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Hepa		
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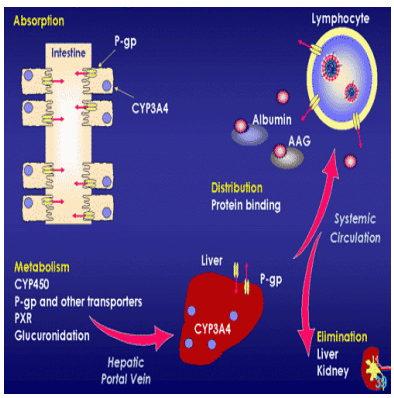
Cirrhosis assessment MUST occur BEFORE treatment

Thompson AJ, Med J Aust 2016; 204 (7): 268-272

Why is cirrhosis important?

- Required for PBS approval
- Determines treatment duration
- Indicates the need for specialist referral
  - Hepatocellular cancer (HCC) screening
  - Portal hypertension screening

Drug-Drug Interactions



www.medscape.com

www.**hep-druginteractions**.org

Prescribing Hep C treatment

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Treatment criteria: Must be treated by a medical practitioner or an authorised nurse practitioner[1] experienced in the treatment of chronic hepatitis C infection; or in consultation with a gastroenterologist, hepatologist or infectious diseases physician experienced in the treatment of chronic hepatitis C infection.
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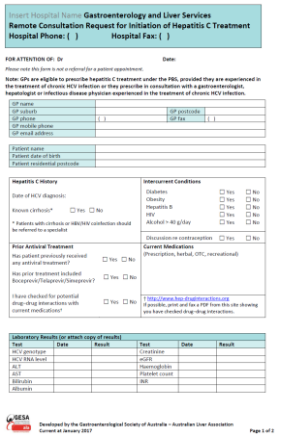
* PBS authority approval from the Department of Human Services (Medicare) — via written or telephone channels — will be required for each prescription; the medicines will not be available under streamlined authority.

"In consultation"

- means that a GP / NP must consult with one of the specified specialists by phone, fax, mail, email or videoconference in order to meet the prescriber eligibility requirements
- **most suitable for people with no cirrhosis**


Insert Hospital Name **Gastroenterology and Liver Services**
Remote Consultation Request for Initiation of Hepatitis C Treatment
Hospital Phone: ( ) Hospital Fax: ( )

FOR ATTENTION OF: Dr Date:

Please note this form is not a referral for a patient appointment.

Note: GPs are eligible to prescribe hepatitis C treatment under the PBS, provided they are experienced in the treatment of chronic HCV infection or they prescribe in consultation with a gastroenterologist, hepatologist or infectious disease physician experienced in the treatment of chronic HCV infection.

GP name			
GP suburb		GP postcode	
GP phone	( )	GP fax	( )
GP mobile phone			
GP email address			

Patient name	
Patient date of birth	
Patient residential postcode	

Hepatitis C History

Date of HCV diagnosis:

Known cirrhosis* ☐ Yes ☐ No

* Patients with cirrhosis or HBV/HIV coinfection should be referred to a specialist

Intercurrent Conditions

Diabetes	☐ Yes	☐ No
Obesity	☐ Yes	☐ No
Hepatitis B	☐ Yes	☐ No
HIV	☐ Yes	☐ No
Alcohol > 40 g/day	☐ Yes	☐ No
Discussion re contraception	☐ Yes	☐ No

Prior Antiviral Treatment

Has patient previously received any antiviral treatment? ☐ Yes ☐ No

Has prior treatment included Boceprevir/Telaprevir/Simeprevir? ☐ Yes ☐ No

I have checked for potential drug-drug interactions with current medications† ☐ Yes ☐ No

Current Medications
(Prescription, herbal, OTC, recreational)

† http://www.hep-druginteractions.org
If possible, print and fax a PDF from this site showing you have checked drug-drug interactions.

Laboratory Results (or attach copy of results)

Test	Date	Result	Test	Date	Result
HCV genotype			Creatinine		
HCV RNA level			eGFR		
ALT			Haemoglobin		
AST			Platelet count		
Bilirubin			INR		
Albumin					

Developed by the Gastroenterological Society of Australia – Australian Liver Association
Current at January 2017

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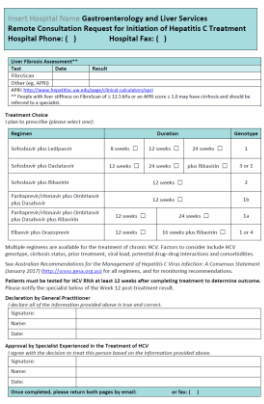

Insert Hospital Name **Gastroenterology and Liver Services**
Remote Consultation Request for Initiation of Hepatitis C Treatment
Hospital Phone: ( ) Hospital Fax: ( )

Liver Fibrosis Assessment**

Test	Date	Result
FibroScan		
Other (eg. APRI)		

APRI: http://www.hepatitis.va.gov/page/clinical-calculators/apri

** People with liver stiffness on FibroScan of ≥ 12.5 kPa or an APRI score ≥ 1.0 may have cirrhosis and should be referred to a specialist.

Treatment Choice
(plan to prescribe (please select one))

Regimen	Duration			Genotype
Sofosbuvir plus Ledipasvir	8 weeks ☐	12 weeks ☐	24 weeks ☐	1
Sofosbuvir plus Daclatasvir	12 weeks ☐	24 weeks ☐	plus Ribavirin ☐	3 or 1
Sofosbuvir plus Ribavirin	12 weeks ☐			2
Paritaprevir/ritonavir plus Ombitasvir plus Dasabuvir	12 weeks ☐			1b
Paritaprevir/ritonavir plus Ombitasvir plus Dasabuvir plus Ribavirin	12 weeks ☐	24 weeks ☐		1a
Ribavirin plus Grazoprevir	12 weeks ☐	16 weeks plus Ribavirin ☐		1 or 4

Multiple regimens are available for the treatment of chronic HCV. Factors to consider include HCV genotype, cirrhosis status, prior treatment, viral load, potential drug–drug interactions and comorbidities.

See *Australian Recommendations for the Management of Hepatitis C Virus Infection: A Consensus Statement (January 2017)* (http://www.gesa.org.au) for all regimens, and for monitoring recommendations.

Patients must be tested for HCV RNA at least 12 weeks after completing treatment to determine outcome. Please notify the specialist below of the Week 12 post-treatment result.

Declaration by General Practitioner
I declare all of the information provided above is true and correct.

Signature:	
Name:	
Date:	

Approval by Specialist Experienced in the Treatment of HCV
I agree with the decision to treat this person based on the information provided above.

Signature:	
Name:	
Date:	

Once completed, please return both pages by email: or fax: ( )

Modified from an original template designed for the ALA by Prof Simone Strasser

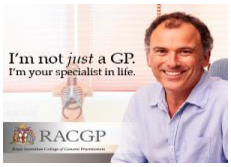
Who needs to see a specialist?

- Cirrhosis
  - Hepatocellular cancer (HCC) screening
  - Portal hypertension screening
- HBV / HIV coinfection
- Renal impairment (eGFR < 50)
- DAA failures
- Complex comorbidities

So - prescribing Hep C treatment is easy

- 5 key questions:
  - What is the HCV genotype?
    - What is the viral load?
    - Is the patient treatment experienced?
  - Is cirrhosis present?
    - FibroScan, APRI, other
  - Is HBV-HCV or HIV-HCV coinfection present?
  - Are there potential drug-drug interactions?
    - www.**hep-druginteractions**.org
  - What is the renal function (eGFR)?

But – system change is hard



The Victorian Model

EC Partnership

Eliminate Hepatitis C (EC) Partnership

Aims to…

- ***Support & enhance*** *programs to* ***increase HCV treatment uptake*** *among* ***people who inject drugs*** *(PWID) using nurse-led models of care in* ***community*** *and* ***prison*** *settings*
- ***Assess the feasibility*** *and* ***impact of treating*** *high enough proportion of PWID (~1,160 annually) to* ***reduce new infections*** *and, inform HCV elimination models in Australia and globally*

EC Partnership

Our Implementation Plan…

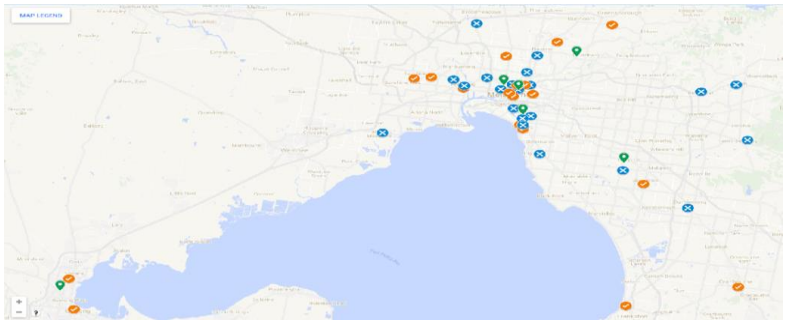
Utilising a health systems framework we aim to….

1. Increase demand through ***health promotion***
2. Increase clinical capacity through ***training & education***
3. Streamline ***clinical pathways*** to increase access to HCV testing & treatment in community & prison serttings
4. Establish integrated HCV ***data and surveillance system*** to monitor trends in HCV prevalence and incidence over time
5. ***Pilot and evaluate*** new interventions to increase uptake of HCV testing & treatment


EC Partnership

Increasing treatment in OST clinics using nurse-led models of care

Mapping Potential EC Sites - OST clinics in Melbourne



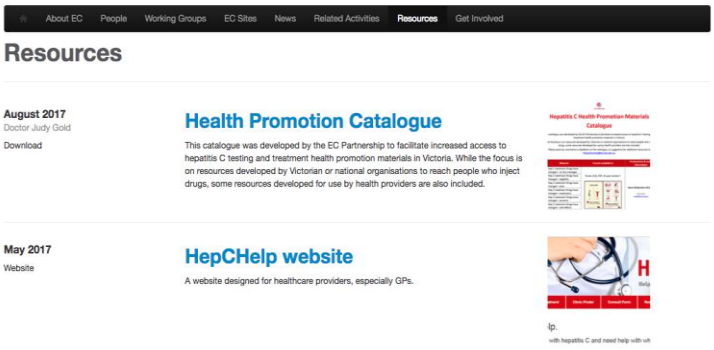
14 hepatitis nurses will support DAA treatment in high case load OST clinics across the state

X **High-case load clinics without access to IHNs**

✓ **High-case load clinics with access to IHNs**

Tertiary centres

ecpartnership.org.au/resources



EC Partnership is currently hiring nurses!

Find out more through Burnet – Careers

EC Partnership

Victorian Statewide Hepatitis Program

- Nurse-led model of care

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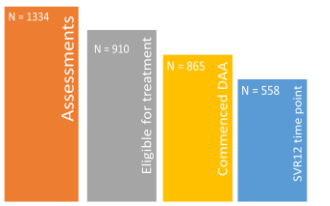
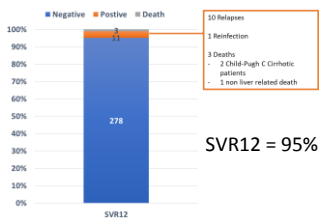
State Government Victoria Department of Justice & Regulation



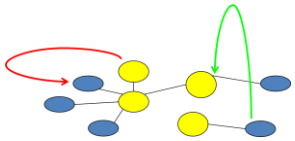


SVR12 = 95%

McDonald L, EASL, 2017 and Papaluca T, AVHEC, 2017

The TAP Study:

HCV-Treatment As Prevention – treating PWID in a the community using a social networks approach.



"Bring Your Friends"
- recruiting:
i) PWID AND
ii) injecting partners

Burnet Institute
Medical Research. Practical Action.

GILEAD
Advancing Therapeutics. Improving Lives.

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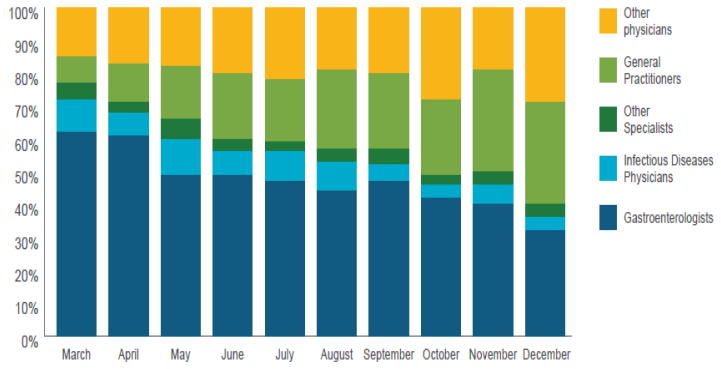
GP treatment is increasing

HCV treatment in Australia: March-September 2016



Other physicians included supervised medical officers (e.g., interns, resident medical officers, and registrars), public health physicians, temporary resident doctors, and non-vocationally registered doctors.

Monitoring hepatitis C treatment uptake in Australia. Issue #7, July 2017.
Available at: https://kirby.unsw.edu.au/sites/default/files/kirby/report/Monitoring-hep-C-treatment-uptake-in-Australia_Iss7-JUL17.pdf

"Now this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning"

Winston Churchill, 1942

Victory over Hep C