Hepatitis C Screening Guideline Development Group
Background to recommendation 5 and 6: People who use unprescribed or illicit drugs

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 adopt/adapt recommendations on PWID from existing guidelines. For non-intravenous drug users determined that further evidence was required on the risk of HCV transmission from non-intravenous drug use?
14/12/2016	GDG subgroup meeting to undertake considered judgement process	Formulation of recommendation
24/01/2017	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: 20/12/2016
Attendees: Margaret Bourke, Austin O'Carroll, Lar Murphy, Sinead Donohue, Ursula Norton, Lelia Thornton, Eve Robinson

Table 1: Considered judgement form

1. What is the question being addressed? Present PICO if relevant
Q2. Who should be offered screening for Hepatitis C? **b. Should the following specified groups be offered screening?** **iii. people who currently use or have a history of unprescribed medications or illicit drug use be offered screening**
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)
For intravenous drug use: relevant guidelines – quality appraised (Section 3) For non-intravenous drug use (NIDU): relevant guidelines and primary research literature – critically appraised (section 3 and 4)
3. What is the body of evidence? Source of evidence: (tick all that apply) Guidelines √ Primary literature √ Other □ ; specify: _____
WHO, 2016: As a population with a high prevalence of HCV infection, all PWID should be offered screening for HCV as an integral component of a comprehensive package of harm reduction interventions. Repeated screening is required in individuals at ongoing risk of reinfection, and the possibility of reinfection after spontaneous clearance or successful treatment should also be considered. Those who have been previously infected should be retested using RNA testing, as the antibody remains positive after the first infection. It is recommended that HCV serology testing be offered to individuals who are part of a population with high HCV seroprevalence or who have a history of HCV risk exposure/behaviour (Strong recommendation, moderate quality of evidence). Populations with a high HCV prevalence or who have a history of HCV risk exposure/behaviour include: People who inject drugs (PWID) and Persons who use/have used intranasal drugs. *(World Health Organization, Guidelines for the screening, care and treatment of persons with hepatitis C infection (1)).* HIQA Quality Score of 148 **NICE, 2013:** HCV screening should be offered to people who have ever injected drugs. GPs and practice nurses should ask newly registered patients if they have ever injected drugs, including image and performance enhancement substances at their first consultation. Drug services should offer and promote hepatitis B and C testing to all service users. *(The National Institute for Health and Care Excellence, Hepatitis B and C: Ways to Promote and Offer Testing to People at Increased Risk of Infection (2)).* HIQA Quality Score of 148

AASLD 2016: Injection drug users (current or ever, including those who injected once) and intranasal illicit drug users should be offered screening for HCV. *(American Association for the Study of Liver Diseases, Recommendations for Testing, Managing, and Treating Hepatitis C (3)).* HIQA Quality Score of 134.5

SIGN 2013: HCV screening should be offered to those with a history of injecting drug use. *(Scottish Intercollegiate Guidelines Network, Management of Hepatitis C A National Clinical Guideline (4)).* HIQA Quality Score of 127.7

US Preventive Services Taskforce 2013: Past or current injection drug users and intranasal drug users should be offered screening for HCV. *(United States Preventive Services Taskforce, Screening for Hepatitis C Virus Injection in Adults).* HIQA Quality Score of 117

KASL, 2016: Intravenous drug abusers should be counselled to stop illicit drug abuse. They should be educated about routes of infection and tested regularly for HCV infection. Persons who have ever injected illicit drugs should be offered screening for HCV. *(The Korean Association for the Study of the Liver, KASL Clinical Practice Guidelines: Management of Hepatitis C (5)).* HIQA Quality Score of 11

CDC, 1998: Persons who ever injected illegal drugs, including those who injected once or a few times many years ago and do not consider themselves as drug users should be screened for HCV. *(Centers for Disease Control and Prevention, Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease (6)).* HIQA Quality Score of 98.

CDC, 2015-webpage: (Viral hepatitis C information (7)) Persons for Whom HCV Testing Is Recommended:

- Currently injecting drugs
- Ever injected drugs, including those who injected once or a few times many years ago.

Persons for Whom Routine HCV Testing Is of Uncertain Need: Intranasal cocaine and other non-injecting illegal drug users.

SASLT, 2012: Individuals with a history of intravenous drug use should be offered screening for HCV. (*Saudi Association for the Study of Liver diseases and Transplantation, SASLT Practice Guidelines: Management of Hepatitis C Virus Infection(8).)*. HIQA Quality Score of 95.3

EASL 2014: People who inject drugs should be routinely and voluntarily tested for HCV antibodies and if negative, they should be continuously tested every 6-12 months. (*European Association for the Study of the Liver, Clinical Practice Guidelines: Management of Hepatitis C Virus Infection (9)).* HIQA Quality Score of 92

Ireland 2004: All those at risk of hepatitis C (including injecting drug users) should be offered testing. *(Dublin Area Hepatitis C Initiative Group, Hepatitis C Among Drug Users: Consensus Guidelines on Management in General Practice (10)).* HIQA Quality Score of 85.5

Literature Review for Non Injecting Drug Use ONLY

A systematic review published in 2007 which included 28 studies, determined the prevalence of HCV in NIDUs to range from 2.3-35.5% (median = 14%). The aim of this review was to synthesise existing data on HCV infection in people who reported never injecting drugs but who did engage in non-injection drug use via sniffing, snorting or smoking heroin, cocaine, crack or methamphetamine--behaviours which could conceivably transmit HCV. Studies that reported a high HCV prevalence tended to have small sample sizes. When the review restricted inclusion criteria to studies that were least likely to misclassify NIDUs (i.e. ensure no IDUs were in the study population), the HCV prevalence range decreased to 2.3-17%. It was concluded that due to quality issues, it could not be statistically determined whether NIDU-specific behaviours were associated with HCV infection. Causal pathway to HCV infection also remained unclear

(Scheinmann et al 2007 (11); Quality SIGN checklist acceptable).

A retrospective cohort of 738 volunteer blood donors positive for HCV in the United States reported that intranasal cocaine use is considered a significant, independent risk factor for HCV infection. The association of intranasal cocaine use and HCV positivity gave an OR of 6.4 (95%CI 3.8-11.2). Multivariate analysis showed HCV positivity and intranasal cocaine use without IDU or blood transfusion to have an OR of 8.5 (95%CI 4.9-15.1) ($p<0.0001$). Risk factor information was self-reported and the veracity of IDU denial cannot be certain. (Allison et al 2012 (12); Quality SIGN checklist acceptable).

A retrospective observational study of blood donors with HCV in the United States used logistic regression to determine an association between intranasal cocaine use and positive HCV infection, the odds ratio was 8.0 (95%CI 3.9 - 16.5). In this study nonparticipants were randomly selected and compared on demographic characteristics. However the validity of the results remains uncertain as other behaviours associated with HCV transmission (sharing of drug use equipment) were not assessed. (Conry-Cantilena et al 1996 (13); EBL checklist 61%).

A cross sectional, blinded survey performed in STD clinics in Texas, US yielded an association on logistic regression analysis between HCV transmission and sharing of straws to snort drugs, OR=2.5 (95%CI 1.2 - 5.4, $p=0.016$). The study may not be representative of the STD population as a clinic based population was used. (D'Souza et al 2002 (14); EBL checklist 63.2%).

A large population based study of homeless and marginally house people in the United States was performed in 2012. After controlling for sociodemographic and other risk factors, multivariate logistic regression concluded that there was a statistically significant negative association between snorting cocaine and HCV (OR=0.39; 95%CI 0.21 - 0.73). No significant association was reported between those sharing snorting equipment and persons with HCV among those who had ever snorted cocaine (OR=1.02; 0.39 - 2.69). Ever smoking crack cocaine was negatively association with HCV antibody positivity (A0R=0.28; 95%CI 0.09 - 0.88). A possible explanation is reporting bias, specifically that some participants who had injected drugs and who are at increased risk of HCV infection may have been uncomfortable reporting any drug use (injection or non-injection). The authors suggested the following under-reporting of injection drug use is plausible given the high overall prevalence (17%) of anti-HCV in this sample of persons who reported no injection drug use.(Hermanstyne et al 2012 (15) ;EBL checklist 68.4%).

A cross sectional seroprevalence anonymous study of university students in the United States found a low prevalence (2%) of injection drug use among US or Canadian born students. Among 5,066 participants without a history of IDU, 12% reported intranasal drug use. The prevalence of HCV was low in those with a history of intranasal drug use at 0.8%. The Authors concluded that the results indicated that routine HCV testing was not warranted in young, low risk adults based solely on history of these procedures and practices (tattooing, body piercing and snorting illicit drugs) (Hwang et al 2006 (16); EBL checklist 70%).

A prevalence study of 300 non-injecting drug users attending drug treatment clinics in Brazil determined that one hundred and six (35%; 95%CI 28.4 - 41.1%) presented anti-HCV antibodies. The HCV-RNA prevalence was 28% (95%CI 20.6 - 35.8%). Univariate analysis reported HCV infection was significantly associated with shared use of drug paraphernalia (EIA positive: OR 6.0; 95%CI 3.1 - 11.6) (HCV-RNA positive: OR 7.7; 95%CI 3.4 - 17.5). Multivariate analysis demonstrated HCV infection was independently associated with shared use of drug paraphernalia (EIA positive: OR 5.6; 95% CI 1.8 - 9.5; $p<0.01$) (PCR positive: OR 4.1; 95%CI 1.9 - 8.4; $p<0.01$). (Oliveira-Filho et al 2014 (17); EBL checklist 66.7%).

A cross sectional study of female drug users in New York, USA, reported 20% (24/123) non IDUs were anti-HCV positive. Univariate analysis noted a significant association between HCV infection and ever sharing heroin implements with an injector (OR 4.38; 95%CI 1.32-14.57); and a significant association between HCV infection and sharing both intranasal and oral implements (regardless of the other user's injection status) (OR 3.44; 95%CI 1.31-9.03). On multivariate analysis, ever sharing both oral and

intranasal implements was independently associated with HCV infection (OR 2.83; 95%CI 1.04-7.72; p=0.04) (Tortu et al 2004(18) ;EBL checklist 76.2%).

A cross sectional study of STD clinic attendees in Miami, US reported the prevalence of antibody HCV in intranasal drug users to be 3.13% (16/522) (P=0.0004). In multivariate analysis the results was not statistically significant (the results were not provided). It should be noted that there was a low response rate for this study (52%) and all risk factor information received was self-reported therefore underreporting of certain social behaviours is a strong possibility. (Weisbord et al 2002 (19); EBL checklist 62%).

The multivariate analysis of a case control study of risk factors for HCV infection in patients with unexplained routes of infection from France showed intranasal cocaine use as an independent risk factor for HCV infection (OR=4.5; 95%CI 1.56 - 13.3; p=0.006). The study recruited 460 HCV infected patients and 757 controls from 1997 - 2001 and risk factors were self-reported. (Karmochkine et al 2006 (20); SIGN checklist acceptable).

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.

Regarding IDU – recommendations are contained in a number of good quality guidelines.

Regarding NIDU: Some of the studies that addressed NIDU do not clearly define what is meant by non-injecting drug use where as other are specific for example intranasal cocaine, smoking crack cocaine, sharing drug paraphernalia. Most of the studies are reliant on self-reported behaviour and were unable to separate out NIDU from other risk behaviours such as IDU and sharing of drug use equipment. These issues are best summarised by the systematic review in 2007 by Scheinmann which concluded that due to quality issues, it could not be adequately determined whether NIDU-specific behaviours were associated with HCV infection.

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

There was consistency in the international guidelines in relation to recommending screening for those with a history of current or past injecting drug use. The evidence and recommendation in relation to NIDU is less clear.

Regarding NIDU: many of the studies did find an association between NIDU and HCV infection on multivariable analysis. However, the quality issues described above need to be noted.

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

IDU: Yes.
NIDU: Many of the studies were conducted in North America and over a decade ago. Patterns of drug use may have changed over time and may be different in Ireland to North America.

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

IDU: Yes and is current practice in Ireland.
NIDU: This population may be more difficult to reach and many may not have come to the attention of drug treatment services.

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.

Possible

5. Additional information for consideration

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

Prevalence of HCV in drug users in Ireland
Studies of PWID in prisons and PWID attending methadone clinics, specialist addiction treatment centres and GPs have estimated the HCV prevalence in this population to be between 62% and 81% (21, 22).
A study amongst prisoners in 1998 showed a prevalence of anti-HCV of 81.3% in prisoners who injected drugs (23).

There have been no recent studies on the prevalence among PWID.
A 2011 prison study found that 54% of prisoners with a history of injecting heroin were anti-HCV positive and 41.5% of prisoners with a history of injecting any drugs were anti-HCV positive (24).

5.2. Relevant national policy/strategy/practice

National HCV strategy 2011-2014: In Ireland those at risk of infection are most often socially excluded groups such as drug users, the homeless and immigrants from endemic countries. All people at risk of hepatitis C should be offered testing and any patient with signs or symptoms suggestive of hepatitis, or requesting testing should also be tested. Patients who should proactively be offered testing for hepatitis C: All drug users, especially those who have injected drugs or shared 'works', including prisoners. Drug users who attend drug addiction services are screened on first presentation for blood borne viral infection, including hepatitis C. Different protocols are employed with regard to the frequency of hepatitis C screening thereafter in those who are either negative or antibody positive but hepatitis C RNA negative. Individuals who are repeatedly exposed to risk factors will require ongoing screening.*(HSE National HCV strategy 2011-2014 Ireland (25)*) HIQA Quality score 98

Standard of care in addiction treatment centres in Ireland:
The standard of care for patients presenting at addiction treatment centres in Ireland involves offering an antibody test for hepatitis C. If found to be antibody positive, a test for hepatitis C antigen or PCR is carried out. If hepatitis C antigen or PCR is positive, the patient is referred for assessment at a hepatology or infectious diseases clinic. If the patient initially tests negative, a repeat test is offered every 6-12 months if the patient continues with risk-taking behaviour. This standard of care is outlined to all doctors in the addiction treatment centres in an algorithm which has been circulated to them. Their contract of service also specifies that they will be required to "Screen patients for relevant viral diseases, evaluate the results, treat and refer to specialist services where appropriate" (26).

5.3. Epidemiology in Ireland if available and applicable

Drug use in Ireland
The National Advisory Committee on Drugs and Alcohol (NACDA) Drug Prevalence Survey 2014/15 reported that 26.4% of the population over 15 years in Ireland reported using any illegal drug in their lifetime; 7.5% in the past 12 months and 4% in the last month. Any illegal drug referred to cannabis, ecstasy, cocaine powder, magic mushrooms, amphetamines, poppers, LSD, new psychoactive substances, mephedrone, solvents, crack, or heroin. Cannabis was the most commonly used drug at 24%, followed by ecstasy at 7.8%; cocaine (including crack) and cocaine powder at 6.6% and 6.4%

There were differences in drug use by age and gender. The survey did not report on route of administration of drugs.

Drug treatment services attendances

The National Drug Treatment Reporting System (NDTRS) collects anonymous data about people in drug and alcohol treatment from general practitioners, low threshold services, outpatient and inpatient centres. In 2014 9046 people entered or re-entered treatment.

Smoking was the most common route of administration at 52% (n=4791). When cannabis smoking was excluded smoking was the route of administration for 24% (n=2216). Injecting was the main route of administration for the main drug used for 20% (n=1776). Snorting or sniffing was reported as the main route of administration for the main drug used for 7% (n=654).

Of note, polydrug use is common and the above results relate to the main drug of use at this treatment episode.

21% (n=1805) of entrants had every injected and 15% (n=1280) were currently injecting. Of those who ever injected 43% (n=1585) were reported as having shared injection equipment. If only those where this was known are considered, the percentage was 57%.

Of those whose main drug of use was benzodiazepines, 12% had every injected any drugs but were not currently injecting, while 4% were currently injecting; these figures were 2% and 0% for cannabis, 10% and 2% for cocaine, 34% and 37% for opiates, and 21% and 12% for other drugs respectively. The injecting status was not calculable for those whose main drug of use was amphetamines, ecstasy or volatile substances as numbers were not reported as they were less than five.

Drug related deaths due to liver disease

The National Drug Related Deaths Index reported that the proportion of drug related deaths due to liver disease increased from under 5% in 2004 to just over 20% in 2014. However, this data does not distinguish between alcohol related deaths and other drug types.

6. Potential impact of recommendation

6.1. Benefit versus harm

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

Benefits:

- Recent advances in treatment options make treatment more acceptable and more successful. Treatment with the new DAAs which are now available results in cure in the majority of patients with shorter duration of treatment and less side effects compared to previous treatments.
- Treatment of current injecting drug users will also limit further transmission to others.
- Testing should be considered a positive thing and promotion and further normalisation of testing may improve uptake
- Highlighting other potential routes of transmission may remove stigma towards IDU.

Harms:

- Detection of cases who may not yet be eligible for treatment may lead to frustration and anxiety
- People with a past history of IDU or NIDU may suffer psychologically from having to admit to past risk behaviours

May result in anxiety amongst certain NIDU who are not at increased risk e.g. those who only ever took drugs orally.

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

Offer of screening is current practice for those in treatment services. The main resource implication will be for those not in services or with a past history drug use, and for those with a history of occasional IDU or NIDU who would not be linked with drug treatment services. If not a medical card or GP-only card holder, they will not be able to avail of free testing. A service or reimbursement scheme may need to be developed to aid implementation.

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

Offers of repeat testing may be considered offensive to patients in drug treatment as it may be perceived as implying they are still involved in risk-taking behaviour.

If a drug user who is in treatment had a once-off lapse in abstinence they may not wish to disclose this to their care provider.

For those with a history of NIDU the communication of possible risk from their behaviour may be difficult and the message may not be accepted.

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

IDU: This is already current practice in Ireland although the coverage may be suboptimal outside of main urban areas. Current projects such as HepCare are developing screening and treatment programmes for marginalised groups.
NIDU: There maybe lack of awareness of the risk among health professionals and the at-risk population and many may not be reached by the current drug treatment services.

6.5. What would be the impact on health equity?

Current or past drug users may have other health problems or have additional risk factors which will exacerbate HCV liver damage. They may also be a difficult to reach population in terms of screening and linkage to care. Improved detection with clear and supported pathways to care and treatment will enable this population benefit from treatment and improved quality of life.

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

Recent advances in treatment options for hepatitis C make treatment more acceptable and more successful. Treatment with the new DAAs which are now available results in cure in the majority of patients with shorter duration of treatment and less side effects than previous treatments. However at present the cost of these treatments is high.

Screening enables early detection, referral for assessment and treatment where indicated. Without screening cases may go undetected for a considerable length of time due to the asymptomatic nature of HCV infection. Individuals often do not present until symptomatic, which is usually indicative of severe liver damage. Early treatment and cure will confer personal, social, and economic benefits. Early treatment and cure will also reduce the risk of transmission to others. A treatment programme exists in Ireland allowing detected cases access treatment.

Given the availability of effective HCV treatments and the ongoing risks of HCV transmission to others through IDU, screening is considered very important for the benefit of the individual and their contacts.

While the risk associated with NIDU is unclear, transmission is biologically plausible for some routes of administration other than injecting e.g. snorting or sniffing, when implements are shared. Polydrug use is common, and a previous history of injecting may be present in those currently using other drugs by routes other than injecting. Given the benefits of treatment it is considered desirable to screen certain NIDU.

8. Final Recommendations

√ Strong recommenda□on for IDU
√ Condi□onal recommenda□on for NIDU

Text:
All those who have ever injected drugs should be offered screening for hepatitis C. This applies to 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.
Retesting of those who are negative should be offered on an annual basis to those who remain in contact with drug treatment services or those who remain at ongoing risk of infection.
Testing should be available during this interval if a known risk exposure incident has occurred.
Those who have been previously infected, but have cleared infection spontaneously or through treatment, should be retested using RNA testing, as antibody remains positive after the first infection.

Screening should be offered to all those who have used unprescribed or illicit drugs but not by injecting, if there is a possibility of transmission of infection by the route of administration. This includes those who currently use intranasal drugs (i.e. snort or sniff), or have done so in the past, or share other equipment or drugs where there is a risk of contamination with the blood of others.

Pre-test counselling is not considered necessary.

9. Justification

There is a clear risk of transmission from IDU.

The risk of transmission through non injecting drug use depends on the potential of exposure to blood of an infected person. The potential exposure may not be obvious as the blood exposure may not be visible. Sharing of implements to snort drugs is likely a risk due to the highly vascular structure of the nasal passages which can be easily damaged by the insertion of implements. Certain drugs which are smoked can cause burning or bleeding of lips which may pose a risk of transmission if drugs or equipment are shared.
Drugs taken orally and most drugs smoked will not pose any risk of HCV transmission.

10. Implementation considerations

People attending drug treatment services, both IDU and NIDU, are currently offered testing on first presentation or on re-entering the service. Thus there should be no implementation considerations for this group in relation to their initial testing. However, re-testing annually may not always take place currently.

Innovative approaches will need to be considered to reach other drug users, such as those who do not perceive themselves to be at risk of HCV (NIDUs, those who injected infrequently in the past, and especially vulnerable hard-to-reach IDUs who traditionally have not attended drug treatment services). Awareness raising, educational approaches, and outreach initiatives may be needed.

In relation to NIDU, it is suggested that the best approach may be to explain the risk and possible exposure routes and for the person to assess the risk themselves.

Peer support such as the Hepfriend initiative and the Hepatitis C/ Liver Health Group operated through Community Response, and the Hepatitis C Partnership may encourage uptake of screening and aid linkage to specialist care where appropriate.

Post test counselling, explaining the results of testing and facilitating access to specialist care as necessary, is important.

Former drug users may not have access to testing as readily if they are no longer in treatment. Although testing can be arranged by a GP, they may not have a medical card.

Testing should be normalised as much as possible in multiple settings in particular in general practice, thus facilitating ease of testing and minimising the stigma attached to HCV.

DBS or oral fluid may improve uptake as the requirement of a venous sample is a barrier for some people.

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.

Studies of how best to link this population into care and retain them in care are needed.

Review by GDG

Date: 24/01/2017

It was agreed that as for other groups at ongoing risk of infection, the interval for repeat testing should be 6 to 12 months.

There was concern expressed over classifying the recommendation for non IDU as 'weak'. GDG members with experience in addiction services believe that it is important to screen this group as a number will not admit or recall IDU and also transmission can occur through sharing intranasal equipment or smoking heroin. It was agreed that the recommendation can be classified as strong but to still acknowledge that the level of evidence supporting it is limited.

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 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

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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

Nil used.

Primary literature

The GDG further evidence was required to formulate a recommendation on HCV screening of non-injecting drug users.
Questions to be addressed?
What have been the results of screening practices in Ireland?

PICO
Population: pregnant women attending antenatal services in Ireland
Intervention: screening for hepatitis C
Comparison: no screening, universal screening, targeted screening
Outcome: detection in mother, acceptability, cost/ cost-effectiveness, transmission to child
Other sources: data directly from maternity hospitals in Ireland where available

Search strategy
Sources:

- Medline
- Embase

See table 2 for search terms used in Medline search

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

Inclusion criteria:

- Low endemicity country
- Subjects had no history of injecting drug use
- Reported on a Non-IDU activity alone (not combined with IDU)
- Reports prevalence or incidence in the risk group, or reports as an independent risk factor
- HCV status based on blood/ saliva rather than self report

Exclusion criteria:

- High endemicity country
- Non HCV
- Not correct population or risk behaviour (e.g. also a history of IDU, combines results for non-IDU and IDU, if not clear that behaviour is illicit e.g. 'smoking')
- Doesn't report on prevalence, incidence, or risk independent of other factors
- HCV status self reported
- Other (eg environmental, animal)

Table 2: Search terms used in Pubmed/Medline search

S1	hepatitis C or HCV or hepacivirus or hep C or hepC	75,099
S2	(MM "Hepatitis C+")	41,215
S3	(MM "Hepacivirus")	17,196
S4	risk factor*	795,348
S5	(MH "Risk Factors")	596,002
S6	S1 OR S2 OR S3	75,099
S7	S4 OR S5	795,348
S8	transmission or transmit or mode of transmission or acquisition or acquire* or transmit*	864,746
S9	(MM "Disease Transmission, Infectious+")	29,905
S10	S8 OR S9	871,458
S11	non-intravenous drug* or non-intravenous drug use* or intranasal or smok* or non-injection drug* or non-injection drug use* or nasal or snort* or sniff*	365,921
S12	S6 AND S11	816
S13	S7 AND S12	446
S14	S10 AND S13	103
S15	S10 AND S13	103
S16	(MM "Inhalant Abuse")	102
S17	S11 OR S16	365,995
S18	S6 AND S17	816
S19	S7 AND S18	446
S20	S10 AND S19	103

Search results

Figure 1: PRISMA flow diagram of review of literature on antenatal HCV screening in Ireland