



Primary Care Providers and Hepatitis C



Recent WHO Global Targets for Elimination include an 80% reduction in new HCV infections by 2030 and a 65% reduction in HCV-related deaths by 2030, compared to 2010 records. The potential to eradicate chronic HCV worldwide including in Australia exists.

On March 1st 2016, Australia entered a new era in chronic hepatitis C (HCV) treatment with the PBS listing of new highly effective, well-tolerated, short duration (mostly only 12 weeks) oral treatments available to all those living with chronic HCV aged over 18 yrs.

All Australians living with chronic HCV should now be considered for direct acting antiviral (DAA) treatment.

Chronic HCV remains one of Australia's most commonly notified infectious diseases. People living with HCV infection are at risk of progressive liver fibrosis leading to cirrhosis, liver failure and hepatocellular carcinoma (HCC). Increasing treatment accessibility is a high priority. Involving more primary care providers in the prescription of DAAs is a major step towards facilitating HCV treatment uptake.

New DAA treatment can be prescribed by primary care practitioners on an S85 authority script following consultation with a gastroenterologist, hepatologist or infectious diseases physician experienced in treating HCV. S85 scripts must be dispensed through community pharmacies.

It is estimated that 25% of HCV infections remain undiagnosed in Australia. Primary care practitioners play a key role in detecting people who are unaware of their HCV infection and in re-engaging those diagnosed some years ago.

The **Australian recommendations for the management of hepatitis C virus infection: a consensus statement**¹ (Consensus Statement) (www.hepcguidelines.org.au) has been prepared by an expert panel to guide all aspects of HCV treatment. It is an online living document that will be updated as new data and treatments become available. A *clinical guidance for treating hepatitis viral infection: a summary*, adapted from the **Consensus Statement**, is an easy reference tool for primary care providers and can be downloaded from the GESA website (www.gesa.org.au).

Chronic HCV can be cured

The benefits of successful treatment include:

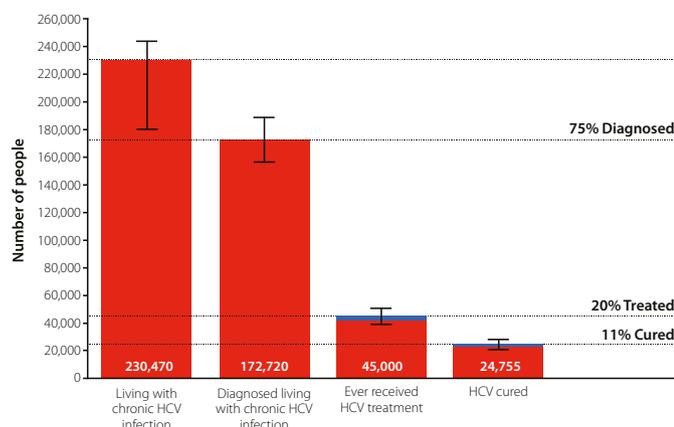
- Reduction of liver disease progression with long-term flow on reduction in decompensated liver disease and hepatocellular carcinoma (HCC).
- Regression of fibrosis and cirrhosis.
- Resolution of HCV symptoms if present, such as tiredness.
- Improved mental, physical wellbeing and quality of life.
- Prevention of extra-hepatic HCV complications such as glomerulonephritis, diabetes, vasculitis, peripheral neuropathy and lymphoma.
- Removal of risk of HCV transmission to others.
- Reduction in rates of HCV transmission in the community. Curing the majority, especially those at higher risk of transmission, can rapidly reduce the number of new infections and re-infections. This is called Treatment as Prevention.

There is still no vaccine for HCV and clearing the virus with treatment does not provide immunity or prevent re-infection.

How common is chronic HCV in Australia?

HCV affects approximately 1.2% of the population with an estimated 230,500 people living with chronic HCV.² The number of new HCV infections is estimated at 9,000/year. With older interferon regimens, treatment rates were low with around 2000-4000 treated /yr. 2015 modelling estimates that approximately 75% of cases are diagnosed, 20% treated and 11% cured. (Figure 1)

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. Reprinted with permission

The virus

Hepatitis C is a ribonucleic acid (RNA) virus, discovered in 1989, belonging to the flavivirus family.³ There are seven major genotypes

with many different subtypes such as 1a or 1b. HCV genotype (and subtype) determines the choice of treatment regimen, though this will change with availability of new pan-genotypic treatments in the future. The most common genotypes in Australia are genotype 1 and 3.

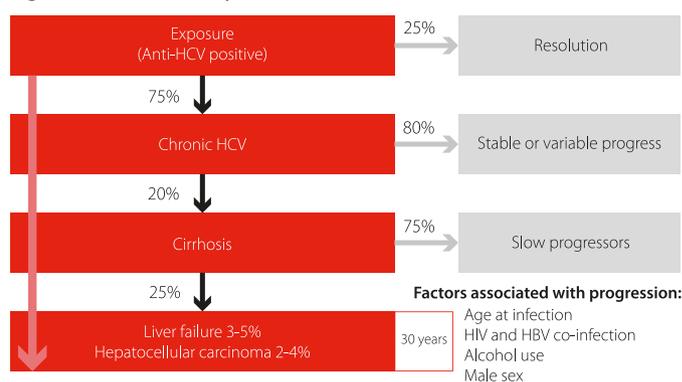
Natural History

Most people are asymptomatic at the time of acute hepatitis infection, however, a few experience symptoms. Those who do experience acute symptoms are more likely to spontaneously clear the virus. Approximately 25% of those infected with HCV clear the virus spontaneously up to 12 months (usually 3-6 months) after infection.

Those that do not clear the virus develop chronic HCV. Many have no symptoms, though some experience non-specific symptoms such as fatigue, brain fog and intolerance to fatty foods. After 20 years, on average, about 7% of people with chronic HCV may have developed liver cirrhosis with this figure increasing to 20% after 40 years. After 40 years of infection about 5% may have developed liver failure or liver cancer.

Outcomes for people with **untreated** chronic HCV are variable as shown in Figure 2. This table does not show the outcome for individual people. Factors such as alcohol intake, age when hepatitis was acquired, insulin resistance, gender and co-infection with HBV and HIV may all influence an individual's outcome.

Figure 2. Natural History of HCV



From HIV, Viral Hepatitis and STIs – A Guide for Primary Health Care Chapter 11, page 127

Primary care provider treatment of chronic HCV

The new DAA therapies have paved the way for a major shift in service provision models of care. Increasingly, HCV treatment will be available in the community through primary care providers, allowing tertiary liver clinics to manage those with advanced liver disease, complex cases with co-morbidities and those who have failed initial DAA treatment.

Advantages of providing care in a primary care setting include:

- Being in a familiar and trusting environment, where one's medical, vaccination and medication history is on record and often the first language is spoken.
- No requirement for a referral and close proximity to place of residence.
- Whole of person health care co-ordination available in one location such as contraception, vaccination, mental health and addiction support and referral to a range of specialist services.

■ Expertise in chronic care disease management, such as diabetes. Advanced liver disease chronic care follow up can be co-ordinated in primary care in partnership with specialists. Refer to *ASHM's Decision-making in Viral hepatitis related advanced liver disease* resource.

■ An opportunity to empower the person to make their own decisions about their treatment and supporting each individual as they manage their infection.

Treating chronic HCV is only one aspect of care for many living with or having lived with chronic HCV. The primary care provider role in HCV has many components: (see Table 1 for a summary).

Prevention & Education	<ul style="list-style-type: none"> ■ Improve health care and reduce stigmatisation of people who inject drugs ■ Reduce sharing of injecting equipment ■ Educate re-transmission and re-infection risks ■ Vaccination - Hepatitis B & A ■ Psycho-social support, alcohol and other drug counselling ■ Opiate Replacement Treatment - methadone or buprenorphine ■ Promote treatment of HCV PCR positive injecting peers
Testing & Diagnosis	<ul style="list-style-type: none"> ■ Identify people at risk and offer testing ■ Think: 'Could this patient have chronic HCV?' <p>Much of the risk of having chronic HCV can be assessed by asking "Have you ever injected drugs?" and identifying if a person was born in a country with high HCV prevalence or has a higher background risk e.g. Aboriginal and Torres Strait Islander (ATSI), men who have sex with men (MSM) or a history of being in a custodial setting.</p>
Assessment & Further Care	<p>Determine:</p> <ul style="list-style-type: none"> ■ Acute or chronic infection. ■ Resolved - spontaneous or after treatment ■ Co-infection HIV, HBV, HAV ■ Assess stage of liver disease <p>Lifestyle Modification:</p> <ul style="list-style-type: none"> ■ Alcohol / drug use / smoking ■ Weight and exercise - obesity associated with non-alcohol fatty liver disease (NAFLD)
Treatment	<ul style="list-style-type: none"> ■ Encourage all to consider treatment ■ Treatment as per Consensus Statement <p>Referral of advanced liver disease and complex cases</p> <ul style="list-style-type: none"> ■ Encourage treatment of HCV PCR positive friends culture
Post Treatment	<ul style="list-style-type: none"> ■ If cirrhosis - ensure linked into HCC and portal hypertension screening surveillance and osteoporosis monitoring ■ Assess re-infection risk, encourage safe behaviours ■ Annual HCV PCR abd LFT in those at higher risk of re-infection ■ Test and follow-up children of those whose mothers were HCV positive during pregnancy (vertical transmission rate approx. 5%).

HCV Prevention and Education

People with HCV express concern about the risk of transmitting the virus to others. It is important to discuss all forms of potential transmission.

HCV transmission occurs primarily through blood-to-blood contact.

The most common mode of transmission in Australia continues to be injecting drug use (IDU). People who inject drugs (PWID) need to be encouraged to use sterile water, needles and syringes as well as new injecting equipment such as spoons, filters and tourniquets each time they inject. Needle and syringe programs for injecting drug users have been proven to reduce the spread of HCV and provide readily available support and safe practice education for PWID.

Transmission can occur through unsterile tattooing especially in prison and some overseas countries. Household transmission (such as via razors, tweezers, toothbrushes) is considered rare. Nevertheless, because the possibility of blood contact exists, these items should not be shared.

Some countries have high rates of HCV related to transmission in healthcare settings such as unsterile vaccinations or medical procedures. People born in and from countries with high prevalence (Egypt, Pakistan, the Mediterranean, Eastern Europe, Africa and Southern Asia) should be tested at least once.

People are frequently concerned about sexual transmission.

There appears to be a very low risk of transmission between heterosexual couples. In contrast, recent increases in acute HCV have been reported among men who have sex with men (MSM) predominantly associated with sexual (per mucosal) transmission. Transmission rates are higher if the patient is co-infected with HIV. Most mucosal sexual transmission occurs via unprotected anal intercourse and when engaging in higher risk sexual activities, such as group sex.

The risk of perinatal transmission varies from 0 to 11% and averages 5%. Co-infection with HIV increases the risk at least two-fold. To date, the National Health and Medical Research Council has not recommended changes to obstetric practice during antenatal care, delivery and post-partum care or in management of the neonate and there is no indication for elective caesarean section in HCV-positive mothers. Despite HCV RNA being detectable in breast milk, breastfeeding has not been directly linked to transmission of HCV. Australian guidelines recommend breastfeeding should not be discouraged unless there are cracked and bleeding nipples.

There is no risk of transmission of HCV through the sharing of cups, plates or via hugging and other such personal contact.

Testing and diagnosis

Identifying people at risk and offering testing is vital in the detection of people living with chronic HCV. Most people are asymptomatic, so it is important to routinely ask the question "Have you ever injected drugs?" in a non-judgemental way and also enquire about country of birth. This will detect many of those at risk and requiring testing. Other opportunities for routine assessment of HCV risk factors include STI screening, contraception, antenatal screening, alcohol and addiction issues, refugee checks.

Persistent elevation of transaminases, in particular ALT, is a prompt to perform HCV screening (although ALT in the context of HCV can be normal). ALT is a marker of liver inflammation but correlates poorly with disease progression risk. Many with normal ALT levels develop significant fibrosis. See Table 2: Who to test.

Table 2: Who to test

- 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 HIV or hepatitis B virus
- People with evidence of liver disease
- People who have had a needlestick injury
- Migrants from high-prevalence regions including Egypt, Pakistan, Mediterranean and Eastern Europe, African and Asia

Obtaining informed consent is an integral part of HCV testing and may require an interpreter. **The National HCV Testing Policy⁴** provides full details of indications for testing, gaining consent and includes access to related resources, guidelines and policies.

The health professional ordering a HCV test is responsible for ensuring the test result is followed up and given to the person tested.

Conveying a negative result

The decision on how a **negative result** is conveyed (e.g. in person, phone, text message) should be based on clinical judgement of the person responsible for conveying the result. It provides an opportunity to reinforce harm reduction strategies, give information about safe behaviours and address addiction issues. There is good evidence Opiate Substitution Therapy (OST) reduces HCV transmission.

Conveying a positive result

A **positive result** should always be provided in person, except in extenuating circumstances. There is often significant emotional reaction to a positive diagnosis. It is good practice to make a longer consultation to discuss results and answer questions. Points to cover include confidentiality, risk of transmission and ways to reduce risk, assessment of individual supports, further investigations and new treatments. Much of any health provider consultation is not remembered, so providing written information and referral to websites and peer support services such as Hepatitis Australia is useful.

The initial screening

Perform an HCV antibodies (anti-HCV) test

■ **Negative anti-HCV** indicates the person has not been exposed to the virus, or is in the window period if recent exposure. Anti-HCVs are usually present within 3 months of exposure.

■ **Positive anti-HCV** indicates exposure to HCV at some time in that person's life but does not prove current infection. Whilst 25% of people will clear the virus spontaneously, anti-HCV remains positive for life even after clearance of the virus spontaneously or post successful treatment.

Confirming current infection

The confirmatory test is a polymerase chain reaction (PCR) assay for HCV RNA

■ **Positive HCV RNA** documents viraemia/current infection. It must be positive before a diagnosis of chronic HCV can be made.

■ **Negative HCV RNA:** in the setting of a positive anti-HCV this indicates the person has cleared the infection spontaneously or been successfully treated in the past.

Management/follow up of spontaneously cleared

Practice Tips

Remember some people have been misdiagnosed with chronic HCV based solely on a positive anti-HCV test and on confirmatory testing the HCV RNA is negative... meaning the person does not have chronic HCV and has been living thinking they have chronic HCV (in some cases for years).

If someone says they have chronic HCV, ensure that a HCV RNA has been performed and the result available. If not, request a blood test for HCV RNA.

A dedicated collection tube is required to undertake the HCV RNA and can be collected at the same time as the initial screening by writing on the pathology form - "If anti-HCV positive please perform a HCV RNA and genotype."

HCV infection

A person can be considered to have cleared HCV infection if they have two negative HCV RNA tests, carried out at least 3 months apart.

People with a negative HCV RNA can be reassured that while they have been exposed to HCV in the past, they have cleared the infection. They need to understand they have no immunity and can be reinfected.

Assess ongoing risk behaviour, such as injecting drug use. When ongoing risk behaviour is identified perform an annual HCV RNA, regardless of ALT level, to detect subsequent re-infection.

Management of chronic HCV

Table 3 for a summary of steps for the primary care provider, highlighting when specialist review is required. Some practice tips follow.

	Primary Care Provider	Specialist review if:
Step 1:	Confirm chronic HCV infection	
Step 2:	Perform baseline tests and check HCV genotype and viral load	Genotype 4,5,6
Step 3:	Determine: could they have cirrhosis?	Cirrhosis
Step 4:	Assess cofactors for liver disease progression	HIV, HBV
Step 5:	Detect other major co-morbidities	Renal impairment (eGFR <50)
Step 6:	Review previous HCV treatment	Treatment failure of DAAs
Step 7:	Select treatment regimen and review drug interactions	Complex interactions
Step 8:	Contraception, pregnancy	
Step 9:	Assess adherence	
Step 10:	Consult with specialist to proceed with treatment	
Step 11:	Treat and monitor	Major adverse events
Step 12:	Post treatment follow-up	Treatment failure of DAAs

Adapted from an article 'Stepping into the Future' by Dr David Baker Australian Doctor 04 March 2016

A person is diagnosed with chronic HCV infection if they have documented active infection for more than 6 months. This means a positive HCV RNA (PCR) 6 months or more after initial infection.

Refer to the *Australian recommendations for the Management of hepatitis C virus infection: a consensus statement*¹ for pre-treatment, treatment and post treatment guidelines.

Step 1: Confirm diagnosis

Undertake a HCV RNA (PCR) test and convey positive results in person

Step 2: Order baseline tests plus medical/physical examination

Baseline testing recommended:	
<ul style="list-style-type: none"> ■ Liver Function Tests (LFT) ■ Full Blood Count (FBC) ■ Electrolytes, Urea, Creatinine (EUC) ■ Fasting blood sugar level & lipids ■ Hepatitis C Genotype 	<ul style="list-style-type: none"> ■ Hep PCR Quantitative (Viral Load) ■ Hepatitis A screen - Check HEP A IgG ■ Hepatitis B screen - Check anti-HBs, Anti-HBc, HBsAg ■ HIV Ab

What is the difference between the HCV RNA PCR tests?

- **HCV RNA Qualitative** is either positive or negative. It is a more sensitive test used to diagnose current HCV and to test for cure 12 weeks post treatment.
- **HCV RNA Quantitative or Viral Load** is reported as a number. If a very low viral load is obtained (e.g. <200,000 IU/ml) and the person has been exposed in the prior 3-6 months they maybe in the process of clearing the virus spontaneously. In this case repeat a HCV RNA qualitative test in 1-2 month. If negative, they have likely cleared HCV and do not need treatment.
- **HCV genotype** currently remains important in determining treatment regime. In Australia, most cases are either genotype 1 (50-55%) or genotype 3 (35-40%).

Undertake full medical, mental health, social, drug and alcohol history and perform physical examination

Depending upon history, consider:

- Risk of re-infection and transmission reduction education
- Referral for opioid replacement treatment, addiction medicine services
- Sexual health screening and contraception
- Addressing modifiable advanced liver disease risk factors such as excessive alcohol and marijuana consumption, obesity, poor diabetes control
- Determining person's need for support services, consider a GPMP and TCA*
- Optimising general health – ensure health screening as per RACGP Guidelines

* GPMP General Practice Management Plan (Medicare Item number 721), TCA Team care arrangement (Medicare Item number 723) - see: www.ashm.org.au

Step 3: Determine stage of liver fibrosis

All people with cirrhosis need specialist referral, additional investigations and lifelong screening for complications such as hepatocellular carcinoma (HCC), portal hypertension and osteoporosis.

How to diagnose cirrhosis? No single test can reliably diagnose all

cases of cirrhosis. One needs to collate clues for each individual from various sources including:

■ Medical history

Cirrhosis clues include: HIV or HBV co-infection, longer duration HCV infection, male, older age at infection, heavy alcohol intake, diabetes, metabolic syndrome. For example, if a person has a 30 year history of chronic HCV, is diabetic, overweight and drinks alcohol excessively, then your suspicion of advanced liver disease is higher compared to a person with chronic HCV for 5 years who is otherwise fit and well.

■ Physical examination

Cirrhosis clues: leukonychia, multiple spider naevi, splenomegaly. Signs such as ascites, peripheral oedema, jaundice, and/or encephalopathy indicate decompensation.

■ Laboratory abnormalities in cirrhosis include:

- Platelet count below $150 \times 10^9/L$ or a reducing platelet count over a couple of years (suggestive of portal hypertension)

Practice Tip

Determining estimated duration of infection is not always easy given the asymptomatic nature of HCV. A patient's age alone can be quite a good indicator. Most patients over the age of 40 who acquired HCV through injecting drug usage are likely to have been infected more than 20 years.

- Reducing albumin, particularly if with low platelet count ($<100 \times 10^9/L$)
- Elevated bilirubin, elevated INR, prolonged prothrombin time (PT),
- Reversal of AST/ALT ratio (normal <1)

However people with well-compensated cirrhosis may have a completely normal platelet count, PT and serum albumin level for many years.

■ Abdominal ultrasound abnormalities cirrhosis clues:

- Irregular liver outline, enlarged portal vein, splenomegaly

■ Non Invasive markers of liver fibrosis have replaced liver biopsy as the best way to exclude or diagnose cirrhosis.

The **Consensus Statement** recommends formal liver fibrosis evaluation with a non-invasive test be performed for all individuals prior to commencing HCV treatment.

Fibroscan is the best non-invasive test to exclude cirrhosis. A liver stiffness measure of >12.5 kPa is the recommended threshold for identifying people with cirrhosis for HCV treatment decision making.

Serum biomarkers such as APRI or Hepascore may be used to exclude cirrhosis where a fibroscan is not available or accessible in a timely fashion.

APRI (AST to Platelet Ratio Index) can be calculated from routine blood tests.

$$APRI = \frac{AST \text{ level } (/ULN)}{\text{Platelet counts } (10^9/L)} \times 100$$

ULN = upper limit of normal

Calculate APRI score to **exclude** cirrhosis for HCV treatment decision making:

<1.0 indicates cirrhosis is very unlikely and patient does not require further staging and can commence therapy

>1.0 indicates cirrhosis is likely and requires referral for Fibroscan and specialist review

An APRI on-line calculator such as: <http://www.hepatitisc.uw.edu/page/clinical-calculators/apri> is a useful tool or download APRI phone app, e.g. MedCalc

If there is any concern about the accuracy of liver fibrosis assessment, specialist referral for further assessment is recommended.

Further information on advanced liver disease see **Decision-Making in Viral Hepatitis Related Advanced Liver Disease**
<http://www.ashm.org.au/resources/Pages/978-1-920773-41-0.aspx>

Practice Tip

If **cirrhosis is likely or detected**, perform abdominal ultrasound prior to specialist appointment.

Step 4: Assess co-factors for liver disease progression

Assess cofactors for liver disease progression including alcohol, marijuana, diabetes, obesity and viral infections (hepatitis B, HIV). Review alcohol and marijuana use, check BMI and offer appropriate ongoing counselling and treatment. Vaccinate for hepatitis A and B if susceptible.

Step 5: Detect other major co-morbidities and those needing referral

When to refer to tertiary liver clinic or experienced specialist:

- Advanced liver disease/cirrhosis
- Decompensated cirrhosis
- Complex cases with co-morbidities, e.g. advanced kidney disease (eGFR < 50)
- Complex cases with co-morbidities on multiple medications
- People with hepatocellular cancer (HCC)
- <18 yrs refer to specialist paediatric liver clinic
- Other associated types of liver disease
- Co-infection HIV/HBV
- When first line DAA therapy has failed

Step 6: History of prior HCV treatment

Assess if treatment naïve or treatment experienced

If prior treatment: document date, regimen and treatment response. Any person who has failed treatment with Interferon free DAA based therapy should be referred for specialist management.

Step 7: Treatment

Practice Tip

If prior treatment, obtain a signed consent to receive medical records with prior results and treatment history at time of consultation.

- Document current medication (including over the counter medication, supplements, natural therapies, and recreational drugs)
- Select appropriate DAA treatment. Treatment choice depends on several factors including: HCV genotype/subtype, presence/absence of cirrhosis, prior treatment history, potential for drug-drug interactions and comorbidities

- Assess for potential drug-drug interactions

All medications need to be checked for potential drug–drug interactions with DAAs. DAA selection and dosage may need to be modified or current medications altered prior to treatment in your specialist consultation.

Refer to the Consensus Statement, Section 5 for treatment details

Practice Tip

DAA Drug to Drug interactions can be checked easily using on-line tools such as The University of Liverpool's Hepatitis Drug Interactions website (www.hep-druginteractions.org) or download free app: HEP iChart.

Certain medications, e.g. Amiodarone and St John's Wort are contraindicated across all DAA classes while other common medications including statins, proton pump inhibitors, antiepileptics, can interfere with all or certain classes of DAAs and need adjustment.

Step 8: Assess contraception, pregnancy status, pregnancy plans

Men and women of childbearing age should avoid pregnancy while on DAAs. Contraception should be arranged for all women of childbearing age and a pregnancy test performed just prior to DAA treatment commencement.

Those prescribed Ribavirin (Category X) need to consent to using double contraception both during and for 6 months post-treatment.

Practice Tip

Prescribing ribavirin is not recommended unless you are an experienced HCV primary care provider who has used ribavirin in the past. Ribavirin has potential serious adverse events, requires closer monitoring, dosage adjustment and is a Category X teratogen.

Step 9: Assess adherence/suitability for treatment

Adherence to the 8-24 weeks of treatment is important. Managing conditions or circumstances that are likely to affect adherence is recommended prior to therapy.

Psychiatric comorbidity or ongoing injecting drug usage are not contraindications to treatment but a person's mental health and lifestyle should be stable enough such that they can complete the proposed treatment.

Practice Tip

Encourage adherence reminder systems such as phone app reminders, webster packs, ticks on a calendar when they take daily medication or if taking opiate replacement therapy, take DAA tablet at time of daily dispensing.

Not all people will be appropriate for treatment or will be interested in treatment immediately. Continue regular ongoing 6 monthly monitoring/review and strongly encourage those most at risk of progression or transmission to be treated at each review.

Treatment is not recommended when a person's overall expected lifespan is less than 12 months.

Step 10: Consultation with specialist

GPs and other medical practitioners can prescribe under the S85 schedule without completing any specific training, provided this is done **in consultation** with a gastroenterologist, hepatologist or infectious diseases physician experienced in HCV treatment.

Formal accreditation is not required, but primary care providers need a working relationship with one or more specialists and up-skilling to be

confident in HCV diagnosis, pre-treatment assessment and management using DAA regimens. Seek specialist advice when in doubt about aspects of HCV care.

Consultation can be by phone, fax, or email. A **Remote Consultation Request for Initiation of Hepatitis C Treatment** template is available on the ASHM or GESA websites. (See contacts section.)

Further information on prescribing is available online at

<https://www.pbs.gov.au/info/publication/factsheets/hep-c/hepatitis-c-medicines-factsheet-for-community-based-prescribers>

Primary care based treatment is most suitable for people with no to moderate liver fibrosis. Some practitioners may prefer to refer patients to primary care providers with a high HCV caseload or to tertiary liver clinic services. See state Hepatitis Council websites for experienced primary care providers and nearest liver clinics.

Step 11: Treatment and monitoring

After receiving approval from the specialist to proceed with treatment, the next step is obtaining PBS Authority and Dispensing. The only PBS population criterion is that the patient must be aged 18 years or older.

A PBS Authority approval is required prior to prescribing.

When seeking an Authority number, prescribers will be asked:

1. Length of treatment required
2. Genotype
3. Cirrhosis present or not
4. Does the patient meet the **General Statement for Drugs for the Treatment of Hepatitis C?** (See PBS General Statement <http://www.pbs.gov.au/info/healthpro/explanatory-notes/general-statement-hep-c>)

Medications will be dispensed monthly (e.g. 28 tabs and 2 repeats for a 12 week course). The cost to the patient will be the usual dispensing pharmacy fees.

Treatment monitoring and side effects

Practice Tips

Many community pharmacies may not stock the medications and will need to order them in. Delivery can take 1-3 days. Inform people at the time of writing the script about this potential delay. Encourage patients to leave repeats at the same pharmacy, to contact the pharmacy a week before the next script is due (to allow preorder of the next month's supply) and to collect medications a few days before they have completed the month's supply to ensure they do not run out of medications if the pharmacy is closed etc.

Remind the person starting HCV treatment to seek advice before starting any other new medication while on DAA treatment, including over the counter medications due to the risk of potential drug interactions.

To assist in 'Treatment as Prevention' encourage people with chronic HCV who inject drugs to consider bringing in their peers (especially those that they inject with) to be tested and treated together at the same time.

Intense monitoring of people undergoing DAA therapy is usually unnecessary due to the high efficacy of these regimens, the lack of a role for response-guided therapy and the considerably improved side effect profile. Refer to **Consensus Statement**, Section 6 p 23-24 for more information.

How to determine if treatment was successful?

An undetectable HCV RNA (Qualitative PCR) 12 weeks post completion of treatment is considered a cure via successful viral eradication. It is the vital test to perform.

Table 4: Treatment Response Definitions

Response	Definition
SVR (sustained virological response)	Undetectable HCV RNA 12 weeks post treatment
Relapse or non-response	Detectable HCV RNA 12 weeks post treatment

Practice Tip

With DAA treatment, HCV cure rates are the same for those co-infected with HIV/HCV as those mono-infected with HCV.

Step 12: Post Treatment follow-up

Establish risk of re-infection and provide education re transmission prevention. Perform annual HCV RNA if at high risk of re-infection (e.g. PWID, HIV positive MSM)

Post treatment care needs to be individualised as below:

If cured:

- People who did not have pre-treatment cirrhosis and who have normal liver function tests after cure can be medically managed as if they never had HCV infection.
- If HCV had caused significant liver damage, clearing the virus does not mean the liver disease will fully regress.
- If cirrhosis was present pre-treatment, ongoing specialist review and monitoring for deterioration is required and patient entered into appropriate surveillance programs for HCC and oesophageal varices (See step 4 of **Decision-Making in viral hepatitis related advanced liver disease** resource). Develop a GP chronic liver disease management care plan (721) and consider a Team Care Arrangement (723) for ongoing chronic disease management.

The current recommendation regarding screening for hepatocellular carcinoma (HCC) is six monthly abdominal ultrasound

Practice Tips

If LFTs do not normalise post HCV treatment, refer to a specialist for alternative causes of liver disease.

Remember to follow-up and test the children born of women with chronic HCV during the pregnancy. If any children have a positive HCV RNA, refer to the nearest major children's hospital for assessment.

If not cured:

Not all patients will be cured. There are still certain genotypes, especially with cirrhosis, with suboptimal cure rates. Refer all that are not cured to specialist services for management and salvage therapy treatment.

If Reinfection Occurs

Encourage retreatment after referral/discussion with specialist. Some patients will be reinfected, but as with other diseases, they need and will have access to retreatment.

Undertake risk management and prevention of advanced liver disease from Alcohol and Non-Alcoholic Fatty Liver Disease:

■ Alcohol intake

Alcohol intake is associated with increased risk of liver damage. Advise any person with excessive alcohol consumption (more than 4 standard drinks per day) of their increased risk of developing advanced liver disease and offer alcohol reduction options. Consider

Naltrexone medication, referral to Addiction Medical Specialist and rehabilitation service as needed. All people with cirrhosis should be encouraged to stop drinking alcohol altogether even after cure of HCV. Brief interventions can assist - see www.health.gov.au for Guidelines for the Treatment of Alcohol Problems.

■ Non-Alcoholic Fatty Liver Disease (NAFLD)

Suspect NAFLD with obesity, T2DM, metabolic syndrome. There is a clear association between obesity and/or insulin resistance with or without diabetes and liver disease progression. Support lifestyle modification, weight loss, exercise, diabetic control.

Discrimination

Australian Commonwealth law prohibits discrimination against someone with an infectious disease, unless the discrimination can be shown to be necessary to protect public health. In addition, most states and territories have laws in the same terms as the Commonwealth law.

HCV is a highly stigmatised condition and many people living with the disease experience discrimination. The Anti-Discrimination Board of NSW found that discrimination in health care settings may take many forms and results in unfair treatment of patients.⁵

Behaviours which reflect stigmatisation towards a patient can also reduce the standard of health care received and lower the quality of life for people with HCV and should be avoided. Such behaviours include:

- Breaches of confidentiality and disclosure related to HCV, even among health care workers;
- Assumptions about how people acquired HCV;
- Assumptions about people's past or present drug use.

Avoiding discrimination

Health care workers should respect the rights of people with HCV. Everyone living with HCV should have access to care and services regardless of transmission route, gender, race, culture, sexual orientation or lifestyle issues (such as injecting drug use).

Needlestick injury and health care workers with HCV

For information on Needlestick Injury and Health Care Workers with HCV, please refer to the **Australian Guidelines for the prevention of Control of Infection in Healthcare (2010)**, published by the National Health and Medical Research Council (NHMRC), available at <http://www.nhmrc.gov.au/node/30290>.

A list of acknowledgements, contacts and resources is available in the downloadable version of this booklet on the ASHM website at www.ashm.org.au/resources

Endorsed by:

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Glossary of Terms

Antibody test – initial screening blood test that looks for antibodies to the virus and not for the virus itself. Anti-HCV antibodies may be detected in anyone who has been infected with hepatitis C. Antibodies may indicate past infection (if PCR is negative – see below).

Fibrosis – formation of scar tissue throughout the liver in response to inflammation or injury. Fibrosis may regress following successful HCV treatment.

Cirrhosis – extensive fibrosis in conjunction with development of regenerative nodules throughout the liver. The endpoint in patients who have progressive liver disease due to any cause. Cirrhosis may regress with successful HCV treatment.

Polymerase chain reaction (PCR) – a laboratory technique that amplifies the genetic material of a virus to a level that can be detected. The presence or absence of the virus can then be determined.

Window period – the period immediately after a person is infected with an agent, during which the infection is not detectable by laboratory tests, although the person may be infectious.

References

1. Australian recommendations for the management of hepatitis C infection: a consensus statement. <http://hepcguidelines.org.au/>
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3. ASHM. HIV, Viral Hepatitis and STIs: a guide for primary care providers 2014 Edition: 15
4. National HCV Testing Policy 2012, 4.0 [Online] [access 2012]. Available from <http://testingportal.ashm.org.au/hcv/informed-consent-for-testing>
5. Anti-discrimination Board of New South Wales. C-Change: Report of the enquiry into hepatitis C-related discrimination. Sydney:2001(Nov)

ASHM offers training in HIV, viral hepatitis and blood-borne viruses for general practitioners, nurses and allied health care workers around Australia.

For information on upcoming courses:

Visit www.ashm.org.au/training or contact the ASHM National Policy and Education Division on education@ashm.org.au or phone 02 8204 0700.



Australian Government

Department of Health

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Supporting the HIV, Viral Hepatitis and Sexual Health Workforce

www.ashm.org.au



Primary Care Providers and Hepatitis C SUPPLEMENTARY

Links to online HCV resources and calculators

Clinical Care Options (CCO) Hepatitis is available at:

<http://www.clinicaloptions.com/Hepatitis/Topics/HCV.aspx>

Clinical Care Options InPractice Hepatology, a clinical decision support tool that helps you find answers to patient care questions quickly, is available at:

<https://www.inpractice.com/Textbooks/Hepatology>

Management of Hepatitis C Infection is available at:

http://www.inpractice.com/Textbooks/Hepatology/ch8_Mgmt_of_Hep_C_Infection/

National Aids Treatment Program for the latest articles about Hepatitis C is available at:

<http://www.natap.org/>

APRI (AST Platelet Ratio Index) Score: $[(AST/upper\ limit\ of\ normal)/platelet\ count\ (expressed\ as\ platelets\ \times\ 10^9/L) \times 100]$ is available at:

<http://www.hepatitisc.uw.edu/page/clinical-calculators/apri>

PBS General Statement available at:

<http://www.pbs.gov.au/info/healthpro/explanatory-notes/general-statement-hep-c>

Australian recommendations for the management of hepatitis C virus infection: Consensus statement available from ASHM and ALA websites or

<http://Hepccguidelines.org.au/>

World Health Organization Guidelines for the screening, care and treatment of persons with hepatitis C infection;

<http://www.who.int/hepatitis/publications/hepatitis-c-guidelines/en/>

Coalition to Eradicate Viral Hepatitis in Asia Pacific

<http://www.cevhap.org/index.php/en/>

For Potential Drug Interactions, see:

University of Liverpool web search, available at: <http://www.hep-druginteractions.org/> or Liverpool HEP iChart - an interaction app for mobile devices, available for download from Google Play (android devices) or the APP Store (IOS devices)

Contacts

Hepatitis C and related organisations/groups can be contacted for further resources and support information.

Hepatitis Australia

Tel: 1800 437 222 (or 1800 HEP ABC)

Web: www.hepatitisaustralia.com

Hepatitis ACT

Tel: 1300 301 383 or 02 6230 6344

Web: www.hepatitisact.com.au

Hepatitis NSW

Tel: 02 9332 1599

1800 803 990 (Freecall country)

Web: www.hep.org.au

Northern Territory AIDS and Hepatitis Council

Tel: 08 8941 1711

1800 880 899 (Freecall)

Web: www.ntahc.org.au

Hepatitis Queensland

Tel: 07 3236 0610

1800 648 491 (Freecall country)

Web: www.hepqld.asn.au

Hepatitis South Australia

Tel: 08 8362 8443

1800 021 133 (Freecall country)

Web: www.hepccouncilsa.asn.au

Hepatitis Victoria

Tel: 03 9380 4644

1800 703 003 (Freecall country)

Web: www.hepcvic.org.au

Hepatitis Western Australia

Tel: 08 9227 9800

08 9328 8538 (Infoline)

1800 800 070 (Freecall country)

Web: www.hepatitiswa.com.au

Tasmanian Council on AIDS, Hepatitis and Related Diseases

Tel: 03 6234 1242

1800 005 900 (Freecall country)

Web: www.tascahrd.org.au

Further resources and support information is available from the following organisations:

Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM)

Tel: 02 8204 0700

Web: www.ashm.org.au

Australian Government Department of Health

Freecall: 1800 020 103

Web: www.health.gov.au

Australasian Hepatology Association

Web: www.hepatologyassociation.com.au

Australasian Society for Infectious Diseases (ASID)

Tel: 02 9256 5475

Web: www.asid.net.au

Australian Drug Foundation

Tel: 03 9278 8100 or 1300 858 584 (Infoline)

Web: www.adf.org.au

Australian Drug Information Network

Tel: 03 9278 8100

Web: www.adin.com.au

Australian Injecting and Illicit Drug Users League (AIVL)

Tel: 02 6279 1600

Web: www.aivl.org.au

Dieticians Association of Australia

Tel: 1800 812 942

Web: www.daa.asn.au

Haemophilia Foundation Australia (HFA)

Tel: 03 9885 7800

Web: www.haemophilia.org.au

Gastroenterological Society of Australia

Tel: 1300 766 176

Web: www.gesa.org.au

For HCV information: <http://www.gesa.org.au/professional.asp?cid=77&id=454>

ASHM resources

Other ASHM resources are available from the ASHM website:

www.ashm.org.au/resources

- B Positive: all you wanted to know about hepatitis B – a guide for primary care
- HIV, Viral Hepatitis and STIs: a guide for primary care providers (4th edition)
- Australasian Contact Tracing Guidelines
- Decision Making in Hepatitis B
- Decision Making in Hepatitis C
- Decision Making in Viral Hepatitis Related Advanced Liver Disease
- Stigma and Discrimination around HIV and HCV in Healthcare Settings: Research Report

Other resources

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

www.hepcguidelines.org.au

Acknowledgments

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