



## **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

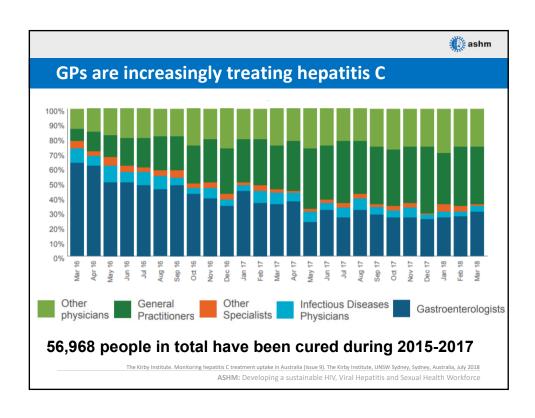
Monitoring hepatitis C treatment uptake in Australia. Issue #9 July 2018. The Kirby Institute.

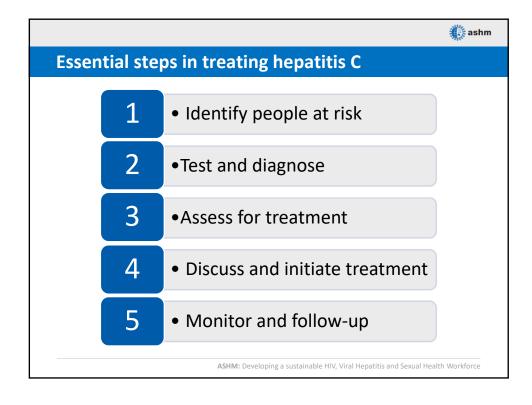


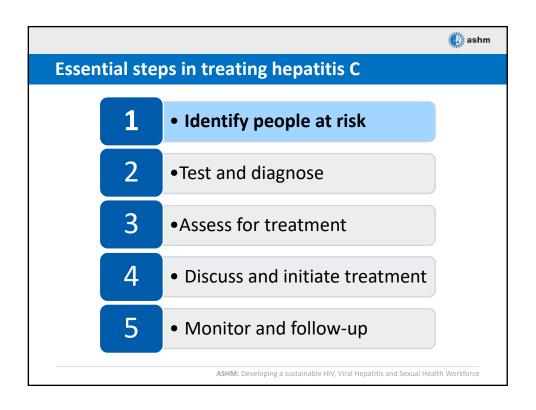
# Consider your role in the hepatitis C response

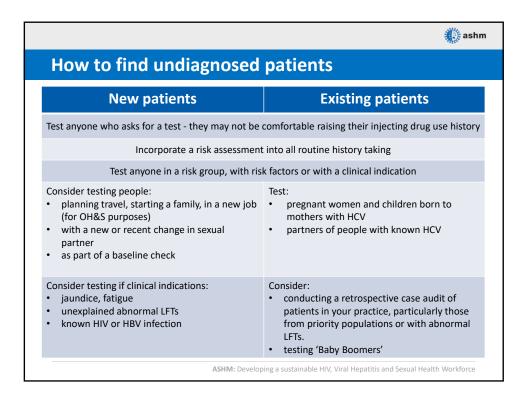
#### Primary care providers have a vital role in:

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









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Case discussion - Tim	
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# **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?

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# ashm

## 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)













Adapted from: Hepatitis C Virus Infection Consensus Statement Working Group. Australian recommendations for the management of hepatitis C virus infection: a consensus statement (Sept 2018). Table 1

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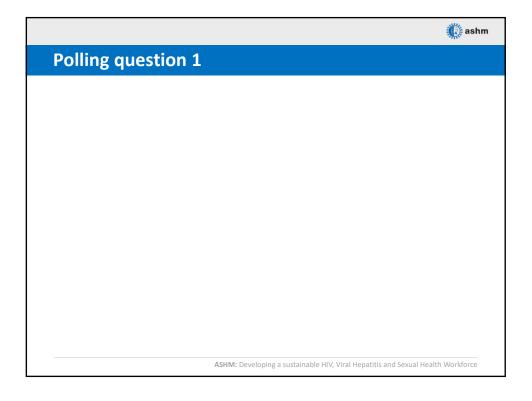


# Test anyone who:

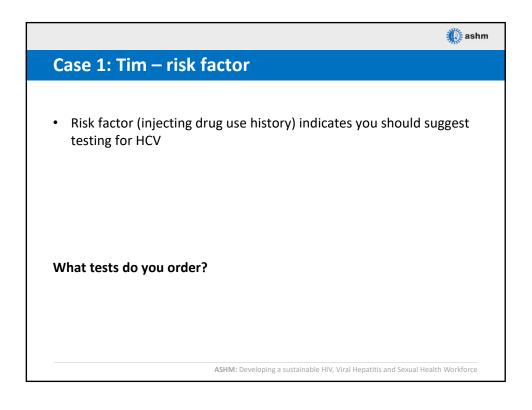
- Has had sex with an HCV+ve person (especially men who have sex with men and people with HCV-HIV coinfection)
- Received a blood transfusion or organ transplantation before 1990
- · Was born to an HCV positive mother
- Has HIV or hepatitis B
- Has liver disease even an ALT slightly out of range (ALT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

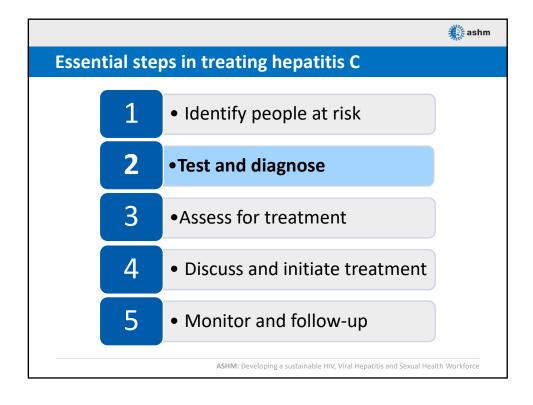
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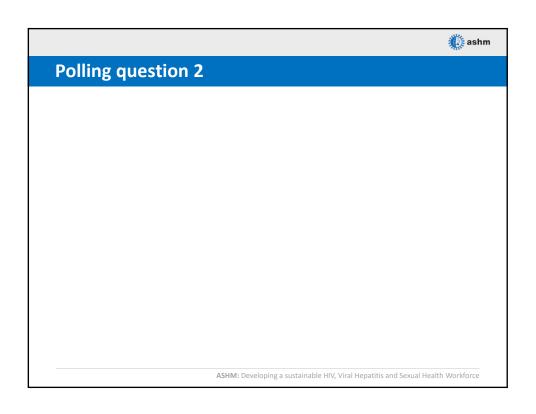
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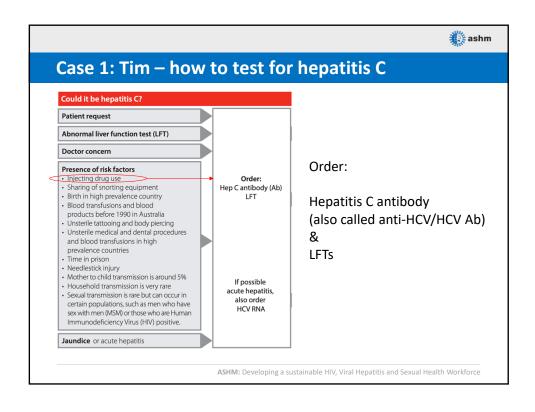


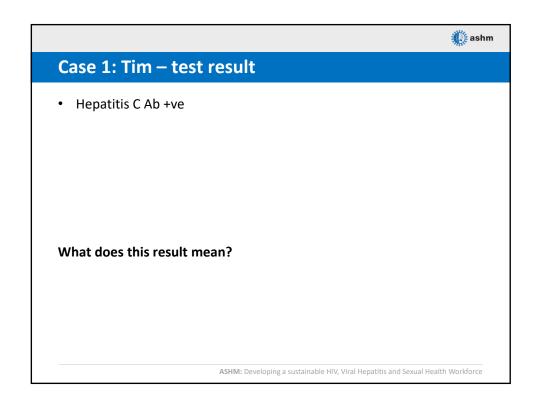
lepatitis C transmission risks							
Sexual	Household	Mother to child transmission					
Sexual activity without blood- blood contact is considered low risk. Transmission occurs in ~5% of monogamous serodiscordant heterosexual couples (risk of 1 in 190,000 sexual contacts)	There are no risks in sharing food, drinks, cutlery, crockery and drink-ware	MTCT risk is approx. 5%. Transmission dependent on viral load (lower risk <10 <sup>6</sup> ) Possible ↑ risk: active IDU, premature rupture of membranes					
Increased sexual transmission risk in MSM, unprotected anal intercourse and people with HCV-HIV coinfection	There are no risks in hugging, kissing, touching a person living with HCV	Mode of delivery (vaginal vs. caesarean) and breastfeeding are not associated with transmission					
Ulcerative STIs (e.g. syphilis) ↑ risk	There are no risks associated with sneezing or coughing, toilet use or mosquito/other insect bites	Babies born to HCV +ve mothers should not be tested until >18 months due to presence of maternal antibodies					
Sexual contact causing bleeding ↑ risk	Avoid sharing of razors, toothbrushes and nail clippers etc as ↑ risk	Breastfeeding is recommended unless there are cracked/bleeding nipples					

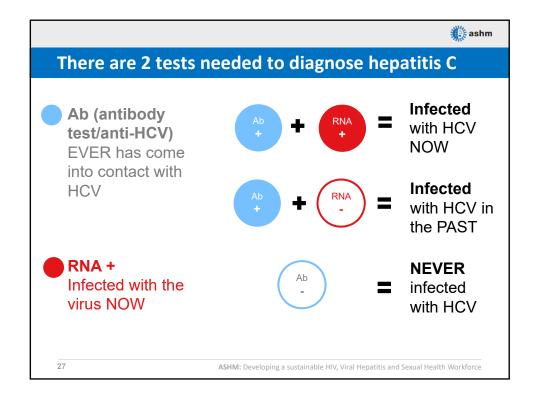














# Perform other investigations if hepatitis C suspected

### 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

	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

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

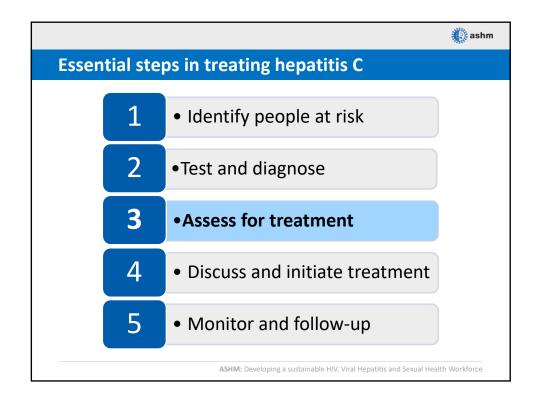
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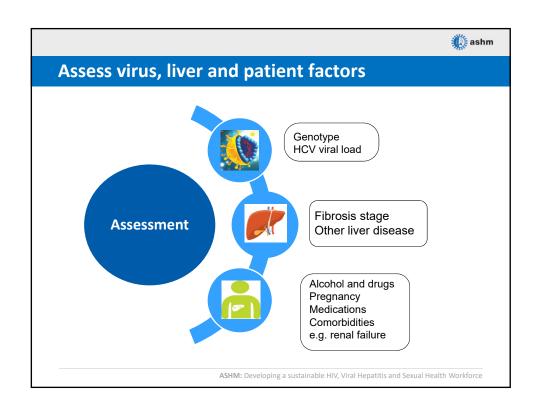


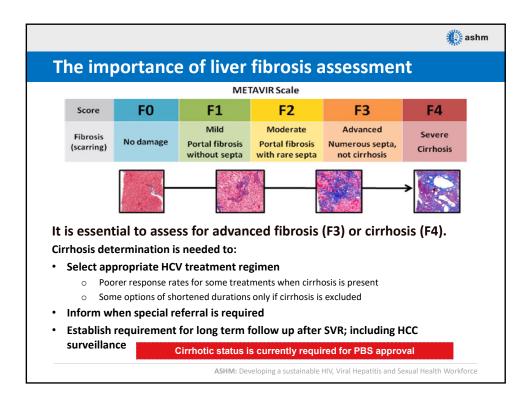
## Case 1: Tim – test results

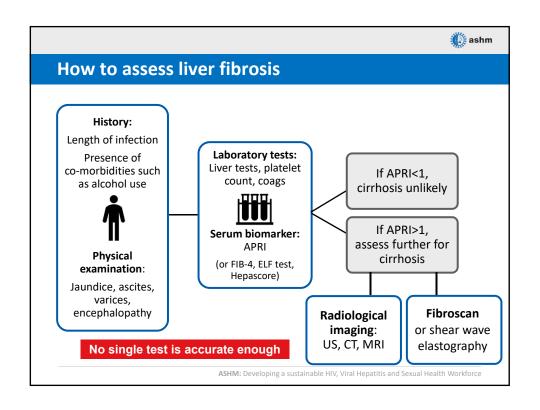
- FBC: Hb 142, WCC 6.0, Plt 270
- EUC: Na 134, K 4.3, eGFR > 90
- LFT: Alb 36, Bil 16, ALT 52, AST 46, GGT 111, ALP 101
- Fasting Chol 5.2, TG 2.3, HDL 1.6, LDL 3.5
- HCV RNA +ve
- HBsAg-ve, HBcAb-ve, HBsAb 56
- HIV-ve
- HAV IgG+ve

Does Tim have hepatitis C? What else should we consider?











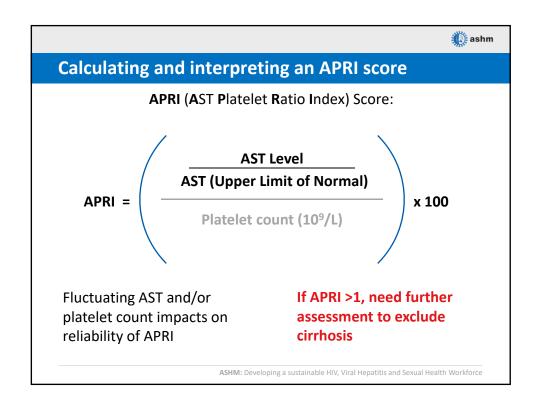
# Using non-invasive serum bio markers to assess for cirrhosis – APRI

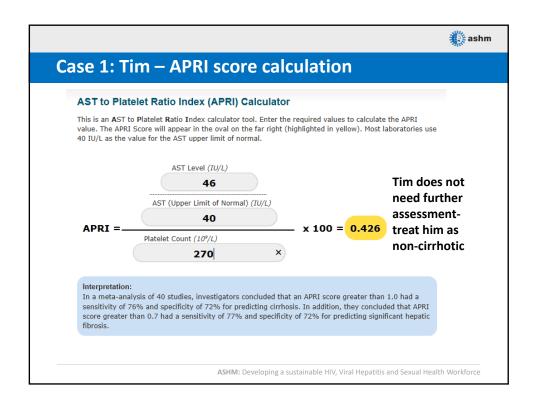
- Non-invasive serum markers can be used for assessing liver fibrosis stage
- In general, they have good performance characteristics for excluding the presence of cirrhosis.
- APRI is a simple, easily calculated method to predict significant, severe fibrosis or cirrhosis

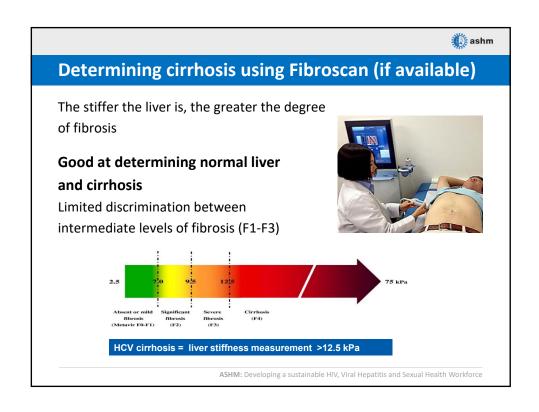


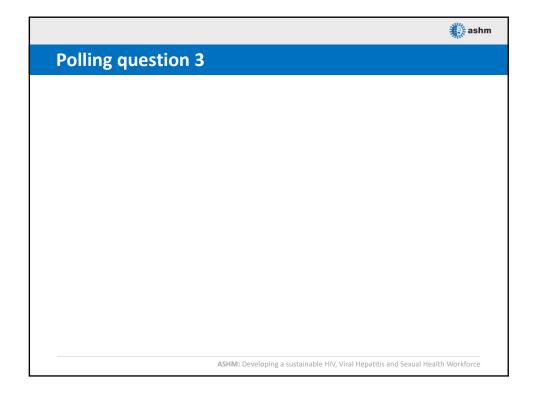
Online calculator e.g.

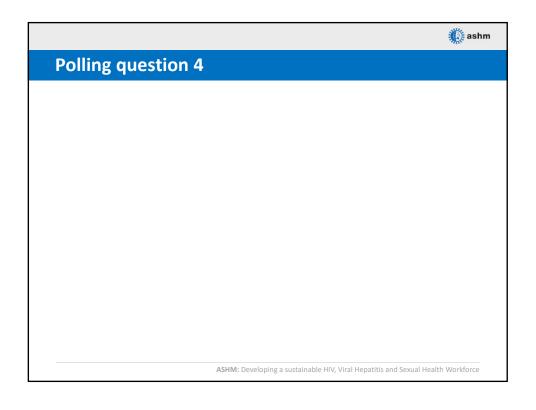
https://www.hepatitisc.uw.edu/page/clinical-calculators/apri













# 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

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#### Assess alcohol use

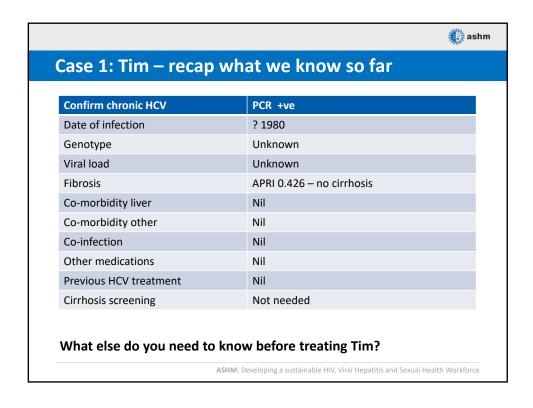
Strong association between excessive alcohol use and liver disease progression / HCC

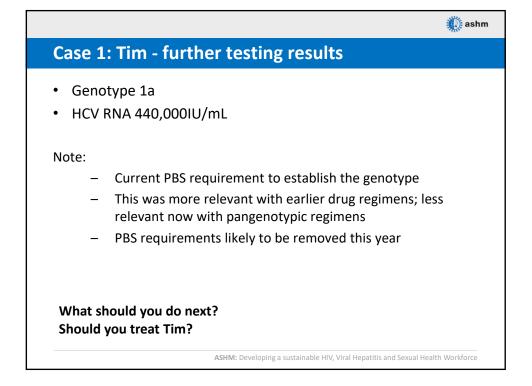
- Increased risk of developing cirrhosis in people with HCV
- Decreased survival, increases risk of HCC
- Light-moderate alcohol use increases risk of HCC in patients with HCV infection and cirrhosis

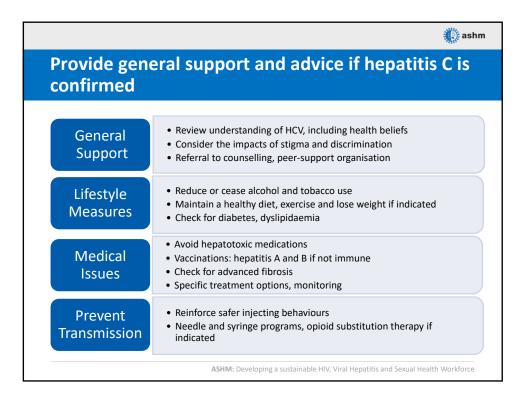
Provide advice to stop and interventions to reduce alcohol consumption

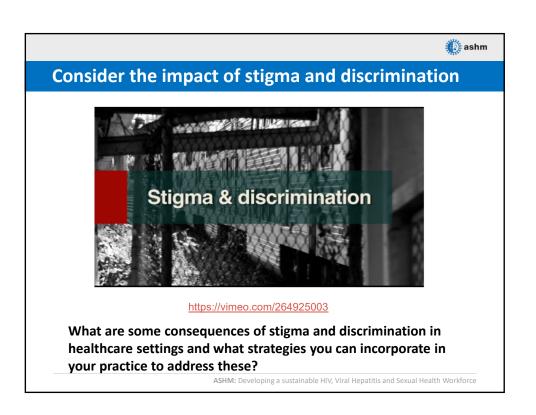


BUT continued alcohol consumption or current injecting should not be used as a reason for withholding treatment









# Preventing HCV transmission and reinfection

#### Multiple prevention strategies are needed

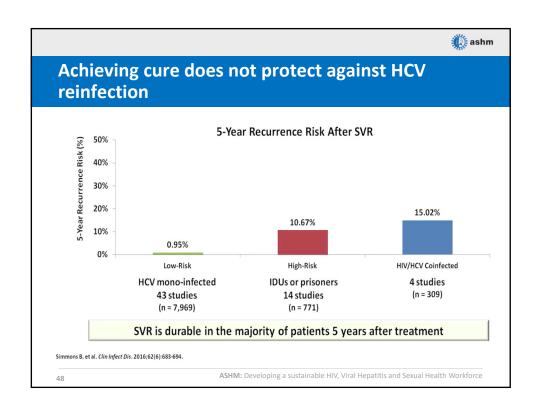
- Treatment alone is not enough: transmission must be stopped
- · Treat injecting social network
- · Treat reinfection

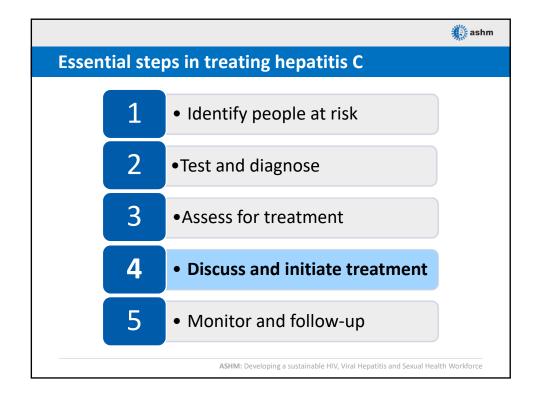


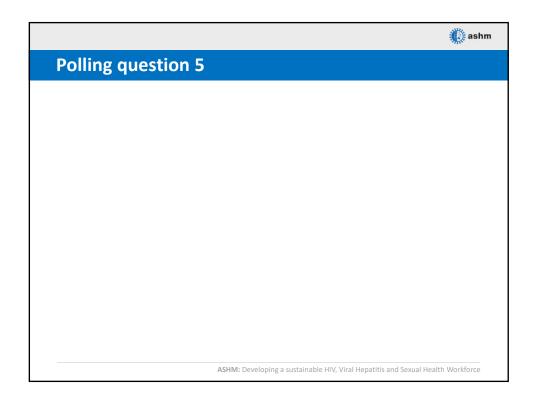
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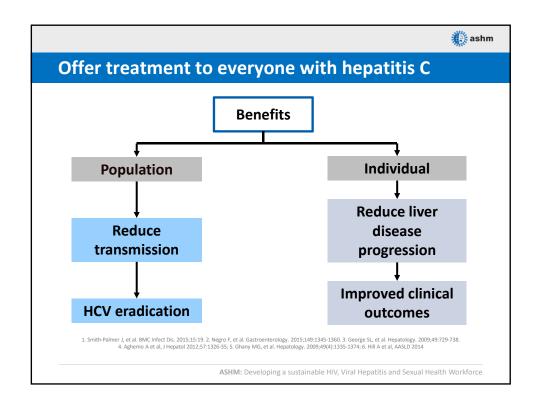
- Among PWID, harm reduction strategies are very effective:
  - Current opioid substitution treatment (OST) reduces HCV acquisition risk by 50%
  - High coverage needle syringe programmes (NSP) reduce HCV acquisition risk by ~21%
  - In combination, both high-coverage NSP and OST can reduce risk of acquiring HCV by 76%

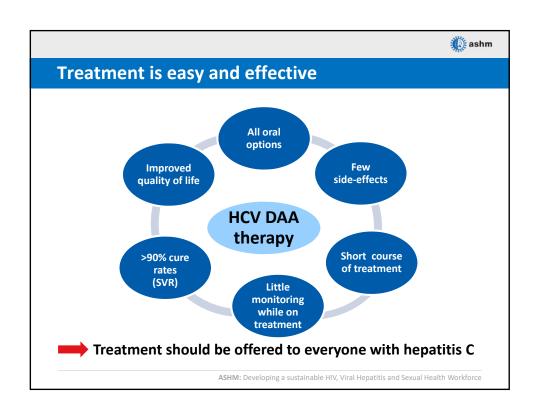
1. Fraser H et al, Hepatology 2018;68:402-11. 2. Platt L et al, Addiction 2017: Epub ahead of print

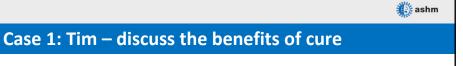




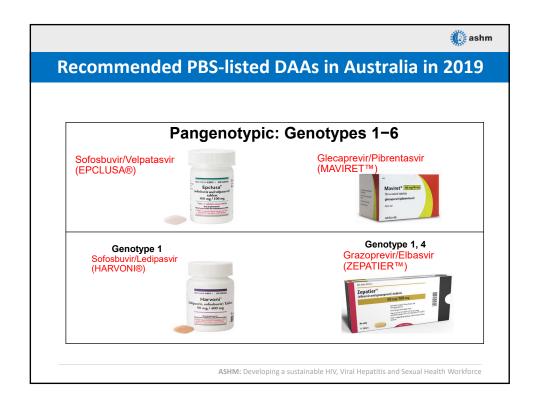


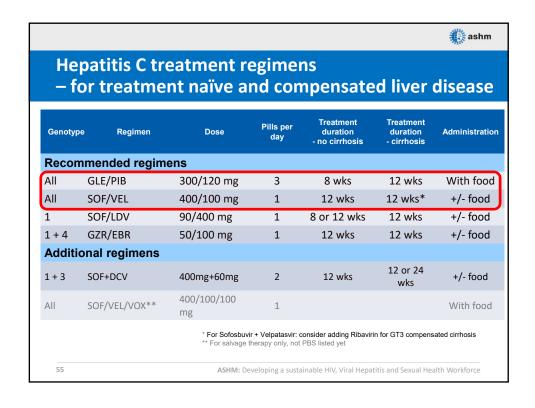


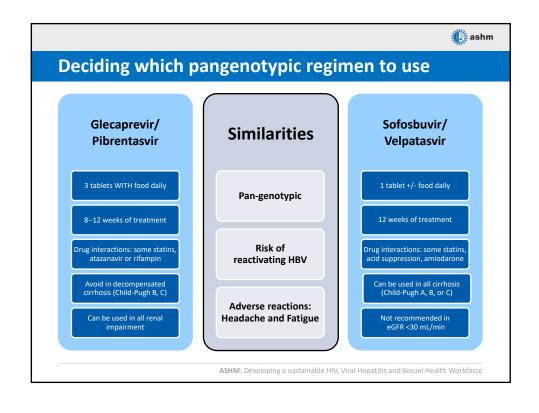


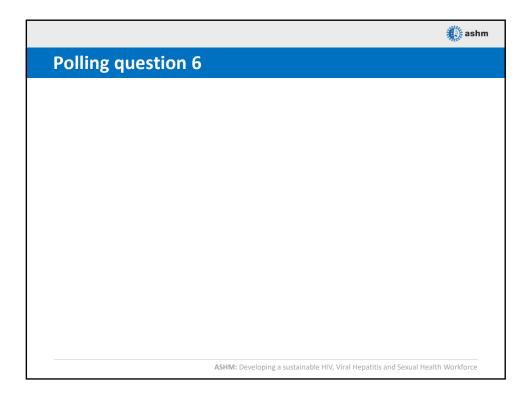


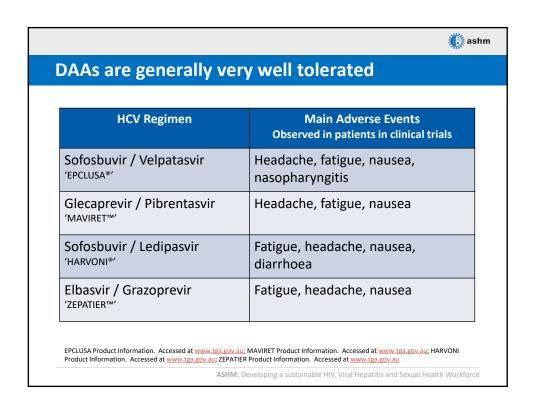
What benefits can Tim experience to his physical and mental health after curing hepatitis C?

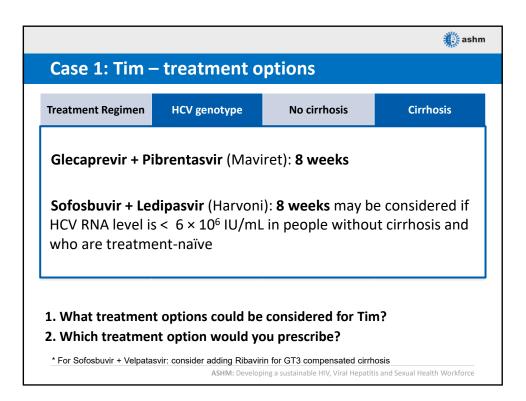


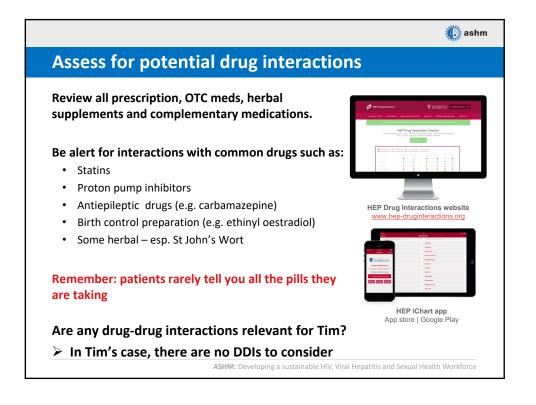














### **Discuss adherence strategies**

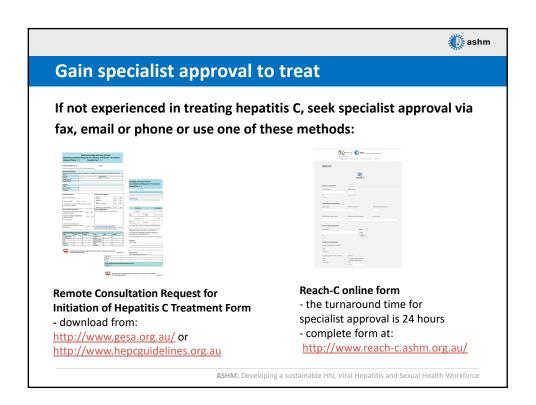
- 1. Are there any consequences if Tim misses a few doses?
- 2. What strategies could be recommended to Tim to support adherence?

#### **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
  - o Start date
  - o Refill due
  - o Labs due
  - Appointments
- Mobile phone alarms
- Looping in caregivers
- Supervised dosing (eg at methadone clinic)





# When to consult with or refer patients to a specialist







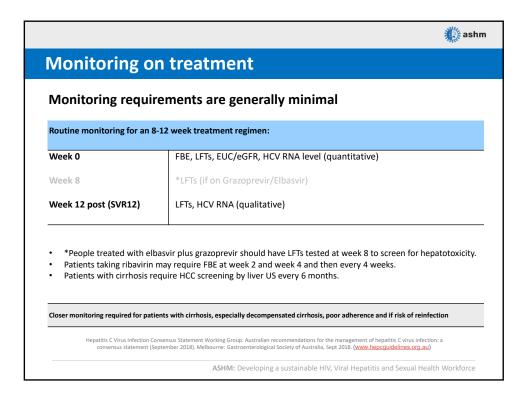




- Patients with advanced fibrosis or cirrhosis
- Patients with extrahepatic manifestations
- Patients with complex co-morbidities
- Patients with renal impairment
- Patients with HIV/HCV or HBV/HCV coinfection
- Patients who failed first line DAA
- Patients with acute HCV

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ashm **Essential steps in treating hepatitis C** 1 • Identify people at risk Test and diagnose 3 Assess for treatment 4 • Discuss and initiate treatment • Monitor and follow-up ASHM: Developing a sustainable HIV, Viral Hepatitis and Sexual Health Workforce





## 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)

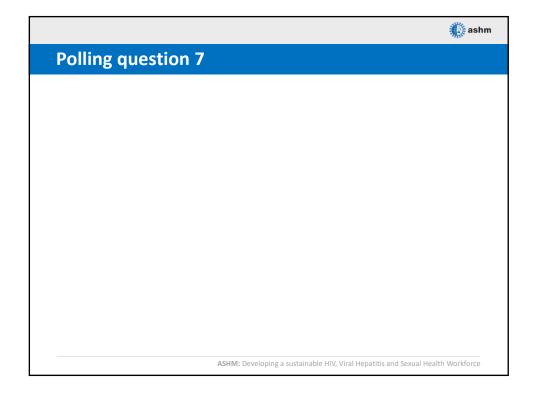
#### Is Tim cured?

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





### Determining post-treatment follow-up: no cirrhosis

#### No cirrhosis, normal LFTs at SVR12

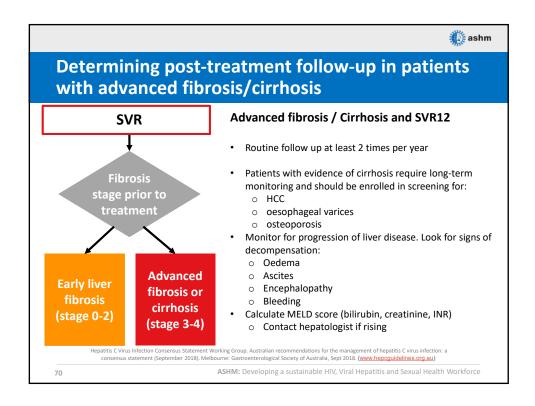
- Patients who are cured do not require clinical follow-up for HCV
- Discussion around moving on as 'hepatitis C free'
- Ongoing HCV monitoring (annual LFTs and HCV RNA) if potential risk of reexposure (PWID, HIV+ve, MSM) or if LFTs abnormal.

#### **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

Hepatitis C Virus infection Consensus Statement Working Group. Australian recommendations for the management of hepatitis C virus infection: a consensus statement (September 2018). Melbourne: Gastroenterological Society of Australia, Sept 2018. (www.hepcquidelines.org.au)





### **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
  - o Diabetes, alcohol abuse, fatty liver, older (≥age 60-65 y)

#### How?

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

#### If AFP or ultrasound is abnormal, refer to specialist

AASLD IDSA Guidelines 2016 (http://www.hcvguidelines.org)

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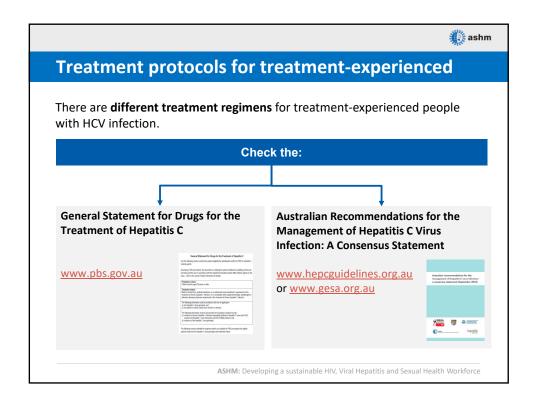


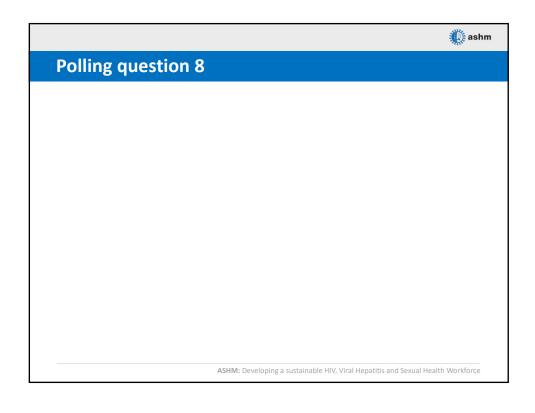
#### Other management issues

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







# 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

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# 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

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