UK National Screening Committee (UK NSC)

Note of the meeting held on the 27 February 2019

in

Holiday Inn, London

This meeting provided recommendation on the following;

Fetal Maternal and Child Health Conditions:

- Screening for Mental health in antenatal and postnatal periods
- Antenatal screening for Fragile X syndrome
- Screening for Permanent Hearing Loss in Children at School entry
- Screening for Gaucher Disease in Newborns

Adult Conditions:

- Breast Screening; Additional screening with ultrasound after negative mammography screening in women with dense breasts: a systematic review
- Cervical Screening; Programme modifications
- Screening for Dementia

Members

Professor Bob Steele	Chair
Claire Bailey	Lead Clinical Nurse Specialist in breast screening, SW London
Professor Roger Brownsword	School of Law, Kings College London
Dr Louise Bryant	Associate Professor in Medical Psychology, University of Leeds
Eleanor Cozens	Patient and Public Voice (PPV)
Dr Paul Cross	Consultant Cellular Pathologist, Queen Elizabeth Hospital Gateshead Health NHS Foundation Trust
Professor Stephen Duffy	Director of the Policy Research Unit in Cancer Awareness, Screening and Early diagnosis and Professor of Cancer Screening, Centre for Cancer Prevention, Wolfson Institute of Preventive Medicine
Professor Gareth Evans	Consultant in Genetics Medicine, St Mary's Hospital, Manchester
Jane Fisher	Patient and Public Voice (PPV)
Professor Alastair Gray	Director at the Health Economics Research Centre, Nuffield Department of Population Health and Professor of Health Economics at the University of Oxford
Hilary Goodman	Operational Manager of Antenatal Services/Screening at Hampshire Hospitals Foundation Trust

Dr John Holden	Joint Head of Medical Division, Medical and Dental Defence Union of Scotland
Professor Chris Hyde	Public Health Specialist, University of Exeter
Dr Jim McMorran	GP, Coventry
Margaret Ann Powell	Patient and Public Voice
Dr Graham Shortland	Consultant Paediatrician, Cardiff and Vale University Health Board, Noah's Ark Children's Hospital for Wales and Executive Medical Director, Cardiff and Vale University Health Board, University Hospital for Wales
Dr Anne- Marie Slowther	Reader in Ethics, University of Warwick

Observers;

Morweena Carrington	Department of Health and Social Science Screening Team, Emergency Preparedness and Health Protection Policy Global and Public Health Group
Dr Heather Payne	Senior Medical Officer for Maternal and Child Health, Welsh Government
Sarah Manson	Scottish Government
Dr Sue Payne	Scottish Government
Dr Carol Beattie	Northern Ireland
Dr David Elliman	Clinical lead for Newborn Infant Physical Examination and Newborn Blood Spot, PHE

Anne Stevenson	Young Persons and Adult National Programme lead
Jacquie Jenkins	NHS Breast Screening Programme Manager
Ruth Stubbs	NHS Cervical Screening Programme Manager
Caroline Vass	Public Health Registrar
Dr Nick Hicks	National Co-ordinating Centre for National Institute for Health Research
Becky Wilkinson	PH trainee, National Institute for Health Research, NETSCC
Iain Smith	NHS England
Heather Lewis	Public Heath Wales
Professor Sir Mike Richards	Leader of the Independent Review of Cancer Screening Services and Diagnostic Capacity
Dr Alan Smith	CMO, National Screening Service Republic of Ireland
Dr Stephen Bergin	Acting Assistant Director of Screening at the Public Health Agency
Dr Sian Taylor- Phillips	University of Warwick
Professor Andy Ewer	University of Birmingham (from 14:20)

Secretariat

Professor Anne Mackie	Director of Programmes - UK National Screening Committee
John Marshall	UK NSC Evidence Lead

Dr Cristina Visintin	UK NSC Evidence Review Manager
Silvia Lombardo	UK NSC Evidence Review Manager
Zeenat Mauthoor	Secretariat
Nick Johnstone- Waddell	Public and professional information lead

Apologies

Members:

Professor Alan Cameron	Consultant Obstetrician at Southern General Hospital, Glasgow
Dr Hilary Dobson	Consultant Radiologist and Deputy Director of the Innovative Healthcare Delivery Programme, University of Edinburgh

Observer's apologies:

Dr Ros Given – Wilson	Chair of the Adult Reference Group (ARG)
Dr Sharon Hillier	Chair of the Fetal Maternal and Child Health Group (FMCH)

1. Welcome and Introductions

1.1. Professor Steele welcomed all to the meeting. A round of introductions was initiated for the benefit of the UK NSC's two newly appointed members; Dr Louise Bryant appointed to fulfil the post of social scientist and Dr Jim McMorran as the GP rep, replacing Dr Greg Irving who stepped down in 2018.

1.2. A warm welcome was also extended to Professor Mike Richards who was in attendance as an observer to gather context on how decisions are made for cancer programmes. Prof Mike Richards provided the Committee with a brief overview on the aims of the Review confirming that an interim report would be published in April 2019 with the full report to be made available in the Summer.

1.3. Members were asked to provide an update on any new declarations of interest which may be relevant to this meeting.

Two conflicts were raised;

i. Prof Hyde's participation in the HTA study 'A programme of studies including diagnostic accuracy of school hearing screening tests and a cost-effectiveness model of school entry hearing screening programmes.'
ii. Dr David Elliman informed the Committee that he was Chair of the sub group who looked at Screening for Permanent Hearing loss in Children at School entry

1.4. Apologies were noted, and the Chair confirmed that the meeting was quorate with 17 members in attendance.

2. Minutes and Matters arising

2.1. The October 2018 minutes were approved as a true and accurate depiction of the meeting held with no amendments made. It was agreed that the October minutes would be published as final.

2.2. Two action points were identified from the October meeting which had been added to the February meeting;

3a. Directors Update on Screening for Severe Combined Immunodeficiency (SCID)

UK NSC to be kept up to date with the outcome of the revised SCID modelling work which would now include neonatal TB —on the agenda under Director's update.

3b. Directors Update on Pulse Oximetry

A report on Pulse Oximetry should be brought to a future UK NSC meeting for further discussion —on the agenda.

3. *Matters arising*

***Director's* Update**

Prof Mackie gave an update on the following

Update on Screening for Severe Combined Immunodeficiency (SCID)

3.1. As discussed at the October 2018 meeting, discussions with the Joint Committee on Vaccinations and Immunisation (JCVI) had flagged a possible issue with timing around the offer of SCID and the newborn BCG programme. Further work to re-examine the SCID model to consider the implications of delivering vaccinations at a later point was still being explored. It is expected that the model will report in Spring 2019 and that the UK NSC meeting will discuss this at its June meeting.

Update on Screening for LCHAD

3.2. Prof Mackie wished to inform the Committee that although the public consultation on screening for LCHAD had closed in January 2019, comments submitted from the consultation as well as from the Fetal Maternal and Child Health Reference group (FMCH) led to further internal work being carried out. It is expected that the document will be submitted for recommendation at the UK NSC's June meeting.

Independent Breast Review

3.3. Prof Mackie provided the Committee with a verbal summary on the published outcomes of the Independent Breast review and the next steps. The review provided six key themed recommendations which included;

i. Breast Screening policy
ii. IT and processes
iii. Governance
iv. Handling of the incident
v. Impact on women
vi. Age X trial

3.4. Relevant to the UK NSC, is the need to understand whether there is any evidence which could usefully inform a discussion about the upper age for breast screening, an item that is on the agenda and to be discussed later in the meeting, as well as providing support for the Age Extension trial.

3.5. In addition to this review is the NAO report, which has commented on the IT infrastructure within the NHS Breast Screening Programme and a Public Accounts Committee hearing.

Action 3a: The report on SCID re- modelling to be added to the UK NSC June meeting

Action 3b: Screening for LCHAD to be added to the June meeting

Action 3c: UK NSC to be kept up to date on the PAC hearing in breast screening

Update on the Ethics Task Group

3.6. The group continues to develop the framework and possible flow charts to help indicate where in the evidence review process formal consideration of the ethical issues should be undertaken. This was more likely to be for those conditions which

may meet the main UK NSC criteria to become a recommended screening programme.

High Risk Screening

3.7. Also included as part of the Director's Update was high risk screening. Although the UK NSC offers population screening for asymptomatic people, some high risk groups are identified as part of routine population screening and are then managed within the screening programme.

3.8. Prof Mackie informed the Committee that queries on the delivery and management of high-risk screening are often directed to the UK NSC, as a positive UK NSC recommendation and ministerial agreement causes the delivery and funding of a complete pathway that is supported by a quality assurance programme. High risk screening is driven by NICE guidance for which there is no delivery arm, and there is an absence in the delivery of such programmes. The UK NSC secretariat is therefore looking to hold exploratory talks with NICE to determine whether there is scope for joint work to evidence and improve the management and delivery for screening groups at high risk.

Action 3d: Zeenat to circulate the high risk paper to the Committee

Upper age limit in Breast screening

3.9. The Committee received an evidence map which was commissioned outside the usual UK NSC review process.

3.10. The evidence map aimed to address the Independent Review of Breast Screening's recommendation, that the screening stopping rule should be clarified with the UK NSC providing advice based on the best available evidence. Following this recommendation, the UK NSC had also formally received a request by the Department of Health and Social Care to advise on this matter.

3.11. Whilst the results of the Age X trial are awaited the UK NSC is required to identity any published evidence which may usefully inform a discussion on what the stopping rule for the screening programme should be.

3.12. The first step produced an evidence map which looked to provide an indication on the volume of published evidence available. This was undertaken in two parts. Firstly, a scoping search looked at international guidelines and standard operating procedures to see if anybody had clearly defined what the age limit is or when the final invite should be issued. Whilst the second part required a systematic search be carried out for any primary research that identified women aged 69-71 and provided an analysis of screening in that age group. Prof Mackie informed the Committee, that the work had been shared continuously through its development with its Adult Reference Group (ARG) which concluded that, based on the work undertaken so far, there is no direct evidence which can inform a discussion on the stopping rule for the final invitation in the breast screening programme.

3.13. The work therefore has been shared with the Committee to ensure it is content with this conclusion and is given the opportunity to comment and suggest whether further literature searching should be considered.

3.14. The Committee stated that they were content with the work undertaken so far and recognised that in the absence of evidence that a pragmatic approach should be taken to help NHS England deliver the breast screening programme.

3.15. Prof Mackie suggested that once the Committee is content with the work, that the four countries should aim to develop a consensus on defining what the stopping rule should be, taking into account current logistics, whilst the UK NSC awaits for the Age X trial to gather new evidence in this upper age cohort.

3.16. The Chair offered the Committee an additional two weeks to thoroughly review the work on upper age limit to ensure that the Committee is content with the work before formal advise on this is issued.

Action 3e: UK NSC given two weeks to review the Upper age limit papers and forward any comments onto Zeenat

Action 3f: UK NSC Secretariat to review any comments submitted.

If there is no objection; to ask Four Countries to develop a statement of clarification to provide a pragmatic approach to defining the breast screening programme stopping rule. In the event of comments and further work the UK NSC secretariat will follow this up

Annual Call for Topics 2018

3.17. The UK NSC ran its third annual call for topics between September to December 2018 and received a total of nine submissions with an internal submission following discussions with the Secretariat; five relating to fetal, maternal and child health conditions and five for adult conditions. Four were rejected, one is to be handled as a major programme modification and five are potential population screening conditions.

3.18. The submissions were reviewed by an evaluation group who provided the following outcomes which were then supported and noted by the UK NSC;

i. Annual screening of 30–75 year olds for all cancers

The proposal is to test all people aged 30–75 years for all cancers using a PanTum test followed by a PET scan if positive.

It was agreed that due to the lack of evidence on the outcomes for individuals entering the screening pathway, and the information provided by RMDM Diagnostics that such evidence might be available in the near future, it was proposed to suggest that RMDM Diagnostics resubmit their application when such information becomes available.

ii. Screening for cutaneous melanoma in adults

The proposal is to screen people under the age of 40 for risk of cutaneous melanoma using ocular/ iris photography.

This is a new condition which falls within the remit of population screening.

It was agreed that an evidence map would be undertaken to scope the volume and direction of any available published peer reviewed evidence on cutaneous melanoma.

iii. Screening for neurofibromatosis type 1 (NF1) in the newborn, 12 months and two years

The proposal is to offer screening in all children up to two years of age to detect café au lait spots early.

This is a new condition which falls within the remit of population screening.

It was agreed that further assessment would be undertaken in the form of an evidence map to scope the volume and direction of any available published peer reviewed evidence on neurofibromatosis type 1 (NF1).

iv. Screening for Klinefelter syndrome in the newborn and adolescence

The proposal is to offer karyotyping to all newborn boys and/or test hormone levels again in boys aged 14 years to detect whether they have 2 XX chromosomes to make up XXY rather than XY

This is a new condition which falls within the remit of population screening.

It was agreed that further assessment would be undertaken in the form of an evidence map to scope the volume and direction of any available published peer reviewed evidence on Klinefelter syndrome (XXY).

v. Newborn screening for 22q11 Deletion Syndrome

The proposal is to screen for 22q11.2 in order to detect whether chromosome 22 was deleted or duplicated.

It was agreed that that further work would be done by the evidence team to check the references in the proposal to see if they provide more information on the screening pathway (especially on the test) and also to undertake an evidence map to understand the volume of literature available.

vi. Newborn Screening for Beta Thalassaemia

The proposal is for beta thalassaemia major to be screened for as a condition rather than be reported as an incidental finding within the existing Sickle Cell and Thalassaemia screening programme.

This would be a major programme modification submission and should therefore be handled in accordance with this process.

vii. Screening for lung cancer in adults

The proposal is screen for lung cancer using low dose computed tomography (T)

This condition is already on the UK NSC's list of conditions which is reviewed regularly as per its published process. No further action is required.

viii. Screening for risk of Sudden Cardiac Death

The proposal is to screen for risk of sudden cardiac death.

This condition is already on the UK NSC's list of conditions which is reviewed regularly as per its published process. No further action is required.

ix. Cascade screening for non Syndromic Thoracic Aortic Diseases (NS-TAD)

The proposal is to screen individuals with a family history of diagnosed conditions. This submission falls outside the UK NSC remit

It was agreed that no further action is needed to look at this as it relates to cascade testing and not population screening.

x. CO based screening to increase smoking cessation rates in pregnancy and improve pregnancy outcomes

The proposal is to offer CO screening to all pregnant women at their booking to deliver the NHSE's 'Saving babies' Lives Care Bundle'

This falls within the remit of the UK NSC

It was agreed that the UK NSC should undertake a rapid review to look at CO screening in pregnancy.

Artificial Intelligence

3.19. Prof Mackie informed the Committee that there is growing interest around the use of artificial intelligence (AI) in health care settings particularly in screening. Several proposals have since been received to consider using AI in the breast and diabetic eye screening programmes.

3.20. In response to this, interim guidance has been developed to look at the purpose of AI in breast screening mammography.

3.21. The Committee was provided with a presentation on how the guidance was developed looking at key aspects of AI, by Dr Sian Taylor- Phillips.

3.22. The Committee supported the interim guidance as a way to assist developers of AI understand the process of adding this technology into screening programmes and the need to have restrictions. On the Committee's approval it was agreed that this would published via the PHE Screening Blog.

Adult Screening

ARG Report

4. In Dr Given-Wilson's absence, the Chair provided the Committee with a summary of developments following the ARG meeting held at the end of January.

4.1 The group had reviewed the consultation comments on the following conditions tabled for recommendation at today's UK NSC meeting;

- Breast Cancer (additional screening with ultrasound after a negative mammography in women with dense breasts)
- Cervical cancer- modification of the programme to extend screening intervals
- Dementia

Screening for Breast Cancer (additional screening with ultrasound after a negative mammography in women with dense breasts)

4.2 This piece of work was commissioned by the UK NSC secretariat and falls outside the usual evidence review process. The work was stimulated given the growing interest in breast density and the current practice in the US where it is mandated that women are informed of their breast density.

4.3 It is suggested that dense breasts can be cause an increased missed rate of screen detected cancers and so as a proactive piece of work, the UK NSC secretariat looked to see if whether it would be of benefit to offer ultrasound within the breast screening programme. To assess the effectiveness of ultrasound it was agreed that this would be offered to women with dense breasts, which then opened the question as to what and how do we define dense breasts and what are the risks of having dense breasts

4.4 The objectives of the review therefore were to determine what is meant by dense breasts and what the balance of benefits and costs of measuring breast density on mammography are.

4.5 The review found that there is a strong consistent association between mammographic breast density and risk of breast cancer meaning that some women with dense breasts may be at a higher risk of developing breast cancer as opposed to women whose breasts tissues are predominantly fatty tissue. As dense breast tissue can make mammograms more difficult to read some abnormal changes may also be missed.

4.6 The evidence of how to measure breast density was found to be less certain. The review reported that it is difficult to validate density methods as there is no gold standard on how this should be measured. Ultrasound is not precise and can lead to large numbers of false positives results as well as detecting additional cancers which would not have been detected when using mammography. Furthermore, it was found that there is little evidence to support that the use of ultrasound would be being cost effective.

4.7 A public consultation was held and the Committee noted that only one comment from CRUK was received which supported the findings of the review to not recommend additional breast density measurements or ultrasound to the breast screening programme. CRUK also informed the UK NSC that it is supporting a study looking at risk adaptive breast screening. The Committee expressed a desire to be kept informed about the study.

The UK NSC supported the recommendation not to offer ultrasound as a supplement to the breast screening programme.

Action 4a: Zeenat to contact CRUK re its study on breast risk and to invite to a future meeting to present findings

Cervical Screening: Programme modifications

4.8 In November 2015, the UK NSC recommended that HPV should be adopted as the primary screen test within the cervical screening programme. Since then there has been discussion on whether the screening intervals for HPV negative women under 50 years could be extended from three to five years.

4.9 Due to the lack of primary evidence on this it was agreed by the Committee in June 2018 that modelling should be used at the interval and surveillance strategy. In addition to this modification it was agreed that a strategy for women exiting the programme at 64 should be considered and that the use of self sampling should also be considered.

4.10 The UK NSC hosted a three month consultation which closed in January 2019 and received a total of 13 responses. In summary the comments indicated a broad consensus on the main components of the proposed strategies: to implement a 5 year screening interval of five years for HPV negative women irrespective of age and to offer HPV positive/ cytology negative women a recall for another test in 12 months. There was a good level of consensus on the strategy for women with persistent HPV infection and negative cytology to undergo two annual tests. However, there was debate about the logistics and clinical value of referring those remaining HPV positive / cytology negative at the second surveillance test. It was suggested that this point of the surveillance strategy could be guided by a clinical consensus process and that a mechanism should be sought to formally evaluate the different approaches following implementation if different strategies were used in the four countries.

4.11 With regards to the proposals on women aged 64 who were exiting the programme comments were generally supportive of the proposal that HPV positive/ cytology positive women should be managed in the same way the other age groups. There was support that HPV positive/ cytology negative women should be recalled at 12 months and that women who were still HPV positive should be referred to colposcopy. However, some comments

suggested that a different surveillance combination could be considered. Again, it was suggested that a clinical consensus process could guide this part of the screening pathway.

4.12 For self-sampling, there was a good level of consensus that further research should be encouraged to explore this strategy further.

The UK NSC therefore recommended the following cervical programme modifications;

- the extension of the screening intervals from three to five years for women who test HPV negative as part of their routine screen test.
- implementation of 2 surveillance tests at 12 month intervals for women who remain HPV positive and cytology negative
- the need to have further research on the feasibility of self sampling

Action 4b: John Marshall to set up a consensus group to discuss the screening pathway for recurrent HPV positive and cytology negative women and women exiting the programme

Screening for Dementia

4.13 Dementia is a term given to a range of symptoms associated with the gradual decline in brain functioning, which can include but not be limited to problems with; memory loss, thinking speed, language, mood and difficulties carrying out daily activities. About 10% of people over the age of 70 have dementia. In 2016 dementia was the most common cause of death in women and the second most common cause of death in men.

4.14 The UK NSC last reviewed the evidence relating to screening for dementia in 2014 and whilst the Committee recognised that this was and would continue to be a growing public health issue, there were various issues at the time around the test accuracy, insufficient evidence on the epidemiology and natural history of mild cognitive impairment (MCI) and the effectiveness of pharmacological and non-pharmacological interventions for MCI or dementia to recommend screening.

4.15 The 2018 review focussed on the following points:

1. What are the early signs and risks that mean someone is likely to develop dementia when they have already developed some deterioration in thinking skills (known as mild cognitive impairment)?
2. Are there screening tests that can accurately identify people likely to have dementia?
3. Are there any treatments that produce better outcomes for people who have been diagnosed with dementia early?
4. Do the public, patients and health professionals think dementia screening is acceptable?

4.16 The review found that although dementia continues to be an important health problem there is still no screening test that can accurately identify people in the general population with dementia who do not have symptoms. The progress of MCI and association to the development of dementia remains unclear. The review found that there is a lack of evidence that cognitive assessment tools for MCI and dementia can provide an effective approach to population screening. The studies reported by 4 good quality meta-analyses were small and subject to bias. The Committee noted that, in relation to biomarkers and brain imaging techniques, the review did not find any evidence that examined the effectiveness of the use of these tools to detect MCI or dementia in asymptomatic adults who are not already suspected of having dementia or MCI.

4.17 Six comments were received following public consultation. Overall, the Committee noted that there is strong support not to offer population screening for dementia as there are clear evidence gaps particularly, the relationship between MCI and dementia, biomarkers and imaging techniques, and the acceptability of screening for dementia in the UK before screening could be feasible.

The UK NSC recommended that population screening for dementia should not be offered.

Based upon the UK NSC criteria to recommend a population screening programme, screening for dementia should not be introduced.

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**
5. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.	**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**
The Screening Programme	
11. There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity. Where screening is aimed solely at providing information to allow the person being screened to make an "informed choice" (such as Down's syndrome or cystic fibrosis carrier screening), there must be evidence from high quality trials that the test accurately measures risk. The information that is provided about the test and its outcome must be of value and readily understood by the individual being screened.	**Not Met**
12. There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/ intervention) is clinically, socially and ethically acceptable to health professionals and the public.	**Not Met**

FMCH Report

5. The Chair provided the Committee with a verbal summary on developments and discussions had at the FMCH meeting in January. A presentation on genome sequencing was delivered and the Chair was in talks with the presenter to have this shared with the NSC at a future meeting. It was agreed that the following conditions should move to public consultation;

- Screening to prevent stillbirth (closes 12 May)
- Antenatal screening for cystic fibrosis in pregnancy (closes 20 May)

Action 5a: Genomic sequencing to be added to a future UK NSC meeting- Zeenat to confirm arrangements

Pulse Oximetry (PO) Report

6.1 The Chair welcomed Professor Ewer to this item to observe and comment on the work undertaken so far given his ongoing commitment, expertise and assistance in this area.

6.2 The Chair drew the Committee's attention to the various pieces of work carried out since the UK NSC evidence review in 2014 which triggered the pilot to gather evidence on screening with PO. Papers on progress have been shared previously with the Committee at various stages. The Committee received a full set of papers from the period between 2014 and now including a cost effectiveness model. The UK NSC has been given the opportunity to review the evidence in its entirety and was asked whether they are content for this to go out for public consultation as a programme modification.

6.3 Prof Ewer stated that as an advocate for PO screening to detect critical congenital heart disease (CCHD) he acknowledges that this test picks up other non-cardiac conditions. The aim of the pilot, was to understand what impact implementing PO would have; looking to see if this would increase hospital neonatal unit admissions, provide better outcomes for the baby through early detection as well as to see how feasible it was to add PO to the Newborn Infant and Physical Examination screening programme (NIPE).

6.4 Prof Ewer said that regarding admissions he supported the verdict that this did not increase the rate for neonatal admissions however did not agree with the outcome of the health economics analysis. It was suggested that it is flawed based on an incomplete set of data. Prof Ewer recognised that although the data from the pilot study was poor and that outcomes had not been collected a consistent outcome in data demonstrates that screening using PO provides benefit through early detection whether it detects CCHD or other non-cardiac conditions.

6.5 The Chair thanked Prof Ewer for his comments and invited Caroline Vass to present the papers on PO to the Committee.

6.6 Pulse oximetry is a quick, non-invasive test that measures the concentration of oxygen in the blood using a sensor applied to the hand or foot of a newborn. Low levels of oxygen, hypoxemia, can indicate that there is a heart problem, infection or other health issue which may require further investigation and which may benefit from early detection whilst the baby is asymptomatic.

6.7 In 2014 the UK NSC reviewed the evidence to screen for congenital heart defects (CHD) using PO. The review found that although screening for CHD was cost effective the work had not taken into account the effect on the whole population of babies who would receive the test. The Secretariat then worked with various clinicians and academics to develop an understanding of whether PO screening does more good than harm at reasonable cost to the whole population being offered screening.

6.8 During 2015 a pilot study took place in which 15 trusts across England offered PO to detect critical congenital heart disease (CCHD) as an additional test in the Newborn Infant Physical Examination(NIPE) screening programme. The pilot provided the following key data:

- 32,836 PO screens completed
- 32, 597 babies received a negative result (normal oxygen level)
- 239 babies received a positive result (abnormal oxygen level) of whom
    - 135 were healthy
    - 14 had CHD (8 CCHD)

- 86 had some other serious (non cardiac) condition detected

6.9 The data above are from units that did screening and found roughly what previous research studies had done. Crucially, however, the pilot had been set up to collect data from units that were not screening using PO in order to provide a baseline (against which we could say PO was better or not). Unfortunately, only very small amounts of data were collected. Admissions to neonatal units were used as a proxy for serious illness; these limited data indicated that there was no significant difference in the number of babies admitted in screening units before and after the introduction of PO.

6.10 In a further attempt to fill evidence gaps produced by having no comparator a workshop was held where clinical expert input was sought. Dr Shortland reported to the Committee that the workshop was set up to look at the potential benefit and harm from PO screening but the group considered and gave a clinical assessment of those conditions for which there was benefit to early diagnosis.

6.11 In addition, a disease and cost effectiveness model was commissioned. The model concluded that without a comparator the estimates of cost and benefit of PO versus usual care was very difficult to ascertain.

6.12 On review of these reports, the Committee noted that by offering screening using PO, then the identification of hypoxemia will be indicative of CHD and other non-cardiac conditions, as well as false positives for any condition.. The work had not been able to reach a robust assessment of benefit and harm and this uncertainty was highlighted in the latest cost effectiveness evaluation. The Committee agree that CHD in newborn is a very important issue but that the evidence thus far did not meet the criteria for a screening programme.

6.13 The Chair asked the Committee if it was content with the proposal to open a public consultation based on the documents circuited, which was approved. Prof Hyde abstained from this decision.

The UK NSC recommended opening a public consultation on the use of using Pulse Oximetry as an additional test in the newborn and infant screening programme

Action 6a: A three month public consultation on the programme modification looking at the use of pulse ox in the newborn and infant screening programme should be opened

Non- invasive prenatal testing: twins and DNA microarray technology

6.14 In 2016 the UK NSC recommended a pragmatic approach to the roll out of non-invasive prenatal testing (NIPT) as part of an evaluation to provide further information on the use of this contingent test to women who have a higher chance (equal or greater than 1 in 150) of having a baby with Down's, Edward's or Patau's syndrome.

6.15 Whilst the programme prepares for this evaluative roll out the UK NSC has been asked to look at proposals which relate to modifications of the offer to see whether DNA microarray, a new method of NIPT, could be used as well as to see if NIPT can be used in twins and other multiple pregnancies.

6.16 The UK NSC reviewed the papers circulated and agreed that the use of microarray represents a minor modification. The review found that there was no statistically significant difference between the sequencing (currently approved) and microarray technologies in either sensitivity and specificity. The Committee noted that this represented no evidence of a difference rather than evidence of no difference. It also noted the test failure rate for microarray based NIPT was estimated to be approximately 1%, which was on a par with the failure rate in sequencing technology in the 2015 review.

6.17 With regards to twins, the Committee recognised that there continues to be very limited evidence for either sequencing/microarray in twin pregnancies. All studies considered had a high risk of bias and only a small number of affected pregnancies had been included in the studies. The Committee supported the use of NIPT as part of the evaluative roll out for this contingent test. The Committee agreed that once NIPT is nationally available programmes will be able to carry out ongoing monitoring and evaluation in such a way that the screening programme can be altered if necessary in light of any real-life findings and be brought back to the UK NSC to consider further.

The UK NSC recommended that the use of the contingent test, NIPT, should be added to the twin pathway and that the newer technology of microarray DNA can also be used.

Screening for mental health in antenatal and postnatal periods

6.18 The Chair informed the Committee that this is the first time the UK NSC has looked at mental health in antenatal and postnatal periods in a single evidence review. Previously, the UK NSC examined 'screening for postnatal depression and 'psychiatric illness in pregnancy' separately. Due to the similarities between these conditions, it was agreed that the two should be combined into a single evidence review document.

6.19 Antenatal and postnatal mental health issues are a cause of significant complications in pregnancy and in the postpartum period. These disorders included depression (from mild to severe), anxiety disorders as well as pregnancy and postpartum psychosis. According to the WHO about 10% of pregnancy women and 13% of women who have just given birth experience a mental health disorder.

6.20 The review looked at four key areas;

i. the negative effect on women and their children of mental health problems during pregnancy and after giving birth
ii. whether the tests available can predict which women are at risk of such problems
iii. whether the treatment for such disorders can help a woman and her baby
iv. whether the national guidance on how to help women with these problems is being followed.

6.21 The review found that although there is a large volume of evidence about the adverse outcomes associated to common mental health problems experienced by women during pregnancy and postpartum. There is a paucity of evidence for effective screening tests for common mental disorders in the antenatal period; however, there is more evidence in relation to screening tests in the postpartum depression. However,

the numbers are still low when considered as evidence for population-based screening. Moreover, these studies suffer from the same heterogeneity problems noted in the antenatal studies. Firm conclusions about the effectiveness the pharmacological and non-pharmacological interventions for these conditions in screen-detected women are difficult to be drawn. This is because of the small number of studies available and the considerable heterogeneity in their methodology, level of bias and consistency of results. The Committee also agreed with the review in recognising that clinical guidance is not fully implemented nor consistent across the service.

6.22 The review received no consultation comments.

The UK NSC recommended that a population screening programme for mental health in antenatal and postnatal period should not be offered.

Based upon the UK NSC criteria to recommend a population screening programme, screening for mental health in antenatal and postnatal periods should not be introduced.

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	
2. 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	
6. There should be a simple, safe, precise and validated screening test.	**Not Met**
7. The distribution of test values in the target population should be known and a suitable cut off level defined and agreed.	
The Intervention	
10. There should be an effective intervention for patients identified through screening, with evidence that intervention at a pre-symptomatic phase leads	**Not Met**

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.	
Implementation	
15. All the cost-effective primary prevention interventions should have been implemented as far as practicable.	**Not Met**

Antenatal and Newborn screening for Fragile X syndrome

6.23 The UK NSC was informed that the evidence team who commission and manage the evidence reviews are trialling a new approach to support the published evidence review process. This new step called 'evidence mapping' is being looked at to help the UK NSC become more efficient when reviewing its regular reviews for its 109 conditions.

6.24 Evidence mapping is a way to gauge the type and volume of published literature to see whether there is sufficient evidence to commission a more in-depth external review. For some conditions, where it is suggested that the evidence base has not changed, an evidence map would be undertaken to scope this and to recommend if further work is needed. If there is no new literature, then this condition would be reviewed again in three years. However, should any evidence be published which may alter the recommendation then a submission can be sent to the UK NSC at any time via its early update process. This additional step will allow the UK NSC to then focus on conditions and commission external reviews where the evidence is developing and changing more rapidly. The Committee stated that it welcomed this step to help better manage the volume of and complexity of the reviews which are brought to the Committee for consideration. The Chair reiterated that it is a trial process but it would still be subject to public consultations and be brought to the Committee to recommend next steps.

6.25 The UK NSC was asked to consider the evidence map undertaken for Fragile X.

6.26 This is the third time the UK NSC has looked at the evidence for antenatal screening for Fragile X. Fragile X is a genetic condition, most commonly found in boys which causes a range of learning disabilities and behavioural problems. It is caused by a mutation in the FMR1 gene on the X chromosome.

6.27 The UK NSC last looked at Fragile X in 2015 and recommended that whilst the natural history and prognosis of full mutations in males is well understood, it was not possible to predict whether a female fetus carrying a full mutation will be affected or to what extent, which highlighted the inaccuracy of prenatal testing. In addition, the test, polymerase chain reaction (PCR) followed by southern blotting, was found to be labour and time intensive and therefore unsuitable for a screening programme.

6.28 One response from the 2015 consultation suggested that the evidence relating to newborn screening should be considered.

6.29 For the 2018 review the UK NSC secretariat undertook two evidence maps to see whether there has been new literature relating to antenatal screening and to see what evidence is available for newborn screening for Fragile X, as this has not been looked at previously.

6.30 The first evidence map looked at literature about whether a suitable screening test had been found for use in the pregnant population. For the second evidence map three key questions were considered; literature on a test for newborns, whether there are any treatments or early interventions and if there are any guidelines around antenatal or newborn screening for Fragile X.

6.31 The result of the first evidence map for antenatal screening for Fragile X suggested that the volume of evidence in this area remains insufficient to change the UK NSC's current position to not offer population screening. As for the second evidence map looking at newborn screening, limited studies were available but the Committee noted that there is growing interest in this area, and indicated that PCR methods need to be explored in larger studies.

6.32 The Committee noted that the three-month consultation resulted in one comment being received which expressed its concern about relying solely on peer reviewed

evidence and the methodology used. The UK NSC suggested that the comment was not pertinent to evidence mapping and that it agreed that the document is clear on its aim and methodology. Furthermore, the Chair stated that the Committee had a responsibility to ensure that the evidential barrier set was high due to the harms screening can cause and this was recognised by the Science and Technology Inquiry in 2014.

The UK NSC recommended that, based on the evidence identified during the mapping exercise looking at the volume and type of literature available, there is not sufficient evidence at the moment to justify commissioning an external review. The UK NSC upholds its 2015 recommendation that antenatal screening for Fragile X should not be recommended. Similarly, the UK NSC recommended that an evidence summary on newborn screening for Fragile X should not be commissioned as the volume and type of the evidence is currently insufficient to justify further work in this area. Since newborn screening for Fragile X has not been previously reviewed by the UK NSC, future consideration of this topic would need to be approved through the annual call for new screening topics.

Screening for Permanent Hearing loss is children at school entry

6.33 The UK NSC was reminded that the School Entry Hearing Screening Programme in the UK was introduced in 1955 and remains in place in many parts of the UK even after the introduction in 2001 of the newborn hearing screening.

6.34 The 2018 review focuses on three key questions around; the prevalence and type of hearing loss, the accuracy of hearing screening tests and the consequences of school entry hearing screening. Dr Visintin informed the Committee that when looking prevalence, only one UK study was identified, in North London. While the review was encouraged by the large sample size, good quality and the results are applicable to the current UK screening context where newborn hearing screening is in place. However, no prevalence figure for temporary hearing impairment was identified and it is not clear

if the prevalence of permanent hearing loss in this area of North-East London is generalisable to the rest of the UK.

6.35 With reference to the diagnostic accuracy of the test one systematic review was identified. The review found that there was a lack of consistency in the results of the included studies (10 small studies), limiting any conclusions that can be drawn about the accuracy of screening tests. Whilst the systematic review was of good quality, there were some concerns about the quality of the included studies. The applicability of the results to the current UK context was questionable.

6.36 Finally, when looking at comparing outcomes of screening versus no screening in an area one study was identified. The study did not find significant difference in the yield of confirmed cases of hearing impairment between such areas. Moreover, there were some concerns about the quality of the study and in the assessment of hearing impairment, and the applicability of the results to the UK population as a whole. No studies were identified assessing the potential impact of a false negative screening test.

6.37 Nine responses were received from the public consultation, two of which were identical. The Committee recognised that generally stakeholders seemed to support the recommendation to not stop school entry screening as there is not enough evidence to support its cessation. Some stakeholders also think that it might be a value in this screening programme in identifying children that either are missed by the newborn hearing screening programme or who were not screened, but they agreed that as there is a lack of evidence to introduce a population screening programme for permanent hearing loss in school entry children this should not be recommended.

6.38 The Committee suggested that there is little evidence to support a change in recommendation, but also noted that if this were presented as a new programme it may not meet the criteria. Therefore, the Committee asked that work be done to characterise current programmes and consider evaluation to assess benefits and hams and brought to the Committee for consideration.

6.39 Prof Mackie agreed that PHE would accelerate the work to try and gain a better understanding of school entry hearing screening and would update the Committee.

The UK NSC recommended that there should be no change to the current guidance on screening for permanent hearing loss in children at school entry but this should remain under review.

Based upon the UK NSC criteria to recommend a population screening programme, Permanent Hearing loss is children at school entry should not be introduced.

Criteria (only include criteria included in the review)	Met/Not Met
The Condition	
3. 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**
The Screening Programme	
11. There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity. Where screening is aimed solely at providing information to allow the person being screened to make an "informed choice" (eg. Down's syndrome, cystic fibrosis carrier screening), there must be evidence from high quality trials that the test accurately measures risk. The information that is provided about the test and its outcome must be of value and readily understood by the individual being screened.	**Not Met**

Action 6b: Prof Mackie to update the UK NSC on the work in England on school entry hearing screening

Screening for Gaucher Disease

6.40 Gaucher disease is an inherited metabolic condition caused by a faulty or missing enzyme used to break down fatty substances from cells which can affect a wide range of body organs and tissues and cause swelling.

6.41 The UK NSC last looked at this condition in 2013 and recommended that population screening should not be offered because were a number of uncertainties. These were difficulty in prediction of the severity of the condition. Gaucher's is divided into classified into three types which have different severity and age of onset of symptoms it was unclear whether earlier treatment following screening would be more beneficial than the current practice of treatment following clinical presentation.

6.42 The 2018 review aimed to assess whether there is new evidence to cause the UK NSC to reconsider the current screening recommendation. The review looked at; whether the treatment of type 1 Gaucher disease at a pre-symptomatic phase results in better health outcomes. No studies were identified that specifically examined the effectiveness of interventions in a pre-symptomatic population.

6.43 An evidence map was developed to provide further background information on the evidence relating to developments in the treatment of Gaucher disease. The Committee was informed that the evidence map did not find any new literature relating to the treatment for the three types of Gaucher disease.

6.44 Five stakeholders commented on the review document following the public consultation which closed on the 17 February. The majority of the responses supported the review's conclusion to not introduce population screening for Gaucher Disease based on the lack of evidence about pre-symptomatic treatment.

6.45 The UK NSC suggested that for the next review it would be useful to see if there is evidence on the diagnostic odyssey.

The UK NSC recommend that population screening for Gaucher Disease in newborns should not be introduced.

Based upon the UK NSC criteria to recommend a population screening programme, Gaucher disease should not be introduced

	Criterion	Met / 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 should not be further considered.	Not met

Updates

NIHR NETSCC Update (for information)

The Committee noted the updates

SIGN Update (for information)

The Committee noted the updates

AOB

None

UK National Screening Committee (UK NSC)

Chair's Action

Following the 27 February 2019 meeting

NOTIFICATION OF CHAIR'S ACTION ON BEHALF OF THE COMMITTEE

Action Number	Item to be addressed	Initial status	Reason for Chair's Action	Decision
1.	Upper age limit in Breast Screening	A recommendation from the Independent Review of Breast Screening is that the UK NSC should provide clarity based on the best available evidence as what the stopping rule should be. Papers have been shared with ARG and were circulated to the Committee. As the papers were sent late it was agreed that an extension for review would be granted.	The UK NSC was presented with the work undertaken at the meeting and an additional two weeks to reflect and comment on the papers. No comments were received from members or officers.	Based on the evidence provided the UK NSC agrees that there is insufficient evidence to propose a change to the upper age limit. The Committee supports the Age X trial. This will gather the evidence needed is this cohort. The UKNSC will review this once the trial reports in 2026. The UK NSC recommends, based on current evidence , that breast screening should end between the 70th and 71st birthday

I confirm that I have taken Chair's action in relation to the decisions recorded above.

Signed: 
Date: 11th April 2019