Hepatitis C: Cure chronic disease in primary care

GoToWebinar tips & tricks

Where is my control panel?

ASHM: Developing a sustainable HIV, Viral Hepatitis and Sexual Health Workforce
GoToWebinar tips & tricks

You have been placed on “mute” to optimise the learning experience for you and your peers.

Use the question box function to talk to us.

Poll test
QI&CPD Requirements

To be eligible for 3 category 2 QI&CPD points participants must:
• attend the entire session
• complete the evaluation questions which will be emailed to in the next couple of days

Presented by:

Dr David Iser
Gastroenterologist and Hepatologist
St Vincent’s Hospital Melbourne, VIC
### Disclosure of interests

<table>
<thead>
<tr>
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<th>Type of relationship</th>
<th>Entity</th>
<th>Comment</th>
<th>Payment received (Y/N)</th>
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<td>Nil to date</td>
<td>-</td>
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<td>2018</td>
<td>Speaker &amp; Advisory Board</td>
<td>AbbVie MSD</td>
<td>GP education, International Ad Boards</td>
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<td>Speaker &amp; Advisory Board</td>
<td>AbbVie Gilead MSD</td>
<td>GP education, International Ad Board</td>
<td>Y</td>
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</tbody>
</table>

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### Learning outcomes

- Identify who to test, how to test and how to interpret the results
- Assess for liver fibrosis and important co-morbidities
- Decide which patients can be treated and followed in General Practice, and identify patients requiring referral for specialist management
**Hepatitis C prevalence in Australia**

![Map showing hepatitis C prevalence in Australia](image)

- **182,144** Australians living with chronic HCV infection at the end of 2017
- About 80% people infected with HCV through injecting drug use.
- 1 in 5 people with HCV don’t know it

The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia, Annual Surveillance Report 2018

**How do we find the estimated 20% still undiagnosed?**

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**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

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ASHM: Developing a sustainable HIV, Viral Hepatitis and Sexual Health Workforce
Consider your role in the hepatitis C response

Primary care providers have a vital role in:

- Screening
- Hepatitis C management and treatment
- Managing comorbidities – drug use, mental health, other chronic diseases etc.

GPs are increasingly treating hepatitis C

56,968 people in total have been cured during 2015-2017
### Essential steps in treating hepatitis C

1. Identify people at risk
2. Test and diagnose
3. Assess for treatment
4. Discuss and initiate treatment
5. Monitor and follow-up
**How to find undiagnosed patients**

<table>
<thead>
<tr>
<th>New patients</th>
<th>Existing patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test anyone who asks for a test - they may not be comfortable raising their injecting drug use history</td>
<td></td>
</tr>
<tr>
<td>Incorporate a risk assessment into all routine history taking</td>
<td></td>
</tr>
<tr>
<td>Test anyone in a risk group, with risk factors or with a clinical indication</td>
<td></td>
</tr>
<tr>
<td>Consider testing people:</td>
<td></td>
</tr>
<tr>
<td>- planning travel, starting a family, in a new job (for OH&amp;S purposes)</td>
<td></td>
</tr>
<tr>
<td>- with a new or recent change in sexual partner</td>
<td></td>
</tr>
<tr>
<td>- as part of a baseline check</td>
<td></td>
</tr>
<tr>
<td>Test:</td>
<td></td>
</tr>
<tr>
<td>- pregnant women and children born to mothers with HCV</td>
<td></td>
</tr>
<tr>
<td>- partners of people with known HCV</td>
<td></td>
</tr>
</tbody>
</table>

Consider testing if clinical indications: |
- jaundice, fatigue |
- unexplained abnormal LFTs |
- known HIV or HBV infection

Consider: |
- conducting a retrospective case audit of patients in your practice, particularly those from priority populations or with abnormal LFTs. |
- testing ‘Baby Boomers’

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**Case discussion - Tim**
Case 1: Tim – history and examination

- 56 year old office worker
- New to your practice after moving into the area
- Experiencing extreme tiredness lately
- Otherwise well, no regular medications
- Minimal alcohol
- During history taking, he tells you he briefly injected drugs in 1980
- Physical examination = no signs of cirrhosis

What do you do next?

Test anyone who:

- Has ever injected drugs (including people who currently inject drugs)
- Has been in prison
- Has tattoos or body piercings
- Identifies as Aboriginal and Torres Strait Islander
- Is from a high-prevalence region (Egypt, Pakistan, Mediterranean, Eastern Europe, Africa and Asia)
Test anyone who:

- Has had sex with an HCV+ve person (especially men who have sex with men and people with HCV-HIV coinfection)
- Received a blood transfusion or organ transplantation before 1990
- Was born to an HCV positive mother
- Has HIV or hepatitis B
- Has liver disease - even an ALT slightly out of range
  (ALT normal range: 5-30 IU/L for men; 5-19 IU/L for women)
- Has had a needle-stick injury


Polling question 1
Hepatitis C transmission risks

<table>
<thead>
<tr>
<th>Sexual activity without blood-blood contact is considered low risk. Transmission occurs in ~5% of monogamous serodiscordant heterosexual couples (risk of 1 in 190,000 sexual contacts)</th>
<th>There are no risks in sharing food, drinks, cutlery, crockery and drink-ware</th>
<th>MTCT risk is approx. 5%. Transmission dependent on viral load (lower risk &lt;10⁶). Possible ↑ risk: active IDU, premature rupture of membranes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased sexual transmission risk in MSM, unprotected anal intercourse and people with HCV-HIV coinfection</td>
<td>There are no risks in hugging, kissing, touching a person living with HCV</td>
<td>Mode of delivery (vaginal vs. caesarean) and breastfeeding are not associated with transmission</td>
</tr>
<tr>
<td>Ulcerative STIs (e.g. syphilis) ↑ risk</td>
<td>There are no risks associated with sneezing or coughing, toilet use or mosquito/other insect bites</td>
<td>Babies born to HCV +ve mothers should not be tested until &gt;18 months due to presence of maternal antibodies</td>
</tr>
<tr>
<td>Sexual contact causing bleeding ↑ risk</td>
<td>Avoid sharing of razors, toothbrushes and nail clippers etc as ↑ risk</td>
<td>Breastfeeding is recommended unless there are cracked/bleeding nipples</td>
</tr>
</tbody>
</table>

**Case 1: Tim – risk factor**

- Risk factor (injecting drug use history) indicates you should suggest testing for HCV

**What tests do you order?**
Essential steps in treating hepatitis C

1. Identify people at risk
2. Test and diagnose
3. Assess for treatment
4. Discuss and initiate treatment
5. Monitor and follow-up

Polling question 2
Case 1: Tim – how to test for hepatitis C

**Could it be hepatitis C?**

- Patient request
- Abnormal liver function test (LFT)
- Doctor concern

**Presence of risk factors**
- Injection drug use
- Sharing of injection equipment
- Birth in high prevalence country
- Blood transfusions and blood products before 1990 in Australia
- Unsafe medical and dental procedures
- Contact with an infected person
- Time in prison
- Needlestick injury
- Mother to child transmission is around 3%
- Household transmission is very rare
- Sexual transmission is rare but can occur in certain populations, such as men who have sex with men (MSM) or those who are human Immunodeficiency Virus (HIV) positive

**Jaundice or acute hepatitis**

**Order:**

- Hepatitis C antibody (also called anti-HCV/HCV Ab) & LFTs

If possible acute hepatitis, also order HCV RNA

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Case 1: Tim – test result

- Hepatitis C Ab +ve

What does this result mean?
There are 2 tests needed to diagnose hepatitis C

- Ab (antibody test/anti-HCV) EVER has come into contact with HCV
- RNA + Infected with the virus NOW

We also need other tests/investigations:
- FBE, LFTs, urea and electrolytes, eGFR, INR
- HBV, HIV and HAV serology
- Pregnancy test for women of child-bearing age
Test for HBV before commencing HCV treatment

Order all 3 tests: HBsAg, anti-HBc, anti-HBs

<table>
<thead>
<tr>
<th></th>
<th>HBsAg</th>
<th>Anti-HBc</th>
<th>Anti-HBs</th>
<th>Recommended action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic HBV</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Consult specialist</td>
</tr>
<tr>
<td>Unexposed</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Vaccinate</td>
</tr>
<tr>
<td>Immune – prior infection</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>Nil needed</td>
</tr>
<tr>
<td>Prior infection - resolved</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>Consult specialist (low risk of HBV reactivation)</td>
</tr>
<tr>
<td>Immune – prior vaccination</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>Nil needed</td>
</tr>
</tbody>
</table>

HBV reactivation (during or after DAA therapy) has been reported in HCV/HBV coinfected patients not on HBV therapy

Case 1: Tim – test results

- FBC: Hb 142, WCC 6.0, Plt 270
- EUC: Na 134, K 4.3, eGFR > 90
- LFT: Alb 36, Bil 16, ALT 52, AST 46, GGT 111, ALP 101
- Fasting Chol 5.2, TG 2.3, HDL 1.6, LDL 3.5
- HCV RNA +ve
- HBsAg-ve, HBcAb-ve, HBsAb 56
- HIV-ve
- HAV IgG+ve

Does Tim have hepatitis C?
What else should we consider?
Essential steps in treating hepatitis C

1. Identify people at risk
2. Test and diagnose
3. Assess for treatment
4. Discuss and initiate treatment
5. Monitor and follow-up

Assess virus, liver and patient factors

- Genotype
- HCV viral load
- Fibrosis stage
- Other liver disease
- Alcohol and drugs
- Pregnancy
- Medications
- Comorbidities
  - e.g. renal failure
The importance of liver fibrosis assessment

METAVIR Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>F0</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosis (scarring)</td>
<td>No damage</td>
<td>Mild</td>
<td>Moderate</td>
<td>Advanced</td>
<td>Severe</td>
</tr>
<tr>
<td>Liver tests, platelet count, coags</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APRI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>or FIB-4, ELF test, Hepascore</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It is essential to assess for advanced fibrosis (F3) or cirrhosis (F4).

Cirrhosis determination is needed to:

- Select appropriate HCV treatment regimen
  - Poorer response rates for some treatments when cirrhosis is present
  - Some options of shortened durations only if cirrhosis is excluded
- Inform when special referral is required
- Establish requirement for long term follow up after SVR; including HCC surveillance

Cirrhotic status is currently required for PBS approval

How to assess liver fibrosis

History:
- Length of infection
- Presence of co-morbidities such as alcohol use

Physical examination:
- Jaundice, ascites, varices, encephalopathy

Laboratory tests:
- Liver tests, platelet count, coags
- Serum biomarker:
  - APRI
  - or FIB-4, ELF test, Hepascore

Radiological imaging:
- US, CT, MRI

Fibroscan or shear wave elastography

If APRI<1, cirrhosis unlikely

If APRI>1, assess further for cirrhosis

No single test is accurate enough
Using non-invasive serum bio markers to assess for cirrhosis – APRI

- Non-invasive serum markers can be used for assessing liver fibrosis stage
- In general, they have good performance characteristics for excluding the presence of cirrhosis.
- **APRI** is a simple, easily calculated method to predict significant, severe fibrosis or cirrhosis

Online calculator e.g. https://www.hepatitisc.uw.edu/page/clinical-calculators/apri

Calculating and interpreting an APRI score

**APRI (AST Platelet Ratio Index) Score:**

\[
\text{APRI} = \left( \frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}} \right) \cdot \frac{\text{Platelet count (10⁹/L)}}{100}
\]

- Fluctuating AST and/or platelet count impacts on reliability of APRI
- **If APRI >1, need further assessment to exclude cirrhosis**
Case 1: Tim – APRI score calculation

**AST to Platelet Ratio Index (APRI) Calculator**

This is an AST to Platelet Ratio Index calculator tool. Enter the required values to calculate the APRI value. The APRI Score will appear in the oval on the far right (highlighted in yellow). Most laboratories use 40 IU/L as the value for the AST upper limit of normal.

\[
\text{APRI} = \frac{\text{AST Level (IU/L)}}{\text{AST (Upper Limit of Normal) (IU/L)}} \times \frac{\text{Platelet Count (10^9/L)}}{270} 
\]

**Interpretation:**

In a meta-analysis of 40 studies, investigators concluded that an APRI score greater than 1.0 had a sensitivity of 79% and specificity of 72% for predicting cirrhosis. In addition, they concluded that APRI score greater than 0.7 had a sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis.

Tim does not need further assessment – treat him as non-cirrhotic.

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**Determining cirrhosis using Fibroscan (if available)**

The stiffer the liver is, the greater the degree of fibrosis.

**Good at determining normal liver and cirrhosis**

Limited discrimination between intermediate levels of fibrosis (F1-F3)

\[ \text{HCV cirrhosis} = \text{liver stiffness measurement} > 12.5 \text{ kPa} \]
Polling question 3

Polling question 4
Remember: no single test is accurate enough! Use All Your Tools to Assess the Liver

- Clinical examination
- AST/ALT ratio >2 suggest advanced fibrosis/cirrhosis if no alcohol
- Platelet count <150,000 especially <100,000 suggest portal hypertension
- APRI ≥ 2 suggest cirrhosis
- Fibroscan ≥ 9.5 suggest advanced fibrosis and ≥ 12.5 suggest cirrhosis
- Abdo ultrasound: splenomegaly or portal vein diameter ≥13 mm suggest portal hypertension

Assess alcohol use

Strong association between excessive alcohol use and liver disease progression / HCC

- Increased risk of developing cirrhosis in people with HCV
- Decreased survival, increases risk of HCC
- Light-moderate alcohol use increases risk of HCC in patients with HCV infection and cirrhosis

Provide advice to stop and interventions to reduce alcohol consumption

BUT continued alcohol consumption or current injecting should not be used as a reason for withholding treatment
### Case 1: Tim – recap what we know so far

<table>
<thead>
<tr>
<th>Confirm chronic HCV</th>
<th>PCR +ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of infection</td>
<td>? 1980</td>
</tr>
<tr>
<td>Genotype</td>
<td>Unknown</td>
</tr>
<tr>
<td>Viral load</td>
<td>Unknown</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>APRI 0.426 – no cirrhosis</td>
</tr>
<tr>
<td>Co-morbidity liver</td>
<td>Nil</td>
</tr>
<tr>
<td>Co-morbidity other</td>
<td>Nil</td>
</tr>
<tr>
<td>Co-infection</td>
<td>Nil</td>
</tr>
<tr>
<td>Other medications</td>
<td>Nil</td>
</tr>
<tr>
<td>Previous HCV treatment</td>
<td>Nil</td>
</tr>
<tr>
<td>Cirrhosis screening</td>
<td>Not needed</td>
</tr>
</tbody>
</table>

**What else do you need to know before treating Tim?**

### Case 1: Tim - further testing results

- Genotype 1a
- HCV RNA 440,000IU/mL

**Note:**
- Current PBS requirement to establish the genotype
- This was more relevant with earlier drug regimens; less relevant now with pangenotypic regimens
- PBS requirements likely to be removed this year

**What should you do next?**

**Should you treat Tim?**
### Provide general support and advice if hepatitis C is confirmed

<table>
<thead>
<tr>
<th>General Support</th>
<th>Lifestyle Measures</th>
<th>Medical Issues</th>
<th>Prevent Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Review understanding of HCV, including health beliefs</td>
<td>• Reduce or cease alcohol and tobacco use</td>
<td>• Avoid hepatotoxic medications</td>
<td>• Reinforce safer injecting behaviours</td>
</tr>
<tr>
<td>• Consider the impacts of stigma and discrimination</td>
<td>• Maintain a healthy diet, exercise and lose weight if indicated</td>
<td>• Vaccinations: hepatitis A and B if not immune</td>
<td>• Needle and syringe programs, opioid substitution therapy if indicated</td>
</tr>
<tr>
<td>• Referral to counselling, peer-support organisation</td>
<td>• Check for diabetes, dyslipidaemia</td>
<td>• Check for advanced fibrosis</td>
<td></td>
</tr>
</tbody>
</table>

### Consider the impact of stigma and discrimination

What are some consequences of stigma and discrimination in healthcare settings and what strategies you can incorporate in your practice to address these?

[https://vimeo.com/264925003](https://vimeo.com/264925003)
Preventing HCV transmission and reinfection

Multiple prevention strategies are needed

• Treatment alone is not enough: transmission must be stopped
• Treat injecting social network
• Treat reinfection
• Among PWID, harm reduction strategies are very effective:
  • Current opioid substitution treatment (OST) reduces HCV acquisition risk by 50%
  • High coverage needle syringe programmes (NSP) reduce HCV acquisition risk by ~21%
  • In combination, both high-coverage NSP and OST can reduce risk of acquiring HCV by 76%


Achieving cure does not protect against HCV reinfection

SVR is durable in the majority of patients 5 years after treatment

5-Year Recurrence Risk After SVR

<table>
<thead>
<tr>
<th></th>
<th>5-Year Recurrence Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-Risk</td>
<td>0.95%</td>
</tr>
<tr>
<td>High-Risk</td>
<td>10.67%</td>
</tr>
<tr>
<td>HIV/HCV Confected</td>
<td>15.02%</td>
</tr>
</tbody>
</table>

- HCV mono-infected 43 studies (n = 7,969)
- IDUs or prisoners 14 studies (n = 711)
- 4 studies (n = 309)


ASHM: Developing a sustainable HIV, Viral Hepatitis and Sexual Health Workforce
**Essential steps in treating hepatitis C**

1. Identify people at risk
2. Test and diagnose
3. Assess for treatment
4. **Discuss and initiate treatment**
5. Monitor and follow-up

**Polling question 5**
Offer treatment to everyone with hepatitis C

Benefits

Population
- Reduce transmission
- HCV eradication

Individual
- Reduce liver disease progression
- Improved clinical outcomes

Individual and Population Benefits:

HCV DAA Therapy
- All oral options
- Few side-effects
- >90% cure rates (SVR)
- Short course of treatment
- Little monitoring while on treatment

Improved quality of life

Treatment is easy and effective

Treatment should be offered to everyone with hepatitis C

ASHM: Developing a sustainable HIV, Viral Hepatitis and Sexual Health Workforce
Case 1: Tim – discuss the benefits of cure

What benefits can Tim experience to his physical and mental health after curing hepatitis C?

Recommended PBS-listed DAAs in Australia in 2019

Pangenotypic: Genotypes 1–6

- Sofosbuvir/Velpatasvir (EPCLUSA®)
- Glecaprevir/Pibrentasvir (MAVIRET™)

Genotype 1
- Sofosbuvir/Ledipasvir (HARVONI®)
- Grazoprevir/Elbasvir (ZEPATIER™)
### Hepatitis C treatment regimens – for treatment naïve and compensated liver disease

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Regimen</th>
<th>Dose</th>
<th>Pills per day</th>
<th>Treatment duration - no cirrhosis</th>
<th>Treatment duration - cirrhosis</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended regimens</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>GLE/PIB</td>
<td>300/120 mg</td>
<td>3</td>
<td>8 wks</td>
<td>12 wks</td>
<td>With food</td>
</tr>
<tr>
<td>All</td>
<td>SOF/VEL</td>
<td>400/100 mg</td>
<td>1</td>
<td>12 wks</td>
<td>12 wks*</td>
<td>+/- food</td>
</tr>
<tr>
<td>1</td>
<td>SOF/LDV</td>
<td>90/400 mg</td>
<td>1</td>
<td>8 or 12 wks</td>
<td>12 wks</td>
<td>+/- food</td>
</tr>
<tr>
<td>1 + 4</td>
<td>GZR/EBR</td>
<td>50/100 mg</td>
<td>1</td>
<td>12 wks</td>
<td>12 wks</td>
<td>+/- food</td>
</tr>
<tr>
<td><strong>Additional regimens</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 + 3</td>
<td>SOF+DCV</td>
<td>400mg+60mg</td>
<td>2</td>
<td>12 wks</td>
<td>12 or 24 wks</td>
<td>+/- food</td>
</tr>
<tr>
<td>All</td>
<td>SOF/VEL/VOX**</td>
<td>400/100/100 mg</td>
<td>1</td>
<td></td>
<td></td>
<td>With food</td>
</tr>
</tbody>
</table>

* For Sofosbuvir + Velpatasvir: consider adding Ribavirin for GT3 compensated cirrhosis
** For salvage therapy only, not PBS listed yet

### 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

**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

**Similarities**
- Pan-genotypic
- Risk of reactivating HBV
- Adverse reactions: Headache and Fatigue
Polling question 6

DAAs are generally very well tolerated

<table>
<thead>
<tr>
<th>HCV Regimen</th>
<th>Main Adverse Events Observe in patients in clinical trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir / Velpatasvir</td>
<td>Headache, fatigue, nausea, nasopharyngitis</td>
</tr>
<tr>
<td>‘EPCLUSA®’</td>
<td></td>
</tr>
<tr>
<td>Glecaprevir / Pibrentasvir</td>
<td>Headache, fatigue, nausea</td>
</tr>
<tr>
<td>‘MAVIRET®’</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir / Ledipasvir</td>
<td>Fatigue, headache, nausea, diarrhoea</td>
</tr>
<tr>
<td>‘HARVONI®’</td>
<td></td>
</tr>
<tr>
<td>Elbasvir / Grazoprevir</td>
<td>Fatigue, headache, nausea</td>
</tr>
<tr>
<td>‘ZEPATIER™’</td>
<td></td>
</tr>
</tbody>
</table>

### Case 1: Tim – treatment options

<table>
<thead>
<tr>
<th>Treatment Regimen</th>
<th>HCV genotype</th>
<th>No cirrhosis</th>
<th>Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glecaprevir + Pibrentasvir</strong> (Maviret): 8 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sofosbuvir + Ledipasvir</strong> (Harvoni): 8 weeks may be considered if HCV RNA level is $&lt; 6 \times 10^6$ IU/mL in people without cirrhosis and who are treatment-naïve</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. What treatment options could be considered for Tim?
2. Which treatment option would you prescribe?

* For Sofosbuvir + Velpatasvir: consider adding Ribavirin for GT3 compensated cirrhosis

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### Assess for potential drug interactions

Review all prescription, OTC meds, herbal supplements and complementary medications.

Be alert for interactions with common drugs such as:

- Statins
- Proton pump inhibitors
- Antiepileptic drugs (e.g. carbamazepine)
- Birth control preparation (e.g. ethinyl oestradiol)
- Some herbal – esp. St John’s Wort

**Remember:** patients rarely tell you all the pills they are taking

Are any drug-drug interactions relevant for Tim?

- In Tim’s case, there are no DDIs to consider

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ASHM: Developing a sustainable HIV, Viral Hepatitis and Sexual Health Workforce
Discuss adherence strategies

1. Are there any consequences if Tim misses a few doses?
2. What strategies could be recommended to Tim to support adherence?

**Recommend 100% adherence**

- Discuss adherence at every visit
  - *What is affecting adherence?*
  - *How does the patient think this may be improved?*
- Check for side effects
- Advise that occasional missed doses may not affect outcome
- Involve and empower patient in decisions about treatment

**Strategies:**

- Pill box
- Dosing time link to routine
- Treatment calendar with important dates
  - Start date
  - Refill due
  - Labs due
  - Appointments
- Mobile phone alarms
- Looping in caregivers
- Supervised dosing (e.g., at methadone clinic)

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**Gain specialist approval to treat**

If not experienced in treating hepatitis C, seek specialist approval via fax, email or phone or use one of these methods:

**Remote Consultation Request for Initiation of Hepatitis C Treatment Form**
- Download from:
  - [http://www.hepcguidelines.org.au](http://www.hepcguidelines.org.au)

**Reach-C online form**
- The turnaround time for specialist approval is 24 hours
- Complete form at:
When to consult with or refer patients to 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

Essential steps in treating hepatitis C

1. Identify people at risk
2. Test and diagnose
3. Assess for treatment
4. Discuss and initiate treatment
5. Monitor and follow-up
Monitoring on treatment

Monitoring requirements are generally minimal

Routine monitoring for an 8–12 week treatment regimen:

<table>
<thead>
<tr>
<th>Week</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>FBE, LFTs, EUC/eGFR, HCV RNA level (quantitative)</td>
</tr>
<tr>
<td>Week 8</td>
<td>*LFTs (if on Grazoprevir/Elbasvir)</td>
</tr>
<tr>
<td>Week 12 post (SVR12)</td>
<td>LFTs, HCV RNA (qualitative)</td>
</tr>
</tbody>
</table>

- *People treated with elbasvir plus grazoprevir should have LFTs tested at week 8 to screen for hepatotoxicity.
- Patients taking ribavirin may require FBE at week 2 and week 4 and then every 4 weeks.
- Patients with cirrhosis require HCC screening by liver US every 6 months.

Closer monitoring required for patients with cirrhosis, especially decompensated cirrhosis, poor adherence and if risk of reinfection


Case 1: Tim – treatment, monitoring and follow-up

- Tim is treated with Sofosbuvir/Ledipasvir for 8 weeks
- Reviewed at week 4 (consultation or phone): slight headache, requiring no treatment. No missed doses
- Seen at 12 weeks after the end of treatment with normal LFT and HCV RNA-ve (SVR12)

Is Tim cured?
Does Tim need any further follow-up?
### Confirming cure

- **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 risk of reinfection is high, test yearly.

- **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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### Polling question 7
Determining post-treatment follow-up: no cirrhosis

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+ve, MSM) or if LFTs 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.

In Tim’s case, he does not need any further follow-up

Determining post-treatment follow-up in patients with advanced fibrosis/cirrhosis

SVR  

Fibrosis stage prior to treatment

Early liver fibrosis (stage 0-2)  
Advanced fibrosis or cirrhosis (stage 3-4)

Advanced fibrosis / Cirrhosis and SVR12

• Routine follow up at least 2 times per year
• Patients with evidence of cirrhosis require long-term monitoring and should be enrolled in screening for:
  o HCC
  o oesophageal varices
  o osteoporosis
• Monitor for progression of liver disease. Look for signs of decompensation:
  o Oedema
  o Ascites
  o Encephalopathy
  o Bleeding
• Calculate MELD score (bilirubin, creatinine, INR)
  o Contact hepatologist if rising
Recommendations for HCC surveillance after cure

Who?
- People with severe fibrosis or cirrhosis (F3 or F4)
- Unclear status: Intermediate stages of fibrosis plus comorbidity with risk for HCC
  - Diabetes, alcohol abuse, fatty liver, older (≥age 60-65 y)

How?
- Abdominal ultrasound every 6 months
- AFP every 6 months
  - Predictive value higher in patients who have achieved SVR

If AFP or ultrasound is abnormal, refer to specialist

Other management issues

We’ve talked through a simple case which is indicative of about 80% of patients that you will manage.

Here are some other management issues you may encounter:
- Treatment-experienced patients
- Pregnancy
- Treatment failure
Treatment protocols for treatment-experienced

There are **different treatment regimens** for treatment-experienced people with HCV infection.

Check the:

- General Statement for Drugs for the Treatment of Hepatitis C
- Australian Recommendations for the Management of Hepatitis C Virus Infection: A Consensus Statement
  - [www.hepcguidelines.org.au](http://www.hepcguidelines.org.au)
  - or [www.gesa.org.au](http://www.gesa.org.au)

Polling question 8
Use of DAAs in pregnancy is contraindicated

Screen for pregnancy pre-treatment and periodically during treatment

Ribavirin free regimens
- Pregnancy category B
- Avoid therapy during pregnancy or lactation
- Recommend contraception during therapy
- According to expert consensus, the washout period for DAAs is 4 weeks

> Ribavirin is teratogenic - avoid during pregnancy

Refer people who do not respond to hepatitis C treatment

Treatment failure is uncommon with DAAs

- Specialist referral is recommended with quantitative HCV RNA & genotype results
- May be relapse or reinfection
- People who become reinfected should be retreated
Summary: essential steps in treating hepatitis C

1. Identify people at risk of HCV infection
2. Test and diagnose
3. Assess for treatment
4. Discuss and initiate treatment
5. Monitor and follow-up

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