UK National Screening Committee

Screening for Hepatitis C Virus in Pregnancy

31 October 2018

Aim

1. To ask the UK National Screening Committee (UK NSC) to make a recommendation, based on the evidence presented in this document, whether or not screening for hepatitis C virus (HCV) in pregnancy meets the UK NSC criteria for a systematic population screening programme.

Current recommendation

2. The 2011 UK NSC review of screening for HCV in pregnancy concluded that systematic population screening is not recommended.

   The conclusions from this review were that:

   - there was a lack of interventions to improve the management of maternal or childhood HCV , therefore, there were no advantages to diagnose HCV during pregnancy but possible psychological disadvantages;
   - there were complications in the assessment of maternal HCV due to pregnancy related changes;
   - there was a lack of data on HCV prevalence in the contemporary pregnant population in the UK; and
   - based on emerging developments, it was recommended that evidence relating to paediatric treatment and issues relating to a postnatal screening strategy for HCV should be kept under review.

Evidence Summary

3. The 2018 evidence summary was undertaken by Solutions for Public Health, in accordance with the triennial review process: https://legacyscreening.phe.org.uk/hepatitisc-pregnancy.

4. The 2018 evidence summary addresses questions generated by uncertainties and lack of evidence identified in the previous review. The aims is to assess whether the volume and direction of the evidence produced since the 2011 UK NSC review is sufficient to change the previous UK NSC recommendation on screening for HCV in pregnancy.

5. The conclusion of the 2018 evidence summary is that population screening for HCV in pregnancy should not be recommended. The volume, quality and direction of evidence published since 2011 does not indicate that there have been significant changes in the evidence base.

   i. The HCV seroprevalence and current infection prevalence for pregnant women for the UK as a whole is unclear, as is the number of new HCV cases that would be detected by screening pregnant women. There are uncertainties about which risk factors increase the risk of vertical HCV transmission and to what extent. **Criterion 1 not met.**

   ii. There is limited information about the performance of HCV screening tests in pregnant women. The limited evidence available suggests a high proportion of false positives would result from screening**. Criterion 4 not met.**

   iii. There is an absence of evidence about the effectiveness of treatment with direct acting antivirals (DAAs) for pregnant women and children with vertically acquired HCV. **Criterion 9 not met.**

Consultation

6. A three month consultation was hosted on the UK NSC website. Direct emails were sent to stakeholders of whom 11 organisations were contacted directly. A further one organisation submitted comments without prior contact. **Annex A**

7. Comments were received from five stakeholders:

   i. British Association of Infection (BIA)
   ii. British Society of Gastroenterology Liver Committee (BSGLC)
   iii. Judith Timms, Consultant Virologist for Coventry and Warwickshire Pathology Services and Laboratory advisor to the Infectious Diseases in Pregnancy Screening Programme
   iv. Royal College of Paediatrics and Child Health (RCPCH)
   v. Royal College of Physicians (RCP)

(See **Annex B** for all comments.)

8. The following themes were reflected across stakeholders' general comments.

a. Screening could improve access to testing and treatment for 'hard to reach' groups and women with risk factors other than intravenous drug use who are currently missed under risk-based screening.

   Response: A UK NSC evidence map on HCV screening pathways and their effectiveness (summarised in the evidence summary document) did not find any studies exploring these outcomes.

b. Screening would allow subsequent highly efficacious treatment in identified mothers and follow up for clearance or treatment in children identified at risk.

   Response: No studies in the evidence map have evaluated clinical outcomes in mothers screened compared with those not screened, nor infants of women screened compared with those not screened.

c. Screening would provide the opportunity to treat positive patients with potential immediate interventions of scalp monitoring/instrumental delivery to reduce vertical transmission, though these treatments are as yet unproven.

   Response: No studies in the evidence map on HCV screening explicitly explored these treatments or their outcomes.

d. Additional intervention opportunities from screening:

   vi. Interventions for drug misuse, addiction, and high risk behaviour support

   vii. Contact screening for other children/family

   viii. If parental high risk behaviour is ongoing, identify children at risk and reduce adverse neonatal outcomes of this additional risk

   Response: No studies exploring these outcomes were identified in the evidence map. Moreover, women with high risk behaviour should be managed by the NICE CG110 guideline on pregnancy and complex social factors.

e. Costs:

   ix. There is no cost-effectiveness analysis for HCV screening in the era of DAAs

   x. Significant costs attached to symptomatic liver disease if HCV infection is not identified by screening

Response: We agree and look forward to hearing the results of DAA studies in pregnant women and children.

f. No evidence of harm from screening but huge potential benefit.

Response: There will always be some harm from a screening programme (for example, anxiety, false reassurance, over-detection and over-treatment). As shown in the evidence map, neither the harm nor the benefit of HCV screening has been quantified.

g. Not offering screening seems counter-intuitive to NHS England's (NHSE) HCV elimination programme.

Response: In the absence of evidence of benefit, the place of screening in the elimination programme is difficult to determine.

h. The following stakeholder comments were on specific issues in the evidence summary:

xi. It is becoming routine in many laboratories to 'reflex' test samples which are screen positive to HCV RNA testing so that only patients with on-going infection are referred.

Response: This information has been considered by the reviewers and has been added into the evidence summary document.

xii. Prevalence is largely unknown and likely much higher than current data predicts (highest risk patients unlikely to be blood donors and demographic changes mean current data likely out of date).

Response: This information has been considered by the reviewers. The evidence in the document is based on the latest published literature up to the date of the search and the included studies on prevalence are not on blood donor data.

9. The general comments show that there is interest in antenatal HCV screening. However, it is generally accepted that there is an absence of evidence relating to the potential benefits of screening which are highlighted by the comments. This draws attention to the need to study the impact of screening. For example, a study of screening would help quantify the outcomes of HCV screening and help inform how it could contribute to the NHSE HCV elimination programme. The UK NSC will await the results of the DAA studies in pregnant women and children to inform the next review.

10. The RCPCH supports the recommendation not to offer population screening.

Recommendation

11. The Committee is asked to approve the following recommendation:

Systematic population screening for hepatitis C virus in pregnancy is not recommended as a population screening programme in the UK.

Criteria (only include criteria included in the review)	Met/Not Met
The Condition	
1. The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease	**Not Met**
The Test	
4. There should be a simple, safe, precise and validated screening test.	**Not Met**
The Intervention	
9. There should be an effective intervention for patients identified through screening, with evidence that intervention at a pre-symptomatic phase leads to better outcomes for the screened individual compared with usual care. Evidence relating to wider benefits of screening, for example those relating to family members, should be taken into account where available. However, where there is no prospect of benefit for the individual screened then the screening programme shouldn't be further considered.	**Not Met**

Annex A

List of organisations contacted:

1. British Association of Infection
2. British Society for Immunology
3. Faculty of Public Health
4. Hepatitis C Trust
5. Kings College Hospital NHS Trust Paediatric Liver Centre
6. Royal College of General Practitioners
7. Royal College of Obstetrics and Gynaecology
8. Royal College of Paediatrics and Child Health
9. Royal College of Physicians
10. Royal College of Physicians and Surgeons of Glasgow
11. Royal College of Physicians of Edinburgh

Annex B

Antenatal screening for Hepatitis C virus

Consultation comments

1. British Infection Association

Name:	XXXX XXXX	**Email address:**	XXXX XXXX
Organisation (if appropriate):	British Infection Association		
Role:	XXXX XXXX		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes ☐ **No** ☒

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
	General	Although the evidence review is clearly comprehensive we differ in our conclusions. In an era of excellent and rapid treatment for Hepatitis C it is clear that a review of antenatal screening policies for this condition is timely. We need to ensure widespread testing for HCV and testing in pregnancy is just one part of this as an opportunity in the life of a healthy asymptomatic woman that she engages with health care providers. This has led to success in treatment for other conditions detected in the antenatal period with effective treatments available. The benefits do not just relate to mother-to-child transmission but also to link hard to reach groups to care and this needs to be taken into account in the conclusions.
	General	There is not a cost-effectiveness analysis for HCV screening in the era of DAAs (as far as we are aware, and the DAAs in pregnancy studies are underway) - there is enough uncertainty in the data synthesis to take into account all the issues eloquently put forwards by the hep C Trust
	General	NHS England have recently announced an HCV elimination programme - not taking the opportunity to offer screening to a key population seems counter-intuitive.

2. British Society of Gastroenterology Liver Committee

1) Prevalence of HCV largely unknown and likely much higher than current data predicts from blood donor data (highest risk patients unlikely to be blood donors!) plus demographic changes meaning current demographic hcv data likely out of date. Screening would be an opportunity to catch such patients that might not otherwise access healthcare, with an ongoing programme eventually encompassing the whole population at some point.
2) Antenatal care provides the opportunity to screen BEFORE the infection has occurred and that there are potential immediate interventions to reduce vertical transmission (scalp monitoring/instrumental delivery however these are as yet unproven) even if specific medication to prevent transmission is not available. It would also allow identification of children at risk of the virus to allow follow up for clearance and subsequent treatment, which is now highly efficacious. It may also identify children at risk if parental high risk behaviour is on-going. Also some evidence of adverse neonatal outcomes so identification of this additional risk would be beneficial - for mother and child.
3) Identification of the mother also allows subsequent treatment of the mother's virus plus opportunity for other interventions such as for drug misuse, addiction and high risk behaviour support etc (if applicable) and contact screening for other children/family etc.
4) If hcv infection NOT identified by screening, many present with symptomatic liver disease with significant costs attached to this.
5) No evidence of harm from antenatal hvc screening, only cost but huge potential benefit (unclear how they have quantified this benefit)
6) This proposal would also capture those that do not frequently attend general practice such as women from high risk countries, those who do not speak English and those who are recently entering the UK. All women attend for antenatal screening, even those would not normally leave their own community, this is an excellent opportunity for public health medicine.

3. The Royal College of Physicians

The Royal College of Physicians is grateful for the opportunity to respond to the above consultation. We would like to endorse the comments made by xxxx xxxx of the British Society of Gastroenterology's Liver Section Committee.

4. Judith Timms, Consultant Virologist

Name:	Judith Timms	**Email address:**	XXXX XXXX
Organisation (if appropriate):	Coventry and Warwickshire Pathology Services and Public Health England		
Role:	Consultant Virologist for CWPS and Laboratory advisor to the Infectious Diseases in Pregnancy Screening Programme		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes √ **No** ☐

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
Page 12	Screening tests	Although positive serological tests cannot differentiate between past and current infection or may even be non-specific, it is becoming routine in many laboratories to 'reflex' test samples which are screen positive (ie antibody positive) for HCV RNA. This can be done from the same sample so that only RNA positive patients are referred ie those with on-going infection. Following such an algorithm
Page 10	Risk factors	Opportunistic screening of pregnant women for HCV infection is already advised if they have identifiable risk factors. However, although iv drug use is widely recognised as a risk there is a lack of appreciation of some of the other risk factors so not all women with risk factors are offered testing. Better information for midwives may increase testing but there are some women with HCV infection in whom no risk factor is ever identified. What this means is that women with on-going HCV infection are not being identified and offered treatment before a subsequent pregnancy. This is what would be offered now if the women were identified although we are not yet at the point of being able to offer treatment during the current pregnancy.

5. Royal College of Paediatrics and Child Health

Name:	Dr MP Ward Platt	**Email address:**	XXXX XXXX
Organisation (if appropriate):	N/A		
Role:	Consultant Paediatrician (neonatal medicine)		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes ☒ **No** ☐

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
All	All	It is believed that the NSC makes a compelling case against any change to the current arrangements whereby pregnant women are not screened for hepatitis C, the NSC decision and the logic behind it is fully supported.