Hepatitis C Screening Guideline Development Group
Background to recommendation 17 and 18: Recipients of substances of human origin

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

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

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

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Contents

History of development of the recommendation

Date	Process	Outcome
02/06/2015	Recommendations from quality appraised national and international guidelines reviewed	Agreed to augment recommendations from guidelines with Irish literature on HCV in this group
20/01/2016	GDG subgroup meeting to undertake considered judgement process	Formulation of recommendation
23/02/2017	Review of subgroup recommendation by GDG	Recommendation accepted
25/04/2017	Consultation feedback reviewed by GDG	No changes to recommendation
June – July 2017	Editing	Recommendation reworded in final editing process

Considered judgement process

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

Date:20/01/2017
Attendees: LT, SD, ER, NOF, CDG, JC

Table 1: Considered judgement form

1. What is the question being addressed? Present PICO if relevant
Should the following groups be screened: Recipients of unscreened blood and blood products in Ireland (pre October 1991) who have not been previously screened? Although not specified in the initial key questions to be addressed decided by the guideline development group (GDG) also considered it necessary to make a recommendation on recipients of **solid organs in Ireland in the past and on recipients of blood and blood products outside of Ireland**.
2. What evidence is being considered to address this question and why? (This section will explain the approach taken to address this question and what GDG members are being asked to consider)
Irish national policy, literature on transmission within Ireland, WHO blood safety database, other international hepatitis C guidelines.
3. What is the body of evidence? Source of evidence: (tick all that apply) Guidelines ã Primary literature Ĭ Other ã ; specify: _Irish national policy, Reviews of transmission and lookbacks conducted in Ireland, WHO blood safety database
For Irish evidence and policy see section 5 **Hepatitis C Guidelines** **AASLD, 2013** (1) The following should be screened: • Prior recipients of transfusions or organ transplants, including persons who were notified that they received blood from a donor who later tested positive for HCV infection. • Received a transfusion of blood or blood components, or underwent an organ transplant before July 1992 • Received clotting factor concentrates produced before 1987 (*American Association for the Study of Liver Diseases, Recommendations for Testing, Managing, and Treating Hepatitis C*). HIQA Quality Score of 134.5 **SASLT, 2012** (2) Prior recipients of transfusions or organ transplants, including those who were notified that they had received blood from a donor who later tested positive for HCV infection, who received a transfusion of blood or blood products before July 1992, and who underwent an organ transplant before July 1992 should be screened for HCV. (*Saudi Association for the Study of Liver diseases and Transplantation, SASLT Practice Guidelines: Management of Hepatitis C Virus Infection*). HIQA Quality Score of 95.3

NASPGHAN, 2012 (3) Earlier recipients of transfusions or organ transplants before July 1992 including persons who were notified that they had received blood from a donor who later tested positive for HCV infection should be offered screening for HCV. Routine hepatitis C virus (HCV) testing is of uncertain need for recipients of transplanted tissue (e.g., corneal, musculoskeletal, skin, ova, sperm). (*North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, NASPGHAN Practice Guidelines: Diagnosis and Management of Hepatitis C Infection in Infants, Children, and Adolescents*). HIQA Quality Score of 88.

NICE, 2013 (4) People who received a blood transfusion before 1991 or blood products before 1986, when screening of blood donors for hepatitis C infection, or heat treatment for inactivation of viruses were introduced, should be offered screening for HCV. *(The National Institute for Health and Care Excellence, Hepatitis B and C: Ways to Promote and Offer Testing to People at Increased Risk of Infection).* HIQA Quality Score of 148

SIGN, 2013 (5) Recipients of blood and blood components before September 1991 and organ tissue transplants in the UK before 1992 should be offered testing for HCV. Recipients of blood clotting factor concentrates prior to 1987 should be offered testing for HCV. *(Scottish Intercollegiate Guidelines Network, Management of Hepatitis C A National Clinical Guideline).* HIQA Quality Score of 127.7

US Preventive Services Taskforce, 2013 (6) All persons who received a blood transfusion before 1992 should be offered screening for HCV. *(United States Preventive Services Taskforce, Screening for Hepatitis C Virus Infection in Adults).* HIQA Quality Score of 117

BASHH, 2015 *(7)*
Offer testing…people with haemophilia or other patients who received blood or blood products pre-1990 and remain untested, (1A). *(British Association for Sexual Health and HIV, United Kingdom National Guideline on the Management of the Viral Hepatitides A, B & C 2015).*

EPHN, 2005 (8) Those who received a blood transfusion or blood products before 1991 should be offered screening for HCV. *(European Paediatric HCV Network, The Management of HCV Infected Pregnant Women and their Children).* HIQA Quality Score of 81.3

IUSTI/WHO Euro, 2010 (9) Testing for HCV should be offered in men with haemophilia or other patients who received blood or blood products pre-1991. *(The International Union Against Sexually Transmitted Infections/WHO Europe, European Guideline for the Management of Hepatitis B and C Virus Infections).* HIQA Quality Score of 66.3

Blood safety literature

WHO Global Database on Blood Safety (10)

Currently, in a number of countries, the safety of blood and blood products cannot be assured. The 2013 WHO Global Database on Blood Safety found that 73% (122/167) of countries had a national blood policy and 65% (108/167) of countries, had specific legislation covering the safety and quality of blood transfusion, including: 79% of high-income countries; 64% of middle-income countries; and 41 % of low-income countries. Sixteen countries were not able to screen for one of more of HIV, hepatitis B, hepatitis C or syphilis. Irregular supply of test kits was one of the most commonly reported barriers to screening. In high-income countries 81% of blood screening laboratories are monitored through external quality assessment schemes compared to 55% in middle-income countries and 34 % in low-income countries. The median prevalence of HCV in blood donations in high-income countries is 0.02% (IQR 0.003% -0.16%), which is considerably lower than in middle-income (0.32%; IQR 0.09%-0.69%) and low-income countries (1.03%; IQR 0.67%-1.8%).

4. What is the quality of the evidence? To be considered if primary literature was reviewed.

4.1. How reliable are the studies in the body of evidence?

If there is insufficient evidence to answer the key question go to section 11. Comment here on any issues concerning the quantity of evidence available on this topic and its methodological quality.

n/a

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

n/a

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

Infected blood components and blood products were issued in Ireland leading to transmission of hepatitis C (see section 5). Assurance programmes were introduced at different times in different countries so dates are not generalisable.

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

Yes but dates will need to be adjusted for Ireland.

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

n/a

5. Additional information for consideration

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

Unscreened and contaminated blood components and blood products issued in Ireland

Routine testing for hepatitis C was introduced into the blood screening process in Ireland October 1991. Incidences of distribution of contaminated blood prior to this have been identified.

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

Infected blood products for the treatment of clotting disorders, both locally produced and imported, were also issued in Ireland. It is estimated that 217 people in Ireland with haemophilia, Von Willebrand's disease or other inherited coagulation disorders were infected with hepatitis C due to infected blood or blood products (locally produced or imported).

Screening which has already taken place

The IBTS have undertaken extensive efforts to trace recipients of potentially infectious products previously issued in Ireland as summarised below. There may still remain a small number of people who received products who have not yet been tested.

Screening of recipients of potentially infectious blood components or blood products already undertaken

Between 1994 and 1995 the Blood Transfusion Service Board (BTSB; now the IBTS) conducted a targeted lookback programme which offered screening to recipients of blood components from donors who were subsequently found to have HCV infection (11).

In September 1995 an optional screening programme was introduced to complement the targeted lookback programme. This programme offered free screening for HCV, through GPs, to anyone who received blood or blood components before October 1991. Of the 14,917 persons who presented for screening, 61 were Anti-HCV positive on confirmatory testing. Of these, five had other risk factors and were not deemed transfusion related. The remainder were deemed transfusion related with 46 being recipients of blood components and 10 recipients of pooled coagulation factor. Thirty eight of the 46 blood component recipients, and eight of the 10 coagulation factor recipients were RNA positive resulting in a HCV rate of 0.3% for blood component recipients presenting voluntarily. Most of those found to be positive received transfusion between 1975 and 1985.

Anti D

The Anti D/Hepatitis C National Screening Programme commenced in February 1994 to offer testing to recipients of Anti-D. All Anti D recipients were invited for testing. Under this programme 65,980 Anti-D recipients were tested. Of the 15,833 recipients tested who indicated exposure to Anti-D from 1977 to 1979, the IBTS have documented records indicating 4,522 actually received Anti D. Of this group, 922 were antibody positive; of whom 459 were PCR positive with viral type consistent with infection though Anti-D. The remainder 3,384 tested HCV negative.

Of the 19,045 recipients tested who indicated exposure to Anti-D in the years 1991 to 1994, the IBTS have documented records indicating 10,558 actually received Anti D. Of this group, 167 were antibody positive of whom 44 were PCR positive with viral type consistent with infection though Anti-D and 10,193 tested HCV negative.

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

In 2011 the Recipient Tracing Unit (RTU) of the IBTS completed the task of tracing and offering testing to known recipients of infectious or potentially infectious Anti-D. An audit of the tracing process found that the RTU had successfully traced 99% of all those identified to the programme. Ninety eight percent of recipients who received potentially infectious batches of Anti-D from both risk periods were tested; 1% were offered testing, but chose not to be tested; 1% were found to be deceased; and less than 1% remained untraced.

Clotting products

Screening of recipients of infected or potentially infected blood products for the treatment of clotting disorders was undertaken by the IBTS in conjunction with the National Centre for Hereditary Clotting Disorders.

5.2. Relevant national policy

See above

5.3. Epidemiology in Ireland if available and applicable

See above for epidemiology of products in Ireland..

Between 2004 and 2016 85 notifications of hepatitis C which reported the most likely risk factor to be the receipt of blood or blood products outside of Ireland. Eight of these were amongst Irish born people and 70 were amongst people born outside of Ireland, and in seven the country of origin was unknown.

6. Potential impact of recommendation

6.1. Benefit versus harm

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

Benefit:
May encourage people not previously screened to come forward and potentially identify undiagnosed cases.

Harms:
May raise anxiety again for those who were infected through blood components or blood products.

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

Extensive screening of recipients of potentially infected blood, blood components and blood products in Ireland has already been undertaken. Extensive efforts were made to contact those who had been screened or traced. Only a very small number of people who have not yet been screened may come forward. Therefore, resource implications are likely to be minimal.
It is not known how many people will be eligible for screening if a recommendation on screening of recipients of blood or blood products overseas is made. The numbers are likely to be small.

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

Likely to be acceptable to highlight recipients of blood components and blood products but will need to be done sensitively and to highlight that the majority have already been screened.
Screening of past recipients of solid organs other than kidneys may not have been previously highlighted and may cause concerns.
Screening of recipients of SoHO overseas is likely to be acceptable although it may be difficult for healthcare providers to risk assess.

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

Extensive efforts have already been made to contact and screen recipients of potentially infected blood components and blood products in Ireland. It is not envisaged that a further active screening programme be established for any remaining unscreened recipients, but that those who have not previously come forward could be offered screening opportunistically or on request.

For screening of recipients of SoHO overseas it is difficult to give a specific recommendation as countries implemented quality assurance programmes at different times. It may be difficult for a healthcare provider to determine if someone should be screened or not.

6.5. What would be the impact on health equity?

The principle of proportionate universalism[1] should underpin the recommendations and the implementation of the guideline in order to have a positive impact on health equity.

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

While the majority of those who received infected or potentially infected blood components or blood products in Ireland have already been traced and offered screening, a small number of people may not yet have been traced or have previously declined screening. While numbers will be small it is important to still acknowledge this group.

Many high income countries had historic hepatitis C transmission episodes due to infected blood components and blood products. In most high income countries, screening began around 1991. There may be historic recipients of unscreened blood or blood products in other countries who have not been screened and now are living in Ireland. In some countries a quality assured donor screening programme is still not in place.

8. Final Recommendations

ã Strong recommendation
Ĩ Conditional/ weak recommendation

Text:

- Recipients of blood or blood components in Ireland prior to October 1991 who have not yet been tested should be offered screening
- All recipients of Anti-D in Ireland between 1st May 1977 and the end of July 1979, and 1st March 1991 to 18th February 1994 who have not yet been tested should be offered screening.
- Recipients of plasma derived clotting factor concentrates in Ireland prior to 1992 who have not yet been tested should be offered screening
- Recipients of solid organ transplants in Ireland who have not yet been tested should be offered screening (see recommendations on dialysis for recipients of renal transplants)
- 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.

9. Justification

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

Many high income countries had historic hepatitis C transmission episodes due to infected blood components and blood products. In most high income countries, screening began around 1991. There may be historic recipients of unscreened blood or blood products in other countries who have not been

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

screened and now are living in Ireland. In some countries a quality assured donor screening programme is still not in place.
10. Implementation considerations
Consultation with relevant bodies including the HPRA, HSE, and the Irish Haemophilia Society should occur. Active screening will not be undertaken.
11. Recommendations for research List any aspects of the question that have not been answered and should therefore be highlighted as an area in need of further research.

Review by GDG

Date: 23/02/2017

Phrasing of recommendation amended.

Consultation feedback and review by GDG

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

No material change to recommendation.

Final recommendation

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

References List

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9. Brook G, Soriano V, Bergin C. European guideline for the management of hepatitis B and C virus infections, 2010. Int J STD AIDS. 2010;21(10):669-78.
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Appendices

Evidence search and results

International and national guidelines

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

Grey literature

Grey literature on HCV transmission through blood and blood products in Ireland identified by expert members of the GDG was included for review.

Primary literature

A systematic literature review was not undertaken. Literature on HCV transmission through blood and blood products in Ireland identified by expert members of the GDG was included for review.