



UK National Screening Committee (UK NSC)

Note of the meeting held on the 8 November 2019

in

London

This meeting provided recommendation on the following;

Fetal Maternal and Child Health Conditions:

- The use of Pulse Oximetry as an additional test in the Newborn and Infant Physical Examination
- Screening for Partner Violence in antenatal and adult populations
- Screening for Dental Disease in Children

Evidence Map outcomes on:

- Screening for Varicella susceptibility
- Screening for Cutaneous Melanoma
- Screening for Klinefelter Syndrome
- Screening for Neurofibromatosis type 1 (NF1)

Adult Conditions:

- Screening for Cardiac conditions associated with Sudden Cardiac Death in the young
- Screening for Type 2 Diabetes in adults
- Screening for Osteoporosis in women after the menopause

➤ Screening for Glaucoma

Members

Professor Bob Steele	Chair
Claire Bailey	Lead Clinical Nurse Specialist in breast screening, SW London
Dr Louise Bryant	Associate Professor in Medical Psychology, University of Leeds
Professor Alan Cameron	Consultant Obstetrician at Southern General Hospital, Glasgow (Skype from 11:00-12:30)
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
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



UK National
Screening Committee

Hilary Goodman

Operational Manager of Antenatal Services/Screening
at Hampshire Hospitals Foundation Trust

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;

Tanya Scanlon

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 (t/c 11:45-13:00)

Sarah Manson

Scottish Government

Dr Sue Payne

Scottish Government

Dr Carol Beattie

Northern Ireland

Invitees;

Dr Hans Houweling

Health Council of the Netherlands

Dr Leo van Rossum

Health Council of the Netherlands



**UK National
Screening Committee**

Dr David Elliman	Clinical lead for Newborn Infant Physical Examination and Newborn Blood Spot, PHE
Nick Hicks	National Co-ordinating Centre for HTA
Dr Ros Given – Wilson	Chair of the Adult Reference Group (ARG)
Dr Sharon Hillier	Chair of the Fetal Maternal and Child Health Group (FMCH)
Dr Alan Smith	CMO, National Screening Service Republic of Ireland
Alex Drew-Hawkins	States of Guernsey
Caroline Vass	PH Consultant
Prof Anneke Lucassen	Clinical Genetics within Medicine, University of Southampton
Patrick Rankin	Programme Manager – Diabetic Eye Screening Programme
Lianne Powell	Fetal Anomaly Screening Programme Project Lead and National Education Manager
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



**UK National
Screening Committee**

Paula Coles	UK NSC Senior Information Scientist
Farah Seedat	UK NSC Evidence Review Manager
Zeenat Mauthoor	Secretariat
Rebecca Oyibo	Screening Administration Support Officer
Mike Harris	IEPP Publications and Information Manager

Apologies

Members:

Professor Roger Brownsword	School of Law, Kings College London
Professor Gareth Evans	Consultant in Genetics Medicine, St Mary's Hospital, Manchester
Dr Hilary Dobson	Consultant Radiologist and Deputy Director of the Innovative Healthcare Delivery Programme, University of Edinburgh
Professor Chris Hyde	Public Health Specialist, University of Exeter
Dr John Holden	Joint Head of Medical Division, Medical and Dental Defence Union of Scotland
Dr Jim McMorran	GP, Coventry

1. Welcome and Introductions

1.1. Professor Steele welcomed all to the meeting with an extended warm welcome to European colleagues' Dr Houwling and Dr van Rossum from the Health Council of



the Netherlands, who were observing the Committee. A round of introductions was initiated for the benefit of all invitees at the meeting.

- 1.2. Members were asked to provide an update on any new declarations of interest which may be relevant to this meeting. No new conflicts were raised. Existing declarations around NIPT had been expressed previously by Alan Cameron and Jane Fisher.
- 1.3. Apologies were noted, and the Chair confirmed that the meeting was quorate with 13 members in attendance.

2. Minutes and Matters arising

- 2.1. The Chair informed the Committee that an updated version of the draft minutes had been circulated in the meeting pack, following comments received from Heart Rhythm Alliance on the UK NSC's recommendation to not offer population screening for AF.
- 2.2. Heart Rhythm Alliance had raised concerns on various matters which the Secretariat had since responded to. The minutes at section 4.9 were revised to provide a more accurate representation of the matters discussed.
- 2.3. Prof Slowther requested two amendments be made on section 3.16 in the confidential section of the ethics task group update.
- 2.4. With these provisos minutes were approved as a true and accurate record of the meeting held. It was agreed that minutes of the June 2019 meeting should be published as final.

11 action points were identified from the June meeting of which nine had been completed while the remaining were on the agenda for discussion. The actions were as follows:

3a. Directors Update on SCID

FMCH to develop questions for the evaluation of SCID and to share with JCVI- *on the FMCH January agenda*



3b, c, d. Directors Update on Genomics Report

Caroline Vass to make amendments on the breast, SCID and polygenic section of the report and to include a digital mammogram picture- *Completed*

UK NSC to send comment on the confidential genomic report and to send comments to Caroline Vass by 16 July- *Completed*

Final Genomics report to be shared with CMOs and then published- *Completed*

3e. Ethics Task Group (ETG) Update: NIPT and Reflex testing

The ETG ethical consideration paper to be discussed at the September meeting- *Completed*

3f. High Risk Screening

UK NSC members to send comments on the confidential high-risk paper to the Chair by 16 July – *Completed*

4a, b, c. AF Screening

Complete set of consultation comments on AF to be shared with the Committee. Members to raise any objection to the recommendation to the Secretariat- *Completed*

Comments on the AF evidence summary to be sent to the reviewers to consider- *Completed*

Chair to take Chair's Action to make a final recommendation- *Completed*

4 d, e. AAA Surveillance- programme modification

John Marshall to share the proposal with HTA to review- *Completed*

Truncated public consultation on the programme modification for the modification of the AAA surveillance intervals to be opened- *Not actioned: on the agenda*

3. Matters arising

Director's Update

Prof Mackie gave an update on the following

Sir Mike Richard's Review

- 3.1. The Professor Sir Mike Richard's [Review](#) on adult screening programmes was published on 16 October.
- 3.2. A total of 22 recommendations were made. The first two relating to governance was of interest to the UK NSC. These were stated as:
 - i. UK Chief Medical Officers bring together an advisory group to agree terms of reference for a new advisory body for both targeted and population screening.
 - ii. Targeted screening should be handled along the same lines as population screening through the Section 7A mechanism.

The Committee were informed that the Government had provided a [Written Ministerial Statement \(WMS\)](#) on this and had stated that it:

- *Agrees that there is a need for robust governance and clarity of responsibility and accountability for the different elements of screening.*
- *PHE and NHS England will produce an implementation plan for publication in spring 2020 that ensures functions are located in the best place to deliver a high-quality service.*
- *There should be a single source of national expert advice on both population-wide and targeted screening and PHE will provide this function. CMO will work with colleagues in the Devolved Administrations to design this.*

- 3.3. Prof Mackie informed the Committee that this review would be considered alongside the various other reviews which had been commissioned. In the meantime, PHE, DHSC and NHSE were working together to produce an implementation plan to be



published in Spring 2020 and would keep the UK NSC secretariat updated on developments. Further information will be shared with the Committee.

- 3.4. There was discussion on the contents of the report.
- 3.5. The Chair focused on recommendation 1 and its impact upon the Committee, highlighting the fact that the report indicates that a new screening advisory body will be set up to consider population and targeted screening. This did not necessarily mean the dissolution or reconstitution of the UK NSC.
- 3.6. Sarah M added that at no point had the CMO in Scotland been consulted on the recommendations made to set up targeted screening, which was echoed by the other UK Health departments. It was stated that although this was outside the scope of the review, it would require early collaborative discussions and engagement to help define what is meant by 'targeted screening'.
- 3.7. The Chair thanked all for their observations and requested that the Committee send any comments on targeted screening to Zeenat to collate

Action 3a: UK NSC to send comments/ observations on 'targeted screening' to Zeenat to collate

Genetic Alliance UK (GAUK) report on newborn blood spot conditions

- 3.8. Prof Mackie informed the Committee that this report had been shared for information.
- 3.9. The report published in July, outlines GAUK's view on the current situation of blood spot screening in the UK whilst offering a number of recommendations for evaluating the evidence relating to rare diseases. The report was critical of the UK NSC and its processes, stating that the UK "lags" behind other countries in terms of the number of conditions for which screening is offered. GAUK call for a separate body to be established which would evaluate the evidence for rare disease giving patient experience and clinician opinion a central role to make recommendations rather than being based on published research evidence.



- 3.10. Prof Mackie stated that the UK NSC had been working on various strands of work to better engage with patient and public voices to better understand the condition where appropriate (e.g. consideration of treatment effects in Tyrosinaemia). There is interest across international screening bodies to work with and consider issues in rare diseases and that this would be explored.
- 3.11. Several members stated that although they didn't agree with all of the report or support all of the recommendations made, they could see how the arrangements for engagement on the UK NSC's update process was frustrating from a patient/public perspective. It was suggested that this could be eased by offering more education to explain the constraints of population screening to the public, and explaining the opportunities of engagement in the process as a whole, for example in cost effectiveness exercises such as those undertaken for SCID and Tyrosinaemia and in screening programme delivery structures.

Action 3b: UK NSC secretariat to explore how better to explain population screening through a variety of channels.

Rubella Susceptibility

- 3.12. Prof Mackie provided a verbal update summarising the discussions from FMCH meeting which took place in September.
- 3.13. FMCH had been made aware of some cases of congenital rubella and Prof Mackie informed the Committee that the Infectious Disease in Pregnancy Screening programme was working with the Institute of Child Health to explore in more detail the circumstances of these. This item would then be discussed at the upcoming FMCH meeting.
- 3.14. Dr Hillier, added that the reference group would in the meantime keep abreast and be alerted to any new developments on suspected congenital rubella given the reduction in uptake of the MMR vaccine.
- 3.15. The Committee accepted this.

Genomics Presentation

3.16. Prof Lucassen had been invited to provide the Committee with an introduction to genomics in screening.

3.17. The presentation highlighted that issues of penetrance remain critical to understanding what the benefits of population screening for genetic mutations might be.

AAA Screening Intervals Strategy Update

3.18. Mr Marshall reminded that Committee that at the last meeting held in June, the Committee had reviewed the proposal, submitted by the National AAA Screening Programme, which sought to extend the screening interval from one to two years in men with aneurysms measuring 3.0-3.9cms.

3.19. It was proposed that by extending this surveillance interval, it would in turn help to reduce the surveillance burden on this group of men, without negatively impacting on the rupture risk. The driver for this move was the growing EU and international interest in this area seen, for example, in the recently published European Society of Vascular Surgery guidelines. The programme was also aware of NICE's consultation on AAA and were concerned that there would be conflicting guidance on the surveillance intervals. Mr Marshall assured the Committee that the possible discordance between the UK NSC and NICE had been addressed. This was because NICE had kindly agreed to withdraw its proposed recommendation and to refer to the UK NSC's recommendation on surveillance intervals, once made.

3.20. Following the presentation at the June meeting the Committee requested that the proposal be shared with the HTA to adapt its existing model in order to quantify the clinical and cost effectiveness of the proposal. The outcome of the HTA's cost effectiveness model had been circulated and was brought to be discussed at this meeting.

- 3.21. The outcome of the HTA's cost effectiveness model estimated that over a 30-year period a monetary saving of £300,000 would be accrued in each annual cohort of screened men. The model also estimated that there would also be a small life year loss of 1.2 years and a 0.9 QALY loss. The Committee noted that the proposal therefore would show an extremely small financial benefit and the potential of a small clinical harm (the risk of rupture in the interval between surveillance scans would increase from 0.1% as it currently stands to be 0.3% if accepted). The Committee stated that it acknowledged that in the wider specialised field this change was endorsed but remained concerned that such change did not benefit the user and the current programme was estimated to be very cost effective. This was supported by Scotland who expressed its concern about the proposed trade-offs between the long-term benefits and savings which could be negated by the implementation costs and risk.
- 3.22. The Committee agreed that a short consultation should be opened to gather views on the proposal, once the period of political sensitivity had ended.

Action 3c: Short public consultation to be opened to gather views on the proposal and cost effectiveness model which looks at altering the surveillance interval change in men from one to two years

Reflex DNA Testing Strategy for Trisomies- proposal

- 3.23. Mr Marshall provided a summary on the developments regarding non-invasive prenatal testing (NIPT) and the proposal of the reflex strategy.
- 3.24. In 2016 the UK NSC recommended that NIPT for Down's, Edward's and Patau's syndromes should be introduced as an additional test into the NHS Fetal Anomaly Screening Programme. This was to be offered, as part of an evaluation, to women with a combined test chance of 1 in 150 or greater of having a baby born with one of the three conditions. To date Wales is the only UK health department that has implemented and rolled out the test.

- 3.25. By offering NIPT in this way, women are then recalled back for a more detailed discussion to support them to make a personal informed choice about their pregnancy.
- 3.26. A proposal to consider reflex DNA strategy was submitted in 2017. This has been discussed within the UK NSC structures.
- 3.27. Reflex DNA testing involves taking two blood samples; one used for the combined test whilst the second sample is kept and used if the result of the combined test is higher than the cut off (the submitters have suggested 1 in 300 and 1 in 800). This automatic testing using DNA analysis is carried out without reporting the combined test result and avoids having to recall the pregnant woman.
- 3.28. The UK NSC considered the proposal to offer reflex DNA testing as a mechanism to deliver NIPT but rejected the proposal, following due consideration at its meeting in October 2018 on the grounds that there was;
- insufficient information on the outcomes as to whether reflex does reduce anxiety as suggested and supports reproductive autonomy
 - a concern that expansion of the use of NIPT might not be acceptable
 - the advantages in terms of reduction of resources used, relative to the recall strategy had not been quantified or confirmed.
- 3.29. Mr Marshall informed the Committee that the papers circulated had also been shared and discussed at length with FMCH who had expressed concerns that the initial reservations and questions asked by the UK NSC had not been addressed satisfactorily. The UK NSC was now being asked to receive and agree with advice from FMCH. FMCH advised that the concerns raised had not been addressed satisfactorily and thus could not be pursued further. Mr Marshall said that the UK NSC had discussed the possibility of research on reflex testing with the HTA. This had not been developed into an active research project because of the concern that, in its current form, reflex testing was unethical.
- 3.30. The Chair opened the item for discussion. Dr Slowther, stated firstly that to say that research on the reflex strategy should not be undertaken due to the ethical



complexities would be incorrect. However, these concerns combined with other more practical obstacles may prevent research being undertaken. If research was possible it would need to be multifactorial covering and providing consideration on elements such as for reduction of autonomy, harms versus benefit, the breakpoint of information and issues of fairness. The discussion reflected on the significant interest in, and concerns around, and there were mixed views on whether research into these areas would be useful.

3.31. Following an extended discussion, the Committee agreed to reaffirm the recommendation that reflex testing should not be pursued as an immediate programme modification proposal. This was because the submitted proposal did not sufficiently address the initial concerns which were raised by the UK NSC. The UK NSC in the meantime awaits the evaluative roll out of NIPT to then be able to review the findings.

3.32. A workshop would be explored to discuss in detail the various ethical points on recall and reflex testing.

Action 3d: Prof Slowther to speak to UK NSC Secretariat about setting up an ethics workshop to discuss the areas of concern on reflex/ recall

4. Adult Screening

ARG Report

4.1. Dr Given-Wilson, provided the Committee with a summary of the ARG meeting held in September, the following items were discussed and were tabled for discussion and final recommendations; sudden cardiac death, type 2 diabetes, osteoporosis and glaucoma. A new programme modification proposal had recently been submitted relating to the Diabetic Eye Screening Programme and stated that ARG expected to review the proposal at its January meeting alongside any annual call for topic proposals relating to adult conditions.



- 4.2. Currently there were no adult conditions out for public consultation and no new consultations would be opened, until a new government had been elected.

Screening for Cardiac Conditions associated with Sudden Cardiac Death in the Young

- 4.3. Sudden cardiac death (SCD) is the sudden and unexpected death of a person caused by a problem with their heart. There are various conditions which can lead to SCD. In people under the age of 35 years, SCD is often caused by a thickening of the heart muscle or an electrical problem with the heart which may have a genetic cause.
- 4.4. It has been proposed that screening would help prevent SCD in young people aged 12-39 years by identifying heart conditions at an early stage before they cause symptoms and offering early treatment.
- 4.5. The UK NSC last looked at the evidence to screen for SCD in 2014 and recognised that it is a very important cause of the loss of young lives. However, the Committee recommended that *population* screening should not be offered. This is because there was uncertainty regarding the incidence of SCD, the accuracy of screening tests and the effect of screening. As part of the UK NSC's review cycle the UK NSC again looked at the evidence to screen for SCD in 2019.
- 4.6. The review this time round focussed on areas of uncertainty from the 2014 review: the incidence of SCD, the accuracy of screening tests and the effectiveness of screening. It was noted that the focus of this review was limited to screening of a general population of asymptomatic young individuals. However, where appropriate, the reviewers included evidence from studies of athletes, whilst acknowledging the limitations of using such indirect evidence. Following a three-month consultation, 81 comments were received of which 72 were from members of the public who described personal accounts of experience with SCD. The Committee reviewed all comments with care recognising the loss experienced by the families, friends and the wider community.
- 4.7. The Committee discussed
 - That SCD continues to be an important health problem.

The Committee expressed gratitude to all the public submissions of personal accounts of how families and wider relations are affected.

The Committee recognises that the death of a young person is tragic and it is incumbent on all involved in health care to determine the best way in which to reduce the numbers of lives lost.

However, due to the current uncertainty in the published evidence, the Committee agreed that, *population* screening was not the best way to help tackle the number of lives lost to SCD.

The reasons underpinning this recommendation are:

➤ Evidence to support a screening programme

Randomised controlled trials (RCTs) are the gold standard in evidence-based medical research but in some cases, they are not practical. RCTs looking at the effectiveness of screening to prevent SCD in young individuals compared to no screening would need to include a large number of people and run for decades to get a convincing outcome. Therefore (as is often the case in screening), alternative study designs will be considered. However, no studies were found that met the inclusion criteria and that would be of sufficient quality to inform a decision

➤ The incidence of SCD is not clear. The published literature suggests it is a very rare event while informal unpublished resources suggest it is much more common.

Rarity of a condition is not necessarily a problem for a screening programme. Many of the bloodspot and antenatal conditions are as rare as the numbers of SCD deaths stated in the literature. But the fact that there is such a divergence between published and informal sources suggests that an acceptable methodology to estimate incidence has not been found. Several stakeholders refer to the paper by Papadakis et al (2009) where the reported incidence is 1.8 deaths per 100,000 per year in the UK which equates to 12 young SCD per week and more than 600 young SCD deaths per year in the UK. This paper was included in the review. The reviewers noted that this estimate is based on death certificate data, which as a methodology is likely

to lead to over-estimation. This is because this type of methodology considers only the cause of death as recorded on the death certificate. However, the precise circumstances of the death are important in determining whether an event meets the definition of SCD, in particular the point in time in which symptoms are first experienced. The paper itself acknowledges this limitation in the methodology and that the estimated incidence may be affected by misclassification.

The UK NSC were informed that, during the development of the review, CRY had been invited to submit peer reviewed evidence on the incidence of SCD or, alternatively, to suggest a source which might provide a dataset for future research, but no response had been received.

The UK NSC stated that it welcomed any peer reviewed data which would allow the UK NSC to take this into consideration when looking at incidence, though this was not the sole reason as to why screening had not been recommended. Should any new data be published during the time of the next review, the UK NSC would welcome an [early update submission](#) on this which could be submitted at any time throughout the year.

➤ Accuracy of screening tests

There is uncertainty on the accuracy of screening tests in the general population because all the studies identified in the review typically relied on an assumption that individuals in whom the screening test was negative did not have the disease. In addition, the tests were usually performed in athletes, which in turn limits the applicability of these studies to the general population. Given the low positive predictive values (PPVs) and the low precision of the PPV estimates, the review noted the tests would cause many individuals to be incorrectly informed that they have a heart problem. Hence uncertainties remain regarding the potential harms of screening.

➤ Amendment of title

It was suggested that the title should be changed to better reflect the various conditions which lead to the outcome of death. This was accepted as it did not change the outcome of the findings.

The Committee agreed that current tests and appropriate treatments for the conditions causing sudden cardiac death are not good enough to recommend a population-wide screening programme, which may ultimately do more harm. However, there are groups of people with symptoms or from families with a sudden unexplained death that could possibly benefit from a targeted screening programme.

Action 4a: Subsequent to ministerial decision to carefully communicate the outcome to stakeholders

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	Severity: met; Incidence: not met; Natural history: not considered
The Test	
4. There should be a simple, safe, precise and validated screening test.	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
13. The benefit gained by individuals from the screening programme should outweigh any harms for example from overdiagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications.	Not Met

Screening for Type 2 Diabetes in Adults

- 4.8. The UK NSC last looked at the evidence to screen for Type 2 Diabetes (T2DM) in adults in 2013.
- 4.9. T2DM is a common condition that causes the level of sugar (glucose) in the blood to become too high. It can affect one's everyday life and most people are required to take medications to control their blood glucose. Not controlling your blood sugar level can lead to serious health complications such as: heart disease, stroke, foot and kidney problems, and vision loss. The main treatment for T2DM is a healthy diet, regular exercise and specific medications.
- 4.10. Currently the UK NSC does not recommend a population screening programme for type 2 diabetes in adults. This is because there was no randomised control trial evidence that demonstrated that screening would lead to better outcomes for people compared to current standard care.
- 4.11. The purpose of the 2019 evidence summary was to examine several key areas of uncertainty. The review looked at four such areas which covered: the proportion of people with non-diabetic hyperglycaemia (NDH) who go on to develop T2DM, which of the current screening tests best predicts who will develop T2DM-related health problems, whether diet and exercise are effective for treating people who have non-diabetic hyperglycaemia and whether there was RCT evidence that showed screening for T2DM was beneficial.
- 4.12. The review found that, although there was evidence which illustrated the natural history of non-diabetic hyperglycaemia (NDH) to T2DM, the frequency and severity had not been considered. The Committee noted that there was still a gap in evidence relating to population screening, thus the effectiveness of large scale population screening had still not measured. There was no consistent evidence that any one of the glycaemic markers was better at predicting micro- and macrovascular complications of diabetes such as retinopathy and nephropathy.



4.13. The Committee discussed the lack of evidence of a benefit of systematic population screening for T2DM and came to the agreement that a screening programme for T2DM should not be recommended.

4.14. As part of the review, a three-month public consultation was hosted on the UK NSC website, which closed on the 20th September 2019. Only one response was received, which said the review was comprehensive and supported its findings.

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	Natural history of NDH (association with T2DM only): met; Frequency, severity, epidemiology, incidence, prevalence: not considered
The Test	
4. There should be a simple, safe, precise and validated screening test.	Comparative validity of tests: Not met (no clear evidence of superior test accuracy of one test over others); Overall validity: not considered; Simplicity, safety, precision: not considered
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.	Effectiveness of lifestyle interventions to reduce progression from NDH to T2DM: Met; Effectiveness of lifestyle interventions to improve health outcomes such as cardiovascular events: not considered; Effectiveness of lifestyle interventions for T2DM: not considered; Benefit of earlier intervention in pre-symptomatic phase: not considered; Evidence



	relating to the wider benefits of screening: not considered
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

Screening for Osteoporosis in women after the menopause

- 4.15. Osteoporosis is a loss of bone density. It weakens the bones causing them to be more fragile and prone to fractures. Women’s bones can become less dense rapidly in the first few years of menopause caused by falling levels of oestrogen.
- 4.16. The UK NSC last looked at the evidence to offer screening for Osteoporosis in 2013 and recommended that population screening should not be established because there were a number of uncertainties in the evidence base relating to screening tests, intervention in screen-detected populations and who to treat. In particular, at the time there was no RCT evidence which assessed the clinical effectiveness of screening and treatment relevant to the UK.
- 4.17. The UK NSC therefore waited for the publication of the SCOOP trial in the UK and the ROSE trial in Denmark to gather necessary RCT evidence.
- 4.18. The 2019 review looked at four key questions:
- i. what is the accuracy of screening tests for osteoporosis in the general population?
 - ii. what is the effectiveness of interventions in reducing the risk of osteoporotic fracture in people found through screening?



- iii. have RCTs demonstrated the clinical benefit of screening in reducing osteoporotic fractures in comparison to standard care?
- iv. have UK evaluations demonstrated that screening for osteoporosis is cost-effective?

4.19. The review found that although there had been changes to the evidence base since the previous review. In particular the two RCTs, although very different in design, suggested that systematic did not improve outcomes compared usual care. The main exception to this related to hip fracture as the SCOOP trial reported a reduction of this outcome compared to usual care. The review recommended that these issues relating to this outcome should be considered further.

4.20. The Committee was informed that 13 stakeholders had been approached to comment on the evidence review during the public consultation. And that one comment was received, from the Royal Osteoporosis Society, drafted by two members of the SCOOP RCT team. The response acknowledged that the trial had not provided a statistically significant reduction of osteoporosis related fractures, all fractures or mortality but stated that it had demonstrated through RCT that systematic screening would improve the number of women identified for assessment of fracture risk and stated that this could be replicated on whole population of women aged 70-85 years.

Having considered the evidence presented, the Committee discussed the report and reached the conclusion that a systematic screening programme for osteoporosis should not be recommended in the UK

The UK NSC stated that avoidance of hip fracture was an important outcome but that it could not currently recommend a population screening programme for osteoporosis in menopausal

women. The Committee agreed that the secretariat should continue to liaise with NICE and European colleagues on this topic. .

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 Test	
4. There should be a simple, safe, precise and validated screening test.	Not Met
The Treatment	
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
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
14. The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (value for money). Assessment against this criterion should have regard to evidence from cost benefit and/or cost effectiveness analyses and have regard to the effective use of available resource.	Uncertain

Screening for Glaucoma

- 4.21. Glaucoma is a common eye condition where the optic nerve, which connects the eye to the brain becomes damaged. Glaucoma can lead to loss of vision if left untreated.
- 4.22. Open angle glaucoma (OAG), is the most common type of the disease accounting for at least 90% of all glaucoma cases, for this reason the UK NSC evidence reviews concentrated its attention on this type of glaucoma. In OAG the drainage canal of the eye gradually becomes blocked allowing less fluid to leave the eye, causing an increase of pressure within the eyeball. Older people are more likely to develop open angle glaucoma. Usually, the condition runs in families and is more common in people of black-African or black-Caribbean origin.
- 4.23. The UK NSC last looked at the evidence to screening for glaucoma in 2015 and concluded that a systematic population screening for OAG in adults should not be recommended. Reasons which led to this decision was because there were no tests a suitable for use in general population screening programme; there was no high-quality evidence demonstrating that strategies to reduce visual damage from chronic OAG are more effective than no treatment; there was no evidence found of whether a general population screening programme would be effective in reducing morbidity.
- 4.24. The 2019 review focussed two key questions on whether there is a valid, accurate screening test for primary open angle glaucoma and if screening reduces morbidity of the condition compared to usual diagnosis and care.
- 4.25. The UK NSC noted that based on the current evidence important areas of uncertainty remain. There is still no agreement on the test, combination of tests or cut-off levels for the tests used for the screening examination. No randomised controlled trials on the effectiveness of screening for OAG to reduce the morbidity of the condition were identified.
- 4.26. The Chair informed the Committee that the consultation on screening for Glaucoma closed on date 03 November 2019. An updated coversheet with the inclusion of the two comments would be circulated after the Committee meeting. Dr Visintin however presented the consultation comments for consideration to the Committee.



4.27. . Only two comments were received from the Royal College of Ophthalmologists (RCO) and the College of Optometrists both supported the UK NSC’s proposed recommendation to not offer population screening

4.28. The UK NSC agreed that a national screening programme should not be offered for screening of glaucoma.

The Committee did note that this condition could be a potential candidate, as well, for targeted screening, based on risk factors.

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 Test	
4. There should be a simple, safe, precise and validated screening test.	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
13. The benefit gained by individuals from the screening programme should outweigh any harms for example from over-diagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications	Not Met

5. Fetal Maternal and Child Health

FMCH Report

- 5.1 Dr Sharon Hillier provided the Committee with a brief summary of the FMCH meeting in September
- 5.2 MPS I was the only condition out for consultation and is due to close on the 14 January.
- 5.3 Consultations for other FMCH conditions will be opened after the period of political sensitivity ends.
- 5.4 Dr Hillier highlighted that that consultation of FH in children that closed on the 27 October had not been brought to the UK NSC for a final recommendation. The secretariat informed the members that this was because a number of comments had been made on the review and that these were being considered carefully. An update would be shared at the FMCH meeting and the Committee would be kept updated on developments.

Evidence Review Summaries

For the use of Pulse Oximetry as an additional test in the Newborn and Infant Physical Examination

- 5.5 The proposal to add pulse oximetry (PO) to the Newborn and Infant Physical Examination screening programme (NIPE) has been under consideration by the UK NSC and FMCH for some time. It was in 2012 when the Committee first received the proposal to use PO as a screening test to help detect critical congenital heart disease (cCHD).
- 5.6 Currently in the UK CHD can be picked up at various points of the antenatal screening pathway, the fetal anomaly scan that is offered at 18-20 weeks gestation and the NIPE screening programme, includes a heart check as part of the screening offer. Although screening is offered at these points not all conditions will be detected.

5.7 In [2014](#) a formal evidence review was published, as commissioned by the UK NSC to evaluate the evidence which looked at screening for cCHD. The review's conclusion suggested that the UKNSC needed to understand what the impact of using PO in all newborn babies is as the test is not for cCHD but rather for mildly lower oxygen levels in the baby's blood (hypoxaemia). More than 95% of babies with low oxygen did not have heart disease. The international literature, suggested that PO is a cost- effective method to find additional babies with cCHD but the benefits harms and costs of finding the other babies with hypoxaemia had not been explored or described.

5.8 Recognising the importance of the issue, a concerted effort was then taken by the UK NSC. PHE provided funding and support to Clinicians supporting PO and to set up a pilot to collect data from services using PO screening and those not doing so. It was practicable low oxygen levels are not rare so a pilot of this sort in England could produce useful results. The aim being to assess the effect of using PO in all babies. A clinical workshop was also organised to discuss the benefits and harms to babies with non-cardiac causes of slightly low oxygen level. Finally, a disease and cost model was commissioned which aimed to demonstrate the effects of a PO within the parameters of a screening programme.

5.9 The pilot did not gather adequate comparable data from the non-screening units.

As a result of this there was no comparator to use in the model so it could not come to a conclusion.

5.10 The UK NSC agreed at its February meeting that it would publicly consult on all work undertaken so far to gather views on whether the evidence presented was sufficient to support the UK NSC's position or whether it was enough to support the establishment of a screening programme.

5.11 Caroline Vass provided the Committee with a presentation on the consultation comments received. Annex A

5.12 The Committee noted the following:

- The members expressed gratitude to all those who participated in the consultation and shared their personal stories. 179 responses were

received from the consultation of which 79 were from affected families.

- The UKNSC members are acutely aware that cCHD is a serious health problem and its effects on families are devastating. The Committee and the secretariat have commissioned and supported work to try to fill gaps in the international evidence base in order to determine whether screening would be of benefit to newborn babies. In addition, the UK NSC is clear that the evidence for PO to find additional babies with cCHD is robust but that there is uncertainty relating to benefit and harm of finding all babies with mild hypoxaemia.
- The key themes of the consultation were; personal experiences, the use of PO as a test, the concept of earlier diagnosis, current screening concerns as well as harms vs benefits. Some senior clinicians called for more research while others stated that there was enough evidence already on PO and lack of ethical discussion
- 116 responses supported the use of PO as an additional test to form part of NIPE. A common comment was that offering PO would prevent cCHD, which is not correct. Many of the supporters for introducing PO stated that the test is simple, cheap, non-invasive and given that there is demand for it should be offered. Furthermore, many felt that the impact of harms from screening had been overstated and that they felt that the benefit to offer screening outweighs the harms.
- Nine responders supported a call for further research.
- The UK NSC was clear that it was looking at the evidence for the use PO as a population screening tool in newborn babies. It was not making any comment on how PO should be used in hospital or in usual care, as this is covered by NICE guidance

- There are established programmes in place which look at screening for cardiac conditions along the various antenatal pathway, though recognise that not all heart conditions will be detected.
- The review agrees that PO appears to be of benefit in identifying a small number of babies with cCHD over and above detection in the current pathway however the consultation sought views on whether there was sufficient evidence which related to the use of PO to screen for non-cardiac conditions.
- The Committee noted that there remains limited understanding of the difference between the use of PO for cCHD and the effect of its application to all well babies.

5.13 The Chair summed up saying that unfortunately, the evidence remained unclear on what the benefits and harms were for non-cardiac conditions when PO is used. The Committee was asked therefore whether, given the public and clinical interest in this area and the Committee's investment, that it would support the call for further research to be undertaken to explore the uncertainties before a final recommendation is made. The members all supported this.

5.14 Subsequent to the acceptance of the proposal, Dr Hicks informed the Committee that the National Institute for Health Research (NIHR- HTA) had put out a call for stage 1 applications to fund some research to determine the clinical and cost effectiveness of PO screening for hypoxaemia in newborn babies. The deadline for applications is the 1st April 2020.

5.15 The Committee acknowledged and welcomed this call.

Action5a: Subsequent to ministerial decision to carefully communicate the outcome to stakeholders

Screening for Partner Violence in antenatal and adult populations

5.16 Partner violence also known as ‘domestic violence/ abuse’ includes physical, psychological, emotional, financial and sexual abuse committed by someone who is or has been an intimate partner

5.17 The UK NSC last conducted a review of the evidence in 2013, which recommended that screening in antenatal and adult populations for partner violence should not be introduced. The review found that there was insufficient evidence for the introduction of a population screening programme for partner violence for various reasons including; offering screening was not the only way to increase the identification of partner violence, it may not improve the uptake of services; there was also a lack of evidence on effective interventions for those who do identify themselves. Therefore, it was concluded that screening may not lead to a reduction in the level of partner violence or increase positive health outcomes.

5.18 Additional comments from stakeholders in response to the 2013 review included a desire to explore existing evidence around partner violence in men. As a result, the aim of the 2019 review was to update the previous reviews undertaken in 2002 and 2013 which focused on partner violence in women, and expand this review to now include partner violence in men.

5.19 The 2019 review focused on low-risk settings because it was specifically interested in whether routine screening of the type practiced in high-risk settings should be adopted in low-risk settings.

5.20 The key questions for the 2019 review were:

- i. What is the prevalence of partner violence in the UK in women and men?
- ii. How accurate are partner violence screening tools in women and men?
- iii. What is the reported effectiveness of interventions after partner violence is disclosed by men and women?

What is the reported effectiveness of partner violence screening for men and women in healthcare settings.

- 5.21 The UK NSC acknowledged that partner violence continues to be an important health problem with partner violence varying between 12% - 24% across the UK.
- 5.22 The review found that there was still very little evidence that a national screening programme would reduce partner violence or improve health outcomes.
- 5.23 There were four studies that showed there are screening tools reporting good sensitivity and specificity in women, however, each study assessed a different tool, only one study was in the UK and one study in men. Thus, there is a low volume of studies to recommend the use of any single tool in the UK.
- 5.24 The Committee noted that on the effectiveness of interventions, studies came from outside the UK, primarily from the USA and Australia and were all based on women. In non-pregnant women the studies showed almost no statistically significant effect on outcomes such as partner violence exposure or mental health, so it was agreed that criterion was not met. Evidence in pregnant women showed mixed results of effectiveness and was still of insufficient quantity and quality.
- 5.25 Two non-UK studies (one good quality RCT) found no statistically significant effect from screening across an important range of outcomes in women and there were no studies on screening in men or pregnant women. The UK NSC agreed that, as the studies were not comparable to the UK, conclusions for the UK could not be drawn.
- 5.26 The Committee noted that the public consultation received no responses though 20 stakeholders had been contacted directly.
- 5.27 The UK NSC agreed that a systematic population screening programme in antenatal and/or non pregnant adult populations for partner violence should not be 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 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 the 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" (e.g. Down's syndrome, cystic fibrosis carrier screening), there must be evidence	Not Met



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.	
13. The benefit gained by individuals from the screening programme should outweigh any harms for example from over diagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications.	Not Met

Screening for Dental Disease in Children

5.28 Dr Visintin presented this item to the Committee. Dental diseases and conditions such as tooth decay, gum disease and trauma can affect children. If left untreated, they can have a harmful impact on the child's general health. The most common type of dental disease is dental caries, known as tooth decay or cavities.

School dental screening was previously offered but was stopped following the publication of a high-quality study in 2006 which stated that screening was not effective.

5.29 In the UK Currently, there is a recommendation that screening for dental disease in children aged 9 years and under should not be offered.

5.30 The 2019 review asked 'Is there evidence that screening children aged 9 and under for dental disease is effective at reducing the level of untreated dental disease in the population?'

5.31 The conclusion of the updated literature review remains unchanged as there was no new evidence to demonstrate that screening for dental disease is effective.

5.32 After a three-month consultation, one response was received. This supported the conclusion of the review, highlighting that screening without preventative



measures will not address this problem. Rather a preventative programme will help more disadvantaged children.

5.33 After careful review of the evidence the UK NSC recommended that a population screening programme for dental disease in children should not be 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 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

Evidence Maps

5.34 The Chair informed the Committee that evidence maps had been undertaken for the following upcoming conditions. Evidence mapping was a new step which the UK NSC was trialling which undertakes a scan for published literature scoping the volume and type of evidence that is available for a topic. This then allows the UK NSC to make a decision as to whether it should commission further work or whether due to limited evidence or unchanged developments in the evidence



base for the condition that it should return to the question in three years. This step will allow the UK NSC to prioritise and focus resources more efficiently.

Antenatal screening for varicella-zoster virus susceptibility

5.35 Varicella zoster virus (VSV) is the virus which causes chickenpox and is contagious. In the UK chickenpox mostly occurs in children under the age of 10 years. Most cases occur through contact with an infected person. Although infection in pregnancy is rare, it can cause serious maternal and neonatal morbidity and mortality.

5.36 The UK NSC last looked at the evidence for antenatal screening for VSV in 2015 and recommended that screening should not be offered. The review highlighted that there was a lack of evidence about VSV exposure in susceptible pregnant women, an absence of evidence on the test in the general pregnant population and that there were no studies on the effectiveness of Varicella Zoster Immunoglobulin to prevent or reduce transmission from mother to baby.

5.37 As absence of evidence was an overriding feature of the previous review, it was agreed that an evidence map would be undertaken which focuses on the evidence base of two key questions: the diagnostic accuracy of VSV screening tests in pregnant populations and the effectiveness of VSV immunoglobulin treatment in pregnancy when VSV susceptibility is known before exposure as opposed to after exposure.

5.38 The 2019 evidence map found no new evidence on either question, concluding that it is currently insufficient to justify an update review at this stage.

5.39 A three-month consultation was held to gather views on the evidence map. Two sets of comments were received which supported the findings of the evidence map.

5.40 The Committee agreed that an update review on antenatal screening for VZV susceptibility should not be commissioned at this time and that the topic should be re-considered in 3 years.



Screening for Cutaneous Melanoma

- 5.41 Screening for cutaneous melanoma is not currently on the UK NSC recommendations list but was a proposal submitted during the 2018 annual call for topics for consideration as a potential candidate for population screening.
- 5.42 It is a type of skin cancer. The most common sign is the appearance of a new mole or a change in an existing mole. Moles can appear anywhere on the body but predominantly affect the back in men and in legs for women.
- 5.43 Ms Coles reminded the Committee that it had agreed at its meeting in February that an evidence map be done to look at the accuracy of using ocular/iris photography to detect iris nevi/iris pigmented lesions to screen for (risk of) cutaneous melanoma.
- 5.44 The search on the evidence map's key question identified a possible 773 unique references, of which 761 were rejected as not being relevant. This left 12 potential references which examined iris nevi or iris pigmented lesions identified by ocular or iris photography. But no studies were identified in respect to the test accuracy to screen for risk of cutaneous melanoma.
- 5.45 The UK NSC noted the outcome of the evidence map and stated that further literature review on screening for risk of cutaneous melanoma using ocular/iris photography to detect iris nevi/iris pigmented lesions should not be commissioned at this time as the volume and type of the evidence is currently insufficient to justify further work in this area. However, should new evidence be published, stakeholders are invited to submit this via the UK NSC's annual call process, so it might be taken into further consideration and evaluated.

Screening for Klinefelter Syndrome

- 5.46 A proposal was submitted during the 2018 annual call for topics to consider the condition Klinefelter syndrome as a potential candidate for population screening.

5.47 Klinefelter syndrome is where boys and men are born with an extra X chromosome. Usually a female baby has 2 X chromosomes (XX) and a male has 1X and 1Y (XY). With Klinefelter syndrome, a boy is born with an extra copy of the X chromosome, so would be XXY. Boys and men with Klinefelter syndrome are still genetically male, and for many will not realise that they have the extra X chromosome but for some the extra X chromosome can increase their risk of certain health problems

5.48 When presented at FMCH and at the UK NSC 's meeting in February it was agreed that the topic fell within the remit of the UK NSC and that an evidence map should be commissioned to address the following questions:

- i. What is the incidence/prevalence of Klinefelter syndrome in the UK?
- ii. Is there a simple, safe, precise and validated screening test for Klinefelter syndrome? Sub-question: are there any incidental findings?
- iii. Are there any national or international guidelines or recommendations on population screening for Klinefelter syndrome in males?

5.49 The evidence map search identified only five potential references which related to question 1 and no references in relation to questions 2 and 3.

5.50 The Committee noted the outcome of the evidence map and concluded that further work on screening for Klinefelter syndrome should not be commissioned at this time as the volume and type of the evidence related to screening is currently insufficient to justify further work in this area. However, the UK NSC stated that should new evidence be published, it would encourage stakeholders to submit this via the UK NSC's annual call process.

Screening for Neurofibromatosis type 1 (NF1)

- 5.51 The UK NSC had not previously looked at the evidence to screen for neurofibromatosis type 1 (NF1). However, the Committee received the proposal to look at the evidence on NF1 following a submission during the 2018 annual call for topics.
- 5.52 NF1 is a genetic condition that causes tumours to grow alongside the nerves of the skin, brain and other parts of the body. It is caused by a faulty gene which in approximately half of the cases is passed from a parent to their child. In some case the faulty gene appears to develop spontaneously, and it is unclear why this happens. It is suggested that by adding a physical examination of the child's skin by a trained clinician to the NIPE screening programme and again at a later point would allow early diagnosis of NF1 via detection of café-au-lait spots, leading to effective treatment at an earlier stage.
- 5.53 The evidence map looked to scope evidence on three key questions:
- i. are there any guidelines and/or recommendations for systematic population screening for NF1?
 - ii. what is the evidence on the diagnostic accuracy of physical examination of the child's skin as a screening test to detect NF1?
Sub-question: are there any incidental findings?
 - iii. what is the evidence exploring the benefits of early pre-symptomatic detection of NF1?
- 5.54 Fifteen references were included in the final evidence map.
- 5.55 The UK NSC recognised that, although there was interest in this condition, the lack of studies directly assessing the diagnostic accuracy of physical examination of a child's skin as a screening test and the lack of studies assessing the benefits of early detection of NF1 prevented any conclusions from being drawn which would be relevant to population screening.
- 5.56 The Committee made the recommendation that a further review of evidence on newborn screening for NF1 should not be commissioned as the volume and type of the evidence related to newborn screening is currently insufficient to justify further work in this area. However, should new evidence be published,



stakeholders would be invited to submit this via the UK NSC's annual call process, so it might be taken into further consideration and evaluated.

Updates

NIHR NETSCC Update (for information)

The Committee noted the updates

SIGN Update (for information)

The Committee noted the updates

AOB

- i. Jane Fisher asked whether given recent activity in Northern Ireland, where abortion has now been decriminalised whether there were plans to review its information, service pathways and guidelines to align with the other UK Health Departments. Dr Beattie stated that discussions on the operational matters to include such services were being examined and would update the UK NSC on developments.

UK National Screening Committee

UK NSC consultation on the addition of Pulse Oximetry to the current newborn and infant physical examination screening programme.

08 November 2019

1. This report summarises the results of the 2019 consultation on the UK National Screening Committee (UK NSC) evidence review of pulse oximetry (PO) as an addition to the current newborn and infant physical examination (NIPE) screening programme.
2. Every consultation response is seen and read by the UKNSC members. All are available on the internet if the consultee permits.
3. Heart disease in newborn babies is a serious and frightening health problem. The UK NSC members are acutely aware of the very distressing experiences that parents, relatives, and friends of families with babies affected by heart disease undergo. These experiences have been brought to life in their responses to the consultation.
4. Recognising this, the Committee members and officers have considered the matter very carefully. This has included designing and funding significant pieces of hospital and university work to try to answer important screening programme questions left by formal research into PO. The Secretariat is also working to support formal research studies to fill evidence gaps.
5. The outcome of this consultation, evidence review and recommendation is not final. The Committee reviews decisions every three years as a minimum and earlier if there is significant new evidence.

Background

6. In 2014 the UKNSC was asked to consider a major modification to the NIPE screening programme. Following a large UK trial and confirmatory results elsewhere it became clear that using PO to find well babies with slightly low levels of oxygen (mild hypoxaemia) is a cost-effective method to find additional babies with critical congenital heart disease (cCHD). The number of extra babies with cCHD found is highly dependent on other screening programmes. In the UK there are likely to be very few additional babies identified as there are other high quality screening programmes in use: the fetal anomaly screening programme (FASP), and the newborn infant physical exam (NIPE).
7. However in studies where PO is undertaken early the overwhelming majority of babies with screen positive results following PO will not have heart disease. However, these studies did not include the impact of finding these babies with non-cardiac problems
8. Therefore, the effect of screening the whole population of babies was unclear. This situation did not allow the committee to assess the balance of good and harm as required by the UK NSC criteria.
9. Recognising the importance of this issue, the UK NSC recommended further work to attempt to understand the effect of a screening programme for mild hypoxaemia. This work was needed to understand not only the impact on cardiac conditions but the *non-cardiac* benefits, harms and costs of finding babies with mild hypoxaemia.
10. Public Health England (PHE) funded a series of pieces of work to attempt to fill this critical gap in the evidence base. These were:
 - a pilot of adding PO to existing NIPE screening services with the intention of collecting data from non-screening hospitals and community services to allow a fair and transparent comparison of screening and usual care.
 - a workshop with clinicians to discuss benefits and harms to babies with non-cardiac causes of slightly low oxygen levels.

- a disease and cost (economic) model to show all the effects of a PO screening programme when compared with usual care (the aim being to use data from the PHE funded pilot).
11. Unfortunately, the pilot study team did not manage to get data from non-screening units.
 12. This meant that the academics developing the economic model had plenty of data to describe the effect on babies with heart problems. But crucially no data to compare screening for mild hypoxaemia with usual practice. They could not therefore conclude the work satisfactorily and were unable to estimate the impact of screening using PO compared to NIPE alone.
 13. The clinicians at the workshop were very positive about the early identification of non-cardiac conditions, but there is very little evidence to estimate the effect of finding babies with mildly reduced oxygen levels by PO screening in comparison with not screening.
 14. Recognising that there was significant interest in the work and there had been no summary since 2014. The UK NSC decided to bring the PHE developed evidence together to inform a new recommendation. This was subject to a formal consultation as per the published UK NSC process.

The consultation sought views on whether there was sufficient evidence relating to the use of PO to screen for non-cardiac conditions **Consultation**

15. A three-month consultation on the PHE evidence and draft recommendation was hosted on the UK NSC website which ran from 9th May to 16th August.
16. There were 179 individual responses received to the consultation.
17. The respondents to the consultation were:
 - 79 responses reflecting personal experiences, predominantly from parents, relatives, or contacts of babies born with congenital heart conditions, and people with congenital heart conditions.
 - 71 responses from clinicians.

- 26 from other members of the public such as councillors, MPs, and charities.
 - 3 duplicates (IT error)
18. Some responses from clinicians were made as a group. And some personal experiences related to the same child.
19. Each consultation response was read and key points identified. The responses were then grouped into themes.
20. There was no additional evidence presented on the key question of outcomes for babies with mild hypoxaemia.
21. Some of the responses suggested that there were some confusions about the recommendation or the use of pulse oximetry.
22. The breakdown of the responses is at **Appendix 1**.

Consultation responses

23. The use of PO as an addition to the NIPE screening programme

- 116 responses support using PO and want the recommendation to be reconsidered
- 5 responses support were concerned about the absence of evidence in key areas and agreed that further research should be undertaken before making a conclusive recommendation on the use of PO
- 23 responders stated that, in their view, there is adequate evidence to make a recommendation for implementing PO.
- 56 responses acknowledged the role of PO in the potential earlier detection of non-cardiac conditions, e.g: sepsis, or respiratory conditions, with some responses citing clinical experience of picking up 'something', and others reflecting anecdotal experience of early detection.

- 14 respondents pointed out there is a lobby for the introduction of PO; that the Americans do screen for heart disease using PO; and the potential backlash for areas not using PO.

24. Research

- 9 responders would welcome further research.
- 4 responses suggest further research would be difficult to design.
- 1 response identified that there was inadequate research reflected about harms to parents, suggesting that specific research around parental anxiety or harms should have been included in the review. This would add evidence based weight to the considerable number of responses which suggested that as parents the potential anxiety was acceptable.

25. Balance of harms and benefits

- 70 respondents thought that the harms of using PO were overstated. These responders raised benefits such as reassurance provided by using PO and the potential for early identification of issues. Also that false positives are a known and accepted fact of screening programmes.
- 1 respondent was of the view that it is an ethical decision to maintain a status quo bias but that the ethics of the discussion were inadequately reviewed.

26. Use as an addition to the current screening programme

- 18 people reported the way in which their baby's heart problem was found: 11 baby's heart problems were found through the antenatal ultrasound scan screening programme and the remaining 7 were found as a result of the physical examination i.e. NIPE screening programme.
- 37 respondents stated their view that the current programme (antenatal ultrasound scanning and NIPE) was poor, or at best variable, in identifying ante- or post-natal conditions, citing practitioner competence, and test limitations. Some suggested staff training was needed.

- 4 respondents stated that observation of signs and symptoms such as cyanosis is less useful for people of colour and that the use of PO would reduce this inequity.
- 8 respondents suggested that the use of PO saved the life of their child, and
- 8 respondents suggested that if PO had been used then their child may not have developed the condition.
- 2 respondents suggested that a better focus would be on improved training in the current FASP and NIPE screening. One of these pointed out that the 2014 review was out of date in terms of antenatal detection of CCHD and that improvements in this area might be a better use of doctor and nurse time.

27. Impact on current pathways

- 11 responses stated that the concern regarding false positives is overstated and that most do not lead to further invasive investigations.
- 2 people said that in their experience of using PO there was no significant increase in echo (expert ultrasound of the heart) referrals.
- 10 responses suggested that there was limited consideration of the impact on the current cardiovascular pathways especially with regards to the locations which did not have easy access to level 3 neonatal units such as were included in the pilot study. Comments included impact of false positives on potential increased antibiotic use, and issues associated with separation from the mother e.g: breast feeding, and attachment issues.
- 1 response submitted the key points from a published analysis of pulse oximetry screening (Banait N, et al / doi: 10.1080/14767052.2018.158348) which analysed 11 years' comparative data. This reported that, in almost 140,000 infants, screening did not statistically affect diagnosis rates after discharge, and that there was no difference in mortality at 1 year in the unscreened population.

28. Early identification

- 38 respondents stated that they think there is benefit of early diagnosis following a PO test.
- 7 respondents felt that early identification of issues using PO would have helped them manage the subsequent trauma experienced.
- 5 acknowledged that using PO may not have changed their outcome, but may have provided an earlier diagnosis or sense that ‘everything possible had been done’.
- 7 respondents felt that a late diagnosis may have been avoided if PO was in use (NB the experiences reflected here were relating to diagnoses from between 4 hours old and 7 years old).

29. *False negatives and false reassurance*

- 4 people identified the potential for false negatives – that is where PO returns a normal result and the child subsequently becomes ill. Some conditions will not show up on PO at the time of screening.

30. *Other comments*

- 9 peoples’ written experiences suggested that they thought that their baby had a PO test and expected the test to improve the outcome for their baby.
- Some responses also questioned whether the weight given to harms and benefits was right: suggesting that the weight for harms should be less than the weight for the benefits.

Clarification of misunderstandings

31. It should be noted that:

- The UK NSC is *not* making a recommendation that affects how PO is used in hospitals or usual care. There is NICE guidance <https://www.nice.org.uk/guidance/qs37> if a doctor or nurse is worried about an infant they should follow this guidance.
- The UK NSC is only considering the use of PO as a screening tool in babies who the hospital or community staff believe to be well.

- Some heart conditions do not show up on PO meaning some babies will still be signed off as well but none-the-less do have heart problems (some of them serious).
- Some responders were under the impression that there were no screening tests in place to detect heart conditions. There are four screening opportunities to find heart disease in apparently well babies in the UK (the first and second trimester scans in pregnancy and the two physical examination tests: one in the few hours after birth and then again by GPs at 6-8 weeks). Of note the USA does not have the newborn screening programme and the Antenatal tests are not organised into a formal quality assured programme
- The workshop tried to establish if non-cardiac conditions would benefit from earlier diagnosis. The panel agreed that in most of the conditions, early diagnosis would benefit the morbidity and mortality outcomes. However, the panel were **not** able to say whether this would be better using PO than usual care.
- Reflecting the emphasis in the international evidence; most of the responses related to heart disease and PO. The review agrees that PO appears to be of benefit in identifying a small number of babies with CCHD over and above detection in the current pathway, however consultation sought views on whether there was sufficient evidence relating to the use of PO to screen for non-cardiac conditions. This is because the introduction of PO as a universal screening test for conditions related to hypoxaemia would significantly change the aims and outcomes of the current NIPE programme.
- This means that the consideration to include PO screening should take all reasons for a baby's hypoxaemia into account not just CCHD.

Summary

32. The majority of consultees were of the view that PO should be added to the NIPE screening programme for CCHD so by implication they thought the conclusions drawn from the literature were incorrect. But the proponents of such an addition did not consider the key question of non-cardiac problems.
33. No new evidence assessing the effects of using PO on the whole well newborn population with a comparison of usual care was found.
34. There was a small group who would favour more research (though some noting it would be difficult to design)
35. The results of the consultation suggest that there is significant appetite for the addition of PO as a test for CCHD as a formal part of the NIPE screening programme
36. There is limited understanding of the difference between the use of PO for CCHD and the effect of its application to all well babies.
37. There is acknowledgement that there are gaps in our understanding and an appetite for research.

Recommendations

This has been an unusually large response to a consultation. When the recommendation and ministerial decision are made public a significant effort to communicate the results should be carried out.

Appendix 1 - Thematic analysis of responses

Response	Personal experience 79	Clinical response 71	Other 26	Total
The recommendation				
Want the recommendation reconsidered / support PO	79	14	23	116
State that the evidence is sufficient to make a recommendation for PO		23		23
Study showed positive results for CCHD	3			3
States that the evidence is not sufficient to support introducing PO		2		2
Does not support introduction of PO		5		5
Problematic consultation, inefficient, not comprehensive, inadequate review, too strict use of screening criteria		5		5
Reflected the use of pulse oximetry in the potential earlier identification of other non-cardiac conditions	7	43	6	56
Research proposal				
Recommends further research		8	1	9
Suggests further research would be difficult		4		4
Inadequate research presented into the harms to parents	1			1
Nature of the test				



Cheap Simple, non-invasive, pain free	15	9	8	32
Inappropriate to recommend not using on the basis of cost	2		4	6
Harms to parents / balance of harms and benefits				
The harms and anxieties to parents are overstated, with reflection that the test is not stressful, that it provides reassurance, that early detection is beneficial for outcomes and cost benefits. False positives are acceptable.	29	30	11	70
It's a test wanted by parents, press, charities, and is used elsewhere (eg USA)/ parental backlash if something is missed and PO not used	2	10	2	14
Specific reflection on equity of current use		1	5	6
Ethical consideration - status quo bias / ranking of benefits and harms as not equally weighted		1		1

Aid to current screening programme				
Own experience indicated scan detected condition	11			11
Own experience indicated NIPE detected condition	7			7
Stated that PO would be useful as an additional test given that the scan and NIPE are unable to pick up all conditions due to test limitations, practitioner competence, variable detection rate / ability of PO to pick up subtle changes	8	22	7	37
Observation of signs and symptoms such as cyanosis dis-benefits people of colour where such observations are rarely made. PO would address this current inequity.		3	1	4
Suggests use of PO would have prevented condition	7		1	8



Suggests use saved the life of the child	8			8
Staff feel reassured by the use of PO		2		2
Should focus on better training for FASP and NIPE, including hip assessments etc.		2		2
Early identification				
Early identification can help with managing the trauma of treatment	7			7
Early diagnosis or detection beneficial, also noted consequences of late diagnosis		33	5	38
Acknowledged that PO may not have changed outcome but would have helped in earlier diagnosis or feeling that everything possible had been done.	5			5
Reflected a late diagnosis which respondent felt might have been identified earlier if PO used - where reflected this was over a wide age range from 4 hours old - 7 years old	7			7
Own panel supports early diagnosis so not taking note of own review and research		3		3
False negatives and false reassurance				
Potential for false reassurance		4		4
Personal experiences reflected (where possible to make the assessment) suggest that PO was used and was negative, but with a subsequent condition identified at a later date.	7			7
Personal experience indicates PO was used or was probably used as it was a clinically indicated situation, but not necessarily benefited outcome	9			9

Continued over



Impact on current CVD pathways				
Concern that the impact of false positives is over stated in the review, that they may not lead to increased Echo, or invasive investigations in most cases.		8	3	11
Introduction may impact on cardiovascular infrastructure, leading to high Echo demand and pathway issues - important to note separation issue potential to impact on breast feeding, bonding, abx use.		10		10
PO reduces admissions / not seen increase in Echo referrals		2		2
Other				
Better education for parents	1		1	2
American responses or reflecting American experiences	2	1	1	4
Parental concerns regarding health of child which came in for clinical criticism may be avoided using PO	2			2
Should be at NIPE and 5 day check or more frequently	1	1		2
Response implies that the person thinks the recommendation is against the clinical use of PO, that is: where the use might be clinically indicated given other symptoms of eg: cyanosis, or birth difficulties.	4	3	1	8