UK National Screening Committee (UK NSC)

Note of the meeting held on the 25 October 2017

at

Coin Neighbourhood Centre, London

This meeting provided recommendation on the following conditions;

- Cytomegalovirus (CMV)
- Human T-Cell Lymphotropic Virus (HTLV)
- Biliary Atresia

Members

Professor Bob Steele	Chair
Dr Paul Cross	Consultant Cellular Pathologist, Queen Elizabeth Hospital Gateshead Health NHS Foundation Trust
Ms Eleanor Cozens	Patient and Public Voice (PPV)
Dr Hilary Dobson	Consultant Radiologist and Deputy Director of the Innovative Healthcare Delivery Programme, University of Edinburgh
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
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
Ms Hilary Goodman	Operational Manager of Antenatal Services/Screening at Hampshire Hospitals Foundation Trust
Mrs 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

Observers;

Ms Natasha Alleyne	Department of Health Screening Team, Emergency Preparedness and Health Protection Policy Global and Public Health Group
Dr Hilary Angwin	Chair of Fetal Maternal and Child Health Group (FMCH)
Dr Carol Beattie	Senior Medical Officer, Northern Ireland
Ms Christine Cook	NHS England
Dr Ros Given – Wilson	Chair of the Adult Reference Group (ARG)
Dr Nick Hicks	National Co-ordinating Centre for HTA
Dr Sharon Hillier	Director of Screening Division, Public Health Wales
Mr Nick Johnstone- Waddell	Head of Communications, National Screening Programmes (PHE)
Dr Sue Payne	Scottish Government
Dr Heather Payne	Senior Medical Officer for Maternal and Child Health, Welsh Government
Prof Catherine Peckham	University College London

Secretariat

Dr Anne Mackie	Director of Programmes - UK National Screening Committee
Ms Zeenat Mauthoor	Secretariat
Mr John Marshall	UK NSC Evidence Lead
Dr Cristina Visintin	UK NSC Senior Evidence Review Manager

Presenters

Dr Sophie Whyte	University of Sheffield; ScHARR

Apologies

Professor Roger Brownsword	School of Law, Kings College London
Professor Alan Cameron	Consultant Obstetrician at Southern General Hospital, Glasgow
Dr David Elliman	Clinical lead for Newborn Infant Physical Examination and Newborn Blood Spot, PHE
Ms Jane Fisher	Patient and Public Voice (PPV)
Mrs Jo Harcombe	National Lead for Stakeholder Information and Profession Education and Training
Professor Chris Hyde	Public Health Specialist, University of Exeter
Dr Greg Irving	GP
Dr John Holden	Joint Head of Medical Division, Medical and Dental Defence Union of Scotland
Ms Sarah Manson	Scottish Government
Dr Ailsa Wight	Deputy Director Emergency Preparedness and Health Protection, Department of Health

Welcome and Introductions

1. Professor Steele welcomed all to the meeting at the earlier start of 11. The Committee were reminded that revised timings allowing for a longer meeting would come into effect next year. A round of introductions was initiated whilst giving members an opportunity to update the Committee on any conflicts of interest which may be relevant to this meeting. No conflicts were raised.

   Apologies were noted.

   Professor Steele welcomed two new officials to the UK NSC; Dr Carol Beattie newly appointed Senior Medical Officer for Northern Ireland and Natasha Alleyne Department of Heath's newly appointed screening lead.

Minutes and Matters arising

2. The minutes were confirmed as a true and accurate record and would be uploaded as final on the webpage.

   Five action points were identified from the June meeting;

   (action 3a) Update on Phase 1 modelling to optimise bowel screening

   ScHARR to be invited to present the second version of the Bowel Optimisation report to the UK NSC when ready – On the agenda

   (action 3b) Pulse Oximetry

   Dr Graham Shortland to review and input on the modelling work- Dr Shortland confirmed that this had been shared with him and that work was progressing well

   (action 3c) UK NSC Task and Finish group

   Task and Finish group to publicly consult on guidance development documents and feedback outcome at a future UK NSC meeting – Mr Johnstone–Waddell informed the Committee that consultation closes on the 16 November. A final social media exercise would take place to encourage any last submissions and that a report would be brought to the February meeting

   (action 5) Screening for Subaneurysmal aortas in AAA

   UK NSC to talk to NICE about developing guidance on subaneurysmal aortas and for data to be reviewed again – In discussions

   (action 6) Fetal Maternal and Child Health

   Four countries to provide Dr Elliman with information on how/if systematic measurement of child weight and height is offered in each country- In hand awaiting feedback from Northern Ireland

   ***Director's* Update**

   Dr Mackie gave an update on the following

Update on Screening for Severe Combined Immunodeficiency (SCID)

3. The Committee has spent a considerable amount of time deliberating whether screening for SCID should be introduced. Although the 2013 evidence review found insufficient evidence to support its introduction the Committee were encouraged by the estimates from the 2016 ScHARR cost effectiveness model which suggested that, from a number of perspectives, it was likely that screening would be cost effective.

3.1 The UK NSC is now publicly consulting on the proposal that a practical evaluation for SCID be undertaken in the NHS. This opened on the 4 August. The aim of the evaluation would be to provide the information needed on key issues to help inform a recommendation on whether screening for SCID should be offered as a population screening programme.

3.2 It was agreed that as the consultation will close on the 4 November the outcome would be authorised via Chair's Action to allow for work to commence sooner rather than later and that this would be appended to the minutes. The Chair stated that if there was significant opposition to the proposal then the issue would be brought back to the February meeting for further Committee discussion. Members supported the plan of action. **Annex A Chairs Action**

Action 3a: Chair's Action to be appended to Minutes of the meeting

Update on Screening for Iron Deficiency anaemia in children under five years of age

3.3 Dr Mackie informed the Committee that this item was also currently out for consultation and was due to close on the 2nd November. The Committee was asked to agree that this too would be carried forward via Chair's Action. Chairs Action in **Annex A**

Action 3b: Recommendation to screen for Iron Deficiency anaemia in children under five years of age to be appended to minutes

Informed Choice

3.4 Dr Mackie drew the Committee's attention to a recently published HTA paper on Provisions of information about newborn screening antenatally. The Committee were informed that the lead author, Dr Fiona Ulph would be presenting the report at an upcoming meeting including bloodspot advisory group and FMCH members.

Action 3c: UK NSC members wishing to attend the presentation of the HTA report to contact Zeenat Mauthoor

Non-invasive prenatal testing (NIPT)

3.5 Work to implement the recommendation that NIPT should be added as an additional test for T21, T18 & T13 in the NHS Fetal Anomaly Screening Programme (NHS FASP) was progressing well. The Committee noted that the 2 day training for Midwives was starting roll out. The UK NSC members expressed their gratitude to the Information and Education for Professionals and Public team (IEPP) for the hard work in developing materials with stakeholders.

3.6 Dr Heather Payne informed the UK NSC that Wales were working hard too to implement next year.

3.7 In discussion it was noted that a proposal to introduce an alternative approach to the use of NIPT, reflex testing, had been considered and rejected in between meetings. This would be discussed at the next UK NSC meeting.

Moratorium on use of newborn screening blood spot cards for research

3.8 Dr Mackie informed the Committee that the moratorium use of newborn blood spot cards for research had been lifted in England only. This meant that research proposals using blood spot cards could now be considered once all necessary ethical and research governance protocols had been approved.

Presentation on the Bowel Optimisation report

3.9 As requested at the June meeting, Dr Sophie Whyte was invited back to present an update on the bowel optimisation work. The UK NSC has commissioned ScHARR to explore the optimisation of the NHS Bowel Cancer Screening Programme following the recommendation to replace gFOBT with FIT as the primary screening test. The report tested various screening strategies to see if they were cost effective. Account was taken of various capacity scenarios.

3.10 The Committee thanked Dr Whyte for the detailed presentation and for the explanation of the report. It was agreed that a formal proposal based on the modelling work would need to be presented to the UK NSC formally to make a recommendation for Ministers to consider.

Action 3d: Confidential report to be shared with ARG

Action 3e: The UK NSC Secretariat to draft a paper to support a consultation. This would be shared with members for their comments before the document was shared more publically.

Ethics Task group update

3.11 The group's first meeting was held in September with the aim to agree terms of reference for the group. It is anticipated that a draft report would to available in time for the February UK NSC meeting

Action 3f: Ethics report to be added to the UK NSC February agenda

Fetal Maternal and Child Health Screening

FMCH Report

4. Dr Angwin summarised the recent September meeting which discussed various review documents in development as well as the CMO's Generation Genome report. Dr Angwin informed the Committee that the proposal on reflex testing, received via the 2016 Annual call for topics had been discussed by the group at length and that further communication about the test would be directed via the FMCH group.

Screening for Cytomegalovirus (CMV)

4.1 Dr Cristina Visintin presented this item to the Committee which was last reviewed in 2012.

4.2 CMV is a common viral infection that once acquired remains in the body, similar to cold sores or chicken pox. Some people will be unaware of the virus and will display no symptoms whilst others may present with some symptoms. Treatment is not needed in the majority of cases. CMV infection is commonly spread through close contact with someone and is passed via bodily fluids such as saliva. In pregnancy an expectant mother can pass the infection onto her unborn baby via the placenta, this is known as congenital CMV infection. In most cases the virus does not cause any harm to the unborn baby however for some it can interfere with the baby's development and cause problems late on, such as hearing loss. It is estimated that around 2,400 babies are born with the infection in the UK each year; most of whom will develop normally. About 10 to 15% of the babies born with infection will present with some moderate to severe symptoms in the first two weeks of life.

4.3 Dr Visintin informed the Committee that there had been a shift in focus when considering screening for CMV from the antenatal to newborn period. This was due to several reasons which included; that there was not a good enough way to detect mother to fetus transmission and that at the time of the review, research was being undertaken to look at saliva PCR and newborn blood spot as potential screen tests for CMV. The 2012 review had found that there was no available test, no screening strategy in pregnancy and no intervention to prevent mother to baby transmission which could support the introduction of screening. The 2017 review therefore looked at whether the

recommendation not to screen antenatally remained valid before considering newborn screening.

4.4 The 2017 review focussed on three key areas; test, treatment for screen detected babies and evidence of a screening pathway that could prevent negative outcomes. The review found that there was not a suitable screening test. Although saliva PCR is considered to be a potential candidate, it was being used as a diagnostic tool. This meant that its performance on a targeted group would not necessarily translate as being a good screen test when used in whole populations. The test's ability to correctly detect individuals who may be at risk, to those who do not have the condition may not be as accurate as expected. Dr Visintin stated that for the test to be considered it would need to be evaluated as a screening test in order to demonstrate its applicability within a screening population. In addition to this, no marker was identified by which the screen test could differentiate between the babies who had the condition but would not be affected and those babies who had the condition and would develop long term problems. It was raised in various consultation comments whether the need for a marker was necessary suggesting that if a baby was screened as being positive for the condition then all babies should be treated. Dr Visintin explained that to employ such practice may in fact cause more harm. Large numbers of asymptomatic babies would be treated unnecessarily for a condition which may not affect them with a drug that is currently not recommended for such babies, leading to overdiagnosis. The Committee noted that there was research ongoing to address this, though the approaches such as blood test results and baby brain scanning would still need to be validated as being safe and reliable.

4.5 The Committee agreed that although the CCMV is an important condition further research was needed to understand what long term benefits would be available, should screening be recommended. The Committee noted that several stakeholders supported the recommendation from the review; i.e. that screening should not be recommended until the following key areas had been addressed;

- more information about the test performance of salivary PCR and/ or extended blood spot testing
- understanding the natural history of CMV and which babies are at a higher risk of adverse outcomes
- the possible harms from the treatment and what the ideal treatment period would be

4.6 The UK NSC reviewed the comments received during the consultation period and noted that 14 stakeholders had responded. Several comments with suggestions to address CMV fell outside the UK NSC's scope (i.e. were related to treatment or prevention) and the Committee noted this.

4.7 The UK NSC agreed that based on the review document presented and the comments from the consultation, screening for CMV should not be recommended. The Committee

noted that the Secretariat would engage with stakeholders to discuss options for taking research forwards, as well as signpost to organisations that could assist with addressing issues which fell outside the UK NSC's scope.

Action 4a: The UK NSC Secretariat to arrange meetings with necessary stakeholders about taking research forwards and signposting where necessary

The Test		
4	There should be a simple, safe, precise and validated screening test.	No screening test had been identified and further research was needed to evaluate Saliva PCR/ blood spot testing
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	Further research is needed
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.	Further research is needed to better understand what the long term benefit to screen would be

Screening for Human T- Cell Lymphotropic Virus (HTLV) in pregnancy

4.8 Human T-Cell Lymphotropic virus (HTLV) is a retrovirus which, like HIV, can be transmitted through sexual contact, blood transfusions from mother to baby. Most people with HTLV do not experience any symptoms but for a small group the condition can cause serious illness such as adult t-cell leukaemia / lymphoma. As there is no treatment for this condition the aim of screening in pregnancy would be to prevent transmission of the condition by avoiding breast feeding or reducing its duration.

4.9 Mr Marshall explained to the Committee that although the condition can result in adverse health outcomes the rate of infection in the UK met current definitions of low prevalence. In the pregnant population no estimate of prevalence had been undertaken since a baseline assessment which was published in 2000. This suggested that, in pregnant women, there was an overall prevalence of 3.1/10,000. However, prevalence declined steeply from first generation migrants from the Caribbean (169/10,000) to women born in non-endemic areas and not resident in inner city areas (1.1/10,000). The 2000 assessment also suggested that the balance of benefit and harm from screening had not been explored in primary research. This was important as the transmission rate and the rate of progression to disease were low compared with other conditions such as HIV. In addition over 200 women with the infection would be identified. The overwhelming majority of these would not be affected and the effect of stigmatisation. The lack of evidence on the psychological harms and the effect of stigmatisation had not been studied. The main focus of subsequent reviews was to establish whether studies had been published which significantly changed the evidence base on issues such as these.

4.10 This was the fourth time the UK NSC had considered the evidence for HTLV. The reviews carried out since 2000 highlighted that little had changed in key areas of the evidence base. The same was found in the current, 2017 review.

4.11 The Committee noted that two responses were received during the public consultation. The Royal College of Midwives supported the findings of the report not to screen. The lack of an intervention for those with the infection was a limiting factor in the case for screening. However, the National Centre for Human Retrovirology (NCHR) expressed concern that their previous comments had not been taken into account by the UK NSC. Mr Marshall informed the Committee that this was not the case. For example the conclusion of the previous, 2012, review cycle noted that there was interest in developing a detection strategy focusing on higher prevalence areas. The Committee had recommended that this should be taken up with specialised commissioners. It was unclear whether this had been clearly communicated with the NCHR and it was agreed that the Secretariat should make contact to clarify this.

4.12 More generally the Committee reviewed the document along with the two comments and agreed that screening for HTLV should not be recommended in the UK.

The Committee suggested that at the next review cycle, before committing to another review, an evidence map should be produced to gauge the volume see if any primary research has been published on the harms and benefits of screening.

Action 4b: The UK NSC Secretariat to contact the NCHR.

Action 4c: The UK NSC Secretariat to do an evidence map before undertaking another regular review of the condition.

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	The prevalence in the UK is low and may only be specific to certain sub groups
The Test		
4	There should be a simple, safe, precise and valid screening test.	Insufficient information to help calculate the test performance but indication of high false positives which would be of concern in the UK due to the low prevalence of the condition

Screening for Biliary Atresia

4.13 Dr Graham Shortland presented this item. Biliary Atresia is a rare condition in which the bile ducts becoming blocked or inflamed. Bile is a digestive fluid produced by the liver and excreted into the small intestine and is needed to help break down fats. The build-up of bile can cause damage to the liver and if left untreated can cause death of an infant by the age of two years. Treatment for the condition involves an operation known as a Kasai portoenterostmy, a surgical procedure to facilitate bile drainage. Dr Shortland informed the Committee that current detection of the condition relies on clinical presentation. Many babies will present as having jaundice. While this is quite common in newborns, babies with biliary atresia will also have dark urine and pale coloured stool. The aim of screening would be to allow for early intervention, preventing further damage to the liver and delay or prevent the need for a liver transplant. The current standard of care is to undertake surgical treatment no later than 90 days.

4.14 The UK NSC had recommended against screening for biliary atresia in 2012 as there was insufficient information to support its introduction. A key area highlighted in the previous review was the absence of published studies about a reliable test. The

aspiration was to identify a dried bloodspot test which could be integrated into the current newborn screening programme. An alternative approach which had been implemented some areas, such as Taiwan, was based on stool colour cards. However, the reported rates of time to surgery in the UK compared favourably with other areas which did not screen and those which had implemented stool colour card screening.

4.15 The 2017 review focussed on test and treatment; whether a more reliable screen test for biliary atresia had been identified and whether there was information about the timeliness of surgical treatment in babies found through normal clinical routes. The review found that no studies had been published since the last review which looked at the use of dried or liquid blood spots in the general population. Furthermore no studies were identified which looked at the mean age of surgery for biliary atresia. The Committee was informed that there was a database which had been in operation for some time, which indicated that surgery was being carried out at a mean age being 56 days. Dr Shortland stated that this would suggest that time to surgery had not slipped since the previous review.

4.16 Two sets of comments were received during the public consultation which supported the findings of the report. The Committee agreed that screening for biliary atresia should not be recommended as a population screening programme.

The condition		
The Test		
4	There should be a simple, safe, precise and validated screening test.	No new evidence available since 2012 on the use of dried blood spots
The intervention		
15	Clinical management of the condition and patient outcomes should be optimised in all health care providers prior to participation in a screening programme.	Current practice is suitable

Adult Screening

Adult Reference Group

5. Dr Ros Given-Wilson, Chair of the ARG, summarised the discussions at the September meeting. The group discussed various programme developments on the horizon in breast screening which included the review of guidance.

Updates

NIHR NETSCC Update (for information)

The Committee noted the updates

SIGN Update (for information)

The Committee noted the updates

AOB

i. Members of the Committee were reminded of the upcoming Annual Stakeholder event to be held on the 24 November

ii. The recruitment campaign to appoint a nurse, social scientist and ethicist had since closed and applications for each type of post had been received.

iii. Information about members appraisals would be circulated in the coming weeks

UK National Screening Committee

Annex A

Chair's Action

November 2017

The Chair of the UK NSC has made recommendations on behalf of the Committee regarding two urgent matters that were not tabled at the October meeting;

- the proposal for a practical evaluation of Severe Combined Immunodeficiency (SCID) to be undertaken in the NHS
- screening for Iron Deficiency Anaemia (IDA) in children under the age of five

Both consultations ended shortly after the Committee met in October. The Committee agreed at the October meeting, that the outcomes of the review should not be delayed till the February meeting.

This document outlines the decision reached by the Chair with corroboration from officials

1. *Proposal for a practical evaluation of Severe Combined Immunodeficiency (SCID) to be undertaken in the NHS*

- It was agreed following a workshop between stakeholders and academics that before screening could be considered as being introduced as a population screening programme, more certainty was needed to support the assumptions of the cost effectiveness model. It was the view of the group that a large practical evaluation of screening in England was needed in order to address the gap identified.

- The UK NSC therefore held a public consultation to see whether a proposal for a practical evaluation would be supported. The aims of the evaluation was set out as to:

- define a cut off for screening and report on clinical outcomes which are achievable in the timeframe and realistic given the rarity of the condition
- identify and undertake research priorities, for example to understand more about the impact of false positive results and the viability of alternatives to universal screening
- clarify the logistics and costs of screening and outcomes monitoring as a basis on which to revisit the cost effectiveness evaluation
- explore the possibility of international collaboration with ongoing pilots and research projects relating to SCID

- The Chair noted that the majority of the consultation responses were supportive for a practical evaluation but were divided on the function. Some suggested that an immediate recommendation to introduce a national screening programme was needed whilst others suggested a reflective approach should be adopted which looked to see whether screening in fact answered some of the concerns raised before a final recommendation is made.

- The Chair stated that the latter suggestion was a more pragmatic approach, as to suggest a final recommendation before the evaluation has commenced would not take into account the implications and concerns the Committee raised about a whole population screening programme. The Chair emphasised that the practical evaluation was a means to allow us to better understand the implications screening in practice.

The Chair recommended that a practical evaluation of SCID using PCR is undertaken in the NHS before a final recommendation is made.

2. *Screening for Iron Deficiency Anaemia in children under five years*

- Iron deficiency anaemia (IDA) is the most common form of anaemia. It is a condition caused by a lack of iron which is needed to help produce red blood cells. The fewer red blood cells being circulating around the body means that not enough oxygen is being transported to organs and tissue than normal. Children under the age of five are especially at risk as it is possible the IDA may affect a child's development.
- The Chair noted that based on the evidence found during the review screening for IDA was not supported. This is because;

  - The prevalence in the UK is unknown
  - It is uncertain whether IDA in children under five causes adverse developmental outcomes
  - If treatment improves long term developmental outcomes in children

- The Chair read the comments received during consultation one which supported the recommendation not to introduce screening whilst the other referenced an unpublished study. The Chair agreed that although this falls out of scope for this review it would be included in the next three yearly cycle.

The Chair recommended that a population screening programme for IDA in children under the age of five should not be introduced