

Evidence evaluation report — Hepatitis C

DRAFT 22 May 2017

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PROCESS OF THE REVIEW

Research questions

- 1 What is the incidence of Hepatitis C in the general Australian child-bearing population (15–45 years)?
- 2 What is the diagnostic value and clinical effectiveness of testing for Hepatitis C?
- 3a What is the potential for transmission of Hepatitis C in labour and birth and breastfeeding?
- 3b What is the potential for the transmission of blood borne viruses through scalp injuries (fetal scalp blood sampling or clips for heart rate monitoring)?
- 4 What are the additional considerations for Aboriginal and Torres Strait Islander women?

Search strategy

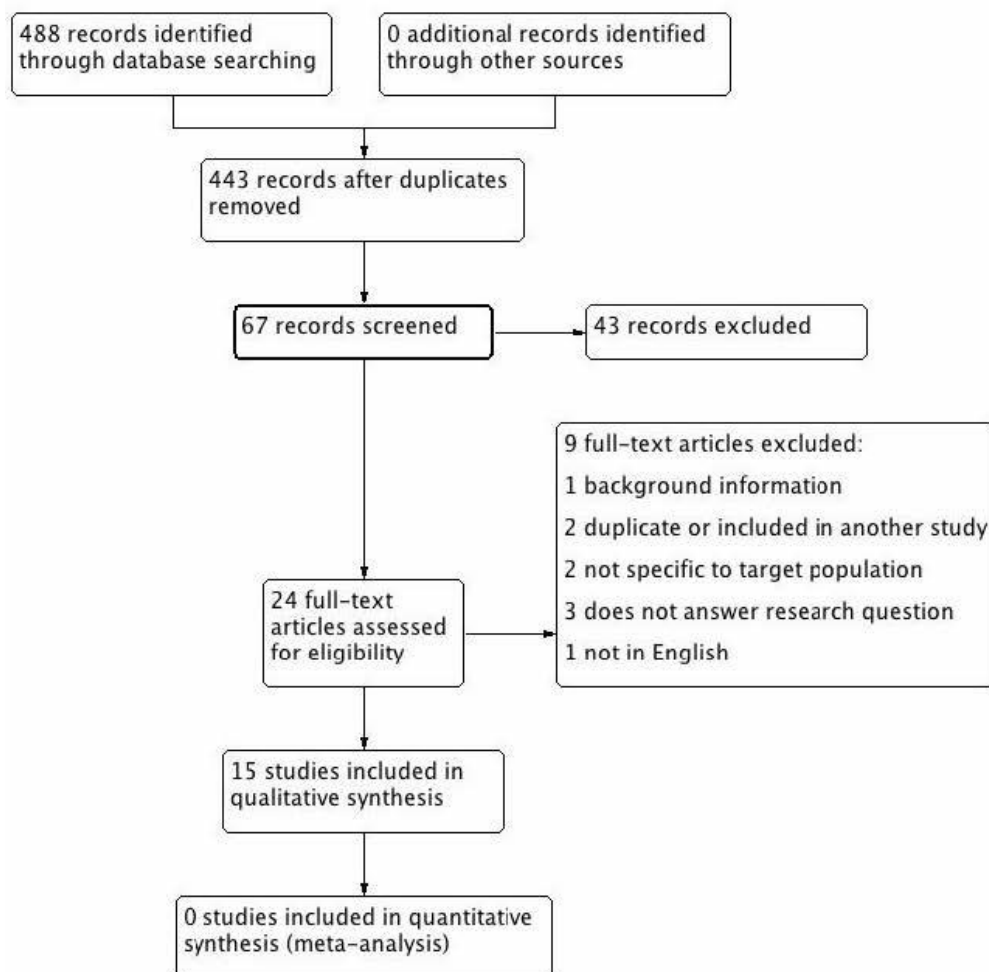
HEPATITIS C: SCREENING

Databases searched:

- EMBASE (OVID) and MEDLINE (OVID) = 449
- COCHRANE LIBRARY = 5
- INFORMIT (HEALTH COLLECTION, ATSIHEALTH) = 3
- AUSTRALIAN INDIGENOUS HEALTHINFONET = 31

Date of searches: 23/08/2016

Dates searched: 2010 to present



PRISMA flow diagram — screening

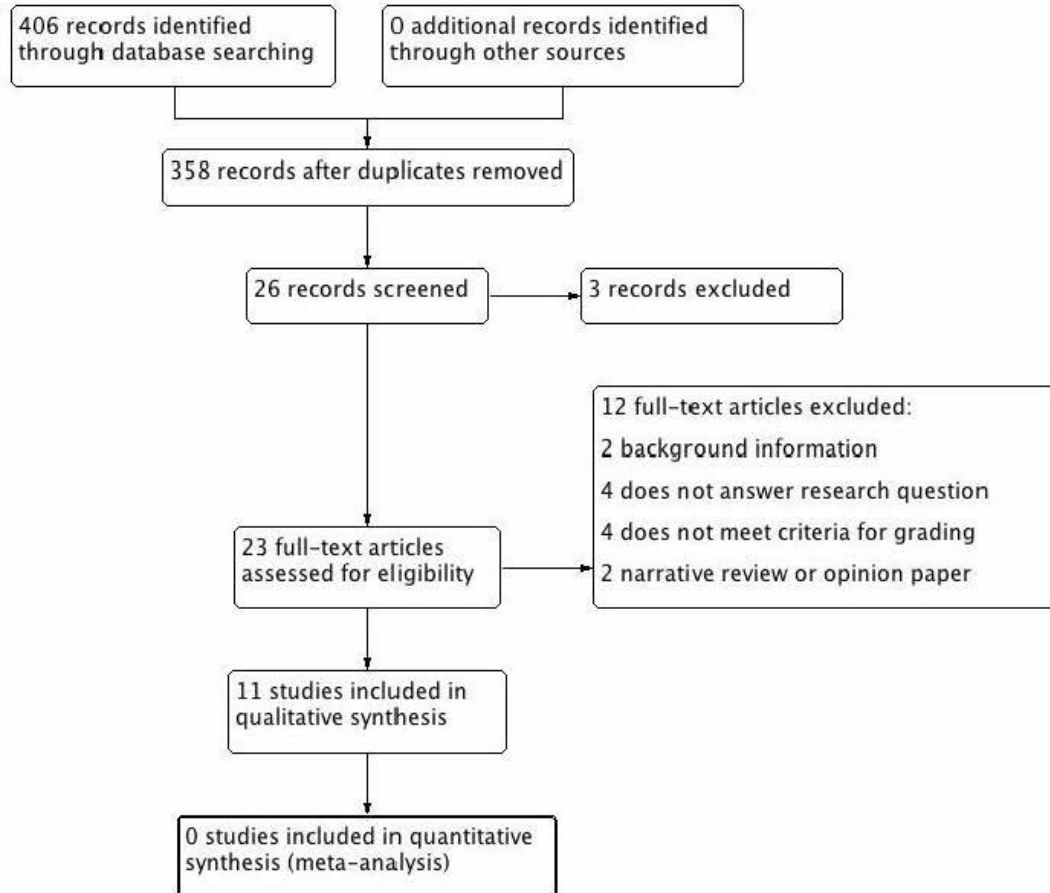
HEPATITIS C: INCIDENCE

Databases searched:

- EMBASE (OVID) and MEDLINE (OVID) and PSYCHINFO (OVID) = 354
- COCHRANE LIBRARY = 6
- INFORMIT (HEALTH COLLECTION, ATSIHEALTH) = 4
- AUSTRALIAN INDIGENOUS HEALTHINFONET = 42

Date of searches: 19/10/2016

Dates searched: 2008 to present



PRISMA flow diagram — incidence

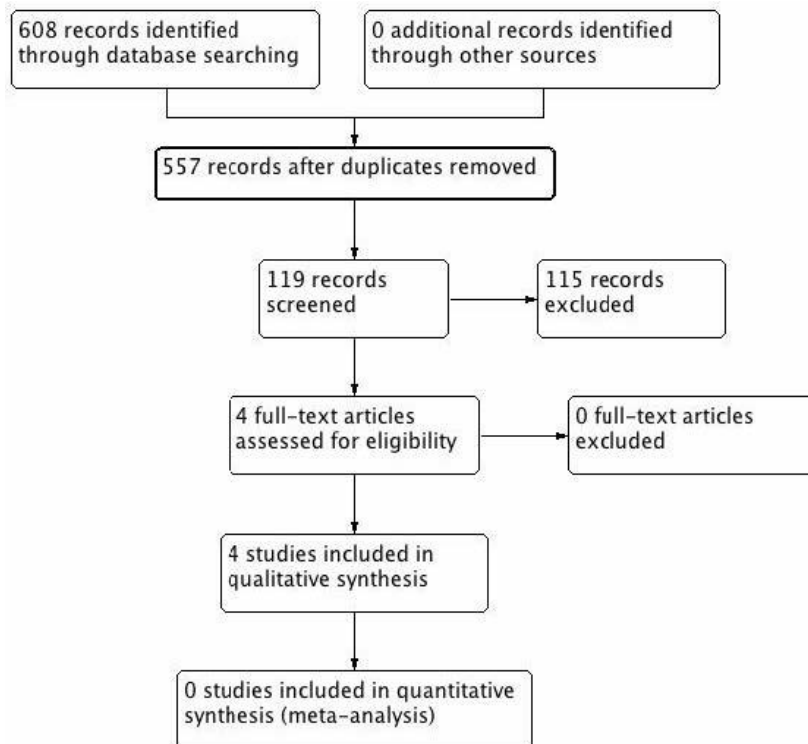
HEPATITIS C: TRANSMISSION

Databases searched:

- EMBASE (OVID) and MEDLINE (OVID) and PSYCHINFO (OVID) = 557
- COCHRANE LIBRARY = 8
- INFORMIT (HEALTH COLLECTION, ATSIHEALTH) = 1
- AUSTRALIAN INDIGENOUS HEALTHINFONET = 42

Date of searches: 14/11/2016

Dates searched: 2008 to present



PRISMA flow diagram — transmission

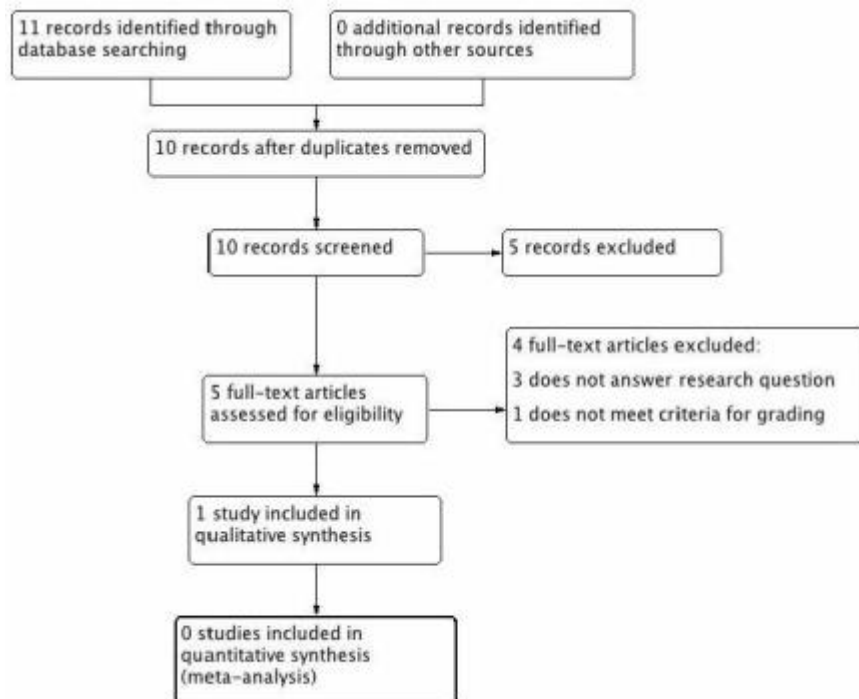
HEPATITIS C: SCALP INJURIES

Databases searched:

- EMBASE (OVID) and MEDLINE (OVID) and PSYCHINFO (OVID) = 10
- COCHRANE LIBRARY = 0
- INFORMIT (HEALTH COLLECTION, ATSIHEALTH) = 1
- AUSTRALIAN INDIGENOUS HEALTHINFONET = 0

Date of searches: 06/12/2016

Dates searched: 2008 to present



PRISMA flow diagram — scalp injuries

Full search strategies

SCREENING

MEDLINE AND EMBASE (OVID)

1. exp Pregnancy/ or exp Pregnancy Complications/ or exp Perinatal Care/ or exp Prenatal Care/
2. (pregnan\$ or antepart\$ or prenatal\$ or antenatal\$ or perinatal\$ or obstetric\$ or maternal\$).mp.
3. 1 or 2
4. exp Hepatitis C/ or Hepacivirus/
5. ((hepatitis adj c) or (hep adj C) or HCV or hepacivirus).mp.
6. 4 or 5
7. exp Mass Screening/
8. (screen\$ or testing).mp.
9. 7 or 8
10. 3 and 6 and 9
11. limit 10 to yr="2010 –Current"
12. remove duplicates from 11

COCHRANE

1. MeSH descriptor: [Mass Screening] explode all trees
2. (screen* or testing):ti,ab,kw
3. MeSH descriptor: [Hepatitis C] explode all trees
4. MeSH descriptor: [Hepacivirus] explode all trees
5. (HCV or hepacivirus or (hep next C) or (hepatitis next C)):ti,ab,kw
6. MeSH descriptor: [Pregnancy] explode all trees
7. MeSH descriptor: [Pregnancy Complications] explode all trees
8. MeSH descriptor: [Perinatal Care] explode all trees
9. MeSH descriptor: [Prenatal Care] explode all trees
10. (pregnan* or antepart* or prenatal* or antenatal* or perinatal* or obstetric* or maternal*):ti,ab,kw
11. #1 or #2
12. #3 or #4 or #5
13. #6 or #7 or #8 or #9 or #10
14. #11 and #12 and #13
15. 2010 to current

AUSTRALIAN INDIGENOUS HEALTHINFONET

Title: Hepatitis C

2010 to current

INFORMIT (HEALTH COLLECTION, ATSIHEALTH)

All fields: (pregnan* OR antepart* OR prenatal* OR antenatal* or perinatal* OR obstetric* OR maternal*)
AND ("hepatitis C" OR "hep C" OR HCV OR hepacivirus)

2010 to current

INCIDENCE

MEDLINE AND EMBASE AND PSYCHINFO (OVID)

1. exp Hepatitis C/ or Hepacivirus/
2. ((hepatitis adj c) or (hep adj C) or HCV or hepacivirus).mp.
3. exp Australia/
4. (Australia* or (New adj South adj Wales) or Victoria* or Queensland* or Tasmania* or (Northern adj Territory)).mp.
5. (prevalence or incidence or epidemiol* or seroprevalence or seroincidence or screen* or test*).mp.
6. exp Prevalence/ or exp Incidence/ or exp Epidemiology/
7. (woman or women or female or girl).mp.
8. 1 or 2
9. 3 or 4
10. 5 or 6
11. 7 and 8 and 9 and 10
12. remove duplicates from 11
13. limit 12 to yr="2008 -Current"

COCHRANE

1. MeSH descriptor: [Hepatitis C] explode all trees
2. MeSH descriptor: [Hepacivirus] explode all trees
3. (HCV or hepacivirus or (hep next C) or (hepatitis next C)):ti,ab,kw
4. MeSH descriptor: [Australia] explode all trees
5. (Australia* or (New next South next Wales) or Victoria* or Queensland* or Tasmania* or (Northern next Territory)):ti,ab,kw
6. MeSH descriptor: [Prevalence] explode all trees
7. MeSH descriptor: [Incidence] explode all trees
8. MeSH descriptor: [Epidemiology] explode all trees
9. (prevalence or incidence or epidemiol* or seroprevalence or seroincidence or screen* or test*):ti,ab,kw
10. (woman or women or female or girl) :ti,ab,kw
11. #1 or #2 or #3
12. # #4 or #5
13. #6 or #7 or #8 or #9
14. #10 and #11 and #12 and #13
15. 2008 to current

AUSTRALIAN INDIGENOUS HEALTHINFONET

Title: Hepatitis C

2008 to current

INFORMIT (HEALTH COLLECTION, ATSIHEALTH)

All fields: ("hepatitis C" OR "hep C" OR HCV OR hepacivirus) AND Australia AND (prevalence OR incidence OR epidemiology OR seroprevalence OR seroincidence OR screen OR test) AND (women OR woman OR female OR girl)

2008 to current

TRANSMISSION

MEDLINE AND EMBASE AND PSYCHINFO (OVID)

1. exp Hepatitis C/ or Hepacivirus/
2. ((hepatitis adj c) or (hep adj C) or HCV or hepacivirus).tw.
3. Infectious Disease Transmission, Vertical/
4. (vertical or mother?to?child or mother?child or mother?to?infant or mother?infant or maternal?to?child or maternal?child or maternal?to?infant or maternal?infant or adult?to?child or adult?to?infant or mother?to?baby or maternal?fetal or MTCT or (perinatal adj transmission) or breast?feed\$.tw.
5. 1 or 2
6. 3 or 4
7. 5 and 6
8. remove duplicates from 7
9. limit 8 to yr="2008 -Current"

COCHRANE

1. MeSH descriptor: [Hepatitis C] explode all trees
2. MeSH descriptor: [Hepacivirus] explode all trees
3. (HCV or hepacivirus or (hep next C) or (hepatitis next C)):ti,ab,kw
4. MeSH descriptor: [Infectious Disease Transmission, Vertical]
5. (vertical or mother?to?child or mother?child or mother?to?infant or mother?infant or maternal?to?child or maternal?to?infant or adult?to?child or adult?to?infant or mother?to?baby or maternal?fetal or MTCT or (perinatal next transmission) or breast?feed*):ti,ab,kw
6. #1 or #2 or #3
7. #4 or #5
8. #6 and #7
9. 2008 to current

AUSTRALIAN INDIGENOUS HEALTHINFONET

Title: Hepatitis C

2008 to current

INFORMIT (HEALTH COLLECTION, ATSIHEALTH)

("hepatitis C" OR "hep C" OR HCV OR hepacivirus) AND ("mother to child" OR "mother-to-child" OR "mother child" OR "mother-child" OR "mother to infant" OR "mother-to-infant" OR "mother infant" OR

"mother-infant" OR "maternal-to-child" OR "maternal to child" OR "maternal child" OR maternal-child OR "maternal to infant" OR "maternal-to-infant" OR "maternal infant" OR "maternal-infant" OR "mother to baby" OR "mother-to-baby" OR "maternal fetal" or "maternal-fetal" OR MTCT OR "perinatal transmission" OR vertical)

2008 to current

SCALP INJURIES

MEDLINE AND EMBASE AND PSYCHOINFO (OVID)

1. Infectious Disease Transmission, Vertical/
2. (vertical or mother?to?child or mother?child or mother?to?infant or mother?infant or maternal?to?child or maternal?child or maternal?to?infant or maternal?infant or adult?to?child or adult?to?infant or mother?to?baby or maternal?fetal or MTCT or transmission).mp.
3. (fetus* or fetal* or foetus* or foetal*).mp.
4. scalp.mp.
5. 1 or 2
6. 3 and 4 and 5
7. limit 6 to yr="2008 –Current"
8. remove duplicates from 7

COCHRANE

1. MeSH descriptor: [Infectious Disease Transmission, Vertical]
2. (vertical or mother?to?child or mother?child or mother?to?infant or mother?infant or maternal?to?child or maternal?to?infant or adult?to?child or adult?to?infant or mother?to?baby or maternal?fetal or MTCT or transmission):ti,ab,kw
3. (fetus* or fetal* or foetus* or foetal*):ti,ab,kw
4. Scalp:ti,ab,kw
5. #1 or #2
6. #3 and #4 and #5
7. 2008 to current

AUSTRALIAN INDIGENOUS HEALTHINFONET

Title: Scalp

2008 to current

INFORMIT (HEALTH COLLECTION AND ATSHI HEALTH)

Scalp AND (fetus* OR fetal* OR foetus* OR foetal*)

2008 to current

Exclusion criteria

Full texts of 56 papers were reviewed and the exclusion criteria outlined below applied.

Reason for exclusion	Number of exclusions		
	Question 1	Question 2	Question 3
Background information	2	1	—
Duplicate or included in another study	—	2	—
Not specific to target population (eg specific to non-pregnant women or high-risk women)	—	2	—
Does not answer research question	4	3	3
Does not meet criteria for grading (eg no outcomes reported or reporting too limited to establish risk of bias, abstract)	4	—	1
Narrative review or opinion paper (editorial, letter, comment)	2	—	—
Not in English	—	1	—
Total exclusions	12	9	4

The analysis included 11 studies for research question 1 (including 1 narrative review, which provided the only information on prevalence in Aboriginal people), 15 studies for research question 2 (including

4 narrative reviews, which were the only identified studies on clinical utility of testing) and 5 studies for research question 3 (including 4 narrative reviews). No studies were identified for research question 4.

Assigning level of evidence

Levels of evidence were assigned using the NHMRC levels and the following definitions.

Level	Aetiology (research question 1)	Screening (research question 2)
I	A systematic review of level II studies	A systematic review of level II studies
II	A prospective cohort study	A randomised controlled trial
III-1	All or none	Pseudo-randomised controlled trial
III-2	A retrospective cohort study	A comparative study with concurrent controls: <ul style="list-style-type: none"> ▪ Non-randomised, experimental trial ▪ Cohort study ▪ Case-control study
III-3	A case-control study	A comparative study without concurrent controls: <ul style="list-style-type: none"> Historical control study Two or more single arm study
IV	A cross-sectional study or case series	Case series

Study design definitions

- **All or none** — all or none of a series of people (case series) with the risk factor(s) experience the outcome. The data should relate to an unselected or representative case series, which provides an unbiased representation of the prognostic effect. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of small pox after large-scale vaccination. This is a rare situation.
- **Case series** — a single group of people exposed to the intervention (factor under study). **Post-test** – only outcomes after the intervention (factor under study) are recorded in the series of people, so no comparisons can be made. **Pre-test/post-test** – measures on an outcome are taken before and after the intervention is introduced to a series of people and are then compared (also known as a 'before- and-after study').
- **Case-control study** — people with the outcome or disease (cases) and an appropriate group of controls without the outcome or disease (controls) are selected and information obtained about their previous exposure/non-exposure to the intervention or factor under study.
- **Cross-sectional study** — a group of people are assessed at a particular point (or cross-section) in time and the data collected on outcomes relate to that point in time ie proportion of people with asthma in October 2004. This type of study is useful for hypothesis-generation, to identify whether a risk factor is associated with a certain type of outcome, but more often than not (except when the exposure and outcome are stable eg genetic mutation and certain clinical symptoms) the causal link cannot be proven unless a time dimension is included.
- **Historical control study** – outcomes for a prospectively collected group of people exposed to the intervention (factor under study) are compared with either (1) the outcomes of people treated at the same institution prior to the introduction of the intervention (ie. control group/usual care), or (2) the outcomes of a previously published series of people undergoing the alternate or control intervention.
- **Non-randomised, experimental trial** - the unit of experimentation (eg. people, a cluster of people) is allocated to either an intervention group or a control group, using a non-random method (such as patient or clinician preference/availability) and the outcomes from each group are compared. This can include:
 - **a controlled before-and-after study**, where outcome measurements are taken before and after the intervention is introduced, and compared at the same time point to outcome measures in the (control) group.

- **an adjusted indirect comparison**, where two randomised controlled trials compare different interventions to the same comparator ie. the placebo or control condition. The outcomes from the two interventions are then compared indirectly.
- **Prospective cohort study** — where groups of people (cohorts) are observed at a point in time to be exposed or not exposed to an intervention (or the factor under study) and then are followed prospectively with further outcomes recorded as they happen.
- **Pseudo-randomised controlled trial** - the unit of experimentation (eg. people, a cluster of people) is allocated to either an intervention (the factor under study) group or a control group, using a pseudo-random method (such as alternate allocation, allocation by days of the week or odd-even study numbers) and the outcomes from each group are compared.
- **Randomised controlled trial** — the unit of experimentation (eg. people, or a cluster of people⁴) is allocated to either an intervention (the factor under study) group or a control group, using a random mechanism (such as a coin toss, random number table, computer-generated random numbers) and the outcomes from each group are compared.
- **Retrospective cohort study** — where the cohorts (groups of people exposed and not exposed) are defined at a point of time in the past and information collected on subsequent outcomes, eg. the use of medical records to identify a group of women using oral contraceptives five years ago, and a group of women not using oral contraceptives, and then contacting these women or identifying in subsequent medical records the development of deep vein thrombosis.
- **Systematic literature review** — systematic location, appraisal and synthesis of evidence from scientific studies.
- **Two or more single arm study** – the outcomes of a single series of people receiving an intervention (case series) from two or more studies are compared.

Source: NHMRC (2009) *NHMRC levels of evidence and grades of recommendations for developers of guidelines*.

Selection of outcomes for GRADE analysis

Outcomes considered for inclusion comprised conditions associated with hepatitis C in pregnancy. Six outcomes were selected on the basis of clinical impact.

Outcome	Importance	Inclusion
Vertical transmission of hepatitis C		<input checked="" type="checkbox"/>
Low birth weight		<input checked="" type="checkbox"/>
		<input checked="" type="checkbox"/>
		<input checked="" type="checkbox"/>
		<input checked="" type="checkbox"/>

Key: 1 – 3 less important; 4 – 6 important but not critical for making a decision; 7 – 9 critical for making a decision

Evidence tables

1. What is the incidence of Hepatitis C in the general Australian child-bearing population (15–45 years)?

1.1 Evidence summary

Results of previous review

This question was not asked in the literature review conducted to inform Module I of the guidelines (Australian Health Ministers' Advisory Council 2012).

Results of the current review

No studies were identified that directly answered the question. Observational studies identified the following groups as at higher risk of testing positive for hepatitis C antibodies or infection:

- *people who inject drugs:*
 - drug users accessing low-threshold primary healthcare in inner-city Sydney had an infection prevalence of 62% (Islam et al 2013);
 - women were at greater risk than men of exposure to hepatitis C infection during the early years of injection (Iversen et al 2010);
 - pregnant women on methadone maintenance treatment had higher rates of seropositivity (84%) than women in the non-methadone group (3%) ($P < 0.001$) (Liu et al 2009)
 - Aboriginal people who injected drugs were more likely to be seropositive (58.7%) than those who did not (2.9%) (Graham et al 2016)
- *people in prison:*
 - seroprevalence was reported as 33.8% in 2004, 30.8% in 2007 and 35.5% in 2010 (Reekie et al 2014) and 42% (Miller et al 2009), incidence as 31.6 per 100 person years (Teutsch et al 2010)
 - women in prison were reported to more likely than men to have positive HCV antibody status (risk ratio 1.39; 95%CI 1.313—1.482; $p < 0.001$) (Miller et al 2009), (incidence rate ratio 1.33; 95%CI 1.00 to 1.77; $p = 0.05$) (Reekie et al 2014) or infection (rate ratio 1.6; 95%CI 1.1 to 2.4) (Teutsch et al 2010)
 - the pooled prevalence of seropositivity was 18.1% among Aboriginal adults in prison (Graham et al 2016)
 - among young offenders (12–19 years), hepatitis C rates were 7.3% for Aboriginal people and 5.3% for non-Aboriginal people (van der Poorten et al 2008)

Additional information

The Australian Annual Surveillance Report (The Kirby Institute 2015) reported that:

- the national rate of diagnosis of hepatitis C infection in 2014 was 46 per 100,000, representing a continuing decline over the past 10 years, from 61 per 100,000 in 2005
- the rate of hepatitis C diagnosis in the Aboriginal and Torres Strait Islander population increased to 164 per 100,000 in 2014 from 119 per 100,000 in 2010 (data from Northern Territory, South Australia, Tasmania, Western Australia), a rate almost five times greater than in the non-Indigenous population (35 per 100,000)
- in the last 10 years, the rate of diagnosis of hepatitis C infection has declined in most age groups, but most markedly in the 25–29 year age group (by 49%), and 20–24 year age group (44%), with declines in these age groups observed in both males and females
- the population rate of newly diagnosed hepatitis C infection in 2014 was highest in the Northern Territory (70 per 100 000 in 2014) and Queensland (57 per 100 000 in 2014)
- the prevalence of hepatitis C in people who inject drugs attending needle and syringe programs was 54%, a level that has remained stable for 5 years
- according to the National Prison Entrants' Bloodborne Virus Survey, prevalence of hepatitis C among people entering prison is 31%.

Advice to EWG

The information from the Kirkby Institute and the evidence from observational studies could be used to inform background discussion.

Women of child-bearing age

Study ref	LoE	N	Aim/ methods	Findings	Comments
(Harrison et al 2015)	IV	7,401	<p>Aim: to compare the incidence of transmissible diseases in infertile couples attending a network of full-service, full-stimulation ART clinics across Queensland and in a low-stimulation, lower-cost ART clinic in south-east Queensland working in association with the full-service clinics.</p> <p>Methods: The incidence of hepatitis B, hepatitis C, HIV I/O/2 and syphilis detection was ascertained in infertile couples.</p>	<p>Hepatitis C was the most commonly detected infection (overall 0.47%) with the highest incidence in the low-cost clinic (1.66%).</p> <p>Transmissible infections were detected more frequently in males (47) than in females (33) with males predominating most in the Springwood low-cost clinic where they were 3.75 times more likely than females to have a transmissible infection.</p>	
(Mapagu et al 2008)	III-2	3,156	<p>Aim: to explore the value of routine HCV testing in a sexual health centre population.</p> <p>Methods: Medical records and pathology data concerning all patients tested for HCV between 2000 and 2002 at Canberra Sexual Health Centre were audited to determine whether the diagnosis of HCV was already known and which, if any, risk factors were identified at the time of testing.</p>	<p>HCV seropositivity was confirmed in 95 patients (3.0%; 95% CI 2.4-3.7), of which 29 (30.5%) were new diagnoses. A total of 85.3% of all patients with confirmed HCV infection reported a history of injecting drug use. Tattoos and body piercings were the most common risk factor in those who denied ever injecting. Risk factor assessment correctly identified all but one positive patient.</p> <p>There were 52 HCV positive females (3.4%; 95% CI 2.4-4.5) and 43 HCV positive males (2.7%; 95% CI 1.9-3.6).</p>	

People who inject drugs

Study ref	LoE	N	Aim/ methods	Findings	Comments
(Graham et al 2016)	IV	15 studies	<p>Aim: to estimate the pooled prevalence of anti-HCV among Aboriginal people in Australia.</p> <p>Methods: A meta-analysis by population-group was conducted if three or more studies reported a prevalence estimate.</p>	<p>The pooled prevalence of anti-HCV was 58.7% (95%CI: 53.9 - 63.5) among Aboriginal people who inject drugs and 2.9% (95%CI: 0.30 - 6.1) among Aboriginal people who did not inject drugs, however there was significant heterogeneity ($I^2 > 90.0\%$, $P < 0.01$). There was significant selection bias in the studies as most included individuals who inject drugs.</p> <p>Our review highlights that unsafe injecting is the main transmission route for HCV infection among Aboriginal people in Australia.</p>	Narrative review
(Islam et al 2013)	IV	500	<p>Aim: to examine prevalence of STIs and perceived barriers to safe sex among drug users accessing low-threshold primary healthcare in inner-city Sydney.</p> <p>Methods: Data were extracted manually from clients' medical records and analysed using STATA.</p>	<p>Prevalence of hepatitis C was 62%. Recent unprotected vaginal and anal intercourse were reported by 85% and 26% of clients, respectively. Younger clients and those with a history of sex work or recent anal intercourse were more likely to report multiple recent unprotected sex partners. Having a regular sex partner was the most prevalent barrier to condom use (37%), and was more likely to be identified by clients who were older, of Indigenous descent, and/or heterosexual. Drug intoxication was a second important barrier (20%), and was more commonly identified by excessive alcohol users.</p>	

Study ref	LoE	N	Aim/ methods	Findings	Comments
(Iversen et al 2010)	II	15,852	<p>Aim: to assess gender differences in hepatitis C antibody prevalence and associated risk behaviours amongst a large sample of people who inject drugs in Australia.</p> <p>Methods: During a one to two week period in October, PWID attending selected NSP sites are invited to participate in the Australian NSP Survey. Between 1998 and 2008, approximately 16,000 individuals completed a self-administered questionnaire and provided a capillary blood sample for HIV and HCV antibody testing. We stratified our sample by time since onset of injecting and analysed the demographic characteristics, injecting behaviours and antibody test results to determine gender differences.</p>	<p>Women were found to be at increased risk of exposure to hepatitis C in all duration of injection categories except those injecting for 17 or more years. In the early years of injecting, women also reported higher rates of receptive sharing of needles and syringe and ancillary equipment when compared to men. Last injecting heroin, methadone or buprenorphine was significantly associated with HCV antibody prevalence amongst both males and females injecting for less than 5 years.</p> <p>Findings indicate that women are at greater risk than men of HCV infection during the early years of injection through higher rates of receptive sharing of needles and syringes and/or ancillary equipment. Our results suggest that women who are new to injecting, and Indigenous women in particular, should be identified as priority populations when developing and implementing harm reduction strategies that target people who inject illicit drugs.</p>	

Study ref	LoE	N	Aim/ methods	Findings	Comments
(Iversen et al 2013)	III-2	724	<p>Aim: To examine trends in HCV incident infection among injection drug users (IDUs) attending needle and syringe programs (NSPs) in Australia in 1995 to 2010.</p> <p>Methods: We created a passive retrospective cohort of 724 IDUs who tested negative for HCV antibodies by a simple deterministic method linking partial identifiers to find repeat respondents in annual cross-sectional serosurveillance.</p>	<p>We identified 180 HCV seroconversions over the study period, for a pooled incidence density of 17.0 per 100 person-years (95% confidence interval [CI]=14.68, 19.66). Incidence density declined, from a high of 30.8 per 100 person-years (95% CI=21.3, 44.6) in 2003 to a low of 4.0 (95% CI=1.3, 12.3) in 2009.</p>	
(Liu et al 2009)	III-2	10,282	<p>Aim: To describe the patterns of testing for hepatitis C virus (HCV) infection in methadone-maintained pregnant women and their infants.</p> <p>Methods: Retrospective review of medical records from one rural and two metropolitan hospitals in New South Wales for pregnant women on methadone maintenance treatment and infants born to these women between 1 January 2000 and 31 December 2006, as well as records for pregnant women who were not on methadone treatment.</p>	<p>Of 295 pregnant women on methadone maintenance treatment, 288 were tested for anti-HCV antibodies (98%), compared with 1,995 of 9,987 women who were not on methadone treatment (20%) (P<0.001). Seropositive results were obtained for 243 women in the methadone group (84%) and 54 in the non-methadone group (3%) (P<0.001), of whom 44 (18%) and 17 (31%), respectively, were subsequently tested for HCV RNA (P=0.03). HCV RNA test results were positive for 31 (70%) and 10 (59%) seropositive women in the methadone and non-methadone groups, respectively (P=0.39). Of infants of HCV-seropositive methadone-maintained mothers, 27% of those for whom we had follow-up attendance data received HCV testing, and one of these infants tested positive for anti-HCV antibodies and HCV RNA.</p>	

People in prison

Study ref	LoE	N	Aim/ methods	Findings	Comments
(Graham et al 2016)	IV	15 studies	<p>Aim: to estimate the pooled prevalence of anti-HCV among Aboriginal people in Australia.</p> <p>Methods: A meta-analysis by population-group was conducted if three or more studies reported a prevalence estimate. Due to a long time period, we separated the studies estimating the prevalence anti-HCV among Aboriginal people in prison into two time periods, 1994–2004 and 2005–2012.</p>	<p>Among Aboriginal people in prison, the pooled prevalence of anti-HCV was 18.1% (95%CI: 6.6 - 29.7). The pooled prevalence among Aboriginal people in prison was 25.7% (95%CI: 4.1-47.3) in studies published between 1994 - 2004 and 14.5% (95%CI: 1.7 - 27.3) in studies published from 2005 - 2012.</p>	Narrative review
(Miller et al 2009)	II	662	<p>Aim: To determine entry antibody seroprevalence and seroconversion to hepatitis C virus (HCV) and associated risk factors in newly incarcerated prisoners.</p> <p>Methods: Males and females entering South Australian prisons completed risk factor surveys and were offered HCV-antibody testing. Participants completed additional surveys and, if HCV-negative at last test, underwent further antibody tests at 3-monthly intervals for up to 15 months. Data were analyzed using univariate and multivariate techniques.</p>	<p>HCV seroprevalence was estimated at 42%. Previous injecting history was highly prevalent at entry (64%) and both community and prison injecting independently predicted entry HCV status. Tattooing was not an important risk factor. While community exposure could not be ruled out, three seroconversions were noted in 148 initially HCV-seronegative individuals occurring in a median 121 days--4.6 per 100 person-years. Prison injecting was infrequently reported, but HCV-seropositive participants were significantly more likely to commence IDU in prison than seronegative participants (p=0.035).</p> <p>Women were significantly more likely than men to have positive HCV antibody status (RR 1.39; 95%CI 1.313—1.482; p<0.001)</p>	

Study ref	LoE	N	Aim/ methods	Findings	Comments
(Reekie et al 2014)	IV	1,742	<p>Aim: To report the prevalence of markers for HIV infection, hepatitis B and hepatitis C among Australian prison entrants.</p> <p>Methods: Cross-sectional survey conducted over 2-week periods in 2004, 2007 and 2010 in reception prisons in New South Wales, Queensland, Tasmania and Western Australia.</p>	<p>The study included 1742 prison entrants: 588 (33.8%) in 2004, 536 (30.8%) in 2007 and 618 (35.5%) in 2010. The age-standardised prevalence estimate for anti-HCV was 29.0%; it decreased over time (33.3% in 2004 v 23.2% in 2010; P = 0.001), and this coincided with a decrease in prison entrants reporting injecting drug use (58.3% [343/588] in 2004 v 45.3% [280/618] in 2010; P < 0.001). Among injecting drug users, the prevalence of anti-HCV was 57.2% and did not change significantly over time. Of those who were anti-HCV positive, 33.7% (140/415) were unaware of their infection status.</p> <p>Participants who were women had an increased risk of testing positive for anti-HCV (IRR 1.33; 95%CI 1.00 to 1.77; p=0.05).</p>	<p>Reports on the National Prison Entrants' Bloodborne Virus Survey. More recent data are available from (The Kirby Institute 2015)</p>

Study ref	LoE	N	Aim/ methods	Findings	Comments
(Teutsch et al 2010)	II	488	<p>Aim: To examine HCV incidence among Australian prisoners with a history of IDU and documented to be seronegative within 12 months prior to enrollment.</p> <p>Methods: Inmates were tested for anti-HCV antibodies and viremia, and interviewed about demographic and behavioral risk factors for transmission.</p>	<p>The cohort was predominantly male (65%) with high rates of prior imprisonment (72%) and tattooing (73%), as well as longstanding IDU (mean 8.5 years). Ninety-four incident HCV cases were identified (incidence 31.6 per 100 person years). Independent associations were observed between incident infection and prior imprisonment ($p = 0.02$) and tattooing ($p = 0.03$), and surprisingly also with methadone maintenance treatment (MMT) ($p < 0.001$).</p> <p>Women were more likely than men to be infected (rate ratio 1.6; 95%CI 1.1 to 2.4).</p>	
(van der Poorten et al 2008)	IV	709	<p>Aim: To define and compare the prevalence, risk factors and understanding of hepatitis C transmission among Aboriginal and non-Aboriginal young offenders.</p> <p>Methods: Young offenders (aged 12-19 years; median age, 16.6 years) in custody or serving community orders with the New South Wales Department of Juvenile Justice who participated in a physical and mental health survey between March 2002 and December 2005, provided blood samples for analysis of biochemistry, bloodborne viruses and sexually transmitted infections.</p>	<p>Of the 1042 young offenders studied, 709 provided blood samples, 179 (25%) of whom identified as Aboriginal. Hepatitis C rates were high in both groups (7.3% v 5.3%; $P = 0.33$). Risk factors for hepatitis C were the same in both groups, the most important being injecting drug use (OR, 19; $P < 0.001$) and prior use of heroin (OR, 15; $P < 0.001$). Current custodial sentence doubled the risk of hepatitis C. Knowledge of hepatitis C transmission was very poor in both groups, with over 50% not knowing how it is transmitted and fewer than 10% able to identify sharing needles as a risk. Being female was a significant risk, with an OR of 3.0, although this may reflect the small sample size of girls ($n=91$).</p>	

1.2 Excluded studies for research question 1

Background papers

Background information will inform revision of the narrative.

(Deacon et al 2011)	As the proportion of cases identified as newly acquired by current New South Wales surveillance methodologies is significantly lower than that identified nationally, the impact on the identification of newly acquired cases of systematic reporting of past negative HCV test results from notifying laboratories was assessed. HCV notifications data for 2007 from two New South Wales laboratories were analysed. Cases with a negative HCV antibody test within the past 24 months were classified as newly acquired. These were linked to the NSW Department of Health (NSW Health)-identified cases to assess the effectiveness of accessing laboratory data. The laboratories accounted for approximately half of all new HCV notifications in 2007. Of the 2,206 newly diagnosed cases, 21 (1.0%) were newly acquired, 18 of which had not been identified under the current surveillance system, increasing the total number of newly acquired cases to 83 from 65. This increased the yield by 28% and increased the proportion of newly acquired cases from 65/4,192 (1.6%) to 83/4,196 (2.0%). Laboratory-identified cases were significantly more likely than NSW Health-identified cases to be aged 30 years or over. Combined with current reporting mechanisms, laboratory data on previous HCV test results have the potential to increase the number of newly acquired cases identified through the New South Wales surveillance system and to enhance the identification of cases among those aged 30 years or more.
(Giles et al 2009)	Among 3,100 general practitioners surveyed, antenatal testing for HCV approached 66% in NSW and 72% in Victoria. Of respondents who have managed a pregnant woman with HCV, 25% inappropriately test infants for infection before one month of age.

Other exclusions

Study	Reason for exclusion
Ahmed, R., et al. (2015). "Clinical management and outcomes of pregnant women with hepatitis C infection and their babies." BJOG: An International Journal of Obstetrics and Gynaecology 122: 362.	Does not meet criteria for grading (abstract)
Ambikaipaker, V., et al. (2010). "Antenatal screening for hepatitis c and adherence to the national hepatitis C testing policy at a large regional centre (pregnancy study, John Hunter Hospital, NSW)." Journal of Gastroenterology and Hepatology 25: A20.	Does not meet criteria for grading (abstract)
Gidding, H. F., et al. (2009). "The epidemiology of hepatitis C in Australia: notifications, treatment uptake and liver transplantations, 1997-2006." Journal of Gastroenterology & Hepatology 24(10): 1648-1654.	Narrative review
Harding, D. J., et al. (2011). "Hepatitis C in pregnancy in Western Australia: A cross-sectional study." Journal of Gastroenterology and Hepatology 26: 104.	Does not meet criteria for grading (abstract)
Mak, D. B. and R. E. Watkins (2008). "Improving the accuracy of Aboriginal and non-Aboriginal disease notification rates using data linkage." BMC Health Services Research 8 (no pagination)(118).	Does not answer research question

Study	Reason for exclusion
Mina, M. (2011). "Blood-borne viruses in New South Wales prisons: Results from a multi-centre study in australiacategory: Clinical lesson." <i>Journal of Infection</i> 63 (6): e3.	Does not meet criteria for grading (abstract)
Quinn, K. and V. <i>Women's Health</i> (2009). "Women and Hepatitis C." <i>Women's Health Issues Paper</i> (3): [i]-[ii], 1.	Narrative review
Razali, K., et al. (2009). "Modelling and calibration of the hepatitis C epidemic in Australia." <i>Statistical Methods in Medical Research</i> 18(3): 253-270.	Does not answer research question
Sacks-Davis, R., et al. (2013). "High rates of hepatitis C virus reinfection and spontaneous clearance of reinfection in people who inject drugs: A prospective cohort study." <i>PLoS ONE</i> 8 (11) (no pagination)(e80216).	Does not answer research question
Stern, R. K., et al. (2008). "The HCV Synthesis Project: scope, methodology, and preliminary results." <i>BMC Medical Research Methodology</i> 8: 62.	Does not answer research question

2 What is the diagnostic value and clinical effectiveness of testing for Hepatitis C?

2.1 Evidence summary

Results of the previous review

This question was asked in the literature review conducted to inform Module I of the guidelines (Australian Health Ministers' Advisory Council 2012). The review identified three level III-2, one level III-3 and five level IV studies that were consistent with the NICE recommendation and the advice of Hepatitis Australia.

The guidelines recommended against routine testing for hepatitis C and included practice points on offering testing to women with identifiable risk factors (intravenous drug use or needle sharing; tattooing or body piercing; incarceration; receipt of blood products or invasive procedures overseas or before 1990 in Australia; country of origin with a high prevalence) and to women having an invasive procedure.

Results of the current review

Universal versus targeted testing

Eight studies were identified that considered the merits of universal versus targeted testing:

- two studies reported increases in prevalence after targeted testing was replaced by universal testing (Martyn et al 2011; Diab-Elschahawi et al 2013)
- three studies reported on universal testing only (McDermott et al 2010; Lambert et al 2013; El-Kamary et al 2015)
- one study reported on risk factors among women previously identified as at high or low risk (Waruingi et al 2015)
- an Australian study reported differences in risk factors between women with a positive or negative test result (Wilson & Beckmann 2015)
- one study compared reported prevalence with an anonymous seroprevalence study (Blasig et al 2011).

Studies were largely consistent in finding an association between hepatitis C seropositivity and the following risk factors:

- injecting drug use (McDermott et al 2010; Diab-Elschahawi et al 2013; Lambert et al 2013; Wilson & Beckmann 2015)
- receipt of blood transfusion or organ transplant (Diab-Elschahawi et al 2013; Wilson & Beckmann 2015)
- history of tattooing or body piercing (Diab-Elschahawi et al 2013; Lambert et al 2013)
- use of intranasal cocaine (Diab-Elschahawi et al 2013; Lambert et al 2013)
- incarceration (Diab-Elschahawi et al 2013)
- origin from a country of high prevalence (Diab-Elschahawi et al 2013; Lambert et al 2013).

Additional findings were:

- only high severity risk factors (exposure to intravenous drug use or to the blood of an HCV-positive individual) were significantly associated with testing positive for hepatitis C antibodies ($P=0.002$) (McDermott et al 2010)
- age, history of prior pregnancy and healthcare employment were additional considerations (El-Kamary et al 2015).

However, studies have estimated that, compared to universal testing, targeted testing would fail to identify 2.5% ($n=7$) (Wilson & Beckmann 2015); 10% ($n=3$) (El-Kamary et al 2015); 21% ($n=14$) (Diab-Elschahawi et al 2013); 24% or 27% ($n=21$) (Lambert et al 2013) of seropositive women.

Reporting of risk factors among women who were seropositive or seronegative was heterogeneous so results were not pooled.

Clinical utility of testing

Narrative reviews noted the lack of effective treatment options to avoid mother-to-child transmission during pregnancy or childbirth (Dunkelberg et al 2014; Rac & Sheffield 2014; Poliquin et al 2015; Aebi-Popp et al 2016).

However, new treatment options (direct-acting antiviral agents) for people living with hepatitis C have become available and were recently listed on the Australian Pharmaceutical Benefits Scheme (PBS). While these treatments have not been proven to be safe in pregnancy or during breastfeeding (Rac & Sheffield 2014;

Aebi-Popp et al 2016), women who are diagnosed with hepatitis C during pregnancy could commence such curative treatment after completion of breastfeeding (or immediately after the birth if the infant is not breastfed), thus reducing their risk of significant liver disease and removing any risk of perinatal infection for subsequent pregnancies.

In addition, knowledge of a woman's hepatitis C status means that interventions that increase the risk of mother-to-baby transmission (fetal scalp blood sampling, internal electronic fetal heart rate monitoring via scalp electrode, episiotomy) (see Section 3.1) can be avoided.

Costs of testing

No cost-effectiveness studies relevant to the Australian context were identified. A study in the Netherlands found a modest cost-effective outcome for testing first-generation non-Western women (Coretti et al 2015) and a study conducted in the United States (Hahne et al 2013) found that neither universal testing with or without elective Caesarean birth were cost-effective. However, a study in the United Kingdom found that antenatal testing and postnatal treatment was feasible and effective at a cost considered acceptable (Selvapatt et al 2015).

Advice to EWG

There is observational evidence that targeted testing fails to identify up to 27% of seropositive women and that invasive interventions (which could be avoided if it was known that a woman was hepatitis C positive) increase the risk of mother-to-baby transmission. Suggest include a consensus-based recommendation on routinely offering hepatitis C testing.

Consensus-based recommendation

Recommend testing for hepatitis C at the first antenatal visit, as interventions that increase the risk of mother-to-baby transmission can then be avoided in women who test positive.

Universal versus targeted testing

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
(Diab-Elshahawi et al 2013)	Historical control	III-3	8,591	<p>Aim: To compare universal vs a targeted hepatitis C virus (HCV) testing policy for identifying pregnant women with the virus.</p> <p>Setting: Vienna University Hospital, Austria</p> <p>Population: pregnant women at risk for pregnancy-related complications, including those enrolled in opiate maintenance therapy programs.</p> <p>Methods: During the first 22 months of the study a targeted HCV testing approach was adopted. Universal testing was implemented for the following 22 months. Medical records of pregnant women who tested positive for HCV during this 44-month period were selected and subsequently reviewed for the distribution and presence or absence of risk factors for HCV.</p>	<p>Universal testing did not yield significantly more identification of patients with HCV than targeted testing. However, 14 of 67 (21%) women with confirmed HCV would not have been detected by targeted risk-based HCV testing.</p> <p>During the targeted testing period, 1,238 of 4,369 (28.3%) pregnant women were tested for HCV antibodies with a prevalence of 1.3% (56 of 4,369). In 54 of 56 women HCV antibody status could be verified by a confirmatory test.</p> <p>During the universal testing period, 4,222 pregnant women were tested for HCV antibodies with a prevalence of 1.7% (73 of 4,222). In 67 of 73 women the HCV antibody status could be verified by a confirmatory test.</p> <p>No significant difference in prevalence (P=0.08), age (P=0.33) and ethnicity (P≥0.2) nor in the prevalence of risk factor distribution could be found in the two study groups, indicating two comparable study populations.</p>	<p>Prevalence in Europe estimated as between 1.7% and 2.5%.</p> <p>Risk factors used in screening:</p> <ul style="list-style-type: none"> • current or former use of illegal drugs, • receipt of blood transfusion, • receipt of organ transplant(s), • long-term haemodialysis, • possible nosocomial transmission, occupational exposure to HCV, • use of intranasal cocaine, • history of tattooing or body piercing, or • possible sexual transmission of HCV.

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
(El-Kamary et al 2015)	Cohort	III-2	1,250	<p>Aim: to determine the reliability of risk-based versus universal HCV testing for pregnant women and to identify additional characteristics that could increase the reliability of risk-based testing.</p> <p>Setting: Cairo University Antenatal Clinic, Egypt (a country with the world's highest HCV prevalence that relies on risk-based testing).</p> <p>Population: Pregnant women with a mean age of 27.4+/-5.5 years (range:16-45)</p> <p>Methods: Women were universally tested for anti-HCV antibodies and RNA, and demographic characteristics and risk factors for infection were assessed.</p>	<p>HCV antibodies and RNA were positive in 52 (4.2%) and 30 (2.4%) women respectively. After adjustment, only age (OR:1.08, 95%CI:1.002-1.16, p < 0.01), history of prior pregnancies (OR:1.20, 95%CI:1.01-1.43, p < 0.04), and working in the healthcare sector (OR:8.68, 95%CI:1.72-43.62, p < 0.01), remained significantly associated with chronic HCV infection.</p> <p>Universal antenatal HCV testing was widely accepted (100%) and traditional risk-based testing alone would have missed 3 (10%) chronically infected women, thereby supporting universal testing of pregnant women whenever possible. Otherwise, risk-based testing should be modified to include history of prior pregnancy and healthcare employment.</p>	<p>Prevalence among pregnant women in Egypt is estimated at 15.7–19%</p> <p>Risk factors assessed:</p> <ul style="list-style-type: none"> • jaundice • liver disease • surgery • blood transfusion • needle-stick injury with a contaminated needle • tattoo • endoscopy • renal dialysis • dental treatment • intravenous injection with needle-sharing

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
(Lambert et al 2013)	Cohort	III-2	8,976	<p>Aim: to pilot universal antenatal HCV testing and to determine the true seroprevalence of HCV infection in an unselected antenatal population.</p> <p>Setting: Rotunda Hospital, Dublin, Ireland</p> <p>Population: Pregnant women</p> <p>Methods: A risk assessment questionnaire for HCV infection was applied to all women booking for antenatal care over a 1-year period. In addition the prevalence of anti-HCV antibody positive serology in this population was determined.</p>	<p>78 (0.9%) women were diagnosed as anti-HCV positive, the majority of whom were Irish (60.3%) or from Eastern Europe (24.4%). 73% of anti-HCV positive women reported one or more known risk factor with tattooing and a history of drug abuse the most commonly reported. 27% (n=21) of anti-HCV positive women had no identifiable risk factors.</p> <p>This provides persuasive evidence for the inclusion of HCV testing or at a minimum highlights the need for ongoing review of selective testing criteria.</p>	<p>Risk factors assessed:</p> <ul style="list-style-type: none"> • HIV, hepatitis B or treponemal infection • current drug user and/or on methadones • ex-intravenous drug user • current or ex-partner a drug user • permanent tattoos • parent(s) are HIV, hepatitis B or hepatitis C positive • recipient of blood products before 1992 • asylum seeker • current or ex-partner known to be HIV, hepatitis B or hepatitis C positive

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
(McDermott et al 2010)	Cohort	III-2	645	<p>Aim: To determine the effectiveness of universal versus targeted testing for hepatitis C (HCV) during pregnancy</p> <p>Setting: Women's Health Care Centre at St Michael's Hospital in Toronto, Canada</p> <p>Population: Obstetric patients aged >15 years</p> <p>Methods: Patients completed a demographic and standardized questionnaire identifying known risk factors for HCV. Patients then underwent blood testing for HCV antibodies. The effectiveness of testing based on risk factors was determined by comparing the number of women who screened positive for HCV risk factors with those who tested seropositive.</p>	<p>Of those who entered the study, 0.5% (3/645) tested positive for HCV. HCV risk factor screening showed that 72% answered Yes to one or more risk factors and 28% answered No to all risk factors. Answering Yes to any risk factor was not associated with testing positive for HCV antibodies ($P > 0.05$). Screening positive for a high severity risk factor (exposure to intravenous drug use or to the blood of an HCV-positive individual) was associated with testing positive for HCV antibodies ($P = 0.002$), but screening positive for a moderate or low severity risk factor was not ($P > 0.05$).</p> <p>During pregnancy, universal testing for HCV and testing based on the presence of any risk factors for HCV is not recommended. HCV testing based on the presence of high severity risk factors, however, may be warranted.</p>	<p>Risk factors assessed:</p> <ul style="list-style-type: none"> • IVDU • Intercourse with IVDU • Transfusion/transplant before 1992 • Blood/organs from HCV-positive donor • Exposure to HCV-positive blood • Clotting factors before 1988 • Hemodialysis treatment • Elevated liver enzymes • Time in correctional facility • HCV-positive mother • HIV positive • Tattoos • Body piercings • Inhaled illicit drugs

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
(Waruingi et al 2015)	Prospective cohort	III-2	419	<p>Aim: to compare the value of HCV universal testing versus risk-based selective testing in pregnant women.</p> <p>Setting: Metro Health Medical Center, Case Western Reserve University, Cleveland, Ohio, United States</p> <p>Population: pregnant women, in a high risk inner city clinic, who were at "low risk" for HCV infection</p> <p>Methods: Women at "low risk" were tested for HCV antibodies (universal testing) and their medical records were compared to the medical records of pregnant women who were at "high risk" (risk based selective testing as assessed by their obstetricians' screening questionnaire).</p>	<p>During the study period, 419 women delivered at our institution with 8.8% (37/419) at high risk for HCV. In 95% (183/193) of available and consenting low risk women, HCV antibody testing was done. The prevalence of HCV was 3.18% (7/220; 95% CI: 1.36-6.50) in all tested women versus 0.95% (4/419; 95% CI: 0.31-2.59) in risk-based selectively tested women. Overall the screening questionnaire had a sensitivity of 0.85 (0.42-0.99) and a specificity of 0.52 (0.45-0.58) in all women who had HCV antibody testing and questionnaire screening.</p> <p>Using a screening questionnaire to identify women at risk for HCV infection during pregnancy underestimates the real prevalence of HCV. A universal testing should be considered in high risk cities.</p>	<p>Risk factors assessed:</p> <ul style="list-style-type: none"> • Received blood, blood products or organ donation before 1992 • Used or injected non-prescription drugs • Been diagnosed with HIV • Had a partner with any of the above • Been treated for sexually transmitted illness • Been diagnosed with hepatitis or abnormal liver function test

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
(Wilson & Beckmann 2015)	Retro-spective cohort	III-2	57,659	<p>Aim: To report the HCV status and risk factors for HCV to better understand the implications of changing from universal to risk factor based HCV testing.</p> <p>Setting: Mater Mothers' Hospitals, Brisbane</p> <p>Population: women delivering at a tertiary metropolitan hospital</p> <p>Methods: An audit of practice was performed using routinely collected data from 2007 to 2013 (n=57,659). The demographic and clinical characteristics of HCV-positive women (n=281) were compared with those with a negative result (n=57,378), and compared for the presence or absence of risk factors for HCV.</p>	<p>From the cohort, 281 (0.5%) women were HCV positive. HCV-positive women were more likely to have received blood products (10.0 vs 3.1%; P<0.001), have a history of illicit drug use (72.2 vs 9.8%; P < 0.001), and have at least one risk factor for HCV infection (92 vs 17%; P < 0.001). Of the HCV-positive women, only seven of the 281 (2.5%) had no identifiable risk factor, whilst most (83%) HCV-negative women did not have any documented risk factor for HCV infection.</p> <p>Most women testing positive for HCV antibodies have identifiable risk factors; however, a small number will not be detected if a risk factor based testing approach is adopted. The benefits of universal testing must be weighed against the potential cost savings of a risk factor based testing program.</p>	<p>Risk factors assessed:</p> <ul style="list-style-type: none"> • Born in country other than Australia or New Zealand • Ethnicity other than Caucasian/European • Previous receipt of blood products • Illicit drug use • HIV positive • Presence of one or more risk factor(s)

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
(Blasig et al 2011)	Historical control	III-3	109,983	<p>Aim: to determine the overall prevalence rate, age and geographic distribution of reported HCV infection and compare results to a previously conducted anonymous seroprevalence survey</p> <p>Setting: British Columbia (BC), Canada</p> <p>Population: pregnant women</p> <p>Methods: Reported HCV prevalence was determined through a confidential database linkage of all prenatal testing results at the Canadian Blood Services (CBS) with all HCV test results at the Provincial Laboratory, from May 2000 to Oct 2002. Data were stratified by age group and geographic location, and subsequently compared to an anonymous prenatal seroprevalence survey conducted in 1994.</p>	<p>The overall HCV prevalence rate was 50.3/10,000 (95% CI 46.3-54.6), or 0.5% of the cohort. Of note, the rate of reported HCV among pregnant women was significantly lower than the anonymous seroprevalence rate: 50.3/10,000 vs. 91.3/10,000 ($p < 0.0001$).</p> <p>Rates of reported HCV among pregnant women were approximately 50% lower than the rates determined by the anonymous seroprevalence survey. Further research is needed to determine the relative merits of the current selective testing policy versus universal prenatal HCV testing in pregnancy.</p>	

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
(Martyn et al 2011)	Historical control	III-3	13,888	<p>Aim: to assess detection rates with universal and targeted testing</p> <p>Setting: Coombe Women and Infants University Hospital, Dublin, Ireland</p> <p>Population: Pregnant women</p> <p>Methods: The policy in the Coombe Women and Infants University Hospital in Dublin changed from targeted testing in 2006 to universal testing in 2007. We audited the two consecutive years.</p>	<p>The prevalence of HCV in our antenatal population was 1.4% for 2006 (67/4666) when targeted testing applied and in 2007 - 0.71% (66/9222) when universal testing came into affect. One woman in 2007 would not have been detected by targeted testing - 1.49% (1/67). In 2006, 55% (37/67) and in 2007 57.5% (38/66) of women were HCV-RNA positive.</p> <p>We conclude that there were similar detection rates for HCV in 2006 and 2007 and that universal testing is not required if inclusive criteria for selective testing are employed but is of use in a research context.</p>	<p>Risk factors used in screening:</p> <ul style="list-style-type: none"> • presence of tattoos and body piercings; • history of injecting drug use, • blood products received, • history of jaundice, • sexual contact with potentially infected partner and • being an immigrant from a country with moderate to high prevalence rate of HCV

Clinical utility of testing (based on narrative reviews)

Study ref	Comments
(Aebi-Popp et al 2016)	<p>At present, routine antenatal hepatitis C virus (HCV) testing is not recommended in pregnant women who do not have known risk factors for infection. The main reason for this has been the lack of effective treatment options to avoid mother-to-child transmission during pregnancy or delivery. Hitherto available treatment regimens based on interferon and ribavirin were associated with sometimes long-lasting and severe side-effects and thus their indication had to be carefully evaluated. In addition, ribavirin has teratogenic and embryocidal effects and is absolutely contraindicated during pregnancy. The situation has substantially changed with the advent of the newly available treatment regimens based on very effective and well-tolerated direct-acting antiviral agents (DAAs).</p> <p>However, the safety and efficacy of DAAs during pregnancy have not yet been studied. Detrimental effects on fetal development during sofosbuvir or ledipasvir treatment have not been seen in animal models. Accordingly, the FDA has classified both antivirals as category B. In consequence, treatment may even become available during pregnancy as soon as these DAAs are proved to be safe and effective in clinical trials. In Europe, both drugs remain currently contraindicated in pregnant and nursing women</p>

Study ref	Comments
(Dunkelberg et al 2014)	No therapeutic agents are yet available or recommended to further decrease the risk of MTCT of HCV, which remains 3 to 10%. HCV MTCT can be minimized by avoiding fetal scalp electrodes and birth trauma whenever possible. Young women with HCV should be referred for treatment post delivery, and neonates should be closely followed to rule out infection. New, better-tolerated treatment regimens for HCV are now available, which should improve outcomes for all infected individuals.
(Poliquin et al 2015)	The availability of efficacious treatments for HCV, with demonstrable benefits to the mother or fetus, is required before antepartum testing can be justified. While the technology to test for HCV, certainly exists, there must be careful consideration of the downstream implications of routine testing at the level of the individual patient, the general population, and other health care resources, including laboratory infrastructure, before recommending routine testing in the antepartum period.
(Rac & Sheffield 2014)	<p><i>Prevention:</i> no vaccine or immunoprophylaxis is available for HCV-positive women or their neonates. Women who are HCV negative but remain at high risk of acquisition should be educated regarding practices that decrease the risk of transmission. Because the risk of sexual transmission is low, serodiscordant monogamous couples do not need to change their sexual practices, but should be tested regularly. HCV disease is not a contraindication to breastfeeding.</p> <p><i>Treatment:</i> The preferred treatment of chronic HCV is a combination of pegylated interferon and ribavirin, both of which are contraindicated during pregnancy. Ribavirin has been shown to be teratogenic and pegylated interferon has been shown to have adverse effects on fetal growth. Newer treatment options include direct-acting antivirals, which target specific steps in the HCV viral replication cycle. These agents have less morbidity than nonspecific therapy, and shorter treatment times. However, their safety during pregnancy has not been established, and studies are needed before recommending treatment with these antivirals. Seropositive women with systemic complications from HCV should be comanaged by both maternal-fetal medicine specialists and gastroenterologists specialising in viral hepatitis.</p>

Cost-effectiveness

Study ref	Design	Aim/methods	Results
(Coretti et al 2015)	Economic evaluation	<p>Aim: To summarize the available evidence on the cost-effectiveness of testing programs for hepatitis C.</p> <p>Methods: A literature search was performed on PubMed and Scopus search engines. Trip database was queried to identify reports produced by the major Health Technology Assessment (HTA) agencies.</p>	<p>One study was identified that was specific to testing in pregnancy in the Netherlands. It found that adding hepatitis C testing to the testing program for pregnant women was not cost-effective for non-migrant women but showed a modest cost-effective outcome for first-generation non-Western women.</p>
(Hahne et al 2013)	Cost-effectiveness study	<p>Aim: To inform testing policies</p> <p>Methods: We assessed (1) the hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus antibody (anti-HCV-Ab) prevalence for 34 European countries; and (2) the cost-effectiveness of testing for chronic HBV and HCV infection.</p>	<p>One economic analysis of antenatal HCV testing was found (conducted in the United States), which considered universal antenatal HCV testing and treatment of HCV infection with or without elective cesarean delivery. Neither of these scenarios was considered cost-effective.</p>

Study ref	Design	Aim/methods	Results
(Selvapatt et al 2015)	Cost-effectiveness analysis	<p>Aim: to assess the cost-effectiveness of a routine universal antenatal hepatitis C virus (HCV) testing programme at a London centre.</p> <p>Methods: Ten years' retrospective antenatal testing and outcome data informed a cost-effectiveness analysis using the previously validated MONARCH model. The cost and quality of life outcomes associated with the testing and treatment of newly identified hepatitis C cases were used to generate cost-effectiveness estimates for the testing programme.</p>	<p>A total of 35,355 women were tested between 1st November 2003 and 1st March 2013; 136 women (0.38%) were found to be HCV antibody positive. Of 78 (0.22%) viraemic cases, 44 (0.12%) were newly diagnosed. In addition, the testing programme identified three (6.8%) vertical transmissions in children of newly diagnosed mothers. Of 16 newly diagnosed mothers biopsied, all were in the F0-F2 METAVIR disease stages, and 50% had HCV genotype 1. Postnatal treatment with pegylated interferon and ribavirin was initiated in 19 women, with 14 (74%) achieving sustained virologic response.</p> <p>The total cost of testing and confirmation of diagnoses was estimated to be 240,641. This translates to 5,469 per newly diagnosed individual. The incremental cost-effectiveness ratio of this testing and treatment strategy was 2,400 per QALY gained. Treatment with newer direct-acting antiviral regimens would have a projected cost of 9,139 per QALY gained, well below the 20,000-30,000/QALY gained willingness-to-pay threshold applied by policy advisory bodies.</p> <p>This study demonstrates that an antenatal testing and treatment program is feasible and effective, at a cost considered acceptable.</p>

2.2 Excluded studies for question 2

Background papers

Background papers will inform revision of the narrative.

(Bottero et al 2016)	In pregnant women, in addition to HIV-HBV testing currently recommended, HCV testing should be routinely performed during the first trimester of pregnancy.
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Other exclusions

Study	Reason for exclusion
Anonymous (2013). "Summaries for patients: screening for hepatitis C virus infection in adults: U.S. Preventive Services Task Force recommendation statement." <i>Annals of internal medicine</i> 159(5): 1-32.	Duplicate

Study	Reason for exclusion
Ceysens, G., et al. (2014). "Blood tests in the first trimester of pregnancy: What to screen?. [French]." <i>Revue Medicale de Bruxelles</i> 35(4): 237-242.	Not in English
Geue, C., et al. (2015). "Cost-Effectiveness of HBV and HCV Screening Strategies – A Systematic Review of Existing Modelling Techniques." <i>PLoS ONE</i> 10(12): e0145022.	Does not answer research question
Kadkhoda, K. and G. Smart (2014). "HCV antigen testing for the diagnosis of hepatitis C infection: A cost-efficient algorithm." <i>Clinical Laboratory</i> 60(4): 677-680.	Not specific to target population
Moyer, V. A. (2013). "Screening for hepatitis C virus infection in adults: U.S. preventive services task force recommendation statement." <i>Annals of internal medicine</i> 159(5): 349-357.	Not specific to target population
Mussi-Pinhata, M. M. and S. M. Quintana (2012). "Screening for infectious diseases during pregnancy: Which test and which situation." <i>Current Women's Health Reviews</i> 8(2): 158-171.	Does not answer research question
Urbanus, A. T., et al. (2013). "Is Adding HCV Screening to the Antenatal National Screening Program in Amsterdam, The Netherlands, Cost-Effective?" <i>PLoS ONE</i> 8 (8) (no pagination)(e70319)	Included in another cost analysis (Coretti et al 2015)
Zuure, F. R., et al. (2014). "Outcomes of hepatitis C screening programs targeted at risk groups hidden in the general population: a systematic review." <i>BMC Public Health</i> 14: 66.	Does not answer research question

3 Transmission

3.1 Evidence summary

Results of the previous review

Questions on transmission were not asked in the literature review conducted to inform Module I of the guidelines (Australian Health Ministers' Advisory Council 2012).

Results of the current review

There are several factors that influence the risk of mother-to-infant transmission:

- if the mother has antibodies for hepatitis C but is not infected, the risk of transmission is approximately 1 to 3%; if the mother is infected, the risk is approximately 4 to 6% (Panda et al 2010)
- the highest reported transmission rates occur in infants born to mothers who are both hepatitis C and HIV positive, with rates as high as 36% (Panda et al 2010; Benova et al 2014)
- risk of transmission is increased with a higher maternal viral load of hepatitis C (Panda et al 2010; Valladares et al 2010), with a threshold of >615 copies/mL (OR 9.3; 95%CI 1.11 to 78.72) (Garcia-Tejedor et al 2015)
- risk is increased with intrapartum invasive procedures (fetal scalp blood sampling or internal electronic fetal heart rate monitoring via scalp electrode) (OR 10.1; 95% CI 2.6 to 39.02) and episiotomy (OR 4.2; 95%CI 1.2 to 14.16) (Panda et al 2010; Gagnon et al 2014; Rac & Sheffield 2014; Garcia-Tejedor et al 2015)
- transmission does not appear to be influenced by mode of birth (Panda et al 2010; Ghamar Chehreh et al 2011; Cottrell et al 2013; Rac & Sheffield 2014) or gestational age at birth (Panda et al 2010)
- prolonged rupture of membranes may increase the risk of transmission (Panda et al 2010; Cottrell et al 2013), however this could be related to maternal viral load and length of membrane rupture (Rac & Sheffield 2014)
- amniocentesis in women infected with hepatitis C does not appear to significantly increase the risk of vertical transmission but very few studies have properly addressed this possibility (Panda et al 2010; Gagnon et al 2014; Rac & Sheffield 2014)
- there is no evidence that breastfeeding is associated with an increased risk of hepatitis C transmission to the newborn (Panda et al 2010; Valladares et al 2010; Cottrell et al 2013; ASHM 2015), unless the nipples are cracked and/or bleeding (Rac & Sheffield 2014; ASHM 2015).

Advice to EWG

These findings support the proposal to include a consensus-based recommendation on routinely recommending hepatitis C testing (see Section 2.1).

Consensus-based recommendation

At the first antenatal visit, recommend testing for hepatitis C.

3a What is the potential for transmission of Hepatitis C in labour and birth and breastfeeding?

Systematic reviews of observational studies

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
{Benova, 2014 #1581}	SLR	IV	109 studies	<p>Aim: To update current estimates of hepatitis C virus (HCV) vertical transmission risk.</p> <p>Methods: PubMed and Embase were searched. Pooled estimates of risk were generated for children born to HCV antibody-positive and viremic women, aged ≥18 months, separately by maternal human immunodeficiency virus (HIV) coinfection.</p>	<p>Meta-analysis of the risk of vertical HCV infection to children of HCV antibody-positive and RNA positive women was 5.8% (95% confidence interval [CI], 4.2%–7.8%) for children of HIV-negative women and 10.8% (95% CI, 7.6%–15.2%) for children of HIV-positive women. The adjusted meta-regression model explained 51% of the between-study variation in the 25 included risk estimates. Maternal HIV coinfection was the most important determinant of vertical transmission risk (adjusted odds ratio, 2.56 [95% CI, 1.50–4.43]).</p>	
{Cottrell, 2013 #1582}	SLR	IV	18 studies	<p>Aim: To evaluate effects of mode of delivery, labor management strategies, and breastfeeding practices on risk for mother-to infant transmission of HCV.</p> <p>Methods: Searches were conducted to identify randomised trials and observational studies on mode of delivery, labor management strategies, and breastfeeding practices and risk for mother-to-infant transmission of HCV.</p> <p>Investigators abstracted and reviewed study details and quality using predefined criteria.</p>	<p>Fourteen studies (2 good-quality, 4 fair-quality, and 8 poor quality studies) found no clear association between mode of delivery (vaginal versus cesarean delivery) and risk for transmission. Two studies (1 good-quality and 1 poor-quality study) reported an association between prolonged duration of ruptured membranes and increased risk for transmission. Fourteen studies (2 good-quality, 2 fair-quality, and 10 poor-quality studies) found no association between breastfeeding and risk of transmission.</p>	

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
{Ghamar Chehreh, 2011 #1584}	SLR	IV	8 studies	<p>Aim: To evaluate the effect of mode of delivery on the risk of perinatal mother-to-infant transmission of HCV.</p> <p>Methods: Only the peer-reviewed published studies that compared perinatal transmission rate of HCV in elective or emergency cesarean section with vaginal delivery in HCVRNA+/HIV- mothers were included.</p>	<p>We identified 8 studies that involved 641 unique mother–infant pairs which fulfilled our inclusion criteria.</p> <p>Aggregation of study results did not show a significant decrease in HCV vertical transmission among study (mothers who underwent C/S) versus control (mothers who gave birth vaginally) patients [pooled odds ratio, 1.1 (95%CI 0.45 to 2.67)]. The P value was 0.35 for our test of heterogeneity.</p>	

Observational studies

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
(Garcia-Tejedor et al 2015)	Retro-spective cohort	III-2	711 infants; 710 mothers	<p>Aim: to analyse the risk factors for the perinatal transmission of hepatitis C virus (HCV).</p> <p>Setting: Spain</p> <p>Population: infants born to HCV-infected mothers</p> <p>Methods: As potential risk factors for transmission we analysed: maternal age, mode of acquisition of HCV infection, HIV co-infection, antiretroviral treatment against HIV, CD4 cell count, HIV and HCV viral load, liver enzyme levels during pregnancy, smoking habit, gestational age, intrapartum invasive procedures, length of rupture of membranes, length of labour, mode of delivery, episiotomy, birth weight, newborn gender and type of feeding.</p>	<p>Overall perinatal HCV transmission rate was 2.4%. The significant risk factors related with HCV transmission were maternal virus load >615 copies/mL (OR 9.3; 95%CI 1.11 to 78.72), intrapartum invasive procedures (OR 10.1; 95% CI 2.6 to 39.02) and episiotomy (OR 4.2; 95%CI 1.2 to 14.16). HIV co-infection and newborn female were near significance (p=0.081 and 0.075, respectively).</p>	

Narrative reviews

Study ref	Comments
(Panda et al 2010)	<p>There are several factors that influence mother-to-infant transmission of HCV. Vertical transmission is greater with a higher maternal viral load of HCV. If the mother is anti-HCV positive but HCV RNA negative, the risk for transmission to the baby is approximately 1% to 3%. If the mother is HCV RNA positive, the risk for transmission is approximately 4–6%. The highest reported transmission rates occur in infants born to mothers who are HCV positive and HIV positive, with rates as high as 36%. The mode of delivery does not seem to influence transmission rates; however, invasive procedures, such as fetal scalp blood sampling or internal electronic fetal heart rate monitoring via scalp electrode should be avoided. Some observations suggest that prolonged rupture of fetal membranes increases the risk for vertical transmission; therefore, early artificial rupture of membranes should be avoided if possible. In the event of preterm premature rupture of membranes in patients infected with HCV, the decision to continue with conservative management versus immediate delivery should be individualized based on gestational age. The risk of transmission seems to be higher with prolonged rupture of membranes; however, in some cases the morbidity associated with prematurity may be greater. There is no association between gestational age at delivery and the risk of vertical transmission. There is no evidence that the small dose of steroids given for fetal lung maturity will have a negative impact on the course of the infection.</p> <p>Amniocentesis in women infected with hepatitis C does not appear to significantly increase the risk of vertical transmission, but women should be counseled that very few studies have properly addressed this possibility. No cases of HCV transmission through breastfeeding are known; therefore, hepatitis C infection is not a contraindication to breastfeeding.</p>
(Prasad & Honegger 2013)	<p>Despite recent advances in the pathogenesis, treatment, and public health response to hepatitis C virus (HCV), HCV as it specifically relates to pregnancy has been a neglected condition. HCV-monoinfected pregnant women have a 2-8% risk of viral transmission to their infant, but the mechanism and timing of mother to child transmission (MTCT) are not fully understood, nor is the natural history of the illness in pregnant women and their offspring. Recognition of HCV-infected pregnant women is relevant because of the long-term health implications for the mother, potential adverse effects of infection on pregnancy outcomes, and the possibility of transmission to their infants. Certain risk factors for MTCT of HCV appear similar to those for human immunodeficiency virus (HIV); however, unlike HIV, effective methods for prevention of HCV vertical transmission have not been developed. It is possible that a better understanding of HCV MTCT and pathogenesis in pregnancy will guide development of useful prevention strategies, particularly as we enter an era where interferon-free drug cocktails may emerge as viable treatment options for HCV.</p>

Study ref	Comments
(ASHM 2015)	<p>There is little evidence that interventions during pregnancy or at the time of delivery reduce the risk of MTCT of HCV. For a woman with a diagnosis of HCV during pregnancy, referral to an infectious diseases specialist or hepatologist, as well as to hepatitis support groups for information and advice, should be made during the pregnancy. This will facilitate provision of accurate information, counselling and linkages for follow up and treatment if desired postpartum.</p> <p>The role of elective caesarean section in the management of women infected with HCV remains uncertain, and further research is required before a recommendation can be made on the mode of delivery used to prevent transmission.</p> <p>Standard precautions and delay of intramuscular injections until after the baby has been bathed to remove all maternal blood are advised.</p> <p>There is no evidence that breastfeeding is associated with an increased risk of HCV transmission to the newborn despite the detection of HCV RNA in breast milk. Consideration should be given to expressing and discarding milk if nipples are cracked and bleeding, until healed.</p>
(Rac & Sheffield 2014)	<p>Rates of transmission have been shown to be as low as 0% to 3% when maternal HCV RNA was undetectable.</p> <p>The mode of delivery has not been shown to affect vertical transmission rates for HCV-positive women. Invasive procedures, such as fetal scalp electrode or fetal scalp sampling, should be avoided, as these procedures have been shown to increase vertical transmission rates. Evidence is lacking regarding the risk of transmission after amniocentesis, although no evidence suggests an increased risk. If amniocentesis is performed, traversing the placenta should be avoided. Vertical transmission has been shown to be higher after premature rupture of membranes. However, this could be related to maternal viral load and length of membrane rupture. Recent data from Japan noted that in women with high viral loads (defined as $>6 \times 10^5$ IU/mL), delivery 4 or more hours after membrane rupture was associated with a significantly higher rate of infected infants. Further studies are needed before recommendations can be made as regards management of PPROM in seropositive pregnancies.</p> <p>Breastfeeding does not seem to increase transmission rates, and is therefore not contraindicated unless the nipples are cracked and/or bleeding.</p>
(Valladares et al 2010)	<p>A high hepatitis C viral load reportedly increases vertical transmission and is higher in women who are coinfecting with HIV or who are intravenous drug users. Prolonged rupture of the membrane for more than 6 h, amniocentesis, and perineal lacerations increase the potential risk of perinatal transmission. Although the hepatitis C virus can be transmitted intrapartum, prevention by caesarean delivery is not generally indicated. The HCV virus can be found in maternal milk; however, breast feeding is not contraindicated. In conclusion, there are no antiviral treatment recommendations for HCV-infected women during pregnancy, or guidelines for the prevention of vertical transmission.</p>

3b What is the potential for the transmission of blood borne viruses through scalp injuries (fetal scalp blood sampling or clips for heart rate monitoring)?

Systematic reviews of observational studies

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
{Gagnon, 2014 #1583}	SLR	IV	Not stated	<p>Aim: To review the risk of in utero infection through prenatal invasive procedures in women with hepatitis B, hepatitis C, and/or human immunodeficiency virus (HIV) infections.</p> <p>Methods: Published literature was retrieved through searches of Medline, CINAHL, and the Cochrane Library using appropriate controlled vocabulary (amniocentesis, chorionic villus sampling, cordocentesis, fetal and neonatal infection) and key words (hepatitis B, hepatitis C, HIV).</p>	<p>For women infected with hepatitis C, and/or human immunodeficiency virus, the use of non-invasive methods of prenatal risk assessment is recommended.</p> <p>Amniocentesis in women infected with hepatitis C does not appear to significantly increase the risk of vertical transmission, but women should be counselled that very few studies have properly addressed this possibility. More research on this topic is recommended.</p> <p>Little information is available on other prenatal diagnostic and therapeutic invasive procedures.</p>	

Observational studies

Study ref	Design	LoE	N	Aim/setting/population/methods	Results	Comments
(Garcia-Tejedor et al 2015)	Retro-spective cohort		711 infants; 710 mothers	<p>Aim: to analyse the risk factors for the perinatal transmission of hepatitis C virus (HCV).</p> <p>Setting: Spain</p> <p>Population: infants born to HCV-infected mothers</p> <p>Methods: As potential risk factors for transmission we analysed: maternal age, mode of acquisition of HCV infection, HIV co-infection, antiretroviral treatment against HIV, CD4 cell count, HIV and HCV viral load, liver enzyme levels during pregnancy, smoking habit, gestational age, intrapartum invasive procedures, length of rupture of membranes, length of labour, mode of delivery, episiotomy, birth weight, newborn gender and type of feeding.</p>	A significant risk factors related with HCV transmission was intrapartum invasive procedures (OR 10.1; 95% CI 2.6 to 39.02).	

Narrative reviews

Study ref	Comments
(Rac & Sheffield 2014)	Invasive procedures, such as fetal scalp electrode or fetal scalp sampling, should be avoided, as these procedures have been shown to increase vertical transmission rates.

3.2 Excluded studies for question 3

Study	Reason for exclusion
Kawakita T, Reddy UM, Landy HJ et al (2016) Neonatal complications associated with use of fetal scalp electrode: a retrospective study. <i>BJOG</i> 123(11): 1797-803.	Does not answer research question
Pinninti, S. G. and D. W. Kimberlin (2014). "Management of neonatal herpes simplex virus infection and exposure." <i>Archives of Disease in Childhood: Fetal and Neonatal Edition</i> 99(3): F240-F244.	Does not answer research question

Study	Reason for exclusion
Pinninti, S. G. and D. W. Kimberlin (2014). "Preventing herpes simplex virus in the newborn." Clinics in Perinatology 41 (4): 945-955.	Does not answer research question
Fleury, C., et al. (2012). "Genitourinary medicine physicians need further training in the management of HSV in late pregnancy." Sexually Transmitted Infections. Conference: 4th Joint BASHH ASTDA Meeting, Brighton United Kingdom. Conference Start 88(no pagination).	Does not meet criteria for grading

4 What are the additional considerations for Aboriginal and Torres Strait Islander women?

Evidence summary

Results of the previous review

This question was asked in the literature review conducted to inform Module I of the Guidelines (Australian Health Ministers' Advisory Council 2012). No evidence was identified.

Results of the current review

No studies identified.

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