

Hepatitis C Screening

National Clinical Guideline No. 15

This National Clinical Guideline has been developed by the National Hepatitis C Screening Guideline Development Group (GDG). The GDG was established in conjunction with the National Hepatitis C Strategy and HSE Primary Care, and the development of the guideline was led by the Health Protection Surveillance Centre (HSE HPSC).

Using this National Clinical Guideline

This National Clinical Guideline applies to those living in Ireland with unrecognised hepatitis C virus (HCV) infection.

The National Clinical Guideline makes recommendations on who should be screened for HCV and how that screening should be done.

Management and treatment of patients with HCV infection will not be addressed.

This National Clinical Guideline is relevant to all healthcare professionals, healthcare managers and policy makers working with those at increased risk of HCV infection. The guideline will also be of value to both statutory and voluntary bodies providing services to those groups at increased risk of HCV infection. It may also be used by those with HCV or in a risk group for HCV and by members of the public.

Disclaimer

National Clinical Effectiveness Committee (NCEC) National Clinical Guidelines do not replace professional judgement on particular cases, whereby the clinician or health professional decides that individual guideline recommendations are not appropriate in the circumstances presented by an individual patient, or whereby an individual patient declines a recommendation as a course of action in their care or treatment plan. In these circumstances the decision not to follow a recommendation should be appropriately recorded in the patient's healthcare record.

Users of NCEC National Clinical Guidelines must ensure they have the current version (hardcopy, softcopy or App) by checking the website: www.health.gov/national-patient-safety-office/ncec/

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Membership of the Guideline Development Group (GDG)

The GDG was chaired by Dr Lelia Thornton, Specialist in Public Health Medicine, HSE Health Protection Surveillance Centre. Membership nominations were sought from a variety of clinical, healthcare management and social care backgrounds so as to be representative of the main key stakeholders involved in the care of those with HCV infection or those at risk of HCV infection. At-risk groups and patients were also represented.

Members of the GDG are listed in Table 1.

Table 1: Members of the Guideline Development Group.

Name	Title/position
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Michele Tait	Programme Manager, HSE National Hepatitis C Treatment Programme

Credits

The role of NCEC is to prioritise, quality assure and recommend clinical guidelines to the Chief Medical Officer for endorsement by the Minister for Health. It is intended through Ministerial endorsement that full implementation of the guideline will occur through the HSE service plan.

The NCEC and the Department of Health acknowledge and recognise the Chair and members of the GDG for development of the guideline. The NCEC and Department of Health wish to express acknowledgement and sincere gratitude to all persons who contributed to this National Clinical Guideline, especially those that give of their time on a voluntary basis.

Acknowledgments

The Chair of the GDG, Dr Lelia Thornton, wishes to acknowledge the support of all members of the GDG who engaged in the planning, interpretation of evidence, formulation of recommendations, development of the implementation plan, and review of the guideline. Particular credit is due to Dr Eve Robinson for her tremendous effort and dedication in seeing this project through from beginning to completion. The work of Dr Chantal Migone, Dr Sinead Donohue, Ms Paula Flanagan, Ms Niamh Murphy, and Dr Eve Robinson who undertook the evidence reviews, analysis of evidence and preparation of evidence for review by the GDG members is acknowledged.

In addition, the contribution of the following to the development of the guideline is acknowledged:

Ms Helen Clark, Library and Information Services Manager, Sligo University Hospital carried out searches for evidence. Professor Declan Devane, Dr Francesca Wuytack and their team in the School of Nursing and Midwifery, National University of Ireland, Galway, conducted a systematic review to address one of the key questions. Professor Devane also provided training to the executive team on the DECIDE evidence to decision (EtD) framework. Ms Lucia Mullen assisted with systematic literature reviews and preparation of considered judgement forms. Ms Niamh Murphy, Surveillance Scientist, HSE HPSC provided Irish epidemiological data. Ms Margaret McIver, HSE HPSC, assisted with the preparation of evidence for review. Ms Kirsty MacKenzie, Mr Gerry Reid and administrative staff of HSE HPSC provided administrative support during the guideline development process and editorial support during preparation for publication. Ms Michelle O'Neill and Dr Mairin Ryan, Health Information and Quality Authority (HIQA) provided advice and support regarding undertaking a review of economic literature and conducting the budget impact assessment. Mr Joe Doyle provided information on HSE Social Inclusion activities. Additional expert advice was provided by Dr Lynda Sisson, Dr Patricia Garvey, Dr Jennifer Kieran, Professor Karina Butler, Professor Suzanne Norris and Dr Mary O'Riordan. We are grateful also for the support received from Mr Niall Mulligan, Professor Joe Barry, Dr John Cuddihy, Dr Julie Heslin and Dr Kevin Kelleher.

The external review was carried out by Dr Susan Hahné, Senior Epidemiologist and Head of Department for Early Warning and Surveillance, National Institute for Public Health and the Environment, the Netherlands, and Dr Magdalena Rosińska, Epidemiologist at the National Institute of Public Health - National Institute of Hygiene, Poland and current chair of the European Centre for Disease Prevention and Control (ECDC) Hepatitis Coordination Committee – we are very grateful for their commitment and expert advice.

The GDG would also like to acknowledge Ms Rosarie Lynch, Dr Kathleen MacLellan and the NCEC team who provided invaluable advice and support throughout the guideline development process.

Dr Lelia Thornton
Chair, Guideline Development Group, July 2017

National Clinical Guidelines

Providing standardised clinical care to patients in healthcare is challenging. This is due to a number of factors, among them variations in environments of care and complex patient presentations. It is self-evident that safe, effective care and treatment are important in ensuring that patients get the best outcomes from their care.

The Department of Health is of the view that supporting evidence-based practice, through the clinical effectiveness framework, is a critical element of the health service to deliver safe and high quality care. The National Clinical Effectiveness Committee (NCEC) is a Ministerial committee set up in 2010 as a key recommendation of the report of the Commission on Patient Safety and Quality Assurance (2008). The establishment of the Commission was prompted by an increasing awareness of patient safety issues in general and high profile health service system failures at home and abroad.

The NCEC on behalf of the Department of Health has embarked on a quality assured National Clinical Guideline development process linked to service delivery priorities. Furthermore, implementing National Clinical Guidelines sets a standard nationally, to enable healthcare professionals to deliver safe and effective care and treatment while monitoring their individual, team and organisation's performance.

The aim of these National Clinical Guidelines is to reduce unnecessary variations in practice and provide a robust basis for the most appropriate healthcare in particular circumstances. As a consequence of Ministerial mandate, it is expected that NCEC National Clinical Guidelines are implemented across all relevant services in the Irish healthcare setting.

The NCEC is a partnership between key stakeholders in patient safety. NCEC's mission is to provide a framework for national endorsement of clinical guidelines and audit to optimise patient and service user care. The NCEC has a remit to establish and implement processes for the prioritisation and quality assurance of clinical guidelines and clinical audit so as to recommend them to the Minister for Health to become part of a suite of National Clinical Guidelines and National Clinical Audit. The aim of the suite of National Clinical Guidelines is to provide guidance and standards for improving the quality, safety and cost-effectiveness of healthcare in Ireland. The implementation of these National Clinical Guidelines will support the provision of evidence-based and consistent care across Irish healthcare services.

NCEC Terms of Reference

1. Provide strategic leadership for the national clinical effectiveness agenda.
2. Contribute to national patient safety and quality improvement agendas.
3. Publish standards for clinical practice guidance.
4. Publish guidance for National Clinical Guidelines and National Clinical Audit.
5. Prioritise and quality assure National Clinical Guidelines and National Clinical Audit.
6. Commission National Clinical Guidelines and National Clinical Audit.
7. Align National Clinical Guidelines and National Clinical Audit with implementation levers.
8. Report periodically on the implementation and impact of National Clinical Guidelines and the performance of National Clinical Audit.
9. Establish sub-committees for NCEC workstreams.
10. Publish an annual report.

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1 Summary of National Clinical Guideline recommendations

Should the following people be offered screening for hepatitis C virus (HCV)?

Pregnant women

Recommendation 1

- 1.1 Standardised targeted risk based HCV screening of antenatal women is recommended (see Appendix 1 for a list of risk populations).
- 1.2 Universal HCV screening of antenatal women is **not** recommended.
- 1.3 Universal antenatal HCV screening may be reconsidered in the future if HCV treatment during pregnancy becomes possible. Also, if national policy progresses to a policy of birth cohort or total population screening, antenatal screening offers an opportunistic method to reach this particular population cohort.

Quality/level of evidence¹: moderate; good consistency between existing high quality guidelines

Strength of recommendation¹: strong

Children born to mother with HCV infection

Recommendation 2

- 2.1 Infants of HCV-RNA positive women should be tested for HCV-RNA at six weeks and six months of age and, if both are negative, anti-HCV at ≥ 18 months of age.
- 2.2 Infants who are HCV-RNA positive at any time, or who are anti-HCV positive at or after 18 months of age, should be referred to the Rainbow Clinic².
- 2.3 Infants of anti-HCV positive but HCV-RNA negative women, where eradication of infection, either spontaneously or by treatment is not assured (i.e. by serial negative HCV-RNA tests), should be tested for anti-HCV at ≥ 18 months of age.
- 2.4 Infants of anti-HCV positive but HCV-RNA negative women, where eradication of infection, either spontaneously or by treatment is assured (i.e. persistent negative HCV-RNA tests and no ongoing risk for reinfection), should be managed as infants of uninfected women and do not require follow-up.

Quality/level of evidence: low to moderate

Strength of recommendation: strong

Recommendation 3

- 3.1 If a woman is found to have current or resolved HCV infection, any previous children she has given birth to should be tested for HCV, unless the woman was known to be HCV-RNA negative at the time of their delivery.

Quality/level of evidence: low to moderate

Strength of recommendation: strong

¹ Please refer to section 3.8 for a description of the grading of recommendations.

² The Rainbow Clinic is Ireland's national centre for paediatric infectious diseases. The service is delivered by a multidisciplinary team in Our Lady's Children's Hospital, Crumlin and Children's University Hospital, Temple Street.

Household contacts of a person with HCV infection

Recommendation 4

Where a household contact is a child who was born to an infected mother or a sexual contact of a HCV-infected person 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) 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

People who use unprescribed or illicit drugs

Recommendation 5

- 5.1 All those who have ever injected unprescribed or illicit drugs should be offered screening for HCV. This includes those who only injected once, and those who injected any type of drug which was not prescribed, including performance enhancing drugs like steroids, and novel psychoactive substances.
- 5.2 Re-testing of those who test HCV negative should be offered on an annual basis, or six monthly if deemed clinically appropriate*, for those who remain at ongoing risk of infection.
- 5.3 Testing should be available during this interval if a risk exposure is known to have occurred.
- 5.4 Re-testing for those who have been previously infected, but have cleared infection spontaneously or through treatment, should be done by HCV-RNA testing, as anti-HCV antibody remains positive after the first infection.

*More frequent testing may be considered in circumstances such as: if a risk exposure is known to have occurred; an unexplained rise in alanine aminotransferase (ALT); a diagnosis of another bloodborne virus (BBV).

Quality/level of evidence: high; good consistency between existing high quality guidelines

Strength of recommendation: strong

Recommendation 6

- 6.1 Screening should be offered to all those who have used unprescribed or illicit drugs by a route other than injecting (i.e. non-injecting drug use (NIDU)), if there is a possibility of transmission of HCV infection by the route of administration. This includes those who currently use intranasal drugs (i.e. snort or sniff), or have done so in the past, or share other equipment or drugs where there is a risk of contamination with the blood of others (e.g. smoking crack pipes).

Quality/level of evidence: low

Strength of recommendation: strong

Prisoners or former prisoners

Recommendation 7

- 7.1 Screening for HCV should be offered to all prisoners on entry to prison. Screening should be offered at a time at which it is most likely to be accepted by the prisoner, while also ensuring the early identification of infections in order to minimise the risk of transmission to others.
- 7.2 Those found to have HCV infection should be linked into specialist care and treatment should be facilitated while in prison.
- 7.3 Prisoners who initially test HCV negative should be offered repeat testing on an annual basis, or six monthly if deemed clinically appropriate*, while in prison. Screening should also be offered at any time if a risk exposure (e.g. tattooing, needle-sharing) is known to have occurred.
- 7.4 Prisoners should be able to access testing on request at any stage of their sentence.

*More frequent testing may be considered in circumstances such as: if a risk exposure is known to have occurred; an unexplained rise in ALT; a diagnosis of another BBV.

Quality/level of evidence: moderate; good consistency between existing high quality guidelines

Strength of recommendation: strong

Recommendation 8

- 8.1 One-off testing of ex-prisoners should be considered, although implementation may be difficult.

Quality/level of evidence: moderate; good consistency between existing high quality guidelines

Strength of recommendation: conditional/weak

Good practice points:

- Education on the risk of HCV should be provided to prisoners upon entry into prison.
- At the time of committal, the interviewing nurse or doctor is best placed to identify the optimal time to carry out HCV screening on an individual prisoner.
- Continuity of care and/or treatment on discharge from prison should be ensured. This should be considered as part of discharge planning. Continuity of care on entry to prison should also be considered.
- Communication about test results or treatment should occur between the prison health service and the prisoner's GP, or other services attended by the prisoner, such as addiction services or psychiatric services.
- Confidentiality at the time of screening offer, during testing, and when communicating results of testing should be ensured as far as possible, while still ensuring a safe environment for prison healthcare staff.

People who are homeless

Recommendation 9

- 9.1 Homeless people who have a history of engaging in risk behaviours associated with HCV transmission, or who have had a potential HCV risk exposure, should be offered screening.
- 9.2 Those who initially test HCV negative should be offered repeat testing on an annual basis, or six monthly if deemed clinically appropriate*, if there is an ongoing risk of transmission.

*More frequent testing may be considered in circumstances such as: if a risk exposure is known to have occurred; an unexplained rise in ALT; a diagnosis of another BBV.

Quality/level of evidence: low

Strength of recommendation: strong

Migrants

Recommendation 10

- 10.1 Migrants from a country with an intermediate to high prevalence of HCV (anti-HCV \geq 2%*) should be offered one-off HCV screening.

* Refer to Appendix 2 for a list of countries with an anti-HCV prevalence of \geq 2%.

Quality/level of evidence: low to moderate

Strength of recommendation: strong

People who received medical or dental treatment abroad

Recommendation 11

11.1 Screening for HCV should be considered in people who have received medical or dental treatment in countries where HCV is common (anti-HCV prevalence $\geq 2\%$ *) and where infection control may be poor.

*Please see Appendix 2 for a list of countries with anti-HCV prevalence of $\geq 2\%$.

Quality/level of evidence: low

Strength of recommendation: conditional/weak

People with tattoos or body piercings

Recommendation 12

12.1 Screening for HCV should be considered for all those with a tattoo. Those most at risk of having acquired HCV through tattooing are those who received tattoos a number of decades ago, in non-professional settings, in prison, in high prevalence countries, or in other circumstances where infection control was poor.

12.2 There is insufficient evidence to support screening of recipients of body piercings (including ear piercings).

Quality/level of evidence: low; good consistency between existing high quality guidelines on screening of those with tattoos

Strength of recommendation: conditional/weak

Heterosexual partners of a person with HCV or a person at risk of HCV infection

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

Men who have sex with men (MSM)

Recommendation 14

14.1 HIV positive MSM should be screened at least annually for HCV. More frequent testing may be required if clinically indicated, e.g. an unexplained rise in ALT, a diagnosis of a new sexually transmitted infection (STI), or if a risk exposure has occurred such as contact with a known case of HCV, or other risk behaviours including chemsex³.

14.2 HIV negative MSM should be offered testing annually for HCV as part of an overall STI screen. More frequent testing may be required if clinically indicated, e.g. an unexplained rise in ALT, a diagnosis of a new STI, or if a risk exposure has occurred such as contact with a known case of HCV, or other risk behaviours including chemsex.

Quality/level of evidence: moderate for HIV positive MSM; low for HIV negative MSM

Strength of recommendation: strong

³ The use of recreational drugs for or during sex.

People attending for a sexual health screen

Recommendation 15

See Recommendation 14 for MSM attending for sexual health screening.

- 15.1 HCV testing should be considered part of routine sexual health screening in the following circumstances:
- People who are HIV positive
 - Commercial sex workers
 - PWID
 - If indicated by the clinical history e.g. unexplained jaundice
 - When other risk factors for HCV as outlined in this guideline are present*

*See Appendix 1 for a list of risk populations.

Quality/level of evidence: *low*

Strength of recommendation: *conditional/weak*

People on renal dialysis or who have had a kidney transplant

Recommendation 16

- 16.1 Patients commencing, or on maintenance, haemodialysis or peritoneal dialysis should be screened according to the current recommendations of the National Standing Advisory Committee on the Prevention of Transmission of Blood-Borne Diseases in the Health-Care Setting⁴ and any ensuing updates from this committee.
- 16.2 All patients having a kidney transplant should be tested for HCV by a combined antigen-antibody test, or anti-HCV test **AND** HCV-RNA at three months post-transplant.
- 16.3 Patients transplanted before the introduction of the above, unless already known to be HCV positive, should be tested on a one-off basis by combined antigen-antibody test, or anti-HCV test **AND** HCV-RNA to out rule the possible acquisition of HCV infection through past treatment for renal failure.

Quality/level of evidence: *moderate; good consistency between existing high quality guidelines*

Strength of recommendation: *strong*

Recipients of substances of human origin

Recommendation 17

- 17.1 Recipients of blood or blood components in Ireland prior to October 1991 who have not yet been tested should be offered screening.
- 17.2 All recipients of anti-D immunoglobulin in Ireland between 1st May 1977 and the end of July 1979, and 1st March 1991 and 18th February 1994 who have not yet been tested should be offered screening.
- 17.3 Recipients of plasma-derived clotting factor concentrates in Ireland prior to 1992 who have not yet been tested should be offered screening.
- 17.4 Recipients of blood components and blood products overseas in any country where a quality assured blood donor screening programme may not have been in place should be offered screening.

Quality/level of evidence: *moderate*

Strength of recommendation: *strong*

Recommendation 18

- 18.1 Screening for HCV should be considered in recipients of solid organ transplants in Ireland who have not yet been tested (see Recommendation 16 for recipients of kidney transplants).

Quality/level of evidence: *low*

Strength of recommendation: *conditional/weak*

⁴ Available from: <http://www.hpsc.ie/A-Z/Hepatitis/GuidanceforRenalUnits/>

Donors of substances of human origin

Recommendation 19

19.1 Screening of donors of blood, organ, tissue and cells, including reproductive cells*, should at a minimum comply with legislative requirements**.

The following screening is also recommended:

- 19.2 NAT for HCV-RNA of donors of blood should be performed and the results available prior to the use of the donation. The test must be designed and approved for screening of blood donations
- 19.3 NAT for HCV-RNA of donors of tissues and cells, including reproductive cells*, and living solid organ donors, should be performed in addition to current legislative requirements.
- 19.4 For deceased donors of solid organs:
- 19.4.1 Anti-HCV and HCV antigen testing should be done and the results available prior to donation***.
- 19.4.2 NAT should be considered where feasible. NAT results may not be available prior to transplantation but NAT testing should still be performed to ensure the rapid identification of the recipients of potentially infectious organs ***.
- 19.5 Any external laboratories used for microbiological screening of donors should be accredited and comply with the standards of the appropriate regulatory authority. Laboratories in Ireland should be accredited by the Irish National Accreditation Board (INAB) to undertake testing in compliance with the International Standard ISO 15189.
- 19.6 A national advisory committee on the safety of blood, organs and tissues should be established to advise on best practice in relation to donor selection, and testing of potential donors.

*In the case of partner donation of reproductive cells for direct use and when no storage or processing of samples will be undertaken, microbiological screening is not required.

**Please refer to the relevant competent authority for legislative requirements.

***It is acknowledged that in some circumstances the balance of risk and benefit may favour the use of potentially infectious donations. Such a risk assessment should be conducted by the transplant centre in discussion with an appropriate microbiologist/virologist.

Quality/level of evidence: moderate

Strength of recommendation: strong

General population or birth cohort

Recommendation 20

- 20.1 Birth cohort screening cannot be recommended at present due to the likely substantial cost implications and uncertain benefit. Such a programme would require a full health technology assessment (HTA) and approval of funding prior to being considered.
- 20.2 Birth cohort screening should be considered if a HTA shows it to be cost-effective and affordable in the Irish context⁵.

Quality/level of evidence: moderate

Strength of recommendation: conditional/weak

⁵ A request to conduct this HTA was submitted to HIQA and was included in the prioritisation process in March 2017. It scored highly on the required criteria and will now be considered for inclusion on the HIQA work programme.

Healthcare workers**Recommendation 21**

- 21.1 All new healthcare workers (HCWs) should be offered HCV screening on a voluntary basis.
- 21.2 Mandatory HCV screening of all new HCWs who will perform exposure prone procedures (EPPs) is recommended.
- 21.3 Existing HCWs who perform EPPs and have not yet been screened should be offered HCV screening.
- 21.4 Mandatory HCV screening of all new healthcare students* is recommended.
- 21.5 Interval HCV testing of HCWs who perform EPPs is **not** recommended. However, HCWs should be informed of their professional responsibility to seek appropriate assessment if any possible risk exposure has occurred.

*this includes students who may be undertaking EPPs as students or in their future careers, such as dental, medical, nursing, midwifery, or paramedical students.

Quality/level of evidence: moderate

Strength of recommendation: strong

How should screening for HCV be performed?**Testing sequence****Recommendation 22**

- 22.1 Individuals being investigated for evidence of HCV infection should be screened with an anti-HCV antibody or combined HCV antigen/antibody enzyme immunoassay (EIA) screening assay*.
- 22.2 If the initial HCV EIA is reactive (positive), then the sample should be tested for the presence of HCV antigen, or HCV-RNA, to test for current infection.
- 22.3 Current infection should be confirmed on a second sample and HCV-RNA should be performed (if not already performed) and HCV genotyping should be carried out.
- 22.4 Those individuals with evidence of a resolved HCV infection (i.e. anti-HCV positive and antigen/RNA negative) should have a further sample drawn after six to 12 months for HCV-RNA testing to confirm their resolved infection status.

*In certain patient groups, initial testing should routinely incorporate HCV-antigen or HCV-RNA testing. Those are: immunocompromised individuals; children (born to HCV-infected mothers) in the first 18 months of life; individuals previously treated for HCV infection; sources of needle-sticks; and those at risk of recent infection in whom an antibody response might not yet have developed (HCV-RNA testing should be performed six weeks post-exposure).

Quality/level of evidence: moderate; good consistency between existing high quality guidelines

Strength of recommendation: strong

Recommendation 23

- 23.1 Individuals who initially test HCV negative but who remain at risk of HCV infection should be offered repeat testing on an annual basis, or six monthly if deemed clinically appropriate*.

*More frequent testing may be considered in circumstances such as: if a risk exposure is known to have occurred; an unexplained rise in ALT; a diagnosis of another BBV.

Quality/level of evidence: low

Strength of recommendation: strong

What specimen type should be used for HCV screening tests?

Recommendation 24

- 24.1 Serum and plasma are the preferred specimen types for screening and diagnostic testing for HCV infection using quality assured assays.
- 24.2 Screening and diagnostic testing for HCV infection should not be performed on oral fluid samples due to the low sensitivity and low positive predictive value.
- 24.3 Dried blood spot testing can be considered for screening for HCV in special circumstances, such as mass screening initiatives e.g. in prisons.

Quality/level of evidence: moderate; good consistency between existing high quality guidelines

Strength of recommendation: strong

What is the role of rapid diagnostic tests and point of care tests in HCV screening?

Recommendation 25

- 25.1 Where concerns exist about hard-to-reach populations or linkage-to-care then consideration could be given to using approved (e.g. CE marked) rapid diagnostic tests/point of care tests (RDTs/PoCTs) on blood specimens.
- 25.2 If RDTs/PoCTs are introduced into standard clinical practice then a quality assurance programme should be established that addresses internal quality control and external quality assurance.

Quality/level of evidence: low

Strength of recommendation: conditional/weak

Screening for other bloodborne viruses

Recommendation 26

- 26.1 When offering screening for HCV, consideration should be given to the need for screening for other BBVs also.

Quality/level of evidence: low

Strength of recommendation: strong

Interventions to increase uptake of screening and subsequent linkage to care

Recommendation 27

- 27.1 Interventions to increase uptake of screening and linkage to care, particularly amongst vulnerable groups, should be supported and evaluated.
- 27.2 A national HCV programme with a mandate spanning the entire HCV continuum of care to include full implementation of the National Hepatitis C Strategy and the National Hepatitis C Treatment Programme (HSE NHCTP) should be established.

Quality/level of evidence: low

Strength of recommendation: strong

Good practice points for healthcare professionals involved in HCV screening

Healthcare professionals should consider the following points:

- Any contact with services provides an opportunity to offer HCV screening to those at risk (see Appendix 1 for a list of risk populations).
- HCWs should be cognisant that a person may fall into a potential risk group for HCV unrelated to their reason for presentation to a health service.
- HCWs should be cognisant that a person may have more than one risk factor for HCV and this should be considered when determining the need for repeat testing e.g. a migrant from an intermediate or high prevalence country may warrant repeat screening rather than one-off screening due to also being a current PWID.
- HCV testing should be considered in those with an unexplained rise in ALT.
- Screening should be undertaken voluntarily*.
- While offering HCV screening, HCWs should counsel on the testing process, the process of receiving results, and the importance of returning for test results.
- Confidentiality should be maintained during the offer of screening and delivery of results.
- An offer of a test or a negative test result provides an opportunity to counsel about prevention and harm reduction.
- Upon a diagnosis of HCV infection newly diagnosed persons should be:
 - o Referred for specialist assessment (further details available at: <http://www.hse.ie/eng/health/az/H/Hepatitis-C/Treating-hepatitis-C.html>). Community based assessment and treatment models are being piloted and may be more widely available in the future.
 - o Informed of the next steps, in terms of subsequent diagnostic tests required, and treatment options.
 - o Provided with information on HCV, including how to reduce the risk of transmission to others.
 - o Counselling on the importance of linkage to care.
 - o Directed to services which can provide support and counselling as needed (see Appendix 12).
- Continuity of care should be maintained as a patient transitions between services, settings, or circumstances (e.g. prison to community, homelessness to home).

*In certain circumstances screening is mandated by legislation (i.e. donors of substances of human origin). In other circumstances, failure to agree to screening may prohibit a person from undertaking certain activities in order to maintain patient safety (e.g. healthcare workers will be prohibited from performing exposure prone procedures).

2

Background**2.1 Overview of hepatitis C virus**

The hepatitis C virus (HCV) was first identified in 1989. At least six different genotypes exist, with more than 90 subtypes.

Transmission of HCV occurs through contact with blood of an infected person. The incubation period is between two weeks and six months. A person remains infectious as long as the virus is detectable in their blood (i.e. they are viraemic).

Between 15% and 45% of those with acute infection (terminology used in this guideline is outlined in Appendix 15) clear the virus spontaneously, while the remaining 55% to 85% of those infected remain viraemic and develop chronic HCV infection (1). Chronic HCV infection is marked by persistence of HCV viraemia for at least six months after infection. Spontaneous clearance of the virus after this is unusual. Chronic infection can cause liver inflammation, fibrosis, cirrhosis, liver cancer (hepatocellular carcinoma (HCC)), liver failure and death. Chronic liver disease develops over many years and signs and symptoms may not be evident for 20 to 30 years until serious liver damage has occurred. For this reason, HCV infection is sometimes called the 'silent killer'.

Advancements in new treatments for HCV infection, which offer a cure in most cases and are more acceptable to patients, have led to a significant shift in direction for HCV care and policy, with the paradigm now focused towards elimination. Further information on the new treatments for HCV is available at <http://www.hse.ie/eng/health/az/H/Hepatitis-C/>.

2.2 Diagnosis of HCV infection

HCV infection is diagnosed by the detection of antibody to HCV (anti-HCV) in blood or oral fluid, or the detection of HCV core antigen (HCV-Ag) or HCV-RNA in the blood.

Antibodies are detectable from seven to eight weeks after infection. In immunocompromised individuals, antibodies may not be detected despite HCV infection. A positive antibody test does not distinguish between acute, chronic, or resolved infection.

Detection of HCV-RNA by nucleic acid testing (NAT) indicates current infection. HCV-RNA can be detected from one to two weeks after infection. However, HCV-RNA tests can fluctuate between positive and negative for a number of months after acute infection.

HCV-Ag can be detected from one to two weeks after infection and remains positive for as long as infection persists. Detection of HCV-Ag by an assay of comparable clinical sensitivity to NAT technologies may be considered an alternative to HCV-RNA testing (2).

A person with resolved infection will be anti-HCV positive, but HCV-RNA and HCV-Ag negative.

It is not possible to differentiate between acute and chronic infection on initial diagnosis, except if a person has had a recent negative test. Infection is deemed chronic if HCV-RNA remains detectable after six months.

2.3 Epidemiology of HCV infection in Ireland

HCV is a major cause of liver disease worldwide. It is estimated that there are 115 million people who are anti-HCV positive worldwide, and 80 million with chronic infection (1). High prevalence countries are mainly in Africa and Asia. Risk factors for HCV differ globally. In developing countries, healthcare associated transmission is the main source of infection due to unsafe injection practices in medical settings or contaminated blood transfusion. In developed countries like Ireland injecting drug use, (IDU) is the major risk factor.

HCV infection has been a notifiable disease in Ireland since 2004 under an amendment to the Infectious Diseases Regulations 1981 (S.I. 707 of 2003). Prior to this, cases of HCV could be notified as “viral hepatitis type unspecified”.

Between 2004 and 2016, 14,107 cases were notified. The highest number of cases was notified in 2007 (n=1,538) (Figure 1). In recent years there has been a decrease in cases notified. However, notification numbers now appear to be stabilising rather than further declining. In 2016, 650 cases were notified.

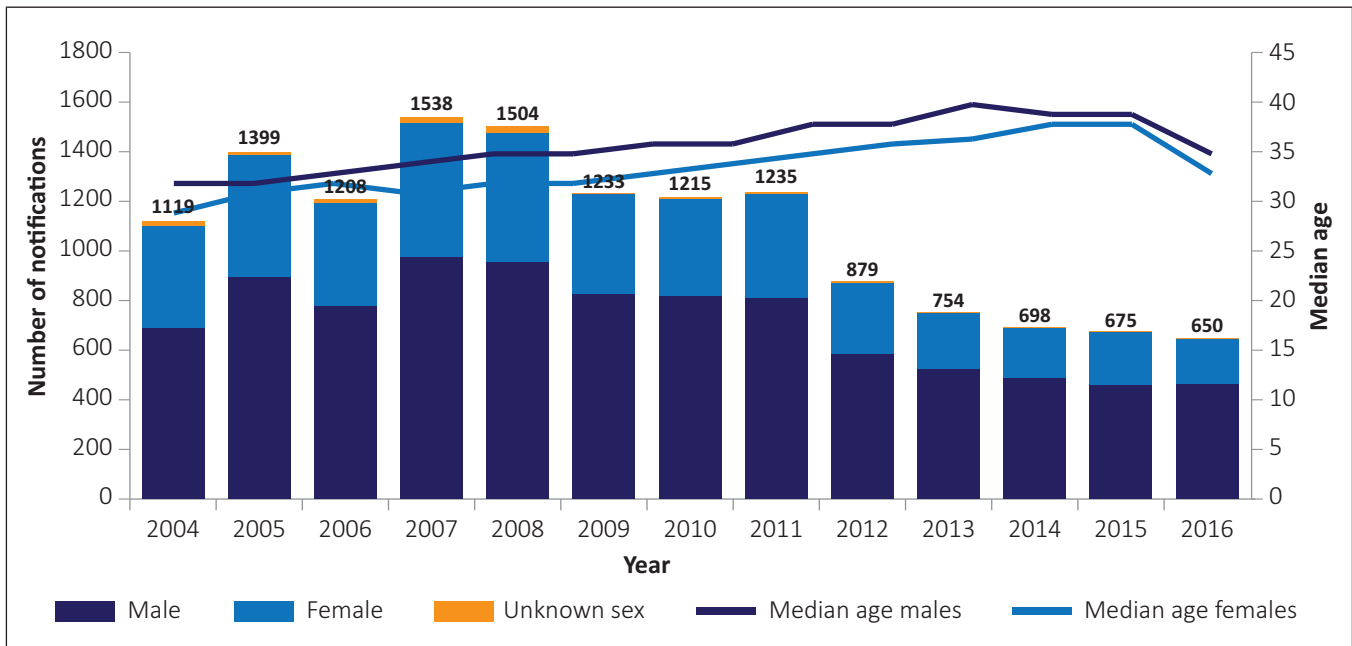


Figure 1: Number of notifications of HCV 2004-2016, by sex and median age (Source: Health Protection Surveillance Centre)

Of note, notifications since 2004 include some (but not all) cases diagnosed before 2004. The proportion of notified cases that were previously diagnosed is likely higher in the earlier years of HCV being notifiable. There may also be some duplicate cases as identifying details are not always available to allow for identification of duplicate notifications.

In addition to data on notified cases, it is known that between 1989, when testing for HCV began, and 2004, 10,384 cases of HCV were diagnosed by the National Virus Reference Laboratory (NVRL) (3). Between 1989 and 2004, of cases diagnosed in the NVRL, 55% were genotype 1, 39% were genotype 3, 4% were genotype 2, and genotypes 4 and 5 and mixed genotypes accounted for 1%.

Amongst cases notified between 2004 and 2016, 66% were male. The median age at notification was 34 years. Information on most likely risk factor for infection has been collected since 2007. Where risk factor

data are available (51%), 80% of cases were people who inject drugs (PWID); possible sexual exposure was reported as the most likely risk factor in 5%, receipt of blood or blood products was reported in 4%, vertical transmission in 2% and tattooing or body piercing in 1%. In 7% of cases no risk factor was identified.

Incidence of HCV infection

Another caveat of HCV notification data is that they are highly influenced by testing practices and may not reflect incidence of HCV infection. In a study of the incidence of HCV in PWIDs in Ireland based on those entering drug treatment between 1991 and 2014, the estimated annual number of new HCV infections among PWIDs increased steeply from the late 1970s and peaked in 1998 (4). An estimated 12,423 (95% Confidence Interval (CI) 10,799-13,161) were infected with HCV, and 9,317 (95% CI 8,022-9,996) became chronically infected. By 2014, almost 30% of injectors were estimated to have been infected for over 20 years.

Prevalence of HCV infection and undiagnosed cases

Notification data can only include diagnosed cases. Given the long period between infection and development of symptoms, a significant proportion of those infected may not be aware of their status. Information on the prevalence of a disease is a better reflection of the burden of disease as it includes undiagnosed cases. A modelling exercise undertaken in 2011 estimated that 20,000–50,000 people in Ireland were chronically infected with HCV, giving a population prevalence of 0.5–1.2% (3). This took account of undiagnosed cases, using undiagnosed proportions previously reported in Scotland and England of between 67% and 80% (5).

A seroprevalence study undertaken in 2016 in Ireland using residual serum specimens at the NVRL found that the prevalence of anti-HCV was 0.98% (95% CI 0.73%-1.3%) in adults and the prevalence of chronic HCV infection in adults was 0.57% (95% CI 0.40%-0.81%) (6). From these findings, it was estimated that 33,708 adults in Ireland have had previous exposure to HCV and that 19,606 have chronic HCV infection. As the study excluded specimens from sources likely to have a higher risk of being HCV positive (e.g. specimens received from addiction services or STI clinics), the estimate obtained is considered the minimum likely prevalence.

Based on this seroprevalence study, and other more recently available data, it is likely that there are between 20,100 and 42,000 people with current infection in Ireland (7). It is estimated that 60% of those have not yet been diagnosed (7).

Further data on HCV prevalence in specific risk groups in Ireland, where available, are provided in the relevant chapters.

2.4 People infected through contaminated blood and blood products in Ireland

Approximately 1,700 people have been infected with HCV through the administration of contaminated blood and blood products in Ireland. These include women infected through anti-D immunoglobulin, recipients of blood transfusion, people with haemophilia and other blood clotting disorders, and people who received treatment for renal disease. The National Hepatitis C Database was established in 2004 to gather important information on an ongoing basis on this group in order to examine the natural history of infection, evaluate the outcomes of treatment, provide information for planning of services, and serve as a resource for research. Of those eligible for inclusion in the database, the participation rate was 77%. The source of infection in participants was anti-D immunoglobulin (61%), blood transfusion or treatment for renal disease (26%) and blood clotting factors (13%). Participants include 1,025 females and 295 males. The most recent follow-up of database participants occurred in 2014. Database reports are available at www.hcvdatabase.ie.

2.5 Clinical impact of HCV infection

Initial infection with HCV is typically asymptomatic or mildly symptomatic. The most common symptoms, if present, are loss of appetite, abdominal discomfort, nausea and vomiting, and jaundice. Infection is rarely detected in the acute phase. Approximately 15-45% of those with acute infection clear the virus spontaneously.

Between 55% and 85% of those infected develop chronic HCV infection and between 15% and 30% of those who are chronically infected will develop cirrhosis after about 20 years (1). An estimated 4% of those with cirrhosis progress to decompensated liver disease annually and 1.6% develop HCC annually (8). Progression to chronic liver disease is associated with excessive alcohol intake, co-infection with hepatitis B virus (HBV) or human immunodeficiency virus (HIV), being male, and older age.

The number of hospital admissions due to end stage liver disease⁶ (ESLD) and HCC in those with HCV infection has been increasing in Ireland (Figure 2). The increasing number of admissions in recent years is likely to be related to the fact that the peak incidence in the largest risk group (PWID) in Ireland was in the late 1990s, and those infected during that period are now developing ESLD or HCC as it can take 20 to 30 years to progress (4).

Between 2005 and 2016, 116 liver transplants were performed in Ireland in people with HCV infection, accounting for 18% of all liver transplants (source: Hospital Inpatient Enquiry System (HIPE) using Health Atlas Ireland⁷).

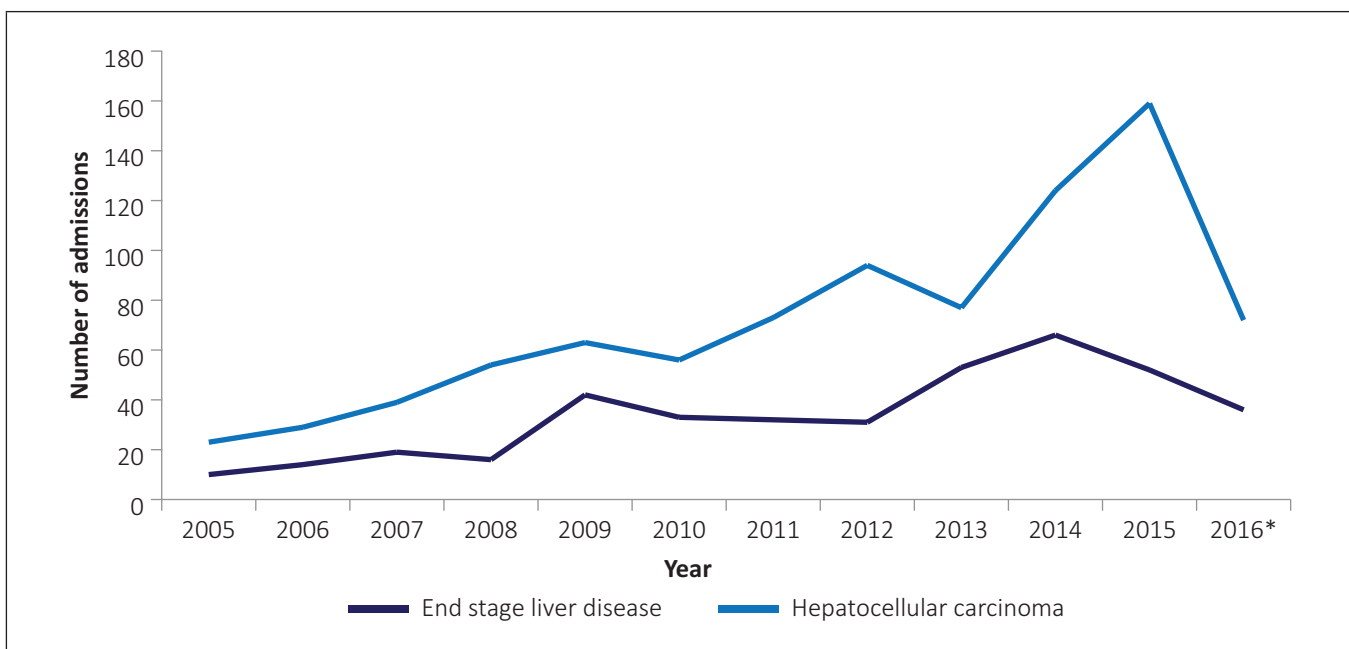


Figure 2: Number of admissions to hospital with a principal diagnosis of ESLD or HCC in people with chronic HCV infection, 2005 to 2016.

(Source: Hospital Inpatient Enquiry System using Health Atlas Ireland; extracted on 22 March 2017; *data for 2016 may not yet be complete)

⁶ Includes admissions (excluding day cases and readmissions) with a principal diagnosis code related to ESLD (ascites (R18), bleeding oesophageal varices (I850), chronic hepatic failure (K721), hepatic failure unspecified (K729), alcoholic hepatic failure (K704), acute and subacute hepatic failure (K720), hepatorenal syndrome (K767), or portal hypertension (K766)) AND a secondary diagnosis of chronic hepatitis C (B182). HIPE uses International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM). The principal diagnosis is defined as: “the diagnosis established after study to be chiefly responsible for occasioning the episode of admitted patient care”. An additional diagnosis is: “a condition or complaint either coexisting with the principal diagnosis or arising during the episode of admitted patient care”.

⁷ Based on a procedural code of ‘Transplantation of liver’ (9031700) AND a diagnostic code of HCV infection (B182). Extracted 10 July 2017.

HCV related morbidity and mortality, and also healthcare resource use, may not yet have peaked in Ireland. Modelling studies in the United Kingdom (UK) predicted that, at current treatment levels, the incidence of ESLD would continue to increase, peaking in 2030 (9). However, the future burden could be significantly altered by the rapid expansion of treatment.

2.6 Financial impact of HCV infection

In an Irish study of the annual cost of ambulatory care for HCV infection, direct medical costs were shown to increase with disease severity as shown in Table 2 (10).

Table 2: Annual mean direct medical costs of chronic HCV care for patient with different stages of liver disease in Ireland

HCV health state	Mean cost €	95% Confidence Interval
Mild liver disease	€398	€336-€482
Moderate liver disease	€417	€335-€503
Compensated cirrhosis	€1,790	€990-€3,164
Decompensated cirrhosis	€8,302	€3,945-€14,637
Hepatocellular liver carcinoma	€21,992	€15,222-€29,467
Liver transplant year 1	€137,176	€136,024-€138,306
Liver transplant after year 1 per annum	€5,631	€4,942-€5,799
Sustained virological response	€44	€16-€73

(Source: adapted from “Hepatitis C in the era of direct-acting antivirals: real-world costs of untreated chronic hepatitis C; a cross-sectional study,” by Kieran JA, Norris S, O’Leary A, Walsh C, Merriman R, Houlihan D, et al., *BMC Infect Dis.* 2015;15:471.)

Between 2001 and 2012, 2,320 patients were treated for HCV infection (11). The highest number of patients on treatment was during 2009. The total cost of HCV treatment was €27,614,326. The mean cost per patient who started treatment was €11,771 (95% CI €11,376-€12,166). Over €2 million of the cost was for drugs to treat adverse effects

In a study of the real-world costs of HCV treatment in Ireland in 2015, the mean cost of treatment with interferon-based regimes was found to be €38,286 (95% CI €35,305-€41,061) and the cost per sustained virological response (SVR) was €62,457 (12). The mean cost of treatment with interferon-free regimes was €55,734 (95% CI €50,906-€60,880) and the cost per SVR was €81,873. The cost of medication accounted for the difference between the treatment regimes. The interferon-free cohort had lower non-drug related costs. The authors noted that patients in the interferon-free cohort had advanced liver disease, and as treatment is extended to those with less severe disease higher SVRs are expected which would reduce the cost per SVR achieved.

2.7 National and international policy

National Hepatitis C Strategy

The *National Hepatitis C Strategy 2011-2014* was the first published strategy relating to all those infected with HCV in Ireland (13). Prior to this, only a statutory health services programme for those infected through contaminated blood or blood products was in place. The *National Hepatitis C Strategy 2011-2014* built on an unpublished report developed in 2004 by the then Eastern Regional Health Authority (ERHA). Because this earlier report was not published, many of its recommendations were not implemented. The 2011-2014 national strategy was devised by a multidisciplinary working group with representation from healthcare providers, voluntary and statutory organisations providing services to those at risk, and users of services. There was a commitment that its implementation would be supported where resources allowed. The strategy contains 36 recommendations spanning surveillance, prevention, screening and treatment of HCV infection. Regarding screening, the strategy made recommendations on: improving facilities for screening and diagnostics in primary care; providing every prisoner on committal a risk assessment for HCV and offering screening if required; developing guidelines with regard to screening of migrants; regularly reviewing the evidence on universal antenatal screening; and offering screening to those attending harm-reduction services (see Appendix 3 for full recommendations).

While progress has been made in a number of the strategy's recommendations, particularly those relating to treatment since the establishment of a National Hepatitis C Treatment Programme (HSE NHCTP), many are still to be implemented. The HSE NHCTP vision and aim is described in detail below, however, in order to fully deliver on the HSE NHCTP's aim of eliminating HCV and making it a rare disease by 2030, it is essential that the HCV Strategy is fully implemented as part of a whole system wide approach to HCV care.

National HCV Treatment Programme

As stated previously, the advances in the treatments available for HCV have changed the landscape for HCV care significantly. In HCV treatment, SVR means that the virus is no longer detectable at a defined period after completion of therapy (either 12 weeks (SVR12) or 24 weeks (SVR24)). SVR is regarded as a virological cure and is associated with improved morbidity and mortality. Older treatment regimes, such as a combination of peginterferon and ribavirin, induced SVR rates of 40-65% depending on the patient's genotype, presence of cirrhosis, HIV status and previous treatment experience (1). Recently introduced new treatment regimes using direct acting antivirals (DAAs) have greatly improved SVR rates to over 90% (1). The new treatment regimes are also of shorter duration with far fewer side effects. In addition to the individual benefit to the patient, the shorter treatment regime and better adverse event profile lead to a freeing-up of capacity within health services. Further details on the new treatments are available at <http://www.hse.ie/eng/health/az/H/Hepatitis-C/>.

In addition to developments in treatment, there have been advances in tests used to assess the severity of HCV associated liver disease. The non-invasive fibroscan is now the preferred diagnostic tool for determining the degree of liver disease and has replaced liver biopsy to a large extent. These advances in treatment and diagnosis/assessment mean that it is feasible for treatment and assessment to be delivered outside of the hospital setting in community and primary healthcare services.

It is now recommended that DAA regimens be used for the treatment of persons with HCV infection (1, 14). The HSE Corporate Pharmaceutical Unit commissions the *National Centre for Pharmacoeconomics* (NCPE; <http://www.ncpe.ie>) to undertake a health technology assessment (HTA) to evaluate the cost-effectiveness and budgetary impacts of new drugs or new indications for existing drugs in accordance with the Health (Pricing and Supply of Medical Goods) Act 2013. This ensures that the HSE has robust budget impact and clinical effectiveness information when deciding whether new drugs should be

reimbursed or not. Although costly, the NCPE has deemed treatment for HCV using DAAs to be cost-effective. DAA therapies for the treatment of HCV were approved for use in Ireland in December 2014.

In order to ensure the most appropriate management of access to these costly new drugs, an Expert Advisory Group was established by the Department of Health (DoH) in 2014 and chaired by the Deputy Chief Medical Officer. The role of the advisory group was to advise on the feasibility of a multi-annual public health treatment plan for patients with HCV infection based on clinical prioritisation criteria. The DoH subsequently published a report: *A Public Health Plan for the Therapeutic Treatment of Hepatitis C* in 2015 which recommended the establishment of the NHCTP in the HSE (15).

The HSE NHCTP is a multi-annual public health programme whose vision and overarching aim is to provide treatment across a range of healthcare settings to all persons living with HCV in Ireland over the coming years with a view to successfully eliminating HCV in Ireland and making it a rare disease by 2030 (16). In order to successfully reach this goal of elimination, significant increases in the number of patients accessing drug treatment is required to invert the infection curve, i.e. the number of patients being treated greatly exceeds the number of patients newly infected thereby reducing the infected cohort. In order to deliver on the DoH Public Health Plan, the strategic objective of the HSE NHCTP is to increase treatment capacity to at least 1,200-1,500 patients per annum during 2017/2018 and a continued increase in numbers being provided with treatment in subsequent years. An aggressive increase in numbers being newly diagnosed and treated is required over the coming years to reduce the burden of HCV in Ireland and achieve elimination.

Access to treatment in Ireland has been introduced through the HSE NHCTP on a phased basis based on clinical criteria with those having greatest clinical need receiving treatment initially. Criteria for treatment are determined by the HSE NHCTP Programme Advisory Group (PAG). Treatment using DAAs is currently only delivered through the acute hospital setting, although pilot programmes of community treatment are planned. Criteria for access to treatment are continuously expanding and communicated with prescribing clinicians by the HSE NHCTP.

The HSE NHCTP is aiming to provide treatment to all persons infected with HCV in the coming years as part of the overall elimination strategy. Since 2015, €30 million has been allocated annually to fund the drug treatment of HCV as governed by the HSE NHCTP. Further development of the HSE NHCTP and the development of new models of care will be subject to the HSE service planning process.

In order to achieve this, all at risk groups must be identified, screened and linked to treatment and care. Implementation of this National Clinical Guideline will be key to the identification and screening of people with undiagnosed HCV infection.

International policy

A resolution on hepatitis (WHA 67.6) was adopted by the World Health Assembly (WHA) in May 2014, calling for an intensified and expanded global hepatitis response and for the World Health Organization (WHO) Secretariat to examine the feasibility of elimination of hepatitis B and C. In addition, goal 3 of the Sustainable Development Goals “Ensure healthy lives and promote well-being for all at all ages” includes a target to combat hepatitis by 2030 (17, 18).

The first global health sector strategy on viral hepatitis was developed and published by WHO in 2016 (19). The strategy covers the period 2016–2021. While it addresses all five hepatitis viruses (A, B, C, D and E), it has a particular focus on HCV. The vision of the strategy is “A world where viral hepatitis transmission is halted and everyone living with viral hepatitis has access to safe, affordable and effective prevention, care and treatment services”. It sets the goal of eliminating viral hepatitis as a major public health threat

by 2030 by reaching the target of 90% of those infected being diagnosed and 80% of those eligible being treated. Other targets include a 90% reduction in new cases of chronic HCV; and a 65% reduction in mortality due to HCV.

The strategy outlines five strategic directions that guide the actions required to achieve these targets. These include information for focused action; identifying interventions for impact; delivery of these interventions in an equitable manner; financing these initiatives; and using innovative approaches to accelerate progress.

The strategy calls for action across the entire continuum of HCV care from primary prevention of infection, to diagnosis, linkage to care, and treatment. Ireland already has a comprehensive national HCV strategy which has been implemented insofar as possible in certain limited areas within existing resources and it now also has a HSE NHCTP which aims to provide treatment to all persons living with HCV in line with the WHO global health sector strategy. However, greater efforts and coordination will be required to meet the goals of the WHO strategy.

Of particular relevance to this guideline, the WHO strategy states that key actions for countries relating to the diagnosis of hepatitis are to:

- *“Integrate viral hepatitis testing into national hepatitis policies and guidelines that defines, among other things, priority populations and locations for testing, testing approaches and strategies”*
- *“Establish key linkages between testing and other services to improve referral and access to quality assured treatment and other support services.”*
- *“The national hepatitis response should be guided by a national plan with a well-defined governance and management structure that can ensure a coordinated and efficient response and clear accountability.”*

At a European level, the WHO Regional Office for Europe, has developed an action plan for the health sector response to viral hepatitis (20). This adapts the *Global Health Sector Strategy on Viral Hepatitis 2016–2021* to the contexts of the countries of the European Region. At an European Union (EU) policy summit on HCV in 2016, a number of European stakeholders in the field of HCV, including the European Association for the Study of the Liver (EASL), European Liver Patients Association (ELPA), and the World Hepatitis Alliance, committed to a declaration on HCV elimination in Europe by 2030 (21).

2.8 Principles of screening

Screening can be defined as “the presumptive identification of unrecognized disease or defects by means of tests, examinations, or other procedures that can be applied rapidly” (22). In 1968 Wilson and Jungner developed a set of criteria by which a proposed screening programme should be evaluated (Box 1) (22). These criteria have been modified over the years by some countries, but in general, criteria regarding the condition, the test, the treatment and the programme should be satisfied before screening is initiated.

Box 1: Wilson and Jungner Criteria (22)

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognised disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognisable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a “once and for all” project.

Screening for HCV infection meets all of these criteria. With regard to the condition, as outlined previously, there is considerable morbidity and mortality associated with HCV infection. The long asymptomatic period provides an opportunity for early detection, early treatment and reduction in morbidity. The natural history of HCV infection has been described. Detection of infection is straightforward and based on a blood sample, with newer tests based on other specimen types becoming available. New, non-invasive techniques, such as fibroscan, for determining the stage of infection are now widely available. Since the advent of the new treatment regimes and the establishment of the HSE NHCTP, successful, acceptable and cost-effective treatments are now available for detected cases. There are clear criteria for who to treat and when to treat, and specialist services are in place to assess patients identified through screening governed by the HSE NHCTP.

3 Development of this National Clinical Guideline

3.1 Rationale for this National Clinical Guideline

With the development of new treatments for HCV, the paradigm has shifted towards elimination. Ireland has committed to a WHO target to eliminate HCV by 2030. Key to reaching the goal of elimination will be treatment of those infected. The establishment of the National Hepatitis C Treatment Programme (HSE NHCTP) is a significant step towards this target.

However, it is estimated that 60% of those with HCV infection in Ireland are undiagnosed (7). Those unaware of their infection status will not access available treatment and also present a risk of ongoing transmission. Screening enables early detection, referral for assessment and treatment thus decreasing progression to chronic liver disease and HCC. This will thus benefit the individual and the health service as a whole. Without screening, cases may go undetected for a considerable length of time due to the asymptomatic nature of HCV infection.

While there is screening for HCV infection ongoing in many settings in Ireland, there has not been a national guideline to guide healthcare providers or services. Also, some at-risk population groups are not covered by current screening services and screening practices vary between institutions and providers. Standardisation of practice will help ensure that all those most at risk are screened in an appropriate manner regardless of setting.

WHO has stated that national testing policies are needed, as are increased investments in HCV screening services in order to reach the goal of elimination. With the commitment to offer treatment to those infected through the establishment of the HSE NHCTP, there has never been a more important time for national screening guidelines to be introduced.

3.2 Aim and objectives

The aim of the guideline is to reduce the overall health and economic impact of HCV infection and contribute to the elimination of HCV as a public health concern in Ireland by 2030.

The objectives of the guideline are:

- to make recommendations on who should be offered screening for HCV infection and how screening should be undertaken
- to enhance and further improve the screening of those at risk for HCV
- to improve the identification of undiagnosed cases of HCV
- to reduce variation in practice relating to screening
- to support the linkage to care of identified cases
- to increase awareness of screening amongst healthcare workers and the public.

3.3 Guideline scope

Population to whom the guideline applies

Those living in Ireland with unrecognised HCV infection.

Intended users of the guideline

All healthcare professionals, healthcare managers and policy makers. The guideline will also be of value to both statutory and voluntary bodies providing services to those groups at increased risk of HCV infection. It may also be used by those with HCV or in a risk group for HCV and by members of the public.

3.4 Conflict of interest statement

The guideline development process followed the conflict of interest policy set out by NCEC. All members of the GDG were required to complete a Conflict of Interest Declaration which were managed by the Chair. Stated conflicts of interest are outlined in Appendix 4.

3.5 Sources of funding

No external funding was received for the development of this guideline. The commissioned literature review (on the risk of HCV sexual transmission amongst heterosexuals) was funded by the National Patient Safety Office (NPSO), Department of Health to support the work of the NCEC.

3.6 Guideline development group

The GDG included professionals with the relevant expertise and experience, and target users of the guidelines. The disciplines represented were infectious diseases, medical microbiology, virology, occupational medicine, obstetrics and midwifery, prison health, general practice, addiction services, and public health. Healthcare management, at-risk groups, and patients were also represented. The members were chosen to represent a professional body, section of the health service, or because of their individual expertise or experience. Members of the GDG are listed in Table 1.

Representation from the population to whom the guideline will apply

HCV affects a heterogeneous group of people. A number of members of the GDG work in services which provide care for groups who are at risk of HCV such as prisoners, migrants, homeless, and MSM.

In Ireland, vulnerable groups, in particular drug users, are most affected by HCV. In addition to the above GDG members, further representation of the population to whom the guideline will apply was provided by Mr Lar Murphy and Ms Nicola Perry. Mr Murphy and Ms Perry work with Community Response, an organisation which works closely with those at risk of HCV, in particular those with alcohol or drug addiction. It is based in the south inner city of Dublin and provides a range of services including education, group support, one-to-one support and referral pathways. Community Response is also collaborating with a number of ongoing projects in Ireland which are developing integrated HCV care pathways for vulnerable groups.

Both Mr Murphy and Ms Perry work closely with people with HCV and people who are at risk for HCV. Mr Murphy is a Project Worker and the facilitator of the Community Response Hepatitis C/Liver Health Group which is a support programme for people with HCV or alcohol related liver disease. Ms Perry is the chair of the Hepatitis C Partnership, which advocates for services and support for those affected by HCV.

3.7 Methodology and literature review

The guideline development process followed the process recommended by NCEC (23).

The key questions to be addressed by the guideline were identified from the recommendations of the National Hepatitis C Strategy and through consultation with the GDG. The key questions are outlined in Appendix 5.

A search for national or international HCV guidelines was conducted to identify recommendations which could be adopted or adapted. The search strategy included a search of Medline, PubMed using search terms related to HCV, screening, and guidelines. The websites of key organisations were also searched. Identified guidelines underwent an initial screening process. This involved reviewing the guideline to determine if it addressed any of the key questions. Guidelines that did then underwent an initial quality screening using the Rigour of Development (ROD) domain of HIQA's National Quality Assurance Criteria (24). Guidelines which addressed key questions and had an acceptable ROD score progressed. An explicit ROD score was not used to exclude guidelines. Guidelines which were of a lower ROD score were excluded if the same recommendation was made in other better quality guidelines. Some guidelines with a low ROD score did progress as they addressed questions not addressed in other guidelines, addressed a key risk group in detail, or were based on a highly relevant context e.g. an Irish guideline. Guidelines which passed the screening stage were then further appraised by two or three members of the GDG using HIQA's National Quality Assurance Criteria. Quality Assurance Scores were collated for each guideline. This and the reviewers' global rating of the guideline were reviewed by the GDG and a decision made to include or exclude the guideline. Again an explicit score was not used. In some instances guidelines of a lower quality were included as they addressed a key risk group in detail or were based on a highly relevant context. The result of the appraisal process of included guidelines is summarised in Appendix 6. For some key questions topic specific guidelines were reviewed and adapted (e.g. screening in renal dialysis setting).

Recommendations from quality approved national and international guidelines relating to key questions were reviewed by the GDG. Taking into account the currency of the guideline, the quality of the guideline, the level of evidence supporting the recommendations, the GDG made a decision on whether or not recommendations could be adopted or adapted.

If a key question was not addressed in existing guidelines, or not adequately addressed, or national and international guidelines conflicted in their recommendation, a review of published research was conducted. Search strategies were tailored to be appropriate to the research question e.g. for searches on diagnostic tests, time limits were restricted to more recent years as technological advances make older literature redundant. As an example, the search strategy and resulting flow diagram for one question is presented in Appendix 7, and others are available on request. One systematic literature review was commissioned and undertaken by the School of Nursing and Midwifery, National University of Ireland, Galway (see Appendix 8).

Retrieved studies underwent an initial title screen to eliminate obviously irrelevant articles. Abstracts were then reviewed by two members of the GDG to determine relevance according to agreed inclusion and exclusion criteria. Where there was disagreement, a third person judged whether the study should be included. Full texts were then reviewed for inclusion or exclusion. Articles that met inclusion criteria underwent quality appraisal appropriate to the study type. If deemed of reasonable quality, the study was included. If an article could not be sourced under existing HSE subscription agreements, the reviewers re-examined the abstract to determine its relevance. If the literature was deemed unlikely to alter the overall body of evidence, further efforts to source it were not undertaken.

Formulation of recommendations

To formulate recommendations, subgroups of the GDG used a considered judgement process adapted from the GRADE Evidence to Decision framework (25, 26). Considered judgement forms (see Appendix 9) were populated for each key question, with recommendations from other guidelines and/ or evidence from primary literature. Considered judgement forms also included relevant Irish epidemiology or national policy where available. Subgroups of the GDG formulated recommendations taking into account the available evidence, the balance of benefits and harms, resource use, acceptability, feasibility of implementation, and the known or estimated values and preferences of patients and society. Links to

considered judgement forms are available in Appendix 9. Recommendations were then presented to the full GDG for final wording and approval.

3.8 Grading of recommendations

Recommendations were graded in two ways: the level and quality of evidence supporting the recommendation and the strength of the recommendation. The criteria used for both grading systems were based on recommendations from GRADE (27, 28).

Table 3 outlines how the quality of evidence was categorised. The level and quality of evidence reflects confidence in estimates of the effect of the outcome under investigation. In determining the level of evidence, factors such as study design, consistency between studies, magnitude of effect, study methodology, and risk of bias were considered. In general, the presence of a number of good quality randomised controlled trials showing consistent results equates to a high level of evidence. Observational studies are generally initially rated low quality but can be upgraded if the magnitude of effect is large, or if there is consistency across multiple studies. Case studies and expert opinion (e.g. in the absence of other evidence) are considered low quality.

Table 3: Categorisation of evidence

Level of evidence	Type of evidence	Rationale
High	Consistent evidence from well performed randomised, controlled trials, meta-analyses, or overwhelming evidence of some other form	Further research is unlikely to change our confidence in the estimate of benefit and risk.
Moderate	Evidence from randomised, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence of some other research design	Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate
Low	Evidence from observational studies, consensus opinion of experts, case studies, or from randomised, controlled trials with serious flaws, or standard of care	Any estimate of effect is uncertain.

When recommendations were adapted from other quality appraised guidelines, the level of evidence described within those guidelines is given. The consistency between different guidelines in the recommendations made and the quality of guidelines is also indicated.

The strength of recommendation reflects the confidence of the GDG that the desirable effects of a recommendation outweighed the potential undesirable effects. In determining the strength of the recommendation the GDG considered the following factors: quality of the evidence, balance of benefits and harms, resource use, acceptability, feasibility of implementation, and the known or estimated values and preferences of patients and society. A two level grading system was used: strong, and conditional/weak (Table 4). If the GDG was confident that the desirable effects outweighed the undesirable effects, a strong recommendation was made. If the GDG believed that the benefits and risks/harms/costs were more finely balanced, or there was uncertainty about the magnitude or value of the benefit, a weak recommendation was made. Some recommendations are conditional as further evidence is required to support the recommendation in the Irish context e.g. a health technology assessment (HTA) is needed, or circumstances may change, e.g. treatment may become available for HCV in pregnancy.

Table 4: Grading of the strength of the recommendation

Strength of recommendation	Rationale
Strong	The potential positive outcome is highly valued. The benefits will outweigh the harms or the cost.
Conditional/Weak	The potential benefit of the recommendation is uncertain, or the balance between benefit and harm, or cost is finely balanced, or dependent on other factors. The feasibility of implementation is uncertain or likely to be difficult.

A strong recommendation may be made despite a low level of evidence. For example, if there was no evidence or only a limited quantity or quality of evidence available to examine the outcome, but the expected benefit was considered to be large, clinically important or highly valued, then a strong recommendation was made. An example of this is the recommendation on screening of migrants from high endemicity countries.

Note on the phrasing of recommendations:

In the case of a strong recommendation to screen a certain group, the phrasing used was that those within this group ‘should be offered screening’.

In the case of conditional/weak recommendation to screen a certain group, the phrasing used was that for those within this group ‘screening should be considered’.

3.9 Stakeholder consultation and external review

Individuals or organisations identified as stakeholders in the health and social care of those who are infected with HCV or at risk of HCV infection were invited to review the guideline and provide feedback (see Appendix 10 for a list of those who were invited to review the guideline).

In addition, a public consultation process was undertaken. The consultation was advertised on the HSE HPSC website, Epi-Insight (a monthly on-line bulletin published by the HSE HPSC), and via the HSE HPSC and HSE social media platforms. The guideline was available online and feedback could be provided via a provided template. The consultation period ran between 31 March and 20 April 2017.

Feedback was requested to be submitted via a template based on that recommended by NCEC (29). Feedback received was reviewed by the GDG and the guideline was amended where appropriate. (Feedback received and the resulting action of the GDG is available in Appendix 10).

External review

International external review of the guideline was undertaken by two experts in the epidemiology and public health management of HCV. Dr Susan Hahné is a Senior Epidemiologist and Head of Department for Early Warning and Surveillance in the Netherlands National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu (RIVM)). Dr Hahné was chair of the European Centre for Disease Prevention and Control (ECDC) Hepatitis Coordination Committee from 2014 to 2016. Dr Magdalena Rosińska (M.D., Ph.D) is an epidemiologist at the National Institute of Public Health - National Institute of Hygiene (Narodowy Instytut Zdrowia Publicznego - Państwowy Zakład Higieny) in Poland and chair of the ECDC Hepatitis Coordination Committee from 2017.

International external reviewers were asked to provide feedback based on questions recommended by National Quality Assurance Criteria for Clinical Guidelines Version 2 (30). The external reviewers were also asked to provide any additional feedback they had. Feedback received was reviewed by the GDG and amendments made where appropriate.

3.10 Procedure to update this National Clinical Guideline

The guideline will be updated three years from publication as per the process recommended by NCEC. Responsibility for update of the guideline will rest with the National Hepatitis C Strategy, or a future governance structure into which the Hepatitis C strategy is incorporated (please see Recommendation 27 regarding the need for a National Hepatitis C Programme). If there is a major change in evidence prior to this, a rapid update may be conducted as per NCEC procedures.

3.11 Implementation

Health equity

As mentioned, HCV is sometimes called the silent killer due to the lack of symptoms until liver disease is advanced. It is also called silent because many of those infected or at risk of infection are from marginalised groups in society. Such people are often poorly reached by health services and may experience many barriers to accessing testing, linking to care, and being retained in care.

Proportionate universalism is the resourcing and delivering of universal services at a scale and intensity proportionate to the degree of need (31). The principle of proportionate universalism should underpin the implementation of this guideline and the entire HCV continuum of care.

Implementation plan

A plan for implementation of this guideline is outlined in Appendix 11. This builds on the work that is already being undertaken by a range of HSE services, non-governmental organisations (NGOs), health and social care professionals, peer workers and volunteers in the areas of screening and care of persons with HCV or at risk of HCV (see Appendix 12).

Support for implementation of this guideline has been cited in the HSE Primary Care and HSE Health and Wellbeing 2017 operational plans (32, 33) with commitment to:

“Support the development and implementation of relevant national clinical guidelines and audits (... hepatitis C screening...) ensuring that the essential clinical leadership is in place

AND

... progress the recommendations of the national clinical guidelines on hepatitis C screening (when published) within available funding”

A key requirement for screening to be effective in reducing the burden of HCV is that people who are diagnosed are linked into care and treated. The HSE NHCTP is working collaboratively with stakeholders to devise pathways to care through existing structures as well as identifying other areas where care can be delivered. New integrated models of care which include shared care programmes across community and acute hospital settings and stand-alone community HCV treatment programmes are also being explored which will facilitate linkage to and retention in care in a wider range of healthcare settings.

One particular initiative of interest is [HepCare Europe](#)⁷ (34). This is a multi-country research collaboration, led by a team in Ireland, which is developing and evaluating targeted community-based interventions for vulnerable groups of people living with HCV or at risk of HCV. It aims to develop an 'integrated care' model for HCV treatment based on the joint participation of primary and speciality care practitioners (see Appendix 12 for further details).

Reaching the goal of elimination

While the scope of this guideline is limited to screening, it is recognised that in order to achieve the goal of elimination by 2030, action is required across the entire continuum of HCV care including reducing vulnerability to HCV infection, primary prevention of infection, diagnosis, linkage to care, treatment, and ongoing care (19). Implementation of this guideline, the work of the HSE NHCTP and the National Hepatitis C Strategy are welcome points of progress in tackling the burden of HCV in Ireland. However, given the complexity of HCV, the vulnerability of many of those at risk of HCV, and the range of actions required across the continuum of care, a co-ordinated approach is required.

The WHO Global Strategy calls for countries to develop national hepatitis response plans and establish governance structures to ensure a coordinated response (19). At present, no such structure exists in Ireland. While the HSE NHCTP has demonstrated a model by which such a structure could operate, it is not currently within the mandate or resources of the HSE NHCTP to address the entire HCV continuum of care.

The GDG recommend that a National Hepatitis C Programme, with a mandate and resources to co-ordinate actions across the entire continuum of care, be established, as recommended by the WHO.

3.12 Economic Impact of this National Clinical Guideline

A review of economic literature was undertaken to inform the guideline process. The considered judgement process through which recommendations were formulated included a consideration of available and relevant economic evidence. A summary of economic evidence is presented in Appendix 13. Of note, the management and treatment of HCV is a rapidly evolving area. New treatments are more effective and also more costly. However the costs of the new treatments are likely to decrease as they become more widely available and production and procurement costs decrease. These factors will impact on the cost-effectiveness of screening interventions into the future. Much of the economic evidence was based on older treatment regimes and therefore not generalisable to the current and changing context.

A Budget Impact Assessment (BIA) is also presented in Appendix 13. It has been estimated that implementation of the guideline will cost is €1.1 million per year over a five year period. Of note, as screening is recommended on a one-off basis for a number of groups, there will be a front-loading of screening in the initial few years. Beyond the five year period, the annual cost is expected to decrease.

The BIA should be reviewed in the context of an annual budget of €30 million which has been allocated for the drug treatment of HCV. The HSE NHCTP aims to offer treatment to all those infected in the coming years. However, without supporting and resourcing screening, those in need of treatment may not be identified. Early detection of cases and early treatment will also have economic benefits in terms of a reduction in future resource use. Detection and treatment will prevent the development of chronic liver disease and the costs of this to the health service.

⁷ <http://www.ucd.ie/medicine/hepcare/>

Funding for implementation of this guideline will be subject to the HSE service planning process for activities within the HSE and the respective funding methods of other organisations to which it applies.

3.13 Monitoring, evaluation and audit

Implementation of the guideline will span a range of sectors and services. Monitoring and evaluation will be required at individual service level, and national service level. Healthcare services which provide care to those at risk for HCV as outlined in this guideline should audit their activity in relation to HCV screening as recommended by this guideline. This applies in particular to addiction services, Methadone Treatment Protocol GPs, the prison service, STI services and maternity services. Audit criteria relating to HCV screening are already components of audit tools in some of these services (35, 36).

Suggested monitoring and audit criteria are presented in Appendix 14. It is recommended that sectors implement a standardised audit plan to allow for audit data from individual services to be collated and fed into a national audit process.

Screening is one part of the continuum of HCV care. The impact of this guideline will depend on the effectiveness of strategies across the whole care pathway. The establishment of a National Hepatitis C Programme, as recommended, will enable the development and monitoring of a suite of metrics across the entire continuum of care in order to comprehensively assess Ireland's progress towards elimination, and the selection of key metrics to be used as national key performance indicators (KPIs).

Appendix 14 presents metrics which reflect key areas of this guideline to be included as national KPIs in the interim.

4

National Clinical Guideline recommendations

4.1 Should the following people be offered screening for HCV?

4.1.1. Pregnant women

Key question

Should pregnant women be screened for HCV infection?

Evidence summary

One of the primary aims of screening pregnant women for infections is to intervene if possible and prevent vertical (mother-to-child) transmission of infection and adverse outcomes for the child.

The risk of vertical transmission of HCV is approximately 4-8% and is substantially higher in infants born to mothers who are HIV-infected as well as HCV-infected (10.8–25%) (1). An Irish cohort study of infants born to HCV positive mothers reported a transmission rate of 6.4% (95% CI 2.8-10%) amongst those where the outcome was known. The rate of vertical transmission was 3.4 times higher for HIV co-infected women.

Transmission occurs in utero or during delivery. Transmission is not associated with breastfeeding. The risk of transmission is correlated with the HCV viral load of the mother. Invasive obstetric procedures, foetal scalp electrodes and prolonged rupture of membranes have been associated with transmission in some studies. Elective caesarean section (ELCS) in order to reduce the risk of transmission is not recommended as the benefit is not clear, and ELCS is associated with increased risk of morbidity for the mother. In HIV negative women, there are currently no interventions which have been shown to significantly reduce the risk of vertical transmission of HCV and routine obstetric care is recommended (37-42).

A number of studies have reported on the prevalence of HCV in the antenatal population in Ireland. A study in 2007-2008 in the Rotunda Hospital determined the prevalence of anti-HCV in an antenatal population to be 0.9% (43). Of those women who tested anti-HCV positive (n=78), 64% were HCV-RNA positive. The majority (60%) of anti-HCV positive women were Irish. A self-reported risk factor for HCV was present in 73% of women. Multiple regression analysis reported an association between HCV infection and both IDU (p<0.001) and tattooing (p<0.05).

In a study comparing targeted screening (i.e. only women with risk factors) and universal screening (i.e. all women) over consecutive years (2006 and 2007) in the Coombe Women & Infants University Hospital (CWIUH), the prevalence of anti-HCV was found to be 1.4% (67/4,666) in the targeted screening programme and 0.7% (66/9,222) in the universal screening programme (44). Approximately half of women attending for antenatal care were eligible for screening as part of the targeted screening programme due to the presence of a risk factor (44). Prior history of drug use and having a tattoo or body piercing were the most common risk factors for being anti-HCV positive in both years. It was estimated that in 2007 when universal screening applied, one case (1/67, 1.5%) would not have been detected through a targeted screening programme. Universal screening has been in place in the CWIUH since 2007. It is estimated that approximately one case of HCV infection per year is detected where there is no obvious risk factor present (personal communication, Orla Cunningham, CWIUH).

In a study in Dublin maternity hospitals between 1994 and 1999, women were tested on the basis of reported risk factors for HCV, clinical indication or self-request. Of detected infections, the most common

risk factor was IDU (83%), followed by heterosexual exposure (8%), infected blood products (7%), and tattoos (<1%). No risk factor was identified in 3% (42).

Currently, HCV treatment during pregnancy is not recommended. Given this, and the lack of effective interventions to reduce vertical transmission, routine testing of pregnant women for HCV is currently not recommended by a number of international bodies (2, 37, 40, 45-50).

Value judgement

The beneficial effects of universal screening in pregnancy do not outweigh the potential cost at present as treatment for HCV infection is not available in pregnancy and there are no interventions to reduce transmission to the baby. The main benefit in screening during pregnancy at present is in identifying women with infection who can be treated after pregnancy. The overall prevalence of HCV in the general antenatal population in Ireland is likely to be low and standardised implementation of targeted risk-based screening is likely to detect most cases of maternal HCV infection. Screening should be undertaken during the booking visit at the same time as other microbiological screening.

HCV treatment is a rapidly evolving area. If HCV treatment during pregnancy becomes feasible in the future, the value judgement may shift in favour of universal screening in pregnancy as it may offer additional benefit by reducing or eliminating the risk of vertical transmission. Also, if national policy progresses to a policy of birth cohort or total population screening, then antenatal screening could be considered as an opportunistic method to offer screening to a particular cohort of the general population.

Recommendation 1

- 1.1 Standardised targeted risk based HCV screening of antenatal women is recommended (see Appendix 1 for a list of risk populations).
- 1.2 Universal HCV screening of antenatal women is **not** recommended.
- 1.3 Universal antenatal HCV screening may be reconsidered in the future if HCV treatment during pregnancy becomes possible. Also, if national policy progresses to a policy of birth cohort or total population screening, antenatal screening offers an opportunistic method to reach this particular population cohort.

Quality/level of evidence: *moderate; good consistency between existing high quality guidelines*

Strength of recommendation: *strong*

The following are responsible for implementation of recommendation 1:

HSE, maternity units, GPs.

4.1.2. Children born to mothers with HCV infection

Key question

Should children born to mothers with HCV infection be offered screening for HCV?

Evidence summary

There is a small risk of transmission of HCV between an infected mother and infant during the perinatal period (see section 4.1.1 for a summary of the evidence). Twenty per cent of infants infected through vertical transmission clear HCV infection spontaneously, usually by 5-6 years of age.

Screening of infants born to infected women permits early identification and linkage to care. It is recommended by a number of international bodies (1, 37, 45, 47-49, 51-55). It was also recommended by the *National Hepatitis C Strategy 2011-2014* (13).

The risk of vertical transmission is related to the HCV viral load of the mother. There is no risk of transmission if a mother is not viraemic (i.e. HCV-RNA negative). Therefore, screening of infants born to women who are HCV-RNA negative is generally not required (37). However, occasionally some women with current infection test anti-HCV positive and HCV-RNA negative, but have a transient or fluctuating viraemia, and may indeed be viraemic at the time of delivery. There is also the possibility that some women may become re-infected during pregnancy. Therefore, screening infants of women who are anti-HCV positive but HCV-RNA negative should be undertaken unless it can be assured that the woman was HCV-RNA negative at the time of delivery.

Maternal anti-HCV is transferred across the placenta, meaning that infants of anti-HCV positive mothers will test anti-HCV positive at birth due to the presence of maternal anti-HCV in the infant's circulation. In the absence of vertical transmission of HCV infection, infants will become anti-HCV negative between six and 20 months of age. Around 80% will be anti-HCV negative by 12 months of age. One study which included an Irish cohort estimated that 50% of uninfected children became anti-HCV negative by eight months of age, with only 5% still having detectable maternal anti-HCV at 13 months of age. Due to this persistence of maternal anti-HCV, serological testing of infants is not recommended before 12 months of age (37, 41). Infants of mothers with HIV co-infection may have negative anti-HCV tests between 12 and 18 months of age despite being HCV-RNA positive.

Testing for HCV-RNA by PCR can be undertaken earlier. In the previously mentioned Irish study the specificity of HCV-RNA PCR was estimated to be 97% (95% CI: 96–99%) and was unrelated to age at testing. PCR sensitivity, by contrast, was age dependent. Estimated sensitivity was 22% (95% CI 7–46%) before one month of age and 97% (85–100%) after that. Some infants who are HCV-RNA positive may clear infection and subsequently become HCV-RNA negative. Also, some infected infants may not become HCV-RNA positive until 12 months of age or older. One study indicated that the sensitivity of a positive HCV-RNA PCR result obtained on two occasions between two and six months of age in predicting infection was 81% (95% CI: 58-97%). Due to the lower sensitivity of HCV-RNA in early life, confirmatory testing will be required at a later stage.

The aim of screening infants born to infected mothers is to identify those with persistent infection and link them to care and treatment, rather than to identify all those to whom the virus was transmitted. Given this and the above issues with the sensitivity and specificity of diagnostic tests in infancy, there are variations in recommendations on the optimal time for testing, with some bodies recommending later testing with initial serology and others earlier testing with HCV-RNA (37, 38).

There is no direct clinical benefit to the child in having a presumptive positive diagnosis earlier in life as treatment is not possible until later in childhood. Early testing can reassure parents of the likely absence of infection. However, the results of early testing are not definitive. An early presumptive positive diagnosis

may result in undue anxiety amongst parents or carers of infants who will spontaneously clear the virus. On the other hand, delaying testing until later (after 12 months) when tests will be more sensitive poses the risk of losing infected infants to follow-up. Screening early confers the benefit of early engagement in care, potentially mitigating losses to follow-up.

The Rainbow Clinic is Ireland's tertiary level clinical service for children with HIV or hepatitis. Current practice in Ireland, as per the Rainbow Clinic guidelines, is to offer HCV-RNA testing at six weeks and six months of age (38). If HCV-RNA is negative, absence of infection is confirmed with an anti-HCV test at 18 months of age. If HCV-RNA is positive at any stage, the infant is referred to the Rainbow Clinic. This testing and referral system has been in place in Ireland for a number of years and is functioning efficiently. It is the experience of the Rainbow Clinic that this testing schedule enables early linkage to care for a sometimes vulnerable population and enables the family to be supported through subsequent follow-up, thus reducing the risk of losing contact with the family and infant.

No formal health economic assessments were retrieved on screening for HCV infection in infants born to infected mothers.

Value judgement

While the GDG recognises that there is not a direct clinical benefit to early detection of infection in infants, the GDG recommends adopting the Rainbow Clinic guidelines on the basis that they have proven to be acceptable and feasible, and that the early testing schedule will link the child and family into care and support subsequent follow-up.

A paediatric treatment programme has been established through the HSE NHCTP will enable future treatment for infected children.

Recommendation 2

- 2.1 Infants of HCV-RNA positive women should be tested for HCV-RNA at six weeks and six months of age and, if both are negative, anti-HCV at ≥ 18 months of age.
- 2.2 Infants who are HCV-RNA positive at any time, or who are anti-HCV positive at or after 18 months of age, should be referred to the Rainbow Clinic.
- 2.3 Infants of anti-HCV positive but HCV-RNA negative women, where eradication of infection, either spontaneously or by treatment is not assured (i.e. by serial negative HCV-RNA tests), should be tested for anti-HCV at ≥ 18 months of age.
- 2.4 Infants of anti-HCV positive but HCV-RNA negative women, where eradication of infection, either spontaneously or by treatment is assured (i.e. persistent negative HCV-RNA tests and no ongoing risk for reinfection), should be managed as infants of uninfected women and do not require follow-up.

Quality/level of evidence: *low to moderate*

Strength of recommendation: *strong*

Recommendation 3

- 3.1 If a woman is found to have current or resolved HCV infection, any previous children she has given birth to should be tested for HCV, unless the woman was known to be HCV-RNA negative at the time of their delivery.

Quality/level of evidence: *low to moderate*

Strength of recommendation: *strong*

The following are responsible for implementation of recommendation 2 and 3:

Maternity units, paediatric units, Rainbow Clinic.

4.1.3. Household contacts of a person with HCV infection

Key question

Should household contacts of those with HCV infection be screened?

Evidence summary

Household contacts are those who share living spaces with each other. Household contacts can be spouses, partners, siblings, children or other family members, or be unrelated.

A household contact of a person who is HCV positive who is also a sexual contact or a child born to a HCV positive mother can be at risk of transmission due to sexual or vertical transmission respectively. The risks of vertical or sexual transmission of HCV are summarised in sections 4.1.2 and 4.1.10 respectively. Household contacts who were born to an infected mother or who have had sexual contact with a HCV infected person should be screened as per Recommendation 2 and Recommendation 13.

There is variation between guidelines from other bodies regarding screening of household contacts. Some guidelines recommend that household contacts be offered screening while others recommend against screening of household contacts or recommend that it be considered on a case-by-case basis (37, 45, 47, 49, 53).

Transmission of HCV to a household contact, who is not a sexual contact or who was not exposed vertically, is termed horizontal transmission. When horizontal transmission occurs between family members it is sometimes termed intrafamilial transmission. A number of studies have examined the risk of horizontal transmission of HCV. A review in 2013 acknowledged that horizontal intrafamilial transmission does occur but data on the epidemiology and routes of transmission are difficult to interpret with any certainty (56). A systematic review from 2000 analysed 23 uncontrolled studies and 5 controlled studies and determined that intrafamilial transmission does occur (57). The prevalence of anti-HCV in siblings and household contacts of paediatric chronic liver disease patients was reported to be 1.1%, while the prevalence in parents was 11.0%. The odds of sibling or household contact of a HCV positive patient being anti-HCV positive was 9.75 (95% CI 0.91 - ad infinitum). The odds of a child of a HCV positive person being anti-HCV positive was 1.12 (95% CI 0.78 - 1.60).

A number of observational studies have found no increase, or a slight increase, in the prevalence of anti-HCV amongst family members or household contacts of a HCV positive individual (58-60). However, the risk of horizontal transmission could not be independently assessed due to other potential routes of transmission between the contact or due to common risk exposures.

While a number of studies demonstrated intrafamilial or household transmission, the evidence on the risk of horizontal transmission is limited. A number of studies were conducted in endemic countries such as Italy where the potential for exposure through other routes outside of the household (e.g. healthcare transmission) could have existed. Even those studies outside of high endemic countries it was not possible to differentiate between sexual transmission and other horizontal transmission pathways in the household or other possible transmission pathways external to the household.

Value judgement

While household transmission can occur, the risk is difficult to quantify and it is difficult to eliminate the contribution of other common exposures amongst household members. The risk of horizontal non-sexual transmission to other household contacts is likely to be very low within normal household settings. The experience of the GDG members is that household horizontal transmission is rare. Promoting screening of household contacts may lead to undue concern amongst those who are HCV positive or their household contacts over the risk posed. It may also lead to stigmatisation of HCV positive people.

Given that the risk within a normal household setting is likely to be low, the possible harms to the HCV positive household member and the resources that would be required for implementation, active screening of all household contacts is not considered justified. The GDG recognises that there are circumstances within a household which may increase the risk, and screening should be considered in such circumstances. The GDG also recognises that testing of household contacts may be requested for reassurance. Testing should not be refused in such circumstances.

Recommendation 4

Where a household contact is a child who was born to an infected mother or a sexual contact of a HCV-infected person 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) 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*

The following are responsible for implementation of Recommendation 4:

Healthcare worker diagnosing HCV in the HCV positive household member, GPs, Departments of Public Health.

4.1.4. People who use unprescribed or illicit drugs

Key question

Should people who currently use or have a history of unprescribed or illicit drug use be offered screening for HCV?

Evidence summary

Injecting Drug Use

People who inject drugs (PWID) are a well-recognised risk-group for HCV infection globally. Screening of current or previous PWID is recommended by all international guidelines (1, 2, 37, 39, 45, 47, 48, 51, 52, 55, 61) and previous Irish guidance (62). A number of guidelines have clarified that this should include those who injected only once (39, 47, 48, 51). Current PWID are at ongoing risk of infection and regular re-testing has been recommended. Recommendations on the frequency of retesting differ between guidelines, from every six to 12 months (61) to annual testing (37). PWID who have been successfully treated or had spontaneous clearance and who continue or return to injecting drug use are at risk of reinfection.

In Ireland, while there have been no recent studies on the prevalence among PWID, previous studies of PWIDs in prisons and PWID attending methadone clinics, specialist addiction treatment centres and GPs have estimated the HCV prevalence in this population to be between 62% and 81% (63, 64). A study amongst prisoners in 1998 showed a prevalence of anti-HCV of 81.3% in prisoners who injected drugs (65). A 2011 prison study found that 54% of prisoners with a history of injecting heroin were anti-HCV positive and 41.5% of prisoners with a history of injecting any drugs were anti-HCV positive (66).

The *National Hepatitis C Strategy 2011-2014* recommended that all drug users, especially those who have injected drugs or shared 'works', including prisoners, be screened (13).

The current standard of care for services offering opioid substitution in Ireland is to offer anti-HCV testing on presentation (67). If a patient initially tests negative, a repeat test is to be offered every six to 12 months if the patient continues with risk-taking behaviour. In an audit of HCV screening and referral in addiction centres in Community Health Organisation (CHO) 7, among those patients for whom audit forms were completed and where data were available, there was a very high level of compliance with the recommendation to test for HCV (98%). A high proportion (95%) of those who were antibody positive were then tested for antigen or HCV-RNA. Compliance was also moderately high with referral of antigen/RNA positive patients for specialist assessment at 86% (36).

Non-injecting drug use

The risk of HCV infection amongst non-injecting drug users is less clear.

A number of guidelines have recommended screening for persons who use/have used intranasal drugs (1), while the US Centers for Disease Control and Prevention (CDC) has stated that testing of intranasal cocaine users and other non-injecting drug users is of uncertain need (48).

A systematic review published in 2007 which included 28 studies, determined the prevalence of HCV in non-injecting drug users to range from 2.3-35.5% (median = 14%) (68). However, the authors concluded that it could not be adequately determined whether non-injecting drug use (NIDU) was associated with HCV infection due to the low quality of evidence available.

A number of observational studies have reported an association between HCV infection and intranasal cocaine use even after adjusting for other possible risk factors, including a history of IDU (69-71). A study

of homeless and marginally housed people in the US found a negative association between snorting cocaine and HCV (OR=0.39; 95% CI 0.21 - 0.73) (72). The authors concluded that there was likely under-reporting of injection drug use as there was a high prevalence (17%) of anti-HCV in those who reported no IDU. Other observational studies have found an association between sharing equipment for snorting or sniffing drugs and HCV infection amongst non-injecting drug users (73-75).

There are several limitations to studies assessing the association between NIDU and HCV infection. Some of the studies do not clearly define what is meant by NIDU. Also, most of the studies are reliant on self-reported behaviour and therefore unreported current or previous IDU may be a confounding factor.

The risk of transmission through NIDU is biologically plausible and depends on the potential for exposure to blood of a HCV positive person. The potential exposure may not be obvious as the blood exposure may not be visible. Sharing of implements to snort drugs is likely a risk due to the highly vascular structure of the nasal passages which can be easily damaged by the insertion of implements. Certain drugs which are smoked can cause burning or bleeding of the lips which may pose a risk of transmission if drugs or equipment are shared with a person who is HCV positive. There is no biologically plausible pathway by which drugs taken orally, and drugs smoked which do not result in any contact with the blood of others, could transmit HCV.

Value judgement

There is a clear risk of transmission of HCV amongst PWID and screening of PWID is current practice.

There is limited and inconsistent evidence on the risk of HCV transmission through NIDU. However, NIDU which results in exposure to blood of an infected person is a biologically plausible transmission route. It is the experience of expert members of the GDG working with drug users that transmission can occur via NIDU as described above. Also, many non-injecting drug users may have a previous history of IDU. Drugs only taken orally, and most drugs smoked, will not pose any risk of HCV transmission.

Recommendation 5

- 5.1 All those who have ever injected unprescribed or illicit drugs should be offered screening for HCV. This includes those who only injected once, and those who injected any type of drug which was not prescribed, including performance enhancing drugs like steroids, and novel psychoactive substances.
- 5.2 Re-testing of those who test HCV negative should be offered on an annual basis, or six monthly if deemed clinically appropriate*, for those who remain at ongoing risk of infection.
- 5.3 Testing should be available during this interval if a risk exposure is known to have occurred.
- 5.4 Re-testing for those who have been previously infected, but have cleared infection spontaneously or through treatment, should be done by HCV-RNA testing, as anti-HCV antibody remains positive after the first infection.

*More frequent testing may be considered in circumstances such as: if a risk exposure is known to have occurred; an unexplained rise in ALT; a diagnosis of another BBV.

Quality/level of evidence: *high; good consistency between existing high quality guidelines*
Strength of recommendation: *strong*

Recommendation 6

6.1 Screening should be offered to all those who have used unprescribed or illicit drugs by a route other than injecting (i.e. non-injecting drug use (NIDU)), if there is a possibility of transmission of HCV by the route of administration. This includes those who currently use intranasal drugs (i.e. snort or sniff), or have done so in the past, or share other equipment or drugs where there is a risk of contamination with the blood of others (e.g. smoking crack pipes).

Quality/level of evidence: *low*

Strength of recommendation: *strong*

The following are responsible for implementation of recommendations 5 and 6:

HSE Social Inclusion/ Primary Care, addiction services, GPs.

4.1.5. Prisoners

Key question

Should prisoners be offered screening for HCV?

Evidence summary

Prisoners are a recognised risk group for HCV infection globally (1). A number of international guidelines recommend screening of prisoners, either by screening of prisoners on entry to prison and during their sentence (45), or by screening of people who have ever been in prison (39, 51, 53, 54).

Prisoners are considered to be a risk group for HCV infection due mainly to the association between IDU, criminality and imprisonment. However, there is a risk of transmission within the prison setting due to factors such as IDU and equipment sharing within prison, tattooing in prison, or other environmental exposure to contaminated blood. Of note, there is a particular practice of tattooing in prison to specifically mark the period of imprisonment. Such a tattoo is sometimes referred to as a borstal mark.

Studies have demonstrated a high prevalence of IDU amongst prisoners in Ireland. In a 2011 study in Irish prisons, 26% of participants reported ever injecting drugs (66). In an older study in 1998, 43% of participants reported ever injecting drugs (65). In this study, a fifth of PWID reported first injecting in prison, and 71% of PWID reported sharing needles in prison. In a study of those entering prison in Ireland in 1999, 29% of participants reported ever injecting drugs (76).

The above studies also revealed a high prevalence of HCV infection amongst prisoners in Ireland. In the 2011 study, an anti-HCV prevalence of 13% (95% CI 10.9–15.2%) was found from the 777 oral fluid samples tested (66). Amongst those with a history of IDU, the anti-HCV prevalence was 41.5%. Drug-related factors which were significantly associated with being anti-HCV positive on multivariable analysis included: being in a very high drug use prison (OR 9.8, 95% CI 3.1–31.1), ever having used drugs intravenously (OR 8.3, 95% CI 3.5–20.0), and ever having shared intravenous drug using equipment (OR 4.5, 95% CI 2.0–10.4). In the 1998 study, an anti-HCV prevalence of 37% (95% CI 34.3–39.9%) was found in total (65). Amongst those with a history of IDU the prevalence was 81%, and amongst those who reported not injecting drugs the prevalence was 4%. In the study of new prison entrants in 1999, an anti-HCV prevalence of 22% (95% CI 18.6–25.4%) was found (76). The prevalence was significantly lower ($p < 0.0001$) in participants who had never been in prison before.

Other factors which have been associated with being anti-HCV positive amongst prisoners in Ireland include: older age, specifically age-group 25–34 years (OR 3.6, 95% CI 1.3–9.7) and age-group 35–64 (OR 7.8, 95% CI 2.7–22.5), female gender (OR 4.5, 95% CI 1.04–20.0), and having had a tattoo done in prison (OR 2.6, 95% CI 1.4–5.10). Of note, 68% of prisoners had tattoos, and of these 35% had a tattoo done in prison.

Notably, these studies have also shown a discrepancy between self-reported HCV status and actual status. In the 2011 study, 8.6% of prisoners self-reported being HCV positive while 12.9% tested anti-HCV positive (66). Ninety five per cent of those who self-reported that they were positive tested positive and 91% of those who self-reported that they were negative tested negative. Five per cent of those who self-reported that they were positive tested negative and 9% of those who self-reported that they were negative tested positive. In the 1998 study, 5% of those who reported being HCV positive tested negative, and 37% who reported a previous negative HCV test tested positive (77).

The *National Hepatitis C Strategy 2011-2014* recommended that every prisoner on committal be provided with a HCV risk assessment, including details of previous testing, and be offered screening if required (13). In Ireland, healthcare is provided to prisoners by the Prison Healthcare Service under the governance of the Irish Prison Service (IPS). Prisoners are entitled to the same quality and range of health

services as that available under General Medical Services (GMS) in the community (78). It is also the duty of the Prison Healthcare Service to do all possible to safeguard the health of those in their care. The *Irish Prison Service Health Care Standards* recommend that: “All persons entering prison who volunteer a background history with risk factors for any infectious disease should be offered any available screening for that condition...” and that “Any therapeutic intervention (screening, treatment, and referral) should be provided on the basis of informed consent”. Specific to HCV, they recommend: “Hepatitis C testing will be offered where clinically appropriate. Testing will be undertaken only when requested by a prisoner or where, following consultation, a prisoner gives informed consent to a test on the clinical recommendation of the doctor involved” and “Prisoners who are infected with Hepatitis C will be given appropriate advice and treatment”.

There are new initiatives underway within some Irish prisons to offer treatment to prisoners within the prison setting, in addition to some of the current in-reach programmes provided by hospital based services and supported by the HSE NHCTP.

Despite the above policy and practice, uptake of HCV screening by prisoners is reported to be low. There are a number of possible reasons for this. Upon committal a prisoner may have many other worries and concerns and HCV screening may not be considered a priority for them. Concerns about confidentiality may also be a barrier to accepting an offer of screening in prison. Communication of HCV test results to a prisoner’s community based healthcare provider on release from prison has also been identified as a difficulty (13).

Value judgement

There is a high prevalence of current or past drug use amongst the prisoner population in Ireland, and the prevalence of HCV amongst prisoners has been shown to be high. Also, transmission can occur in prison through various mechanisms. In general, prisoners are from marginalised groups who are otherwise poorly reached by healthcare services. Their time in prison may offer a unique opportunity for the diagnosis, assessment and treatment of HCV infection.

Screening should be undertaken early during committal to enable an opportunity to link into care, and to minimise the risk of transmission to others within the prison setting.

While screening is being offered currently, uptake is low. Novel approaches will be required to improve uptake.

Recommendation 7

- 7.1 Screening for HCV should be offered to all prisoners on entry to prison. Screening should be offered at a time at which it is most likely to be accepted by the prisoner, while also ensuring the early identification of infections in order to minimise the risk of transmission to others.
- 7.2 Those found to have HCV infection should be linked into specialist care and treatment should be facilitated while in prison.
- 7.3 Prisoners who initially test HCV negative should be offered repeat testing on an annual basis, or six monthly if deemed clinically appropriate*, while in prison. Screening should also be offered at any time if a risk exposure (e.g. tattooing, needle-sharing) is known to have occurred.
- 7.4 Prisoners should be able to access testing on request at any stage of their sentence.

*More frequent testing may be considered in circumstances such as: if a risk exposure is known to have occurred; an unexplained rise in ALT; a diagnosis of another BBV.

Quality/level of evidence: moderate; good consistency between existing high quality guidelines
Strength of recommendation: strong

Recommendation 8

8.1 One-off testing of ex-prisoners should be considered, although implementation may be difficult.

Quality/level of evidence: moderate; good consistency between existing high quality guidelines

Strength of recommendation: conditional/weak

Good practice points

- Education on the risk of HCV should be provided to prisoners upon entry into prison.
- At the time of committal, the interviewing nurse or doctor is best placed to identify the optimal time to carry out HCV screening on an individual prisoner.
- Continuity of care and/or treatment on discharge from prison should be ensured. This should be considered as part of discharge planning. Continuity of care on entry to prison should also be considered.
- Communication about test results or treatment should occur between the prison health service and the prisoner's GP, or other services attended by the prisoner, such as addiction services or psychiatric services.
- Confidentiality at the time of screening offer, during testing, and when communicating results of testing should be ensured as far as possible, while still ensuring a safe environment for prison healthcare staff.

The following are responsible for implementation of recommendation 7:

Irish Prison Service.

4.1.6. People who are homeless

Key question

Should those who are homeless be offered screening for HCV?

Background

The term homelessness can include a broad range of circumstances from people who are sleeping rough to people living with family or friends. There is no broadly accepted terminology around homelessness. FEANTSA, a European Federation of National Organisations Working with the Homeless has developed the European Typology of Homelessness and Housing Exclusion (ETHOS) to provide a common language around homelessness (79). ETHOS uses the term rooflessness to describe people living rough and people living in emergency accommodation. The Dublin Region Homeless Executive uses the term visibly homeless to describe people who are living rough or sleeping in designated emergency accommodation such as a hostel (80).

While the term homeless will be used here, it is generally referring to those who are roofless or the visibly homeless.

Evidence summary

A number of studies in Ireland have shown an association between homelessness, IDU and HCV infection. In a study of homeless people in Dublin and Limerick in 2013, 78% of participants reported illicit drug use ever, 55% reported illicit drug use in the last three months, 43.5% reported IDU ever, and 24% reported IDU in the last 12 months (81). Drug use was higher in Dublin compared to Limerick, with 46% of participants from Dublin reporting IDU ever and 25% reporting IDU in last 12 months compared to 22% and 15% respectively of participants from Limerick. Amongst participants from Dublin, 28.5% self-reported a diagnosis of HCV. No participants from Limerick self-reported a diagnosis of HCV infection.

In a study of active PWID presenting to an Emergency Department in inner city Dublin over a three month period in 2010 the prevalence of homelessness was high with 37% of participants residing in a temporary homeless hostel and 13% having “no fixed abode” (82). Amongst all participants, 74% were HCV positive. In a census of homeless adults in north Dublin city conducted in 2005, 31% reported drug or alcohol misuse as the reason for homelessness, 23% reported being a current drug user, 42% reported ever using drugs, and 36% of participants self-reported a diagnosis of HCV infection (83). Data from the National Drug Treatment Reporting System (NDTRS) showed that 13% of those entering or re-entering addiction services in 2014 had an unstable accommodation status. Amongst attendees of addiction services in Community Health Organisation 7 (formerly Dublin Mid Leinster) 35% are reported to be rough sleepers, sleeping in rolling emergency beds, or in six month beds (personal communication, Dr Margaret Bourke, HSE Addiction Services).

The above studies and the experiences of members of the GDG working with homeless people show that there is a clear association between homelessness and IDU. However, studies have been mainly concentrated in Dublin, and the association may not be reflected in other regions. Also, in recent years there may be an increasing number of people becoming homeless due to altered financial circumstances, and these people may not have the same risk profile.

While IDU is the main reason that people who are homeless are at risk of HCV infection, other risk factors may be present, such as being from a country where HCV is common. Also, those who do not use drugs but share sleeping space with drug users may have been exposed to environmental risks, such as discarded needles.

In the UK, it is recommended that people living in hostels for the homeless or sleeping on the streets should be offered HCV screening as they are considered a group at increased risk of HCV infection (45).

Value judgement

The prevalence of current or previous drug use is high, as is HCV infection, amongst some homeless populations such as rough sleepers. The homeless are a marginalised population with often greater healthcare needs than other population groups. Drug using homeless people are a particularly vulnerable population who are sometimes poorly reached by health and addiction services. Extra support will be required to pro-actively identify and access this population, and to facilitate uptake of screening. In addition, support will be required to enable linkage to care and treatment.

Recommendation 9

- 9.1 Homeless people who have a history of engaging in risk behaviours associated with HCV transmission, or who have had a potential HCV risk exposure, should be offered screening.
- 9.2 Those who initially test HCV negative should be offered repeat testing on an annual basis, or six monthly if deemed clinically appropriate*, if there is an ongoing risk of transmission.

*More frequent testing may be considered in circumstances such as: if a risk exposure is known to have occurred; an unexplained rise in ALT; a diagnosis of another BBV.

Quality/level of evidence: *low*

Strength of recommendation: *strong*

The following are responsible for implementation of recommendation 9:

HSE Social Inclusion/Primary Care, addiction services, GPs, homeless services.

4.1.7. Migrants

Key question

Should migrants from a country where HCV is common be offered screening for HCV?

Background

The term 'migrant' is taken to include any person who was not born in Ireland but who is currently living here temporarily or permanently. This includes: all persons who have migrated to this country voluntarily for whatever reason, including migrant workers and foreign students; international adoptees; those who have been compelled to leave their original country of nationality or residence for whatever reason and have come to this state to seek its protection as asylum seekers or refugees; undocumented or irregular migrants including those who are trafficked.

Evidence summary

In 2015 the *Infectious Disease Assessment for Migrants* developed by the Migrant Health Assessment Sub-committee of the HSE HPSC, Scientific Advisory Committee recommended that migrants who originate from countries with a prevalence of chronic hepatitis C of 3% or higher should be offered HCV testing (84). However, at present in Ireland, apart from screening being offered to asylum seekers and some screening of migrants attending antenatal services, screening for migrants is not routine.

WHO states that migrant populations represent a heterogeneous group and HCV seroprevalence estimates vary widely (2). It recommends that migrant populations from high/intermediate endemic countries be offered screening. SIGN recommends that testing be offered to migrants from countries with a medium or high prevalence of HCV (37). NICE lists people born or brought up in a country with an intermediate or high prevalence of chronic HCV as a risk group for HCV, specifying intermediate prevalence to be a prevalence of at least 2% (45).

There is limited data available on the prevalence of HCV among migrants living in Ireland. The Reception Centre in Baleskin reported that, between 2004 and 2012, amongst the 10,014 asylum seekers or refugees accommodated in the centre who accepted voluntary testing, the prevalence of HCV was 0.95% (n=96) (85). Only one country-specific prevalence rate was calculable from the information available: the prevalence amongst those from Pakistan was 3.3%.

An audit of screening services provided to asylum seekers presenting to reception centre clinics in what was previously the Eastern Region Health Authority (ERHA) determined that between 1999 and 2003 the anti-HCV prevalence amongst those screened was 1.5% (86). Breakdown by country of origin was not reported.

Information on country of birth for statutory notifications of HCV in Ireland is limited. On a review of notifications received between 2004 and 2015⁸, country of birth is known for 16.5%. Where country of birth is known, 46% are Irish born (source: CIDR; HSE HPSC). However, this is likely to under-represent Irish born people as country of birth may be less likely to be completed for Irish born people.

ECDC compared the anti-HCV prevalence in migrants living in Europe to the prevalence in their country of origin (in-country) (87). They compared 43 estimates of anti-HCV prevalence among migrant populations in the EU/EEA to an in-country or regional estimate. Studies included migrants from 38 countries. They found that 18 estimates were lower, 15 were comparable, and 10 were higher than the in-country estimate. There was heterogeneity in the populations from which the migrant estimates in the EU/EEA

⁸ Please note CIDR is continuously being updated and numbers may differ from those published elsewhere

were determined making it difficult to clearly determine if the prevalence differs in migrants compared to the country of origin. Ten estimates were from the general migrant population, which ECDC suggests is the most valid comparison. Of these 70% were comparable to the in-country prevalence, and 30% are lower. Of note, in general the prevalence in migrant populations in Europe was higher than the prevalence in the general population of the new country.

Assuming migrants have a similar prevalence of HCV as in their country of origin, it has been estimated that adult migrants contribute 20% (lowest to highest estimate: 7- 47%) of the total burden of chronic HCV cases in Ireland (87).

As per the 2011 census there were 766,700 migrants resident in Ireland. Assuming a prevalence of anti-HCV equivalent to that in their country of origin and that 75% of those who are anti-HCV positive have current infection, it is estimated that there are over 8,000 migrants in Ireland with HCV infection. There are approximately 145,000 migrants from countries with an anti-HCV prevalence of 2% or greater, of whom approximately 4,300 are estimated to be chronically infected. There are 90,000 migrants from a country with an anti-HCV prevalence of 3% or greater, amongst whom 3,200 are estimated to have chronic infection.

Value judgement

Migrants from intermediate and high prevalence countries can have a prevalence of HCV comparable to their country of origin. There is some evidence that even when the prevalence is lower than the prevalence in the country of origin, it is still higher than that of the general population of the country of residence.

While data on HCV in migrants in Ireland is limited, it is estimated that migrants contribute significantly to the burden of HCV in Ireland. A recommendation to offer one-off screening to those from a country with a prevalence of 2% or greater would potentially detect half of chronic infections amongst migrants. While the recommendation will result in a large number of people being eligible for screening, given the increased risk of chronic infection in migrants, it is considered appropriate to offer one-off screening to those from a country with a prevalence greater than 2%.

There are a number of points for consideration around making a recommendation on screening of migrants. The recommendation and implementation must not lead to any stigmatisation. There may be economic, language or cultural barriers to migrants accessing healthcare and testing, in particular migrants who are undocumented.

Of note, migrants, from high or low endemicity countries may fall into another risk group for HCV infection and should offered screening as appropriate for this risk group.

Recommendation 10

10.1 Migrants from a country with an intermediate to high prevalence of HCV (anti-HCV \geq 2%*) should be offered one-off HCV screening.

*Please refer to Appendix 2 for a list of countries with an anti-HCV prevalence \geq 2%.

Quality/level of evidence: *low to moderate*

Strength of recommendation: *strong*

The following are responsible for implementation of recommendation 10:

HSE Primary Care and Social Inclusion; antenatal services.

4.1.8. People who received medical or dental treatment abroad

Key question

Should those who received medical or dental treatment in high prevalence countries be screened for HCV?

Background

This includes travellers and migrants who have required medical or dental treatment while abroad and people who have travelled for the purpose of medical or dental treatment. It also includes migrants who may have received medical treatment in their country of origin or in another country. Please refer to Recommendation 10 on screening migrants from intermediate and high prevalence countries also. There is also a separate recommendation on those who have received blood or blood products abroad (Recommendation 17).

Guidance on screening of dialysis patients who have had dialysis abroad has been issued by the subgroup of the Standing Advisory Committee on the Prevention of Transmission of Blood-Borne Diseases in the Health-Care Setting and so will not be addressed in this guideline (88).

Evidence summary

There is limited published literature on the risk of HCV transmission from medical or dental treatment abroad, apart from case reports of transmission events associated with dialysis or transplants abroad. Dialysis and transplant surgery are recognised risks for HCV transmission and are not within the scope of this question.

However, WHO recognises that there is a risk of parenteral transmission of HCV in healthcare settings where there is a higher background prevalence of HCV and where infection control practices are inadequate (e.g. around diagnostic and therapeutic procedures), and where blood transfusions and other tissue donations are not screened for viral hepatitis (2). WHO thus recommends that persons who have received medical or dental interventions in healthcare settings where infection control practices are substandard should be offered testing for HCV (1).

The number of Irish residents who travel abroad for medical and dental treatment, and the countries they travel to, is not known. In addition, the number of people resident in Ireland who may have received medical or dental treatment while travelling or living abroad is not known.

Between 2004 and 2016 there were 30 notifications of HCV in Ireland (of a total of >14,000 HCV notifications) in which surgical or dental treatment outside of Ireland was cited as the most likely risk factor (source: CIDR; HSE HPSC). The majority of these (n=25) were born outside of Ireland. Four were Irish born, and for one the country of origin was unknown.

Value judgement

The number of Irish residents infected with HCV or at risk of infection through medical or dental treatment abroad is not known. However, the numbers are not likely to be large, except amongst migrants from intermediate and high prevalence countries for whom screening has been recommended.

It is recognised that implementation of this recommendation will be difficult and will be likely to be done on an opportunistic basis.

Recommendation 11

11.1 Screening for HCV should be considered in people who have received medical or dental treatment in countries where HCV is common (anti-HCV prevalence $\geq 2\%$ *) and where infection control may be poor.

*Please see Appendix 2 for a list of countries with anti-HCV prevalence of $\geq 2\%$.

Quality/level of evidence: *low*

Strength of recommendation: *conditional/weak*

The following are responsible for implementation of recommendation 11:

HSE Social Inclusion; Reception and Integration Agency; HSE Social Inclusion and Safety Net Mobile Health and Screening Unit; GPs and other health professionals on an opportunistic basis.

4.1.9. People with tattoos or body piercings

Key question

Should those who have tattoos or body piercings be offered screening for HCV?

Evidence summary

A number of guidelines make recommendations on screening of those with tattoos or body piercing. Some guidelines specify that this applies only to those who have had tattoos in unregulated settings (39, 51) or where infection prevention and control procedures may have been poor (1, 37). Others do not specify any conditions to the recommendations (53, 54). CDC in the US has stated that screening of those with tattoos or body piercings is of uncertain need (47).

Tattoos

A large, global systematic review and meta-analysis in 2010 identified a strong association between HCV infection and tattooing (89). The overall pooled odds ratio (OR) was 2.74 (95% CI 2.38-3.15). The association varied when stratified by the place where the tattoo was done. The OR for tattoos carried out in non-professional parlours or by 'friends' was 2.8 (95% CI 1.29-6.08). The OR for tattoos done in professional parlours was lower and non-significant (OR 1.28, 95% CI 0.68-2.39). When stratified by study population type, the strongest association was found amongst non-injecting drug users (OR 5.74; 95% CI 1.98-16.66), blood donors (OR 3.73, 95% CI 2.46-5.67) and hospitalised patients (OR 3.2; 95% CI 1.95-4.0).

An observational study from the Netherlands determined that people with multiple tattoos were not at increased risk of HCV infection (90). From a cohort (n = 434) of tattoo artists, body piercers, and people with multiple tattoos and/or body piercings, only one participant (who had other risk factors for HCV infection) was HCV positive.

A number of studies have found that the association between tattooing and HCV infection differs by the date of tattooing. In a study in Australia, ever having received a tattoo was statistically significantly associated with being anti-HCV positive (OR 3.73; 95% CI 2.32-5.99). When stratified by date of tattooing, the highest association was found amongst those tattooed between 1980 and 1990 (OR 5.92; 95% CI 1.46-24.06). Amongst those tattooed before 1980, the association was lower, but still statistically significant (OR 3.28; 95% CI 1.11-9.67). Amongst those tattooed after 1990, no association was found (OR 0.37; 95% CI 0.15-1.02). In a study amongst blood donors in Canada in 2006, having received a tattoo more than 10 years ago was significantly associated with HCV infection (OR 5.43; 95% CI 1.82 - 16.2), while receiving a tattoo within the last 10 years was not found to be statistically significantly associated with HCV infection (OR 2.35; 95% CI 0.77 - 7.22) (91).

Studies on the association between tattooing and HCV infection in Ireland are limited. Two studies determined the association between tattooing and HCV in the prison population (66, 76). In one study, tattooing in prison was the only independent risk factor identified for being anti-HCV positive amongst those who had never injected drugs (76). In another study, the presence of tattoos, and tattoos acquired in prison, were associated with being anti-HCV positive on univariable analysis (66). However on multivariate analysis only having had a tattoo done in prison remained significant (OR 2.6, 95% CI 1.4-5.1).

Of note, in the most recent prison study, 68% of prisoners had tattoos (66). In 71% of those with a tattoo, they had a tattoo done by a professional, 24% had a tattoo done by a friend, 18% had a tattoo done by another prisoner, and in 20% had a self-done tattoo. Thirty five per cent of those with tattoos had a tattoo done in prison.

In a study of HCV screening in the antenatal population in Dublin, 47% of anti-HCV positive women had a tattoo, and tattooing was significantly associated with being anti-HCV positive on multiple regression ($p < 0.05$) (43).

Body piercing

Studies examining the association between body piercing and HCV infection have been conducted in a range of countries and amongst a range of study groups.

One systematic review was identified but it was of poor quality, with a number of methodological and presentation flaws (92). A number of observational studies found an association between HCV infection and ear piercing (93, 94), body piercing, or an unspecified piercing on univariable analysis (93, 95-97). However, when multivariable analysis was undertaken the associations did not persist (91, 93, 95), except for one study where the OR decreased but remained significant for any piercings (OR 2.0, 95% CI: 1.1-3.7) (97). This study was conducted between 1994 and 1995, and therefore may not be relevant now due to improved infection prevention and control practices after this time.

Other observational studies did not find an association with HCV infection and ear piercing (95, 98), body piercing (99-102), the number of body piercings (101), the setting where piercings were performed (101), or the type of disinfection method used (101).

As mentioned previously, an observational study from the Netherlands determined that people with multiple tattoos and body piercings were not at increased risk of HCV (90).

Irish data

At present in Ireland there is no regulation of the tattoo or body piercing industry. There are no available data on the prevalence of tattoos or body piercing in the general population in Ireland.

Tattooing or body piercing were cited as the most likely risk factor for 38 of greater than 4,200 notifications of HCV in Ireland between 2011 and 2015 (source: CIDR; HSE HPSC). Amongst the 28 of these with a country of infection stated, 21 were reported to be infected outside Ireland.

Value judgement

The evidence demonstrates a link between tattooing and HCV infection. The factors associated with increased risk of transmission are not clear but it is likely that those most at risk of having acquired HCV through tattooing are those who received tattoos a number of decades ago, in non-professional settings, in prison, in high prevalence countries, or in other circumstances where infection control was poor. Within Ireland, there is evidence of an association between HCV infection and tattoos done in prison. The risk of HCV transmission from tattooing in commercial premises or other settings in Ireland is not known. While many commercial premises are likely to employ appropriate infection prevention and control practices, there is no regulation of the industry in Ireland to assure standards. It is not considered appropriate to ask recipients of tattoos to self-assess whether or not infection prevention and control practices were adequate. For these reasons, offering HCV screening to all recipients of tattoos should be considered.

The evidence on the risk of HCV transmission with body piercing is inconsistent and limited in quantity and quality, and thus does not support a recommendation for offering screening to those with body piercings.

Recommendation 12

- 12.1 Screening for HCV should be considered for all those with a tattoo. Those most at risk of having acquired HCV through tattooing are those who received tattoos a number of decades ago, in non-professional settings, in prison, in high prevalence countries, or in other circumstances where infection control was poor.
- 12.2 There is insufficient evidence to support screening of recipients of body piercings (including ear piercings).

Quality/level of evidence: *low; good consistency between existing high quality guidelines on screening of those with tattoos*

Strength of recommendation: *conditional/weak*

The following are responsible for implementation of recommendation 12:

GPs and other health professionals on an opportunistic basis; antenatal services.

4.1.10. Heterosexual partners of a person with HCV or a person at risk of HCV infection

Key questions

Should the following be offered screening for HCV:

- Sexual partners of a person with HCV or a person at risk of HCV infection?
- Sexual contacts of known cases of HCV?
- Sexual contacts of a person who injects drugs?
- Those with high risk sexual behaviour?

These questions address the risk of sexual transmission amongst heterosexuals. The risk of sexual transmission amongst men who have sex with men (MSM) is considered in section 4.1.11.

Evidence summary

While a number of guidelines recommend that screening of sexual partners of those who are HCV positive be considered (37, 45, 52, 54, 55), others only recommend it if either partner is HIV positive (53, 103), or there are other shared risk factors for HCV between partners, such as needle-sharing (53). Others have stated that testing of long term steady sexual partners of a HCV positive person is of uncertain need (47). The *National Hepatitis C Strategy 2011-2014* did not propose any recommendations on sexual partners due to the limited evidence in relation to sexual transmission (17).

Recent evidence reviews by WHO and others concluded that the risk of sexual transmission of HCV is strongly linked to pre-existing HIV infection and that there is low or no risk of sexual transmission of HCV among HIV-negative heterosexual couples (1, 2, 51, 53).

In a systematic review of studies assessing sexual transmission of HCV, several large prospective cohort studies included did not show an increased risk for HCV transmission amongst heterosexual couples (104). The review reported that the risk of sexual transmission of HCV is increased in persons with multiple sexual partners (adjusted OR 2.2 to 2.9) and those who are HIV positive. The authors did acknowledge that a limitation in assessing the risk of sexual transmission of HCV is the potential confounding effect of drug use, as most studies were reliant on self-reporting of drug use.

A subsequent case control study of 500 index cases and their partners found a HCV prevalence rate of 4% amongst among partners of HCV positive persons (105). 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 sexual transmission of HCV was 0.07% per year (95% CI, 0.01–0.13%) equating to approximately one episode of transmission per 190,000 sexual contacts. No specific sexual practices were related to HCV transmission among couples.

Others potentially at risk of sexual transmission of HCV

Outside of the context of a heterosexual relationship there is limited evidence on what, if any, sexual behaviours present an increased risk of sexual transmission of HCV.

Screening of sex workers is recommended by some guidelines (53, 54). WHO states that overall the risk of sexual transmission of HCV is low amongst sex workers. However, there may be a small increased risk of transmission among persons with multiple sex partners which may place sex workers at increased risk. Also, sex workers may be more likely to belong to other high risk populations, such as PWID and persons in prisons or closed settings, which may be the main reason for the higher prevalence among sex workers (2). In a study of 150 female sex workers attending the Women's Health Project in Dublin between 1991 and 1997, 8.1% (8/99) were anti-HCV positive (16). Amongst women who were not PWID, 3.2% (3/93) were HCV positive. Amongst women who injected drugs, 83.3% (5/6) were positive.

CDC has stated that routine HCV testing is of uncertain need for persons with a history of multiple sex partners or sexually transmitted diseases (47).

In a systematic review to determine what factors were associated with an increased risk of sexual transmission of HCV infection in a heterosexual population, eight studies examining seven risk factors (multiple sex partners, receiving or providing sex commercially, having a PWID partner, and unprotected vaginal, oral or anal sex) were included (106). One included study did find that, in an antenatal population in Scotland, the prevalence of anti-HCV amongst those who reported not injecting drugs but had a sexual partner who did was 15% compared to 0.6% in the overall study population (107). The relative risk of being anti-HCV positive for a sexual partner of a PWID compared to those who were not PWID or have a partner who was a PWID was 48 (95% CI 5-32). Multivariable analysis was not conducted. A second included study which examined the risk in sexual partners of PWID did not find an association. None of the other factors examined in the systematic review were found to be statistically significant risk factors for HCV infection. However, the authors concluded that there was uncertainty about these results due to limited quantity of evidence and the very low quality of evidence.

Irish data

Between 2004 and 2016 there were 171 cases of HCV notified in Ireland (of a total of >14,000 HCV notifications) where the most likely risk factor was reported to be possible sexual exposure (75 heterosexual, 41 MSM, and 55 of unknown sexual orientation) (source: CIDR, HSE 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).

Value judgement

Testing of heterosexual sexual partners of people who are HCV positive is not routine practice in most settings in Ireland at present. The risk of sexual transmission amongst heterosexual partners is low. However, there are circumstances that increase the risk of sexual transmission, including if either partner is HIV positive.

There is no clear evidence to suggest that any particular sexual practices or behaviours increase the risk of sexual transmission amongst heterosexuals. There is very limited evidence that sexual partners of PWID and commercial sex workers may be at increased risk of HCV infection. This may be due to other non-sexual transmission routes of exposure. Commercial sex workers may be more likely to belong to other risk groups. Sexual partners of PWID 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.

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*

The following are responsible for implementation of recommendation 13:

Addiction services, Hepatology/infectious diseases/STI/GUM services; Departments of Public Health.

4.1.11. Men who have sex with men

Key question

Should men who have sex with men (MSM) be offered screening for HCV?

Evidence summary

To date, the risk of sexual transmission of HCV amongst MSM who are HIV negative has been considered to be low (1). A number of guidelines have limited recommendations on HCV screening amongst MSM to those that are HIV positive (45, 51, 53, 54). More recent guidance has recommended that MSM engaging in chemsex⁹ be screened for HCV (53).

A number of systematic reviews and meta-analyses have examined the prevalence or incidence of HCV in HIV positive and/or HIV negative MSM. These have shown an increased prevalence or incidence of HCV amongst HIV positive MSM compared to HIV negative MSM, and when stratified by IDU, an increase amongst HIV positive MSM who engaged in IDU. Jordan et al. (108) reported a pooled prevalence of anti-HCV of 8.2% (95% CI 6.6%-9.7%) amongst HIV positive MSM. Among HIV positive MSM who did not engage in IDU the prevalence was 6.7% (95% CI 5.3%-8.1%) and among HIV positive MSM who engaged in IDU it was 40.0% (95% CI 28.0%-51.0%). Yaphe et al. (109) reported a pooled incidence, amongst HIV negative MSM of 1.48/1000 person years (PY) (95% CI 0.75 to 2.21). The pooled incidence amongst HIV positive MSM was 6.08/1000 PY (95% CI 5.18% to 6.99%). Ghisla et al. (2016) reported a pooled incidence amongst MSM regardless of HIV status of 6.3/1000 PY (95% CI 5.0%-7.5%) (110). Amongst HIV negative MSM the pooled incidence was 0.4/1000 PY (95% CI 0.0%-0.9%). The pooled incidence amongst HIV positive MSM was 7.8/1000 PY (95% CI 6.0%-9.7%).

A number of meta-analyses have also shown a change in the association between HCV infection and MSM over time. One study showed that while a statistically significant increase in anti-HCV prevalence amongst all HIV positive MSM over time was found, increasing by 0.334% a year (108), the increase was only seen amongst HIV positive MSM who did not engage in IDU. In this group, the prevalence increased by 0.367% a year ($p < 0.001$), while there was a statistically significant decrease in the prevalence amongst MSM who engaged in IDU by 1.44% a year ($p < 0.001$). In another study, an increasing trend over time in HCV incidence amongst HIV positive MSM was observed until 2010, after which a levelling off was observed (110). The pooled incidence of studies pre 2000 was 2.6/1000 PY (95% CI 0-5.8); between 2000 and 2005 it was 6.8/1000 PY (95% CI 3.0-10.6); between 2006 and 2010 it was 10.1/1000 PY (95% CI 5.8-14.3); and after 2010 it was 8.1/1000 PY (95% CI 2.7-13.5). In a meta-analysis, which included more than 13,000 HIV positive MSM followed for over 91,000 PY, and excluded studies which did not exclude PWID, it was found that the pooled incidence rate increased from 0.42/100 PY (95% CI 0.23-0.77) in 1991 to 1.09/100 PY (95% CI 0.73-1.61) in 2010 and 1.34/100 PY (95% CI 0.076-2.36) in 2012 (111).

Studies have shown sexual transmission of HCV amongst HIV positive MSM to be associated with unprotected anal intercourse (UAI); the number of sexual partners; recent ulcerative STIs, in particular syphilis and lymphogranuloma venereum (LGV); group sex; fisting; rectal trauma with bleeding; use of sex toys/and or anal enema; and recreational drug use before or during sex (e.g. chemsex) (104, 110-113). Mucosal damage is proposed as the facilitator of transmission.

Proposed reasons for the increased risk of HCV amongst HIV positive MSM include direct effects of HIV infection and behavioural factors amongst HIV positive MSM. It has been proposed that HIV leads to deterioration of the gastrointestinal (GI) mucosa making a person more susceptible to HCV infection when exposed via the GI tract. Also, HIV positive men may have higher HCV viral loads and therefore

⁹ The use of recreational drugs for or during sex.

have high HCV viral loads in their semen making them more infectious. The above two factors, coupled with serosorting, may explain the increases in HIV positive MSM and the limited transmission amongst HIV negative MSM. Another hypothesis proposed is that the association is not due to any biological interaction between the two viruses resulting in increased infectivity or susceptibility, but that co-infections are occurring amongst a particular high risk cohort of MSM, and that HIV is preceding HCV infection due to the fact that HIV is more easily transmissible through sexual contact.

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 under-reported NIDU (1). Chemsex may also be a contributing factor. Some drugs used for chemsex are injected and chemsex may increase the risk of HCV due to the sharing of injecting equipment. Another mechanism by which chemsex may increase the risk of HCV infection is due to less safe sex and mucosal trauma due to disinhibition.

Risk behaviours amongst MSM in Ireland

The Men who have Sex with Men Internet Survey in Ireland (MISI) conducted in 2015 reported a high prevalence of sexual risk behaviour and drug use amongst MSM in Ireland, particularly HIV positive MSM (114). Overall, 36% of participants reported drug use in the previous 12 months, 7% had used drugs associated with chemsex and 1.6% reported ever injecting drugs. Amongst HIV positive MSM, 53% had used drugs in last 12 months compared to 36% of HIV negative MSM (this included those who have tested HIV negative and not those who have never tested for HIV). IDU was more common amongst HIV positive MSM with 15% reporting ever injecting compared to 1% of HIV negative MSM. The use of drugs associated with chemsex in the previous 12 months was 25% in HIV positive MSM compared to 8% in HIV negative MSM.

Sixty-one percent of men had sex with one or more non-steady male partners in the last 12 months. Of these, 18% had one non-steady partner, 34% had 2-4 partners, 21% had 5-9 partners and 27% had 10 or more partners. Forty-two percent of men who had sex with a non-steady partner had UAI. HIV positive men were more likely to have UAI.

HCV amongst MSM in Ireland

A cluster of acute HCV amongst MSM in Ireland was reported in 2016 (115). As of March 2017, there were 19 cases associated with the cluster. Of these, 74% had a positive STI screen in the previous year, and a number had STIs diagnosed after their HCV diagnosis indicating that the cluster may be occurring in a particularly high risk behaviour cohort. Twenty percent of cases involved in this cluster were HIV negative.

In the national HCV surveillance system information on acute/chronic status and mode of transmission data are incomplete. During 2016, there were 28 notifications of HCV identified as MSM, compared to eight, three and 13 in the previous three years, respectively (source: CIDR, HSE HPSC). Amongst those notified in 2016, 68% (n=19) were HIV positive. In addition, 36% (n=10) had recently been diagnosed with gonorrhoea, 29% (n=8) had recently been diagnosed with chlamydia, and 29% (n=8) had recently been diagnosed with syphilis.

Value judgement

HCV amongst MSM in Ireland is an emerging issue. The number of cases of HCV appears to be increasing in MSM in Ireland. The risk appears to be particularly high in those who are co-infected with HIV and in those who engage in high risk sexual behaviour, as evidenced by the high proportion of cases in this population who have had multiple recent sexually transmitted infections. However, in a recent cluster of acute HCV amongst MSM in Ireland, at least 20% of cases were known to be HIV negative.

While up until recently the global epidemiology of HCV amongst MSM has indicated that HCV infection has been mainly confined to HIV positive MSM, the epidemiology of HCV amongst HIV negative MSM may change with greater use of treatment as prevention, post-exposure prophylaxis, and the advent of pre-exposure prophylaxis for HIV, changes in sexual networks, and changes in sexual practices.

There is evidence of high risk sexual and drug taking behaviour amongst some MSM in Ireland as reported by MISI and evident in the increasing rates of STIs. These behaviours may lead to increased HCV transmission amongst MSM. Early detection of acute infection in MSM through screening may reduce transmission within MSM sexual networks and limit the propagation of the epidemic amongst MSM in Ireland.

Recommendation 14

- 14.1 HIV positive MSM should be screened at least annually for HCV. More frequent testing may be required if clinically indicated, e.g. an unexplained rise in ALT, a diagnosis of a new STI, or if a risk exposure has occurred such as contact with a known case of HCV, or other risk behaviours including chemsex.
- 14.2 HIV negative MSM should be offered testing annually for HCV as part of an overall STI screen. More frequent testing may be required if clinically indicated, e.g. an unexplained rise in ALT, a diagnosis of a new STI, or if a risk exposure has occurred such as contact with a known case of HCV, or other risk behaviours including chemsex.

Quality/level of evidence: *moderate for HIV positive MSM; low for HIV negative MSM*

Strength of recommendation: *strong*

The following are responsible for implementation of recommendation 14:

HIV services, STI/GUM clinics.

4.1.12. People attending for a sexual health screen

Key question

Should those attending for a sexual health screen be offered screening for HCV?

Evidence summary

The risk of sexual transmission of HCV amongst heterosexuals and MSM are presented in sections 4.1.10 and 4.1.11 respectively.

International recommendations limit the screening of asymptomatic attendees of sexual health services to those who fall into other risk groups (37, 45, 103, 116, 117).

Value judgement

The risk of sexual transmission of HCV is generally low amongst heterosexuals and there is limited evidence on particular high risk behaviours which increase the risk.

A sexual health screen is an opportunity to screen those with other identified risk factors for HCV.

Recommendation 15

See Recommendation 14 for MSM attending for sexual health screening.

15.1 HCV testing should be considered part of routine sexual health screening in the following circumstances:

- People who are HIV positive
- Commercial sex workers
- PWID
- If indicated by the clinical history e.g. unexplained jaundice
- When other risk factors for HCV as outlined in this guideline are present*

* See Appendix 1 for a list of risk populations.

Quality/level of evidence: *low*

Strength of recommendation: *conditional/weak*

The following are responsible for implementation of recommendation 15:

STI/GUM clinics, HIV services, GPs.

4.1.13. People on renal dialysis or who have had a kidney transplant

Key question

Should people on renal dialysis or who have had renal dialysis in the past be offered screening for HCV?

Evidence summary

The dialysis setting is recognised as a high risk environment for the transmission of HCV and other bloodborne viruses (BBV), in the absence of strict infection prevention and control practices, including appropriate screening. Screening of people commencing or on haemodialysis or who have ever been on haemodialysis in the past is recommended by other international guidelines (37, 47, 49, 51, 52, 55).

In 2014, the National Standing Advisory Committee on the Prevention of Transmission of Blood-Borne Diseases in the Health-Care Setting updated its guidance on screening requirements in the dialysis setting: *Blood-Borne Viruses in the Haemodialysis, CAPD and Renal Transplantation Setting July 2014* (88). The guidance within that document on screening of those commencing or on dialysis is still considered best practice, and the GDG recommends that this guidance and any ensuing updates made by the Committee are followed.

Value judgement

The dialysis setting is a high risk environment for transmission of HCV and other BBVs. In addition, patients in renal failure or post-transplant are a vulnerable population with sometimes complex healthcare needs. In patients on haemodialysis, HCV infection is associated with an increased risk for all-cause and liver-related mortality.

Screening is part of the suite of strict infection prevention and control practices required to prevent the transmission of HCV and other BBVs in the dialysis setting. Detection of cases prior to commencing haemodialysis will ensure the appropriate procedures are followed. Regular screening while on dialysis will also detect any transmission events early and allow the appropriate action to be taken. Detection of cases will also enable the patient to receive appropriate treatment either pre- or post-transplant as indicated.

The existing national guidance recommended that one-off testing of kidney transplant patients three months post-transplant be considered. It also recommended that one-off testing be considered for patients transplanted before the introduction of this post-transplant screening, unless known to be HCV-infected. It is not known to what extent these recommendations on post-transplant screening have been implemented. The reasoning behind these recommendations is that it is possible for transmission to occur during dialysis just prior to kidney transplant. The GDG consider that screening of this group of patients is important to detect any transmission which may have occurred in the final months of dialysis prior to transplantation, or in those who were on dialysis in the past and successfully transplanted prior to the introduction of screening and current infection prevention and control standards.

Recommendation 16

- 16.1 Patients commencing, or on maintenance, haemodialysis or peritoneal dialysis should be screened according to the current recommendations of the National Standing Advisory Committee on the Prevention of Transmission of Blood-Borne Diseases in the Health-Care Setting and any ensuing updates from this committee.
- 16.2 All patients having a kidney transplant should be tested for HCV by a combined antigen-antibody test, or anti-HCV test **AND** HCV-RNA at three months post-transplant.
- 16.3 Patients transplanted before the introduction of the above, unless already known to be HCV positive, should be tested on a one-off basis by combined antigen-antibody test or anti-HCV test, **AND** HCV-RNA to out rule the possible acquisition of HCV infection through past treatment for renal failure.

Quality/level of evidence: moderate; good consistency between existing high quality guidelines

Strength of recommendation: strong

The following are responsible for implementation of recommendation 16:

Dialysis centres, transplant centres, renal services.

4.1.14. Recipients of substance of human origin

Key question

Should recipients of unscreened blood and blood products in Ireland (pre October 1991) who have not been previously screened be offered screening for HCV?

Evidence summary

In many countries across the world there have been episodes of HCV transmission related to receipt of blood or blood products either before HCV was recognised as a disease, or before quality assured blood safety programmes were put in place.

Routine testing for HCV was introduced into the blood screening process in Ireland in October 1991. Incidences of distribution of contaminated blood prior to this did occur leading to HCV transmission. HCV transmission also occurred in Ireland due to distribution of contaminated blood products, either locally produced or imported. The main products implicated were anti-D immunoglobulin and clotting factors.

In Ireland two transmission periods of HCV due to infected anti-D immunoglobulin have been described. The first period was between 1 May 1977 and 31 July 1979, during which a total of 4,062 vials of infectious or potentially infectious anti-D immunoglobulin were manufactured and issued by the Blood Transfusion Service Board (BTSB; now the Irish Blood Transfusion Service (IBTS)). The second period was between 1 March 1991 and 18 February 1994, during which a total of 14,946 vials of infectious or potentially infectious anti-D immunoglobulin were issued.

People with haemophilia, Von Willebrand's disease or other inherited coagulation disorders were particularly affected by HCV infection due to exposure to both blood and blood products for the treatment of clotting disorders.

In Ireland, 1,694 persons are known to have been infected with HCV through blood or blood components (source: National Hepatitis C Database, HSE HPSC). Of these, 1,051 were infected through anti-D immunoglobulin, 418 through blood transfusions, and 225 through clotting factors.

Screening of recipients of blood or blood products which has already taken place

The BTSB and subsequently the IBTS have undertaken extensive efforts to trace recipients of potentially infectious products previously issued in Ireland. Between 1994 and 1995 the BTSB conducted a targeted lookback programme which offered screening to recipients of blood components from donors who were subsequently found to have HCV infection (118). In September 1995 an optional screening programme was introduced to complement the targeted lookback programme. This programme offered free screening for HCV, through GPs, to anyone who received blood or blood components before October 1991. Close to 15,000 people presented for screening as part of this programme. The Anti D/Hepatitis C National Screening Programme commenced in February 1994 to offer testing to recipients of anti-D immunoglobulin. All anti-D immunoglobulin recipients were invited for testing and 65,980 were tested.

The Anti-D/Hepatitis C Reassurance Programme was established to offer repeat testing to women who originally tested HCV negative under the Anti D/Hepatitis C National Screening Programme and it is now known received infectious or potentially infectious anti-D immunoglobulin. To date 9,882 recipients have re-tested negative under this programme.

In 2011 the Recipient Tracing Unit (RTU) of the IBTS completed the task of tracing and offering testing to known recipients of infectious or potentially infectious anti-D immunoglobulin. An audit of the tracing process found that the RTU had traced 99% of all those identified to the programme. Ninety eight percent of recipients who received potentially infectious batches of anti-D immunoglobulin from both risk periods

were tested; 1% were offered testing, but chose not to be tested; 1% were found to be deceased; and less than 1% remained untraced.

While extensive screening has occurred, there may be a small number of people remaining who have not yet been tested.

Organ recipients

HCV can be transmitted by the transplantation of an organ from an infected person. There have also been cases of transmission reported when the donor was anti-HCV negative due to being within the window period of seroconversion (119, 120). The currently recommended screening regime for solid organ donors will minimise the risk of HCV transmission through solid organ transplantation. However, there may be patients who had a solid organ transplant prior to these standards being implemented.

Recipients of products overseas

Many other developed countries had historical HCV transmission events due to unscreened or contaminated blood or blood products. In most high income countries, screening for HCV began around 1991. In many developing countries, quality assured programmes will not have been introduced until much later than 1991. Also, in some areas the quality assured programmes may have been periodically disturbed due to conflict or other factors. Currently, in a number of countries, particularly in low income countries, the safety of blood and blood products cannot be assured (121). The 2013 WHO Global Database on Blood Safety found that 73% (122/167) of countries had a national blood policy and 65% (108/167) of countries had specific legislation covering the safety and quality of blood transfusion, including: 79% of high-income countries; 64% of middle-income countries; and 41% of low-income countries. Sixteen countries were not able to screen for one or more of HIV, HBV, HCV or syphilis. Irregular supply of test kits was one of the most commonly reported barriers to screening. In high-income countries, 81% of blood screening laboratories are monitored through external quality assessment schemes compared to 55% in middle-income countries and 34% in low-income countries. The median prevalence of HCV in blood donations in high-income countries is 0.02% (interquartile range (IQR) 0.003% -0.16%), which is considerably lower than in middle-income (0.32%; IQR 0.09%-0.69%) and low-income countries (1.03%; IQR 0.67%-1.8%).

There may be people resident in Ireland who have been recipients of blood or blood products overseas where a quality assured programme was not in place.

Between 2004 and 2016 there were 85 notifications of HCV in Ireland (of a total of >14,000 HCV notifications) in which receipt of blood or blood products outside of Ireland was cited as the most likely risk factor (source: CIDR, HSE HPSC). The majority of these (n=70) were born outside of Ireland. Eight were born in Ireland and the country of origin was unknown for seven cases.

Value judgement

Extensive efforts have already been made to contact and screen recipients of potentially HCV-infected blood and blood products in Ireland. While the majority of those who received infected or potentially infected blood or blood products in Ireland have already been traced and offered screening, a small number of people may not yet have been traced or have previously declined screening. It is not recommended that a further active screening programme be established for any remaining unscreened recipients, but that those who have not previously come forward could be encouraged to present for screening or be offered screening opportunistically.

Many high income countries had historical HCV transmission episodes due to infected blood components and blood products. There may be historical recipients of unscreened blood or blood products in other

countries who have not been screened and who are now are living in Ireland. In some countries a quality assured donor screening programme is still not in place.

Recommendation 17

- 17.1 Recipients of blood or blood components in Ireland prior to October 1991 who have not yet been tested should be offered screening.
- 17.2 All recipients of anti-D immunoglobulin in Ireland between 1st May 1977 and the end of July 1979, and 1st March 1991 and 18th February 1994 who have not yet been tested should be offered screening.
- 17.3 Recipients of plasma-derived clotting factor concentrates in Ireland prior to 1992 who have not yet been tested should be offered screening.
- 17.4 Recipients of blood components and blood products overseas in any country where a quality assured blood donor screening programme may not have been in place should be offered screening.

Quality/level of evidence: *moderate*

Strength of recommendation: *strong*

Recommendation 18

- 18.1 Screening for HCV should be considered in recipients of solid organ transplants in Ireland who have not yet been tested (see Recommendation 16 for recipients of kidney transplants).

Quality/level of evidence: *low*

Strength of recommendation: *conditional/weak*

The following are responsible for implementation of recommendation 17 and 18:

Renal, hepatology and transplant services, GPs, IBTS.

4.1.15. Donors of substances of human origin

Key question

What screening of blood, tissue or organ donations, or donors should be undertaken?

Evidence summary

Screening of donors of substances of human origin (SoHO) for HCV and other infectious diseases is regulated under EU legislation and national legislation, and the respective competent bodies are responsible for implementation. The Health Products Regulatory Authority (HPRA) is the designated competent authority responsible for human blood and blood components and for tissues and cells (122, 123). The HPRA and the HSE are the competent authorities responsible for organs intended for transplantation (124). Within the HSE, Organ Donation Transplant Ireland (ODTI) is responsible for implementation of their relevant aspects of legislation. In Ireland, ODTI in conjunction with the HPRA have developed *A Framework for quality and safety of human organs intended for transplantation* as required by legislation (125).

Legislative requirements will only be briefly summarised here. The original legislation should be consulted. Legislation requires that at a minimum anti-HCV testing be performed on donors of whole blood and apheresis donations, at each donation (122, 126). Donors of blood, tissues and cells, and organs must be tested for anti-HCV, and testing must be carried out on the donor's serum or plasma (123, 127, 128). In addition to biological testing, legislation requires the exclusion or deferral of donors (either living or deceased) where the medical or behavioural history, or physical examination show evidence of HCV, or evidence of risk factors for HCV (123, 129).

Legislative requirements for screening of reproductive cells for donation differ from other tissues and cells as less stringent biological testing is considered to be justified if the donation is between partners with an intimate physical relationship. Legislation requires that when partner reproductive cells are donated for direct use, donor selection criteria and laboratory testing do not need to be applied (123, 127). However, if partner-donated gametes will be stored or processed in any way, or will result in the cryopreservation of embryos, anti-HCV testing must be performed. In the case of sperm processed for intrauterine insemination and not to be stored, if the tissue establishment can demonstrate that the risk of cross-contamination and staff exposure has been addressed through the use of validated processes, biological testing may not be required.

Legislation requirements regarding the timing of the above screening of blood, organs, tissues and cells, and any re-testing or quarantine periods required are outlined in the respective statutes and relevant amendments and these should be consulted directly (122, 123, 126, 127, 130-132). In addition there are legislative requirements relating to quality and safety standards of licenced establishments (123, 124, 126-129, 131-138). Imported blood or blood components, tissue or cells must meet equivalent quality standards (139).

In addition to the legislation, European level best practice guidance is provided by the European Directorate for the Quality of Medicines & HealthCare of the Council of Europe (EDQM) in the following guides:

- *Guide to the quality and safety of organs for transplantation* (140)
- *Guide to the preparation, use and quality assurance of blood components* (141)
- *Guide to the quality and safety of tissues and cells for human application* (142)

The UK's Advisory Committee on the Safety of Blood Tissues and Organs (SaBTO) *Guidance on the microbiological safety of human organs, tissues and cells used in transplantation*, also provides further best practice guidelines which in some instances exceeds legislative requirements (143). For blood and

blood components, the UK equivalent is *The Guidelines for the Blood Transfusion Services in the UK* (referred to as the 'Red Book'), published by the Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) (144).

In relation to testing of donors of blood, in addition to the legislative requirement for anti-HCV testing, JPAC mandates HCV-RNA by NAT of blood donations (144). EDQM recommend that If screening of blood donations by NAT is required by national authorities for the release of blood components, the NAT assays must be validated to detect 5,000 IU/mL for HCV-RNA (142).

Regarding the testing of donors of tissues and cells, legislation requires that for donations from living allogeneic donors which can be stored for long periods, repeat microbiological sampling and testing is required after an interval of 180 days. If the initial donation sample is tested by NAT, testing of a repeat blood sample is not required. Re-testing is also not required if the processing includes an inactivation step that has been validated for the viruses concerned. EDQM states due to the increased sensitivity of NAT assays for the detection of recently acquired infections, testing of both deceased and living allogeneic donors of tissues and cells using this technology is highly recommended as standard practice (142). JPAC recommend optional testing with HCV-Ag and/or HCV-Ag/Ab or HCV-RNA for tissues and cells (144).

For solid organ donors, EDQM indicate that NAT is encouraged where appropriate and available (140). They recommend that in donor populations at an increased risk for HCV, in addition to serology testing, prospective NAT is undertaken in order to rule out window period infections. They advise to screen living donors by NAT shortly (one week) before organ donation in order to minimise risks due to undisclosed risk behaviours. SaBTO recommends NAT for HCV-RNA for organ transplantation to be good clinical practice and replaces the need for any quarantine or follow-up serological screening (143). SaBTO recognises that in the case of deceased solid organ donors, NAT results may not be available prior to transplantation but they should still be performed to ensure the rapid identification of the recipients of potentially infectious organs. SaBTO also recommends that if NAT is either not done, or the results are not available prior to organ donation, combined HCV-Ag and anti-HCV assays should be considered rather than anti-HCV alone.

Current practice in Ireland

All blood donated to the IBTS is tested for anti-HCV. In addition, Individual Donation (ID)-NAT using a multiplex assay testing for HIV-RNA, HCV-RNA and HBV-DNA is undertaken. IBTS also screen tissue and cell donors with NAT.

Screening of solid organ donors is done in the National Virus Reference Laboratory where combined anti-HCV/HCV-Ag tests are performed for deceased donors which exceeds the current legislative requirements.

Value judgement

Recipients of donated SoHO often have complex health needs and infection with HCV may cause further morbidity. Therefore prevention of transmission will have a positive impact.

Best practice, where it exceeds legislative requirements, should be implemented where feasible. However, it is acknowledged, that in some circumstances, particularly the case of solid organ donation from deceased donors, time factors may limit the feasibility of NAT, and in those circumstances the balance of risk and benefit to the recipient may favour the use organs from donors where infection has not been comprehensively outruled.

A national advisory committee for safety and quality of blood, organs and tissues similar to SaBTO in the UK is required to advise on, and provide a governance framework for best practice in this area beyond legislative requirements.

Recommendation 19

19.1 Screening of donors of blood, organ, tissue and cells, including reproductive cells*, should at a minimum comply with legislative requirements**.

The following screening is also recommended:

19.2 NAT for HCV-RNA of donors of blood should be performed and the results available prior to the use of the donation. The test must be designed and approved for screening of blood donations.

19.3 NAT for HCV-RNA of donors of tissues and cells, including reproductive cells*, and living solid organ donors, should be performed in addition to current legislative requirements**.

19.4 For deceased donors of solid organs:

19.4.1 Anti-HCV and HCV-antigen testing should be done and the results available prior to donation***.

19.4.2 NAT should be considered where feasible. NAT results may not be available prior to transplantation but NAT testing should still be performed to ensure the rapid identification of the recipients of potentially infectious organs ***.

19.5 Any external laboratories used for microbiological screening of donors should be accredited and comply with the standards of the appropriate regulatory authority. Laboratories in Ireland should be accredited by the Irish National Accreditation Board (INAB) to undertake testing in compliance with the International Standard ISO 15189.

19.6 A national advisory committee on the safety of blood, organs and tissues should be established to advise on best practice in relation to donor selection, and testing of potential donors.

*In the case of partner donation of reproductive cells for direct use and when no storage or processing of samples will be undertaken, microbiological screening is not required.

**Please refer to the relevant competent authority for legislative requirements.

***It is acknowledged that in some circumstances the balance of risk and benefit may favour the use of potentially infectious donations. Such a risk assessment should be conducted by the transplant centre in discussion with an appropriate microbiologist/ virologist.

Quality/level of evidence: *moderate*

Strength of recommendation: *strong*

The following are responsible for implementation of recommendation 19:

IBTS, HPRA, ODTI, Department of health, transplant centres, blood, tissue and cell establishments.

4.1.16. General population or birth cohort

Key question

Is there a role for birth cohort screening for HCV?

Evidence summary

WHO states that the best approach to screening will depend on a country's unique HCV epidemiology. They recommend that whenever there is an easily identified demographic group that has a high HCV prevalence, such as all individuals born in a certain time period i.e. a birth cohort, routine testing for HCV within that cohort will likely be cost-effective and should be considered. However, this is a conditional recommendation mainly because of low quality of evidence (52).

In the US, a recommendation was made in 2012 by CDC to offer one-time screening for HCV infection to adults born between 1945 and 1965, in addition to screening in persons at high risk of infection (145). This decision was based on the finding of a national seroprevalence study which found that the anti-HCV prevalence in this birth cohort was 3.25%, five times higher than adults born outside these years. In addition it was estimated that 45% - 85% of HCV infections in the US were undiagnosed. Another factor in selecting this particular birth cohort in the US was that the 1945–1965 birth cohort is a recognised subpopulation in the US known as the “baby boomers” and familiarity with this subpopulation and the term used to describe it likely would facilitate adoption and implementation of the recommendation.

A number of other countries have considered birth cohort screening following the US recommendation, although none have yet introduced a similar recommendation.

A number of economic modelling studies of birth cohort screening have been undertaken, mainly from the US, with one from Italy and one from Canada. Studies compared birth cohort screening to either no screening or risk based screening in the particular age cohort. *Coward et al.* (2016) (146), in a systematic review which summarised the economic evaluations of birth cohort screening, reported that the incremental cost per quality adjusted life year (QALY) gained in included studies ranged between £3,706 and £45,123 (using data from original articles this corresponds to between €7,769 and €64,650¹⁰). In studies which evaluated different treatment regimes, the addition of DAAs increased the cost per QALY gained. The authors concluded that treatment of choice and cost of treatment can change the conclusion of the model. They also reported that the main source of variation was due to prevalence estimates, and screening and treatment uptake estimates used. *Correti et al.* in their systematic review, concluded that studies generally proved the cost-effectiveness of screening for specific age cohorts in which the disease prevalence is high and life expectancy sufficiently long (214). *Coward et al.* discussed how the cost-effectiveness of a programme will depend on the prevalence, acceptability of screening, and uptake of treatment. The economic evaluations to date have not included the costs of implementation. It is likely that the implementation plan required to achieve the necessary uptake of screening and treatment in order for a birth cohort programme to be cost-effective will be high. The authors conclude that a thorough budget impact assessment, including the implementation plan, would be required to assess any such programme.

Identification of a suitable birth cohort in Ireland

A review of epidemiological information was undertaken to determine if a specific birth cohort for which HCV screening could be recommended exists in Ireland.

¹⁰ Inflated to 2014 and converted to Irish euro.

Data from the national HCV surveillance system shows that, of notifications of HCV reported in Ireland between 2004 and 2016, 72.5% fall into the birth cohort 1965-1985, while 81.1% fall into the birth cohort 1960-1985. Of note, these only represent diagnosed cases of HCV. Figure 3 shows the distribution of notified (diagnosed) cases of HCV by birth year.

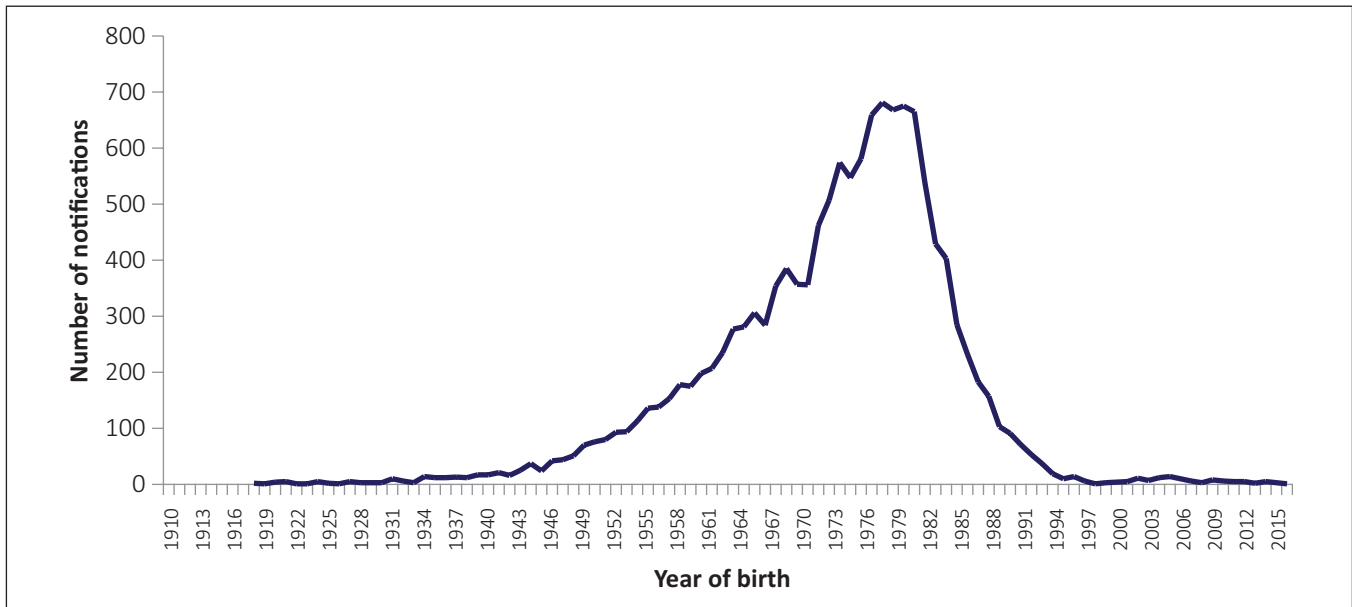


Figure 3: Birth year of diagnosed cases of HCV notified in Ireland, 2004-2016 (Source: CIDR, HSE HPSC).

A HCV seroprevalence study conducted in Ireland using residual sera in 2016 showed an anti-HCV seroprevalence among adults of 0.98% (0.73%-1.3%) and a prevalence of chronic infection of 0.57% (0.40%-0.81%) (6). The prevalence of chronic infection was significantly higher among persons aged 30-49 years. Adult males born between 1965 and 1984 from the east of the country had the highest rate of chronic HCV infection (males in east aged 40-49 years 5.2% (2.8%-9.3%), males in east aged 30-39 years 3.5% (1.8%-6.9%)). The estimate obtained is likely to be the minimum prevalence value as the sampling specifically excluded specimens that would be expected to have a higher risk of being HCV positive (e.g. from drug treatment services, or samples submitted for HCV testing).

The predominant risk factor for HCV in Ireland has been IDU. A study of the incidence of HCV amongst PWID, based on the incidence of IDU, estimated that the annual number of new HCV infections among PWID increased steeply from the late 1970s and peaked in 1998 (4). This finding is consistent with the age-profile identified in the notification data and the seroprevalence study.

Triangulation of data from the above sources indicates that the prevalence of HCV infection in Ireland is highest in those born between 1965 and 1985. Thirty one per cent of the Irish population (n=1,426,156) was born between these years.

Value judgement

One-off birth cohort screening offers the advantage of avoiding the need to identify specific risks as the basis for screening. Healthcare workers may not be skilled at identifying risk factors, and individuals may not recall or wish to disclose a risk factor. Economic literature from other countries suggests that birth cohort screening is cost-effective.

However, the generalisability of birth cohort studies from the US or elsewhere to the Irish population needs to be considered as the HCV epidemic differs in each country. Also, more recent data suggest that

a significant proportion of the HCV-infected population is not captured as part of birth cohort screening. The yield from birth cohort screening may be considerably lower in healthcare settings serving lower risk populations. The birth cohort studies also did not analyse the distribution of benefits which may be achieved with birth cohort screening, only the total benefit. Any birth cohort programme would need to consider the health equity impact and also the impact it may have on onward transmission compared to risk-based screening or targeting those at risk of onward transmission.

Triangulation of data from a number of sources identified the birth cohort born between 1965 and 1985 as being most affected by HCV infection in Ireland. However, the implementation of any birth cohort screening recommendation would require substantial resources and the impact is uncertain as it will be influenced by factors such as the uptake of screening and linkage to care. The GDG considers that there is insufficient cost-effectiveness evidence to support a recommendation on birth cohort screening at present.

A health technology assessment (HTA) and comprehensive budget impact assessment should be undertaken prior to further consideration of birth cohort screening. This HTA should also take into account the costs of implementation of birth cohort screening beyond laboratory and personnel testing costs, such as the costs of marketing and communication. A request to conduct this HTA was submitted to HIQA and was included in the prioritisation process in March 2017. It scored highly on the required criteria and will now be considered for inclusion on the HIQA work programme.

Recommendation 20

- 20.1 Birth cohort screening cannot be recommended at present due to the likely substantial cost implications and uncertain benefit. Such a programme would require a full health technology assessment (HTA) and approval of funding prior to being considered.
- 20.2 Birth cohort screening should be considered if a HTA shows it to be cost-effective and affordable in the Irish context.

Quality/level of evidence: *moderate*

Strength of recommendation: *conditional/weak*

4.1.17. Healthcare workers

Key question

What HCV screening of healthcare workers should occur?

Background

The guideline will make recommendations relating to screening of healthcare workers (HCWs) for HCV pre-employment or during employment, for the purpose of minimising healthcare provider to patient transmission of HCV in the healthcare setting.

For recommendations on the management of HCWs following an exposure to potentially infected material, *HSPC Guidelines on the Emergency Management of Injuries* should be consulted (147).

Recommendations on the assessment of HCWs found to be infected with HCV or management of their employment while undergoing treatment or post-treatment will not be addressed as this is not within the scope of the guideline. Also, this guideline will not address wider issues relating to prevention of HCV transmission in the healthcare setting (e.g. patient to patient transmission due to poor infection control practices).

Evidence summary

Provider to patient transmission of HCV during exposure prone procedures (EPPs¹¹) has been documented. These include transmission events in the UK, Spain and Germany during cardiovascular, gynaecological or obstetric, and orthopaedic surgery (148-151). A cluster of cases was associated with an anaesthetic assistant who worked with a weeping wound on his finger without wearing gloves. It is thought that viral burden was likely to have been very high during this period, contributing to the transmission (152). A case of transmission from a mother with chronic infection who administered clotting factor infusions to her child with haemophilia was also reported (153). The mother did not wear gloves and reported instances of needle stick injuries.

A number of reports, from the US, Spain and Israel, have described transmission from an anaesthetist or anaesthetic assistant who was, or was suspected of, diverting drugs, self-injecting and re-using needles on patients (154).

When the risk of provider to patient transmission is summarised based on published studies of patient notification exercises (PNEs), studies from the UK yield a transmission rate of 0.19% (15/7656 patients tested) and 0.26% if index cases are included (155). Studies from Germany found no transmission in lookback exercises, but a transmission rate of 0.13% if index cases are considered (155).

No known cases of provider to patient transmission of HCV have been reported in Ireland. In 2009 a lookback exercise was conducted in HSE West after a HCW was identified as being HCV positive (156). The lookback invited 454 patients who had EPPs involving the HCW for testing. No cases of transmission were identified.

¹¹ These include procedures where the worker's hands may be in contact with sharp instruments, needle tips or sharp tissues (e.g. spicules of bone or teeth) inside a patient's open body cavity, wound or confined anatomical space where the hands or fingertips may not be completely visible at all times. There is a risk that injury to the worker may result in the exposure of the patient's open tissues to the blood of the worker. They have been more precisely defined as procedures which involve surgical entry into tissues, cavities or organs or repair of major traumatic injuries, vaginal or Caesarean deliveries or other obstetric procedures during which sharp instruments are used; the manipulation, cutting or removal of any oral or perioral tissues including tooth structure, during which bleeding may occur. EPPs would not usually include giving injections, taking blood, setting up IV lines, minor surface suturing, and the incision of abscesses, routine vaginal or rectal examinations or uncomplicated endoscopies.

A review of PNEs in Ireland between 1997 and 2011 involved a survey of those with regional and national responsibility for the management of incidents of possible BBV transmission in healthcare settings to identify incidents (157). No other PNE due to an HCW infected with HCV were identified other than the one described above. In PNEs due to HCWs with others BBVs, no cases of provider to patient transmission were identified amongst almost 500 patients tested.

The Society for Healthcare Epidemiology of America (SHEA), in *SHEA Guideline for Management of Healthcare Workers Who Are Infected with Hepatitis B Virus, Hepatitis C Virus, and/or Human Immunodeficiency Virus* does not recommend mandatory HCV screening of HCWs (155). It recommends that a provider who conducts category III (equivalent to EPPs) procedures is ethically obligated to know his or her infection status and that institutions should provide voluntary confidential testing for their employees. The UK Department of Health policy *Health clearance for tuberculosis, hepatitis B, hepatitis C and HIV: New healthcare workers (2007)* recommends that standard health clearance which includes testing for HCV be offered to all categories of new HCWs. Additional health clearance, which involves anti-HCV testing, and HCV-RNA testing if positive, is required for all new HCWs who will perform EPPs.

A number of policies and guidance documents refer to HCWs professional duty to seek testing if they believe themselves to be at risk and that this professional duty obviates the need to recommend interval testing of HCWs. The Irish Medical Council's *Guide to professional conduct and ethics for registered medical practitioners* and the Dental Council's *Code of Practice Relating to: Infection Prevention and Control* state that members must seek medical advice if they think they might be infected with a serious communicable disease or BBV (158, 159). The Nursing and Midwifery Board of Ireland *Code of Professional Conduct and Ethics* has a similar statement regarding seeking help if health may affect ability to practice safely, although not confined to infectious diseases (160).

Existing guidance on HCW screening in Ireland was made by the DoH Standing Advisory Committee on the Prevention of Transmission of Blood-Borne Diseases in the Health-Care Setting in 2005 (161). The policy applies to all HCWs in Ireland, in both public and private healthcare settings. It recommends that screening of all HCWs who perform EPPs should be initiated in Ireland. The implementation of this policy within the HSE was outlined in HSE HR Circular 19/2008: *Implementation of Recommendations of Report on The Prevention of Transmission of Blood Borne Diseases in the Health Care Setting* issued by the National Director of Human Resources in July 2008 (162). An amendment was issued in April 2009 (163). This stated that from 7 July 2008, all new staff commencing in a post which involves EPPs should be tested for HCV. New staff was defined as those staff entering the Irish public health system for the first time or those staff currently in the system but now transferring to or taking up employment in an area that involves EPPs e.g. a nurse undertaking midwifery or a medical intern taking up a post of surgical Senior House Officer.

Healthcare students

The Irish DoH 2005 policy does state that it applies to students (161) although the HSE circular does not make reference to undergraduate students training within the HSE (162). The *Infectious disease policy for medical students in Ireland (2011)*¹² agreed by the six medical schools in Ireland states that any student who suspects he or she may have been exposed to HCV must notify the relevant office immediately for advice and support. However, no specific guidance on HCV screening is provided. Some universities in Ireland do offer HCV screening to all healthcare students, and require it for dental related students.

¹² Available at the following link <https://www.ucc.ie/en/media/support/studenthealthservice/Infectious-Diseases-Policy-for-Medical-Students-in-Ireland.pdf>

In the UK, the medical and dental school councils, Public Health England, Health Protection Scotland, the Association of UK University Hospitals, and Higher Education developed guidance on health screening for medical and dental students. For medical students it recommends voluntary testing early in training before exposure to EPPs. If testing is refused, or the student is found to be positive, the student will only be allowed to continue the course and proceed to registration with the Medical Council, provided that they formally accept the requirement they will not be allowed to perform EPPs or enter postgraduate clinical training in certain specialties until they have satisfied the requirements of the Department of Health clearance guidance. Potential dentistry students must undergo additional health clearance before acceptance onto the course.

Value judgement

Although rare, provider to patient transmission of HCV can occur. In the context of healthcare provision any risk of provider to patient transmission of HCV needs to be minimised.

Screening of HCWs who undertake EPPs is current recommended practice in Ireland. The team that conducted the PNE in HSE West recommended that the HSE examine the feasibility of performing an evaluation of the compliance with the requirement for occupational screening for BBV among HCW carrying out EPPs (156). The PNE survey respondents did recommend more rigorous occupational health screening for BBVs and an audit of compliance with occupational health screening (157).

While there is negligible risk of provider to patient transmission of HCV in HCWs who do not perform EPPs, the offer of HCV screening to all new HCWs confers a personal benefit to HCWs by identifying undiagnosed cases and allowing linkage to care and treatment.

Screening of healthcare students early in the course of their training is recommended to identify undiagnosed cases and link them to care and treatment. Successful treatment will avoid implications for their future career choices.

Healthcare workers should discuss screening with their occupational health service.

Recommendation 21

- 21.1 All new healthcare workers should be offered HCV screening on a voluntary basis.
- 21.2 Mandatory HCV screening of all new HCWs who will perform EPPs is recommended.
- 21.3 Existing HCWs who perform EPPs and have not yet been screened should be offered HCV screening.
- 21.4 Mandatory HCV screening of all new healthcare students* is recommended.
- 21.5. Interval HCV testing of HCWs who perform EPPs is **not** recommended. However, HCWs should be informed of their professional responsibility to seek appropriate assessment if any possible risk exposure has occurred.

*This includes students who may be undertaking EPPs as students or in their future careers, such as dental, medical, nursing, midwifery, or paramedical students.

Quality/level of evidence: *moderate*

Strength of recommendation: *strong*

The following are responsible for implementation of recommendation 21:

HSE occupational health, employers in private healthcare, healthcare training bodies.

4.2 How should screening for HCV be performed?

4.2.1. What test should be used for HCV screening?

Key questions

What test should be used?

What should the screening sequence process be?

How frequently should those who remain at risk be screened?

Note:

The testing process following injuries that involve possible exposure to HCV is not being considered within this guideline - please refer to the EMI Guidelines (www.EMIToolkit.ie) (147).

The test and the timing of testing for children born to infected mothers has been considered in section 4.1.2.

Evidence summary

WHO recommends that the initial test for HCV infection is a HCV serological assay (i.e. anti-HCV or antibody/antigen) using either rapid diagnostic test (RDT) or a laboratory-based immunoassay format that meets minimum safety, quality and performance standards (2).

A reactive anti-HCV test can be due to current infection, past infection that has resolved either spontaneously or due to treatment, or it can be a false positive. Supplementary nucleic acid testing (NAT) to detect HCV-RNA is required to determine current infection. Detection of HCV-RNA indicates current infection.

WHO recommends that directly following a positive anti-HCV test, the use of quantitative or qualitative NAT for detection of HCV-RNA is recommended as the preferred strategy to diagnose HCV viraemic infection. WHO also states that an assay to detect HCV core (p22) antigen, which has comparable clinical sensitivity to NAT, is an alternative to NAT to diagnose HCV viraemic infection.

Chronic infection is confirmed if an HCV-RNA assay is positive six months after the first positive test. Patients with low-level viraemia may require HCV-RNA testing on two or more occasions to confirm infection (5, 16).

The above strategy of initial anti-HCV followed by NAT if reactive is consistent with other guidelines except for specific circumstances as outlined below (61).

Considerations

Those who are HIV positive or immunosuppressed

In a person who is immunosuppressed, antibody may not be generated resulting in a false negative anti-HCV test in a person who is in fact infected. In people who are HIV positive, this may occur in up to 6% of persons who undergo testing using a second-generation anti-HCV enzyme immunoassay (EIA), but may occur more often among persons with advanced immunosuppression due to HIV and during early HCV infection. Therefore HCV-RNA should be considered in some people who are immunosuppressed if HCV infection is suspected and anti-HCV is negative.

Those previously infected

Re-infection can occur after spontaneous clearance or successful treatment. As anti-HCV generally remains positive for life, testing should be by HCV-RNA in those who were previously infected (37, 39).

Recent infections

While anti-HCV can usually be detected seven to eight weeks after infection, it may not be detectable for three or more months. HCV-RNA will be detectable after two weeks.

If the potential exposure was recent, testing for HCV-RNA or HCV-Ag should be considered.

Of note, following acute infection, HCV-RNA can oscillate between positive and negative for several months. If an individual is anti-HCV positive, but HCV-RNA negative, a second sample should be tested at a later stage to confirm current HCV status if recent infection is suspected (6).

Frequency of testing for those at ongoing risk

Repeated testing of those with an ongoing risk is recommended (39, 45, 53). Guidelines that refer to the need for regular retesting in those with ongoing risk of infection vary slightly in their recommendations. Some are not definite about the interval (45) while others recommend an interval of six months, 12 months (37, 39, 54, 62) or six to 12 months (53, 164).

Value judgement

A standard approach to the sequence of testing will ensure that testing is carried out with maximum efficiency and will minimise the risk of missed diagnoses or inappropriate testing.

For population groups at continuing risk of infection, frequent re-testing will ensure early detection and linkage to care.

Recommendation 22

- 22.1 Individuals being investigated for evidence of HCV infection should be screened with an anti-HCV antibody or combined HCV antigen/antibody EIA screening assay*.
- 22.2 If the initial HCV EIA is reactive (positive), then the sample should be tested for the presence of HCV-antigen, or HCV-RNA, to test for current infection.
- 22.3 Current infection should be confirmed on a second sample and HCV-RNA should be performed (if not already performed) and HCV genotyping should be carried out.
- 22.4 Those individuals with evidence of a resolved HCV infection (i.e. anti-HCV positive and antigen/RNA negative) should have a further sample drawn after six to 12 months for HCV-RNA testing to confirm their resolved infection status.

*In certain patient groups, initial testing should routinely incorporate HCV-antigen or HCV-RNA testing. Those are: immunocompromised individuals; children (born to HCV-infected mothers) in the first 18 months of life; individuals previously treated for HCV infection; sources of needle-sticks; and those at risk of recent infection in whom an antibody response might not yet have developed (HCV-RNA testing should be performed six weeks post-exposure).

See algorithm for testing sequence – Box 2 and Figure 4

Quality/level of evidence: moderate; good consistency between existing high quality guidelines

Strength of recommendation: strong

Recommendation 23

23.1 Individuals who initially test HCV negative but who remain at risk of HCV infection should be offered repeat testing on an annual basis, or six monthly if deemed clinically appropriate*.

*More frequent testing may be considered in circumstances such as: if a risk exposure is known to have occurred; an unexplained rise in ALT; a diagnosis of another BBV.

Quality/level of evidence: *low*

Strength of recommendation: *strong*

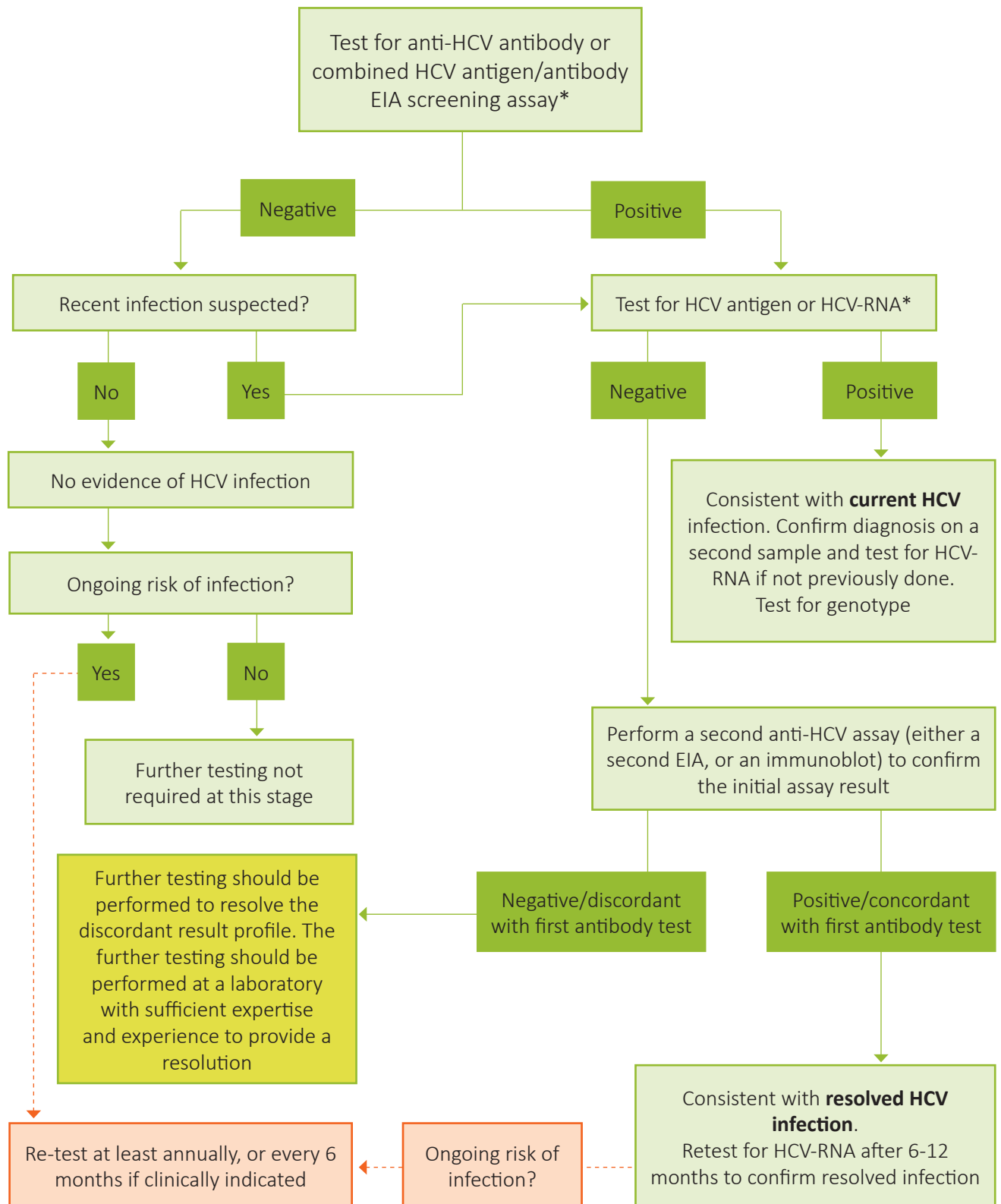
The following are responsible for implementation of recommendation 22 and 23:

Healthcare professionals carrying out HCV testing, diagnostic laboratories, NVRL.

Box 2: Proposed testing sequence for HCV infection

- 1) Individuals being investigated for evidence of HCV infection should be screened with an anti-HCV antibody* or combined HCV antigen/antibody EIA screening assay.
 - a) If this initial test is negative, and recent infection is not suspected, then no further testing is indicated.
- 2) If the initial HCV EIA is reactive (positive), then the sample should be tested for the presence of HCV antigen, or HCV-RNA.
 - a) If the individual tests positive for HCV antigen or HCV-RNA, then the results should be reported with an interpretative comment along the lines of “consistent with current HCV infection” (Proceed to 3 below).
 - b) If an individual tests HCV antibody positive, but antigen/RNA negative, then a second anti-HCV assay (either a second EIA, or an immunoblot) should be performed to confirm the screening assay result.
 - i) If the second anti-HCV assay confirms the initial result, then the results should be reported with an interpretative comment along the lines of “consistent with HCV infection at some time” or “HCV serology suggestive of resolved infection” (Proceed to 5 below).
 - ii) If the second anti-HCV assay does not confirm the initial result, then further testing should be performed with a view to resolving the discordant result profile: the further testing should be performed at a laboratory with sufficient expertise and experience to provide a resolution.
- 3) All individuals testing positive for current infection should have a second serum sample drawn to confirm their HCV diagnosis.
- 4) Those individuals testing positive for current infection should also have a sample drawn for HCV-RNA (if not already performed) and HCV genotyping.
- 5) Those individuals with evidence of a resolved HCV infection (i.e. anti-HCV positive and antigen/RNA negative) should also have a further sample drawn after six to 12 months for HCV-RNA testing to confirm their resolved infection status.

*In certain patient groups, initial testing should routinely incorporate HCV-antigen or HCV-RNA testing. Those are: immunocompromised individuals; children (born to HCV-infected mothers) in the first 18 months of life; individuals previously treated for HCV infection; sources of needle-sticks; and those at risk of recent infection in whom an antibody response might not yet have developed (HCV-RNA testing should be performed six weeks post-exposure).



*In certain patient groups, initial testing should routinely incorporate HCV antigen or RNA testing. Those are: immunocompromised individuals; individuals previously treated for HCV infection; and those at risk of recent infection in whom an antibody response might not yet have developed (RNA testing should be performed 6 weeks post-exposure).

Figure 4: Testing sequence for HCV infection

4.2.2. What specimen type should be used for HCV screening?

Key question

What specimen type should be used for HCV screening?

Evidence summary

HCV testing can be performed on a number of different types of specimens including serum, plasma, dried blood spots (DBS), and oral fluid.

While DBS and oral fluid specimens may confer advantages in terms of ease of use and acceptability any such advantage needs to be weighed against their diagnostic accuracy.

Diagnostic accuracy of alternative types of specimens

Dried blood spot

WHO states that DBS specimens for anti-HCV testing may be considered in settings where there are no facilities or expertise to take venous whole blood specimens, where there are persons with poor venous access or where rapid diagnostic tests are not available or their use is not feasible (2). Regarding the use of DBS for HCV-RNA testing, WHO states that DBS may be considered in settings where there is a lack of access to sites or nearby laboratory facilities for NAT or provision for timely delivery of specimens to a laboratory or there are persons with poor venous access.

A number of other guidelines recognise serum or plasma as the gold standard specimen type, but that the DBS should be considered in certain settings (e.g. prisons) or in certain populations (e.g. PWID), where facilities to take venous blood may be lacking or venous access may be difficult, in order to improve uptake (37, 45).

Studies examining the performance of DBS in the diagnosis of HCV have found the sensitivity of DBS in detecting anti-HCV ranged from 70-98.3% and the specificity ranged from 98.9-100% (165-171).

In a systematic review examining the performance of DBS specimens for detection and quantification of HCV-RNA the sensitivity of DBS in included studies ranged from 93.8–100%, specificity ranged from 94.0–100%, positive predictive value (PPV) ranged from 96.1-100%, and negative predictive value (NPV) ranged from 90-100% (172). HCV-RNA was detected by DBS in 100% of HCV-positive samples with serum viral loads as low as 150–250 IU/mL up to 4,830-24,160 IU/ml. In additional studies that examined performance of DBS samples in detection of HCV-RNA the sensitivity ranged from 65.9-97.8% and the specificity in all studies was 100% (165, 166, 168, 169). The low sensitivity of 65.9% was found in an in-house PCR test compared to all other studies that modified existing PCR tests. Excluding this in-house PCR test, the sensitivities ranged from 88-97.8%. In two studies that examined performance of DBS samples in detection of HCV-Ag/Ab the sensitivity ranged from 80-98.2% and the specificity ranged from 96-100% (173, 174).

Of note, currently available commercial assays have not been approved for use on DBS. Therefore the use of DBS specimens would be considered “off-label”.

Oral fluid

Note: HCV-RNA is not detectable in oral fluid. Therefore oral fluid can only be used for testing of anti-HCV or HCV-Ag serological testing.

Studies examining the performance of saliva/oral fluid specimens in the diagnosis of HCV have found the sensitivity of oral fluid in detecting anti-HCV ranged from 73-93.9% and the specificity ranged from 92.5-100% (171, 175-179). Amongst HIV positive individuals, the sensitivity was found to be 73% and the

specificity 93% (175). In one study examining the performance of saliva/oral fluid samples in detection of HCV-Ag/Ab, the sensitivity ranged from 71.7-94.6% and the specificity ranged from 94.3-100% (174).

Regarding the use of oral fluid specimens, NICE guidance concluded that, given the lower sensitivity and specificity of oral fluid, if an oral fluid specimen was used, a blood sample would be required to confirm the initial positive results, and for HCV-RNA testing to diagnose chronic HCV infection (45).

Acceptability of alternative specimen types

Alternative specimen types such as DBS or oral fluid have been proposed as they may be more acceptable because they are less invasive and therefore uptake of screening would be improved.

In a systematic review of studies that contained quantitative data on the frequency of testing and/or new diagnoses after the introduction of DBS testing of high-risk populations, five of the six included studies provided evidence that the introduction of DBS testing increased the number of tests, new diagnosis or both (180). However, variable effect sizes were found and all included studies that were judged to have a high risk of bias.

In one RCT, PWID were randomly allocated to either screening via venepuncture or via oral fluid (181). While the study was not specifically designed to assess the acceptability and impact on uptake of the different specimen types, it was found that uptake of screening was higher in those offered oral fluid testing, resulting in a higher detection rate of anti-HCV positive individuals (10.3% vs. 8.6%). One third of participants randomised to the venepuncture arm of the study could not be tested due to poor venous access. However, venepuncture sampling enabled a greater number of anti-HCV positive patients to be tested for HCV-RNA (91% vs. 53%).

In a qualitative study exploring the acceptability of oral fluid specimen collection, DBS from finger-prick, and venepuncture amongst PWID all three collection methods were found to be highly acceptable (182). Oral fluid sampling was reported as the preferred method of testing and finger-prick was the least preferred method.

Value judgement

Alternative specimen types such as DBS and oral fluid offer potential advantages over venous blood. They are easier to obtain from patients, particularly those with poor venous access. Currently, the evidence to support the improved acceptability and uptake of testing with DBS or oral fluid is limited.

DBS and oral fluid offer other logistical advantages. Neither requires trained healthcare professionals and both can be used for self-sampling. DBS samples can be transported without the need for refrigeration and do not require plasma separation within a specified time period. These benefits may be particularly useful in settings where larger numbers of tests are being done e.g. prisons, addiction services, etc.

However, the sensitivity of testing on oral fluid samples is low, with poor PPV and therefore not considered an acceptable specimen.

While the sensitivity of DBS is considered acceptable, there are some issues. There is currently no approved assay for use with DBS specimens. In the absence of an authorised commercial assay, considerable resources would need to be invested in validation, standardisation, quality assurance and quality control.

Recommendation 24

- 24.1. Serum and plasma are the preferred specimen types for screening and diagnostic testing for HCV infection using quality assured assays.
- 24.2. Screening and diagnostic testing for HCV infection should not be performed on oral fluid samples due to the low sensitivity and low positive predictive value.
- 24.3. Dried blood spot testing can be considered for screening for HCV in special circumstances, such as mass screening initiatives e.g. in prisons.

Quality/level of evidence: *moderate; good consistency between existing high quality guidelines*

Strength of recommendation: *strong*

The following are responsible for implementation of recommendation 24:

Healthcare professionals carrying out HCV testing, diagnostic laboratories, NVRL.

4.2.3. What is the role of rapid diagnostic tests and point of care tests in HCV screening?

Key question

What is the role of rapid diagnostic tests and point of care tests in HCV screening?

Definitions

A rapid diagnostic test (RDT) is a test which provides a result in a short time period, typically less than 30 minutes. While laboratories do undertake some RDTs, the term is typically used to describe rapid tests performed at the point of care. A point of care test (PoCT) involves the performance of a test in the immediate vicinity of a patient to provide a rapid result outside the conventional laboratory environment (183).

Evidence summary

The advantages of RDTs/PoCTs are that they can be used in the community and therefore may lead to greater access to testing. The rapid result can facilitate patient management and improve linkage to care, and some can be used with less invasive specimens that do not require venepuncture, such as capillary whole blood or oral fluid. However, they must also be accurate and reliable.

WHO has recommended the use of RDTs in settings where there is limited access to laboratory infrastructure and testing and/or in populations where access to rapid testing would facilitate linkage to care and treatment (2). In the USA, CDC recommends that testing for HCV begin with either a rapid or a laboratory conducted assay for HCV antibody in blood.

Diagnostic accuracy of RDTs/PoCTs

In a systematic review and meta-analysis evaluating RDTs/PoCTs pooled accuracy was high overall. The overall pooled sensitivity, specificity, positive likelihood-ratio, negative likelihood-ratio and diagnostic odds ratio for all tests were 97.4% (95% CI: 95.9%–98.4%), 99.5% (99.2%–99.7%), 80.17 (55.35–116.14), 0.03 (0.02–0.04), and 3032.85 (1595.86–5763.78), respectively (184). Performances varied widely among individual RDTs/PoCTs. Of the seven tests evaluated in the meta-regression model, OraQuick® HCV Rapid Antibody Test had the highest test sensitivity and specificity and showed better performance than a third generation EIA in seroconversion panels.

Acceptability of RDTs/PoCTs and impact on uptake of screening

In a systematic review on the effect of RDTs/PoCTs on increasing uptake of screening or improving the detection of HCV infection, no studies that contained quantitative data on the frequency of testing and/or new diagnoses after the introduction of RDTs/ PoCTs were identified (180).

In a qualitative study of provider attitudes to RDTs/PoCTs (OraQuick® HCV Rapid Antibody Test on oral fluid) staff had a significantly more positive attitude to RDTs/PoCTs compared to the standard blood test with regards to explaining test procedure, administering the test, integrating prevention messages and appropriateness of the test (185). The service providers were more likely to recommend the RDTs/PoCTs to clients. Key themes in support of RDTs/PoCTs were that there was no need for follow-up appointments, education and counselling could be provided during the time waiting for results, ability to focus attention then on those who test positive, ability to provide testing in more settings, reduced risk to staff, challenges that phlebotomy can cause for many clients, challenges accessing sufficiently skilled phlebotomists due to limited resources, and potential to incorporate rapid HCV testing in combination with rapid HIV testing. Limitations identified were that RDTs/PoCTs could result in increased testing and the measures that would be required to address this. In addition there would be a need for blood testing for some populations e.g. immigrant populations, who also require HBV screening.

In a study in which a RDT/PoCT (OraQuick® HCV Rapid Antibody Test) was performed on venous blood samples in an urban STD clinic and HIV testing facility in the US, HCV negative patients (n=9) reported being pleased with the RDT/PoCT and the fact that they received their test results on the same day (186). For HCV positive patients (n=3), one said that the rapidity of the test made it easier and one patient said that because all tests were carried out at the same time it made it easier. Staff reported that the RDT/PoCT was quick, accurate and simple to use.

In a study in the US of high risk patients attending a mobile clinic, participants were offered a choice between RDT/PoCT (OraQuick® HCV Rapid Antibody Test) with finger-stick and standard test with venepuncture (187). Of the 32.6% who accepted testing, 47.7% chose the RDT/PoCT and 52.3% chose the standard phlebotomy test. Interestingly, PWID patients were less likely to choose the RDT/PoCT. Those choosing a RDT/PoCT were significantly more likely to be linked to care within 30 days. The study findings are potentially biased by the fact that the RDT/PoCT only tested for HCV whereas standard venepuncture tested for HCV, HBV, HAV, HIV and syphilis.

In a separate US study in which patients were offered either RDT/PoCT (OraQuick® HCV Rapid Antibody Test) with finger-prick or standard test with venepuncture, 82.9% chose to receive the RDT/PoCT (188). Getting results fast was cited as the main reason for choosing the RDT/PoCT by 60.2%. Most (84.4%) who received the RDT/PoCT agreed that they preferred receiving their results the same day, 53.5% reported that the finger-prick was less or much less painful. The majority (93.9%) would recommend the RDT/PoCT to a friend. Amongst those who opted for the standard venepuncture HCV test the most common cited reason, cited by 38.1%, was that they felt it was older and more trusted. Other participants stated that they did not want their results that day (14.3%), felt that the standard test was more convenient (14.3%), were afraid of fingers-pricks (9.5%), or felt that the standard test was less painful (4.8%). The study findings are potentially biased by the fact those who had the RDT/PoCT were aware of their test result prior to completing the survey.

Value judgement

As oral fluid is not considered an acceptable specimen type (see section 4.2.2), only RDTs/PoCTs using blood were considered.

RDTs/PoCTs may confer some benefit in preventing loss to follow-up, particularly amongst hard-to-reach populations. RDTs/PoCTs which use finger-prick blood could increase the accessibility of testing. In addition RDTs/PoCTs that use finger-prick blood do not require specially trained phlebotomists or clinicians.

HCV RDTs/PoCTs are not routinely used in clinical practice in Ireland. To date, they have only been used for research purposes. HCV RDTs/PoCTs can use oral fluid or finger-prick blood, and/or venous blood. As discussed in section 4.2.2 oral fluid is not considered an acceptable specimen type for routine HCV diagnosis. RDTs/PoCTs performed on venous blood remove many of the potential advantages of RDTs/PoCTs.

Currently available RDTs/PoCTs only test for anti-HCV, meaning traditional venepuncture and laboratory based diagnostics will still be required to test for HCV-Ag or HCV-RNA to confirm current infection. In addition, some RDTs/PoCTs require serum or plasma samples with centrifugation before testing. Therefore it is recommended where possible to screen using a plasma or serum sample to enable a more complete diagnosis be made.

Where concerns exist about loss to follow-up, RDTs/PoCTs using finger-prick or DBS specimens can be considered. Any RDT/PoCT programme should follow the recommendations set out in *Guidelines for Safe and Effective Management and Use of Point of Care Testing in Primary and Community Care* (183).

Recommendation 25

- 25.1 Where concerns exist about hard-to-reach populations or linkage-to-care then consideration could be given to using approved (e.g. CE marked) rapid diagnostic tests/point of care tests on blood specimens.
- 25.2 If RDTs/PoCTs are introduced into standard clinical practice then a quality assurance programme should be established that addresses internal quality control and external quality assurance.

Quality/level of evidence: *low*

Strength of recommendation: *conditional/weak*

The following are responsible for implementation of recommendation 25:

HPRA, healthcare professionals carrying out HCV testing, diagnostic laboratories, NVRL.

4.2.4. Screening for other bloodborne viruses

It was not within the scope of this guideline to make recommendations on the need for screening for other bloodborne viruses (BBV) such as HIV and HBV.

At present, national guidelines on screening for other BBVs do not exist. Guidelines on HIV testing are in development.

Some risk groups for whom offering HCV screening is recommended, in particular PWID, migrants from endemic countries, and MSM, may also be at risk for other BBVs.

When offering screening for HCV, consideration should be given to the need for screening for other BBVs also.

Recommendation 26

26.1 When offering screening for HCV, consideration should be given to the need for screening for other BBVs also.

Quality/level of evidence: *low*

Strength of recommendation: *strong*

4.3. Interventions to increase uptake of HCV screening and subsequent linkage to care

Key question

How can those at risk be communicated with and encouraged to take up screening?

How can those identified as being infected through screening be linked into care?

Note

The impact of this guideline will depend on the uptake of screening by at risk populations and the subsequent linkage to care and treatment of detected cases.

Evidence Summary

Uptake of screening

Guidelines from the UK recommend that methods to raise awareness and highlight information regarding HCV amongst at risk groups and the general public be considered and that awareness campaigns be targeted to particular audiences (37, 45). Initiatives by local organisations in venues and at events popular among groups at increased risk are recommended (45). Training for healthcare professionals and other staff providing services for people at increased risk of HCV infection is also recommended (37, 45).

A number of studies have examined interventions to increase uptake of screening and/or linkage to care. Of note, most of the studies were conducted prior to the introduction of newer treatment regimes. In a systematic review of interventions to increase HCV testing uptake amongst high risk groups, eight controlled studies were included in the final narrative analysis (189). Included studies showed a positive impact on test uptake using targeted case finding in primary care, support and training for primary care practitioners, offering alternative testing and provision of outreach testing. However, intervention effects were variable. Of the eight studies included in the systematic review, six had available data to calculate effect size. The largest effect sizes were associated with interventions based on delivery of services in non-specialist community settings.

A systematic review and meta-analysis investigated the effectiveness of targeted HCV testing interventions compared to no targeted interventions or routine practice (190). The number of people needed to be tested to detect one anti-HCV case was highest when all risk groups were targeted (range 19-118), and lowest when those at risk of being an injecting drug user were targeted (range 8-36), or individual injecting drug users were targeted (range 1-4).

On pooled analysis, exposure to a targeted testing intervention compared to no intervention was associated with an increased number of people tested, anti-HCV cases detected, referrals to a specialist, attendance at a specialist, and cases commencing treatment. Targeted testing interventions were not associated with a difference in achieving sustained virological response.

Practitioner based targeted testing interventions (i.e. where a health or social care professional was given support to offer risk assessment and/or testing) compared to no targeted testing increased the number of people tested and the number of anti-HCV positive cases detected.

A media/information-based targeted approach (i.e. television, newspaper, radio advertisements, posters, leaflets) compared to no targeted testing, was found to be less effective in increasing the number of people tested, and the number who tested positive.

Targeting of individuals known to be PWID, compared to no targeted testing, increased the number of tests and the number who tested positive. Targeted testing of individuals with any risk factor for HCV,

compared to no targeted testing, was less effective in both increasing the number of tests, and the number of positive tests. The authors concluded that targeted practitioner based interventions have the greatest impact in terms of numbers tested and cases detected.

Settings for testing

The European Monitoring Centre for Drugs and Drug Addiction recommend that facilities most suitable for screening for infectious diseases such as HCV among PWID include: primary healthcare, including general practitioners and family doctors; special health services for PWID delivered through mobile clinics, in other community settings, through harm reduction programmes or through other types of outreach; low threshold service centres visited by PWID (164). NICE recommended that all venues where testing and treatment services are, or could be offered that can also ensure continuity of care and onward referral to specialist treatment for people who test positive be considered (45). In addition to outreach testing this could include pharmacy testing, although there was not sufficient evidence at the time to uniformly support community pharmacy testing. Pilot studies of community pharmacy testing in the UK have shown good acceptability and detection rates (191, 192).

Linkage to care

A number of studies have assessed the HCV care cascade and ways to improve linkage to care. It should be noted that the majority of these were undertaken in the US, where the insurance-based funding model for healthcare has a major influence on access to care.

Interventions aimed specifically at improving adherence to treatment have not been considered here as any such interventions are not within the scope of the guideline. However, some studies have reported on the entire care cascade. Where the outcome of treatment adherence is reported it is included.

A systematic review of interventions to improve linkage to care identified 20 studies for inclusion. Linkage to care was defined broadly as interventions with the common purpose of shifting HCV-diagnosed individuals towards HCV-specific care for further evaluation and treatment.

Interventions based in addiction treatment centres all used multidisciplinary approaches combining medical and addiction treatment with intensive social support. Peer driven interventions were found to be well accepted and efficient ways to facilitate linkage to care. Correctional settings, primary care settings, and clinics that have prolonged engagement with homeless, substance using populations or PWIDs were reported as ideal settings for interventions for linkage to care (193).

A number of studies have evaluated the impact of a care co-ordinator or patient navigator on linkage to care (194-202). In the included studies, care co-ordinators undertook tasks such as assisting with insurance applications, scheduling appointments, reminding patients about appointments, linking with social care services, escorting patients to appointments, arranging transport, outreach to patients who did not attend for follow-up, and counselling. While results varied between studies, a number showed improvements in referrals to specialist care and attendance with the use of care co-ordinators.

Value judgement

A key requirement for Ireland to meet its goal of elimination by 2030 is for undiagnosed cases to be detected through screening and subsequently linked to care and treatment. Those most at risk of HCV are often from marginalised groups of society and may experience barriers to accessing healthcare services such as screening.

Studies examining how to improve uptake of screening have shown that targeted strategies in community settings are successful. Strategies to improve linkage to care which have been found to be successful include outreach services in the community, peer support and care co-ordinators. There are a number

of initiatives already underway in Ireland employing such strategies (see Appendix 12). Such initiatives should be supported and evaluated to inform the best way to improve uptake and linkage to care in the Irish setting.

While the scope of this guideline is limited to screening, it is recognised that in order to achieve the goal of elimination by 2030, action is required across the entire continuum of hepatitis C care. A National Hepatitis C Programme with a mandate and resources to co-ordinate actions across the entire continuum of care should be established as recommended by WHO. Such a programme will enable Ireland reach the target of elimination by 2030 – this is the ultimate goal of the NHCTP and is in line with the 2016 WHO global health strategy on viral hepatitis.

Recommendation 27

- 27.1 Interventions to increase uptake of screening and linkage to care, particularly amongst vulnerable groups, should be supported and evaluated.
- 27.2 A national hepatitis C programme with a mandate spanning the entire hepatitis C continuum of care to include full implementation of the National Hepatitis C Strategy and the National Hepatitis C Treatment Programme should be established.

Quality/level of evidence: *low*

Strength of recommendation: *strong*

5

Good practice points for healthcare professionals involved in HCV screening

Healthcare professionals should consider the following points:

- Any contact with services provides an opportunity to offer HCV screening to those at risk (see Appendix 1 for a list of risk populations).
- HCWs should be cognisant that a person may fall into a potential risk group for HCV unrelated to their reason for presentation to a health service.
- HCWs should be cognisant that a person may have more than one risk factor for HCV and this should be considered when determining the need for repeat testing e.g. a migrant from an intermediate or high prevalence country may warrant repeat screening rather than one-off screening due to also being a current PWID.
- HCV testing should be considered in those with an unexplained rise in ALT.
- Screening should be undertaken voluntarily*.
- While offering HCV screening, HCWs should counsel on the testing process, the process of receiving results, and the importance of returning for test results.
- Confidentiality should be maintained during the offer of screening and delivery of results.
- An offer of a test or a negative test result provides an opportunity to counsel about prevention and harm reduction.
- Upon a diagnosis of HCV infection newly diagnosed persons should be:
 - o Referred for specialist assessment (further details available at: <http://www.hse.ie/eng/health/az/H/Hepatitis-C/Treating-hepatitis-C.html>). Community based assessment and treatment models are being piloted and may be more widely available in the future.
 - o Informed of the next steps, in terms of subsequent diagnostic tests required, and treatment options.
 - o Provided with information on HCV, including how to reduce the risk of transmission to others.
 - o Counselling on the importance of linkage to care.
 - o Directed to services which can provide support and counselling as needed (see Appendix 12).
- Continuity of care should be maintained as a patient transitions between services, settings, or circumstances (e.g. prison to community, homelessness to home).

*In certain circumstances screening is mandated by legislation (i.e. donors of substances of human origin). In other circumstances, failure to agree to screening may prohibit a person from undertaking certain activities in order to maintain patient safety (e.g. healthcare workers will be prohibited from performing exposure prone procedures).

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6 Appendices

Appendix 1: Risk populations for HCV

Risk populations for HCV to guide screening decisions:

- Those who have ever injected drugs
- Those who have used unprescribed or illicit drugs by a route other than injecting (non-injecting drug use (NIDU)), if there is a possibility of transmission of infection by the route of administration
- Prisoners or former prisoners
- Homeless people who have a history of engaging in risk behaviours associated with HCV transmission, or who have had a potential HCV risk exposure
- Migrants from a country with an intermediate and high prevalence of HCV (anti-HCV \geq 2%*)
- People who are HIV positive
- Infants of HCV-RNA positive women
- Men who have sex with men
- People on renal dialysis or who have had a kidney transplant
- Recipients of blood or blood components in Ireland prior to October 1991 who have not yet been tested
- Recipients of anti-D immunoglobulin in Ireland between 1st May 1977 and the end of July 1979, and 1st March 1991 to 18th February 1994 who have not yet been tested
- Recipients of plasma derived clotting factor concentrates in Ireland prior to 1992 who have not yet been tested

**Strong
recommendation
– Screening
should be offered**

- Those with a tattoo, particularly those who received tattoos a number of decades ago, in non-professional settings, prisons, countries with a high prevalence of HCV, or in circumstances where infection control was poor
- Household contacts of a person who is HCV positive in circumstances where household transmission is more likely to have occurred
- Recipients of solid organ transplants in Ireland prior to the introduction of routine screening
- Recipients of blood components and blood products overseas in any country where a quality assured blood donor screening programme may not have been in place
- People who have received medical or dental treatment in countries where HCV is common (anti-HCV prevalence \geq 2%*) and infection control may be poor
- Sexual partners of known HCV cases:
 - o If the case or contact is also HIV positive
 - o If the HCV-infected case is an injecting drug user
- Sexual contacts of persons who inject drugs, but where HCV status is unknown or where there is evidence of resolved infection
- Commercial sex workers

**Weak
recommendation
– Screening
should be
considered**

* A list of countries this includes is available in Appendix 2.

Appendix 2: HCV endemic countries

Table A 1 lists the countries known to have a prevalence of anti-HCV $\geq 2\%$.

Table A 1: Anti-HCV prevalence of countries with a prevalence $\geq 2\%$

Country	Anti-HCV prevalence	Country	Anti-HCV prevalence
Albania	2.4	Kyrgyzstan	2.5
Angola	4.2	Latvia	2.4
Armenia	5.4	Lebanon	3.1
Azerbaijan	3.1	Liberia	5.3
Bahrain	3.1	Lithuania	2.9
Benin	3.6	Mali	5.3
Burkina Faso	5.3	Republic of Moldova	4.5
Cambodia	2.3	Mongolia	10.8
Cameroon	11.6	Niger	5.3
Cape Verde	5.3	Nigeria	8.4
Central African Republic	4.2	Oman	3.1
Chad	5.3	Pakistan	5
Congo	4.2	Palestinian Territory, Occupied	3.1
Congo, the Democratic Republic of the	4.3	Puerto Rico	2.3
Côte d'Ivoire	3.3	Romania	3.2
Egypt	15.7	Russian Federation	4.1
Equatorial Guinea	4.2	Sao Tome and Principe	5.3
Estonia	3.3	Senegal	5.3
Gabon	11.2	Sierra Leone	5.3
Gambia	2.1	Syrian Arab Republic	3.1
Georgia	6.7	Taiwan, Province of China	4.4
Ghana	5.3	Tajikistan	3.1
Guinea	5.3	Thailand	2.7
Guinea-Bissau	5.3	Togo	5.3
Iraq	3.2	Turkmenistan	5.6
Italy	4.4	Ukraine	3.6
Ivory Coast	5.3	United Arab Emirates	3.1
Jordan	3.1	Uzbekistan	11.3
Kazakhstan	3.3	Western Sahara	3.1
Kuwait	3.1	Yemen	2.2

(Source: adapted from “Epidemiological assessment of hepatitis B and C among migrants in the EU/EEA” by European Centre for Disease Prevention and Control. Stockholm: ECDC; 2016. Available from: <http://ecdc.europa.eu/en/publications/Publications/epidemiological-assessment-hepatitis-B-and-C-among-migrants-EU-EEA.pdf> (87))

Appendix 3: Recommendations from the National Hepatitis C Strategy 2011-2014

Table A 2: Recommendations relevant to screening from the National Hepatitis C Strategy 2011-2014

Recommendation 23a	Provide ready access for GPs and other community healthcare providers to diagnostic facilities.
Recommendation 24b	Provide every prisoner on committal with a hepatitis C risk assessment, including details of previous virological tests, and offer screening for blood-borne viruses, including hepatitis C, if required.
Recommendation 26	Establish guidelines with regard to hepatitis C screening of individuals from endemic countries/ new entrants to the Irish healthcare system.
Recommendation 27a	Continue targeted antenatal screening for those with risk factors for hepatitis C infection.
Recommendation 27b	Regular review of the evidence with regard to universal antenatal screening.
Recommendation 28	Offer and promote screening for hepatitis C and other blood-borne diseases to those who attend services such as Needle-Exchange programmes and other harm-reduction services.
Recommendation 29b	Develop standard protocols for testing, diagnosis, evaluation, referral for treatment, monitoring of treatment and monitoring of patients not on treatment.

(Source: Adapted from “National Hepatitis C Strategy 2011-2014”. By Health Service Executive. Dublin: HSE; 2012. Available from: <https://www.hse.ie/eng/services/Publications/HealthProtection/HepCstrategy.pdf> (13))

Appendix 4: Conflict of interest declarations

Conflict of interest statements were submitted by members of the GDG and renewed annually. The chair reviewed all conflict of interest statements. No interests stated were deemed to be conflicts in relation to the recommendations of this guideline.

Appendix 5: Key questions

The following is a list of key questions which are to be addressed by the guideline:

1. Is screening for hepatitis C beneficial?
 - a. For the individual?
 - b. For society?
2. Who should be offered screening for hepatitis C?
 - a. Who is at risk for hepatitis C infection?
 - b. Should the following specified groups be offered screened?
 - i. Migrants
 - ii. Prisoners
 - iii. People who currently use or have a history of unprescribed or illicit drug use
 - iv. Sexual contacts of PWID
 - v. Pregnant women
 - vi. Men who have sex with men
 - vii. People who are homeless
 - viii. Healthcare workers
 - ix. People having an STI screen/test
 - x. Those engaging in, or with a history of, high risk sexual behaviour
 - xi. People on renal dialysis or who have had renal dialysis in the past
 - xii. Recipients of unscreened blood and blood products in Ireland (donated pre October 1991) who have not been previously screened
 - xiii. Recipients of tattoos and body piercings
 - xiv. Those who received medical treatment in high prevalence countries
 - c. Should the following contacts of known cases of hepatitis C be screened?
 - i. Sexual contacts
 - ii. Household contacts
 - iii. Children of infected mothers
 - d. Any other group identified from 2.a
 - e. Should there be screening of the general population?
 - f. Is there a role for birth cohort screening?
3. What screening of blood, tissue or organ donations, or donors should be undertaken?
4. How should screening be implemented for each group for which screening is recommended, including:
 - a. Should screening be universal or selective?
 - b. What settings should screening be offered in?
 - c. What specimen type should be used?
 - d. What test should be used?
 - e. What is the role for point-of-care tests?
 - f. What should the screening sequence process be?
 - g. How frequently should those who remain at risk be screened?
5. For those being screened for hepatitis C – should they be screened for other bloodborne infections at the same time?
6. How can those at risk be communicated with and encouraged to take up screening?
7. How can those identified as being infected through screening be linked into care?
8. What are the economic implications of screening?

Appendix 6: Quality scores of included guidelines

Table A 3: HCV guidelines included for adaptation or adoption and their quality appraisal score.

Publisher/ organisation	Guideline name	Country/ Region	Year of publication	Rigour of development score	Quality appraisal score	Reasoning for decision
WHO	Guidelines on hepatitis B and C testing (2)	Global	2007	50	147	Included as it scored well in methodology; includes up to date literature on testing.
WHO	Guidelines for the screening, care and treatment of persons with hepatitis C infection (1)	Global	Updated 2016	51	148	Included as it scored well in methodology; addressed a key questions and is from a key organisation
British Association of Sexual Health and HIV (BASHH)	United Kingdom National Guideline on the Management of the Viral Hepatitides A, B & C (53)	UK	2008; updated 2016	41	97	Included as it addressed questions around screening in GUM setting, sexual contacts and MSM in more detail than other guidelines
BASHH	Sexually Transmitted Infections: UK National Screening and Testing Guidelines (116, 117)	UK	2006 and 2015 update	36	122	Included as it addressed questions around screening in GUM setting, sexual contacts and MSM in more detail than other guidelines
European Association for the Study of the Liver (EASL)	Clinical Practice Guidelines: Management of hepatitis C virus infection (61)	Europe	2014	26	92	Included as it addressed questions on how to test in more detail than other guidelines and from a key organisation
American Association for the Study of Liver Disease (AASLD)	Recommendations for Testing, Managing, and Treating Hepatitis C (51)	US	2014	38	135	Included as it scored well in methodology and addressed a number of the key questions
The Korean Association for the Study of the Liver (KASL)	KASL clinical practice guidelines: Management of Hepatitis C (52)	Korea	2014	38	111	Included as it scored well in methodology and addressed a number of the key questions
US Preventive Services Taskforce	Screening for Hepatitis C Virus Infection in Adults (39)	US	2013	37	117	Included as it scored well in methodology and addressed a number of the key questions
CDC	Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratories (203)	US	2013	15	75	Scored low because methodology not outlined but does address questions around testing practices
CDC	Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965 (145)	US	2012	49	147	Included as it scored well in methodology and addressed a key question

Publisher/ organisation	Guideline name	Country/ Region	Year of publication	Rigour of development score	Quality appraisal score	Reasoning for decision
Scottish Intercollegiate Guidelines Network (SIGN)	Management of hepatitis C A national clinical guideline (37)	Scotland	2013	44	128	Included as it scored well in methodology; addresses a number of the key questions; and Scottish context similar to Ireland
National Institute for Health and Care Excellence	Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection (45)	UK	2013	44	148	Included as it scored well in methodology; addresses a number of our questions; and UK context similar to Ireland
British HIV Association	British HIV Association guidelines for the management of hepatitis viruses in adults infected with HIV 2013 (204)	UK	2013	47	122	Included as it addressed questions around screening in GUM setting, sexual contacts and MSM in more detail than other guidelines
Saudi Association for the Study of Liver diseases and Transplantation	SASLT practice guidelines: management of hepatitis C virus infection (55).	Kingdom of Saudi Arabia	2012	29	95	Included as it scored well in methodology and addressed a number of the key questions
North American Society for Pediatric Hepatology, Gastroenterology and Nutrition (NASPHGN)	NASPGHAN Practice Guidelines: Diagnosis and Management of Hepatitis C Infection in Infants, Children, and Adolescents (49)	North America	2012	29	88	Included as it addressed some questions around children not addressed in other guidelines
International Union against Sexually Transmitted Infections (IUSTI)/ WHO Euro	European guideline for the management of hepatitis B and C virus infections, 2010 (54)	Europe	2010	30	66	Included as it addressed a number of key questions
European Monitoring Centre for Drugs and Drug Addiction (EMCDDA)	Guidelines for testing HIV, viral hepatitis and other infections in injecting drug users (164)	Europe	2010	18	91	Included as it contained recommendations relating to PWID in more detail than other guidelines and is a key organisation in Europe
European Paediatric HCV Network (EPHN)	The management of HCV-infected pregnant women and their children European paediatric HCV network (40)	Europe	2005	19	81	Scored low as methodology was not detailed. Included as it contained recommendations on testing of children born to infected women in more detail than other guidelines
Ireland	Hepatitis C among drug users: consensus guidelines on management in general practice (62)	Ireland	2004	21	86	Included as it is an Irish guideline and also applies to primary care.
CDC	Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease (47)	US	1998	16	95	Scored low because methodology not outlined. It is also old but included because it is one of the key guidelines from the USA

Appendix 7: Example of search strategy and results

The search strategy and results for the systematic review to address the question: ‘what is the risk of hepatitis C from tattooing?’ is presented here as an example. Other search strategies are available on request.

Table A 4: EMBASE search strategy on risk of HCV from tattooing

#	Query	Limiters/Expanders	Results
S1	hepatitis C or HCV or hepacivirus or hep C or hepC	Search modes - Boolean/Phrase	74,953
S2	(MM «Hepatitis C+»)	Search modes - Boolean/Phrase	41,127
S3	(MM «Hepacivirus»)	Search modes - Boolean/Phrase	17,165
S4	risk factor*	Search modes - Boolean/Phrase	793,591
S5	(MH «Risk Factors»)	Search modes - Boolean/Phrase	594,724
S6	S1 OR S2 OR S3	Search modes - Boolean/Phrase	74,953
S7	S4 OR S5	Search modes - Boolean/Phrase	793,591
S8	transmission or transmit or mode of transmission or acquisition or acquire* or transmit*	Search modes - Boolean/Phrase	863,409
S9	(MM «Disease Transmission, Infectious+»)	Search modes - Boolean/Phrase	29,862
S10	S8 OR S9	Search modes - Boolean/Phrase	870,117
S11	tattoo* or body art or body ornament*	Search modes - Boolean/Phrase	4,340
S12	(MM «Body Modification, Non-Therapeutic»)	Search modes - Boolean/Phrase	81
S13	(MM «Tattooing»)	Search modes - Boolean/Phrase	2,160
S14	S11 OR S12 OR S13	Search modes - Boolean/Phrase	4,408
S15	S6 AND S14	Search modes - Boolean/Phrase	404
S16	S7 AND S15	Search modes - Boolean/Phrase	288
S17	S10 AND S16	Search modes - Boolean/Phrase	197
S18	S10 AND S16	Limiters - Date of Publication: 19900101-20151231 Search modes - Boolean/Phrase	197
S19	S10 AND S16	Limiters - Date of Publication: 19900101-20151231; Human Search modes - Boolean/Phrase	183

Table A 5: Medline search strategy on risk of HCV from tattooing

1. (hepatitis c or HCV or hepacivirus or hep c or hepc).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	119677
2. exp *hepatitis C/ or exp *Hepatitis C virus/	61876
3. risk factor*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	879512
4. exp *risk factor/	32466
5. 3 or 4	879512
6. (transmission or transmit* or mode of transmission or acquisition or acquire*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	927221
7. exp *disease transmission/	30705
8. 6 or 7	935740
9. (tattoo* or body art or body ornament*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	5338
10. exp *tattoo/	1180
11. exp *body modification/	1440
12. 9 or 10 or 11	5667
13. 1 or 2	119677
14. 12 and 13	721
15. 5 and 14	454
16. 8 and 15	274

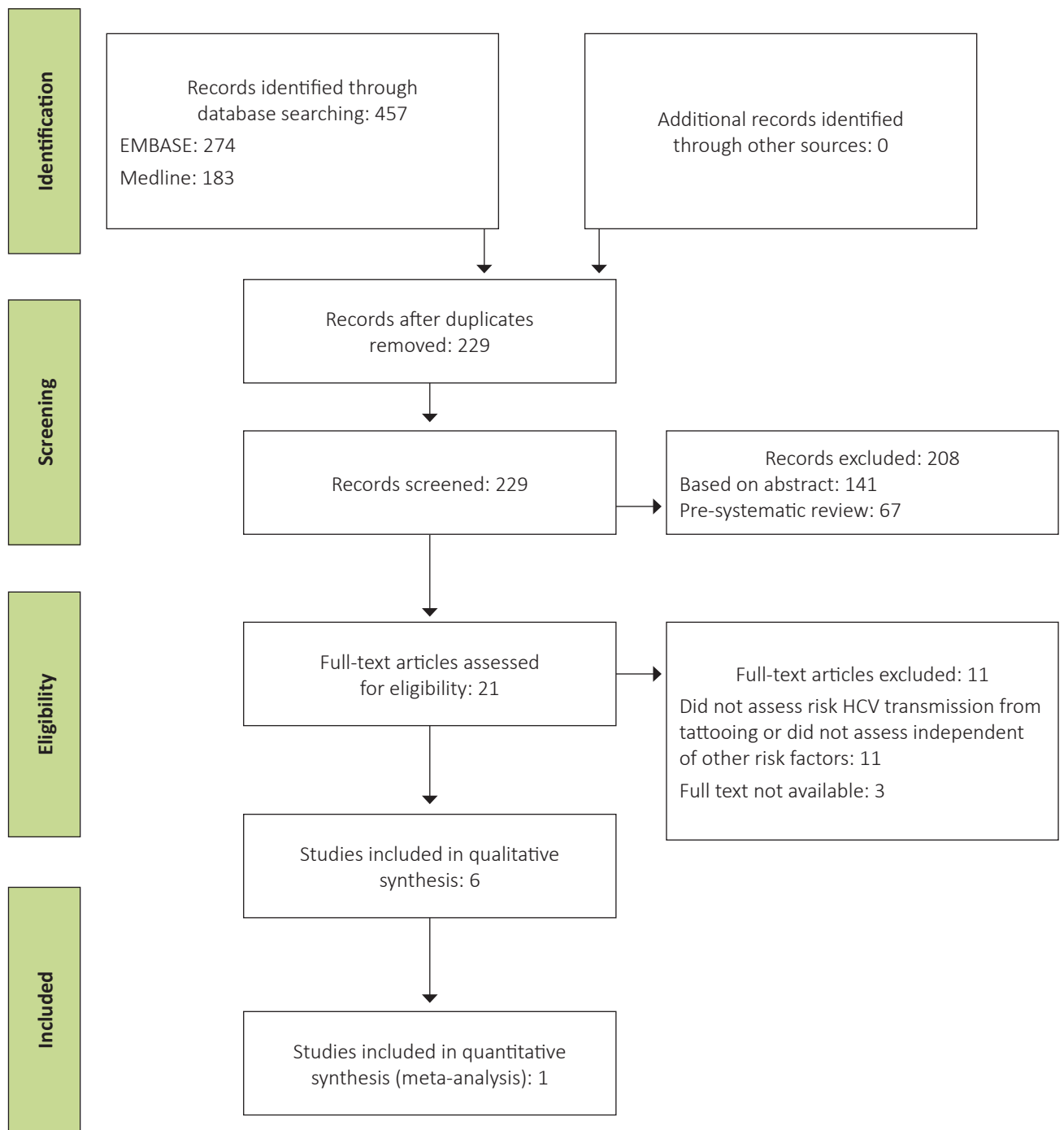


Figure A 1: PRISMA flow diagram of systematic review of literature on the risk of HCV from tattooing.

Appendix 8: Commissioned systematic literature review

The School of Nursing and Midwifery National University of Ireland, Galway was commissioned by the CEU/NCEC Department of Health under a contract agreement to undertake one systematic literature review to support the development of this guideline.

The systematic literature review addressed the risk of HCV sexual transmission amongst heterosexuals. The abstract is presented here below.

The full review is available at:

<http://health.gov.ie/national-patient-safety-office/ncec/national-clinical-guidelines>

ABSTRACT

Wuytack F, Lutje V, Tohme R, Jakobsen JC, Weiss KH, Flanagan P, Smith V, Gethin G, Murphy L, Smyth S, Devane D (2017). Sexual transmission of hepatitis C virus infection in a heterosexual population, a systematic review. National Clinical Effectiveness Committee, Department of Health: Dublin.

Background

Hepatitis C virus (HCV) infection is an important cause of liver disease worldwide and an estimated 130 to 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 have examined 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 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 2nd to 4th November 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, people who inject drugs (PWIDs), 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. Case studies, case series and reviews were excluded.

Data collection, analysis and quality assessment

Studies were screened 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 using 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 a PWID 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 a PWID 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 liberal approach to review study inclusion criteria (i.e., including the 67 studies in which participants were mostly heterosexuals but samples included some (but not all) PWIDs) 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 applied when doing so to avoid the impact of confounders on the findings and we would recommend conducting subgroup analyses in such case.

Appendix 9: Considered judgement form

The considered judgement forms for each of the questions addressed are available here: <http://www.hpsc.ie/A-Z/Hepatitis/HepatitisC/Guidance/Backgrounddocuments/>

Figure A 2: Considered judgement form used in developing the recommendations

Hepatitis C Screening Guideline Development Group Considered judgement to formulate recommendations

Subgroup:

Date:

Attendees:

1. What is the question being addressed?
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)
3. What is the body of evidence? Source of evidence: (tick all that apply)
<input type="checkbox"/> Guidelines
<input type="checkbox"/> Primary literature
<input type="checkbox"/> Other; specify: Economic literature; surveillance data; Irish prevalence study
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? If there is insufficient evidence to answer the key question 10 to section 11. Comment here on any issues concerning the quantity of evidence available on this topic and its methodological quality.
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
4.3 Generalisability - are the patients in the studies similar to our target population for this guideline? Is it reasonable to generalise
4.4. Applicability - Is the evidence applicable to Ireland? Is the intervention/action implementable in Ireland?
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
5. Additional Information for consideration
5.1. Additional literature if applicable e.g. Irish literature
5.2. Relevant national policy/strategy/practice

5.3. Epidemiology in Ireland If available and applicable
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?
6.2. What are the likely resource implications and how large are the resource requirements? Consider cost effectiveness, financial, human and other resource implications
6.3. Acceptability - Is the intervention/option acceptable to key stakeholders?
6.4. Feasibility - Is the Intervention/action implementable in the Irish context?
6.5. What would be the 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
8. Final Recommendations
<input type="checkbox"/> Strong recommendation <input type="checkbox"/> Conditional/weak recommendation
Text:
9. Justification
10. Implementation considerations
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.

Appendix 10: Consultation process

Table A 6: List of individuals and organisations who were invited to participate in the consultation process

Groups or representative bodies	
Academy of Clinical Science and Laboratory Medicine	Irish College of Psychiatrists
Addiction service pharmacists	Irish Dental Association
Balseskin Centre doctors and nurses	Irish Faculty of Primary Dental Care
Chrysalis Drugs Project	Irish Haemophilia Society
Community Response	Irish Kidney Association
Consultants in Emergency Medicine	Irish National Accreditation Board
Consultant Hepatologists/Gastroenterologists	Irish Patient's Association
Consultant Microbiologists	Irish Penal Reform Trust
Consultant Obstetricians	Red Cross (prison liaison)
Consultant Paediatricians	Irish Prison Service
Consultative Council on Hepatitis C	Irish Prison Doctors group
Cork University Dental School and Hospital	Irish Society of Clinical Microbiologists
Crosscare	Irish Society of Community and Public Health Medicine
Department of Health Chief Medical Officer's office	Irish Society of Gastroenterology
Department of Health Drugs Policy Unit	Level 1 & 2 GPs in addiction services Merchants Quay Project
Directors of Public Health	Migrant Rights Centre Ireland
Directors of Public Health Nursing	National Addiction Advisory and Governance Group
Dublin Dental University Hospital	National Bloodborne Virus Committee (healthcare setting)
Focus Ireland	National Centre for Pharmacoeconomics
Garda National Drugs Unit	National Drug Advisory and Treatment Centre
Gay Mens Health Service	National Hepatitis C Strategy Implementation Committee
GUM Physicians	National Virus Reference Laboratory
Health Information and Quality Authority	Nursing and Midwifery Board of Ireland
Health and Safety Authority	Occupational Health Nurses Association of Ireland
Hepatitis C liaison nurses	Occupational Medicine Consultants
Hepatitis C Partnership	Organ Donation and Transplant Ireland
Hospital Pharmacists Association of Ireland	Office of the Nursing and Midwifery Services Director, HSE
Health Products Regulatory Agency	Pavee Point
HPSC	Peter McVerry Trust
HPSC Scientific Advisory Committee	Principal Medical Officers, HSE
Health Research Board (HRB), Drugs and Alcohol Section	Probation Officers (prisons)
HSE Clinical Strategy and Programmes Division	Rainbow Clinic
HSE Drug Treatment Services – clinics	Reception and Integration Agency
HSE Drugs/HIV helpline	Royal College of Physicians of Ireland (RCPI)
HSE Health and Wellbeing	RCPI Faculty of Occupational Medicine
HSE Health Promotion	RCPI Faculty of Paediatrics
HSE Hepatitis C Treatment Programme	RCPI Faculty of Pathology
HSE Infection Prevention and Control Nurses	RCPI Faculty of Public Health Medicine
HSE Integrated Services Directorate	Royal College of Surgeons in Ireland (RCSI)
HSE National Lead for Primary Care	RCSI Faculty of Dentistry
HSE National Lead for Neonatology	SafetyNet
HSE National Lead for Obstetrics	SAOL Project
HSE Occupational Health	Sexual Assault Treatment Units
HSE Quality Improvement Division	Sexual Health and Crisis Pregnancy Programme
HSE Social Inclusion	Simon Community
Infection Prevention Society	Specialists in Public Health Medicine
Infectious Diseases Physicians	Society for the Study of Sexually Transmitted Diseases in Ireland (SSSTDI)
Infectious Disease Society of Ireland	Transfusion Positive
Institute of Obstetrics and Gynaecology	Union for Improved Services Communication and Training (UISCE)
Irish Blood Transfusion Service	
Irish College of General Practitioners	

Individuals:	
Dr Susan Hahné (External reviewer)	Dr Mairin Ryan, HIQA
Dr Magda Rozinska (External reviewer)	Ms Helen Clark, Librarian, HSE
Dr Kevin Kelleher, Assistant National Director Public Health and Child Health, HSE Health and Wellbeing	Ms Lucia Mullen
Dr Stephanie O’Keeffe, Director, HSE Health and Wellbeing	Dr Lynda Sisson, HR Lead - Staff Health and Wellbeing and Occupational Health, Office of the National Director of HR, HSE
Mr John Hennessy, HSE Director Primary Care	Mr Niall Mulligan, HIV Ireland
Professor Joe Barry, HSE Consultant in Public Health Medicine and Professor of Population Health, Trinity College Dublin	Ms Erin Nugent, HIV Ireland
Dr Jean Long, HRB	Dr Cliona Ni Cheallaigh, Inclusion Medicine Service, St. James’s Hospital
Professor Declan Devane, School of Nursing and Midwifery, NUIG	Mr Tim Bingham, Irish Needle Exchange Forum
Dr Francesca Wuytack, School of Nursing and Midwifery, NUIG	Dr Erika Duffell, ECDC
Dr Jennifer Kieran, Consultant in Infectious diseases, St. James’s Hospital	Dr Lara Tivoschi, ECDC
Ms Michelle O’Neill, HIQA	

The template asked for comments on the questions outlined in Box 3 with an option for additional feedback if required.

Box 3: Questions reviewers were asked to comment on

<ol style="list-style-type: none"> 1. User friendliness <ol style="list-style-type: none"> a) Is the draft guideline easy to read? b) Do you think the guideline will be easy to use in practice? 2. Content <ol style="list-style-type: none"> a) Do the recommendations cover the scope of the draft guideline? b) Do the recommendations clearly link to the evidence presented? c) Does the draft guideline consider the views and needs of specific population groups? d) Does the draft guideline consider gaps in the current evidence? 3. Implementation <ol style="list-style-type: none"> a) Do any recommendations change current practice substantially? If so, do you consider that the reasons given in the draft guideline explain why the change is necessary? b) Which areas do you think may be difficult to put into practice? Please explain why. c) What would help users to implement the guideline? (For example, useful checklists, patient information leaflets etc.)

External review

International external reviewers were asked to provide feedback based on the questions outlined in Box 4 as recommended by NCEC/HIQA National Quality Assurance Criteria for Clinical Guidelines Version 2 (30). The external reviewers were also asked to provide any additional feedback they had.

Box 4: Questions asked of the international external reviewers

<ol style="list-style-type: none"> 1. Has the appropriate evidence been identified and reviewed in line with the scope and clinical questions posed by this guideline? 2. Are there specific links between decisions and the available scientific evidence? 3. Have the risks and potential harms of recommendations been fully considered in the context of clinical practice? 4. Is the guideline clearly written, user friendly and allows for individual clinician decisions? 5. Is the guideline suitable for routine use as intended (in so far as you are able to comment on the Irish situation)? 6. Are there relevant international or well referenced guidelines (recommendations) on the same topic that these guidelines are in conflict with, and if yes are the reasons for this justified in the guidelines?
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Feedback received was reviewed by the GDG and amendments made where appropriate. The feedback received and response of the GDG is available to review here:

<http://www.hpsc.ie/A-Z/Hepatitis/HepatitisC/Guidance/Backgrounddocuments/>

Appendix 11: Implementation plan

Table A 7 outlines the current barriers and facilitators to the implementation of each recommendation, possible actions to facilitate implementation, key stakeholders and the actions to be undertaken by the GDG.

Table A 7: Implementation plan

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
Recommendation 1 - Women who are pregnant					
Standardised targeted risk based HCV screening of antenatal women is recommended.					
Will require a standardised list of risk factors. Large numbers may be eligible due to having a tattoo. Laboratory resources.	Current practice in the majority of units. New National Medical Laboratory Information System (MedLIS).	Develop and make available a standardised list of risk factors; Incorporate this into the new maternity IT system. Education and training for staff; Information leaflets for mothers.	Maternity units, GPs who are involved in antenatal care,	HSE Clinical programmes Relevant facilities and societies (ICGP, O&G Society, IDSI, ISCM, SSSTDI, Public Health, Paediatrics, Pathology) IT system Diagnostic laboratories	Consult with stakeholders and disseminate final recommendations. Develop standardised list of risk factors. Request inclusion in IT system. Review recommendation if treatment guidelines change. Develop promotional and educational materials.
Recommendation 2 and 3 - Children born to HCV-infected mothers					
Infants of HCV-RNA positive women should be tested for HCV-RNA checked at six weeks and six months of age, and if both are negative, anti-HCV at ≥ 18months of age.					
Loss to follow-up of infants due to lack of understanding of parents, language barriers, moving, or chaotic lifestyles. If living outside of Dublin area, attendance at Rainbow Clinic might be difficult. Access to test results.	Current practice The National Medical Laboratory Information System (MedLIS)	Education of HCPs. Clear pathway for referral to paediatrics for follow-up and to Rainbow Clinic if required. Information leaflets for parents. Potentially follow-up could be coordinated by the proposed perinatal hepatitis B programme.	Maternity units, paediatric units, Rainbow Clinic, proposed perinatal hepatitis B programme	Obstetrics and paediatric clinical programmes GPs Relevant facilities and societies (ICGP, O&G Society, IDSI, ISCM, SSSTDI, Public Health, Paediatrics, Pathology) Diagnostic laboratories	Consult with stakeholders and disseminate final recommendations. Inform relevant HSE department, maternity units, relevant faculties. Awareness raising for public/ risk group. Develop promotional and educational materials.

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
<p>If a woman is found to have current or resolved HCV infection, any previous children she has given birth to should be tested unless the woman was known to be HCV-RNA negative at the time of their delivery.</p> <p>Determining retrospectively if a mother was HCV negative at the time of delivery may be difficult and time consuming. It may not be possible if the birth occurred outside of Ireland. Services where a mother is diagnosed may not provide a service for children e.g. addiction services and a referral mechanism for testing will be required. Depending on the age of the child GPs may not take bloods and referral may be required to paediatrics OPD. Payment for testing.</p>	<p>MedUIS Rainbow Clinic</p>	<p>Awareness raising. Easy access to maternity records from previous births. Clear pathway for referral for testing for children if needed. Referral pathways to care for detected cases.</p>	<p>Diagnosing healthcare worker, maternity units, GPs</p>	<p>Rainbow Clinic Diagnostic laboratories</p>	<p>Consult with stakeholders and disseminate final recommendations. Inform relevant HSE department, maternity units, relevant faculties. Awareness raising for public/ risk group. Develop promotional and educational materials.</p>
<p>Recommendation 4 - Household contacts of those with HCV infection In general HCV screening of household contacts (with no sexual or vertical exposure to the HCV positive household member) 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 the HCV positive household member is on dialysis in the home; if there are environmental risks within the household such as discarded needles.</p>					
<p>HCPs may not feel competent or have the resources to undertake the risk assessment. Index case may be diagnosed in a setting which does not provide general medical care to others or may not be acceptable to the household contact to attend e.g. addiction services or STI services. The index case may not wish to disclose their infection status to household contacts. It may be difficult to identify and contact eligible contacts. Lack of resources within Public Health Departments or other services for contact tracing. Payment for testing if person does not have GMS card. Lack of resources within Public Health Departments for contact tracing.</p>	<p>Public health and STI services currently undertake contact tracing in some circumstances for some infectious diseases. New methods for contact tracing are being considered under the National Sexual Health Strategy.</p>	<p>Where resources allow, active contact tracing could be undertaken by Public Health, primary care or other services. Where resources are not available, a passive approach could be taken where the index case advises household contacts of the need for screening. Awareness raising that testing is not generally needed and on circumstances where it should be considered. Information leaflets on the risk for cases and household contacts. Means of referring household contacts for testing if required. Involve patient in method of contact tracing. Include in any new contact tracing service which may be developed by the Sexual Health Strategy.</p>	<p>Diagnosing healthcare worker, GPs, Departments of Public Health</p>	<p>Patient groups, services offering testing, Clinical Lead for sexual health. Clinical programmes. Relevant faculties and societies (ICGP, O&G Society, IDSI, ISCM, SSSTD), Public Health, Paediatrics, Pathology Diagnostic laboratories</p>	<p>Consult with stakeholders and disseminate final recommendations. Develop promotional and educational materials.</p>

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
<p>Recommendation 5 and 6 - People who currently use or have a history of unprescribed medications or illicit drug use All those who have ever injected unprescribed or illicit drugs should be offered screening for HCV. This includes those who only injected once, and those who injected any type of drug which was not prescribed, including performance enhancing drugs like steroids, and novel psychoactive substances.</p>					
<p>Some may not perceive they are at risk (e.g. those that inject steroids). Poor venous access. Fear of testing of subsequent treatment. Unwillingness to admit behaviour to HCW. Access to testing for those not in services. Payment for testing if not in addiction services or don't have GMS card. Resources within addiction services. Lack of computerised system to indicate when last test performed Laboratory resources.</p>	<p>Current practice for those attending HSE Addiction Services and methadone level 1 and 2 GPs. HepCare project. A number of NGOs providing education and peer support. Needle exchange sites could be a setting to encourage testing. Safe injecting facilities being developed. MedLIS.</p>	<p>Awareness raising amongst public and other HCPs for those not attending addiction services and for those who have used drugs in the past. Outreach testing services. Targeted testing outside addiction services e.g. in GP. Education programmes in addiction services. Needle exchange as an opportunity to encourage testing (statutory, NGO and pharmacy). Safe injecting facilities being developed which provide a setting for education or testing. Audit of practice. Reminder systems on addiction services IT system.</p>	<p>HSE Social Inclusion/ Primary Care, Addiction services, GPs, HSE NHCTP and those providing outreach community treatment</p>	<p>Patient groups, NGOs, needle exchange sites, new consultants responsible for vulnerable patients in St James's Hospital and Mater Hospital. Relevant facilities and societies (ICGP, IDS), ISCM, Public Health, Pathology Diagnostic laboratories</p>	<p>Consult with stakeholders and disseminate final recommendations. Awareness raising for public/risk group.</p>
<p>Screening should be offered to all those who have used unprescribed or illicit drugs by a route other than injecting (non-injecting drug use (NIDU)), if there is a possibility of transmission of infection by the route of administration. This includes those who currently use intranasal drugs (i.e. snort or sniff), or have done so in the past, or share other equipment or drugs where there is a risk of contamination with the blood of others.</p>					
<p>Some may not perceive they are at risk. Lack of awareness amongst HCWs. Fear of testing. Unwillingness to admit behaviour to HCW. Access to testing for those not in services. Payment for testing. Laboratory resources.</p>	<p>Current practice in addiction services.</p>	<p>Awareness raising amongst public and other HCPs for those not attending addiction services and for those who have used drugs in the past. Outreach testing services. Targeted testing outside addiction services e.g. in GP. Education programmes in addiction services. Referral pathways to care for detected cases. Care co-ordinator and/ or peer support (e.g. HepFriend) to support retention in care. Community treatment services.</p>	<p>HSE Social Inclusion/ Primary Care, Addiction services, GPs, HSE NHCTP and those providing outreach community treatment</p>	<p>Patient groups, NGOs, new consultants responsible for vulnerable patients in St James's Hospital and Mater Hospital. Relevant facilities and societies (ICGP, IDS), ISCM, Public Health, Pathology Diagnostic laboratories</p>	<p>Consult with stakeholders and disseminate final recommendations; Awareness raising for public/ risk group Develop promotional and educational materials</p>

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
<p>Recommendation 7 and 8 - Prisoners Screening should be offered to all prisoners on entry to prison. Screening should be offered at a time at which it is most likely to be accepted by the prisoner, while also ensuring the early identification of infections in order to minimise the risk of transmission to others. Those found to have HCV infection should be linked into specialist care and treatment should be facilitated while in prison. Prisoners who initially test HCV negative should be offered repeat testing on an annual basis, or six monthly if deemed clinically appropriate, while in prison. Screening should also be offered at any time if a risk exposure (e.g. tattooing, needle-sharing) is known to have occurred. Prisoners should be able to access testing on request at any stage of their sentence.</p>					
<p>Prisoners have other concerns at the time of committal. Lack of confidentiality. Resources of prison health service. Prison IT system does not currently facilitate easy retrieval of previous testing results. Prisoners may not perceive they are at risk/ Lack of awareness of HCV. Fear of testing or subsequent treatment. Continuity of care or communication of test results on transfer or release. Access to treatment while in prison may not be universally available. Continuation of treatment on discharge if required.</p>	<p>It is current practice to offer screening although the timing of the offer at present may not be ideal and uptake is low. There are initiatives underway for treatment while in prison. MedUIS may facilitate access to testing history.</p>	<p>Designated nurse within each IPS complex, and regional nurses within the stand-alone prisons to coordinate. Adequate resourcing of prison health services to improve drop-in testing service. Testing drive days.</p>	<p>Irish Prison Health Service, GPs working in prisons, HSE NHCTP, hospital HCV services (providing in-reach)</p>	<p>HSE NHCTP, NGOs working in prisons e.g. the Red Cross Prison Programme – Community Health and First Aid Diagnostic laboratories</p>	<p>Consult with stakeholders and disseminate final recommendations. Support IPS in providing education, awareness raising and testing. Advocate for improved transition of prisoners on release, e.g. GMS application prior to discharge.</p>
<p>One-off testing of ex-prisoners should be considered, although implementation may be difficult.</p>					
<p>There is no specific health service for former prisoners. They may be difficult to reach.</p>	<p>Some prisoners may attend other services in the community where testing could be offered.</p>	<p>Awareness raising amongst public and healthcare professionals. Peer groups to have awareness sessions. Probation services could recommend.</p>	<p>HSE Primary Care/ social inclusion. Probation services</p>	<p>GPs Support services such as Red Cross Prison Programme – Community Health and First Aid with ex-prisoners</p>	<p>Awareness raising for public/ risk group.</p>
<p>Good practice points:</p>					
<p>Education on the risk of HCV should be provided upon entry into prison.</p>					
<p>There may be literacy issues.</p>	<p>Peer education by groups such as Red Cross taking place for other health topics</p>	<p>Development of educational materials, peer education session e.g. by Red Cross.</p>	<p>Irish Prison Health Service; HSE Primary Care/ Social inclusion</p>	<p>NGOs working in prisons e.g. the Red Cross</p>	
<p>At the time of committal, the interviewing nurse or doctor is best placed to identify the optimal time to carry out HCV screening on an individual prisoner.</p>					
<p>Irish Prison Health Service</p>					

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
Continuity of care and/or treatment on discharge from prison should be considered. This should be considered as part of discharge planning. Continuity of care on entry to prison should also be considered.	Probation services. Clinical services within some prisons provided by local hospitals. Existing relationships between prison health services and some addiction services.	Templates for discharge with relevant information. Care worker to liaise with patients during transition. Peer support on discharge to remain in care. Ensure patient has a GP prior to discharge from prison.	Irish Prison Health Service, HSE NHCTP, Probation services	Red Cross	Advocate for improved transition of prisoners on release, e.g. GMS application prior to discharge.
Communication about test results or treatment should occur between the prison health services and the prisoner's GP, or other services attended by the prisoner such as addiction services or psychiatric services.					
On release the place of follow-up may not be known.		Medical discharge planning to be part of release planning. Template letters from prison health service to other services. Ensure prisoner has a GP prior to release.	Irish Prison Health Service, addiction services, GPs, probation services	Community groups	Advocate for improved transition of prisoners on release, e.g. GMS application prior to discharge.
Confidentiality at the time of offering screening, during testing, and when communicating results of testing should be ensured as far as possible while still ensuring a safe environment for prison healthcare staff.					
Safety of staff to be maintained			Irish Prison Health Service staff and prison staff		
Recommendation 9 - People who are homeless					
Homeless people who have a history of engaging in risk behaviours associated with HCV transmission, or who have had a potential HCV risk exposure, should be offered screening.	A number of services are already offering testing and/or education to homeless people. In some areas there are outreach health services for homeless people (e.g. SafetyNet). Homeless people registered for emergency accommodation are assigned key workers. HepCare Europe project offering PoC testing to at-risk populations including homeless. MedLIS	Continue with and expand current initiatives. Awareness raising amongst public and HCPs, organisations providing health services for the homeless. Development of educational materials for homeless. Information sessions in homeless centres. Outreach/ mobile services for testing.	HSE Social Inclusion/ Primary Care to continue their own services and to continue to support NGOs that run services providing clinical, social or education, GPs, prevention services	NGOs, New consultants responsible for vulnerable patients in St James's Hospital and Mater Hospital, GPs, homeless services, addiction services, Relevant facilities and societies (ICGP, IDSI, ISCM, SSSTDI, Public Health, Pathology) Diagnostic laboratories	Consult and disseminate recommendations to stakeholders. Prepare educational material in different languages. Advocate with HSE for extension of NHCTP to cover entire spectrum of HCV care.

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
Recommendation 10 - Migrants					
Migrants from a country with an intermediate to high prevalence of HCV (anti-HCV $\geq 2\%$) should be offered screening.					
There is no dedicated health service for screening of migrants except for those who are asylum seekers. Many migrants may have poor access to health services due to language, financial, cultural, or legal barriers. Migrants are a diverse group with varying health needs and social circumstances. Different strategies are needed for different groups. There may be a lack of perceived risk. Fear of stigmatising migrants. Access to and payment for testing Laboratory resources.	Asylum seeker and refugee health programme is in place. HSE Social Inclusion/ Primary Care have commissioned SafetyNet to provide outreach services for some newly arrived refugees. This sets a precedent model for outreach services. Migrant screening guidelines are already in place for a range of infectious diseases including HCV (level of 3%). Some GPs are offering services to migrant populations in different languages. New HSE Intercultural Health Strategy is being developed.	Awareness raising amongst public and HCPs. Culturally appropriate information material. Education sessions in community venues frequented by migrants. Outreach testing in community (e.g. religious venues, cultural centres). Establishment by HSE of a testing service or HSE support for outreach testing services by NGOs as for HIV. Translation and interpretation services. Targeted programmes within GP. Inclusion in the new intercultural health strategy	HSE Social Inclusion/ Primary Care; GPs, asylum health services; antenatal services; NGOs commissioned to provide care	Migrant organisations including religious and cultural groups, NGOs, Relevant faculties and societies (ICGP, Public Health, IDSI) Laboratories	Consult with stakeholders and disseminate final recommendations; Awareness raising for public/ risk group Prepare educational material in different languages. Advocate with HSE for extension of NHCTP to cover entire spectrum of HCV care. Advocate for improved healthcare access for migrants
Recommendation 11 – People who received medical treatment abroad					
Screening for HCV should be considered in people who have received medical or dental treatment in countries where HCV is common (anti-HCV prevalence $\geq 2\%$) and where infection control may be poor.					
Payment for testing Difficulty in assessing the risk Lack of awareness of the risk		Awareness raising amongst public and HCPs	GPs	Relevant faculties and societies (ICGP, Public Health, IDSI)	Consult and disseminate recommendations to stakeholders Awareness raising for public/ risk group
Recommendation 12 – Those who have tattoos or body piercings					
Screening should be considered for all those with a tattoo. Those most at risk of having acquired HCV through tattooing are those who received tattoos a number of decades ago, in non-professional settings, in prisons, or in other circumstances where infection control was poor.					
The number of people in Ireland with a tattoo is not known but is likely to be large. Payment for screening. Lack of perceived risk. Negative reaction by tattooists or those with a tattoo. Laboratory resources.	Tattooing is one of the risk factors included in screening questions in maternity services at present.	It is not anticipated that an active screening programme be implemented for this group but that screening is offered on an opportunistic basis or as part of other screening programmes (e.g. antenatal). Awareness raising amongst public and HCPs.	GPs, maternity services, STI clinics	Department of Health in publishing infection prevention and control guidance Relevant faculties and societies (ICGP, O&G Society, IDSI, ISCM, SSSDI), Public Health, Pathology Diagnostic laboratories	Consult with stakeholders and disseminate final recommendations. Awareness raising for public/ risk group. Approach a maternity unit to study the proportion of women booking for antenatal care who have tattoos or other risk factors for HCV.

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
Recommendation 13 – Heterosexual partners of those who are HCV positive					
<p>In general, screening of sexual partners of known HCV 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:</p> <p>If the HCV-infected case is PWID</p> <p>If the case or contact is also HIV positive.</p> <p>Sexual contacts of PWID, but where HCV status is unknown or where there is evidence of resolved infection, should be considered for screening. If testing of a sexual partner of a HCV-infected case is requested for reassurance, then this should not be denied.</p>					
Willingness to disclose injecting drug use status of partner. Resources for follow-up of sexual contacts of injecting drug users. Access to and payment for testing.	Current practice not to test sexual contacts MedLIS HIV positive people should be screened annually as part of HIV care Contact tracing system to be developed by National Sexual Health Strategy	Information material on the risk of sexual transmission for cases. Raise awareness amongst HCPs. Where resources allow, active contact tracing could be undertaken by Public Health, primary care or other services. Where resources are not available, a passive approach could be taken where the index case advises contacts of the need for screening. Screening of sexual contact of an IDU is likely to be done on an opportunistic basis	HIV clinics, STI/GUM clinics, GPs	Sexual Health Strategy, respective faculties and societies.	Consult and disseminate recommendations to stakeholders
Recommendation 14 - MSM					
<p>HIV positive MSM should be screened at least annually for HCV. More frequent testing may be required if clinically indicated e.g. an unexplained rise in ALT, a diagnosis of a new STI, or if a risk exposure has occurred such as a contact with a known case of HCV, or other risk behaviours including chemsex.</p>					
Nil expected as it is current practice	Current practice MedLIS	Awareness raising amongst public and HCPs. Referral pathways to care for detected cases.	HIV clinics, STI/GUM clinics, GPs	HIV and MSM NGOs, respective faculties and societies, Sexual Health Strategy	Consult and disseminate recommendations to stakeholders
<p>HIV negative MSM should be offered testing annually for HCV as part of an overall STI screen. More frequent testing may be required if clinically indicated eg. an unexplained rise in ALT, a diagnosis of a new STI, or if a risk exposure has occurred such as a contact with a known case of HCV, or other risk behaviours including chemsex.</p>					
Thought to be current practice in most STI/GUM clinics but not stated as national policy Laboratory resources	Thought to be current practice in most STI/GUM clinics but not stated as national policy MedLIS	Communicate recommendation. Link with National Sexual Health Strategy.	HIV clinics, STI/GUM clinics, GPs	HIV and MSM NGOs, Sexual Health Strategy Relevant faculties and societies (ICGP, IDSI, SSSTDI, Public Health) Laboratories	Consult and disseminate recommendations to stakeholders Awareness raising for public/ risk group

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
Recommendation 15 - People having sexual health screening					
HCV testing should be considered part of routine sexual health screening in the following circumstances: MSM, People who are HIV positive, commercial sex workers, PWID, if indicated by the clinical history, when other risk factors for HCV as outline in this guideline are present.					
Nil expected as current practice	Current practice	Awareness raising amongst public and HCPs. Referral pathways to care for detected cases.	STI clinics, GPs	Sexual Health Strategy, respective faculties and societies.	Consult and disseminate recommendations to stakeholders
Recommendation 16 - People on renal dialysis or who have had a kidney transplant					
Patients commencing, or on maintenance, haemodialysis or peritoneal dialysis should be screened according to the current recommendations of the Standing National Advisory Committee on the Prevention of Transmission of Blood-Borne Diseases in the Health-Care Setting and any ensuing updates from this committee. All patients having a kidney transplant should be tested for HCV by a combined antigen-antibody test or anti-HCV test AND HCV-RNA at three months post-transplant. Patients transplanted before the introduction of the above, unless already known to be HCV positive, should be testing on a one-off basis by a combined antigen-antibody test or anti-HCV test AND HCV-RNA to out rule the possible acquisition of HCV infection through past treatment for renal failure.					
Nil expected for those on dialysis; For testing post-transplant there may be a lack of awareness amongst HCPs. There may be a perception that the risk was due to surgery rather than pre-surgery dialysis.	Screening during dialysis is current practice. Screening post-transplant was previously recommended although compliance is unknown. MedLIS	Annual audits of compliance in dialysis units should be undertaken. Awareness raising amongst HCPs and transplant units re post-transplant screening	Dialysis units, transplant centres, ODTI	Irish Kidney Association (IKA) and other patient groups, GPs Relevant faculties and societies (ICGP, IDSI, micro, renal societies, surgical societies) Diagnostic laboratories	Consult with stakeholders and disseminate final recommendations; Awareness raising for public/ risk group
Recommendation 17 and 18 - Recipients of SoHo					
Recipients of blood or blood components in Ireland prior to October 1991 who have not yet been tested should be offered screening. All recipients of anti-D immunoglobulin in Ireland between 1st May 1977 and the end of July 1979, and 1st March 1991 to 18th February 1994 who have not yet been tested should be offered screening. Recipients of plasma derived clotting factor concentrates in Ireland prior to 1992 who have not yet been tested should be offered screening.					
Nil expected.	Majority already screened.	Further screening will be on an opportunistic basis. Raise awareness among public and HCPs.	GPs	Patient support groups, GPs, Relevant faculties and societies (ICGP, IDSI, ISCM, haematology) Laboratories	Consult with stakeholders and disseminate final recommendations; Awareness raising for public/ risk group
Screening for HCV should be considered in recipients of solid organ transplants in Ireland who have not yet been tested (see recommendations on dialysis for recipients of kidney transplants).					
Resistance by HCPs. Lack of awareness of risk by HCPs. Fear of negativity towards transplantation process.	This has been recommended previously for recipients of kidney transplants. Compliance not known	Further screening will be on an opportunistic basis. Raise awareness among public and HCPs.	HSE specialist follow-up services and transplant services	Patient support groups, HPRa and ODTI Laboratories	Disseminate recommendation

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
Recipients of blood components and blood products overseas in any country where a quality assured blood donor screening programme may not have been in place should be offered screening.		Likely to be implemented on an opportunistic basis. Raise awareness among public and HCPs.	GPs, other clinical services attended by patients		Consult with stakeholders and disseminate final recommendations; Awareness raising for public/ risk group
Recommendation 19 - Donors of substances of human origin (SoHO)					
Screening of donors of blood, organ, tissue and cells, including reproductive cells, should at a minimum comply with legislative requirements.					
Nil expected as current practice	Current practice	Nil	IBTS, HPRA, ODTI		
NAT for HCV-RNA of donors of blood should be performed and the results available prior to the use of the donation. The test must be designed and approved for screening of blood donations. NAT for HCV-RNA of donors of tissues and cells, including reproductive cells, and living solid organ donors, should be performed in addition to current legislative requirements.					
The practice in other establishments not known. Other establishments may not be using laboratories currently accredited for NAT. This is not required by legislation. There is no body to ensure implementation of this. Tissues and cells are often imported.	Current practice in IBTS for blood	Discuss with HPRA and ODTI. Awareness raising amongst HCPs and establishments. Establishment of a body to recommend best practice.	HPRA, ODTI; Establishments involved in organ, tissue and cell donations, NVRL or other laboratories currently testing donors.		Advocate with HPRA to recommend NAT testing to tissue establishments as best practice.
For deceased donors of solid organs: Anti-HCV and HCV antigen testing should be done and the results available prior to donation.					
Nil expected.	Current practice in NVRL	Current practice in NVRL	NVRL or other laboratories currently testing deceased donors, transplant centres, transplant co-ordinators, ODTI		
NAT should be considered where feasible. NAT results may not be available prior to transplantation but NAT testing should still be performed to ensure the rapid identification of the recipients of potentially infectious organs.					
Not requested by transplant teams	NVRL supportive of this	Awareness raising amongst healthcare professionals. Support of recommendation by ODTI. National advisory body	NVRL or other laboratories currently testing deceased donors, transplant centres, transplant co-ordinators, ODTI		
Any external laboratories used for microbiological screening of donors should be accredited and comply with the standards of the appropriate regulatory authority. Laboratories, in Ireland should be accredited by the Irish National Accreditation Board (INAB) to undertake testing in compliance with the International Standard ISO 15189.					
Some labs may not have sufficient throughput to maintain standards.	Majority of laboratories compliant with quality assurance procedures	Relevant establishments to ensure they use only accredited laboratories or only import from other establishments which use accredited laboratories. Awareness raising.	Laboratories, regulatory bodies, establishments commissioning laboratory services.		

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
A national advisory committee on the safety of blood, organs and tissues should be established to advise on best practice in relation to donor selection, and testing of potential donors. Will need to be established by the DoH	Similar committees exist for other health issues e.g. NIAC.	Advise DoH on recommendation	Department of Health	HSE, HPRA, ODTH, Micro, relevant facilities and societies (ICGP, IDSI, micro, haematology)	
Recommendation 20 - Birth cohort screening for HCV					
Birth cohort screening cannot be recommended at present due to the likely substantial cost implications and uncertain benefit. Such a programme would require a full health technology assessment (HTA) and approval of funding prior to being considered.					
No recommendation made	No recommendation made	Inform Department of Health (DoH) of recommendation for a HTA	DoH, Health Information and Quality Authority (HIQA)		Inform DoH of recommendation for a HTA
Recommendation 21 - HCWs					
All new HCWs should be offered HCV screening on a voluntary basis.					
Not current practice. Not all new HCWs will require a blood sample to which HCV testing could be added. Additional occupational health resources. Cost to occupational health Laboratory resources.	All new HCWs do have an occupational health assessment which can require a blood sample to be done for other tests (e.g. HBV immunity).	Incorporation into pre-employment occupational health review. Referral pathways to care for detected cases. Clear protocol in place for employment if positive.	Occupational health, HSE	Relevant facilities and societies (Occ health), unions, private healthcare providers Laboratories	Consult with stakeholders and disseminate final recommendations; Awareness raising for public/ risk group
Mandatory HCV screening of all new HCWs who will perform EPPs is recommended.					
	Current practice although compliance not known. A new national HR IT system is being established for NCHDs which will allow checking of results on transfer to another hospital. MedLIS		Occupational health, HSE	Relevant facilities and societies (surgery, nursing, midwifery), unions Laboratories	Dissemination of recommendations
Existing healthcare workers who perform EPPs and have not yet been screened should be offered HCV screening.					
New practice, may be resistance from HCWs and possible IR issues. Cost to occupational health.		Occupational health in individual units to invite staff for testing or to make testing available for staff on request	Occupational health, HSE	Relevant facilities and societies (surgery, nursing, midwifery), unions Laboratories	Dissemination of recommendations. Liaison with HSE Occupational Health and Human Resources and with healthcare providers in the private sector

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
Mandatory screening of all new healthcare students is recommended.	Healthcare students must currently show evidence of immunity to HBV at start of training.	Inform healthcare training institutes. Referral pathways to care for detected cases.		Laboratories	Dissemination of recommendations
Resistance by universities to implement. Linkage to care of detected cases, particular if a migrant. Impact on studies. Confidentiality. Payment Laboratory resources.					
Interval testing of HCWs who perform EPPs is not recommended. However, HCWs should be informed of their professional responsibility to seek appropriate assessment if any possible risk exposure has occurred.					
Occupational health resources		Incorporation into induction for HCWs doing EPPs. May also need periodic reminders.			
Recommendation 22 - Test and test sequence					
See algorithm					
Recommendation 23 - Frequency of testing					
Individuals who initially test HCV negative but who remain at risk of HCV infection should be offered repeat testing on an annual basis, or six monthly if deemed clinically appropriate.					
Not all those at risk will be regularly attending services If attending different services testing history may not be known	Currently recommended in OST treatment guidelines MedLIS would allow access to testing history	IT systems which flagged when repeat testing due	Mainly addiction services		Consult with stakeholders and disseminate final recommendations; Awareness raising for public/ risk group
Recommendation 24 and 25 - Specimen type and RDT/ POCTs					
Serum and plasma are the preferred specimen types for screening and diagnostic testing for HCV infection using quality assured assays.					
Other specimen types may be currently used in research settings.	Current practice in clinical practice	Raise awareness among HCPs and laboratories	All those who test people for HCV; NVRL; other diagnostic laboratories	Relevant facilities and societies (ICGP, IDSI, Public Health, ISCM/ pathology)	Consult and disseminate recommendations to stakeholders

Barriers to implementation	Facilitators to implementation	Possible actions to facilitate screening	Who will be responsible for implementation	Other stakeholders	Specific action required by GDG
<p>Screening and diagnostic testing for HCV infection should not be performed on oral fluid samples due to the low sensitivity and positive predictive value.</p> <p>Other specimen types may be currently used in research settings.</p>		<p>Raise awareness among HCPs and laboratories</p>	<p>All those who test people for HCV; NVRL; other diagnostic laboratories</p>	<p>Relevant faculties and societies (ICGP, IDSI, ISCM, Faculty of Public Health Medicine, Faculty of Pathology)</p>	<p>Consult and disseminate recommendations to stakeholders</p>
<p>Where concerns exist about hard-to-reach populations or linkage-to-care then consideration could be given to using approved (e.g. CE marked) RDT/PoC tests on blood specimens.</p>			<p>Individual HCPs or services planning to introduce these and the NVRL</p>		
<p>If RDT/PoC tests are introduced into standard clinical practice then a quality assurance programme should be established that addresses internal quality control and external quality assurance.</p> <p>Will require collaboration between the service offering testing and an accredited laboratory</p>			<p>Individual HCPs or services planning to introduce these and the NVRL</p>		

Appendix 12: Summary of information services, tools, and services to assist implementation

Screening related leaflets and promotional material is in development and will be available from:
<http://www.hpsc.ie/A-Z/Hepatitis/HepatitisC/Guidance/Backgrounddocuments/>

Information sources on HCV for patients/ risk groups and healthcare professionals

Information on HCV is available from the following sources:

- Health Protection Surveillance Centre
<http://www.hpsc.ie/a-z/hepatitis/hepatisc/factsheetleaflets/>
- Health Service Executive
<http://www.hse.ie/eng/health/az/H/Hepatitis-C/Treating-hepatitis-C.html>
- Hepatitis C Partnership
<http://hepinfo.ie/hepc-information.aspx>
- National Hepatitis C Treatment Programme
<http://www.hse.ie/eng/about/Who/primarycare/hepcprogramme%20.html>
- European Centre for Disease Prevention and Control
http://ecdc.europa.eu/en/healthtopics/hepatitis_C/factsheet-general-public/Pages/factsheet-general-public.aspx
- World Health Organization
Hepatitis: <http://www.who.int/hepatitis/en/>
Hepatitis C factsheet: <http://www.who.int/mediacentre/factsheets/fs164/en/>
- World Hepatitis Alliance
<http://www.worldhepatitisalliance.org/what-viral-hepatitis-0>

Services involved in HCV screening and care

A plan for implementation of this guideline is outlined in Appendix 11. This builds on the work that is already being undertaken by a range of HSE services, non-governmental organisations (NGOs), and health and social care professionals, peer workers and volunteers in relation to HCV screening and care. Some of the key services or organisations providing services are described below. Please note that this list is not exhaustive.

NGOs

Community Response

Community Response is based in the Liberties in the south inner city of Dublin and provides alcohol and HCV services. It offers a range of services in relation to HCV such as group support, one-to-one support and referral pathways to treatment. They also deliver outreach educational support such as in homeless centres. www.communityresponse.ie

Hepatitis C Partnership

The Hepatitis C Partnership is a network of stakeholders, from statutory, community and voluntary sectors, working in the area of HCV. Organisations in the network include: Community Response, Irish Haemophilia Society, Coolmine Drug Treatment, UISCE (Union for Improved Services Communication and Training), the HSE Addiction Services, the National Drug Treatment Centre. The Partnership provides

information and support for all those affected by HCV and those working with them. They undertake and participate in public awareness campaigns which promote testing, treatment and general health promotion in relation to HCV. <http://hepinfo.ie/>

SafetyNet

The SafetyNet service provides primary care services to people who are homeless and to other marginalised members of society. It operates clinics in a range of homeless and addiction centres across Dublin. It also operates a mobile service. <http://primarycaresafetynet.ie/services>

Crosscare

Crosscare is a social support service which provides a range of social care, community and youth work services across the Dublin Archdiocese. They offer residential and day services for the homeless, and also an alcohol and drug programme which provides counselling and support. <http://www.crosscare.ie/index.php/about-us>

Irish Red Cross

The Irish Red Cross Prison Programme - Community Based Health and First Aid offers peer to peer education in prisons on a range of health topics including hepatitis. Education is delivered by Irish Red Cross Volunteer Inmates. The programme operates under a partnership of the Irish Red Cross, the Irish Prison Service and Education and Training Boards (ETBs). <https://www.redcross.ie/CBHFA>

Dublin Simon Community

In addition to the Soup Run, which goes out 365 nights of the year, Dublin Simon Community provide many services which aim to help those who are sleeping rough on the streets, people who are in their own accommodation but at risk of homelessness and those who are at any of the stages in between. In 2003, Dublin Simon expanded into addiction treatment services for homeless clients, opening up the first Residential Treatment and Recovery Centre specifically for people who were homeless or at risk of becoming homeless. In 2012, Simon further expanded the service and added a HIV respite / stabilisation unit. In 2017 they expanded the remit of this unit to include all BBVs. Presently the treatment service has 64 beds that offer an array of services such as detox, recovery, BBV Respite/Stabilisation, counselling. Other support services such as gyms, yoga, health, wellbeing, literacy, personal development, arts drama, dance and social enterprise complete the holistic approach and are all provided onsite.

HIV Ireland

HIV Ireland was established to improve conditions for people living with HIV and acquired immunodeficiency syndrome (AIDS), their families and their caregivers, while actively promoting HIV and sexual health awareness in the general population. They offer HIV and STI testing, including HCV in their base office and also in range of locations including Baleskin Reception Centre, and the Front Door in Drogheda. <http://www.hivireland.ie/>

GOSHH

GOSHH is a regional project working in the mid-west of Ireland in the areas of gender, orientation, sexual health, and HIV and hepatitis. The range of services to people living with HCV include a peer support group, free counselling, personal support, HCV testing, accompaniment to attend appointments, information and training for professionals. <http://goshh.ie/>

The Mid Western Regional HCV Network

The Mid Western Regional HCV Network is a collective of agencies whose service users are affected by HCV. Their aim is to improve the outcomes for people living with HCV through advocacy, awareness raising, information sharing and upskilling of staff teams. Members include people living with HCV, Novas, the Ana Liffey Drug Project, Health Equity Partnership, GOSHH, and drug and alcohol clinics.

Other organisations providing support to specific groups

There are a number of other organisations providing support to those who were exposed to HCV in the healthcare setting including:

- The Irish Kidney Association (IKA) (<http://www.ika.ie>)
- Irish Haemophilia Society (<http://www.haemophilia.ie/>)
- Transfusion Positive is a support and action group for people infected with the Hepatitis C Virus as a direct result of having received contaminated blood or blood products administered within the Irish State. Their aim is to provide a supportive and informative network and to be proactive at all times in advocating on behalf of the health needs of our members. (<http://www.transfusionpositive.ie/index.html>)

HSE Services

HSE National Hepatitis C Treatment Programme

The National Hepatitis C Treatment Programme (HSE NHCTP) is a multi-annual public health plan working collaboratively with stakeholders in the treatment, management and care of people who have HCV infection or are at risk of HCV. Its aim is to provide access to treatment across a range of healthcare settings to all persons infected with HCV over the coming years so that it becomes a rare disease in Ireland by 2030. The HSE NHCTP is responsible for devising strategies to help improve surveillance, the identification of patients, education, and pathways to care and treatment. New integrated models of treatment and care including shared care across community and acute hospital setting, stand-alone HCV treatment programmes in primary care healthcare services including drug treatment centres and prisons are being explored.

The HSE NHCTP is supported by a Programme Advisory Group (PAG) whose role is to provide strategic advice and direction in relation to the implementation of the programme over the coming years. Clinical advice to the programme is provided through a Clinical Advisory Group (CAG). The CAG has developed and recommended clinical guidelines for the HSE NHCTP and will continue to revise and recommend new clinical guidelines in line with best practice and international developments throughout the duration of the treatment programme.

The HSE NHCTP is also supported by a national HCV disease and treatment registry. The registry is pivotal in providing information and data to the programme on numbers being treated, numbers approved for treatment, duration of treatment, treatment data (throughput) per treatment site, regimens used, outcome data (SVR rates), relapse rates, discontinuation rates and other clinical/performance datasets. The registry is also an invaluable source of data and information to clinicians and researchers giving real world data on patient outcomes etc. <http://www.hse.ie/eng/about/Who/primarycare/hepcprogramme%20.html>

HSE Social Inclusion

The HSE National Social Inclusion Office supports equity of access to services and aims to improve the health outcomes of minority and vulnerable groups. The Social Inclusion Office works in partnership with other sectors of the HSE and external bodies to support a range of services for vulnerable groups. It supports the HSE Homeless Service which oversees and manages a range of services and supports provided through outreach specialist services, specialised teams and individuals, or by services contracted through the voluntary sector. Examples of these services include emergency, supported or long term accommodation units or facilities, medical homeless outreach clinics, community houses, settlement services, drop in and day centres.

It is responsible for the delivery of a wide range of national policy objectives outlined in the National Drugs Strategy (interim) 2009-2016. It also supports the National Addiction Training Programme and the Pharmacy Needle Exchange programme.

In relation to migrants, it is responsible for implementation of the HSE National Intercultural Health Strategy 2007-12. It also is responsible for the health needs of refugees settled in Ireland under arrangements agreed with the United Nations High Commissioner for Refugees (UNHCR) and supports asylum seekers access to health services in association with the Reception and Integration Agency. It also supports the health services to provide services in a variety of languages.

Mobile health screening unit

In 2016, HSE Social Inclusion received funding of €1,460,000 allocated from dormant accounts to develop a mobile health screening unit. This unit aims to provide an accessible, targeted screening and primary care service to vulnerable groups including those affected by homelessness, migrants and asylum seekers and people who suffer from addiction.

HSE addiction services

HSE addiction services provide a range of preventative, therapeutic and rehabilitation services for those with substance misuse problems. Addiction services are provided through the Local Health Offices across the country. In addition to opioid substitution therapy, the addiction services provide a range of other services including nursing interventions, counselling and outreach work.

HSE Hepatitis C Liaison Nurse Specialists

The HCV liaison nurse specialists work within the HSE addiction services to deliver care to those with HCV infection. They act as a liaison between the addiction services, other primary care services and specialist care. They also provide education and training on HCV to healthcare professionals and to those attending addiction services.

Methadone prescribing GPs

Opioid substitution treatment (OST) is also provided by GPs in the community. Level 1 GP prescribers treat stabilised opioid dependent persons. Patients are referred to Level 1 GPs from HSE addiction services or a Level 2 GP. Level 2 GP prescribers can assess, initiate treatment, and stabilise opioid dependent people as well as providing maintenance treatment.

HSE Sexual Health Services

HSE public STI screening services offer free STI screening around the country. The Gay Men's Health Service (GMHS) provides services for gay, bisexual and men who have sex with men, through counselling and STI clinical services. The Women's Health Project offers sexual health screening and counselling services, and a methadone and needle exchange programme, to women in prostitution.

The National Sexual Health Strategy 2015-2020 (205) is Ireland's first national framework for sexual health and wellbeing. The strategy contains 71 recommendations across the spectrum of sexual health services. Some of the actions relevant to this guideline include: an evaluation of novel HIV and STI testing services, the development of national HIV and STI testing guidelines, and a review of partner notification procedures.

The Rainbow Clinic

The Rainbow Clinic is the national centre for Paediatric Infectious Diseases/Immunology and for HIV related medicine in children. It is delivered by a multidisciplinary team in Our Lady's Children's Hospital, Crumlin and Temple Street Children's University Hospital. It offers both inpatient and outpatient services in both hospitals for investigation, diagnosis and management of paediatric infectious disease and immune deficiency. Key areas include the prevention of mother to child transmission of HIV, management of children with HIV, HBV, HCV, TB, congenital and other infections.

HepCare Europe project

HepCare Europe, a European Union-funded initiative, is a multi-country collaboration developing and evaluating targeted community-based interventions for vulnerable groups of individuals living with HCV. Ireland's participation is led by the Mater Misericordiae University Hospital, general practitioners in Dublin's north inner city and University College Dublin. It aims to improve the efficacy of HCV treatment by providing an 'integrated care' model for HCV treatment based on the joint participation of primary and speciality care practitioners. <http://www.ucd.ie/medicine/hepcare/>

The main branches of HepCare are:

- HepCheck which seeks to identify patients not accessing care by using point of care rapid tests in hard to reach settings (homeless, in shelters, prisons, etc.)
- HepLink seeks to develop an integrated model of HCV care
- HepEd will develop and implement a multidisciplinary inter-professional education resource for healthcare professionals on HCV care.
- HepFriend recognises the importance of peer support to ensure treatment adherence and will recruit, train and support credible advocates to support the clinical care team
- HepCost will assess the cost-effectiveness of the specific case-finding interventions across different EU countries to inform the development of public health policy in member states.

The HepCare Ireland team is focusing on HepCheck, HepLink and HepFriend. They are working in collaboration with Merchant's Quay and SafetyNet Primary Care Services, HSE Addiction Services, Community Response, HIV Ireland and the Ireland East Hospital Group. A number of projects have already been initiated. A liaison nurse is performing fibroscan tests to evaluate patients' HCV status in general practices, addiction clinics, and prisons, with the aim to improve the currently suboptimal level of referrals to secondary care. Community nurse outreach and peer advocacy support projects are offering testing in the community.

Appendix 13: Economic impact report

Part A: Review of economic literature

Methods

Review question

Patient, intervention, comparator, outcome (PICO) format for review question:

Population: Those unaware of HCV status/ populations listed in the key questions

Intervention: Screening for HCV

Comparison: No screening, screening using different methodology, setting or frequency, targeted screening vs. universal screening

Outcome: Compares cost to outcomes

Search Strategy

A systematic review for relevant literature was conducted using the following databases and information sources:

- The medical database Medline
- Database of Abstracts of Reviews of Effects, NHS Economic Evaluation Database and Health Technology Assessment Database using the University of York, Centre for Reviews and Dissemination search tool
- Reference lists of relevant articles and reviews.

Search terms were combinations of free text and medical subject heading terms (MeSH). The search strategies employed are detailed below.

Search limits

The review was limited to articles published between January 2000 and December 2015 and published in English.

Inclusion criteria

Studies were included if they were:

- Published in English
- Published between January 2000 and 2015
- Compared costs to health outcomes
- The intervention was related to one of the guideline key questions.

Studies were excluded if they:

- Reported on an economic evaluation of screening of substances of human origin or their donors only*
- Reported on an economic evaluation of screening of dialysis patients only*
- Reported on an economic evaluation of screening of healthcare exposure only
- Reported on costs alone
- Were conducted in a high-endemicity country.

*These were excluded as screening in these contexts is defined by legislation or existing guidelines already in practice.

Conduct of the review

Due to the large number of records identified, a title review was first conducted to remove all obviously irrelevant records prior to abstracts being screened for relevance. Abstracts were then reviewed to

identify studies which met the inclusion criteria. The full text of potentially eligible papers was then reviewed to confirm eligibility for inclusion.

Articles which, after full text review, met the inclusion criteria were quality appraised using the Scottish Intercollegiate Guidelines Network checklist for economic evaluations.

Presentation of results

A qualitative analysis of results is presented here. Costs presented in italics and brackets represent the cost converted and inflated to Irish Euro (€) 2014.

Results

Figure A 3 shows the results of the review process. After removal of duplicates 1,949 records were identified. Sixty-nine records underwent abstract review of which 45 were selected for full text review. Of these, 33 were included in the final qualitative analysis, four of which were systematic reviews. The most recent systematic review was updated to July 2015.

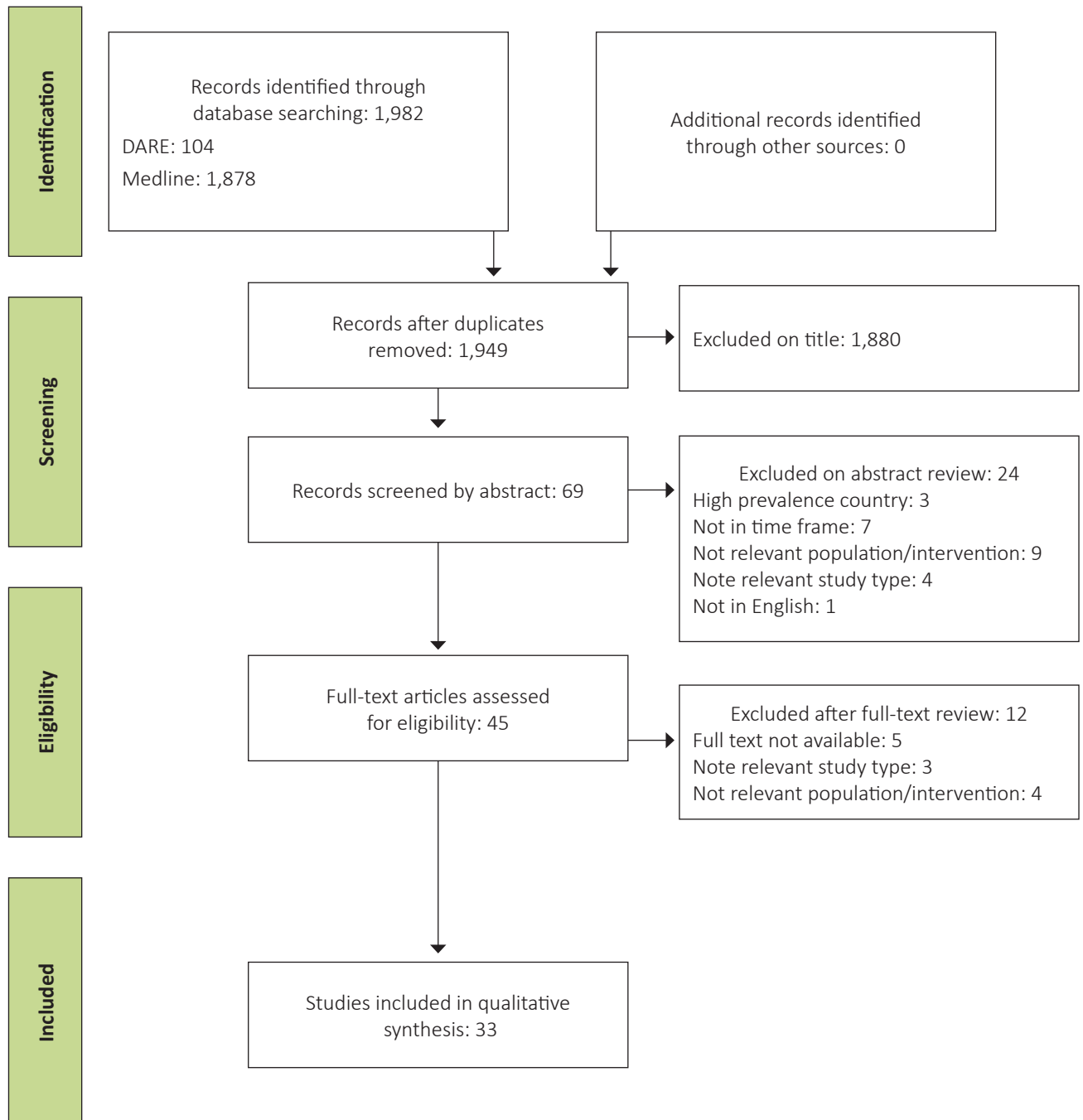


Figure A 3: PRISMA flow diagram of review of economic literature.

Pregnant women

Three studies reporting on cost-effectiveness of HCV screening in the antenatal setting were identified. Studies were from the US, the UK and the Netherlands.

Plunkett et al. (2005) compared universal screening of low risk asymptomatic pregnant women with and without a caesarean delivery for positive cases to a scenario without screening using a Markov model (206). The study was based on a population of HIV negative women without risk factors receiving routine antenatal care in the US. Positive cases were treated with pegylated-interferon and ribavirin (Peg-IFN+RBV). A lifetime time horizon was used, and costs and utilities for both mother and child considered. Costs and utilities were discounted at 3%. The base case assumed a prevalence of 1%, a rate of vertical transmission of 0% for elective caesarean section, and 7.7% for emergency section or vaginal delivery. Neither screening scenario was found to be cost-effective. Screening followed by caesarean section delivery and treatment of mother had an incremental cost-effectiveness ratio (ICER) of \$1,170,000 (€1,504,411) per quality adjusted life year (QALY) gained. When examined separately for mother and child, screening followed by caesarean had an ICER of \$3,019/ QALY (€3,882) for the child, but for the mother it added to the cost and decreased the utility due to the disutility of a caesarean. The screening without caesarean section delivery scenario was dominated (more costly and less effective) by the no screening scenario. Sensitivity analysis did not result in the interventions being cost-effective.

In the Netherlands, *Urbanus et al.* (2013) analysed the effect of adding universal screening, or screening of non-Western migrants to current antenatal screening programmes using a Markov model (207). They also considered various subsequent treatment scenarios. Costs were discounted at a rate of 4% and life years at a rate of 1.5%. The base case assumed a prevalence of 0.2% in all women, and 0.43% in non-Western women. The scenario of universal screening and treatment with IFN+RBV for genotypes 2 to 4, with the addition of a protease inhibitor (PI) for genotype 1 had an ICER of €52,473 (€58,265) while screening of non-Western migrants had an ICER of €47,113 (€52,314). They reported that a reduction in treatment costs to €3,750 would make both screening options cost-effective at a threshold of €20,000. In a different scenario where all genotypes received PIs, universal screening had an ICER of €88,162, (€97,894) and screening of non-western migrants had an ICER of €88,005 (€97,720). Sensitivity analysis showed that the ICER for both groups was most sensitive to changes in transition probabilities to cirrhosis, followed by treatment costs and successful treatment outcome.

In the UK, *Selvapatt et al* (2015) used the results of a 10 year universal screening programme in a London unit to determine the cost-effectiveness of this strategy (208). This programme found that of 35,355 women screened, 136 (0.38%) were anti-HCV positive, 78 (0.22%) were viraemic with 44 (0.12%) new chronic infections identified. Of these new infections, 11 had a history of injecting drug use. It is also reported that 14 were from the UK, 14 from Eastern Europe, three from Western Europe, four from Africa and nine from Asia. The model used a discount rate of 3% for costs and utilities. Based on treatment with IFN+RBV, simeprevir+IFN+RBV for all, or simeprevir+IFN+RBV for IFN+RBV treatment failures, universal screening was found to be cost-effective with ICERs of £2,400 (€2,537), £9,139 (€11,3641) and £3,105 (€3,861) respectively. Screening was found to be cost-effective under all sensitivity analyses performed. It was most sensitive to the prevalence of infection.

Summary

While one recent study from the UK showed universal antenatal screening to be cost-effective, other studies did not find universal screening cost-effective. Underlying differences in the demographics of antenatal populations will likely impact on the cost-effectiveness of universal antenatal screening.

Prisoners

Three studies of screening in the prison setting were identified. All studies were UK based. In the most recent study, *Martin et al. (2013)* performed a cost utility analysis of introducing dried blood spot (DBS) testing for current or former PWID in the prison setting (209). They assumed a 2.6 fold increase in the uptake of testing with the availability of DBS testing. They estimated an ICER of £59,400 (€77,874)/QALY gained. DBS testing in prison was not cost-effective without continuity of treatment between prison and the community. If continuity of care of >40% was ensured, the ICER would fall to below £20,000.

Sutton et al. (2008) determined that offering screening to all prisoners at reception was not cost-effective with an ICER of £54,852 (€88,558)/QALY gained (210).

Castelnuovo et al. (2006) examined the impact of two different case finding strategies in the prison setting (211). In one strategy new entrants received a general lecture on BBVs during induction. Prisoners were then offered an opportunity to make an appointment for individual discussion and confidential testing. It was assumed that 8.5% would be tested with 16% of those testing would be anti-HCV positive. This strategy had an ICER of £20,083 (€33,586). In the second scenario the lecture focused on intravenous drug use as a risk factor for HCV. Here it was assumed that 12% would be tested and 42% of these would be anti-HCV positive. The ICER in this scenario was £16,484 (€26,613).

Sutton et al (2006) compared the cost per chronic case detected for a range of testing scenarios based on verbal screening (212). They found that testing based on a negative response to verbal screen on having a past positive test, and positive response to a verbal screen on ever having injected illicit drugs was the most cost-effective strategy with an incremental cost of £2,102 (€3,394) per chronic case detected. The verbal screen based on ever having injected illicit drugs had in an incremental cost of £16,625 (€26,841), while no verbal screening had an incremental cost of £6,338 (€10,234). Offering screening based on a negative response to a verbal question on past positive test was dominated.

Summary

The results from economic evaluations of screening of prisoners vary. Strategies targeting prisoners with a history of IDU appear to be more cost-effective and less costly to implement. It appears that the cost-effectiveness of screening of prisoners is dependent on access to treatment, and when there is continuity of care after release, screening may be cost-effective.

Migrants

One study from the UK was identified which analysed an intervention aimed at migrants in general practice (213). Migrants from the Indian sub-continent registered with GPs were invited through a letter to opt out of the programme. Those who did not opt out were telephoned and invited for testing. The model was based on a prevalence of 3.2% in the target population and a testing rate of 20%. An ICER of £23,200 (€30,415)/QALY was determined for the base case. The ICER was found to be sensitive to the prevalence, intervention cost, uptake of screening, and the referral and treatment rate.

Birth cohort screening

A number of studies identified in the economic literature review evaluated birth cohort screening. Two systematic reviews were also identified which summarised economic evaluations of birth cohort screening (146, 214). Most identified studies were from the USA, with one from Italy and one from Canada. Studies compared birth cohort screening to either no screening or risk based screening in the particular age cohort.

McGarry et al. (2012) performed a CUA using a Markov model on a hypothetical cohort in the US (215). They compared a risk based screening approach to birth cohort screening of those born between 1946 and 1970. The birth cohort screening approach would last 5 years and then return to risk based screening. A lifetime time horizon was used. A payer's perspective was used and only direct medical costs were considered. Cost and utilities were discounted at 3%. Screening was with enzyme linked immunoassay (ELISA) followed by HCV-RNA PCR if positive. They assumed eligible patients were treated with Peg-IFN+RBV, with genotype 1 patients receiving DAA combination therapy. It was assumed that over 5 years all eligible persons were screened. Birth cohort screening resulted in an ICER of \$37,700 (€37,073)/QALY gained compared to risk based screening. Sensitivity analyses showed that the ICER was sensitive to the reducing the time horizon, treatment rates and treatment efficacy.

McEwan et al. (2013) used a Markov model to compare risk based screening to birth cohort testing in the US based on a birth cohort of 1945 to 1965 (216). They assumed a healthcare payer's perspective and included only direct medical costs. A lifetime horizon was used. Costs and utilities were discounted at 3.5%. Birth cohort screening was found to be cost-effectiveness with an ICER of \$28,602 (€26,331). This assumed 91% of the population is tested, and at least 278,000, 26% of identified population, were treated to generate sufficient cost offsets and QALY gains at a willingness to pay threshold of \$50,000. Cost-effectiveness was optimised when patients were treated immediately and those with more advanced disease are prioritised.

Rein et al. (2012) used a Markov model to compare a range of screening and treatment strategies in a US population born between 1945 and 1965 (217). They used a societal perspective and lifetime time horizon. Scenarios included no screening, risk based screening and Peg-IFN-RBV treatment; birth cohort screening and Peg-IFN-RBV treatment; and birth cohort screening with DAA treatment for genotype 1. Screening was with a one-off anti-HCV. Birth-cohort screening followed by Peg-IFN-RBV resulted in an ICER of US \$15,700 (€15,966)/QALY gained compared to risk based screening. When birth cohort screening was followed by DAA treatment for genotype one an ICER of \$35,700 (€36,304)/QALY resulted compared to risk based screening and \$73,700 (€74,947) when compared to birth cohort screening with Peg-IFN+RBV. Sensitivity analysis showed the ICER to be most sensitive to sustained viral response of antiviral therapy, the cost of therapy, the discount rate, and the QALY losses assigned to disease states.

Coffin et al. (2012) used a Markov model to compare risk based screening, general population (20-69 year olds) screening and birth cohort screening (1945 -1965) (218). A payer's perspective was taken and only direct medical costs considered. A lifetime time horizon and a discount rate of 3% were used. General population screening resulted in an ICER of between \$7900 and \$49000 (€7,769 and €48,185) depending on uptake and disease progression compared to risk based screening. The birth-cohort scenario which assumed 15% of those born between 1945 and 1965 were screened had an ICER of \$5400 (€5,310) compared to risk based screening and dominated general population screening scenarios.

Liu et al. (2013) undertook CUA using a Markov model. Costs included healthcare costs including out-of-pocket costs (219). The population included the general population aged between 40 and 74 years. They compared no screening and standard treatment to risk based screening and birth cohort screening with various treatment regimens (standard therapy (Peg-IFN+RBV), IL28B guided triple therapy (Peg-IFN+RBV+PI), and universal triple therapy. One time screening was undertaken at a routine medical visit with an ELISA, followed by two ELISAs, a RIBA, and an RNA test in those initially positive.

Birth cohort screening with triple universal triple therapy and IL28B guided triple therapy had ICERs of US \$65,749 and US \$60,590 (€64,656 and €59,582) respectively compared to no screening and standard therapy. No screening and IL28B guided triple therapy had an ICER of \$50417 (€49,632) compared to no screening and standard therapy. Other scenarios were dominated by the reference scenario of no screening and standard therapy. The age of the target population and disease prevalence were significant

on sensitivity analysis. The author's concluded that one time, birth cohort (40-64 years) screening of asymptomatic adults is likely to be cost-effective provided healthcare system has capacity to deliver prompt treatment and appropriate follow-up care.

Ruggeri et al. (2013) used a CUA to compare no screening and treatment of patients with cirrhosis of HCC to screening of the general population aged 35 years and older in Italy (220). A health service perspective and a lifetime horizon were used. Costs and utilities were discounted at 3.5%. Screening was with anti-HCV Ab followed by HCV-RNA PCR if positive. Treatment was Peg-IFN+RBV. An ICER of €5,171 (not adjusted)/ QALY gained was determined compared to no screening. Results were sensitive to the age of the target population, the prevalence, and the time horizon used.

Wong et al. (2015) undertook a CUA based on a Canadian monoinfected hypothetical cohort (221). They compared no screening to one-off general population screening of those aged 25-64, and no screening to one-off screening of those aged 45-64. For both age groups various treatment scenarios were used including: Peg-IFN+RBV; simeprevir-based combination therapy (genotype 1), sofosbuvir-based combination therapy (genotype 2 and 3) or Peg-IFN+RBV (other genotypes); and a third scenario where patients with genotype one were treated with ABT-450-based interferon-free combination therapy. In the screening arms individuals were offered screening by a primary care physician at a visit for another reason. Screening was by anti-HCV followed by HCV-RNA if positive. A payer's perspective was used. Costs and benefits were discounted at 5%.

The ICER for screening of the 45-64 year age cohort ranged between CA \$34,359 and CA \$55,151 (€23,394 and €37,551; assuming cost year of 2013) compared to no screening. For the 25-64 year age cohort screening followed by treatment with Peg-IFN+RBV had an ICER of \$38,117 (€25,953); and when followed by treatment with interferon-free DAA for genotype 1 was \$34,783 (€23,683). The treatment scenario using the interferon based DAAs dominated.

Coward et al. (2016) (146), in a systematic review which summarised the economic evaluations of birth cohort screening, reported that the incremental cost per QALY gained in included studies ranged between £3,706 and £45,123 (using data from original articles this corresponds to between €7,769 and €64,650) (9). In studies which evaluated different treatment regimes, the addition of DAAs increased the cost per QALY gained. The authors concluded that treatment of choice and cost of treatment can change the conclusion of the model. They also reported that the main source of variation was due to prevalence estimates, and screening and treatment uptake estimates used.

Coretti et al. in their systematic review, concluded that studies generally proved the cost-effectiveness of screening for specific age cohorts in which the disease prevalence is high and life expectancy sufficiently long (214).

Summary

As summarised by *Coward et al.*, the cost-effectiveness of a birth cohort screening programme will depend on the prevalence, acceptability of screening, and uptake of treatment, which will be unique to each country. Of note, the economic evaluations to date haven't included the costs of implementation. It is likely that the implementation plan required to achieve the necessary uptake of screening and treatment in order for a birth cohort programme to be cost-effective will be high. *Coward et al.* conclude that a thorough budget impact plan, including the implementation plan, would be required to assess any such programme.

The generalisability of birth cohort studies from the USA to the Irish population also needs to be considered. Of note, the studies compared birth cohort screening to either no screening or risk based screening within the same cohort. If implemented, other screening strategies would likely still be required

for those at risk outside of this cohort. Birth cohort screening would be additional to, rather than in place of, other screening strategies. If the budget for screening implementation is limited, prioritising other strategies targeted at those at risk of ongoing transmission may be better.

The birth cohort studies also did not analyse the distribution of benefits which may be achieved with birth cohort screening, only the total benefit. Any birth cohort programme would need to consider the health equity impact and also the impact it may have on onward transmission compared to risk based screening or targeting those at risk of onward transmission.

General population

WHO's *Guideline on hepatitis B and C testing* concluded that general population screening was generally not cost-effective outside specific settings with high general population prevalence (2). The WHO guideline development group considered that one-off birth cohort screening would be more widely applicable.

A systematic review by *Coward et al.* evaluated five studies which examined the cost-effectiveness of general population screening. Studies were from the United States, the Netherlands and Egypt and were conducted between 2001 and 2013 (146). The findings of the studies ranged from £66.5 to £62,452/QALY. The study with the low cost per QALY was from Egypt, a high prevalence country. Amongst the studies included in the systematic review, a study from the Netherlands found that a campaign using advertising aimed at the general population was not cost-effective (222). When a support programme for primary care was added to the campaign an ICER of €11,297/QALY was estimated. In the US *Eckman et al.* found general population to be cost-effective with an ICER of \$47,276/QALY based on modelling in a hypothetical population with a prevalence of 1.4% (223). They reported that screening remained cost-effective once the prevalence remained above 0.84%. *Coffin et al.* found general population screening to be cost-effective compared to no screening, but it was dominated by birth cohort screening (218). *Coward et al.* report that prevalence was the main source of variation between the study results.

Summary

The cost-effectiveness of general population screening will likely depend on the prevalence in the underlying population, and also on the uptake of treatment. General population screening has been dominated by birth cohort screening in economic evaluations. The epidemiology of HCV differs between countries, but as state by WHO, birth cohort screening is likely to be more appropriate in most countries.

PWID

A number of economic evaluations of screening of PWID have been reported (209, 211, 222, 224-227). Settings varied from general practice to drug treatment services.

Martin et al. carried out a cost-effectiveness study of DBS use in specialist drug treatment services using a dynamic model (209). They compared offering DBS testing in specialist addiction services to the current practice of testing by venepuncture only. A health service perspective was taken and lifetime time horizon used. Costs and utilities were discounted at a rate of 3.5% per year. The model assumed a 3.6 fold increase in testing in addiction services based on published studies. They demonstrated that for a £20,000/QALY gained willingness-to-pay threshold, DBS testing in addiction services is cost-effective (ICER of £14,600/QALY gained (€19,141)). Results were robust to changes in HCV prevalence. Increasing PWID treatment rates to those for ex-PWID considerably reduced the ICER (£4,500 (€5,900)/QALY gained).

Schackman et al. compared the cost-effectiveness of no HCV testing referral or offer, offsite HCV testing, onsite rapid HCV testing (with OraQuick® HCV Rapid Antibody Test), and onsite rapid HCV and HIV testing

in a substance abuse treatment programme (224). They took a lifetime horizon and discounted costs and utilities at a rate of 3% per year. Compared to no testing, onsite rapid HCV testing had an ICER of \$18,300 (€17,464)/QALY compared with no testing. Offsite referral was dominated by onsite rapid testing. Onsite rapid HCV and HIV testing had an ICER of \$64,500 (€61,554) compared to onsite rapid HCV testing alone. Results were similar when different treatment regimes, including an interferon-free regime were considered.

Cipriano et al. used a dynamic compartmental model of HIV and HCV in a population of PWIDs and non-IDUs in the US to estimate the cost-effectiveness of adding HCV to HIV screening of PWID in opioid replacement therapy (ORT) (225). They examined what test sequence to use and also evaluated one-time and repeat screening at intervals from annually to once every three months. They found that adding HCV testing to HIV testing was dominated in all scenarios except for when anti-HCV was added to 3-monthly anti-HIV plus RNA testing. However, the ICER was US \$168,600 (€171,453). All testing scenarios had ICERs exceeding \$100,000 (€101,692)/QALY gained unless awareness of HCV-infection status resulted in a substantial reduction in needle-sharing behaviour.

Stein et al. undertook a CUA using a Markov model in the UK (226). The study population was PWID in contact with drug treatment services. The cost per QALY was £28,000 (€49,371) when treatment was with IFN+RBV and £14,000 (€24,685) when treatment was with Peg-IFN+RBV. Cost were sensitive to the proportion of positives people accepting liver biopsy, proportion accepting treatment, treatment response, and the proportion eligible for treatment.

Summary

While studies varied in terms of setting, and other factors, screening of PWID was generally found to be cost-effective using the respective willingness to pay thresholds.

STI clinic attendees

Two studies examining the cost-effectiveness of screening for HCV in the STI/GUM setting were identified (228, 229).

Stein et al. (2003) undertook a cost utility analysis of screening for HCV in people attending GUM clinics in the UK (228). They compared universal screening, screening of former or current PWID, and selective screening of 'at risk' groups. A health service perspective was taken. Screening was with ELISA followed by HCV-RNA PCR if positive. Costs were discounted at 6% and benefits at 1.5% a year. Universal screening (assuming a prevalence of 1.5%) had an ICER of £85,000 (€149,875)/QALY and a total cost of £4,808,373. Screening only PWID (assuming 3% of attendees were PWID and a prevalence of 48.6% in this group) had an ICER of £32,138 (€56,667)/QALY and a total cost of £982,832. Selective screening was based on criteria such as IDU, sexual behaviours and contacts. If 10% of attendees were screened (assuming a prevalence of 9.9%) an ICER of £34,288 (€60,458)/QALY was estimated and a total cost of £1,530,547 (€2,698,715) in addition to no screening. Selective screening of 20% who present (with prevalence of 6.2%) had an ICER of £39,647 (€69,907)/QALY and a total cost of £2,168,860 (€3,824,211) in addition to no screening. When treatment was with PEG-IFN the ICER of universal screening decreased to £46,389 (€81,795). The ICER was sensitive to prevalence, increasing once prevalence decreased below 3%. It was also influenced by acceptance rates, but remained above £60,000 (€105,794) even with 100% acceptance. It was also sensitive to acceptance of treatment, and eligibility for treatment. The PWID and selective screening strategies were also sensitive to acceptance of screening and treatment.

Honeycutt et al. estimated the cost and cost-effectiveness ratio of testing STD clinic attendees for HCV (229). The cost per anti-HCV positive tester returning for results was estimated. No further costs or utilities were considered. Testing was with EIA followed by RIBA for those with a low positive EIA.

In the baseline scenario only PWID were offered screening. This was compared with testing of other subpopulations: non-PWID males aged over 40 with more than 100 sex partners; non-PWID males over 40 with less than 100 sex partners; and non-PWID females over 40 years. The prevalence of anti-HCV in these groups was taken from the National Health and Nutrition Examination Survey and was 57%, 16%, 2% and 0.9% respectively. The CER of testing these subpopulations compared to testing IDUs only was \$179 (€203), \$1,386 (€1,575) and \$2,986 (€3,393) respectively.

Summary

Studies of STI clinic attendees have not shown universal screening of all attendees to be cost-effective. The applicability of these however is limited as one was conducted in 2003 and was modelled on different management and treatment strategies than are current practice. The second only considered the cost of detecting anti-HCV positive cases.

Type of test

Linás et al. estimated the cost-effectiveness of screening for acute hepatitis C infection in HIV infected MSM (230). All patients had an anti-HCV test at enrolment, followed by one of 10 screening strategies involving symptom-based screening, or screening with LFTs, anti-HCV, or HCV-RNA in various combinations and intervals. A societal perspective was used. Costs and utilities were discounted at a rate of 3% per year. The model assumed 81% of detected acute cases started treatment. Chronic cases also had treatment. The ICER with six monthly LFTs and an annual anti-HCV test compared to symptom base screening was \$43,700 (€41,704)/QALY when treated with PEG-IFN+RBV and \$57,800 (€55,160) when a PI was added to treatment. Three monthly LFTs compared to symptom based screening had an ICER of \$129,700 (€123,776) and \$229,000 (€218,541), while three monthly RNA and LFTs had ICERs of \$1,700,000 (€1,622,354) and \$1,400,000 (€1,336,056) when treatment was PEG-IFN+RBV and PEG-IFN+RBV+PI respectively. All other strategies dominated.

Specimen type

Martin et al. carried out a cost-effectiveness study of DBS use in prisons and specialist drug treatment services using a dynamic model (209). They compared offering DBS testing in prison or specialist addiction services to the current practice of testing by venepuncture only. A health service perspective was taken and lifetime time horizon used. Costs and utilities were discounted at a rate of 3.5% per year. The model assumed a 3.6 fold increase in testing in addiction services and a 2.6 fold increase in testing in prisons based on published studies. They demonstrated that for a £20,000/QALY gained willingness-to-pay threshold, DBS testing in addiction services is cost-effective (ICER of £14,600/QALY gained (€19,141)). Under the base-case assumption of no continuity of treatment/care when exiting/entering prison, DBS testing in prisons is not cost-effective (ICER of £59,400/QALY gained (€77,874)). Results were robust to changes in HCV prevalence. Increasing PWID treatment rates to those for ex-PWID considerably reduced the ICER (£4,500 and £30,000/QALY gained for addiction services and prison, respectively). If continuity of care is >40%, the prison DBS ICER falls below £20,000/QALY gained.

Summary

DBS testing may be cost-effective in certain settings by increasing the uptake of screening. While it was not cost-effective in the prison setting in this study, when continuity of care on release was improved, it did become cost-effective.

Rapid diagnostic tests

Schackman et al. compared the cost-effectiveness of no HCV testing referral or offer, offsite HCV testing, onsite rapid HCV testing (with OraQuick® HCV Rapid Antibody Test), and onsite rapid HCV and HIV testing

in a substance abuse treatment programme (224). They took a lifetime horizon and discounted costs and utilities at a rate of 3% per year. Compared to no testing, onsite rapid HCV testing had an ICER of \$18,300 (€17,464)/QALY compared with no testing. Offsite referral was dominated by onsite rapid testing. Onsite rapid HCV and HIV testing had an ICER of \$64,500 (€61,554) compared to onsite rapid HCV testing alone. Results were similar when different treatment regimes, including an interferon-free regime were considered.

Summary

While this study found onsite rapid testing to be cost-effective the comparator used was no testing or offsite testing. In settings in Ireland, the alternative to rapid testing will likely be onsite testing by venepuncture.

Summary

HCV screening of high risk populations has generally been shown to be cost-effective. Birth cohort screening is also likely to be cost-effective. Universal screening in low risk populations such as the antenatal setting or STI clinics has generally shown not to be cost-effective. However, the currently available economic literature needs to be considered in the context of major developments in the care and treatment of HCV. The cost-effectiveness of HCV screening will be dependent on the prevalence of HCV in the targeted population, uptake of screening, linkage to care, and treatment success. The majority of retrieved economic evaluations were conducted when the standard of care involved invasive evaluation tests (i.e. liver biopsies) and older treatment regimes. In addition to the difference in cost and clinical effectiveness compared to new standards of care, these older standards of care are likely to have been less acceptable to patients resulting in fewer patients accepting screening, linkage to care and/ or treatment.

While some studies did include the newer treatments in their analysis, the costs of the new treatments are likely to decrease as their use becomes more widespread. The cost-effectiveness of screening programmes for HCV is likely to change significantly in coming years as these new treatments become standard of care and their costs decrease. Therefore, much of the economic evidence available is now of limited value.

References are incorporated into the main reference list.

Search terms used in PubMed search

(mass screening[MeSH Terms] OR mass screening[Title/Abstract] OR screen*[Title/Abstract] OR diagnosis[MeSH Terms] OR diagnos*[Title/Abstract] OR test*[Title/Abstract] OR population surveillance[Title/Abstract] OR detect*[Title/Abstract] OR case finding[Title/Abstract])

AND

(hepacivirus[MeSH Terms] OR hepatitis c, chronic[MeSH Terms] OR hepatitis C[MeSH Terms] OR hepatitis C[Title/Abstract] OR HCV[Title/Abstract] OR Hepatitis C virus[Title/Abstract])

AND

(((((economics[MeSH Terms]) OR (models, economic[MeSH Terms]) OR (analysis, cost benefit[MeSH Terms]) OR (analysis, cost[MeSH Terms]) OR (cost of illness[MeSH Terms]) OR (economics, medical[MeSH Terms]) OR economics, hospital[MeSH Terms]) OR economics, pharmaceutical[MeSH Terms]) OR economics, nursing[MeSH Terms]) OR (health care economics and organizations[MeSH Terms]) OR (healthcare economics and organizations[MeSH Terms]) OR (costs and cost analysis[MeSH Terms]) OR (economics[MeSH Subheading]) OR healthcare costs[MeSH Terms]) OR decision support techniques[MeSH Terms] OR cost savings[MeSH Terms] OR (healthcare costs[MeSH Terms]) OR (chains, markov[MeSH Terms]) OR (monte carlo method[MeSH Terms]) OR (quality of life[MeSH Terms]) OR (quality-adjusted life years[MeSH Terms]) OR (quality-adjusted life year*[Title/Abstract] OR quality adjusted life year*[Title/Abstract] OR quality-adjusted life expectanc*[Title/Abstract] OR quality adjusted life expectanc*[Title/Abstract]) OR (economic impact[Title/Abstract] OR economic value[Title/Abstract] OR pharmacoeconomics[Title/Abstract] OR healthcare cost[Title/Abstract] OR economic factors[Title/Abstract] OR cost analysis[Title/Abstract] OR economic analysis[Title/Abstract] OR cost-effectiveness[Title/Abstract] OR cost effectiveness[Title/Abstract] OR costs[Title/Abstract] OR healthcare cost[Title/Abstract] OR cost savings[Title/Abstract] OR cost-benefit analysis[Title/Abstract] OR hospital costs[Title/Abstract] OR medical[Title/Abstract] AND costs[Title/Abstract] OR quality-of-life[Title/Abstract] OR quality adjusted life year[Title/Abstract]) OR (qol[Title/Abstract] OR qoly[Title/Abstract] OR hrqol[Title/Abstract] OR qaly[Title/Abstract] OR qalys[Title/Abstract] OR qale[Title/Abstract] OR qales[Title/Abstract]))))

Part B: Budget impact analysis of this National Clinical Guideline

A more detailed version of the budget impact assessment is available at:

<http://www.hpsc.ie/A-Z/Hepatitis/HepatitisC/Guidance/Backgrounddocuments/>

Background

Screening for HCV in Ireland is currently undertaken in several different settings and services. However, to date there has been no comprehensive national screening guideline to guide which population groups should be offered testing, and how it should be done. These new guidelines presented here make recommendations on the specific population groups to whom HCV testing should be offered, the frequency with which testing should be offered, the specimen and test method to be used, the setting for testing and the suggested approach to encourage uptake of screening and linkage to care.

This budget impact analysis considers the additional resources that will be required to implement the recommendations outlined in the new guidelines. Many of the recommendations are budget neutral as they mainly involve specifying and standardising practices that are largely already in place. However, there are some anticipated additional resource requirements in order for some of the recommendations to be implemented.

Four key types of additional resources have been identified:

1. Additional testing
 - a. Extra HCV testing, through both improved coverage of population groups for whom screening was previously recommended and increased frequency of testing for some population groups for whom screening was previously recommended. The resource implications of this extra testing include staff time, consumables and laboratory costs.
2. Additional services to enable risk groups access testing
3. Communicable disease nurse in Department of Public Health in the greater Dublin area to undertake risk assessments for contacts of identified cases.
4. Information and promotion
 - a. Amongst health professionals.
 - b. Amongst the public
 - i. A public information campaign among the general population
 - ii. Specific information campaigns targeting individual risk populations.

Approach taken

The recommendations having a resource impact will be considered and then the additional resources quantified under the type of resource. Potential cost savings will also be described. Finally, the additional resources required for all recommendations will be combined and costed. A five year time horizon was taken, with annual costs over the five year period estimated.

Limitations

Of note, there are a number of significant limitations to the budget impact analysis which should be kept in mind. One of the main limitations is in estimating the number of additional tests which will result from the guideline implementation. The change in resource use due to additional testing is difficult to estimate for a number of the recommendations. The size of the eligible population is not known for certain risk groups, the number of undiagnosed cases within certain populations is not known, and the amount of screening currently taking place within certain risk groups is not known. The amount of additional testing will also depend on the uptake of screening, which is not known. An attempt has been made, in consultation with key stakeholders working in the relevant areas, to estimate the amount of additional

testing by risk group. However, some estimates are still very uncertain. Such estimates are in italics and shaded (like this) to highlight the uncertainty around them.

There will be overlap between risk groups (i.e. a number of people will fall into multiple risk groups). It is not possible to quantify this, and therefore the estimated number of additional tests may be an overestimate.

There will be variability in how screening is implemented for different risk groups and in different settings, which will result in different costs. It is not possible to take into account all of these variations within the scope of this budget impact analysis.

Recommendations with a resource impact

Table A 8 summarises the estimated resource change for each recommendation.

Table A 8: Change in resources for each recommendation.

	Change in resources	Annual Budget Impact
Recommendation 1 Women who are pregnant		
1.1. Standardised targeted risk based screening of antenatal women is recommended. 1.2. Universal screening of pregnant women is not recommended. 1.3. Universal screening may be reconsidered in the future if HCV treatment during pregnancy becomes possible. Also, if national policy progresses to a policy of birth cohort or total population screening, antenatal screening offers an opportunistic method to reach this particular population cohort.	There will be no change in the majority of maternity units. The standardisation of criteria for screening may result in an increased number of tests. One large Dublin maternity hospital (>8,000 births per year) currently offers universal HCV testing to all women. Therefore, if this unit changes to targeted screening, there may be a net decrease in the number of tests in the antenatal population. Information and promotional material.	See later for information and promotional material.
Recommendation 2 Children born to HCV positive women		
2.1. Infants of HCV-RNA positive women should be tested for HCV-RNA at 6 weeks and 6 months of age and, if both are negative, HCV antibody at ≥ 18 months of age. 2.2. Infants who are HCV-RNA positive at any time or who are HCV antibody positive at or after 18 months of age should be referred to the Rainbow Clinic. 2.3. Infants of anti-HCV positive but HCV-RNA negative women, where eradication of infection, either spontaneously or by treatment is not assured (i.e. by serial negative HCV-RNA tests) should be tested for anti-HCV at ≥18 months of age. 2.4. Infants of anti-HCV positive but HCV-RNA negative women where eradication of infection, spontaneously or by treatment is assured (i.e. persistent negative HCV-RNA and no ongoing risk for reinfection), should be managed as infants of uninfected women and do not require HCV follow-up.	Nil additional resources anticipated as current practice (38). Information leaflets for parents explaining follow-up.	See later for information and promotional material.
Recommendation 3		
3.1. If a woman is found to have current or resolved HCV infection, any previous children she has given birth to should be tested, unless the woman was known to be HCV-RNA negative at the time of their delivery.	Unlikely to result in substantial numbers of additional tests.	Nil

Recommendation 4 Household contacts of a person who is HCV positive		
<p>4.1. In general screening of household contacts (with no sexual or vertical exposure to the HCV positive household member) 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 the HCV positive household member is on dialysis in the home; or if there are environmental risks within the household such as discarded needles.</p> <p>4.2. Where a household contact requests testing for reassurance, this should not be denied.</p>	<p>May result in some additional testing. The number of those eligible for screening or who will present for screening is not known.</p> <p><i>if 10% of PWID cases which are notified per year were assessed to be at higher risk of transmitting infection to their household contacts, and each of these has two household contacts which present for testing an estimated 100 additional tests would be carried out each year (75% of 660 notifications in 2016 were amongst PWID=495; 10% of these=50; 50 x 2 household contacts=100).</i></p> <p>Additional staff in Public Health to carry out risk assessment and follow-up contacts. As the majority of cases occur in HSE East this resource should be placed in HSE East.</p> <p>Information and promotional material</p>	<p>100X€55.12 = €5,512</p> <p>0.5 WTE communicable disease control nurse = €33,897/ year based on general nurse CNM 2, point 1 salary scale including PRSI, pension and overheads.</p> <p>See later for information and promotional material.</p>
Recommendation 5 People who use unprescribed or illicit drugs		
<p>5.1. All those who have ever injected unprescribed or illicit drugs should be offered screening for HCV. This includes those who only injected once, and those who injected any type of drug which was not prescribed, including performance enhancing drugs like steroids, and novel psychoactive substances.</p> <p>5.2. Re-testing of those who test HCV negative should be offered on an annual basis, or six monthly if deemed clinically appropriate, for those who remain at ongoing risk of infection.</p> <p>5.3. Testing should be available during this interval if a known risk exposure incident has occurred.</p> <p>5.4. Re-testing for those who have been previously infected, but have cleared infection spontaneously or through treatment, should be done by HCV-RNA testing, as anti-HCV antibody remains positive after the first infection</p>	<p>Current practice for those attending addiction services (36, 67).</p> <p>There may be some additional testing among people who use illicit drugs but do not attend addiction treatment centres and those who may have used illicit drugs in the past.</p> <p><i>It has been estimated that between 1991 and 2014, approximately 2,062 PWID never attended drug treatment (4). If 50% of these presented for screening over 5 years then an additional 1,000 tests would be carried out, or 200/year.</i></p> <p>Repeat testing for those at ongoing risk is currently recommended within addiction services but it is not known to what extent it is implemented so it is possible that this recommendation may result in some increase in the level of testing.</p> <p><i>Approximately 10,000 attend addiction treatment services (personal communication Eamon Keenan). An estimated one third of these are anti-HCV negative and should be retested annually if still risk-taking. It is estimated that 50% of these may still be engaging in risk taking behaviour (n=1,650). If re-testing is currently being carried out in only 50% of these, then implementation of the guidelines would result in an additional 825 tests per year.</i></p>	<p>1,025X€55.12 = €56,498</p>

Recommendation 6		
<p>6.1. Screening should be offered to all those who have used unprescribed or illicit drugs by a route other than injecting (non-injecting drug use (NIDU)), if there is a possibility of transmission of infection by the route of administration. This includes those who currently use intranasal drugs (i.e. snort or sniff), or have done so in the past, or share other equipment or drugs where there is a risk of contamination with the blood of others.</p>	<p>This is current practice for those attending addiction services. There may be some additional testing among people who do not attend addiction treatment centres and those who may have used illicit drugs in the past. The number of such people who will be eligible for screening or who will present for screening is not known.</p> <p><i>The NACDA 2016 drug prevalence study reports on the lifetime prevalence of different drugs in the adult population (231). While it doesn't report on route of administration, the non IDU drug with the highest prevalence, which also has a biologically plausible transmission potential for HCV, was cocaine with a lifetime prevalence of 6.6%. Applying age specific prevalence of use to 2016 Census data, it can be estimated that 226,935 persons have used cocaine in their lifetime. Between 2004 and 2014 there were approximately 7,000 new entrants to drug treatment services where cocaine was the main problem drug. Of note polydrug use is common in Ireland. If it is assumed that the majority of PWID are also included in this prevalence estimate, then excluding PWID and those who have entered treatment for cocaine results in approximately 200,000 being eligible for screening. This is likely an overestimate as a number may have attended addiction services with other drug problems and have been tested. If 5% of the 200,000 present for screening over 5 years then 10,000 additional tests would be performed, or approximately 2,000 per year.</i></p>	<p>2,000X€55.12 = €110,240</p>
Recommendation 7 Prisoners or former prisoners		
<p>7.1. Screening should be offered to all prisoners on entry to prison. Screening should be offered at a time at which it is most likely to be accepted by the prisoner, while also ensuring the early identification of infections in order to minimise the risk of transmission to others.</p> <p>7.2. Those found to have HCV infection should be linked into specialist care and treatment should be facilitated while in prison.</p> <p>7.3. Prisoners who initially test HCV negative should be offered repeat testing on an annual basis, or six monthly if deemed clinically appropriate, while in prison. Screening should also be offered at any time if a risk exposure (e.g. tattooing, needle-sharing) is known to have occurred.</p> <p>7.4. Prisoners should be able to access testing on request at any stage of their sentence.</p>	<p>Additional testing. The exact number of additional tests is not known. It is estimated that current uptake of screening is 5%-10% (personal communication Ursula Norton). This equates to 650-1,300 of the approximately 13,000 people committed to prison each year being tested currently.</p> <p><i>If 80% of prisoners with a history of IDU were tested on committal, and 20% of those without a history of IDU were tested, this would result in approximately 2,470-3,120 additional tests per year. These figures are based on the following: 15% have a history of IDU: 1,950 x 80% = 1,560 85% without a history of IDU: 11,050 x 20% = 2,210 (26% in 2011 prison study had a history of IDU (66), however the proportion of committals having a history of IDU is likely to be lower given that, in 2015, 9,883 committals were for the non-payment of court ordered fines (232)).</i></p> <p>Information and promotional material.</p>	<p>3,120X€55.12 = €171,974</p> <p>See later for information and promotional material.</p>

Recommendation 8		
<p>8.1. One-off testing of ex-prisoners is recommended, although implementation may be difficult.</p>	<p>The size of this population is unknown, but the expected number of additional tests is expected to be low. It is likely that many will already have been tested through the prison service or through other services such as addiction services.</p> <p>The rate of reoffending, or recidivism, for prisoners released in 2010 was 45.1% (defined as an individual committing a criminal offence within a three year period following their release from prison and being subsequently convicted for that offence) (233), thus some will be offered testing in the future on committal to prison.</p>	<p>Nil</p>
Recommendation 9 People who are homeless		
<p>9.1. Homeless people who have a history of engaging in risk behaviours associated with HCV transmission, or who have had a potential HCV risk exposure, should be offered screening.</p> <p>9.2. Those who initially test HCV negative should be offered repeat testing on an annual basis, or six monthly if deemed clinically appropriate, if there is an ongoing risk of transmission.</p>	<p>Implementation of the guideline may result in additional testing. The exact number of additional tests is not known. It is estimated that the majority of at risk people in homeless hostels and emergency accommodation in Dublin are offered screening for HCV currently as HCV testing is part of the usual health needs assessment in these services (personal communication Joe Doyle, HSE Social Inclusion). Uptake is not known.</p> <p><i>In February 2017, the number of homeless adults in temporary emergency accommodation and supported temporary accommodation was 2,604 (234). If it is estimated that 50% are at risk of HCV infection (1,300) and current uptake of HCV testing is 60%, and raising awareness increases this to 80%, then an additional 260 tests would be carried out over 5 years on the existing cohort of homeless people, or 52 per year. There are approximately 4,500 new presentations per year to homeless accommodation services (235). Assuming that 53% are to temporary emergency accommodation and supported temporary accommodation (2,400), and 50% are at risk of HCV infection (1,200) and current uptake of HCV testing is 60%, and raising awareness increases this to 80%, then an additional 240 tests would be carried out per year on the new cohort of homeless people.</i></p> <p>In order to improve the availability and accessibility of screening for homeless people at risk of HCV infection, current services to homeless people (e.g. HSE services, SafetyNet and HepCare Europe) should continue to be supported and may need to be expanded.</p> <p>Information and promotional material.</p>	<p>292X€55.12 = €16,095</p> <p>See later for information and promotional material.</p>

Recommendation 10 Migrants		
10.1. Migrants from a country with an intermediate to high prevalence of HCV (anti-HCV \geq 2%) should be offered one-off screening.	<p>Although it has already been recommended that those from a country with a prevalence > 3% be offered testing it is not known and how many of these people have been tested.</p> <p>The guideline will result in additional testing.</p> <p><i>According to the 2011 census there were 164,820 residents in Ireland from countries with an anti-HCV prevalence greater than 2%. If 10% of these present for testing over five years, this would result in approximately 3,296 tests per year.</i></p> <p><i>There will be new migrants each year to Ireland from intermediate and high prevalence countries. Based on PRSI allocations, there were approximately 26,000 new entrants from countries with a prevalence of 2% or greater in 2016. This number will include children who are less likely to be at risk as in a number of countries the increased risk is due to historically poor infection prevention and control practices. If it is assumed that 60% are eligible for screening, and 10% of this present for screening then there could be an additional 1,560 tests per year.</i></p> <p>Culturally appropriate information and promotional material</p>	<p>4,856x€55.12 = €267,663</p> <p>See later for information and promotional material.</p>
Recommendation 11 People who received medical or dental treatment abroad		
11.1. Screening for HCV should be considered in people who have received medical or dental treatment in countries where HCV is common (anti-HCV prevalence \geq 2%) and where infection control may be poor.	<p>There may be some additional testing but the numbers are likely to be low.</p> <p>Information and promotional material.</p>	<p>See later for information and promotional material.</p>
Recommendation 12 People with tattoos or body piercings		
<p>12.1. Screening should be considered for all those with a tattoo. Those most at risk of having acquired HCV through tattooing are those who received tattoos a number of decades ago, in non-professional settings, in prison, in high prevalence countries, or in other circumstances where infection control was poor.</p> <p>12.2. There is insufficient evidence to support screening of recipients of body piercings (including ear piercings).</p>	<p>The recommendation will result in additional number of people tested.</p> <p>The number of people eligible for screening or who will present for screening is not known.</p> <p><i>If it is estimated that 20% of the adult population aged 20 to 50 years have a tattoo, and 60% of females have been tested as part of antenatal screening, and 10% of the remainder have been screened through other services, then approximately 253,265 persons would be eligible for screening. If 5% of these present for screening then 12,663 would be screened over five years, or 2,533 per year</i></p> <p>Information and promotional material.</p>	<p>2,533x€55.12 = €139,619</p> <p>See later for information and promotional material</p>

Recommendation 13 Heterosexual partners of those who are HCV positive		
<p>13.1. In general, screening of sexual partners of known HCV cases is not recommended in heterosexual couples who are both HIV negative.</p> <p>13.2. Sexual partners of known HCV cases should be considered for screening in the following situations:</p> <p>a) If the HCV-infected case is a PWID (caution: the case may not have disclosed this to the partner). 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.</p> <p>b) If the case or contact is also HIV positive</p> <p>13.3. Sexual contacts of PWID, but whose HCV status is unknown or there is evidence of resolved infection, should be considered for screening.</p> <p>13.4. If testing of a sexual partner of a HCV-infected case is requested for reassurance, then this should not be denied.</p>	<p>Current practice and therefore any change in the number of those tested is likely to be small.</p> <p>Where required, contact tracing could be undertaken by Public Health. The additional resources required are listed under Recommendation 4.</p> <p>Information and promotional material</p>	<p>Costed under Recommendation 4.</p> <p>See later for information and promotional material.</p>
Recommendation 14 Men who have sex with men		
<p>14.1. HIV positive MSM should be offered screening at least annually for HCV. More frequent testing may be required if clinically indicated e.g. an unexplained rise in ALT, a diagnosis of a new STI, or if a risk exposure has occurred such as contact with a known case of HCV, or other risk behaviours including chemsex.</p>	<p>Nil additional anticipated as current practice.</p>	<p>Nil</p>
<p>14.2. HIV negative MSM should be offered testing annually for HCV as part of an overall STI screen. More frequent testing may be required if clinically indicated eg.an unexplained rise in ALT, a diagnosis of a new STI, or if a risk exposure has occurred such a contact with a known case of HCV, or other risk behaviours including chemsex.</p>	<p>This may result in some additional testing as not current practice in all centres. However, as testing is only undertaken annually rather than at each visit as is being done in some high volume centres there would be a saving so there will not be a net increase in resources</p> <p>Information and promotional material.</p>	<p>See later for information and promotional material</p>
Recommendation 15 Those having sexual health screening		
<p>15.1. HCV testing should be considered part of routine sexual health screening in the following circumstances:</p> <ul style="list-style-type: none"> • Men who have sex with men • People who are HIV positive • Commercial sex workers • PWID • If indicated by the clinical history e.g. unexplained jaundice • When other risk factors for HCV as outlined in this guideline are present 	<p>Nil additional anticipated as current practice.</p>	<p>Nil</p>

Recommendation 16 People on renal dialysis or who have had a kidney transplant		
16.1. Patients commencing, or on maintenance, haemodialysis or peritoneal dialysis should be screened according to the current recommendations of the National Standing Advisory Committee on the Prevention of Transmission of Blood-Borne Diseases in the Health-Care Setting and any ensuing updates from this committee.	Nil additional anticipated as current practice (88).	Nil
16.2. All patients having a kidney transplant should be offered testing for HCV by a combined antigen-antibody test, or anti-HCV test AND HCV-RNA at 3 months post-transplant.	Although this is currently recommended, adherence to the existing recommendation is not known. This guideline may reinforce practice resulting in some additional testing. Between 2011 and 2015 the average annual number of kidney transplants was 169. If at present only 50% are tested post-transplant, and implementation of this guideline increases this to 100%, this would result in an additional 85 tests per year . The laboratory costs are the only additional resources as these patients are already attending services and having regular blood samples taken.	85X€41 = €3,485
16.3. Patients transplanted before the introduction of the above, unless already known to be HCV infection, should be tested on a one-off basis by a combined antigen-antibody test or anti-HCV test AND HCV-RNA to out rule the possible acquisition of HCV infection through past treatment for renal failure.	May result in some additional testing. The number eligible for testing and that will come forward is not known. At the end of 2014 there were 2,300 recipients of kidney transplants alive. If it is estimated that 80% of the 1,149 people who had a transplant between 2008 and 2014 were still alive, then approximately 1,380 of the 2,300 alive in 2014 were transplanted before 2008 and the issuing of the recommendation on post-transplant screening. Also, if only half of those transplanted since 2008 had post-transplant screening then 460 of this group would require screening. In total there may be 1,840 eligible for screening under this recommendation. If 50% presented for screening over 5 years then 920 additional tests would be performed or approximately 184 per year .	184X€14 = €2,576
Recommendation 17 Recipients of substances of human origin		
17.1. Recipients of blood or blood components in Ireland prior to October 1991 who have not yet been tested should be offered screening. 17.2. All recipients of anti-D immunoglobulin in Ireland between 1st May 1977 and the end of July 1979, and 1st March 1991 to 18th February 1994 who have not yet been tested should be offered screening. 17.3. Recipients of plasma derived clotting factor concentrates in Ireland prior to 1992 who have not yet been tested should be offered screening.	Nil additional anticipated as the majority of those affected have already been screened. The number of any additional people coming forward for testing is likely to be very low.	Nil
17.4. Recipients of blood components and blood products overseas in any country where a quality assured blood donor screening programme may not have been in place should be offered screening.	May result in additional testing but the numbers are likely to be low.	Nil
Recommendation 18		
18.1. Screening should be considered in recipients of solid organ transplants in Ireland who have not yet been tested.	It is estimated that approximately 2,000 solid organ transplants other than kidney transplants have taken place in Ireland since 1964. Approximately 1,300 of these have been since 2010 when screening practices will have been adequate. Given the survival rates post-transplant in previous years, the number of historical transplant recipients from a time before screening was adequate who are still alive is likely to be low.	Nil

Recommendation 19 Donors of substances of human origin		
19.1. Screening of donors of blood, organ, tissue and cells, including reproductive cells, should at a minimum comply with legislative requirements	Nil additional anticipated as current practice.	Nil
19.2. NAT testing for HCV of donors of blood should be performed and the results available prior to the use of the donation. The test must be designed and approved for screening of blood donations. 19.3. NAT testing for HCV of donors of tissues and cells, including reproductive cells, and solid organ donors should be performed in addition to current legislative requirements.	<p><u>Blood</u> Nil additional anticipated as current practice.</p> <p><u>Living organ donors</u> Ab/Ag test is current practice. NAT testing will be additional. Between 2012 and 2015 the average annual number of living solid organ donors was 34. As this group is already having microbiological testing undertaken, the laboratory cost is the only additional resource.</p> <p><u>Other tissues and cells</u> It is not known if NAT testing is current practice in other services that process tissues and cells. Also the number of donors is not known. Donations within the fertility sector are likely to be the largest group.</p> <p>Of note, most tissues and cells for use in Ireland, including reproductive cells are imported.</p>	34X€55 = €1,870
19.4. For deceased donors of solid organs: <ul style="list-style-type: none"> • HCV antibody and HCV antigen testing should be done and the results available prior to donation. • NAT testing should be considered where feasible. NAT results may not be available prior to transplantation but NAT testing should still be performed to ensure the rapid identification of the recipients of potentially infectious organs. 	<p>Combined Ab/Ag testing is current practice. NAT testing will be additional. No additional staff time or consumables will be required as microbiological testing is already being undertaken for this cohort.</p> <p>Between 2013 and 2015 the average annual number of deceased organ donors was 77.</p>	77X €55 = €4,235
19.5. Any external laboratories used for microbiological screening of donors should be accredited and comply with the standards of the appropriate regulatory authority. Laboratories, in Ireland should be accredited by the Irish National Accreditation Board (INAB) to undertake testing in compliance with the International Standard ISO 15189.	Current regulatory requirement. No additional resources required.	Nil
19.6. A national advisory committee on the safety of blood, organs and tissues should be established to advise on best practice in relation to donor selection, and testing of potential donors.	The resources required for this is not within the remit of implementation of this guideline.	Nil
Recommendation 20 People in a birth cohort		
20.1. Birth cohort screening cannot be recommended at present due to the likely substantial cost implications and uncertain benefit. Such a programme would require a full health technology assessment (HTA) and approval of funding prior to being considered. 20.2. Birth cohort screening should be considered if a HTA shows it to be cost-effective and affordable in the Irish context.	No action at present pending a HTA	No action at present pending a HTA.

Recommendation 21 Healthcare workers		
21.1. All new healthcare workers (HCWs) should be offered HCV screening on a voluntary basis.	<p>Additional testing as it is not current practice to offer to HCW who will not perform EPPs.</p> <p><i>There are approximately 16,000 new appointments to the HSE each year. However, a significant number of these will not be new employees. If it is estimated that half of new appointments are new employees, and half of these are healthcare workers, there would be approximately 4,000 new staff eligible for screening. It is known that there are approximately 1,000 new entrant NCHDs each year who are all screened at present. A number of other new employees will be involved in EPPs and are screened under existing practice. If this number is assumed to be 500, then there would remain 2,500 newly eligible for screening. As these groups will likely be having blood tests as part of their occupational health screening anyway, uptake is likely to be reasonable. If 25% of these accept screening this would result in an additional 625 tests per year. As bloods are already been taken for offer testing, the laboratory cost is the only additional cost.</i></p>	625X€14= €8,750
21.2. Mandatory HCV screening of all new HCWs who will perform exposure prone procedures (EPPs) is recommended.	Nil additional anticipated as current practice (162).	Nil.
21.3. Existing healthcare workers who perform EPPs and have not yet been screened should be offered HCV screening.	<p>May result in additional testing.</p> <p><i>It is estimated that there are approximately 4,000 HCWs (2,000 doctors and 2,000 nurses or midwives) who perform EPPs and were appointed prior to the commencement of screening. If 10% of doctors accept an offer of screening, and 50% of nurses or midwives this would result in 1,200 additional tests on a one off basis. If these occur over a five year period, this would result in 240 additional tests per year. Staff time and consumables are included in the cost for this group.</i></p>	240X€55.12 = €13,229
21.4. Mandatory HCV screening of all new healthcare students is recommended.	<p>This will result in additional number of tests. As this group are already being tested for other BBVs the additional resource is only the cost of HCV laboratory testing.</p> <p>There are approximately 2,500 new entrants to medicine, nursing, midwifery or dental courses each year (236).</p>	2,500X€14 = €35,000
21.5. Interval HCV testing of HCWs who perform EPPs is not recommended. However, HCWs should be informed of their professional responsibility to seek appropriate assessment if any possible risk exposure has occurred.	Nil	Nil
Recommendation 22 Testing sequence		
<p>22.1. Individuals being investigated for evidence of HCV infection should be screened with an anti-HCV antibody or combined HCV antigen/antibody EIA screening assay.</p> <p>22.2. If the initial HCV EIA is reactive (positive), then the sample should be tested for the presence of HCV antigen, or HCV-RNA, to test for current infection.</p> <p>22.3. Active infection should be confirmed on a second sample and HCV-RNA should be performed (if not already performed) and HCV genotyping should be carried out.</p> <p>22.4. Those individuals with evidence of a resolved HCV infection (i.e. anti-HCV positive and antigen/RNA negative) should have a further sample drawn after six to 12 months for HCV-RNA testing to confirm their resolved infection status.</p>	Nil additional anticipated as current practice.	Nil

Recommendation 23		
23.1. Individuals who initially test HCV negative but who remain at risk of HCV infection should be offered further testing on an annual basis, or six monthly if deemed clinically appropriate.		
Recommendation 24 What type of specimen should be used for screening tests		
24.1. Serum and plasma are the preferred specimen types for screening and diagnostic testing for HCV infection, using quality assured assays. 24.2. Screening and diagnostic testing for HCV infection should not be performed on oral fluid samples due to the low sensitivity and low positive predictive value. 24.3. Dried blood spot testing can be considered for screening for HCV in special circumstance such as mass screening initiatives e.g. in prisons.	Nil additional anticipated as current practice in clinical settings.	Nil
Recommendation 25 What is the role of rapid diagnostic tests or point of care tests?		
25.1. Where concerns exist about hard-to-reach populations or linkage to care then consideration could be given to using approved (e.g. CE marked) RDT/PoC tests on blood specimens. 25.2. If RDT/PoC tests are introduced into standard clinical practice then a quality assurance programme should be established that addresses internal quality control and external quality assurance.	If introduced, RDT/PoC tests are unlikely to have a significant resource implication.	Nil
Recommendation 27 How can uptake of screening be increased and detected cases be linked to care and treatment?		
27.1. Interventions to increase uptake of screening and linkage to care, particularly amongst vulnerable groups, should be supported and evaluated.	Continue to support	Nil
27.2. A national hepatitis C programme with a mandate spanning the entire HCV continuum of care to include full implementation of the <i>National Hepatitis C Strategy</i> and the NHCTP should be established and resourced.	Not costed	

Additional resources and costs

In this section the cost of the additional resources identified are considered.

1. Additional testing

The cost of additional testing will vary by risk group and setting. For some, the additional laboratory test will be the only additional cost as the patient will already be attending a healthcare service and having a blood sample taken. For others there will be additional costs from any pre- and post-test counselling required, staff time for taking blood, and consumables.

Of note, there will be overlap between risk groups. The extent of this is not known. Therefore the estimated number of additional tests is likely to be an overestimate.

Laboratory tests

The cost of the additional HCV testing includes the cost of the initial screening assay and the cost of any subsequent confirmatory tests required. The initial anti-HCV test costs €11 per test (personal communication; Cillian De Gascun, NVRL). An antigen test is needed on approximately 10% of those who have an antibody test and costs €30 per test (personal communication; Cillian De Gascun, NVRL). Taking this into account the average cost of the initial screening tests is €14.

In those with resolved infection screening should be by HCV-RNA, at a cost of €55 per test (personal communication; Cillian De Gascun, NVRL). This will increase the cost of screening. The number this will apply to is not known. In most settings it is likely to be low.

Those who are anti-HCV positive will have HCV-RNA testing on the same sample to confirm current infection at a cost of €55 per test. The number who will require this is not known and will likely vary by source of referral. It is assumed that 10% of anti-HCV tests will be positive and will have a HCV-RNA test on the same sample.

For those who are anti-HCV positive, repeat RNA testing is also recommended after 6 months to confirm chronic or resolved infection.

Laboratory capacity

As of 2013, there were 13 laboratories nationally carrying out HCV testing on behalf of the HSE, with the National Virus Reference Laboratory carrying out over 50% of total tests annually (237). The total number of HCV tests carried out nationally in 2013 was estimated at 135,112 antibody tests, 21,251 antigen tests and 10,881 RNA tests. Extra laboratory capacity may be required but this would not be a new service.

It is estimated that the new guideline could result in an increase of approximately 20,000 anti-HCV tests and 2,000 RNA tests annually.

Blood sampling - consumables

The cost of materials of €1.19 per blood sample was assumed (based on a HTA undertaken by HIQA (238)). This cost includes gloves, cotton wool balls, swabs, needles, blood bottles and tape.

Staff time – assessment, blood sampling, communication of results, counselling, referral

The exact funding mechanism for screening is not decided and will differ by setting and method of presentation of the patient. For the purpose of the budget impact the human resource costs were estimated based on the opportunity cost of staff time.

Staff time for assessment, counselling, and taking the blood samples may differ by setting and population group e.g. taking blood may take longer in PWID with difficult venous access. It will also differ depending

on the type of staff that undertake the work. The time taken to communicate results and counsel will also depend on the result, being longer when positive. It is not possible to account for all these variations at this stage.

Counselling and testing will likely be performed by a range of staff. In some services, it will be mainly nurse-led and in others it may be doctor-led. To calculate an average staff time it was assumed that half of staff time will be nurse time and half will be GP time. GP time was costed at €4.50 per minute and nurse time at €0.33 per minute giving an average cost of €2.42 per minute (239).

Assessing a patient's risk, taking of blood, and communicating a negative test result were assumed to take five minutes each. Communicating a positive result and arranging follow-up was assumed to take 20 minutes. If it is assumed that 10% of anti-HCV tests will be positive, then the average staff time used from assessment to referral will be 16.5 minutes.

Table A 9: Costs of screening process

Resource	Cost
Staff time	€39.93
Consumables	€1.19
Laboratory costs	
Anti-HCV	€11.00
HCV-Ag	€30.00
Anti-HCV + HCV-Ag in 10%	€14.00
HCV-RNA/ NAT testing	€55.00
Total testing cost	
Initial screen with anti-HCV (anti-HCV test+ Ag for 10% + staff time+ consumables)	€55.12
Confirmatory repeat HCV-RNA six months later (staff time (20 mins), consumables, laboratory costs)	€96.12

2. Additional services to provide testing for risk groups

For many population groups a service already exists through which they can be screened. However, for others, there may not be a service or they may be poorly accessed by existing services. A new service or a new approach will be needed. There are some existing initiatives currently funded to improve access for marginalised risk groups. There may be a need in the future to expand these initiatives or develop new ones to, which will be new resources. However, these are not costed at the minute as it is not within the scope of the guideline or current structures to implement these.

3. Communicable disease nurse

A communicable disease nurse in the Department of Public Health in the greater Dublin area will be required to undertake risk assessments for contacts of identified cases. It is estimated that this would be 0.5 WTE position. A cost of €33,897/year is used based on a general nurse CNM 2 position at point 1 of the salary scale, including PRSI, pension and overheads.

4. Information and promotional material

The publication of the guideline should be accompanied by awareness-raising among relevant health professionals and services. This will be done by email communication direct from HPSC to well defined health professional groups; and also through HSE Health Matters bulletin and by HSE Broadcast mail. This will be budget neutral and will not be considered further here.

A public information campaign to raise awareness among the general population will be required, in particular to reach those people who may have had a risk exposure in the past but who are not currently engaged in services where HCV testing would be offered. The purpose would be to raise awareness of HCV and risks of transmission. This campaign would be supported by HSE Communications and would include PR, social media and digital support, using HSE owned assets.

For defined populations there will be a requirement for the development of a targeted information campaign. This would involve the development of information leaflets and posters. Translation of leaflets and posters into different languages will be a necessity. The content of the leaflets and posters will be developed by HPSC, with support from HSE Communications. There would be no costs attached to this. There would be additional costs involved in the design and layout, translation and printing of the leaflets and posters. Posters and leaflets will be distributed to key healthcare and other settings where risk groups congregate. Promotion of testing will also occur digitally via existing HSE communication channels.

The estimated costs of the information and promotional campaign are outlined in Table A 10.

Table A 10: Costs of information and promotion campaigns

Resource	Cost (including VAT at 23%)	Source of cost data
Design of posters (6 at €529 each)	€3,174 in total or €635 per year over five years	Quotation received by HSE HPSC for similar campaign (personal communication; Kirsty MacKenzie, HPSC)
Design of double sided A4 leaflets (10 different designs at €554 each)	€5,535 or €1,107 per year over five years	Quotation received by HSE HPSC for similar
Translation of leaflets into different languages (9 different leaflets at €2,793 each; HCW leaflets not translated)	€25,137 or €5,027 per year over five years	Quotation received by HSE HPSC for similar campaign
Printing of information leaflets: Generic leaflets – 10,000 Prisoners – 14,000 Migrants – 10,000 Antenatal women – 10,000 Parents of children born to infected mothers - 250 MSM – 10,000 Healthcare workers - 1000 For cases on sexual and household transmission - 1000 Homeless people - 2000 People who use drugs - 2000	Annual cost: €1,138 €1,593 €1,138 €1,138 €134 €1,138 €178 €178 €178 €683 €683	Quotation received by HSE HPSC for similar campaign
Printing of posters: Generic posters – 2000 Prisoners – 1000 Migrants – 1000 Antenatal women – 500 MSM – 1000 People who use drugs - 1000	€228 €178 €178 €154 €178 €178	
Social media and internet information and promotional material	Neutral – cost of leaflets and posters above includes digital friendly versions. Other material will be generated by HSE staff. Promotion will be by HSE communications.	
Total (annual)	€15,864	

Table A 11 summarises the anticipated annual additional resources and costs for implementation of this guideline over a five year period. The annual cost is estimated to be €1 million. The main cost is due to the increased testing.

Table A 11: Summary of annual budget impact over five years.

Resource	Costs included	Annual cost (€)
Additional initial HCV screening tests	Number of tests and costs included	
Household contacts	100 anti-HCV tests (staff, consumable and lab costs)	5,512
PWID	200 anti-HCV tests (staff, consumable and lab costs)	11,024
Repeat screening of PWID	825 anti-HCV tests (staff, consumable and lab costs)	45,474
Non injecting drug users	2000 anti-HCV tests (staff, consumable and lab costs)	110,240
Prisoners	3,120 anti-HCV tests (staff, consumable and lab costs)	171,974
Homeless	292 anti-HCV tests (staff, consumable and lab costs)	16,060
Migrants	4,856 anti-HCV tests (staff, consumable and lab costs)	267,663
People with tattoos	2,533 anti-HCV tests (staff, consumable and lab costs)	139,619
Post kidney transplant	85 anti-HCV+Ag tests (lab costs)	3,485
Historical kidney transplant recipients	184 anti-HCV tests (lab costs)	2,576
Deceased solid organ donors	77 HCV-RNA tests (lab costs)	4,235
Living solid organ donors	34 HCV-RNA tests (lab costs)	1,870
Healthcare workers		
New entrants	625 anti-HCV test (lab costs)	8,750
Existing HCWs performing EPPs	240 anti-HCV (staff, consumable and lab costs)	13,229
Healthcare students	2500 anti-HCV tests (lab costs)	35,000
Additional RNA tests		
On those who are anti-HCV positive	Unknown and will differ by risk group. If 10% of those tested are anti-HCV positive then there would be 2,190 additional RNA tests on the initial sample (lab cost only)	96,580
	If 60% return in six months for repeat RNA testing (consumables, staff time and lab test)	101,272
Subtotal – testing costs		1,034,563
Other costs		
0.5 WTE communicable disease nurse for contact tracing	CNM 2 at point 1 of salary scale	33,897
Information and promotion campaign		15,864
Total		1,084,324

Other potential additional resources which are not costed

Additional healthcare for detected cases

It is expected that implementation of the guideline will result in increased numbers of people diagnosed with HCV. Therefore, there will be an increase in the numbers of patients being referred for specialist assessment and treatment.

Their eligibility for antiviral treatment will be subject to prioritisation on the basis of clinical need as defined in the clinical guidelines developed by the HSE National Hepatitis C Treatment Programme. The NHCTP has a fixed annual budget. Therefore, there should be no additional impact on this budget.

There will be an increase in the number of newly diagnosed patients who will be referred for an initial assessment, advice and possibly ongoing monitoring until eligible for treatment. The number of new cases that will be diagnosed and so require additional care is not known. However, it is likely that existing services will have the capacity within their current resources to meet this need. An increasing number of patients currently attending services are now being treated with newer treatments which have a shorter duration, require less monitoring and have fewer adverse events and so place less of a burden on services (10). Also, given the high SVR rates, treated patients will no longer need care and may be discharged from the services.

New services for testing

A challenge to the success of this guideline is ensuring that those at risk are offered screening and that uptake is high. A number of those for whom screening is recommended will not be currently attending specific health services. They also may be poorly reached by existing healthcare services such as primary care services.

There are a number of initiatives underway, funded or partly funded by the HSE, to improve access to testing and to treatment for certain at risk groups. One such example is the HepCare Europe project. Such initiatives should continue to be supported and expanded if shown to be effective in reaching their target risk groups. Further initiatives such as walk-in services or outreach testing may be required to reach certain risk groups, such as migrants or homeless people.

While the GDG recommends that these be considered, their implementation is not within the scope of the guideline and not costed here.

A national hepatitis C programme

One of the recommendations of this guideline is that a national hepatitis C programme be established with a remit across the entire HCV continuum of care. While the scope of this guideline is limited to screening, it is recognised that in order to achieve the goal of HCV elimination by 2030, action is required across the entire continuum of HCV care including reducing vulnerability to HCV infection, primary prevention of infection, diagnosis, linkage to care, treatment, and ongoing care.

Although a commitment of €30 million a year has been made by the Department of Health to the HSE to fund the antiviral drug treatment for HCV, resources have not been allocated to support other activities along the continuum of care. The National Hepatitis C Treatment Programme (NHCTP) aims to treat all those infected with HCV in order to reach elimination. However, this requires that cases are first identified and linked into care. Therefore, additional resources to support access to screening and linkage to care are needed to reach the goal of HCV elimination by 2030.

Potential cost saving

It is anticipated that the implementation of these screening guidelines will result in the identification of previously undiagnosed cases of HCV infection, many of whom will be asymptomatic. They are likely to be

diagnosed at an earlier stage of infection, rather than presenting when they become symptomatic in the later stages of advanced liver disease. Diagnosis of HCV infection with referral for specialist assessment has the following advantages: the patient can be advised about lifestyle factors such as alcohol use which can have an additive harmful effect on the liver; the patient can be advised about how to prevent onward transmission of infection to others; the patient can be offered antiviral treatment. Antiviral treatment is now highly effective. Treatment at an earlier stage of infection is more effective and may involve a shorter course of treatment, but is still effective in many cases of advanced liver disease. Treatment and cure of infection in these population groups will result in improved survival, improved quality of life, reduced requirement for inpatient and outpatient hospital care, some of which would otherwise be very high cost such as intensive care for decompensated liver disease and liver transplantation. However, these savings may not be realised on any significant scale within the next five years. There are also advantages to the wider population in terms of reduced opportunities for transmission of infection to others.

Summary

The estimated annual cost of implementation of this guideline is €1.1 million. A budget of €30 million has been allocated for antiviral drug treatment of HCV infection. However, in order to avail of drug treatment, cases need to be first diagnosed, linked into care and retained in care. Given that those most at risk of HCV are often from marginalised groups, resources will be required in these aspects of care.

References are incorporated into the main reference list.

Appendix 14: Audit and monitoring criteria

Implementation of the guideline will span a range of sectors and services. Monitoring and evaluation will be required at individual service level, and national service level. Suggested audit and monitoring criteria are presented in Table A 12. Services should adapt and develop those relevant to their service as appropriate. This list is not exhaustive and services should develop their own audit plans.

It is recognised that, at present, information systems are not in place to easily monitor many of these criteria at a national level. For some, there are information systems in development that will assist e.g. the Maternal and Newborn Clinical Management System (MN-CMS) and National Medical Laboratory Information System (MedLIS), and others are being further developed e.g. the National HCV Registry.

Screening is one part of the continuum of HCV care. The impact of this guideline will depend on the effectiveness of strategies across the whole care pathway. Therefore, monitoring and audit criteria will overlap with other aspects of the care pathway. The NHCTP currently monitors metrics in relation to access to treatment, such as the time from referral to first appointment with specialist, time from first appointment to treatment initiation, time from funding approval to treatment commencement.

The establishment of a National Hepatitis C Programme, as recommended, will enable the development and monitoring of a suite of metrics across the entire continuum of care in order to comprehensively assess Ireland's progress towards elimination, and the selection of key metrics to be used as national KPIs.

In the interim, Table A 13 presents metrics to be included as national KPIs. They reflect key areas of this guideline. These have been selected because screening of key risks groups and linkage to care of those diagnosed through screening are key recommendations in order to reduce the burden of HCV.

Table A 12: Suggested audit and monitoring criteria.

Criteria	Target	Audited/ monitored by	Possible source of data
Process audit criteria			
Percentage of those attending the service in a risk group who have been offered screening	To be determined by individual services as will vary by risk group	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system
Percentage of those who are at ongoing risk who have been tested in the last 12 months.	As above	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system
Percentage of those tested for anti-HCV who are informed of their test result	As above	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system
Percentage of those who are anti-HCV positive who have a subsequent HCV-RNA or HCV-Ag test	As above	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system, laboratory information systems/MedLIS

Criteria	Target	Audited/ monitored by	Possible source of data
Percentage of those tested for HCV-RNA or HCV-Ag who are informed of their test result	As above	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system
Percentage of those with current infection referred to specialist care or evaluation	As above	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system
Percentage of infants born to HCV-RNA positive women who are referred for follow-up screening	As above	Maternity services/ relevant national HSE divisions	Patient notes, IT system
Percentage of infants born to HCV-RNA positive women who have follow-up HCV-RNA at 6 weeks of age	As above	Paediatric services/ Rainbow clinic	Patient notes, IT system, laboratory information systems/ MedLIS
Percentage of infants born to HCV-RNA positive women who have follow-up HCV-RNA at 6 months of age	As above	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system, laboratory information systems/ MedLIS
Percentage of screening test requests with a risk factor stated	90%	Individual service/ healthcare provider/ relevant national HSE divisions	Laboratory information systems/ MedLIS
Percentage of samples which are anti-HCV positive but RNA or Ag negative which have a second anti-HCV assay to confirm the initial results	90%	Laboratories	Laboratory information systems/ MedLIS
Outcome monitoring criteria			
Percentage of those in a risk group who have accepted screening	To be determined by individual services as will vary by risk group	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system
Percentage of those offered screening who are anti-HCV positive	n/a	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system
Percentage of those who are anti-HCV positive who are HCV-RNA or HCV-Ag positive	n/a	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system, laboratory information systems/ MedLIS
Percentage of those referred to specialist care who attend	To be determined by individual services as will vary by risk group	Individual service/ healthcare provider/ relevant national HSE divisions	Patient notes, IT system

Criteria	Target	Audited/ monitored by	Possible source of data
Anti-HCV positivity rate by risk group	n/a	Individual service/ healthcare provider/ relevant national HSE divisions/ HSE HPSC/ NVRL	Patient notes, IT system, laboratory information systems/ MedLIS
Chronic infection rate by risk group	n/a	Individual service/ healthcare provider/ relevant national HSE divisions/ HSE HPSC/ NVRL	Patient notes, IT system, laboratory information systems/ MedLIS

Table A 13: Suggested national KPIs

Criteria	Target	Possible source
Percentage of PWID who are offered screening on presentation to addiction services	100%	TBC. At present there is not a national IT system for addiction services.
Percentage of those with current HCV infection referred to specialist care	90%	At present there is not a single national information system from which this could be monitored and there is not integration between information systems. The number of diagnosed cases identified through CIDR divided by the number of referrals to treatment centres could be used as a proxy. The proposed new National HCV Registry electronic platform may also be a data source.
Percentage of those referred to specialist care who are offered an appointment	100%	Treatment centres, NHCTP/National HCV Registry
Percentage of those who are referred who then attend a first appointment with specialist care		Treatment centres, NHCTP/National HCV Registry

Appendix 15: Glossary of terms and abbreviations

Definitions within the context of this document

Acute infection	HCV infection is classified as acute if detected within six months after exposure. Determination of infection as acute is difficult unless a person has had a recent negative test.
Anti-HCV antibody	Antibody to HCV, which can be detected in the blood usually within two or three months of HCV infection or exposure.
Anti-HCV antibody positive	Being anti-HCV positive indicates that a person has been infected with HCV at some stage. However, infection may have resolved spontaneously or due to treatment. Further testing is required to establish if the person is currently infected.
Chronic infection	Persistence of HCV-RNA for at least six months after infection.
Cirrhosis	An advanced stage of liver disease characterized by extensive hepatic fibrosis, nodularity of the liver, alteration of liver architecture and disrupted hepatic circulation.
Chemsex	The use of recreational drugs for or during sex.
Endemic	The constant presence of a disease or infectious agent within a given geographic area or population group; may also refer to the usual prevalence of a given disease within such area or group.
Enzyme immunoassay (EIA)	Laboratory-based serological immunoassays that detect antibodies, antigens, or a combination of both.
Exposure incident	A specific exposure to the eye, mouth, other mucous membrane, non-intact skin, or parenteral exposure to blood or other potentially infectious materials.
Exposure prone procedures	These include procedures where the worker's hands may be in contact with sharp instruments, needle tips or sharp tissues (e.g. spicules of bone or teeth) inside a patient's open body cavity, wound or confined anatomical space where the hands or fingertips may not be completely visible at all times. There is a risk that injury to the worker may result in the exposure of the patient's open tissues to the blood of the worker. They have been more precisely defined as procedures which involve surgical entry into tissues, cavities or organs or repair of major traumatic injuries, vaginal or Caesarean deliveries or other obstetric procedures during which sharp instruments are used; the manipulation, cutting or removal of any oral or perioral tissues including tooth structure, during which bleeding may occur. EPPs would not usually include giving injections, taking blood, setting up IV lines, minor surface suturing, and the incision of abscesses, routine vaginal or rectal examinations or uncomplicated endoscopies (162).
HCV-Ag	HCV core antigen which is released into plasma can be detected from early on and throughout the course of infection.
HCV-RNA	HCV viral genomes that can be detected and quantified in serum by nucleic acid testing (NAT).

HCV-RNA positive/ Viraemic/ current infection	A person is HCV-RNA positive when virus is detectable in their circulation. This is also referred to as being viraemic or having current or active infection. While viraemic, a person is infectious, although the risk of transmitting infection is related to the viral load.
Hepatocellular carcinoma (HCC)	Primary cancer of the liver arising from the hepatocytes.
Incidence	The number of new cases of a disease that develop in a given period of time.
Men who have sex with men (MSM)	Any male who engages in sexual activity with a male regardless of sexual identity or sexual desire.
Migrant	The term 'migrant' is taken to include any person who was not born in Ireland but who is currently living here temporarily or permanently. This includes: all persons who have migrated to this country voluntarily for whatever reason, including migrant workers and foreign students; international adoptees; those who have been compelled to leave their original country of nationality or residence for whatever reason and have come to this state to seek its protection as asylum seekers or refugees; undocumented or irregular migrants including those who are trafficked.
Multiplex or multidisease testing	Refers to testing using one specimen in the same test device (or reagent cartridge) that can detect other infections (e.g. HIV, syphilis, HCV, HBV).
Predictive value	The probability that a person's test result truly reflects their infection/disease status. Negative predictive value (NPV) is the probability that when a person's test result is negative, they truly do not have the infection/disease. Positive predictive value (PPV) is the probability that when a person's test result is positive, they truly do have the infection/disease. Predictive values are influenced by the prevalence of the disease in the population.
Nucleic acid testing (NAT)	A molecular technology, for example, polymerase chain reaction or nucleic acid sequence-based amplification that can detect very small quantities of viral nucleic acid (RNA or DNA), either qualitatively or quantitatively.
Parenteral	Piercing the skin barrier or mucous membranes e.g. by needlestick.
Percutaneous	An exposure through the skin (e.g. a needlestick or cut with a sharp object) or contact of non-intact skin (e.g. exposed skin that is chapped, abraded, or afflicted with dermatitis) with blood, tissue, or other body fluids that are potentially infectious.
Point of care test (PoCT)	A test performed in the immediate vicinity of a patient to provide a rapid result outside the conventional laboratory environment
Post-exposure prophylaxis (PEP)	The administration of a drug to prevent the development of an infection after the patient has been exposed to the infection.
Pre-exposure prophylaxis (PrEP)	The administration of a drug to prevent the development of an infection before the patient has been exposed to the infection.
Prevalence	The proportion of individuals in a population having a disease at a given time.

Rapid diagnostic test (RDT)	A test which provides a result in a short time period, typically less than 30 minutes. While laboratories do undertake some RDTs, the term is typically used to describe rapid tests performed at the point of care
Risk factors	An aspect of personal behaviour or lifestyle, an environmental exposure, or an inborn or inherited characteristic that is associated with an increased occurrence of disease.
Sensitivity of a test	The ability of a test to correctly identify those with the infection or disease (i.e. true positives/true positives + false negatives).
Serological assays	Assays that detect the presence of either antigens or antibodies.
Seroprevalence	The level of a pathogen in a population, as measured in blood serum.
Sharps	Any items that have the potential to puncture the skin and inoculate the recipient with infectious material.
Substances of human origin (SoHO)	Includes blood and blood products, organs, tissues, and cells, including reproductive cells and human embryonic stem cells.
Specificity of a test	The ability of a test to correctly identify those without the infection or disease (i.e. true negatives/true negatives + false positives).
Sustained virological response (SVR)	Undetectable HCV-RNA in blood by 12 weeks (SVR12) and/or 24 weeks (SVR24) after the end of treatment.
Vertical transmission	Vertical transmission or mother-to-child transmission of an infectious disease is when infection passes from an infected mother to her infant. This can occur in utero, during delivery, or through breastfeeding.
Viral load	Viral load relates to the amount of HCV virus which is detectable in a person's blood.
Window period	The time interval after infection during which serological assays for antigen and/or antibody are negative.

Abbreviations

The following abbreviations are used in this document:

AAP	American Academy of Pediatrics
AASLD	American Association for the Study of Liver Disease
Ab	Antibody
Ag	Antigen
AIDS	Acquired immunodeficiency syndrome
ALT	Alanine aminotransferase
Anti-HCV	Antibody to hepatitis C virus
ARR	Absolute risk reduction
BASHH	British Association of Sexual Health and HIV
BBV	Bloodborne virus
CAG	Clinical Advisory Group (referring to the CAG of the NHCTP)
CDC	Centers for Disease Control and Prevention
CE	Conformité Européene
CER	Cost-effectiveness ratio
CI	Confidence Interval
CIDR	Computerised infectious disease reporting system
CUA	Cost utility analysis
DAA	Direct acting antiviral agents
DBS	Dried blood spot
DoH	Department of Health
EASL	European Association for the Study of the Liver
ECDC	European Centre for Disease Prevention and Control
EEA	European economic area
EIA	Enzyme immunoassay
ELCS	Elective Caesarean Section
ELISA	Enzyme linked immunoassay
ELPA	European Liver Patients Association
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
EPHN	European Paediatric Hepatitis C Virus Network
EPP	Exposure prone procedure
ERHA	Eastern Regional Health Authority
ESLD	End stage liver disease
ETB	Education and Training Board
ETHOS	European Typology of Homelessness and Housing Exclusion
ETR	End of treatment response
EU	European Union
FEANTSA	European Federation of National Organisations Working with the Homeless
FDA	Food and Drug Administration, USA
GDG	Guideline Development Group
GI	Gastrointestinal
GMHS	Gay Men's Health Service
GMS	General Medical Services
GP	General Practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation

GUM	Genitourinary medicine
HCC	Hepatocellular carcinoma
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HCV-RNA	Hepatitis C virus ribonucleic acid
HCW	Healthcare worker
HIPE	Hospital Inpatient Enquiry System
HIQA	Health Information and Quality Authority
HIV	Human immunodeficiency virus
HPRA	Health Products Regulatory Authority
HPSC	Health Protection Surveillance Centre
HRB	Health Research Board
HSE	Health Service Executive
HTA	Health technology assessment
IBTS	Irish Blood Transfusion Service
ICER	Incremental cost-effectiveness ratio
ICGP	Irish College of General Practitioners
IDU	Injecting drug use
IDSi	Infectious Disease Society of Ireland
IFN	Interferon
IKA	Irish Kidney Association
INAB	Irish National Accreditation Board
INF	Interferon
IPS	Irish Prison Service
IQR	Interquartile range
ISCM	Irish Society of Clinical Microbiologists
IUSTI	International Union against Sexually Transmitted Infections
JPAC	Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee
LGV	Lymphogranuloma venereum
LFTs	Liver function tests
MedLIS	National Medical Laboratory Information System
MISI	Men who have sex with men Internet Survey Ireland
MN-CMS	Maternal and Newborn Clinical Management System
MSM	Men who have sex with men
NASPHGN	North American Society for Pediatric Hepatology, Gastroenterology and Nutrition
NAT	Nucleic acid testing
NCEC	National Clinical Effectiveness Committee
NCPE	National Centre for Pharmacoeconomics
NGO	Non-governmental organisation
NHCTP	National Hepatitis C Treatment Programme
NICE	National Institute for Health and Care Excellence (formerly National Institute for Clinical Excellence, and National Institute for Health and Clinical Excellence)
NIDU	Non-injecting drug use
NPSO	National Patient Safety Office
NPV	Negative predictive value
NUIG	National University of Ireland, Galway
NVRL	National Virus Reference Laboratory

ODTI	Organ Donation and Transplant Ireland
OR	Odds Ratio
OST	Opioid substitution therapy
PAG	Programme Advisory Group (referring to the PAG of the NHCTP)
PCR	Polymerase chain reaction
PEP	Post-exposure prophylaxis
PI	Protease inhibitor
PICO	Patient, intervention, comparator, outcome
PNE	Patient notification exercise
PoC	Point of care
PPV	Positive predictive value
PrEP	Pre-exposure prophylaxis
PWID	People who injects drugs
PY	Person years
QALY	Quality adjusted life year
RBV	Ribavirin
RCPI	Royal College of Physicians of Ireland
RCSI	Royal College of Surgeons in Ireland
RCT	Randomised controlled trial
RDT	Rapid diagnostic test
RIBA	Recombinant immunoblot assay
RNA	Ribonucleic acid
ROD	Rigour of Development
RR	Relative risk
RTU	Recipient Tracing Unit
SaBTO	Safety of Blood Tissues and Organs (refers to the UK's Advisory Committee on the Safety of Blood Tissues and Organs)
SHEA	Society for Healthcare Epidemiology of America
SI	Statutory Instrument
SIGN	Scottish Intercollegiate Guidelines Network
SoHO	Substances of human origin
SSSTDI	Society for the Study of Sexually Transmitted Diseases in Ireland
STI	Sexually transmitted infection
SVR	Sustained virological response
TasP	Treatment as prevention
UISCE	Union for Improved Services Communication and Training
UK	United Kingdom
UNHCR	United Nations High Commissioner for Refugees (also known as the UN Refugee Agency)
USA	United States of America
USPSTF	United States Preventive Services Taskforce
WHA	World Health Assembly
WHO	World Health Organization



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