

Hepatitis C Screening

National Clinical Guideline No. 15

Summary

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, HSE Primary Care, and the development of the guideline was led by the Health Protection Surveillance Centre (HSE HPSC).

Using this Summary National Clinical Guideline

This Guideline Summary should be read in conjunction with the full version National Clinical Guideline.

The full National Clinical Guideline and Summary versions are available at:

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

The complete list of references and appendices can be found in the full version of the National Clinical Guideline. The same number for appendices have been retained in both versions.

This Summary National Clinical Guideline is relevant to all healthcare professionals, healthcare managers and policy makers working with those at increased risk of hepatitis C virus (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.

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Membership of the Guideline Development Group

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.

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Nicola Perry	Manager, Community Response and Chair of the Hepatitis C Partnership (representing at risk groups/patients)
Michele Tait	Programme Manager, HSE National Hepatitis C Treatment Programme

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* The same numbers for appendices, tables and figures have been retained in both full and summary version guidelines. The numbers relate to the appendix sequence in the full version National Clinical Guideline.

1 Background

1.1. Overview of hepatitis C virus

Hepatitis C virus (HCV) is a major cause of liver disease worldwide. Globally, it is estimated that there are 115 million people who have had HCV infection, and 80 million with chronic infection (1).

Transmission of HCV occurs through contact with the blood of an infected person. Risk factors for HCV differ globally. In developed countries like Ireland, injecting drug use (IDU) is the major risk factor.

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. Between 15% and 45% of those infected clear the virus spontaneously, while the remaining 55% to 85% of those infected develop chronic HCV infection (2). 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’. An estimated 4% of those with cirrhosis progress to decompensated liver disease annually and 1.6% develop HCC annually (3). 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.

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 strategy direction for HCV care and policy, with the paradigm now focused towards elimination.

1.2. Epidemiology and clinical impact of HCV infection in Ireland

HCV infection, has been a notifiable disease in Ireland since 2004. Between 2004 and 2016, 14,107 cases were notified. In recent years there has been a decrease in cases, notified (Figure 1). However, the number of new cases now appears to be stabilising rather than further declining.

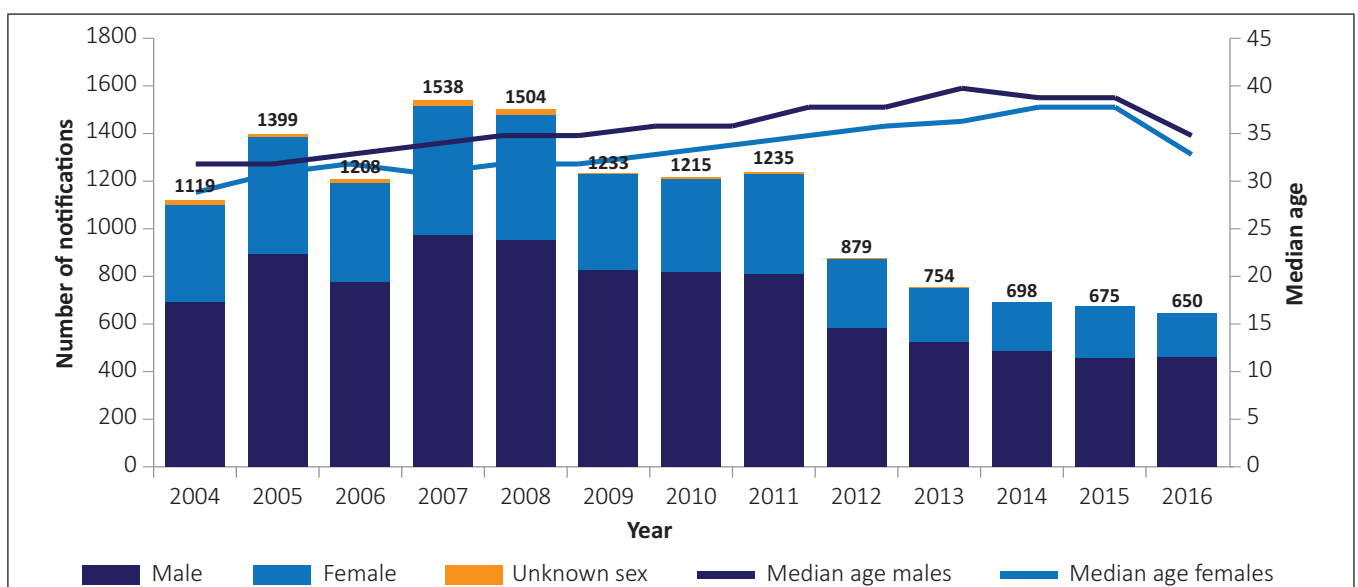


Figure 1: Number of notifications of HCV 2004-2016, by sex and median age. (Source: HSE Health Protection Surveillance Centre)

Where risk factor data are available, IDU is the most common risk factor reported (80%), followed by possible sexual exposure (5%), receipt of blood or blood products (4%), vertical transmission (2%) and tattooing or body piercing (1%). In 7% no risk factor was identified.

Notification data can only include diagnosed cases. Information on the prevalence of a disease is a better reflection of the burden of disease as it includes undiagnosed cases (4). A 2016 study found that the adult seroprevalence of HCV was 0.98% (95% confidence interval (CI) 0.73%-1.3%) and the adult prevalence of chronic HCV infection was 0.57% (95% CI 0.40%-0.81%) (5). Based on this and other available data it is likely that there are between 20,100 and 42,000 people with current infection in Ireland, and that 60% of those have not yet been diagnosed (4, 6).

The number of hospital admissions due to end stage liver disease (ESLD) and HCC in those with HCV infection has been increasing in Ireland. This increase is likely related to the fact that the peak incidence in the largest risk group, people who inject drugs (PWID), in Ireland was in the late 1990s, and those infected during that period are now developing ESLD or HCC (7). Between 2005 and 2016, 116 liver transplants were performed in Ireland in people with HCV infection, accounting for 18% of all liver transplants (source: HIPE via Health Atlas Ireland¹ (8)).

HCV related morbidity and mortality, and also healthcare resource use, may not yet have peaked. Modelling studies in the UK predicted that, at current treatment levels, the incidence of ESLD would continue to increase, peaking in 2030 (9).

1.3. 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 (10). The strategy spans surveillance, prevention, screening and treatment of HCV infection. 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.

National Hepatitis C Treatment Programme

Direct acting antiviral (DAA) therapies are now the standard of care for HCV infection (11). In HCV treatment, sustained virological response (SVR) means that the virus is no longer detectable at a defined period after completion of therapy. SVR is regarded as a virological cure and is associated with improved morbidity and mortality. Older treatment regimes induced SVR rates of 40-65% (2). DAA treatment regimes are of shorter duration, with far fewer side effects, and have SVR rates of over 90% (2). Further details on the new treatments are available at <http://www.hse.ie/eng/health/az/H/Hepatitis-C/>

It is now recommended that DAA regimens be used for the treatment of persons with HCV infection (2, 12). 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 (13).

¹ Based on a procedural code of 'Transplantation of liver' (9031700) AND a diagnostic code of HCV infection (B182). Extracted 10 July 2017.

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). Criteria for access to treatment are continuously expanding. The HSE NHCTP is aiming 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 the HCV in Ireland and making it a rare disease by 2030 (14).

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

The first global health sector strategy on viral hepatitis, covering the period 2016–2021 was published by the World Health Organization (WHO) in 2016 (15). 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 having been treated. The strategy calls for action across the entire continuum of hepatitis care from primary prevention of infection, to diagnosis, linkage to care, and treatment.

1.4 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”(16).

Screening for HCV infection meets all of the criteria by which a proposed screening programme should be evaluated (16).

2 Development of this National Clinical Guideline

2.1. 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 as a major public health concern HCV by 2030. Key to reaching the goal of elimination will be treatment of those infected. However, it is estimated that 60% of those with HCV infection in Ireland are undiagnosed. 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.

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.

2.2. 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 HCV screening
- to support the linkage to care of identified cases
- to increase awareness of HCV screening amongst healthcare workers and the public.

2.3. 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 agencies 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.

2.4. 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 of the full guideline.

2.5. Sources of funding

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

2.6. Guideline development group (GDG)

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. Members of the GDG are listed in Table 1.

2.7. Methodology and literature review

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. Key questions are outlined in Appendix 5.

Recommendations from high quality national or international guidelines were adopted or adapted where feasible. Included guidelines and their quality appraisal scores are summarised in Appendix 6 of the full guideline. 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 altered to be appropriate to the research question (see Appendix 7 of the full guideline). One systematic literature review was commissioned and undertaken by the School of Nursing and Midwifery, National University of Ireland, Galway (see Appendix 8 of the full guideline).

To formulate recommendations, subgroups of the GDG used a considered judgement process adapted from the GRADE Evidence to Decision (EtD) framework (17, 18). Recommendations were formulated 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 of the full guideline). Recommendations were then presented to the full GDG for approval.

2.8. Grading of recommendations

Recommendations were graded in two ways: the level and quality of evidence supporting the recommendation (Table 3) and the strength of the recommendation (Table 4), based on recommendations from GRADE (19, 20).

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'.

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

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.

2.9. 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, and members of the public were invited to review the guideline and provide feedback.

International external review of the guideline was undertaken by two experts in the epidemiology and public health management of HCV: 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.

Feedback received was reviewed by the GDG and the guideline was amended where appropriate. Further detail on the consultation process, the feedback received and the resulting action of the GDG is available in Appendix 10 of the full guideline.

2.10. 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 National Hepatitis C Strategy is incorporated (please see Recommendation 27 regarding the need for a national HCV programme). If there is a major change in evidence prior to this, a rapid update may be conducted as per NCEC procedures.

2.11. Implementation

A plan for implementation of this guideline is available in Appendix 11 of the full guideline. The plan builds on the work that is already being undertaken by a range of HSE services, NGOs, health and social care professionals, peer workers and volunteers (see Appendix 12 of the full guideline for a summary of services). Support for implementation of this guideline has been stated in the HSE Primary Care and HSE Health and Wellbeing 2017 operational plans (21, 22).

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 (15). The GDG recommends that 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.

2.12. Economic impact of this National Clinical Guideline

A review of economic literature was undertaken to inform the guideline process and, where appropriate, was considered in the formulation of recommendations. A summary of economic evidence is presented in Appendix 13 of the full guideline. Of note, much of the economic evidence was based on older treatment regimes and therefore not generalisable to the current and rapidly changing HCV treatment context.

A Budget Impact Assessment (BIA) is also presented in Appendix 13 of the full guideline. It has been estimated that implementation of the guideline will cost is €1.1 million per year over a five year period.

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.

2.13. 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. Suggested monitoring and audit criteria are presented in Appendix 14 of the full guideline. 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.

Appendix 14 of the full guideline presents metrics which reflect key areas of this guideline which should be considered for inclusion as national key performance indicators.

3 National Clinical Guideline recommendations

3.1. Should the following people be offered screening for HCV?

3.1.1. Pregnant women

One of the primary aims of screening pregnant women for infections is to intervene if possible and prevent vertical (mother-to-child) transmission of the 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 also HIV-infected (10.8–25%) (2). The risk of transmission is correlated with the HCV viral load of the mother. 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 (23-28). Currently, HCV treatment during pregnancy is not recommended.

A number of studies have reported on the prevalence of HCV in the antenatal population in Ireland. A study in 1997-1998 in the Rotunda Hospital determined the prevalence of anti-HCV in an antenatal population to be 0.9% (29). 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, the prevalence of anti-HCV was found to be 1.4% in the targeted screening programme and 0.7% in the universal screening programme (30). Approximately half of women attending for antenatal care were eligible for screening as part of the targeted screening programme (30). It was estimated that in the universal programme, one case (1/67, 1.5%) would not have been detected through a targeted screening programme.

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 infant. The 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. If HCV treatment during pregnancy becomes feasible in the future, the value judgement may shift in favour of universal HCV screening in pregnancy.

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

3.1.2. Children born to mothers with HCV infection

There is a small risk of transmission of HCV between an infected mother and her infant during the perinatal period (see section 3.1.1). There is no risk of vertical transmission if a mother is not viraemic (i.e. HCV-RNA negative).

Screening of infants born to infected women permits early identification and linkage to care.

Due to the transfer of maternal anti-HCV across the placenta, infants born to infected mothers may be anti-HCV positive in the first few months of life, in the absence of vertical transmission of HCV infection. Due to this persistence of maternal anti-HCV, serological testing of infants is not recommended before 12 months of age (23, 27). Testing for HCV-RNA can be undertaken earlier. However, the sensitivity of HCV-RNA in early life is low and confirmatory testing will be required at a later stage.

Current practice in Ireland, as per the Rainbow Clinic² guidelines, is to offer HCV-RNA testing at six weeks and six months of age (24). 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.

Value judgement

While the GDG recognises that there is not a direct clinical benefit to detecting infection in infants early, 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.

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, 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*

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.

3.1.3. Household contacts of a person with HCV infection

Household contacts are people who share living spaces with each other. They can be spouses, partners, siblings, children or other family members, or be unrelated. Transmission of HCV to a household contact (excluding vertical or sexual transmission) is termed horizontal transmission. When horizontal transmission occurs between family members it is sometimes termed intrafamilial transmission.

Some studies have identified a risk of horizontal transmission of HCV (31, 32). Other studies have found no increase or only a slight increase in the prevalence of anti-HCV amongst family members or household contacts of a HCV positive individual (33-35).

The epidemiology and routes of transmission between household members are difficult to interpret with any certainty. A number of studies showing an increased risk were undertaken in high endemicity countries where the potential for exposure through other routes outside of the household (e.g. healthcare transmission) could have existed. Even those studies in non-endemic countries were not able to differentiate between sexual transmission, horizontal transmission, 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 infected person 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.

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*

3.1.4. People who use unprescribed or illicit drugs

People who inject drugs (PWID) are a well-recognised risk-group for HCV infection globally. Current PWID are at ongoing risk of infection and regular re-testing has been recommended, although recommendations on the frequency of re-testing vary (23, 36). The current standard of care for services offering opioid substitution in Ireland is to offer anti-HCV testing on presentation (37). 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.

There is limited and inconsistent evidence on the risk of HCV amongst non-injecting drug users. A systematic review published in 2007 determined the prevalence of HCV in those engaging in non-injecting drug use (NIDU) to range from 2.3-35.5% (median = 14%) (38). However, the authors concluded that it could not be adequately determined whether 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 (39-41). Other observational studies have found an association between sharing equipment for snorting or sniffing drugs and HCV infection (42-44). However, the quality of studies is limited by a lack of clarity on the definition of NIDU used, and reliance on self-reported behaviours.

Value judgement

PWID are a recognised risk group for HCV infection. NIDU which results in exposure to blood of another person is a biologically plausible transmission route. 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.

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 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

3.1.5. Prisoners

Prisoners are a recognised risk group for HCV infection globally (2). Prisoners are considered to be a risk group mainly due 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, tattooing, or other environmental exposure to contaminated blood while in prison.

Studies have demonstrated a high prevalence of IDU amongst prisoners in Ireland and a high prevalence of HCV (45-47). In a 2011 study, an anti-HCV prevalence of 13% (95% CI 10.9-15.2%) was found amongst prisoners (45). Amongst those who were also PWID, the anti-HCV prevalence was 41.5%.

The *Irish Prison Service Health Care Standards* recommend that all those entering prison be offered HCV testing where clinically appropriate and that prisoners who are infected with HCV be given appropriate advice and treatment (48). However, 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.

Value judgement

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. 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.

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. 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 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.

3.1.6. People who are homeless

A number of studies in Ireland have shown an association between some homeless populations such as rough sleepers, IDU and HCV infection (49-51).

The results of these studies are consistent with the experiences of members of the GDG working with people who are homeless. 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 some 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.

Value judgement

The homeless are a marginalised group with often greater healthcare needs than other population groups. Homeless people who are PWID 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*

3.1.7. Migrants

WHO recommends that migrant³ populations from high/intermediate endemic countries be offered screening (52). 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.

There is limited data available on the prevalence of HCV among migrants living in Ireland. The Reception Centre in Baleskin reported that, amongst those accepting voluntary screening between 2004 and 2012, the prevalence of HCV was 0.95%, with a prevalence of 3.3% amongst certain nationalities (53). 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% (54).

Migrants from high prevalence countries can have a prevalence of HCV comparable to their country of origin (55). 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 (55).

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 (55). Based on the census data, and assuming a prevalence equal to that in their country of origin, it is estimated that there could be 8,000 migrants in Ireland with HCV infection.

Value judgement

One-off screening of migrants from intermediate to high prevalence countries 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 screening to those from a country with a prevalence greater than 2%.

This recommendation and its 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, and these should be addressed.

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*

³ The term migrant in this guideline refers to anyone born outside of Ireland but currently living in Ireland. See glossary for definition.

3.1.8. People who received medical or dental treatment abroad

There is limited evidence on the risk of HCV transmission from medical or dental treatment abroad. 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, and where blood transfusions and other tissue donations are not screened for viral hepatitis (52). WHO thus recommends that persons who have received medical or dental interventions in health-care settings where infection control practices are substandard should be offered testing for HCV (2).

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.

It is recognised that implementation of this recommendation will be difficult and will be likely to be 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*

3.1.9. People with tattoos or body piercings

A number of studies have identified an association between tattooing and HCV infection (56). When stratified by the place where the tattoo was done the association persisted for tattoos carried out in non-professional parlours or by ‘friends’ but was lower and not significant for tattoos done in professional parlours.

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, the highest association was found amongst those tattooed between 1980 and 1990. 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, while receiving a tattoo within the last 10 years was not (57).

No studies, outside of the prison context, were identified which determined the risk of HCV from tattoos in Ireland.

A number of observational studies found an association between HCV infection and ear piercing, body piercing, or an unspecified piercing, on univariable analysis (58-62). However, when multivariable analysis was undertaken the associations generally did not persist (57, 58, 60, 62). Other observational studies did not find an association with HCV infection and piercing (60, 63-67).

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 long time ago, in non-professional settings, in prison, in high prevalence countries, or in other circumstances where infection control was poor. 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. For this reason, 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*

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

The risk of sexual transmission of HCV is strongly linked to HIV co-infection and there is low or no risk of sexual transmission of HCV among HIV-negative heterosexual couples (2, 52, 68-71).

Amongst heterosexuals, outside of the context of monogamous relationships, there is limited evidence on what, if any, sexual behaviours present an increased risk of sexual transmission of HCV. The risk associated with multiple sexual partners or sexually transmitted infections is not clear (72). 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 (52). In a systematic review to determine what factors were associated with an increased risk of sexual transmission of HCV infection in a heterosexual population, the included studies examined seven risk factors (multiple sex partners, receiving or providing sex commercially, having a PWID partner, and unprotected vaginal, oral or anal sex) (73). One included study in an antenatal population in Scotland, found an increased risk of HCV amongst those who reported not injecting drugs but had a sexual partner who did (74). None of the other factors examined in the systematic review were found to be statistically significant risk factors. However, the authors concluded that there was uncertainty about these results due to limited quantity of evidence and the very low quality of evidence.

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.

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*

3.1.11. Men who have sex with men

To date, the risk of sexual transmission of HCV amongst men who have sex with men (MSM) who are HIV negative has been considered to be low (2). A number of systematic reviews and meta-analyses have shown an increased prevalence or incidence of HCV amongst HIV positive MSM compared to HIV negative MSM, in particular HIV positive MSM who are PWID (75-77).

Mucosal damage is proposed as the facilitator of sexual transmission of HCV amongst MSM. Studies have shown sexual transmission of HCV amongst MSM to be associated with unprotected anal intercourse (UAI); the number of sexual partners; recent ulcerative sexually transmitted infections (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. chemsex³) (70, 77-80). Some drugs used for chemsex are injected, which may pose a transmission risk. Another mechanism by which chemsex may increase the risk of HCV infection is due to less safe sex and mucosal trauma due to disinhibition.

HCV amongst MSM in Ireland

A cluster of acute HCV amongst MSM in Ireland was reported in 2016 (81). Twenty percent of cases involved in this cluster were HIV negative. An increase in notifications of HCV in men identified as MSM has also been observed in the national HCV surveillance system. During 2016, there were 28 cases, compared to eight, three and 13 in the previous three years (source: Computerised Infectious Disease Reporting system before (CIDR), HSE HPSC). In both the cluster and the notification system, a high proportion of cases have had multiple STI events suggesting that transmission may be occurring in a particularly high risk group.

Value judgement

HCV amongst MSM in Ireland is an emerging issue. 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. However, cases have occurred in HIV negative MSM.

There is evidence of high risk sexual and drug taking behaviour amongst some MSM in Ireland as reported by the Men who have Sex with Men Internet Survey 2015 and evident in the increasing rates of STIs amongst MSM (82, 83). 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 HCV 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 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 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

³ The use of recreational drugs for or during sex.

3.1.12. People attending for a sexual health screen

The risk of sexual transmission of HCV amongst heterosexuals and MSM are presented in sections 3.1.10 and 3.1.11 respectively.

International recommendations limit the screening of asymptomatic attendees of sexual health services to those who fall into other risk groups (23, 84-87).

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.

Value judgement

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*

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

The dialysis setting is recognised as a high risk environment for the transmission of HCV and other BBVs, in the absence of strict infection prevention and control practices, including appropriate screening. 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.

The 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 considers 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 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.

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

Strength of recommendation: strong

3.1.14. Recipients of substances of human origin

In many countries there have been episodes of HCV transmission related to the 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.

In Ireland, 1,694 persons are known to have been infected with HCV through blood or blood components (89). Of these, 1,051 were infected through anti-D immunoglobulin, 418 through blood transfusions, and 225 through clotting factors. Routine testing for HCV was introduced into the blood screening process in Ireland in October 1991.

The Irish Blood Transfusion Service (formerly the Blood Transfusion Service Board) has undertaken extensive efforts to trace recipients of potentially infectious products previously issued in Ireland (90). 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 may 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 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 living in Ireland. Also, in some countries a quality assured donor screening programme is still not in place (91).

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 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.
- 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

3.1.15. Donors of substances of human origin

European Union legislation and national legislation requires that, at a minimum, donors of blood, tissues and cells⁵, and organs must be tested for anti-HCV (92-100).

In addition to the legislative requirement, HCV-RNA testing of blood donations by nucleic acid testing (NAT) is considered to be best practice and is current practice in Ireland (101). Regarding the testing of donors of tissues, cells, and organs, due to the increased sensitivity of NAT assays. NAT is also encouraged as good clinical practice to rule out window period infections, and replaces the need for any quarantine or follow-up serological screening (102-104). If NAT is either not done, or the results are not available prior to organ donation, testing by a combined HCV-Ag and anti-HCV assay test is recommended rather than anti-HCV alone (104).

A national advisory committee for safety and quality of blood, organs and tissues 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 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 requirements⁶.

***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

⁵ Legislative requirements for screening of reproductive cells 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.

⁶ The Health Products Regulatory Authority (HPRA) for human blood and blood components and for tissues and cells. The HPRA and the HSE for organs intended for transplantation. Within the HSE, Organ Donation Transplant Ireland (ODTI) is responsible for implementation of their relevant aspects of legislation.

3.1.16. General population or birth cohort

WHO states that the best approach to screening will depend on a country's unique HCV epidemiology. It recommends 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 (52).

A review of epidemiological information was undertaken to determine if a specific birth cohort for which HCV screening could be recommended exists in Ireland. Triangulation of data from a number of sources indicates that the prevalence of HCV infection in Ireland is highest in those born between 1965 and 1985. 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 (source: CIDR, HSE HPSC). A HCV seroprevalence study conducted in Ireland in 2016 showed that the prevalence of chronic infection was significantly higher among persons aged 30-49 years (5). Adult males born between 1965 and 1984 from the east of the country had the highest rate of chronic HCV infection.

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 (7). This finding is consistent with the age-profile identified in the notification data and the seroprevalence study.

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.

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. Thirty one per cent (n=1,426,156) of the Irish population were born between these years. 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. A request to conduct this HTA was submitted to the Health Information and Quality Authority (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*

3.1.17. Healthcare workers

For recommendations on the management of healthcare workers (HCWs) following an exposure to potentially infected material, *HSPC Guidelines on the Emergency Management of Injuries* should be consulted (105).

Provider to patient transmission of HCV has been documented, including transmission events in the UK, Spain and Germany during cardiovascular, gynaecological or obstetric, and orthopaedic surgery (106-109). However, the transmission rate from infected HCWs to patients, as determined from published patient notification exercises, is low (110). No cases of provider to patient transmission of HCV have been reported in Ireland (111, 112).

In 2005 the Department of Health Standing Advisory Committee on the Prevention of Transmission of Blood-Borne Diseases in the Health-Care Setting recommended HCV screening of all HCWs who perform exposure prone procedures (EPPs) (113). Since 2008 it is policy that all new HSE staff who perform EPPs are screened (114, 115).

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.

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 and avoid restrictions to their activities during training. Successful treatment will avoid implications for their future career choices.

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 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

3.2. How should screening for HCV be performed?

3.2.1. What test should be used for HCV screening?

WHO recommends that the initial test for HCV infection is a HCV serological assay (i.e. anti-HCV or antibody/antigen) (52). If positive this should be directly followed by testing for the detection of HCV-RNA to confirm current infection. Detection of HCV core (p22) antigen, with an assay which has comparable clinical sensitivity to NAT, is an alternative to diagnose current 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).

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. Therefore HCV-RNA testing should be considered in some people who are immunosuppressed if HCV infection is suspected and anti-HCV remains negative.

Those previously infected

As anti-HCV generally remains positive for life, testing should be by HCV-RNA in those who were previously infected (23, 25).

Recent infections

Anti-HCV may not be detectable for three or more months after infection. HCV-RNA will be detectable after two weeks. If the potential exposure was recent, HCV-RNA or HCV-Ag should be considered.

Frequency of testing for those at ongoing risk

Repeated testing of those at ongoing risk is recommended, although there is no clear consensus on the frequency of repeat testing (23, 25, 68, 86, 116-118).

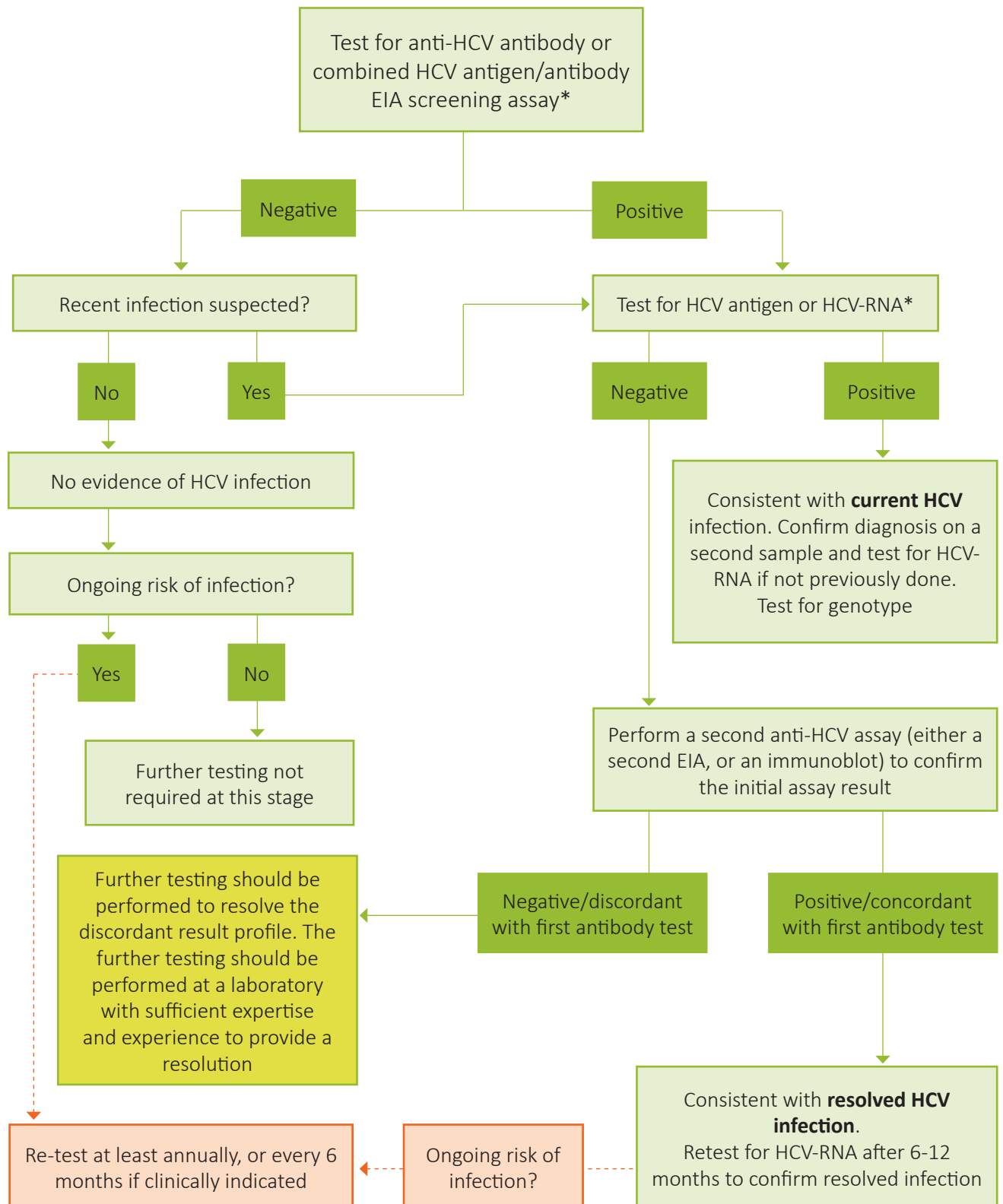
Recommendation 22

- 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 Figure 4.

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



*In certain patient groups, initial testing should routinely incorporate HCV antigen or HCV-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 (HCV-RNA testing should be performed 6 weeks post-exposure).

Figure 4: Testing sequence for HCV infection

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*

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

Anti-HCV testing can be performed on a number of different types of specimens including serum, plasma, dried blood spots (DBS), and oral fluid. HCV-RNA testing is restricted to serum, plasma or DBS.

Studies examining the performance of DBS in the diagnosis of HCV have found the sensitivity and specificity of DBS in detecting anti-HCV to be high (119-125). WHO and other bodies state 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 (23, 52, 86).

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 to be lower than DBS (125-130). Amongst HIV positive individuals, the sensitivity was particularly reduced (126).

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 (131). However, variable effect sizes were found and all included studies that were judged to have a high risk of bias. 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 (132). 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. There is some evidence to support improved acceptability and uptake of testing with DBS or oral fluid, although it is still limited. However, the sensitivity of testing on oral fluid samples is low, and therefore it is not considered an acceptable specimen.

While the sensitivity of DBS is considered acceptable, there are some limitations. There is currently no approved laboratory 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

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

A rapid diagnostic test (RDT) is a test which provides a result in a short time period, typically less than 30 minutes. The term is typically used to describe rapid tests performed at the point of care (PoC) i.e. in the immediate vicinity of a patient, and commonly also called PoC tests (PoCT).

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. 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 (52).

In a systematic review and meta-analysis evaluating RDTs/PoCTs pooled accuracy was high overall.

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 (131). A number of qualitative studies have suggested positive attitudes to RDTs/PoCTs amongst providers and patients (133-136).

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. 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 RDTs/PoCTs 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* (137).

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*

3.2.4. 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 (BBVs).

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

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

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*

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

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.

Interventions which have been shown to have a positive impact on the uptake of screening amongst high risk groups include targeted case finding in primary care, support and training for primary care practitioners, offering alternative testing and provision of outreach testing (138). Delivery of services in non-specialist community settings have, in particular been found to be effective. Targeted HCV testing interventions have been shown to be more effective compared to no targeted interventions, or routine practice, in increasing the number of people tested, anti-HCV cases detected, referrals to a specialist, attendance at a specialist, and cases commencing treatment (139). Practitioner based targeted testing interventions (i.e. where a health or social care professional was given support to offer risk assessment and/or testing) were found to be most effective.

Recommended settings for testing include: mobile clinics, community settings, harm reduction programmes or low threshold service centres visited by PWID, correctional settings, primary care settings (118, 140). NICE determined that while pilot studies of community pharmacy testing in the UK have shown good acceptability and detection rates, there was not yet sufficient evidence to uniformly support community pharmacy testing (86, 141, 142).

A number of studies have showed improvements in referrals to specialist care and attendance with the use of care co-ordinators, patient navigators, or peer driven interventions (143-151).

Value judgement

There are a number of initiatives already underway in Ireland employing such strategies (see Appendix 12 of the full guideline). 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 HCV care. A national HCV programme with a mandate and resources to co-ordinate actions across the entire continuum of care should be established as recommended by WHO.

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*

4

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 of the full guideline).
- 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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5 Appendices

Only appendices 1, 2, 5 and 15 are presented here as they are key to interpretation of the recommendations presented in this Summary Guideline.

Please refer to the full guideline report for the following appendices.

Appendix 3	Recommendations from the National Hepatitis C Strategy 2011-2014
Appendix 4	Conflict of interest declarations
Appendix 6	Quality scores of included guidelines
Appendix 7	Example search strategy and results
Appendix 8	Commissioned systematic literature review
Appendix 9	Considered judgement form
Appendix 10	Consultation process
Appendix 11	Implementation plan
Appendix 12	Summary of tools/ services to assist implementation
Appendix 13	Economic impact report
Appendix 14	Audit and monitoring criteria

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: Hepatitis C 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> (55))

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> (10)

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 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 characterised 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 (114).
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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