UK National Screening Committee

Antenatal screening for HSV-1 and HSV-2 infection to prevent neonatal herpes infection

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 antenatal screening for herpes simplex virus (HSV) to prevent neonatal herpes infection meets the UK NSC criteria for a systematic population screening programme.

Current recommendation

2. The UK NSC's 2006 review of antenatal screening for herpes concluded that systematic population screening is not recommended.

   This was because the 2006 review concluded that there was:

   - no evidence that universal serologic screening in pregnancy to identify women at risk of new infections will effectively decrease the incidence of neonatal infections in the perinatal period
   - limited evidence that drug treatment or the performance of elective Caesarean section in seropositive women or those with a history of genital infection reduces transmission of neonatal infections to infants born to this group of women.

   The 2006 review recommended that efforts should be focused on:

   - improving the early diagnosis and treatment of neonatal HSV
   - ensuring appropriate action where primary maternal infection occurs during late pregnancy

Evidence Summary

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

4. The current 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 2006 UK NSC's review is sufficient to reconsider the current UK NSC recommendation on antenatal screening for herpes simplex virus (HSV) to prevent neonatal herpes infection.

5. The conclusion of the current evidence summary is that antenatal screening for herpes simplex virus (HSV) to prevent neonatal herpes infection should not be recommended. This is because the volume, quality and direction of evidence published since October 2005 does not indicate that there have been significant changes in the evidence base. Key areas of concern relate to:

    - Uncertainties about the seroprevalence of HSV-1 and HSV-2 in UK pregnant women. **Criterion 1 not met**

    - An absence of evidence about the performance of screening tests for HSV-1 in pregnant women, and uncertainties about the performance of screening tests for HSV-2 in pregnant women, particularly around the number of false positive tests that might be expected. The evidence summary did not identify any studies reporting seroprevalence for HSV-2 in pregnant women in the UK. If seroprevalence in a population is low, this would generate more false positive screening tests than would be found in populations with a higher seroprevalence. **Criterion 4 not met**

    - There is some evidence that intervention can reduce behaviours which increase risk of acquisition of HSV-2 infection in women seronegative for HSV-2 (and at known risk of infection), and evidence that intervention can reduce risk factors for vertical transmission for women with HSV infection, however the resulting impact on neonatal infection was not established. **Criterion 9 not met**

Consultation

6. A three month consultation was hosted on the UK NSC website. Direct emails were sent to 15 stakeholder organisations. **Annex A**

7. Responses were received from the following stakeholders:

    i. Dr Dushyant Batra, Consultant Neonatologist, Nottingham University Hospitals

    ii. British Association for Sexual Health and HIV (BASHH)

    iii. British Infection Association

    iv. Chezelle Craig, neonatal herpes awareness campaigner

    v. Herpes Viruses Association

    vi. Kit Tarka Foundation

    vii. National Infection Service, Public Health England

    viii. Royal College of Midwives

    ix. Royal College of Paediatrics and Child Health

    All comments can be found in **Annex B** below.

8. The following themes were reflected across the consultation responses:

    a. Several stakeholders acknowledged that the evidence base does not support systematic population screening for antenatal HSV infection in the UK.

    b. Some stakeholders noted that a positive herpes diagnosis can be psychologically harmful.

    c. One stakeholder suggests that potential benefits of oral antivirals (reduced viral shedding and reduced Caesarean sections), should be considered for inclusion, as a way to sign post clinicians to this treatment option.

    Response: The evidence summary acknowledges the evidence for the effectiveness of oral antiviral therapy in the summary of findings relevant to criterion 9. This includes the potential benefits from oral antivirals including reduction of shedding

and Caesarean section. Some additional information about the interventions identified in the evidence summary has been added to the concluding statements.

d. One stakeholder was concerned that the summary of findings regarding risk reduction in seronegative pregnant women suggests that current advice about risk reduction in serodiscordant couples is unsupported. They suggest that this section should include a caveat.

Response: The statement referred to is part of the critique of an individual study. The text has been amended to make this clearer.

The concluding statements for the evidence summary acknowledge that there is some evidence that intervention can reduce behaviours which increase risk of HSV acquisition. An example of an intervention with some evidence of effectiveness (knowledge of a sex partner's HSV status) has been added to the concluding statements.

e. A suggestion that the evidence summary should consider recommending an updated report of UK neonatal herpes incidence. The stakeholder referred to information from conference presentations about clusters of neonatal HSV cases.

Response: The evidence summary states that there is uncertainty about the incidence of neonatal herpes for the UK as a whole and highlights a number of areas in which further research would be beneficial.

Conference abstracts were not eligible for inclusion in the evidence summary.

f. Some stakeholders suggested that the avoidance of postnatal transmission should be part of the review.

Response: The evidence summary looked at screening pregnant women antenatally to prevent neonatal herpes transmission. Prevention of postnatal transmission is important, however, it is outside the screening context for this review.

g. Some stakeholders suggested that increased awareness amongst health care professionals, parents, and the public in general should be considered.

Response: Increased awareness of neonatal herpes is an important factor in prevention and improving early diagnosis and treatment when infection occurs. However, awareness raising is outside the direct remit of the UK NSC.

h. One stakeholder raised issues relating to the inclusion and exclusion criteria for the evidence summary, and some of the figures used.

Response: The consultation comments were considered by the reviewer and alterations made to the evidence summary where appropriate.

Recommendation

8. The Committee is asked to approve the following recommendation:
A systematic population screening programme for herpes simplex virus (HSV) in pregnancy is not recommended.

Criteria (only include criteria included in the review)	Met/Not Met
Section 1 - Criteria for appraising the viability, effectiveness and appropriateness of a screening programme	
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 Screening Programme	
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 should not be further considered.	**Not Met**

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Annex A

List of organisations contacted:

1. Association for Improvements in the Maternity Services
2. British Association for Sexual Health and HIV
3. British Infection Association
4. British Maternal & Fetal Medicine Society
5. Faculty of Public Health
6. Infectious Diseases in Pregnancy Screening Programme
7. MBRRACE-UK
8. National Childbirth Trust
9. Royal College of Midwives
10. Royal College of Paediatrics and Child Health
11. Royal College of Physicians
12. Royal College of Physicians and Surgeons of Glasgow
13. Royal College of Physicians of Edinburgh
14. Royal College of General Practitioners
15. Royal College of Obstetricians and Gynaecologists

Annex B

Dear PHE Screening team.
I am a consultant neonatologist based in Nottingham and have interest in neonatal viral infections. I wanted to thank your team for looking into above review and asking for comments.
https://legacyscreening.phe.org.uk/genitalherpes
In your review, you have referenced a study my team conducted in our region. It is a well-structured and thorough review. I agree with your recommendations based on the evidence that is available. I would be extremely grateful if the following could be taken into account when the final review is published.
In relation to following question:

is there a way of reducing the risk that pregnant women will be infected with HSV during pregnancy?

1. Although the highest risk of transmission is from maternal primary herpes during last few weeks of pregnancy, there is a 1-2% risk of neonatal herpes transmission from active recurrent herpes at the time of delivery. You review has looked at the results from Cochrane review (Hollier & Wendel, 2008) which shows oral antivirals to mothers from 36wks reduces the recurrence of genital herpes at delivery, presence of detectable HSV and reduces the likelihood of caesarean section. Your review has concluded " there is some evidence that intervention can reduce risky behaviours in women seronegative for HSV-2 or reduce risk factors for vertical transmission for women with HSV infection. However the resulting impact on neonatal infection was not established." I would request you to consider including details of potential benefits from oral antivirals in terms or reduction of viral shedding and caesarean section. Individual centres can draw their own conclusions from this but specific mention of oral antivirals would signpost treating clinicians to appraise this treatment modality.
2. I feel increased awareness in health-care professionals and public in general has not been explored and, in my view, is a missed opportunity. Simple education measures on safe sex, awareness about symptoms and signs of HSV, seeking medical help can be invaluable in prevention and early diagnosis of neonatal herpes.
3. On a similar note, avoiding post-natal transmission of herpes should be included and be part of this important review.

I hope your team finds these comments helpful. My apologies if they have already been considered. Let me know if I or my team can help in any way or you have any questions about my feedback.
I wish to thank you again for seeking comments on your thorough review.
Best wishes
Dush
Dr Dushyant Batra
Consultant Neonatologist
Nottingham University Hospitals

UK National Screening Committee

UK National Screening Committee
Antenatal screening for HSV-1 and HSV-2 infection to prevent neonatal herpes infection –an evidence review

Consultation comments pro-forma

Name:	Rajul Patel	**Email address:**	xxxx xxxx
Organisation (if appropriate):	BASHH		
Role:	**Chair of the HSV Special Interest Group**		

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

Yes ☐

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		Multiple typos exist across the document which would benefit from correction
Page 18	The 2006 UK NSC evidence review reported that about 60 UK neonatal herpes cases were identified in 2004-2005 with a prevalence of 4 per 100,000 live births2. This was an increase from a previously reported prevalence of 1.65 per 100,000 live births	We are aware of a number of presentations at conference of clusters of neonatal HSV cases. The historical UK reporting rate of neonatal disease has always been unusually low compared to other European countries and the last National study doubled the previous estimate- this is now out of date.

	from 76 cases identified between 1986 and 19912.	The report should consider calling for an uptodate report of incidence based on current disease patterns
Page 30/31	The 2006 UK NSC evidence review discussed management strategies, stating that seronegative women could be offered advice about potential ways to reduce their risk of acquiring HSV but did not find any evidence UK NSC external review – Antenatal screening for HSV-1 and HSV-2 infection, May 2018 about whether such strategies would be effective. A small study identified for the current review suggests that knowing that they are at risk of acquiring HSV through knowledge of their sex partner's HSV status may reduce risky behaviours in women at risk of HSV-2 but not HSV-1. Whilst a reduction in risky behaviours should reduce the risk of HSV acquisition in seronegative women this study does not provide information about whether HSV was acquired or not acquired by these women or their neonates.	The evidence required for a national screening and intervention program is different to that needed for individual patient care. We are concerned that this statement suggests that giving careful advice about risk reduction in serodscordant couples is not supported. Recent medicolegal cases as well as BASHH/RCOG guidance advise that risk reduction be advised (when male partners are infected and female partners are asymptomatic/uninfected)- ranging from abstinence to full antiviral suppression of the male partner. This statement should have a caveat.
Overall		BASHH is supportive of the general advice that population level screening is not supported by the evidence

Please return to the Evidence Team at screening.evidence@nhs.net **by Thursday 13th September 2018.**

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Consultation comments pro-forma

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	We support this decision

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Submitted by xxxx xxxx

Hi there,

Firstly I apologise for submitting this request through this platform however the link I used to submit the application does not allow me to submit my request to be a stakeholder and I do not want to miss the deadline.

Please see below what I had originally submitted:

My name is xxxx xxxx and xxxx xxxx founded the 'What's in a kiss? campaign in 2012 following the death of xxxx xxxx, to Neonatal Herpes Simplex . We were the first organisation in the UK to create resources for medical professionals available on the NHS improvement platform and to have them available in hospitals.

Having never suffered Herpes in my life, or even being aware that babies could contract it, the campaign was never really intended to be a campaign, but more a desperate search for answers.

Throughout xxxx xxxx journey, xxxx xxxx was shocked by the misleading and severe lack of credible information out there, but also by discovering a lot of medical staff from midwives, GP's, neonatal consultants had limited experience, exposure and awareness of the condition as it is so rare. As a result, opportunities to diagnose babies earlier are missed because the illness is often mistaken for other sepsis related illnesses. Therefore the biggest weapon we have against this is around prevention and informing people what to look for.

xxxx xxxx grief was undoubtedly more challenging because information was so scarce in the UK and xxxx xxxx had to try and piece together small bits of knowledge to try and build a picture of how xxxx xxxx had contracted it. xxxx xxxx had to source a lot of information from America. Due to the negative stigma attached to adult herpes, mothers can sometimes find themselves in a position where they are blamed or indeed blame themselves for the death of their baby and this can cause them to feel further isolated.

The shock and trauma xxxx xxxx felt spurred xxxx xxxx into raising awareness about Neonatal Herpes Simplex. xxxx xxxx began by targeting midwives and medical professionals, who are often the first people involved in informing and supporting parents. During pregnancy xxxx xxxx had read so many pregnancy journals, apps, books - none of which highlighted any dangers about neonatal herpes. xxxx xxxx do not want the first time parents hear about the illness to be when it's too late - as it was for xxxx xxxx.

xxxx xxxx campaign is largely focused on raising awareness amongst health professionals however, as xxxx xxxx continued xxxx xxxx work xxxx xxxx recognised public awareness is also very important. After all, if xxxx xxxx had seen a poster or an article about this illness, maybe xxxx xxxx would have recognised the signs and avoided the devastating results. xxxx xxxx also want to support parents and families on their grief journey as xxxx xxxx know only too well the devastating aftermath that neonatal death, especially from neonatal herpes can cause.

Over the last 6 years xxxx xxxx been partnering with NHS England and NHS -Improvement to conduct workshops and raise awareness with medical teams, encouraging them to pay more attention to symptoms and also looking at how they can support parents if a baby sadly dies from the virus.

To date xxxx xxxx achievements with the campaign include:

* Campaigning for and co-authoring a neonatal herpes simplex page on the NHS choices website https://www.nhs.uk/conditions/neonatal-herpes/
* Creating the awareness poster, (attached) distributed across neonatal units in London, (St Georges, Kings college, UCH, Southampton, St Barts, Royal London), GP's, sexual health clinics and dental surgeries
* Collaborating with Bounty baby to create a neonatal herpes awareness leaflet (attached) which is featured on their Bounty baby app
* Written various articles in the Bounty journal and British Journal of Midwifery (attached)
* Speaking at various patient safety events https://youtu.be/2UsjEzcO9Yk
* Created an awareness film called 'What's in a kiss?' launched at the Royal College of Nursing, in conjunction with Fixers charity https://youtu.be/dhH4Jai869A
* Being part of the patient advocacy team working on the NHS bereavement pathway on how we care and manage grieving parents
* Creating and conducting workshops for medical professionals to raise their awareness about symptoms management and how to support grieving parents who have lost their babies to HSV / bereavement workshops

As neonatal herpes is so rare I fear it will never capture the attention or publicity of higher profile conditions. I would very much appreciate the opportunity to be able to be a stakeholder on the review.

Thank you for your consideration.
Kind regards,
xxxx xxxx xxxx xxxx

WIAK - Neonatal Herpes awareness lea


WIAK Awareness poster.png

UK National Screening Committee
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Consultation comments pro-forma

Name:	Marian Nicholson	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Herpes Viruses Association		
Role:	Director		
Do you consent to your name being published on the UK NSC website alongside your response? **Yes**			

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.*
Whole draft		This is a valuable review. It has established that there are no new data to suggest that testing pregnant women for asymptomatic herpes simplex would be useful. We thank the UK NSC for undertaking this work.
Whole draft		A positive result for HSV-2 will often create a serious psychological burden for the patient, so testing should not be undertaken until it has been shown that the results of such testing outweigh the harm of informing asymptomatic patients that they carry the virus.

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Consultation comments pro-forma

Name:	Sarah Higson	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Kit Tarka Foundation		
Role:	Chief Executive		

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

Yes X **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 8	Focus of the review	We would like postnatal transmission and education of parents to also be considered.
Page 10	Mortality is cited at 20%	This seems very low compared to other studies e.g. Meeting report: Initial World Health Organization consultation on

		herpes simplex virus (HSV) vaccine preferred product characteristics, March 2017, Gottlieb et al cites mortality at 60% and the Batra et al study which cites 53%.
Page 19	Exclusion of the Batra et al study	We believe this study should form a key part of the screening consideration. The number of confirmed cases is small but indicates a much higher incidence rate than previously thought. The review states that it is not clear if the higher incidence in this population would apply to the UK as a whole but there are no reasons given as to why it would not. The doctors involved in this study see no reason why it would not be indicative of the rest of the UK. Excluding this study means the review is relying on outdated reported incidence rates against a backdrop of International reports of increasing infection rates.
Page 19	Reference to the 2000 Vyse et al study (ref 3)	We are concerned that the screening review is using a study of over 18 years old as the basis for the screening decision.
Page 20	Exclusion of studies of prevalence of a general population	We believe these studies should be considered as we are not aware of any reasons why HSV in the general population is not indicative of the pregnant population.
Page 20	No studies reporting UK seroprevalence	We are concerned that the screening review is not using any UK studies as the basis.
Page 30	Unable to draw conclusions re impact of antiviral prophylaxis on neonatal herpes	This appears to be due to the low sample not because antivirals were ineffective so we would like to see the other relevant studies considered.
Page 33	Lack of evidence	It is clear a lack of evidence has led to the conclusions of the screening review. The Kit Tarka Foundation is able to fund relevant studies into neonatal herpes so would ask interested

		parties to get in touch to ensure the next review has sufficient evidence to make a informed decision.

Please return to the Evidence Team at screening.evidence@nhs.net **by Thursday 13th September 2018.**

National Infection Service, Public Health England

I have asked colleagues within NIS, and have received the following response (and other respondents who had no comments)
‘ I think looks comprehensive and only have a couple of minor comments.
Perhaps the introduction could be rephrased to highlight that HSV1, according to 2014 BASHH guidelines, is the commoner cause of genital herpes in the UK.
Also, my understanding is that ‘condomless’ sex is increasingly being used in place of ‘unprotected’ sex, although think this has been more in the setting of HIV.’

Best wishes

xxxx xxxx

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Consultation comments pro-forma

Name:	Rachel Scanlan	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Royal College of Midwives		
Role:	**Practice and Standards Advisor**		

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

Yes x☐ 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.*
		Having read the review, RCM agrees there is insufficient evidence to recommend screening all pregnant women for HSV, nor is there enough evidence to change the conclusions of the previous UK NSC review.

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Submitted by the Royal College of Paediatrics and Child Health

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Consultation comments pro-forma

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.*
General	**All**	The review makes a strong case for not introducing screening for maternal HSV. The evidence base for doing so is either very weak or non-existent.

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