Hepatitis C Screening Guideline Development Group

Background to recommendation 13: Heterosexual partners of a person with HCV or a person at risk of HCV infection

The purpose of this document is to provide the background information to the formulation of recommendations by the Guideline Development Group (GDG).

Not all evidence in this document is presented in the National Clinical Guideline.


Please note, that this document is being made available for information purposes only. It should not be reproduced or cited. Please refer to the National Clinical Guideline for the final evidence analysis, value judgements and recommendations.

Contents

History of development of the recommendation ................................................................. 1
Considered judgement process ............................................................................................. 2
Review by GDG .................................................................................................................. 11
Consultation feedback and review by GDG ...................................................................... 11
Final recommendation ....................................................................................................... 11
References List .................................................................................................................. 12
Appendices ........................................................................................................................ 13
   Evidence search and results........................................................................................... 13
   International and national guidelines........................................................................... 13
   Grey literature............................................................................................................... 13
   Primary literature ......................................................................................................... 13

History of development of the recommendation

<table>
<thead>
<tr>
<th>Date</th>
<th>Process</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>02/06/2015</td>
<td>Recommendations from quality appraised national and international guidelines reviewed</td>
<td>Agreed that further evidence was required on the risk of HCV transmission from sexual practices, and what factors increase the risk of sexual transmission through sexual contact</td>
</tr>
<tr>
<td>02/02/2017</td>
<td>GDG subgroup meeting to undertake considered judgement process</td>
<td>Formulation of recommendation</td>
</tr>
<tr>
<td>23/02/2017</td>
<td>Review of subgroup recommendation by GDG</td>
<td>Recommendation accepted</td>
</tr>
<tr>
<td>25/04/2017</td>
<td>Consultation feedback reviewed by GDG</td>
<td>No changes to recommendation</td>
</tr>
<tr>
<td>June – July 2017</td>
<td>Editing</td>
<td>Recommendation reworded in final editing process</td>
</tr>
</tbody>
</table>
**Considered judgement process**

The considered judgment form completed by the GDG subgroup in formulating the recommendations is presented below. Please note the final wording of the recommendation may have changed after review of the GDG, after the consultation process, or during the editing process.

Date: 2/2/2017  
Attendees: LT, PF, ER, SK, OE, CB

<table>
<thead>
<tr>
<th>Table 1: Considered judgement form</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. What is the question being addressed? Present PICO if relevant</strong></td>
</tr>
<tr>
<td>Should sexual contacts of known cases of hepatitis C be screened?</td>
</tr>
<tr>
<td>Should sexual contacts of a person who injects drugs be screened?</td>
</tr>
<tr>
<td>Should those with high risk sexual behaviour be screened?</td>
</tr>
</tbody>
</table>

**This CJF is covering sexual transmission amongst heterosexuals. Sexual transmission amongst MSM is considered in a different CJF**

<table>
<thead>
<tr>
<th><strong>2. What evidence is being considered to address this question and why?</strong> (This section will explain the approach taken to address this question and what GDG members are being asked to consider)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendations and evidence from other high quality guidelines and primary literature. The risk of transmission and recommendation amongst sexual partners is considered. The risk for those who engage in high risk sexual behaviours is also considered.</td>
</tr>
<tr>
<td><strong>A systematic literature review was undertaken by NUIG on factors which increase the risk of sexual transmission amongst heterosexuals. Please review the draft report of this review also.</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>3. What is the body of evidence?</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Source of evidence: (tick all that apply)</td>
</tr>
</tbody>
</table>
| Guidelines  
  Primary literature |
| Other |

**Current Guidelines – Sexual partners of a person with hepatitis C**

**WHO, 2016 (1)**

No specific recommendation is made. Evidence on sexual transmission amongst people with sexual partners who are HCV infected:

- There is low or no risk of sexual transmission of HCV among HIV-uninfected heterosexual couples and HIV-uninfected men who have sex with men (MSM). The risk of sexual transmission is strongly linked to pre-existing HIV infection.
- People with HIV infection: Persons with HIV infection, in particular MSM, are at increased risk of HCV infection through unprotected sex.

*(World Health Organization, Guidelines for the screening, care and treatment of persons with hepatitis C infection (1)).* HIQA Quality Score of 148

**WHO (2)**

No specific recommendation. Evidence statement on sexual transmission:

Sexual transmission of HCV occurs infrequently in heterosexual couples. It is more common in HIV-positive persons, particularly in MSM. In several recent outbreaks of HCV infection among MSM in Europe, Australia and the United States, transmission has been linked to sexual exposure as well as potentially to underreported use of non-injecting recreational drugs. HIV-infected Heterosexual partners of HCV-infected people are also more likely to acquire HCV; this may be due to sexual transmission or other exposure to blood or due to unreported injection or non-injection drug use, such as sharing of straws for inhaling cocaine.

*(WHO 2017 Guidelines on hepatitis B and C testing)*
Evidence statements on risk of sexual transmission:

- Sexual transmission is extremely unlikely in heterosexual relationships (<0.1% /10 years) but the rate increases if the index patient is also HIV infected.
- There is also evidence of increased rates of infection in sex workers.

Recommendations on sexual contacts:

- Partner notification should be performed and documented and the outcome documented at subsequent follow-up. Contract tracing to include any sexual contact if the index patient or partner are HIV+ (penetrative vaginal or anal sex) or needle sharing partners during the period in which the index case is thought to have been infectious (1D).
- In patients with chronic infection, sexual transmission should be discussed. It seems likely that if condoms are used consistently then sexual transmission will be avoided, but given the very low rates of transmission outside of HIV co-infection..., monogamous partners may choose not to use them. Sexual contacts with HIV should be advised of the risk of sexual transmission, with regular testing and condom use encouraged (1D).

Recommendations on who to screen:

- Other groups to be tested include: the sexual partners of HCV positive individuals, sex workers, tattoo recipients, migrants from highly endemic countries, alcoholics, people who snort cocaine and ex-prisoners (1B).

(British Association for Sexual Health and HIV; United Kingdom National Guideline on the Management of the viral hepatitides A, B and C 2015 (3))

CDC 2015 (4)
Advice on management of sex partners:
Because incident HCV has not been demonstrated to occur in heterosexual couples followed over time, condom use might not be necessary in such circumstances. Persons with HCV infection with one long-term, steady sex partner do not need to change their sexual practices. However, they should discuss the low but present risk for transmission with their partner and discuss the need for testing. Heterosexuals and MSM with HCV infection and more than one partner, especially those with concurrent HIV infection, should protect their partners against HCV and HIV acquisition by using male latex condoms. Partners of persons with HCV and HIV infection should be tested for HCV and HIV, if not known to be infected. (CDC Sexually Transmitted Diseases Treatment Guidelines, 2015 (4))

NICE, 2013 (5)
Close contacts of someone known to be chronically infected with hepatitis C should be offered HCV screening. The definition of a close contact is the people in close contact with someone infected with hepatitis B or C, where there is a risk of transmitting the infection (through blood or body fluids). This could include their family members, close friends, household contacts or sexual partners. (The National Institute for Health and Care Excellence, Hepatitis B and C: Ways to Promote and Offer Testing to People at Increased Risk of Infection). HIQA Quality Score of 148

SIGN, 2013 (6)

1 Grade 1 recommendation is a strong recommendation to do (or not do) something, where benefits clearly outweigh risks (or vice versa) for most, if not all, patients. Grade D evidence is based only on case studies, expert judgement or observational studies with inconsistent effects and a potential for substantial bias, such that there can be little confidence in the effect estimate.
People who have had a sexual partner who is HCV infected should be offered HCV screening. ([Scottish Intercollegiate Guidelines Network, Management of Hepatitis C A National Clinical Guideline](https://www.scipgn.org/)). HIQA Quality Score of 127.7

**KASL, 2016 (7)**
Screening should be offered to persons who have current sexual contact with HCV-infected persons. ([The Korean Association for the Study of the Liver, KASL Clinical Practice Guidelines: Management of Hepatitis C](https://www.kasl.or.kr)). HIQA Quality Score of 111

**SASLT, 2012 (8)**
Sexual partners of HCV-infected persons should be offered screening. ([Saudi Association for the Study of Liver diseases and Transplantation, SASLT Practice Guidelines: Management of Hepatitis C Virus Infection](https://www.saslt.org)). HIQA Quality Score of 95.3

**NASPGHAN, 2012 (9)**
HCV screening is not recommended for monogamous relations but is recommended for polygamous relationships. ([North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, NASPGHAN Practice Guidelines: Diagnosis and Management of Hepatitis C Infection in Infants, Children, and Adolescents](https://www.naspghan.org)). HIQA Quality Score of 88

**IUSTI/WHO Euro, 2010 (10)**
Other groups to be considered for testing are sexual partners of HCV-positive individuals. ([The International Union Against Sexually Transmitted Infections/WHO Europe, European Guideline for the Management of Hepatitis B and C Virus Infections](https://www.iusti.org)). HIQA Quality Score of 66.3

**BASHH, 2006 (11)**
Evidence statements:

- The rate of seroconversion after unprotected vaginal or anal sex is about two percent per year if neither partner is HIV-positive but the risk rises to over ten percent if there is HIV infection in either partner
- Hepatitis C virus (HCV) is transmitted parenterally although there is a low rate of sexual and vertical transmission, which is more likely to occur within the setting of HIV/HCV co-infection

**Recommendations:**

- Repeat screening should be offered to contacts with an HCV-infected partner who continue to be exposed to infection. The optimum frequency has not been defined but may be every 6-12 months.
- Diagnostic tests for HCV are recommended in anyone presenting with suspected acute hepatitis, and in those with symptoms or signs of chronic liver disease, or abnormal LFTs consistent with acute or chronic hepatitis.
- Screening of asymptomatic STD clinic attendees is recommended if they fall into one of the groups at increased risk which includes intravenous drug users, recipients of blood/blood products, needlestick recipients, HIV-positive people and sexual partners of HCV-positive people.

([British Association for Sexual Health and HIV, BASHH Sexually Transmitted Infections: UK National Screening and Testing Guidelines](https://www.bashh.org)) HIQA Quality Score of 121.5

**CDC, 1998 (12)**
Routine hepatitis C virus (HCV) testing is of uncertain need for long-term steady sex partners of HCV-positive persons and for persons with a history of multiple sex partners. ([Centers for Disease Control and Prevention, Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic](https://www.cdc.gov))
Disease). HIQA Quality Score of 98

Current guidelines – others potentially at risk of sexual transmission/ high risk sexual behaviours

WHO (unpublished) (2)
No specific recommendation. Evidence statement on risk in sex workers:

Sex workers – overall the risk of sexual transmission of HCV is low. There may be a small increased risk of transmission among persons with multiple sex partners. Sex workers may be more likely to belong to other high risk population, such as PWID and person in prisons or closed settings, which is the main reason for the higher prevalence among sex workers

(WHO 2016 (draft report) Guidelines on hepatitis B and C testing)

BASHH 2015 (3)
Evidence statements on risk of sexual transmission:

- There is also evidence of increased rates of infection in sex workers.

Recommendations on who to screen:

- Other groups to be tested include: the sexual partners of HCV positive individuals, sex workers, tattoo recipients, migrants from highly endemic countries, alcoholics, people who snort cocaine and ex-prisoners (1B).

(British Association for Sexual Health and HIV; United Kingdom National Guideline on the Management of the viral hepatitides A, B and C 2015 (3))

IUSTI/WHO Euro, 2010 (10)
Female sex workers should be offered HCV testing. (The International Union Against Sexually Transmitted Infections/WHO Europe, European Guideline for the Management of Hepatitis B and C Virus Infections). HIQA Quality Score of 66.3

CDC, 1998 (12)
Routine hepatitis C virus (HCV) testing is of uncertain need for persons with a history of multiple sex partners or sexually transmitted diseases. (Centers for Disease Control and Prevention, Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease). HIQA Quality Score of 98

AASLD 2016 (13)
Consider screening sexually active persons about to start pre-exposure prophylaxis (PreP) for HIV

Primary literature

THE ABSTRACT OF THE REVIEW UNDERTAKEN BY NUIG IS PRESENTED BELOW. PLEASE REVIEW THE DRAFT REPORT ALSO.

Background

Hepatitis C (HCV) infection is an important cause of liver disease worldwide and an estimated 130-150 million people have chronic HCV infection globally. Identification of risk factors for HCV is essential in guiding screening and designing prevention strategies to improve health outcomes and reduce costs. The role of sexual transmission of HCV infection is not fully understood and an increasing number of studies examine this question. Sexual transmission in people in monogamous heterosexual relationships is rare and there is uncertainty on what specific sexual behaviours in heterosexuals are linked to HCV transmission.
Aim
To determine what factors are associated with an increased risk of sexual transmission of HCV infection in a heterosexual population.

Search methods
A comprehensive search of both electronic databases (Medline (OVID), Embase (OVID), Science Citation Index-Expanded, Social Sciences Citation index, Conference proceedings (Web of Science), Cinahl (EBSCOHost), Scopus and LILACS (Bireme), pubmed (conducted up to 02-04/11/2016)) and grey literature (9 resources) was conducted.

Selection criteria
Studies examining sexual risk factors for HCV infection (determined by antibody/antigen or PCR RNA test) other than interspousal transmission in heterosexual adults (≥18 years), excluding prisoners, injecting drug users (IDUs), people co-infected with HIV and people from high prevalence countries. Only cohort studies, case-control studies, cross-sectional studies published in or after the year 2000 were included, and case studies, case series and reviews were excluded.

Data collection, analysis and quality assessment
Studies were selected by two reviewers independently by title/abstract and full-text. We assessed Risk of Bias (ROB) using the Quality In Prognosis Studies (QUIPS) tool with two independent reviewers. Data extraction and quality of evidence assessment (GRADE) was completed by two reviewers independently. Since it was not appropriate to carry out meta-analysis, findings were presented in evidence tables and summarised narratively.

Main results
Eight studies were included, examining seven risk factors (multiple sex partners, receiving or providing sex commercially, having an IDU partner, and unprotected vaginal, oral or anal sex). None of these factors seemed to be significant risk factors in the included studies, except the evidence for having an IDU partner as a risk factor was conflicting. However, we are uncertain about these results due to the very low quality of evidence (GRADE).

Conclusion
More high quality studies examining sexual risk factors for HCV in heterosexuals are required to further examine the impact on HCV transmission. A more inclusive approach (including the 67 studies that included heterosexuals and other groups including IDUs, prisoners or homo/bisexuals along with) might be useful in further identifying factors associated with an increased risk of sexual transmission of HCV infection in a heterosexual population. However, caution should be had when doing so to avoid the impact of confounders on the findings and we would recommend conducting subgroup analyses in such case.

Other literature
Tohme and Homberg (2010)(14) undertook a systematic review of studies assessing sexual transmission of hepatitis C infection. Studies published between 1995 and 2009 were eligible for inclusion. Eighty studies in total were included in the review (including studies amongst MSM). They report that several large prospective cohort studies did not show an increased risk for HCV transmission among heterosexual discordant couples. They report that the risk of hepatitis C infection through sexual contact is increased in persons having multiple sexual partners (aOR 2.2 to 2.9) and those who are HIV positive. The authors do acknowledge that a limitation in assessing the risk of sexual transmission is the potential confounding effect of IDU, with studies often reliant on self reporting.

A subsequent case control study of 500 index cases and their partners found a HCV prevalence rate of 4% amongst among partners (15). Nine couples had concordant genotype/serotype. Viral isolates in three couples (0.6%) were highly related, consistent with transmission of virus within the couple. Based on 8,377 person-years of follow-up, the maximum incidence rate of HCV transmission by sex was 0.07% per year (95% confidence interval, 0.01–0.13) or approximately one per 190,000 sexual contacts. No specific sexual practices were related...
4. What is the quality of the evidence? To be considered if primary literature was reviewed.

4.1. How reliable are the studies in the body of evidence?
If there is insufficient evidence to answer the key question go to section 11. Comment here on any issues concerning the quantity of evidence available on this topic and its methodological quality.

A number of high quality of guidelines have considered the risk of sexual transmission

PLEASE REFER TO NUIG DRAFT REPORT FOR EVALUATION OF QUALITY OF EVIDENCE REGARDING THAT PIECE OF WORK

4.2. Are the studies consistent in their conclusions? comment on the degree of consistency within the available evidence. Highlight specific outcomes if appropriate. If there are conflicting results highlight how the group formed a judgement as to the overall direction of the evidence

General consistency in determining the risk of heterosexual transmission amongst HIV negative people to be low. Variation is recommendations on testing though. Other risk factors associated with increased risk of sexual transmission are not clearly outlined or consistent between guidelines.

4.3. Generalisability - are the patients in the studies similar to our target population for this guideline? is it reasonable to generalise

Yes

4.4. Applicability - Is the evidence applicable to Ireland? Is the intervention/ action implementable in Ireland?

Yes

4.5. Are there concerns about publication bias? Comment here on concerns about all studies coming from the same research group, funded by industry etc

Not applicable for guidelines

5. Additional information for consideration

5.1. Additional literature if applicable e.g. Irish literature

In a study of 150 female sex workers attending the Women’s Health Project in Dublin between 1991 and 1997 99 were tested for anti-HCV and 8.1% (8/99) were positive (16). Amongst women who were not IDU 3.2% (3/93)
were positive. Amongst women who were IDU 83.3% (5/6) were positive. Almost all the women reported using condoms on all occasions with clients, but the majority also reported burst condoms on at least one or more occasions.

### 5.2. Relevant national policy

The 2004 Eastern Regional Health Authority (ERHA) Regional Hepatitis C Strategy advised that screening should be considered for sexual partners of people who have hepatitis C. However the National Hepatitis C Strategy which supersedes the ERHA document did not propose any recommendations on sexual partners due to the limited evidence in relation to sexual transmission (17).

### 5.3. Epidemiology in Ireland if available and applicable

Between 2004 and 2016 there were 171 cases of hepatitis C notified in Ireland where the most likely risk factor was reported to be possible sexual exposure (75 heterosexual, 41 MSM, and 55 unknown sexual orientation) (personal communication – Niamh Murphy, HPSC). There were a further 77 notifications where sexual contact with a case was reported as the most likely risk factor. (49 heterosexual, 1 MSM, 27 unknown sexual orientation) Between 2004 and 2016 there were 171 cases of hepatitis C notified in Ireland where the most likely risk factor was reported to be possible sexual exposure (75 heterosexual, 41 MSM, and 55 unknown sexual orientation).

### 6. Potential impact of recommendation

#### 6.1. Benefit versus harm

What factors influence the balance between benefit versus harm? Take into account the likelihood of doing harm or good. Do the desirable effects outweigh the undesirable effects?

**Benefits:**
- Linkage to care and treatment will result in improved quality of life for detected cases.
- The offer of screening also provides an opportunity to raise awareness and educate on hepatitis C.
- Promotion and further normalisation of testing may improve uptake and reduce stigma around hepatitis C.
- Detection and treatment of undiagnosed cases will reduce the risk of transmission to others.

**Harms:**
- False positives. The rate of false positive screening results depends on the population being screened. In high risk populations false positive rates are acceptable. However, in low risk populations the positive predictive value of the screening test decreases and may not be acceptable. False-positive test results incur costs and can also cause psychological harm. Confirmatory testing reduces the false-positive rate but increases the cost.
- Detected cases may suffer from stigmatisation.

#### 6.2. What are the likely resource implications and how large are the resource requirements?

Consider cost effectiveness, financial, human and other resource implications

As screening of sexual partners, except for particular circumstance, is not likely to be recommended then there will not be a significant impact on resources.

#### 6.3. Acceptability – Is the intervention/ option acceptable to key stakeholders?
Testing of sexual partners is not routine practice in most settings at present and therefore this will not lead to a change. Some clinicians do report that they offer testing to partners as this is usually requested for reassurance and a recommendation which would prohibit this may not be accepted.

6.4. Feasibility - Is the intervention/action implementable in the Irish context?

Likely to be implemented on an opportunistic basis rather than active screening.

6.5. What would be the impact on health equity?

The principle of proportionate universalism\(^{2}\) should underpin the recommendations and the implementation of the guideline in order to have a positive impact on health equity.

7. What is the value judgement? How certain is the relative importance of the desirable and undesirable outcomes? Are the desirable effects larger relative to undesirable?

The risk of sexual transmission of hepatitis C is low in HIV negative heterosexuals. There are some circumstances which increase the risk such as HIV infection. Sexual partners may share other risk factors for hepatitis C infections such as IDU.

Where a sexual partner is an IDU screening should be considered as there may be additional risk factors for transmission such as needlestick injury.

8. Final Recommendations

<table>
<thead>
<tr>
<th></th>
<th>Strong recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Conditional/ weak recommendation</td>
</tr>
</tbody>
</table>

Text:

- In general, screening of sexual partners of known hepatitis C cases is not recommended in heterosexual couples who are both HIV negative.
- Sexual partners of known HCV cases should be considered for screening in the following situations:
  - If the HCV infected case is an injecting drug user (caution: the case may not have disclosed this to the partner). Partners of HCV infected IDU may be at increased risk as they may themselves have a history of IDU, or due to environmental exposure to discarded needles, or they may have been involved in commercial sex work.
  - If the case or contact is also HIV positive.
- Sexual contacts of persons who inject drugs, but where HCV status is unknown or there is evidence of resolved infection, should be considered for screening.
- If testing of a sexual partner of a HCV infected cases is requested for reassurance then this should not be denied.

Level of supporting evidence: low

9. Justification

---

\(^{2}\) Proportionate universalism is the resourcing and delivering of universal services at a scale and intensity proportionate to the degree of need.

The risk of sexual transmission amongst heterosexual partners is low. However there are circumstances that increase the risk of sexual transmission including being HIV positive. Sexual partners may also be at increased risk of transmission from an infected partner through other routes such as sharing injecting drug use equipment, or environmental exposure to needles.

<table>
<thead>
<tr>
<th>10. Implementation considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opportunistically through GP, or through sexual health clinic or drug treatment clinics.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>11. Recommendations for research</th>
</tr>
</thead>
<tbody>
<tr>
<td>List any aspects of the question that have not been answered and should therefore be highlighted as an area in need of further research.</td>
</tr>
</tbody>
</table>
Review by GDG
Phrasing of recommendation amended.
Date: 23/02/2017

To be clarified that sexual partners of an IDU who is hepatitis C positive are at increased risk not due to sexual transmission but because they may also be an IDU or have environmental exposure. They may not have presented for testing themselves.

Recommendation accepted.

Consultation feedback and review by GDG
Please see Report of the consultation process for feedback received.

No material change to recommendation.

Final recommendation

Recommendation 13

13.1. In general, HCV screening of sexual partners of known HCV cases is not recommended in heterosexual couples who are both HIV negative.

13.2. Sexual partners of known HCV cases should be considered for screening in the following situations:
   a) If the HCV infected case is a PWID. *
   b) If the case or contact is also HIV positive.

13.3. Sexual contacts of PWID, but whose HCV status is unknown or where there is evidence of resolved infection, should be considered for screening.

13.4. If testing of a sexual partner of a HCV-infected case is requested for reassurance, then this should not be denied.

*Partners of HCV-infected PWID may be at increased risk as they may themselves have a history of IDU, or due to environmental exposure to discarded needles, or they may have been involved in commercial sex work.

Quality/level of evidence: low
Strength of recommendation: conditional/weak
References List

Appendices

Evidence search and results

International and national guidelines
HCV guidelines identified, reviewed, and quality appraised as described in the National Clinical Guideline.

Grey literature
Nil used.

Primary literature
The School of Nursing and Midwifery, National University of Ireland, Galway were commissioned to undertake a systematic literature review on the risk of HCV transmission through heterosexual sexual contact.

This can be viewed at: http://health.gov.ie/wp-content/uploads/2017/08/Hep-C-Review-REPORT-FINAL-FOR-WEB.pdf