## Hepatitis C Screening Guideline Development Group
## Background to recommendation 4: Household contacts of a person who is HCV positive

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.

The National Clinical Guideline is available from: http://health.gov.ie/national-patient-safetyoffice/ncec/national-clinical-guidelines/

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## Contents

# History of development of the recommendation

| Date | Process | Outcome |
|---|---|---|
| 02/06/2015 | Recommendations from quality appraised national and international guidelines reviewed | Agreed to augment evidence from existing guidelines with literature search on the risk of horizontal transmission of HCV. |
| 14/12/2016 | GDG subgroup meeting to undertake considered judgement process | Subgroup did not reach consensus on a recommendation. Decision to present options of GDG to decide on recommendation. |
| 24/01/2017 | Review of subgroup recommendation by GDG | Recommendation formulated by the GDG |
| 25/04/2017 | Consultation feedback reviewed by GDG | No changes to recommendation |
| June – July 2017 | Editing | Recommendation reworded in final editing process |

# 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: 14/12/2016
Attendees: ER, PF, LT, CDG, OC, JL, SD
Not in attendance but reviewed evidence and provided commentary: RD

**Table 1:** Considered judgement form

| 1. **What is the question being addressed? Present PICO if relevant** |
|---|
| Q2. Who should be offered screening for Hepatitis C?<br>    c. Should the following contacts of known cases of hepatitis C be screened?<br>        ii. **Household contacts** |

| 2. **What evidence is being considered to address this question and why?** (This section will explain the approach taken to address this question and what GDG members are being asked to consider) |
|---|
| Relevant guidelines – quality appraised<br>Primary literature search – critically appraised<br><br>This question considers household contacts other than sexual or vertical contacts. |

| 3. **What is the body of evidence?** |
|---|
| Source of evidence: (tick all that apply)<br>        Guidelines ✓<br>        Primary literature ✓<br>        Other □ ; specify: _____ |

**Current Guidelines**

**BASSH, 2015** For other non-sexual contacts thought to be at risk, consider on a case-by-case basis (British Association for Sexual Health and HIV, United Kingdom. National Guidelines on the Management of Viral Hepatitides A, B & C 2015 (1)) *HIQA Quality Score 97*

**NICE, 2013** Close contacts of someone known to be chronically infected with hepatitis C, including household contacts, should be offered screening for Hepatitis C. (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 (2)). *HIQA Quality Score of 148*

**SIGN, 2013** Screening for HCV should be offered to people who have a household contact who is HCV positive. (Scottish Intercollegiate Guidelines Network, Management of Hepatitis C A National Clinical Guideline (3)). *HIQA Quality Score of 127.7*

**CDC, 1998** Routine hepatitis C virus (HCV) testing is not recommended for household contacts. (Centers for Disease Control and Prevention, Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease (4)). *HIQA Quality Score of 98*

**North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN), 2012** Present evidence does not support routine HCV screening of household contacts. (North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, Practice Guidelines: Diagnosis and Management of Hepatitis C Infection in Infants, Children, and

Adolescents (5)). *HIQA Quality Score of 88*

**Literature Review**

A review in 2013 summarises the current knowledge of epidemiology, risk factors and molecular biology of horizontal intrafamilial transmission of HCV infection (6). This review acknowledged that horizontal intrafamilial transmission does occur but data on the epidemiology and routes of transmission are difficult to interpret with any certainty.

A systematic review from 2000 analysed 23 uncontrolled studies and 5 controlled studies and determined that intrafamilial transmission does occur (7). From the uncontrolled studies, the authors reported prevalence of HCV in siblings and household contacts of paediatric chronic liver disease patients to be 1.14%. The prevalence of HCV in parents of paediatric chronic liver disease patients was 10.96%. From a review of the controlled studies, this paper found the odds of HCV for siblings and household contacts of HCV positive patients was 9.75 (95% CI 0.91 - ad infinitum). From a review of 7 controlled studies for offspring of HCV positive individuals, OR=1.12 (95% CI 0.78 - 1.60).

A seroprevalence study from two regions in Tunisia determined HCV prevalence among household contacts to be low (8). However risk factors within families could not be independently separated.

A combined case control and seroprevalence study from Brazil determined transmission of HCV to be 2.2% within family members (9). It should be noted that all HCV positive family members were spouses and it was not possible to independently assess risk factors within families.

A seroprevalence study from Korea in 1998 stated there was no evidence of familial clustering of HCV (10). This study reported a 2.2% prevalence of HCV positivity among household contacts of index cases and a 1% prevalence among household contacts of control cases. All cases were spousal however and the study was unable to separate out other risk factors.

| |
|---|
| **4. What is the quality of the evidence?** To be considered if primary literature was reviewed (also apply where appropriate to guidelines) |
| **4.1. How reliable are the studies in the body of evidence?**<br>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. |
| Some of the primary research studies that were included took place in Italy, which is considered to be a high endemnicity country.  While a few of the above findings report an occurrence of intrafamilial transmission of HCV, it was impossible to differentiate between sexual transmission and other horizontal transmission pathways in the household or other possible transmission pathways external to the household. Screening may be recommended based on a risk assessment for factors such as HIV, co-infection, high viral load in the index case, index case is or has a history of IVDU, poor hygiene, environmental risks such as needles, index case is on dialysis in the home. |
| **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 |

The recommendations from the guidelines (n = 4) reviewed were inconsistent.  Two recommended screening for household contacts and two did not.

There was also a lack of consistency in the primary research reviewed and a lack of high quality studies that separated out the risk of non-sexual horizontal transmission within households from transmission due to other behaviours and risks within households or from outside the household.

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

The populations in which the studies have been performed may not be similar to the Irish population

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

There is an absence of evidence to apply

**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

No

**5.   Additional information for consideration**

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

No relevant studies carried out in Ireland were retrieved

**Relevant national policy/strategy/practice**

None

**5.2. Epidemiology in Ireland if available and applicable**

None available

**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 of screening household contacts:
- 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.
- Household transmission does occur and may explain cases where no other mode of transmission is evident. This possible risk group may not be offered screening at present.

Harms of screening household contacts:

- 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.
- Detection of cases who may not yet be eligible for treatment may lead to frustration and anxiety.
- Detected cases may suffer from stigmatisation.
- Opportunity cost. Diversion of resources from screening of other groups who are at greater risk.
- May cause undue anxiety amongst those who have lived or live with someone who has HCV.
- May cause anxiety amongst those with HCV who may worry that they are a risk to those they live with.
- May increase stigma towards those with HCV if there is a perceived risk from living with them.
- The requirement to disclose healthcare information to others given the extremely low likelihood or risk of transmission. The index cases is very likely to be identifiable to the household contacts.
- Transmission in normal household setting is likely to be extremely low so screening of all household contacts may have a low yield.
- If there are clear pathways to care and treatment available, there is limited foreseeable harm for a person knowing they are infected.

| **6.2. What are the likely resource implications and how large are the resource requirements?** Consider cost effectiveness, financial, human and other resource implications |
|---|

Resource implications would be large. Identification of contacts, contacting contacts and testing would be time consuming and resource intensive. Annually between 600 and 700 notifications of hepatitis C are received in Ireland.

| **6.3. Acceptability – Is the intervention/ option acceptable to key stakeholders?** |
|---|

A recommendation to screen household contacts is not likely to be accepted by those who typically do contact tracing (Public Health or GUM/ STI services or GPs) due to resource constraints. At present some services are not able to undertake contact tracing for other infections for which there is a greater risk of household transmission.

Infected person may not find it acceptable to disclose household contacts.

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

Due to resource constraints Departments of Public Health are not always able to undertake contact tracing for HBV which has a higher risk of horizontal transmission within a household.

It may be more difficult to arrange testing of household contacts than for other diseases as cases may be less likely to have a traditional family household unit. There may be multiple household contacts, and different types of accommodation such as hostels or institutions.

The likelihood of identifying historical household contacts may be low. Also some people with HCV may have led chaotic lives creating further difficulties in identifying and contacting household contacts. Also, it would need to be determined who constituted a household contact eg. if a person resided in a hostel or institution.

If screening is recommended based on a risk assessment it is not clear who would be the most appropriate person to undertake the risk assessment or how to judge the risk.

### 6.5. What would be the impact on health equity?

If the principle of proportionate universalism[1] underpins the recommendations and implementation of the guideline then there will be a positive impact on health equity.

Screening of all household contacts may divert resources away from other risk groups which require greater support.

Contact tracing of household contacts by public health would also divert resources from other the surveillance and public health management of other diseases.

### 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

Recent advances in treatment options for hepatitis C make treatment more acceptable and more successful. Treatment with the new DAAs which are now available results in cure in the majority of patients with shorter duration of treatment and less side effects than previous treatments. Screening enables early detection, referral for assessment and treatment where indicated. Without screening cases may go undetected for a considerable length of time due to the asymptomatic nature of HCV infection. Individuals often do not present until symptomatic, which is usually indicative of severe liver damage. Early treatment and cure will confer personal, social, and economic benefits. Early treatment and cure will also reduce the risk of transmission to others. A treatment programme exists in Ireland allowing detected cases access treatment. However, at present the cost of these treatments is high.

Screening of household contacts may identify cases who would not otherwise be screened and detected. However, it would be difficult to implement and the benefit is uncertain. The risk of transmission within a household is not clear.

It may be a better use of resources at present to ensure other risk groups are appropriately screened and linked to care and treatment

The group was divided in opinion regarding the value of screening of this group.

Some members consider that screening should be recommended given that there is a risk of transmission. Other members consider that the risk is extremely low in a normal stable household setting but that a risk assessment could be carried out for factors that increase the risk of transmission.

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[1] Proportionate universalism is the resourcing and delivering of universal services at a scale and intensity proportionate to the degree of need.
http://www.healthscotland.com/documents/24296.aspx

Two potential recommendations emerged. This question is to be referred to the main GDG to decide.

## 8. Final Recommendations

□ Strong recommenda on
√ Conditional/ weak recommendation

**Text:**
Household contacts of those with HCV infection should be screened

OR

Screening of household contacts is not recommended. However, there may be circumstances where household transmission is more likely to have occurred. Screening may be recommended based on a risk assessment for factors such as HIV, co-infection, high viral load in the index case, index case is or has a history of IVDU, poor hygiene, environmental risks such as needles, index case is on dialysis in the home.

## 9. Justification

Justification for screening of all household contacts
The evidence suggests that household transmission can occur. Given the benefit of detection and treatment of undiagnosed cases it is considered appropriate to offer screening to household contacts.

Justification against screening of all household contacts
While household transmission can occur the risk is difficult to quantify and other common exposures amongst household members are difficult to eliminate. The risk of transmission is likely to be very low within many household settings. Given the number of diagnosis of hepatitis C each year in Ireland, the chronic nature of infection and the potential number of household contacts implementation of this recommendation would be difficult. Given that the risk within a normal household setting is likely to be low, the harms to the index case and the resources that would be required for implementation, screening of all household contacts is not considered justified. . The GDG recognises that there are circumstances within a household which may increase the risk. It is considered a better use of resources to focus on identifying contacts where these circumstances exist.

## 10. Implementation considerations

Screening of all household contacts
Difficult to implement as resources not available for contact tracing. There are between 600 and 700 notifications each year in Ireland. Each index cases will likely have multiple household contacts. Also it may be difficult to reach contacts.

Screening if there are increased risks of transmission
It may be difficult to ascertain if any risks are present. This will still require public health resources as it is additional to the current follow up undertaken. It still may be difficult to identify and trace contacts.

## 11. Recommendations for research
List any aspects of the question that have not been answered and should therefore be highlighted as an area in need of further research.

## Review by GDG

Date: 24/01/2017
It was agreed that while active follow up of all household contacts is not necessary it may be warranted in some situations where there is an increased risk of transmission and also should not denied if requested by an index case or their family for reassurance.
The recommendation was amended.

## Consultation feedback

Please see *Report of the consultation process* for feedback received.

No material change to recommendation.

## Final recommendation

*Recommendation 4*

Where a household contact is a sexual contact of a HCV-infected person or is a child who was born to an infected mother please refer to Recommendation 2 and Recommendation 13, respectively.

4.1. In general, HCV screening of household contacts (with no sexual or vertical exposure to the HCV positive household member case) is not necessary due to the low risk of horizontal household transmission. However, there may be circumstances where household transmission is more likely to have occurred. Screening may be considered based on clinical judgement or a risk assessment for factors such as:

• HIV co-infection or high HCV viral load in the HCV positive household member

• A history of current injecting drug use in the HCV positive household member

•If there has been a potential exposure to blood of the HCV positive household member e.g. sharing razors

• If the HCV positive household member is on dialysis in the home

• If there are environmental risks within the household such as discarded needles.

4.2. Where a household contact requests testing for reassurance, this should not be denied.

*Quality/level of evidence:* low; inconsistent recommendations from existing guidelines
*Strength of recommendation:* conditional/weak

# References

1.       Brook G, Bhagani S, Kulasegaram R, Torkington A, Mutimer D, Hodges E, et al. United Kingdom National Guideline on the management of the viral hepatitides A, B and C 2015. Int J STD AIDS. 2016;27(7):501-25.

2.       National Institute for Health and Care Excellence. Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection. NICE Public Health Guidance 43. NICE; 2012. Available from: https://www.nice.org.uk/guidance/ph43.

3.       Scottish Intercollegiate Guidelines Network. Management of hepatitis C; A national clinical guidance. Edinburgh: SIGN; 2013. Available from: http://www.sign.ac.uk/pdf/sign133.pdf.

4.       Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. Centers for Disease Control and Prevention. MMWR Recomm Rep. 1998;47(Rr-19):1-39.

5.       Mack CL, Gonzalez-Peralta RP, Gupta N, Leung D, Narkewicz MR, Roberts EA, et al. NASPGHAN practice guidelines: Diagnosis and management of hepatitis C infection in infants, children, and adolescents. J Pediatr Gastroenterol Nutr. 2012;54(6):838-55.

6.       Indolfi G, Nesi A, Resti M. Intrafamilial transmission of hepatitis C virus. J Med Virol. 2013;85(4):608-14.

7.       Ackerman Z, Ackerman E, Paltiel O. Intrafamilial transmission of hepatitis C virus: a systematic review. J Viral Hepat. 2000;7(2):93-103.

8.       Mejri S, Salah AB, Triki H, Alaya NB, Djebbi A, Dellagi K. Contrasting patterns of hepatitis C virus infection in two regions from Tunisia. J Med Virol. 2005;76(2):185-93.

9.       Keiserman DR, Both CT, Mattos AA, Remiao J, Alexandre CO, Sherman KE. Intrafamilial transmission of hepatitis C virus in patients with hepatitis C and human immunodeficiency virus coinfection. Am J Gastroenterol. 2003;98(4):878-83.

10.     Kim YS, Chi HS, Ahn YO, Lee HS, Klag MJ. Lack of familial clustering of hepatitis C virus infection. Int J Epidemiol. 1998;27(3):525-9.

# 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 GDG determined that to formulate a recommendation further information was required on the the risk of HCV transmission through household contact.

**PICO**
**Population:** Household contacts of people with HCV infection
**Intervention:** n/a
**Comparison:** n/a
**Outcome:** prevalence of HCV, incidence of HCV, diagnosis, detection rate

**Search strategy**
**Sources:**
- Medline
- Embase

See table 2 for search terms used in Medline search

**Study type/ limits:** experimental or observational studies, case studies, case reports; published between 1 January 1990 and 30 June 2015

**Inclusion criteria:**
- Low endemicity country
- Reports on prevalence/ incidence in a household contact where there has not been sexual contact with known case and where no other risk factors are apparent; or in a chid of an infected mother where the mode of transmission was not vertical
- HCV status based on blood/ saliva rather than self report
- From 1990

**Exclusion criteria:**
- High endemicity country
- Non HCV
- Not correct population (not household contact of child of infected mother)
- Doesn't report on prevalence, incidence, or risk independent of other factors
- HCV status self reported
- Other (eg environmental, animal)

**Table 2**: Search terms used in Pubmed/Medline search

| S1 | hepatitis C or HCV or hepacivirus or hep C or hepC | Search modes - Boolean/Phrase | 76,787 |
|----|----|----|----|
| S2 | (MM "Hepatitis C+") | Search modes - Boolean/Phrase | 41,868 |
| S3 | (MM "Hepacivirus") | Search modes - Boolean/Phrase | 17,492 |
| S4 | risk factor* | Search modes - Boolean/Phrase | 812,653 |
| S5 | (MH "Risk Factors") | Search modes - Boolean/Phrase | 606,129 |
| S6 | S1 OR S2 OR S3 | Search modes - Boolean/Phrase | 76,787 |
| S7 | S4 OR S5 | Search modes - Boolean/Phrase | 812,653 |
| S8 | transmission or transmit or mode of transmission or acquisition or acquire* or transmit* | Search modes - Boolean/Phrase | 876,190 |
| S9 | (MM "Disease Transmission, Infectious+") | Search modes - Boolean/Phrase | 30,305 |
| S10 | S8 OR S9 | Search modes - Boolean/Phrase | 882,975 |
| S11 | S6 AND S7 AND S10 | Search modes - Boolean/Phrase | 3,341 |
| S12 | household contact* or housemate* or house mate* or horizontal* N3 (transmission or transmit*) | Search modes - Boolean/Phrase | 4,408 |
| S13 | household* N5 contact* | Search modes - Boolean/Phrase | 2,322 |
| S14 | (family or families) N5 member* or familial | Search modes - Boolean/Phrase | 241,512 |
| S15 | S12 OR S13 OR S14 | Search modes - Boolean/Phrase | 246,184 |
| S16 | S11 AND S15 | Search modes - Boolean/Phrase | 138 |
| S17 | S11 AND S15 | Limiters - Date of Publication: 19900101-20151231<br>Search modes - Boolean/Phrase | 136 |

**Figure 1: PRISMA flow diagram of review of literature on horizontal transmission of HCV**