Patient Workup for the Treatment of Hepatitis C

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Perth Infectious Diseases

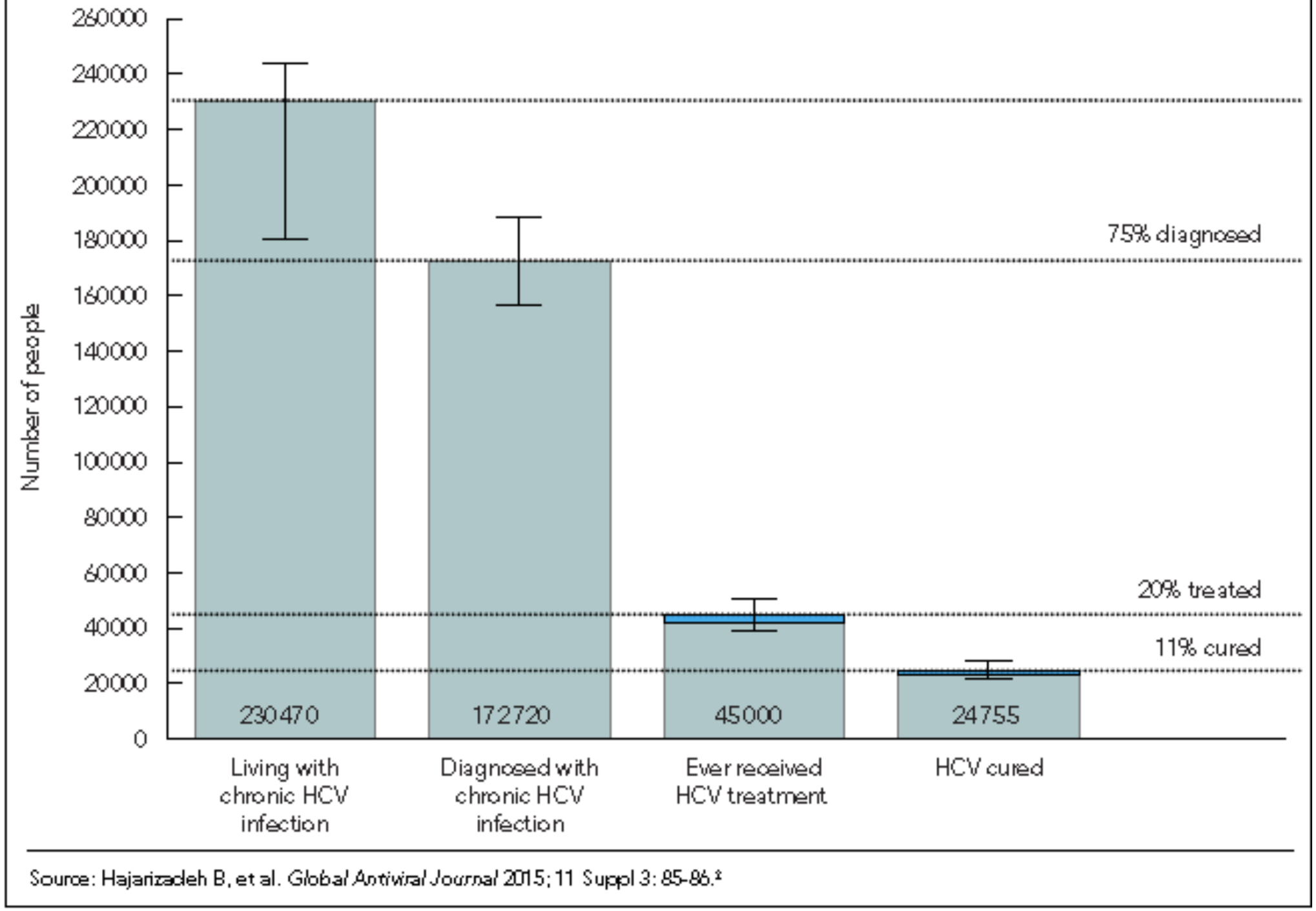
Outline

- Hepatitis C overview
- New Treatments
- Assessment of patients and workup for treatment

Hepatitis C

- Major PH challenge- 75% chronic disease
- 20-30 years on- 1/3 develop cirrhosis and HCC
- Notifiable disease- 75-85% HCV infected diagnosed
- Decreased new cases BUT complications increasing

Figure 1. Estimates of the cascade of care for people with chronic hepatitis C virus (HCV) infection in Australia

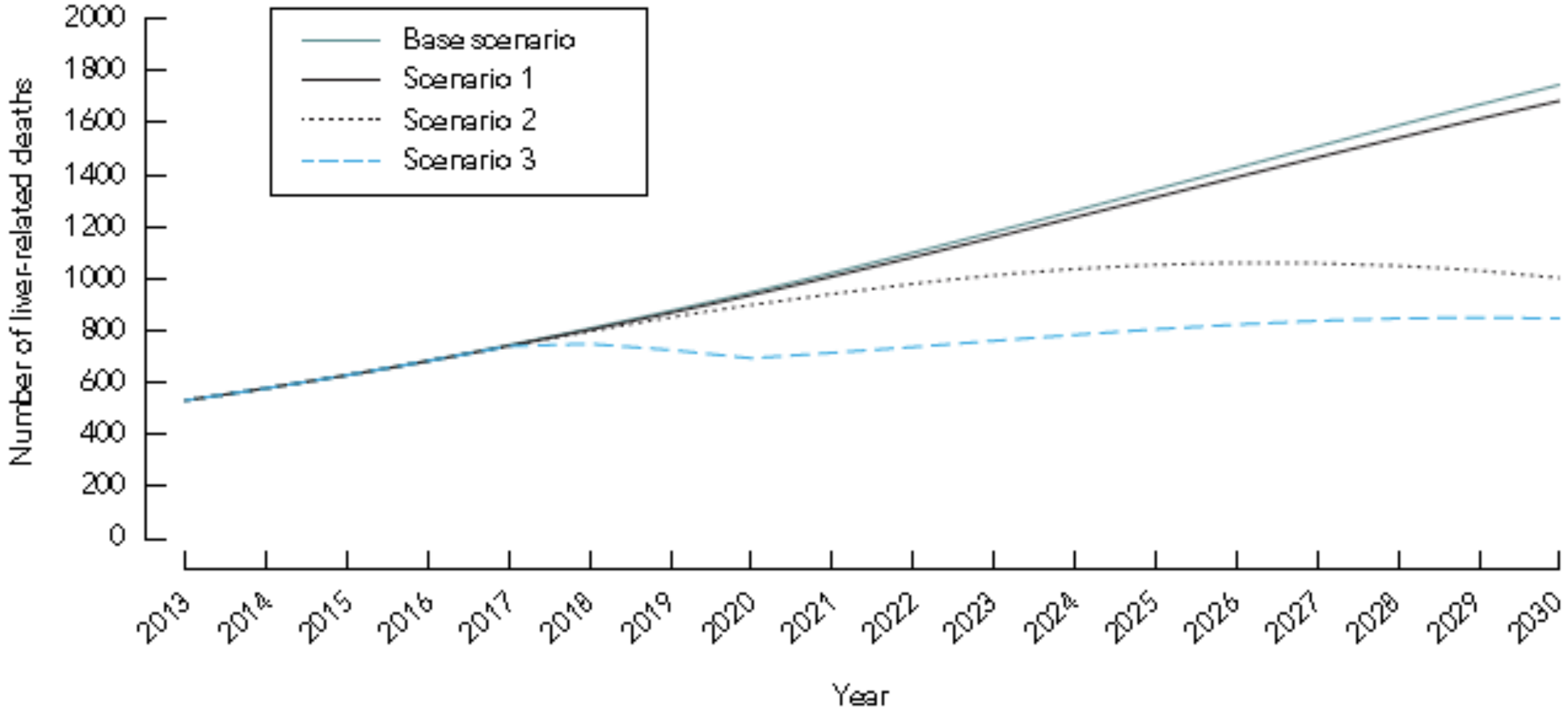


Source: Hajarizadeh B, et al. *Global Antiviral Journal* 2015; 11 Suppl 3: 85-86.[1]

Burden of Disease

- Only 1-2% treatment uptake (toxicity)
- 2013 most mild liver fibrosis (6% or 13,000)
- 2030 liver fibrosis will triple (38,000) with >2000 HCC and >1700 liver deaths

Figure 2. Projected burden of disease: liver-related deaths, 2013–2030



Model inputs for scenarios:

Scenario 1: increase sustained virological response (SVR) only, with no increase in annual treated population and treatment eligibility not restricted by fibrosis stage.

Scenario 2: increase SVR and annual treated population, with treatment eligibility not restricted by fibrosis stage.

Scenario 3: increase SVR and annual treated population, restricted to fibrosis stage ≥ F3 in 2015–2017, then unrestricted (all stages ≥ F0) from 2018.[5]

These scenarios illustrate that it will be necessary to increase both treatment efficacy AND treatment uptake rates to reduce the projected burden of liver-related deaths due to HCV infection in Australia by 2030.

Australian recommendations for the management of Hepatitis C infection:
A consensus statement 2016, Gastroenterological Society of Australia

Timeline of Hepatitis C

1970s **Non-A, non-B hepatitis recognised**

1989 Hepatitis C virus identified

1991 First HCV Rx- Intron A

1997 Interferon

1998 Ribavirin

2001 Pegintron (Peginterferon alfa-2b)

2002 Pegasys (Peginterferon alfa-2a)

2011 Boceprevir, Telaprevir

2013 Simeprevir
Sofosbuvir

2014 **Harvoni (Sofosbuvir, Ledipasvir)**
Genotype 1

Viekira Pak (ombitasvir, paritaprevir, ritonavir, dasabuvir)

2015 **Daclatasvir and Sofosbuvir**
Genotype 3

Technivie (Ombitasvir, Paritaprevir, Ritonavir)
Genotype 4

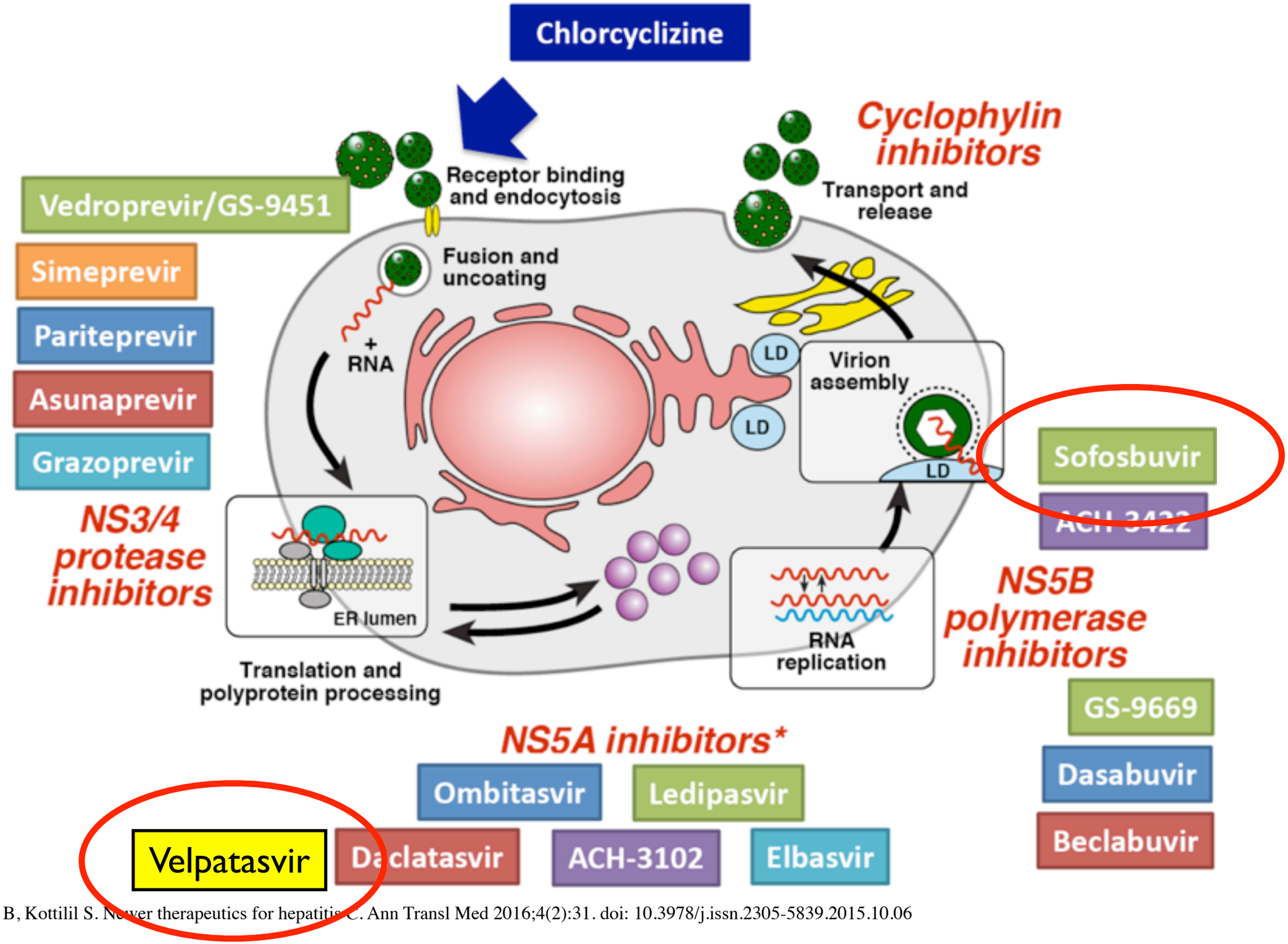
2016 **Elbasvir and Grazoprevir +/- Ribavirin**
Genotype 1 SVR 97%
Genotype 4 SVR 100%

Sofosbuvir and Velpatasvir
Genotype 1-6 SVR 98%
(94% cirrhosis)

Directly Acting Antivirals- DAAs

- Target multiple steps in HCV replication
- Highly effective
- Safe
- Short term treatments- 12 weeks even cirrhosis

DAAs mechanisms of action



Poonia B, Kottilil S. Newer therapeutics for hepatitis C. Ann Transl Med 2016;4(2):31. doi: 10.3978/j.issn.2305-5839.2015.10.06

Hep C Treatment Choices

Genotype	No Previous Treatment (naïve)		Previously Received Treatment (experienced)	
	No cirrhosis	With cirrhosis	No cirrhosis	With cirrhosis
1 a/b	**Ledipasvir/sofosbuvir** [8 or 12 weeks]	**Ledipasvir/sofosbuvir** [12 weeks] or **Sofosbuvir** and **Peg-Interferon alfa-2a/ribavirin** [12 weeks]	**Ledipasvir/sofosbuvir** [12 weeks] or **Sofosbuvir** and **Peg-Interferon alfa-2a/ribavirin** [12 weeks]	**Ledipasvir/sofosbuvir** [24 weeks] or **Sofosbuvir** and **Peg-Interferon alfa-2a/ribavirin** [12 weeks]
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http://www.gesa.org.au/professional.asp?cid=77&id=454
http://www.hepatitisaustralia.com/hepatitis-c-facts/treatment-for-hep-c.

Decision Making in Hepatitis C

- Could it be Hep C?
- Confirm the diagnosis
- Treat
- Refer for treatment
- Follow up

Decision Making in Hepatitis C

- ***Could it be Hep C?***
  - Patient request, abnormal LFTs, doctor concern
  - Risk factors*

Table 1. High-risk populations for hepatitis C virus (HCV) infection

- People who inject drugs or who have ever injected drugs
- Sex workers
- People in custodial settings
- People with tattoos or body piercing
- People who received a blood transfusion or organ transplant before 1990
- Children born to HCV-infected mothers
- Sexual partners of an HCV-infected person
- People infected with human immunodeficiency virus or hepatitis B virus
- People with evidence of liver disease (persistently elevated alanine aminotransferase level)
- People who have had a needlestick injury
- Migrants from high-prevalence regions (Egypt, Pakistan, Mediterranean and Eastern Europe, Africa and Asia)

Decision Making in Hepatitis C

- ***Confirm the diagnosis***
- Order Hepatitis C Antibody test
- Order Hepatitis C RNA PCR

*Consent needs to include reasons for testing, meaning of a positive test, positive results in person

Decision Making in Hepatitis C

- Hep C Ab positive
- HCV RNA PCR not detected
- Cleared infection (only 25%)

Decision Making in Hepatitis C

- Hep C Ab positive
- HCV RNA PCR detected (>6 months)
- Chronic Hepatitis C infection

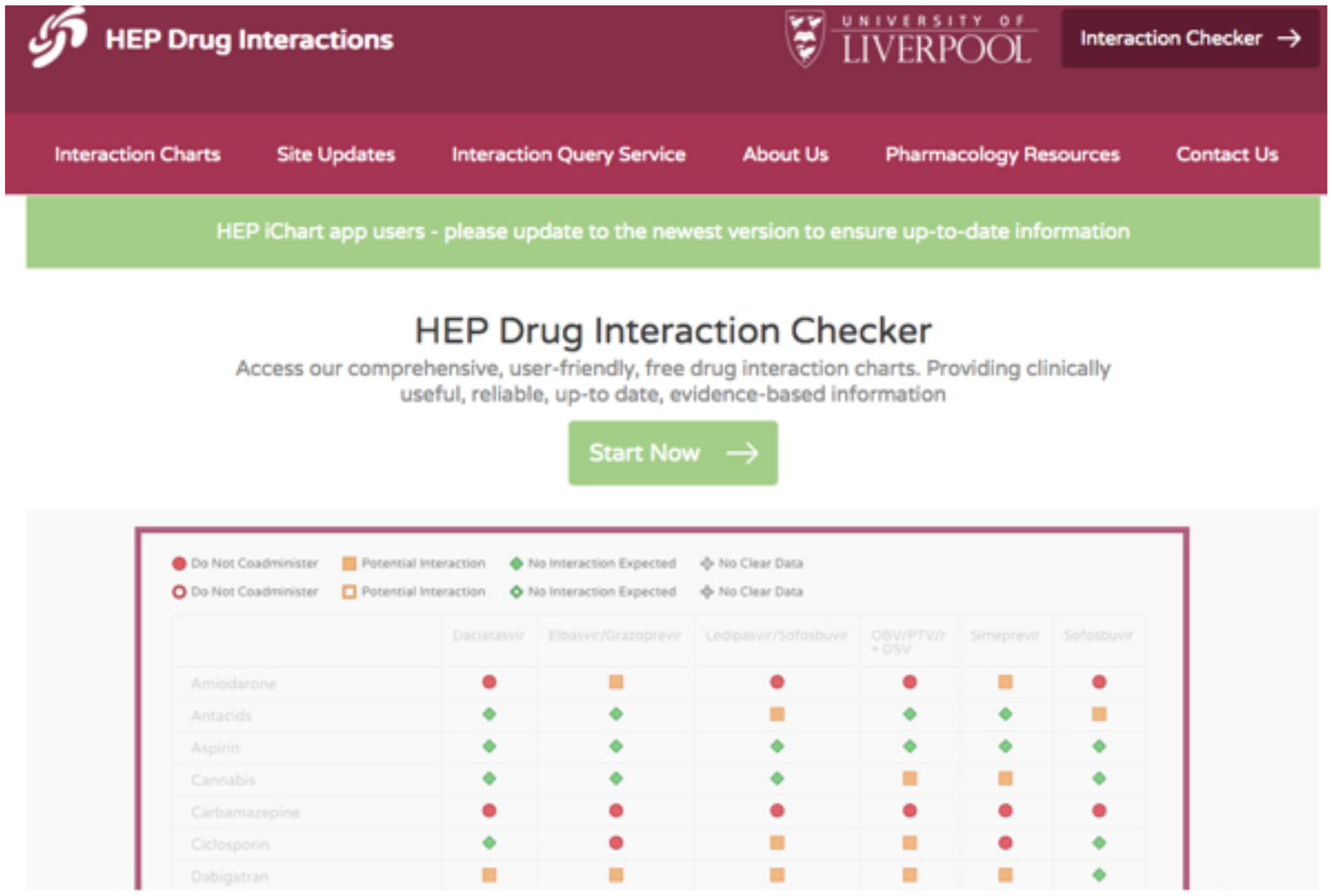
Decision Making in Hepatitis C

- ***Follow up and/or referral?***
- Aim should be to treat
- Assess and treat
- Assess and refer

History

- Estimate duration of HCV infection
- Previous HCV treatment
- Factors for liver disease progression: alcohol intake, marijuana, co-infection with HIV or HBV, diabetes, obesity
- IHD/cardiovascular risk factors (ribavirin)
- HAV and HBV vaccination
- Ongoing risk behaviours/education about reducing transmission/reinfection

Medications



- Prescription
- Over the counter
- Illicit

http://www.hep-druginteractions.org/

Physical Exam

- Features of cirrhosis: hard liver edge, spider naevi, gynaecomastia
- Decompensation: jaundice, ascites, oedema, bruising, muscle wasting, encephalopathy
- Body weight and BMI

Virology

- Further Viral-related tests
  - HCV genotype (*treatment regimen)
  - HCV RNA quantitative (viral load)
  - HBV (HbsAg, anti-HBc, anti-HBs), HAV, HIV serology

Investigations

- FBP, LFTs, Urea and electrolytes, eGFR, INR
- Pregnancy test
- Liver fibrosis assessment
  - Elastography
  - Biomarkers (APRI, Hepascore, ELF test)
- Liver ultrasound
- Electrocardiogram if ribavirin therapy planned, >50 years and cardiac risk factors

Liver fibrosis assessment

- Cirrhosis affects treatment choice and duration
- Requirement for PBS Authority
- Patients with cirrhosis require lifelong HCC and portal hypertension surveillance

Factors associated with progression to liver disease in chronic HCV
Age at acquisition of infection (>40 years)
Heavy alcohol intake (>40g/day)
Male gender
Longer duration of infection
Moderate-severe fibrosis on baseline Elastography
Co-infection with HBV or HIV
Obesity
NB Viral load is not associated with progression

Liver fibrosis assessment

- Peripheral stigmata of chronic liver disease
- Portal hypertension: splenomegaly, thrombocytopaenia
- Low albumin, raised bilirubin, raised INR

Liver fibrosis assessment

- Liver biopsy is rarely performed
- Non-invasive tests such as Elastography are now routine
- These techniques outperform biomarkers for the assessment of fibrosis
  - *Hepascore/APRI/others
- No method is totally accurate
- Patients with cirrhosis need endoscopy

Cirrhosis

- Should be referred to a specialist
- Need evaluation for decompensation
- Need endoscopy
- Certain DAAs are contraindicated in this group because of hepatic toxicity (NS3-PI)

Other considerations

- Adherence
- Stable psychiatric
- Stable injecting drug use
- No fibrosis- alcohol acceptable 2 std/day
- Cirrhosis- total alcohol abstinence

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http://www.hepatitisaustralia.com/hepatitis-c-facts/treatment-for-hep-c.

Treatment monitoring

- Intense monitoring not necessary
- Non-cirrhotic: baseline and FBP/LFTs/ adherence/side effects/cardiac risk factors at week 4.
- Cirrhotic: baseline and FBP/LFTs/adherence/ side effects/cardiac risk factors at week 4, 8 and 12.
- HCV RNA PCR at week 12 and 24
- Poor response: non-adherence, reinfection

Monitoring after SVR

B. Monitoring after SVR
SVR, no cirrhosis and normal LFT results (males, ALT < 30 U/L; females, ALT < 19 U/L): • Patients who are cured do not require clinical follow-up for HCV
SVR and abnormal LFT results (males, ALT ≥ 30 U/L; females, ALT ≥ 19 U/L): • Patients with persistently abnormal LFT results require evaluation for other liver diseases and should be referred for gastroenterology review. Investigations to consider include: fasting glucose level, fasting lipid levels, iron studies, ANA, ASMA, anti-LKM antibodies, total IgG and IgM, AMA, coeliac serology, copper level, caeruloplasmin level and α-1-antitrypsin level

SVR, cirrhosis:
• Patients with cirrhosis require long-term monitoring and should be enrolled in screening programs for:
  ▸ hepatocellular carcinoma — liver ultrasound ± serum α-fetoprotein level
  ▸ oesophageal varices — gastroscopy
  ▸ osteoporosis — dual emission x-ray absorptiometry

EOT = end of treatment. SVR = sustained virological response at least 12 weeks after treatment (cure). FBE = full blood examination. LFT = liver function test. INR = international normalised ratio. PCR = polymerase chain reaction. ALT = alanine aminotransferase. ANA = anti-nuclear antibodies. ASMA = anti-smooth muscle antibodies. LKM = liver–kidney microsome. AMA = anti-mitochondrial antibody.

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NPS MEDICINEWISE LEARNING

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- Get it right! Taking a Best Possible Medication Hi...
- **Managing hepatitis C in primary care**
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- Medication safety
- National Inpatient Medication

Managing hepatitis C in primary care

This module will provide you with training in the diagnosis, treatment and ongoing management of people with chronic hepatitis C infection. Hepatitis C (HCV) remains a significant public health issue in Australia and GPs are an essential part of the management team, from identifying people who may be at risk of infection to diagnosis and monitoring of liver disease. In addition, with the new direct-acting antiviral (DAA) agents now available on the PBS general schedule it is even more vital that GPs are aware of HCV treatment strategies.

View the learning outcomes.

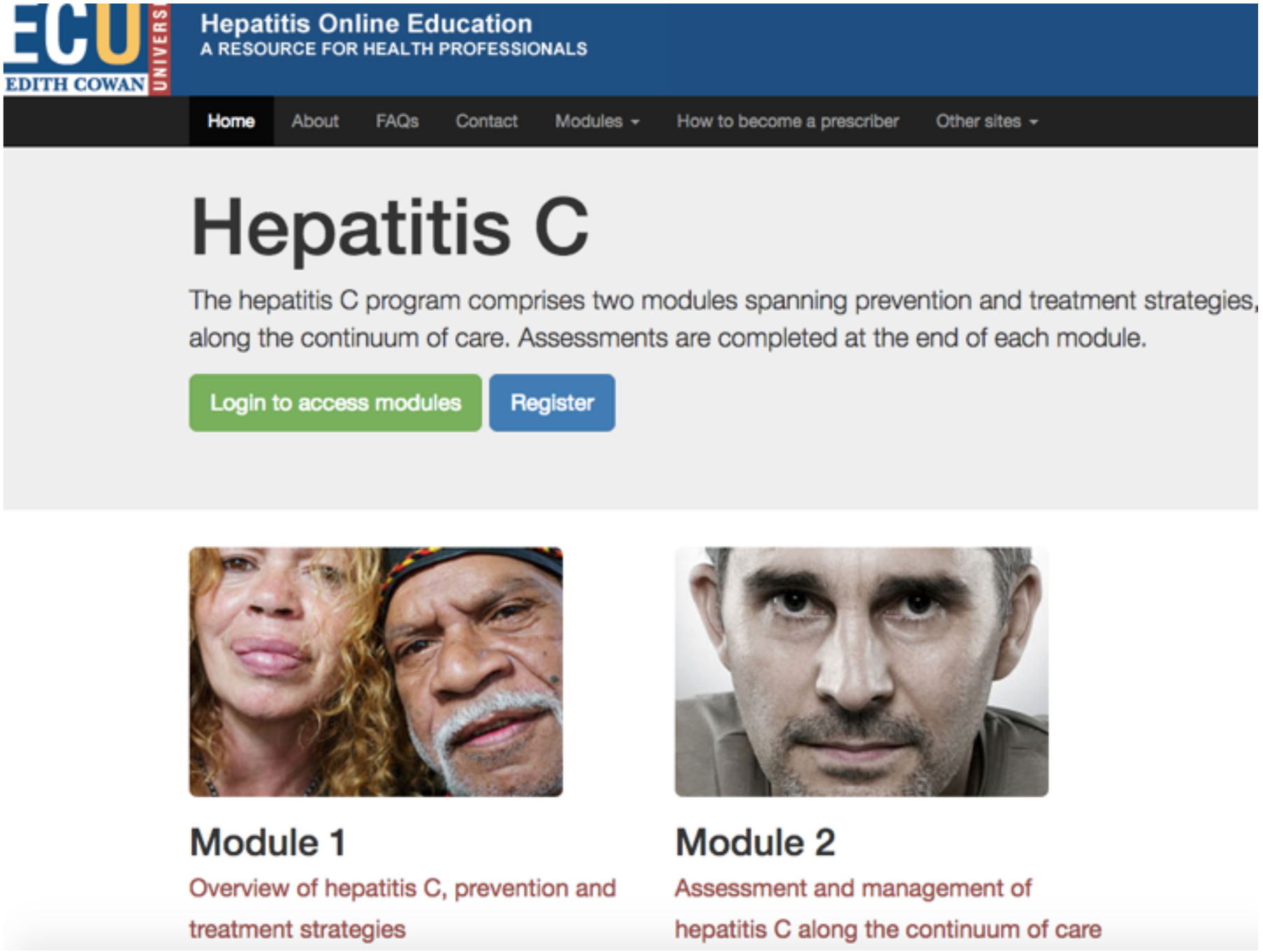
Target audience: GPs

Open to: GPs, Pharmacists, Nurses, Students

Cost: Free

CPD points: GPs - view details

http://learn.nps.org.au/mod/page/view.php?id=7278



http://hepatitis.ecu.edu.au/hepc/index.php

Take Home Messages

- Think about Hep C in at risk groups and test
- Confirm the diagnosis
- Work up patients for treatment
- Treat (Educations Modules)
- Refer (Shared Care)
- Challenges: access to treatment, rapidly changing landscape of DAAs, pitfalls of therapy, developing models of care.

Thank you for listening!

Perth Infectious Diseases

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