

Eliminating hepatitis C

Part 5. Practical steps in your practice

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For most people with chronic hepatitis C, treatment with direct-acting antiviral (DAA) therapy is simple and easily incorporated into primary care. GPs can help in the push to eliminate hepatitis C by 2030 through strategies to eliminate hepatitis C from their own practices. This includes finding their patients with hepatitis C, assessing, treating and following up after DAA therapy.

KEY POINTS

- GPs can help achieve the goal of eliminating hepatitis C in Australia by 2030 through 'microelimination' in their own practices.
- Since 2016, over 6000 Australian GPs have treated patients with direct-acting antiviral (DAA) therapy.
- For most people with chronic hepatitis C, treatment with DAA therapy is simple and easily incorporated into primary care.
- Patients can be tested for hepatitis C, assessed, treated and followed up for cure in four GP visits, with an optional fifth visit during treatment.
- Ongoing care for patients after DAA therapy includes care of comorbidities and strategies to prevent and detect reinfection in those with ongoing risk.

Australia aims to eliminate hepatitis C by 2030. The contribution of GPs is essential to achieving this goal, and Australian GPs are leading the world in treating their patients with hepatitis C in primary care. Since the arrival of direct-acting antiviral (DAA) therapy in March 2016, over 6000 GPs have treated one or more people living with hepatitis C.¹ GPs are also treating an increasing proportion of patients.² At the same time, there have been steady improvements in assessment and therapy, which have made the treatment pathway even more straightforward.³

This is the final article in the series on eliminating hepatitis C. Previous articles have reviewed patient testing, assessment, treatment and follow up after DAA treatment.⁴⁻⁷ This article summarises practical ways for GPs to eliminate hepatitis C in their individual practices.

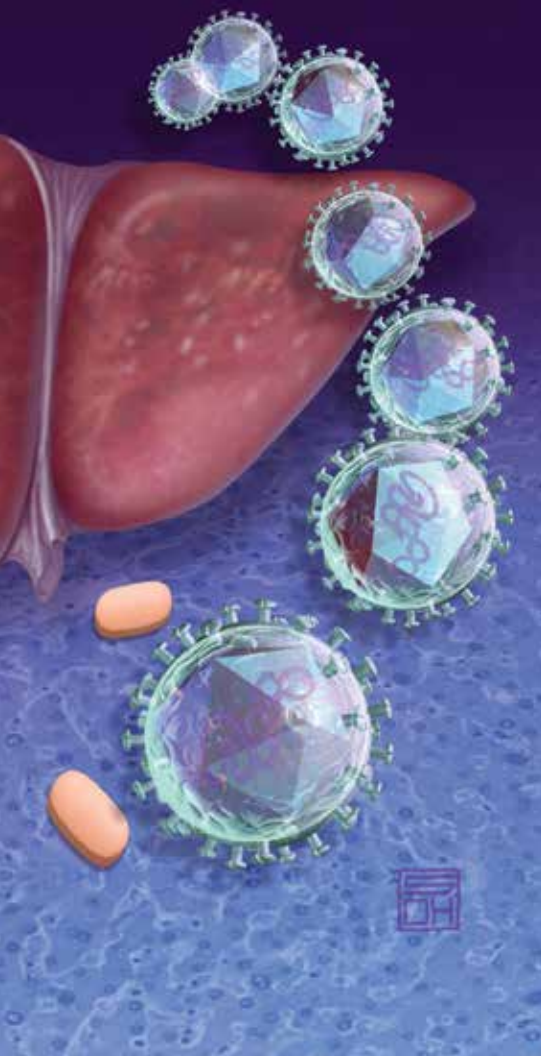
Microelimination in your practice

A useful approach for GPs to help achieve the goal of eliminating hepatitis C is 'microelimination'. This is the concept that we as GPs can focus on pursuing hepatitis C elimination in our own



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practice or community.⁸ This involves some planning to tailor an approach for our individual clinic. An example of a hepatitis C elimination plan is shown in Box 1.⁹

Eliminating hepatitis C involves four steps: finding patients with hepatitis C, assessing, treating and following up. These steps can be achieved in four patient visits, with an optional fifth visit during treatment, as summarised in Box 2. Depending on patient circumstances, medical practitioners experienced in hepatitis C management may be able to achieve the steps in three visits.

Find patients with hepatitis C

There are two main groups of people with hepatitis C who need DAA treatment:¹⁰

- people who are undiagnosed (estimated to be about 20%)
 - those who have been diagnosed previously with hepatitis C but remain untreated.
- Both groups are important to reach.

1. EXAMPLE OF A HEPATITIS C ELIMINATION PLAN*⁹

General

- Develop a practice plan or policy to test for and treat hepatitis C
- Support doctors and practice nurses to attend a hepatitis C training course or to undertake online courses
- Make the waiting area 'hepatitis friendly' by providing information booklets in appropriate languages
- Consider possible barriers to patients, such as stigma and discrimination, and consider whether specific training is needed
- Consider choosing a lead doctor or nurse to co-ordinate the hepatitis C elimination plan

Finding hepatitis C

- Develop a testing and screening policy for your practice
- Promote your practice as offering hepatitis C treatment, for example on the practice website
- Set up a template for test batteries on practice computers, for example bloodborne virus testing: anti-HCV, anti-HIV, HBsAg, anti-HBc, anti-HBs
- Include reflexive testing for HCV RNA in the template; for example 'If anti-HCV +ve then perform HCV RNA (PCR) test'
- Implement a policy to ask all new patients if they would like bloodborne virus screening
- Offer bloodborne virus screening to existing patients after risk assessment
- Audit the existing patient database to review all patients with known hepatitis C to determine their treatment status
- Consider using a software tool such as POLAR or PenCat to conduct a practice audit. Training and support may be available from the local Primary Health Network

Assessment

- Review staff training, for example in fibrosis assessment with the APRI score
- Set up a template for test batteries for patients with hepatitis C as per the guidelines: HCV genotype, HBV (HBsAg, anti-HBc, anti-HBs), anti-HIV, anti-HAV, FBC, LFT, UEC, INR, beta-hCG
- Establish links to tertiary centres when further assessment is needed and not available in the community (e.g. FibroScan)

Treatment

- Access current treatment guidelines:
 - Australian recommendations for the management of hepatitis C virus infection: a consensus statement³
 - Local Health Pathways
- Establish links with a dispensing pharmacy regarding stocking direct-acting antivirals (DAAs)
- Prepare an HCV-specific GP management plan
- Review adherence support if needed

Follow up

- Review recall systems and establish practice policy about recording hepatitis C and cirrhosis
- Establish a system to review the GP management plan
- Support patients to reduce reinfection: discuss opioid substitution treatment and needle and syringe programs
- Set up recall systems for patients who are at risk of reinfection after SVR to retest annually with HCV RNA (PCR)
- Set up recall systems for patients with cirrhosis to undertake six-monthly liver ultrasound examinations to screen for hepatocellular carcinoma and ensure linkage to specialist care

Abbreviations: anti-HAV = antibody to hepatitis A virus; anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; anti-HCV = antibody to hepatitis C virus; anti-HIV = antibody to HIV; APRI = aspartate aminotransferase to platelet ratio index; beta-hCG = beta human chorionic gonadotrophin; FBC = full blood count; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; LFT = liver function tests; UEC = urea, electrolytes, creatinine; SVR = sustained virological response.

* Based on the Burnet Institute Eliminate Hepatitis C Partnership. EC Partnership practice support toolkit (2018).⁹

Patients who are undiagnosed

Your approach to testing for hepatitis C will depend on your practice profile. One approach is to test everyone. Universal

testing (or screening) is recommended as part of antenatal screening in Australia.¹¹ GPs working in high-prevalence practices, such as in homeless health or opioid

2. FOUR-VISIT PLAN FOR HEPATITIS C TREATMENT*

Visit 1. Find

- Obtain informed consent
- Undertake bloodborne virus screening, including reflexive HCV RNA testing

Visit 2. Assess

- Discuss results; if positive for HCV RNA then proceed to pretreatment assessment
- Prepare a General Practice Management Plan (GPMP) and Team Care Arrangement (TCA) if indicated

Visit 3. Treat

- Assess APRI score, check for drug interactions, determine treatment, prescribe DAA, discuss adherence

Visit 3a. On treatment (optional)

- After one month of treatment, review side effects and adherence
- Provide pathology form for an SVR test (HCV RNA, liver function tests) for next visit

Visit 4. Follow up

- Twelve weeks after treatment is completed, check HCV RNA and liver function test results
- Review GPMP (TCA)

Abbreviations: APRI = aspartate aminotransferase to platelet ratio index; DAA = direct-acting antiviral; HCV = hepatitis C virus; SVR = sustained virological response.

* This plan could be completed in three to five visits depending on patient circumstances and medical practitioner experience.

substitution therapy, might consider offering testing to all patients.

Otherwise, testing for hepatitis C is generally based on risk, as discussed in Part 1 of this series.⁴ Sometimes, risk factors for hepatitis C may be difficult to identify during a busy GP consultation. In addition, for many patients, risk factors may have occurred in the distant past, such as a period of injecting drug use in their youth.

Most GPs take a social history from new patients, and this is an opportunity to enquire sensitively about risk factors such as current or past injecting drug use, along with recording demographic

Figure 1. Bloodborne virus screen and pretreatment assessment for patients with hepatitis C.⁹ Note that the quantitative hepatitis C virus RNA test is optional. A pregnancy test should also be performed if indicated.

variables such as country of birth and sexual behaviour. This information is also crucial for establishing whether there is a need to test for bloodborne viruses such as hepatitis B virus and HIV along with hepatitis C, which can all be performed as part of 'a new patient screen'. Tests included in bloodborne virus screening are shown in Figure 1.⁹

Existing patients also need to be tested for hepatitis C. There are many opportunities for testing as part of general health checks, sexual health screens, pre-travel check-ups and antenatal screening.

Patients with hepatitis C can also be found by searching the practice management system. Third-party tools such as POLAR (<https://outcomehealth.org.au/polar.aspx>) and PenCat (<https://help.pencs.com.au/dashboard.action>) can help find patients with potential risk factors (e.g. abnormal liver function test results) for testing. Advice on using these tools can be obtained from your local Primary Health Network.

Patients who are diagnosed but not treated

Most people living with hepatitis C have been previously diagnosed. This group of patients includes those who have declined treatment and others who are not engaged in regular medical care. Many people living with hepatitis C belong to marginalised populations and may have limited contact with the health-care system. They are also an important group to engage and to support into treatment. A GP outreach project, the Kombi Clinic, that aims to engage and support people with hepatitis C, especially marginalised populations, into treatment is described in Box 3.

Assess patients

Assessment of patients was covered in Part 2 of this series.⁵ The initial test to diagnose hepatitis C is a hepatitis C antibody test. If the result is positive then current infection needs to be confirmed with a qualitative hepatitis C virus (HCV)

3. THE KOMBI CLINIC: ENGAGING AND SUPPORTING PEOPLE WITH HEPATITIS C INTO TREATMENT

The Kombi Clinic is a mobile hepatitis C diagnostic and treatment clinic run by Brisbane GPs Matt Young and Joss O'Loan. They take the clinic, housed in a 1975 pine lime-coloured Kombi van, to drug rehabilitation centres, hostels, homeless shelters and the streets of South East Queensland. The clinic has a team of four: two GPs, a phlebotomist and a registered nurse who performs transient elastography scans (FibroScans).

'Destigmatising hepatitis C and intravenous drug use by rocking up in a Kombi, wearing loud pink flamingo Hawaiian shirts and cranking out the rock 'n' roll is vital', said GP Matt Young. 'It helps engage people who have been marginalised by mainstream, more formally dressed medical professionals.'

The clinic also embeds medical students, registrars and other GPs to encourage their learning 'the ropes' of hepatitis C eradication.



Figure. Clinic staff Joss O'Loan, Mim O'Flynn, Matt Young and Christie Hoger outside the Kombi Clinic.

Photo courtesy of Andrea Macleod, City North News, Brisbane, Qld.

RNA (PCR) test. If this result is positive then it is followed by HCV genotyping.

Other recommended blood tests after diagnosis of chronic hepatitis C are shown in Figure 1. They include tests:

- to detect hepatitis A, hepatitis B and HIV infection (if not already performed)
- to assess renal and liver function
- to exclude pregnancy.

The most complex part of pretreatment investigation is assessing for advanced liver disease. Patients with cirrhosis need specialist referral and may require changes to the treatment regimen. Most patients

do not have cirrhosis and can be treated easily in general practice.

Steps in patient assessment for advanced liver disease are shown in the Flowchart.⁹ A simple assessment that can be performed with the results of a full blood count and liver function testing is the aspartate aminotransferase to platelet ratio index (APRI). APRI calculators are available online (e.g. www.hepatitisc.uw.edu/page/clinical-calculators/apri). If the APRI score is less than 1.0 then cirrhosis is unlikely, and the patient can be treated without further investigation (see the case study in Box 4). If the APRI

score is 1.0 or more then the patient needs further assessment.

The most useful next investigation is transient elastography, such as FibroScan. In many parts of Australia, this investigation can be performed by a specialist nurse at the GP clinic or local hospital (Figure 2).

Treat with DAAs

Hepatitis C treatment is straightforward, as described in Part 3 of this series.⁶ DAA therapy for hepatitis C became available in March 2016 and has continued to evolve. Treatment options are based on the national guidelines, *Australian recommendations for the management of hepatitis C virus infection: a consensus statement (September 2018)*.³

The choice of DAA medication depends on:

- HCV genotype
- presence of cirrhosis
- patient's renal function
- potential drug interactions and
- patient or provider preference.

Potential drug interactions can be checked using the University of Liverpool's online interaction checker (www.hep-druginteractions.org/checker).

There are two regimens that can be used for any HCV genotype (pangenotypic). Their characteristics are summarised in the Table.

Minimal monitoring is required during treatment. Many medical practitioners see the patient after four weeks to check on adherence and side effects, but pathology testing is no longer generally needed.

GPs who are not experienced in hepatitis C treatment need to have the treatment plan signed off by a specialist (gastroenterologist, hepatologist or infectious diseases physician). They can communicate with the specialist by telephone, email or fax. A proforma can be used, such as:

- *Remote consultation request for initiation of hepatitis C treatment* form from the Gastroenterological Society of Australia (<http://cart.gesa>).

PATHWAYS TO LIVER FIBROSIS ASSESSMENT IN PRIMARY CARE FOR PATIENTS WITH HEPATITIS C^{9*}

Patient confirmed with chronic hepatitis C (HCV PCR positive)

Initial liver fibrosis assessment using APRI score[†]

APRI <1.0

APRI ≥1.0

Patient needs FibroScan to exclude cirrhosis

If patient is suitable, perform FibroScan[‡]

If patient is not suitable for FibroScan,[‡] refer to specialist[§]

FibroScan reading <12.5 kPa

FibroScan reading ≥12.5 kPa

No cirrhosis
Patient suitable for hepatitis C treatment in primary care

Likely cirrhosis
Refer to specialist for assessment and treatment[§]

Abbreviations: APRI = aspartate aminotransferase to platelet ratio index; PCR = polymerase chain reaction.

* Adapted from Burnet Institute Eliminate Hepatitis C Partnership. EC partnership practice support toolkit (2018).⁹

[†] An APRI calculator is available at: www.hepatitisc.uw.edu/page/clinical-calculators/apri

[‡] FibroScan is not approved for use in people younger than 18 years, pregnant women, people with ascites and people with a pacemaker or implantable defibrillator. FibroScan and APRI results should be interpreted in conjunction with a full clinical picture by a trained clinician.

[§] Appropriate specialists include gastroenterologists, hepatologists and infectious disease physicians, depending on local referral processes.

[org.au/membes/files/Resources/Hepatitis%20C/Remote_consultation_form_updated_Aug_2017.pdf](https://reach-c.ashm.org.au/membes/files/Resources/Hepatitis%20C/Remote_consultation_form_updated_Aug_2017.pdf)

- Reach-C interactive webpage (<https://reach-c.ashm.org.au>).

Follow up

Follow up of patients is essential after DAA treatment, as described in Part 4 of this series.⁷ The key date for follow up is 12 weeks after completion of therapy. A negative HCV RNA result at this time indicates hepatitis C cure, termed a sustained virological response (SVR12). This is truly a 'miracle of modern medicine' and a delightful message to convey to a patient.

Patients who are cured and have normal liver function test results and early liver disease need no further follow up, unless there is ongoing exposure to HCV, such as continuing injecting drug use. If liver function test results continue to be raised, indicating liver disease, or the patient has been diagnosed with cirrhosis then they need specialist review.

Patients with cirrhosis need lifelong monitoring with six-monthly liver ultrasound examinations because of the risk of hepatocellular carcinoma. Monitoring can be done by the GP or specialist. Built-in recall systems in GP software are helpful for this.

Figure 2. Hepatology nurse specialists can provide support to GPs managing patients with hepatitis C, performing mobile FibroScan assessments and giving advice to patients around treatment. Here, hepatitis nurse specialist Dianne How Chow advises GP registrar Jacqueline Nicholson on FibroScan results of a patient presenting for hepatitis C treatment.



HCV reinfection is possible as past infection does not provide any immunity to reinfection. Patients with an ongoing risk of HCV infection (e.g. continuing injecting drug use) need regular HCV RNA tests at least once a year as long as they remain at risk. Note that the anti-HCV test will give positive results for life, and this test is thus not useful for monitoring for reinfection and does not need to be repeated.

Complete patient care

Most people living with hepatitis C have comorbidities.¹² These can be:

- hepatitis C-related, such as cirrhosis, liver failure and type 2 diabetes
- associated with hepatitis C acquisition, such as injecting drug use and imprisonment
- associated with marginalisation and poverty, such as smoking, alcohol abuse and mental illness.

These problems require ongoing GP care and sometimes referral to other healthcare workers.

Some health problems that are more common in people living with hepatitis C are listed in Box 5. These health problems will probably persist after curative treatment of hepatitis C and impact on quality of life. Patient engagement in hepatitis C care can provide an opportunity to consider other health problems. Patients should be offered appropriate health screening according to the guidelines of the Royal Australian College of General Practitioners.¹³

Preventing reinfection is important. This may include offering opioid substitution therapy and encouraging safer

4. CASE STUDY: A PATIENT WITH A PAST DIAGNOSIS OF HEPATITIS C

Presentation

Tim is a 48-year-old new patient to your practice. He has heard from a friend that you 'know something about hepatitis C'. He reports that he was diagnosed with hepatitis C in the early 1990s after a car accident and blood transfusion when he was overseas. He has not done anything about it in the past but is now keen to have treatment. He is well apart from mild asthma treated with a regular inhaled corticosteroid and as-required inhaled salbutamol. He smokes about 10 cigarettes daily and drinks two to four beers on an average day.

Assessment

You order hepatitis C virus (HCV) genotyping and standard pathology tests. Results show that Tim is infected with HCV genotype 1. His AST to platelet ratio index (APRI) calculated with an online calculator is 0.609 (Figure). Hepatitis B serology indicates he is immune to hepatitis B. All other test results are normal.

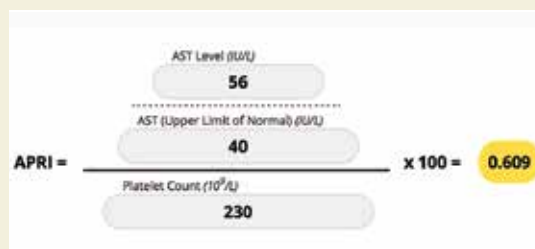


Figure. APRI result for Tim from an online calculator (www.hepatitisc.uw.edu/page/clinical-calculators/apri).

Management

You check for any potential drug interactions between Tim's current medication and hepatitis C direct-acting antiviral (DAA) therapy at the University of Liverpool online checker (www.hep-druginteractions.org/checker). As you are a new DAA prescriber, you complete and submit the Reach-C interactive form with the suggestion that Tim could be treated with either of the two pangenotypic DAA regimens. You receive a response the following day confirming your choice of DAA.

At Tim's next visit you discuss with him the results of the blood tests and his preference between the two DAA regimens. After telephoning the PBS for a PBS authority, you write Tim a DAA prescription and advise him that the pharmacy will likely need 24 hours' notice to fill the prescription.

Follow up

Tim returns to see you 12 weeks after he completes DAA treatment. He reports taking almost all doses of the DAA with mild nausea as the only adverse effect. You order a hepatitis C RNA (PCR) test, which is negative, and liver function tests, which have normal results.

Tim is delighted when you tell him that he is cured and does not need any further follow up. As part of his long-term care you discuss his smoking and alcohol use.

injecting (e.g. needle and syringe exchange). It is also helpful to encourage patients to support their partner and friends to access hepatitis C treatment, which will also reduce the likelihood of reinfection.

Treating hepatitis C around Australia

GP referral to a specialist is a longstanding model, and referral is appropriate for patients with advanced liver disease or major comorbidities, such as chronic

TABLE. PANGENOTYPIC DAA REGIMENS FOR PEOPLE WITH HEPATITIS C WHO ARE TREATMENT-NAÏVE WITH NO CIRRHOSIS^{3*}

Formulation (daily dose)	Tablets per day	Treatment duration	Recommended relation with food	Renal impairment (eGFR <30 mL/min/1.73 m ²)
Glecaprevir/pibrentasvir (300 mg/120 mg)	Three once daily	8 weeks	With food	No dose adjustment required
Sofosbuvir/velpatasvir (400 mg/100 mg)	One once daily	12 weeks	With or without food	Not recommended

Abbreviation: eGFR = estimated glomerular filtration rate.

* Adapted from Hepatitis C Virus Infection Working Group. Australian recommendations for the management of hepatitis C virus infection: a consensus statement (September 2018).³

5. COMMON COMORBIDITIES IN PATIENTS WITH HEPATITIS C

Social

- Poverty
- Imprisonment
- Unemployment
- Homelessness

Physical

- Smoking, chronic obstructive pulmonary disease (COPD)
- Type 2 diabetes
- Cardiovascular disease
- Obesity
- Lung and other smoking-related cancers
- Liver cancer

Mental health

- Alcohol dependency
- Opioid and amphetamine dependency
- Depression
- Psychosis

hepatitis B or HIV infection. However, treatment of chronic hepatitis C for most people is now simple and can be easily incorporated into primary care. Less experienced GPs can obtain specialist support and advice on a treatment plan by contacting a specialist by telephone, by email using the Reach-C proforma or by fax using the GESA proforma.

Rural GPs may need to manage all stages of diagnosis and treatment of hepatitis C, including the care of patients with cirrhosis (Box 6). GP outreach models have also been developed, in which GPs provide assessment and care in the community, as described above (Box 3).

Conclusion

Australian GPs are leading the world in curing hepatitis C. GPs can treat and cure most people living with hepatitis C with well-tolerated DAA therapy. Finding and treating patients with hepatitis C is straightforward and fits well with the skills that GPs use every day. Curing hepatitis C can be rewarding for the treating doctor as well as life changing for the patient. Eliminating hepatitis C from your practice is a great

6. HEPATITIS C TREATMENT IN RURAL AND REMOTE AREAS

Outside major centres, GPs often have to manage patients with all stages of hepatitis C, including cirrhosis, because of the lack of specialists. Rural GP Annie Balcomb has established a dedicated viral hepatitis clinic within a busy general practice in Orange, NSW, and treated over 150 patients with hepatitis C, including 30% with compensated cirrhosis. She collaborates with specialists via telephone and email as needed. Her success rates for treatment of patients with cirrhosis are the same as those of tertiary centres.

'Many specialists are supportive of GPs in rural and remote communities and keen to see patients with cirrhosis treated', said Dr Balcomb. 'Reach out for support if you cannot get the patient to a specialist.'



Figure. Rural GP Annie Balcomb.

step towards hepatitis C elimination in Australia.

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