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|  **National Screening Advisory Committee (NSAC)** **National Screening Unit (NSU)** |
| **Minutes Wednesday 16 March 2016** |
| Venue | Ministry of Health (MOH), Freyberg Building, Aitken St, Wellington  |
| Start time | 1000hrs |
| NSAC members present  | Professor Ross Lawrenson (Chair)Dr Jane O’Hallahan (Deputy Chair) Dr Carol AtmoreProfessor Jackie Cumming Associate Professor Brian Cox (1145-1600hrs)Dr Joanne Dixon John Forman Dr Bryn Jones Professor John McMillan Dr Deborah Rowe Professor Diana SarfatiDr Andrew Simpson (1200-1400hrs)  |
| Ministry of Health attendees | **NSU: all items** Anne McNicholas Dr Bronwyn Rendle **Items 6-9: antenatal screening programme and non-invasive prenatal testing (NIPT)** Moira McLeod, *Acting Antenatal & Newborn Screening Programme Manager,* Sian Burgess, *Antenatal Screening Programme Leader*Dr Dianne Webster, *Auckland District Health Board* **Item 9: NIPT economic analyses** Dr Gary Jackson, *Ernst & Young (via videoconference)* | **Item 10: primary HPV screening**Helen Colebrook, *Programme Manager, National Cervical Screening Programme (NCSP)*Dr Karen Canfell, *Director, Cancer Research Division, Cancer Council of NSW (via telefconference)* **Item 11: NIPT** Dr Jeanne Snelling, *Bioethics Dept, Otago University*  |
| Apologies | Astrid KoornneefProfessor John PotterDr Pat Tuohy  |

| **Item** | **Subject and summary** |
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| **1.** | **Welcome, apologies and introductions** Ross Lawrenson welcomed the NSAC members, noting that Professor John Potter, recently appointed as the Ministry of Health’s Chief Science Advisor, has agreed to become a member of NSAC.  |
| **2.** | **Declaration of conflicts of interest (COI)**COI register tabled with no additions. Ross Lawrenson advised of his recent appointment as Clinical Director, Strategy and Funding, at the Waikato DHB and also as Professor of Population Health with the National Institute of Demographic and Economic Analysis at the University of Waikato.  |
| **3.** | **Minutes of 18 November 2015** Confirmed as a true and accurate record. Moved by Deb Rowe. Seconded by Joanne Dixon.  |
| **4.**  | **Correspondence** 1. Chair’s letter to Bowel Screening Programme (action from 18 Nov 2015 meeting)
2. Chair’s letter in reply to Brian Cox correspondence (tabled) re: (i) NSAC’s consideration of the proposal to introduce primary HPV screening: (ii) NSAC’s consideration of the report on the Breastscreen Aotearoa Programme’s effectiveness at reducing breast cancer mortality.
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| **5.**  | **Conduct of meetings and terms of reference** In committee discussion. |
| **6.**  | **Antenatal screening for Down syndrome and other conditions** Sian Burgess explained the quality improvements for antenatal screening or Down syndrome and other conditions. Areas covered included:* history of the quality improvements and conditions screened for
* quality improvement initiatives introduced in 2010
* screening pathway, uptake and outcomes
* variations in screening rates and diagnostic testing by ethnicity, deprivation and DHB
* ongoing quality improvements particularly nuchal translucency (NT) and crown-rump length (CRL) ultrasound measurements, with NSU Guidelines released in 2015. The NSU now provides feedback to radiology practices, reporting radiologists and individual practitioners on the quality of their NT and CRL measurements.

Discussion included:* responsibility for advising availability of antenatal screening lies with who sees the women at the relevant time (under Section 88) with 40% of ultrasound scans ordered by GPs (first trimester single episode claim)
* two laboratories test/report risk results, but with single database so results are aligned
* equity of screening access and uptake, with information and research required on underlying drivers of decisions, noting it is a voluntary programme with individual beliefs inherent, especially given termination of pregnancy is an option. There is a need to differentiate those who choose not to participate versus, for example, access barriers such as rurality or co-payments
* name of the screening initiative
	+ name “Antenatal screening for Down syndrome and other conditions” regarded by some as very confusing
	+ name drives perception of women and society - not appreciated by many that the scan is screening for a number of problems
	+ suggested name be simplified in line with the UK approach ie their “Fetal Anomaly Screening Programme”, so it is clear the programme is offering a suite of tests for mothers and healthy babies
	+ no disorder should be named at all in programme title; protects integrity of programme and means can add or subtract conditions without a name change
* concerns regarding radiology sector with variable quality of ultrasound and a lack of specialist sonographers. For example, issues around measurement of the nasal bone with this measure missing too often. A number of sonographers lack confidence in correctly interpreting the nasal bone, noting it has a large weighting in risk algorithm. Also a large number of sonographers perform < 25 scans annually
* suggested that NSU should provide first trimester ultrasound monitoring reports to DHBs to further leverage improvements
* QC regarded as very robust for tertiary level providers - diagnostic services/fetal medicine.

**Action.** The NSU will consider changing the programme name to the “Fetal Anomaly Screening Programme”. |
| **7.** | **Fetal anomaly screening** Jane O’Hallahan outlined the UK’s Fetal Anomaly Screening Programme and discussed their approach as a potential screening model for New Zealand.* The UK programme includes a first trimester combined test and a second trimester quadruple test (for women too late for first trimester screen or when NT cannot be measured) – similar to New Zealand’s antenatal screening programme.
* In addition, the UK programme includes the second trimester fetal anomaly ultrasound scan (between 18 to 20 weeks+5days). Their ultrasound scan base menu specifies the measuring techniques and structures to be assessed and a fetal cardiac protocol defines views required.
* Their overall programme has national standards, formal quality assurance and audits.

Discussion included whether the NSU should consider a broader approach to antenatal screening and include second trimester fetal anomaly screening in its programme. * There are believed to be a number of quality issues with second trimester scans.
* The NSU’s experience implementing quality improvements for first trimester ultrasounds is potentially useful for helping address second trimester scan quality.
* There is concern that the number of scans per pregnancy is increasing, with impacts on women and on budgets. The ultrasound budget is not capped and is not held by the NSU.
* Consideration of an expanded programme would be some time away given current NSU priorities, including the need to address the fast moving area of cell-free DNA testing of maternal blood for trisomies.
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| **8.** | **Non-invasive prenatal testing (NIPT)** Diane Webster presented on the science behind NIPT, its advantages and also areas of uncertainly. Areas covered included: * ability of the test to detect cell-free fetal DNA in maternal blood from week five
* potential position of NIPT in the screening pathway ie as a primary test or contingent on the risk estimate from the combined first trimester screen
* much higher sensitivity and specificity of NIPT compared to current screening
* cut-off level options if NIPT is offered as a contingent test
* loss of information provided through current antenatal screening eg very high risk results potentially indicative of other aneuploidies, and structural anomalies through NT screen
* requirement remains for diagnostic testing (amniocentesis) following positive NIPT result.
* the range of conditions that could be added to the test panel, and the poorer test performance and uncertain clinical significance of many compared with Trisomy 21 detection
* impact of increased maternal weight on fetal fraction and NIPT performance; and importance of laboratories reporting fetal fraction
* infrastructure requirements, particularly changes that would be needed for a wide range of provider and consumer resources
* commercial sector has largely led test development and introduction, noting aggressive marketing
* $ costs are falling but still remain very high, creating inequities in access.

It was noted that the aim of screening is to provide reproductive autonomy as well as information to allow choices in clinical care, for example, the place of delivery.  |
| **9.** | **NIPT: economic analysis within New Zealand’s publicly funded antenatal screening for Down syndrome and other conditions** The NSU commissioned Gary Jackson (Ernst & Young) to undertake an economic evaluation of the potential cost-effectiveness of introducing NIPT. This analysis was to assist with the evaluation of options for the introduction if NIPT into the screening pathway. Gary Jackson presented the analysis findings. Key conclusions were that:* from an economic standpoint, the contingent testing scenario could be cost saving to the New Zealand funded health system (due the substantial decrease in the number of diagnostic amniocentesis tests), while detecting more cases
* the universal scenario would incur a larger step wise increase in total costs and has a larger incremental cost pre additional case detected
* all NIPT scenarios significantly reduced the number of invasive tests (amniocentesis/CVS).

Additional points noted: * all NIPT options assumed routine scans would continue as these are embedded in maternity care
* costs were based on the information provided by the commercial sector following a formal request for information process, but were agnostic on whether the tests were done off shore or in New Zealand
* cost of change, re-organisation, training or additional counselling were not included.

A NSU noting memo was included with the NSAC meeting papers regarding issues that the Down Syndrome and Other Conditions Technical Working Group (TWG) raised at their 2 March 2016 meeting about the cost effectiveness report. * The TWG expressed concerns that the report included age to determine eligibility for NIPT (women aged ≥ 35 years to have universal access to NIPT and those < 35 years to have NIPT as a contingent test).
* The NSU has clarified it is not considering using age to determine eligibility for NIPT.
* The TWG believed that the modelling does not properly represent the full range of options for introduction of contingent NIPT. They recommended that contingent screening should be modelled using risk data available from the current screening strategy to provide a better positive predictive value.
* The NSU has clarified that it will undertake further economic modelling and policy development to develop the preferred option for the inclusion of NIPT. The modelling will more fully consider the costs of other aspects of NIPT, including:
	+ varying pathways and thresholds for offering NIPT as a contingent screen
	+ pathway options for women where NIPT results in a failed screen, including those due to low fetal fraction
	+ the continued clinical requirement for ultrasound around 12 weeks to date the pregnancy, confirm viability, determine multiple pregnancy, chorionicity and amnionicity, and identify any early fetal abnormalities.

Discussion included: * reasons for continuing 12-13 week scan when NIPT is introduced eg, for dating, viability, identifying multiple births and also some gross abnormalities
* consideration of altering the risk algorithm to adjust for impact of missing or poor quality scan data, but the best approach is to work further to improve quality of NT (eg review outliers in current reports; set minimum annual scan number) and identify the best cut off for NIPT.
* significant risk noted if sex chromosomes are included in panel given discrepancy in sex numbers is already apparent in particular cultural groups.
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| **10.** | **Cervical cancer: analysis of New Zealand trends** At the 18 November 2015 meeting NSAC agreed that the NSU would undertake additional analyses of the incidence and patterning of cervical cancer in New Zealand women aged 20-24 years to assist consideration of maintaining LBC screening in this age group for a transitional period. Karen Canfell (Cancer Council NSW) noted that their previous presentation to the NSAC looked at New Zealand modelling with a switch from LBC in women aged 20-24 years to primary HPV starting at 25 years. This modelling did not support continued LBC screening in women aged 20 to 24 years. Karen presented preliminary analysis of the trends in cervical cancer in New Zealand since the inception of the National Cervical Screening Programme (NCSP). Conclusions were as follows:* in women aged 25 and older, the rate of cervical cancer incidence was 49-66% lower in the most recent five year period (2009-2013) than it was in the five year period immediately prior to NCSP (1985-1989)
* reductions of ~50% in 25-49 and 50-69 age groups are consistent with findings from other countries
* in contrast, rates in women aged 20-24 appeared higher in 2009-2013 than in 1985-1989
* difference is statistically significant for non-Māori but not for Māori (although point estimate also suggests possible increase in Māori)
* the relative reduction in cervical cancer incidence in 2009-2013 compared to 1985-1989 is similar in Māori and non-Māori women aged 25-49 and 50-69
* incidence rates appeared to have plateaued in recent years in women aged 25-49 and possibly 70+.

Discussion included: * It was asked if there was an impact from detecting cervical dysplasia in 20-24 year age group on reduction in cancer in 25-29 year age group.
* Canfell advises there is no protection in 25-29 year age group from screening women under 25 years. Cited paper by Sasieni and colleagues, a case control audit, as one of the best controlled examinations of protective effect in next age group if screened before 25 years, and that it concluded there was none
* Canfell noted that when starting screening in the 25-29 age group it is critical to screen close to age 25 rather than age 29, with modelling quantifying that effect as significant.
* It was suggested that any benefit at age 20-24 would be small and very difficult to detect, with exponential gain in next age group; and that five year age groups are arbitrary and a screening starting age could be in-between age bands, eg, from 23 years.

**NSU concluding remarks**The NSU asked NSAC to note the preliminary results on cervical cancer incidence trends; and advised that the memo provided on screening women aged 20 to 24 years is for noting only. Given the current stage of policy development, the NSU will seek NSAC endorsement of recommendations on cervical screening in women aged 20 to 24 years once it has finalised its advice. **Action:** The NSU will bring a recommendation paper to NSAC on whether to continue cervical screening in women aged 20 to 24 years.  |
| **11.**  | **NIPT: ethical considerations** John McMillan and Jeanne Snelling led a session considering the ethical and legal issues related to NIPT. Initial considerations related to how well the National Health Committee (NHC) 2003 Screening Criteria worked for genetic screening tests. NSAC 2010 papers on informed consent and ethical and social considerations in screening were provided as further background. Discussion included: * the priority of informational openness
* that antenatal screening is providing information for one person (baby) through another (the mother) for the mother to make an informed choice
* that screening may benefit the next child not the current foetus, and may benefit the entire family unit eg, there is value in information early in pregnancy/before the next pregnancy for inherited conditions that are not diagnosed in an older child until they become symptomatic
* families’ perspective often that there is value in knowing about a condition in advance
* not specifically addressed in the NHC screening criteria is the importance of equity; and that the issue of over-diagnosis is also not explicitly mentioned, although the consequences of false positives and negatives are included in the wider document
* assessing benefit of screening in neonatal period can differ eg, the benefit of screening for cystic fibrosis was not able to be demonstrated in a trial, but through post-implementation
* complex consent issues when there is no longer a single disease of interest; added issues of incidental genetic findings and continuing panel extensions, with serial consenting a suggested approach
* consideration of future review of screening criteria in light of increased genetic screening, with a view the criteria may only need small amendments. In the interim, NSAC could look at UK criteria which were recently updated to better account for genetic screening.

Other socio-ethical and socio-legal aspects covered in the presentations and discussions included: * relative benefits of NIPT eg, safety, reliability, reduction in invasive tests
* cost-effectiveness, noting the move away from measuring wider societal costs as is now regarded as unethical to measure dollar cost of looking after a disabled child. Focus is on cost-effectiveness of providing information through different ways of testing, as information is the aim of antenatal screening
* importance of consent and autonomy, including capacity to provide counselling
* tensions between reproductive choice, disability rights and fetalist critiques eg, increased pressure on women to use NIPT, potential stigmatisation if choose not to use NIPT or have a disabled child
* cultural context with different communities varying in their acceptance of disability
* aggressive marketing, with direct to consumer marketing outside public sector
* capacity of system to provide counselling and information
* issues related to risks around sex selection
* duty of care with duty to inform - “information that a reasonable person in that person’s circumstances would expect to receive” - includes understanding and consenting to a range of tests, and understanding implication of results eg, false positives
* genetic literacy of health professionals and difficulties with field moving quickly
* routinisation of NIPT, and also testing for additional conditions (tick box “trap”) could see testing occur without consent
* commercial companies determining what conditions are included on screening panels
* issue with reporting some micro-deletions eg, there can be a wide variation in outcome, including from early death through to being able to attend university
* regulatory oversight and quality assurance requirements eg, reporting fetal fraction, standardisation of results
* accessing NIPT outside public system

**Next steps** The NSU will review additional cost benefit analyses and options for inclusion of NIPT by year end. In particular, the NSU will look at varying pathways and thresholds for offering NIPT as a contingent screen. Noted that consensus will be required on what should be included in the publicly funded screening programme; that a process for public consultation will be required; and that implementation of NIPT needs to be done in a thorough and systematic way. Noted that early consideration must be given to equity with introduction of NIPT, as well as improving equity in current services. There is a need for a better understanding of the current inequities. User charges were thought likely to be key. More information on access to and uptake of first trimester screening by DHB was requested.**Action:** NSU to review and table recent changes to UK screening criteria designed to better account for genetic screening. **Action:** NSU to provide an update on NIPT at the July 2016 meeting, and anticipates providing a recommendation paper for NSAC endorsement at the November 2016 meeting. **Action:** NSU to provide further information on uptake of first trimester screening by DHB**.**  |
| **12.** | **Work Programme** The updated work programme was tabled. Topics NSAC will likely consider at July and November 2016 meetings: * NIPT: update and recommendations regarding implementation
* NHC screening criteria: review UK changes to their screening criteria in relation to genetic testing
* primary HPV screening: recommendations re screening 20-24 age group using LBC
* AAA screening: review of National Health Committee report and recommendations
* breast cancer age extension: review and recommendations
* bowel cancer screening programme: update.
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| **13.** | **Other business** Next meeting Wed 6 July 2016  |
|  | The meeting closed at 1600hrs |