Hepatitis C epidemiology, screening and treatment

Date Wednesday 29 August 2018: 7.00-8.00pm

Presenter Professor Greg Dore

This education activity has been developed in association with:

- Kirby Institute, UNSW & St Vincent's Hospital
- Aboriginal Health and Medical Research Council of NSW and NSW Health

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Aboriginal Health & Medical Research Council of New South Wales

NSW GOVERNMENT Health

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Acknowledgement of Country

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

We pay our respects to Elders past and present.

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Hepatitis C epidemiology, screening and treatment

Professor Greg Dore

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Infectious Diseases Physician, St Vincent's Hospital, Sydney
NHMRC Practitioner Fellow

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Learning Outcomes

- Identify risk factors and increase appropriate screening strategies for Hepatitis C within a community setting.
- Discuss barriers to effective implementation of Hepatitis C diagnosis and treatment.
- Outline the role of general practitioners (GPs) and other health practitioners in the context Hepatitis C treatment for Aboriginal and Torres Strait Islander people.
- Discuss the importance of harm reduction for prevention of Hepatitis C, including following successful treatment (reinfection).

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Session outline

- Introduction to hepatitis C
- Identify priority populations for hepatitis C testing
- Interpret test results for hepatitis C
- Primary care based management and specialist referral
- Pre-treatment assessment, including liver fibrosis
- Treatment of hepatitis C and post-treatment monitoring

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Introduction to hepatitis C

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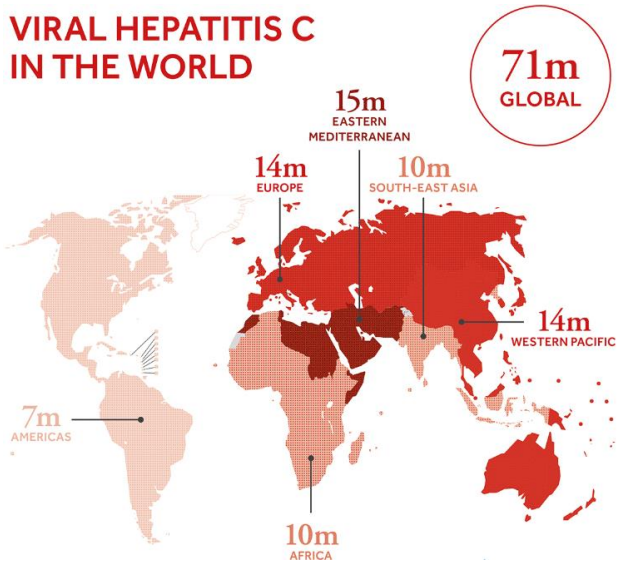
Global HCV burden: 2016 chronic HCV



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WHO Global Hepatitis Report 2017. Centre for Disease Analysis.

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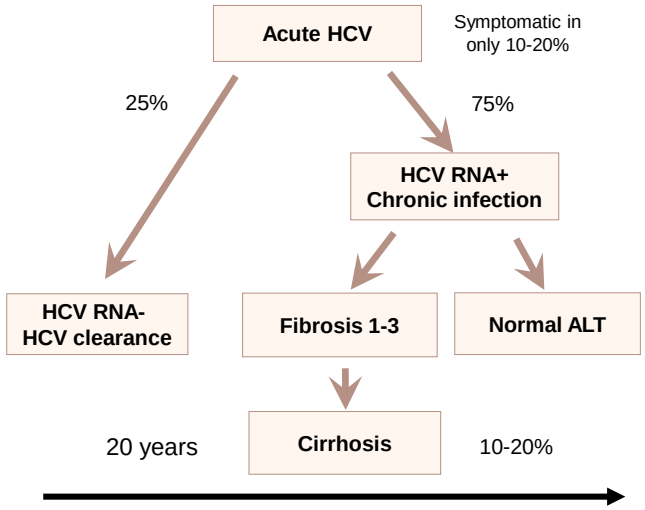
Natural history of HCV infection



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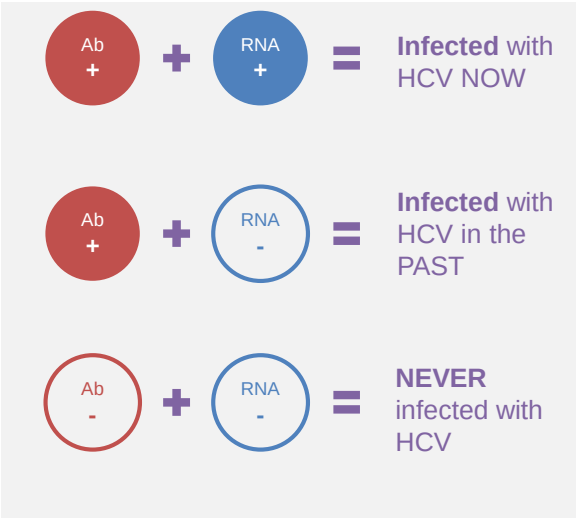
Testing for HCV infection

There are two blood tests:

Ab
Antibody test
EVER come into contact with HCV

RNA
Infected with the virus NOW



Spontaneous clearance OR Treatment-induced clearance

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HCV transmission risk levels

Risk group	Level of risk
Regular IDU (lifetime)	50-60%
Regular IDU (< 3 years)	20-40%
Occasional IDU	10-20%
Born in highly endemic country	10-20% Egypt, 5% SEA
Infant of HCV+ mother	3-5%
Infant of HIV/HCV+ mother	10-15%
Heterosexual partner of HCV+	<1% over 10-20 years
HIV- MSM	1%
HIV+ MSM (+/- IDU)	10-15%

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Screening for HCV infection

Populations to consider for a HCV screening test:

- **People who inject drugs or who have ever injected drugs**
- **People in custodial settings**
- People with tattoos or body piercing
- **Aboriginal and Torres Strait Islander peoples**
- People who received a blood transfusion or organ transplantation before 1990
- **Children born to HCV-infected mothers**
- Sexual partners of an HCV-infected person (individuals at higher risk of sexual transmission include men who have sex with men and people with HCV–HIV coinfection)
- People infected with human immunodeficiency virus or hepatitis B virus
- People with evidence of liver disease, such as elevated alanine aminotransferase level
- People who have had a needle-stick injury
- Migrants from high-prevalence regions (Egypt, Pakistan, Mediterranean and Eastern Europe, Africa and Asia)

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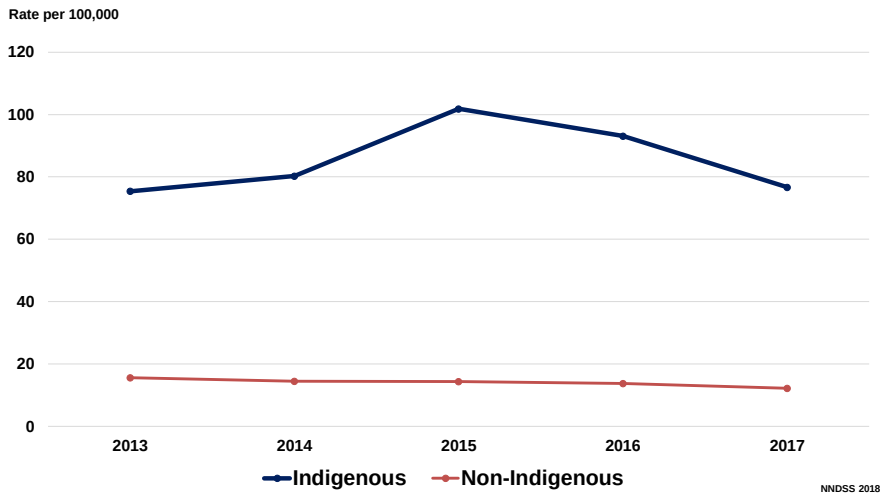
HCV notifications: 15-24 years



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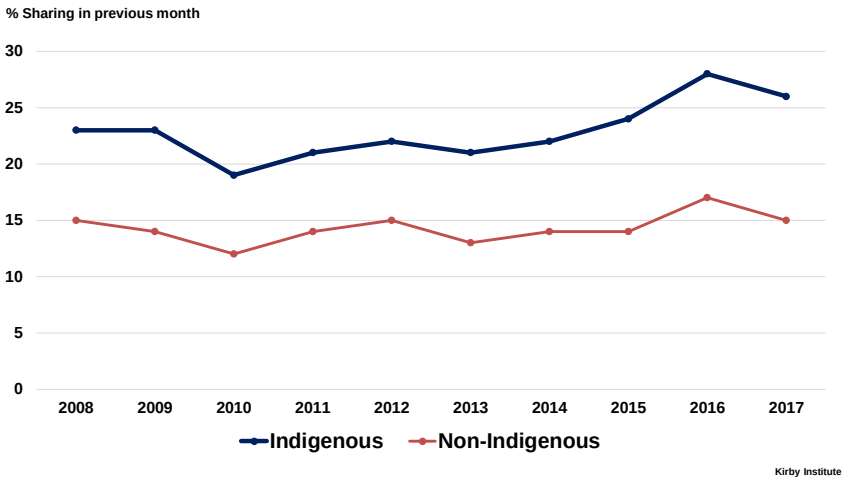
Needle syringe sharing (last month): ANSPS



Kirby Institute 2018

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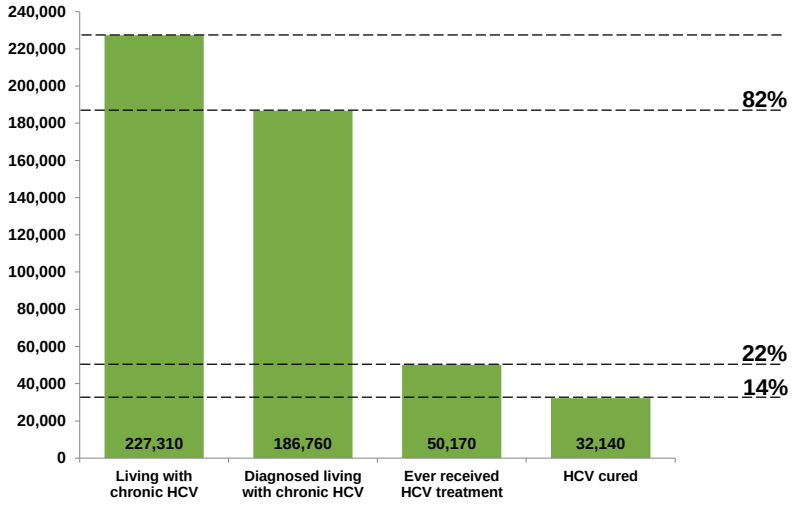
HCV in Australia: 2015 cascade of care



The Kirby Institute. Hepatitis B and C in Australia Annual Surveillance Report Supplement 2016

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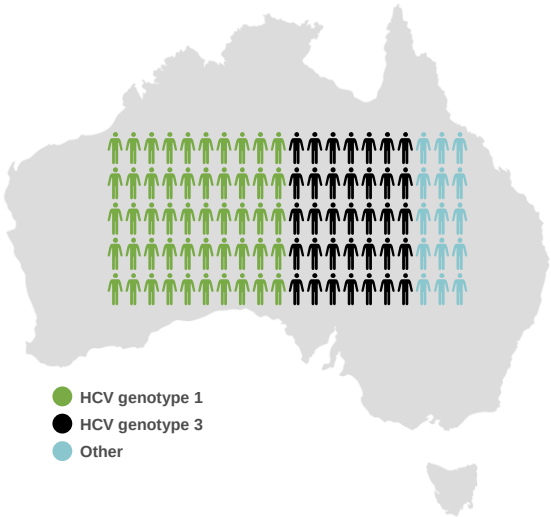
HCV in Australia: 2015 by genotype

227,000
Australians live with chronic HCV infection



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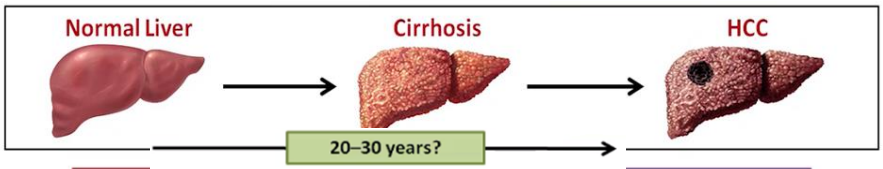
HCV liver disease progression



Disease State Factors
- Liver fibrosis stage
- Inflammation grade
- Persistently elevated ALT levels

Patient/Viral Factors
- Male gender
- Age
- Obesity, diabetes
- HIV, HBV coinfection
- Immunosuppression
- Hepatic steatosis
- Iron overload
- Genotype 3

Lifestyle Factors
- Heavy alcohol use
- Tobacco use
- Daily cannabis use

1. Hajarizadeh B et al. Nat Rev Gastroenterol Hepatol 2103;10(9):553-62. 2. Poynard A. Antivir Ther 2010;15:281-91

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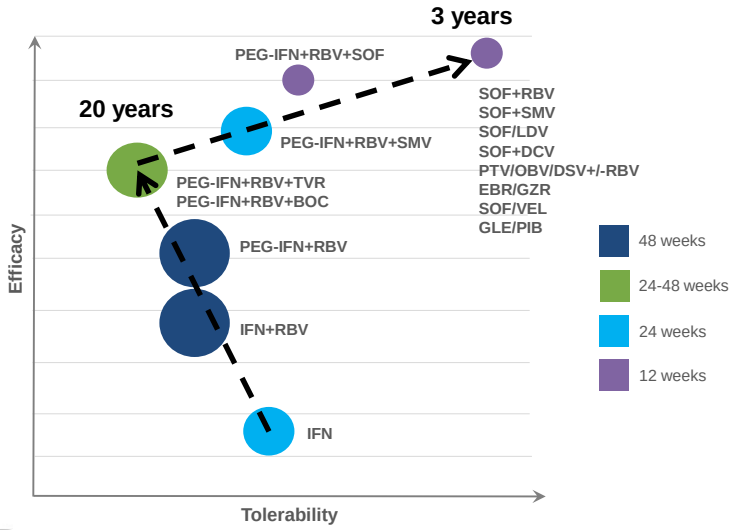
Evolution of HCV therapy



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Dore GJ & Feld J. CID 2015 (revised)

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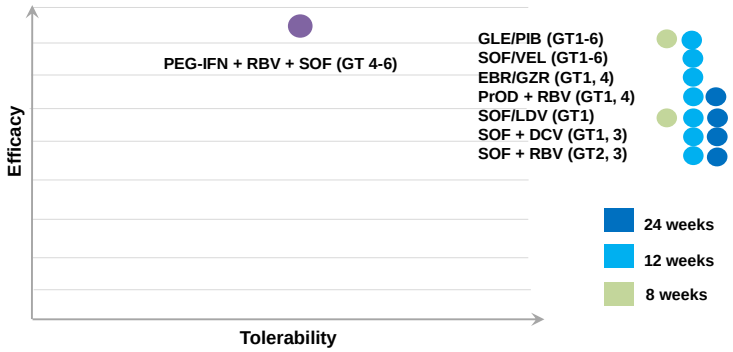
Australian PBS listed HCV treatments



Gilead Sciences, SOVALDI Australian PI, March 2015; Gilead Sciences, HARVONI Australian PI, June 2016 Bristol-Myers Squibb, DAKLINZA Australian PI, August 2016; AbbVie, VIEKIRA PAK-RBV PI, August 2016 Merck Sharp & Dohme, ZEPATIER ARTG August 2016; Gilead Sciences, EPCLUSA Australian PI August 2017

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Australian PBS listed HCV treatments

Pangenotypic: GT 1-6

Sofosbuvir/Velpatasvir

Glecaprevir/Pibrentasvir

Genotype 1
Sofosbuvir/Ledipasvir

Genotype 1, 4
Grazoprevir/Elbasvir

Genotype 1, 3
Sofosbuvir + Daclatasvir

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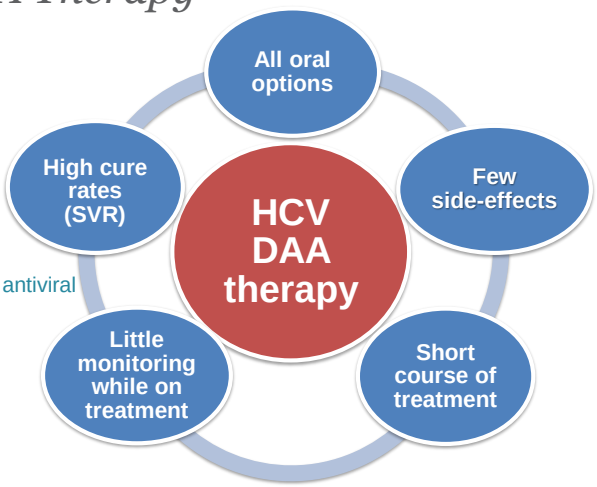
Advantages of DAA Therapy



DAA = direct acting antiviral

Increasing number of candidates for treatment

+ Guidelines to follow: Australian Recommendations for the Management of Hepatitis C Virus Infection: a Consensus Statement

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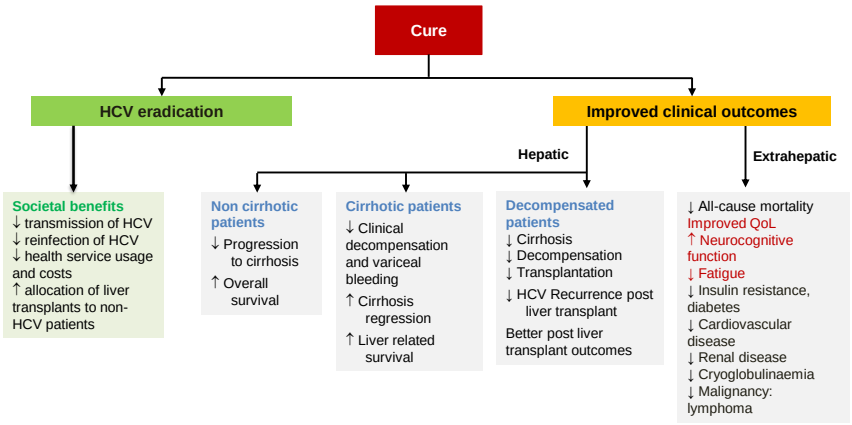
Rationale for universal HCV treatment



1. Smith-Palmer J, et al. BMC Infect Dis. 2015;15:19. 2. Negro F, et al. Gastroenterology. 2015;149:1345-1360. 3. George SL, et al. Hepatology. 2009;49:729-738. 4. Aghemo A et al, J Hepatol 2012;57:1326-35; 5. Ghany MG, et al. Hepatology. 2009;49(4):1335-1374; 6. Hill A et al, AASLD 2014

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PBS requirements for DAA treatment

Population criteria:
Patient must be aged 18 years or older.

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.

Information that must be provided on application:
a) the hepatitis C virus genotype; and
b) the patient's cirrhotic status (non-cirrhotic or cirrhotic)

The patient's medical records must document:
a) evidence of chronic hepatitis C infection; and
b) evidence of the hepatitis C virus genotype

1. Medicines for the treatment of hepatitis C are listed for prescribing by authorised nurse practitioners under the General Schedule only.
2. General Statement for Drugs for the Treatment of Hepatitis C http://www.pbs.gov.au/healthpro/explanatory-notes/general-statement-pdf/general-statement-hepatitis-c.pdf

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Specialist approval: remote consultation

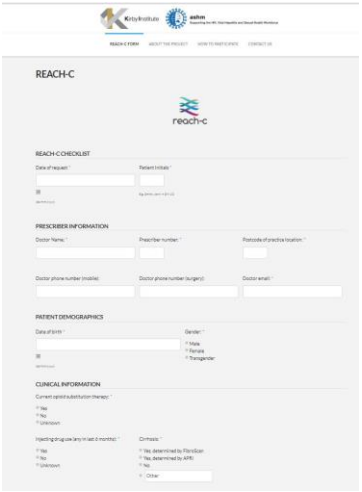
The **REACH-C study** aims to evaluate uptake and real world outcomes of HCV DAA therapy in Australia.

As part of the REACH-C study, ASHM and the Kirby Institute have developed **an online form** that medical practitioners can complete to gain specialist approval to initiate DAA therapy.

The turnaround time for specialist approval is 24 hours.

By completing the online form, the medical practitioner is giving approval for the de-identified data entered to be collected for the REACH-C Study.

Access the online form at: http://www.reach-c.ashm.org.au/



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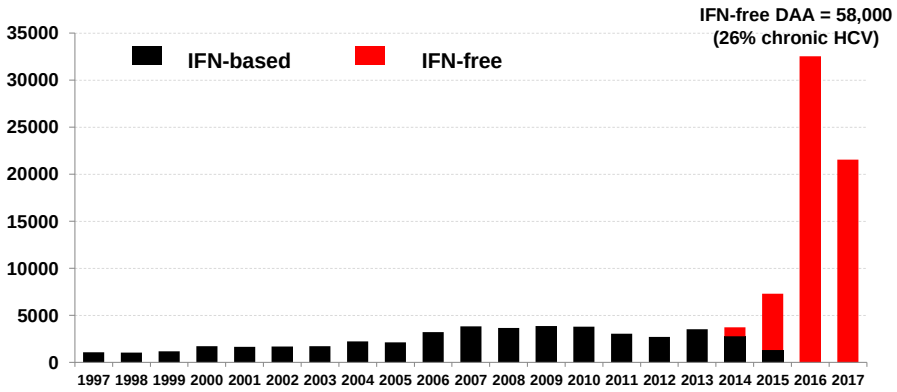
HCV treatment in Australia



Dore GJ & Hajarizadeh B. ID Clinics 2018

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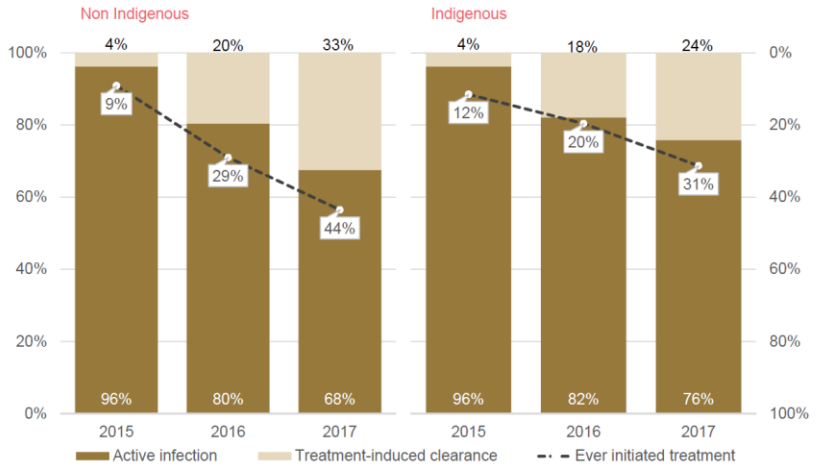
HCV treatment uptake among current PWID



^ Treatment eligible respondents: Ever exposed excluding those with spontaneous clearance

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Iversen J, et al. AVHC 2018

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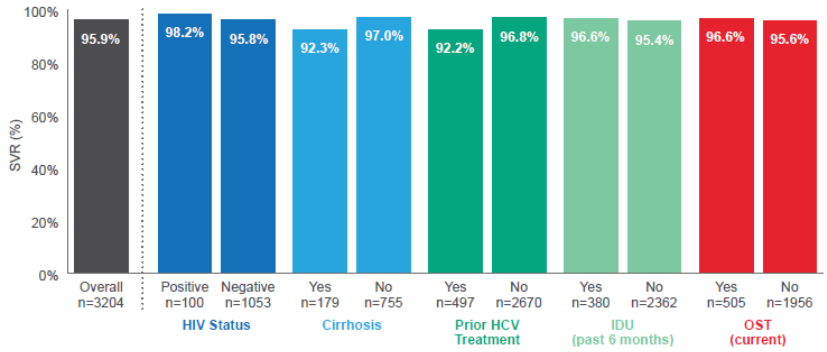
High DAA efficacy across all sub-populations

REACH-C study: Per protocol analysis* (n=3,204)



***(n=576 with unknown SVR; 16%)**

Yee J, et al. GHS 2018 (P1-062); Kirby Institute 2018

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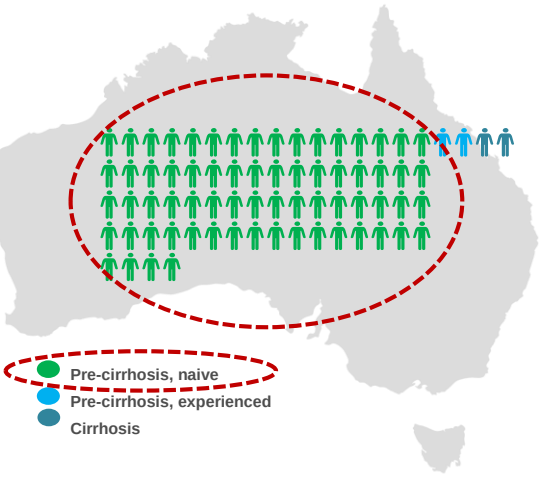
HCV in Australia: 2017 by disease stage

182,000

Australians live with chronic HCV infection



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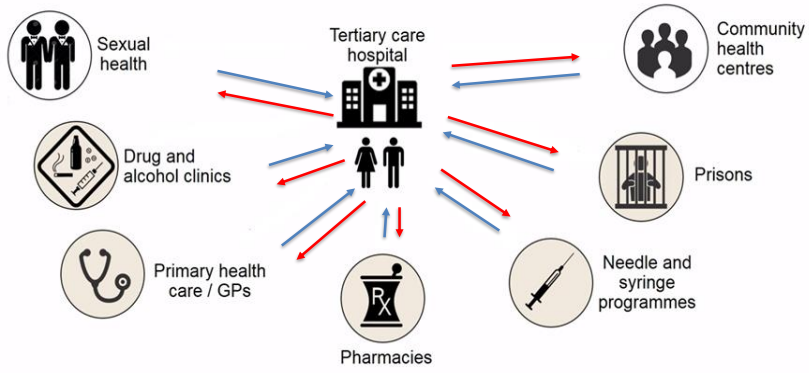
A diverse range of models of HCV care

- Need to bring HCV care to the community where patients access services



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Primary care pivotal to HCV response

- Primary care is first line of engagement for majority of patients
- Primary care is central to management of chronic disease
- HIV treatment by GPs provides an important precedent
- Large number of GPs involved in addiction medicine, so able to reach critical population for HCV elimination
- Primary care is best suited to treat because HCV should not be treated in isolation but in the context of the whole person
  - Allows co-management of HIV, drug use disorders, psychiatric disease, and other chronic diseases

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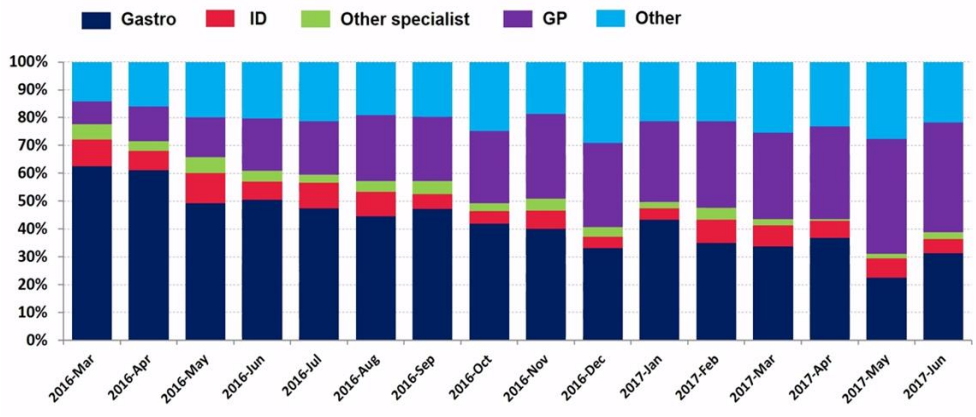
DAA prescriber distribution in Australia



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

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Pre-treatment Assessment including Liver Fibrosis

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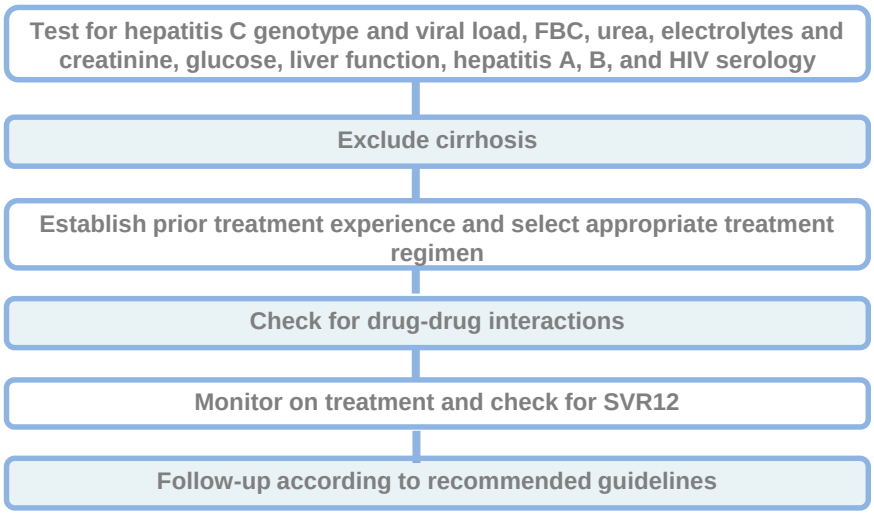
Pre-treatment assessment in primary care



Adapted from *Managing hepatitis C in general practice.* Australian Prescriber Volume 40 : Number 2 : April 2017

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Assessment for liver fibrosis

History	Physical examination	Laboratory tests	Biomarker panels	Transient elastography	Imaging	Liver biopsy
Length of infection Presence of co-morbidities such as alcohol use	Jaundice, ascites, varices, encephalopathy	Liver tests, platelet count, coagulation profile	APRI, FIB-4 Hepascore	Fibroscan , shear wave elastography	US, CT, MRI	

It is a PBS requirement that you know the patient's cirrhotic status (non-cirrhotic or cirrhotic)

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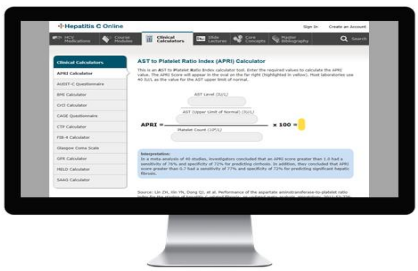
Assessment for liver fibrosis: APRI Score

APRI = (AST [IU/L] ÷ AST ULN [IU/L] x 100) ÷ platelet count (x10⁹/L)

Use an online calculator, such as: https://www.hepatitisc.uw.edu/page/clinical-calculators/apri

Critical to assess for advanced fibrosis or cirrhosis

- Informs when specialist referral needed
- Indicates need for post-SVR HCC monitoring
- Affects HCV regimen selection



Fluctuating AST and/or platelet count impacts on reliability of APRI

- **If APRI >1 : need further assessment to exclude cirrhosis**

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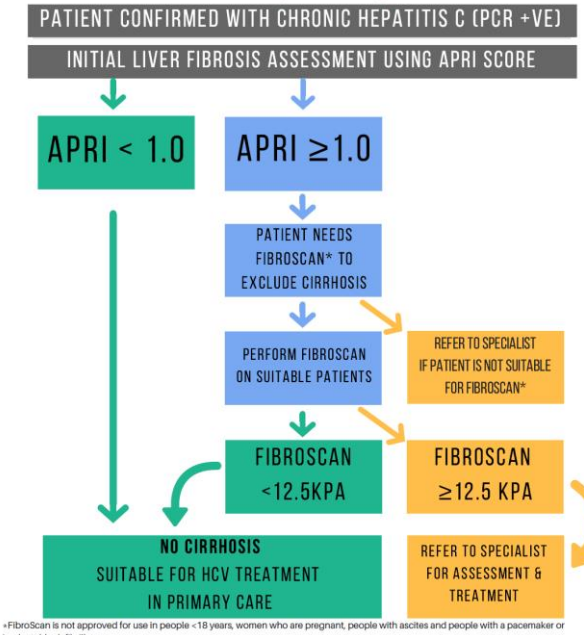

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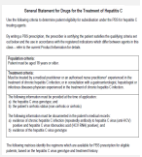
DAA treatment guidelines in Australia

Current PBS listed treatments and management recommendations

General Statement for Drugs for the Treatment of Hepatitis C



www.pbs.gov.au

(Always up to date)

Australian recommendations for the management of hepatitis C virus infection: a consensus statement

www.hepcguidelines.org.au or www.gesa.org.

(Note: updates re new DAAs may be delayed)

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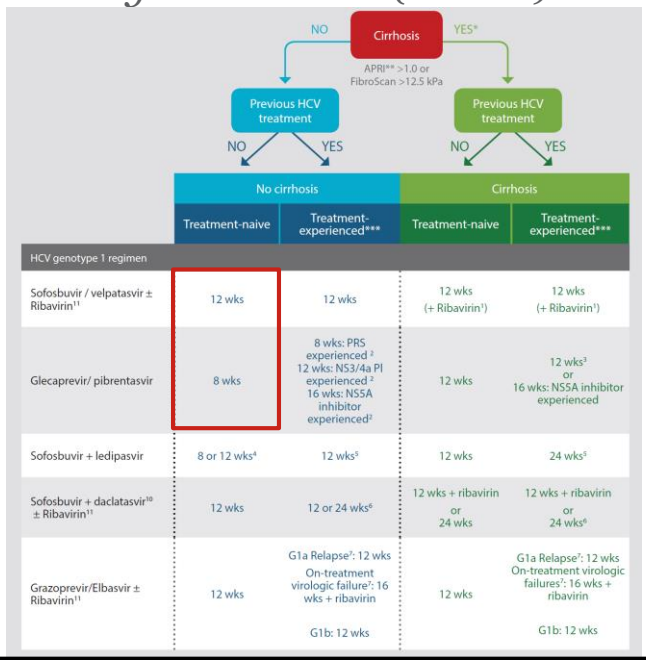
DAA treatment algorithm: GT1 (ASHM)



	No cirrhosis		Cirrhosis	
	Treatment-naive	Treatment-experienced***	Treatment-naive	Treatment-experienced***
HCV genotype 1 regimen				
Sofosbuvir / velpatasvir ± Ribavirin[11]	12 wks	12 wks	12 wks (+ Ribavirin[1])	12 wks (+ Ribavirin[1])
Glecaprevir/ pibrentasvir	8 wks	8 wks: PRS experienced[2] 12 wks: NS3/4a PI experienced[2] 16 wks: NS5A inhibitor experienced[2]	12 wks	12 wks[3] or 16 wks: NS5A inhibitor experienced
Sofosbuvir + ledipasvir	8 or 12 wks[4]	12 wks[5]	12 wks	24 wks[5]
Sofosbuvir + daclatasvir[10] ± Ribavirin[11]	12 wks	12 or 24 wks[6]	12 wks + ribavirin or 24 wks	12 wks + ribavirin or 24 wks[6]
Grazoprevir/Elbasvir ± Ribavirin[11]	12 wks	G1a Relapse[7]: 12 wks On-treatment virologic failure[7]: 16 wks + ribavirin G1b: 12 wks	12 wks	G1a Relapse[7]: 12 wks On-treatment virologic failures[7]: 16 wks + ribavirin G1b: 12 wks

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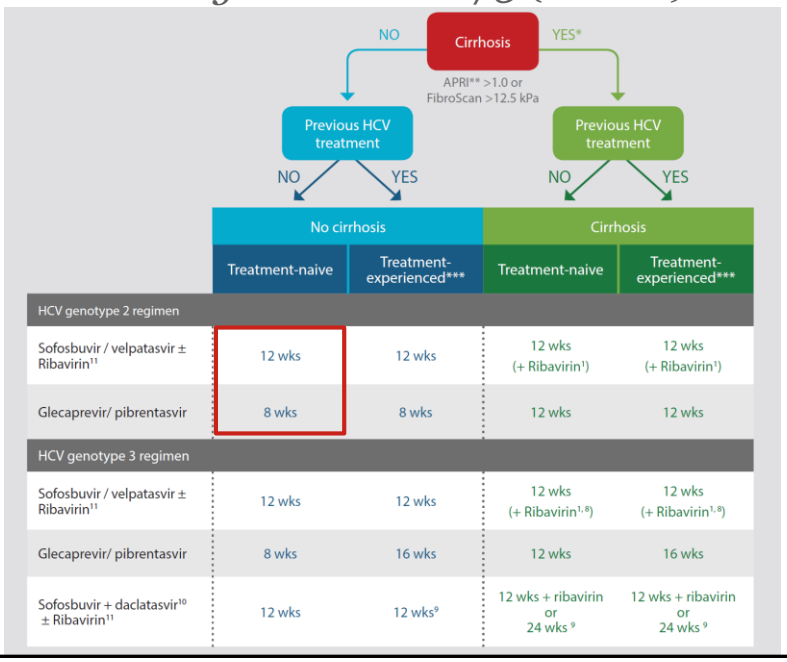
DAA treatment algorithm: GT2/3 (ASHM)



	No cirrhosis		Cirrhosis	
	Treatment-naive	Treatment-experienced***	Treatment-naive	Treatment-experienced***
HCV genotype 2 regimen				
Sofosbuvir / velpatasvir ± Ribavirin[11]	12 wks	12 wks	12 wks (+ Ribavirin[1])	12 wks (+ Ribavirin[1])
Glecaprevir/ pibrentasvir	8 wks	8 wks	12 wks	12 wks
HCV genotype 3 regimen				
Sofosbuvir / velpatasvir ± Ribavirin[11]	12 wks	12 wks	12 wks (+ Ribavirin[1,8])	12 wks (+ Ribavirin[1,8])
Glecaprevir/ pibrentasvir	8 wks	16 wks	12 wks	16 wks
Sofosbuvir + daclatasvir[10] ± Ribavirin[11]	12 wks	12 wks[9]	12 wks + ribavirin or 24 wks[9]	12 wks + ribavirin or 24 wks[9]

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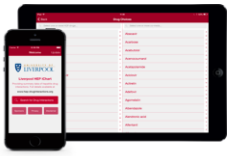
Drug to drug interaction

- **Review all prescription and OTC meds, herbal supplements and other complementary medications**
- **Be alert for interactions with common drugs such as:**
  - Statins
  - Proton pump inhibitors
  - Antiepileptic drugs (e.g. carbamazepine)
  - Birth control preparation (eg. ethinyl oestradiol)
  - Some herbal – esp. St John's Wort
- **Remember: patients rarely tell you all the pills they are taking**

HEP Drug Interactions website
www.hep-druginteractions.org



HEP iChart app
App store | Google Play

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HBV reactivation during DAA Therapy

- Patients at risk: prior, resolved, or active HBV infection
- HBV reactivation (during or after DAA therapy) has been reported in HCV/HBV coinfected patients not on HBV therapy
  - Severity: mild to severe fulminant liver injury (life threatening)
  - Frequency: low to very low
- Seen with different HCV genotypes and DAA combinations
- Mechanism of reactivation unknown
- **Important to screen for HBV prior to starting HCV treatment: HBsAg, HBcAb, HBsAb**

	HBsAg	Anti-HBc	Anti-HBs	Recommended action
Chronic HBV	+	+	-	Consult specialist
Unexposed	-	-	-	Vaccinate
Immune - prior infection	-	+	+	Nil needed
Prior infection - resolved	-	+	-	Consult specialist (low risk of HBV reactivation)
Immune – prior vaccination	-	-	+	Nil needed

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When to consult a specialist

- Patients with advanced fibrosis or cirrhosis
- Patients with extrahepatic manifestations
- Patients with complex co-morbidities
- Patients with renal impairment
- Patients with HIV/HCV or HBV/HCV coinfection
- Patients who failed first line DAA
- Patients with acute HCV

Australian Recommendations for the Management of HCV Infection: A Consensus Statement 2018

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Post-treatment follow up: liver disease and reinfection monitoring

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Confirming cure post-treatment

- **SVR12** = undetectable HCV RNA 12 weeks post treatment completion
  - Don't need another repeat SVR after SVR12 (=cure) but consider on a case by case basis – if significant risk of reinfection, annual HCV RNA testing recommended
- Note that **HCV antibody tests will remain positive after cure and should not be repeated**
  - Important to **warn patients that this can happen** in case the test is repeated by another doctor
- **Treatment failure** = detectable HCV RNA 12 weeks post treatment completion

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Post-treatment follow-up

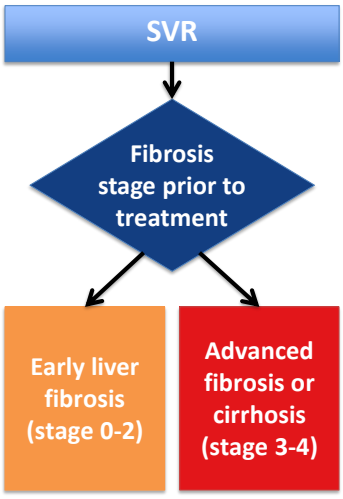
No cirrhosis, normal LFTs at SVR12

- Patients who are cured do not require clinical follow-up for HCV
- Discussion around moving on as "hepatitis C free"
- Ongoing HCV monitoring (annual LFTs and HCV RNA) if potential risk of re-exposure (PWID, HIV+ MSM) or if LFTs become abnormal

Abnormal LFTs at SVR12

- Patients with persistently abnormal LFTs require evaluation for other liver diseases and should be referred for gastroenterology review.
- Check for other causes of liver disease including alcohol, metabolic syndrome

Australian Consensus Statement 2018 (www.hepcguidelines.org.au)



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Hepatitis C online learning

- ASHM eLearning: https://lms.ashm.org.au
- NPS MedicineWise eLearning: https://learn.nps.org.au/mod/page/view.php?id=7278
- mdBriefCase eLearning: http://au-mdbriefcase.lmscentral.net/lms/default.aspx?program_id=16709&section=mp

Hepatitis C web resources

- GESA: http://www.gesa.org.au/resources/hepatitis-c-treatment/
- ASHM: http://www.ashm.org.au
- ASID: https://www.asid.net.au/

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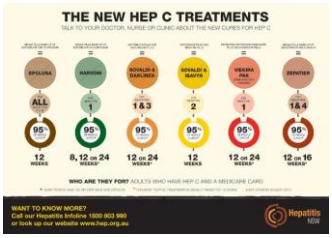
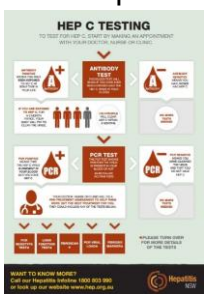
Patient Support and Resources

- Hepatitis NSW https://www.hep.org.au/
- National hepatitis Information Line: **1800 437 222**
- Provide information and support services to people affected by hepatitis (primarily hepatitis C) and to support the reduction of hepatitis C transmission:





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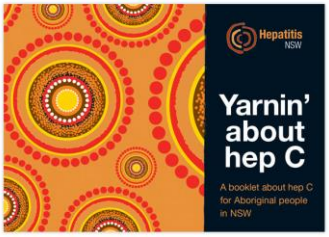
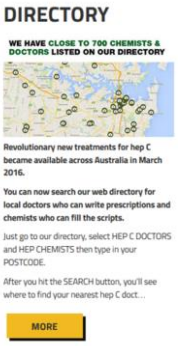
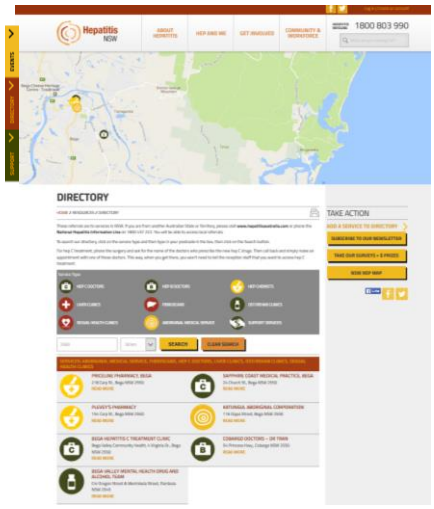
Hepatitis NSW

Directory of local doctors prescribing HCV and dispensing pharmacies: https://www.hep.org.au/





HOW MANY SERVICES ARE LISTED WITHIN YOUR AREA?



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Summary

T
- Screen all people at risk for hepatitis C. Hepatitis C infection can be cured
- Test for HCV to confirm current infection (= anti-HCV +ve and HCV RNA +ve)
- All people with HCV infection should be considered for treatment, including people who inject drugs

R
- Assess for liver fibrosis and other co-morbidities
- Refer patients with cirrhosis, renal failure, HBV or HIV coinfection to a specialist

E
- Evaluate for DDIs at http://hep-druginteractions.org
- Select appropriate treatment regimen, assess adherence

A
- Approval from a specialist to prescribe (using a remote consultation request form or similar) is required if GPs are not experienced in HCV treatment
- Dispensing of S85 scripts are from a community pharmacy

T
- Monitor on treatment and check for SVR 12 weeks after treatment completion
- Tailor post- treatment follow-up according to treatment outcome, liver disease stage, reinfection risk
- Patients with cirrhosis need ongoing lifetime surveillance for liver cancer
- Re-treatment should be offered to people who become reinfected

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Q & A

With thanks to:

Kirby Institute

UNSW SYDNEY

ashm
Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine

Aboriginal Health & Medical Research Council of New South Wales

NSW GOVERNMENT Health

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