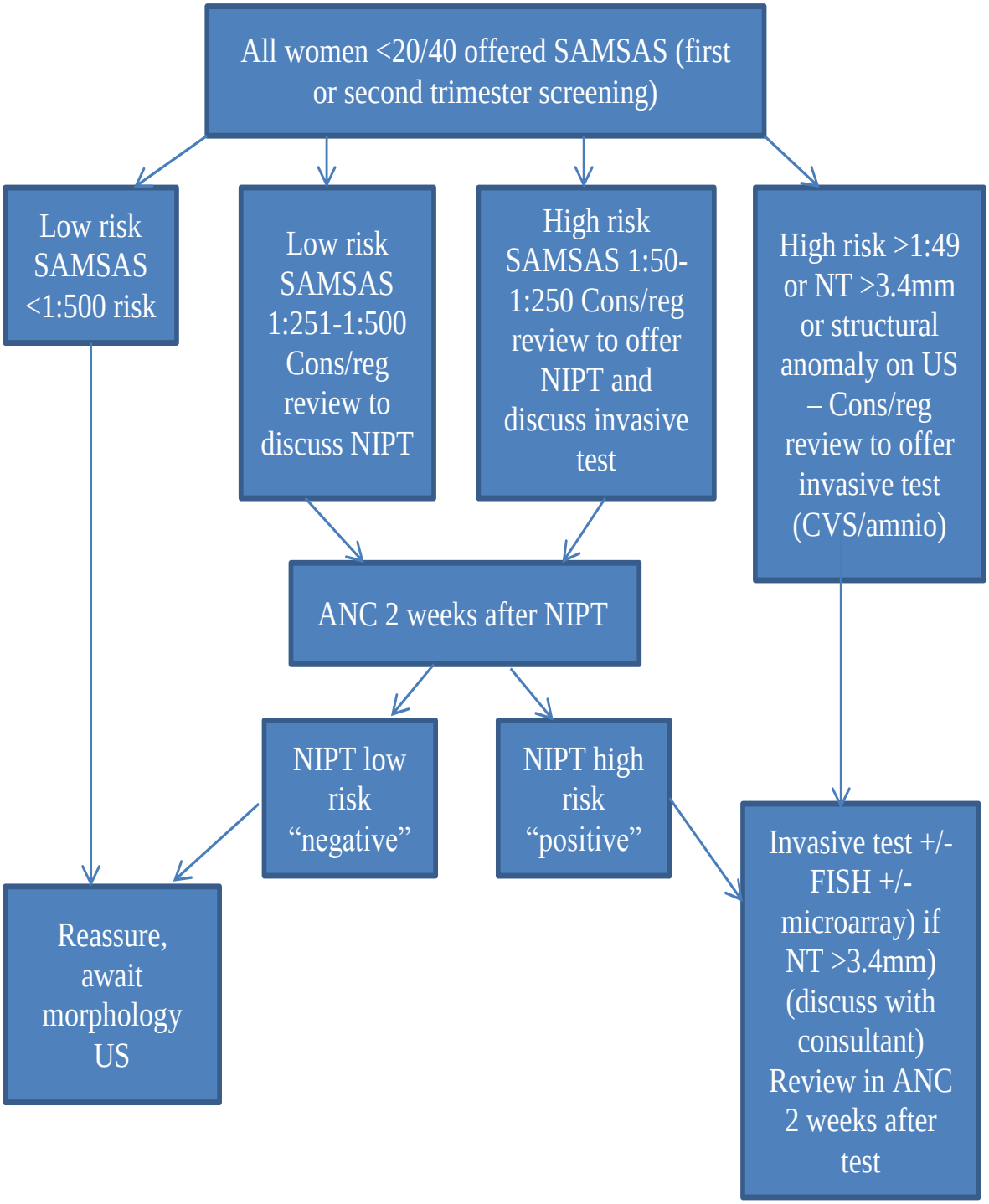
SSI03491

Aneuploidy Screening and NIPT (Non Invasive Prenatal Testing) in Obstetrics



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Effective Date	04/2018		**Review date**: 04/2021
Scope (indicate those that apply ☒)	☐Organisation Wide (OW) NALHN		☒Service/Site Specific (SS) ☒ Division Women & Children's ☒Clinical Area Obstetrics & Gynaecology ☒Site Lyell McEwin and Modbury Hospitals
Application (indicate those that apply ☒)	☐All Staff	☒Medical ☒Nursing ☒Midwifery ☐Allied Health ☐Administration ☐Pharmacy	☒Students ☐Volunteers ☐Contractors ☒Agency ☐Consumers ☐Other Insert details

Roles and Responsibilities

Medical Officers and Registered Midwives are responsible for discussing and offering aneuploidy screening to all pregnant women, including discussing the limitations of screening tests and the possible need for further diagnostic testing. Medical Officers are responsible for requesting screening ultrasounds/blood tests and for counselling those with elevated risk results.
Individual Clinicians are responsible for:

- Discussing care with consumers in an environment enabling respectful, culturally appropriate, confidential care.
- Advising consumers of their choice and obtaining informed consent.
- Documenting all care in accordance with mandatory and organisation guidelines.

Purpose

The purpose of this procedure is to outline the responsibilities of the Medical Officer/Registered Midwife seeing the woman after aneuploidy screening.

Aneuploidy screening for trisomy 18 and 21 has evolved from screening based on maternal age alone to current practice of ultrasound assessment of nuchal thickness (NT) with serum screening (utilising PAPP-A and bHCG) in the first trimester and serum screening (AFP, unconjugated estradiol bhcg) alone in the second trimester.

New technology for non-invasive prenatal testing (NIPT) utilising cell free foetal DNA (cfDNA) has greater sensitivity and sensitivity than current serum/US screening programs, but is associated with a significant cost to the patient.

This guideline aims to assist with managing the woman with low/intermediate/high risk of aneuploidy based on serum/US screening.

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Procedure Detail

Currently the first/second trimester aneuploidy screening program is conducted by SAMSAS (South Australian Maternal Serum Antenatal Screening) through SA Pathology – see http://www.wch.sa.gov.au/services/az/divisions/labs/geneticmed/samsas.html for further information.

All women less than 20 weeks gestation should be offered aneuploidy screening utilising the SAMSAS program, and should be counselled as to the limitations of screening prior. They should also be advised that SAMSAS provides information other than just aneuploidy risk. Women who decline aneuploidy screening may still want SAMSAS screening for the additional information:

- Low PAPP-A (< 0.37 MoM) is associated with a 3 x higher risk for SGA. These patients require an additional uterine artery Doppler at the time of the morphology scan and may require additional growth surveillance and CTG monitoring in labour. See SA Health "Management of women with a low PAPP-A and normal chromosomes".
- Early US - US in the first trimester has the additional benefits of confirmation of gestational age, early diagnosis of twins/chorionicity as well as early structural/morphological assessment of the foetus.
- Increased NT is associated with significant structural anomalies even when there is a normal karyotype. NT 3-3.4mm (approx 5%centile) should proceed to early tertiary morphology US. NT >3.5mm should be offered invasive testing with microarray, early tertiary morphology +/- foetal echo.

Gestational Age Windows for Antenatal Screening for Birth Defects (from SAMSAS)

1st Trimester	Blood sample	9w0d –14w0d	*Optimal gestation 10 - 12 weeks
	Ultrasound	11w0d – 14w0d	*Optimal gestation 11 - 12 weeks

* The blood sample and nuchal translucency measurement can be done on different days.

2nd Trimester	Blood sample	14w1d – 20w6d	*Optimal gestation 16 weeks

US assessment of NT must be performed by NT accredited sonographers, therefore referral to an appropriate US practice is required. To facilitate Medicare billing the requesting medical officer must state "risk of foetal abnormality" on the request form. Currently Lyell McEwin Hospital refers to Radiology SA and Modbury Hospital to Benson's Radiology.

Bloods are requested on the SAMSAS form, with inclusion of maternal age, gestation, maternal weight, smoking, IVF etc important for accurate calculation of risk, therefore these parameters must be included before informed counselling.

SAMSAS coordinates blood and US results and calculate a risk of aneuploidy (T21, T18), and for second trimester also calculates the risk of open neural tube defect.

Risk results:

SAMSAS considers high risk to be those with a risk >1/250, and previously those woman have been offered invasive testing (either referral for CVS at WCH or amniocentesis at Lyell McEwin). With the introduction of cfDNA, a new category of intermediate risk has been suggested, encompassing those with a risk between 1:500 - 1:50.

NIPT using cfDNA:
The presence of cell free foetal DNA in maternal serum was first described in 1997. This "foetal" DNA originates from the placenta and is rapidly cleared after delivery.

NIPT using cfDNA screening of maternal plasma can be performed from 10 weeks gestation and has greater sensitivity and sensitivity than combined serum/US screening described above, however there is no Medicare or private health insurance funding and therefore is completely funded by patients. Currently this is around $400.

Some women will opt to fund cfDNA as a primary screening tool, it is then advised that they do not proceed with SAMSAS screening as this may increase the false positive rate without increasing sensitivity. Women who opt for cfDNA as a primary screening tool should still be offered first trimester NT US to screen for structural anomalies, and if their US demonstrates anomalies may be offered invasive testing even with a low risk cfDNA result.

Three cfDNA tests are currently commercially available, are processed in Australia and have a turnaround time of approximately 1 week. SA Pathology is in the process of developing a NIPT, this is not currently available.

Harmony (Ariosa) through Clinpath utilises single nucleotide polymorphism technology. https://www.sonicgenetics.com.au/nipt/ . Harmony publish the foetal fraction and will rule a test unsatisfactory with no result if the foetal fraction is <4%. Obese women are more likely to have a foetal fraction <4%, as are women with an aneuploid foetus. Women with a test failure may be offered a repeat test at a later gestation or will be refunded their money.

Generation Test through Abbott Pathology utilises whole genome sequencing with massively parallel sequencing. http://www.abbottpathology.com.au/IamaPatient/MyTesting/NoninvasivePrenatalTesting(NIPT).aspx . The Generation Test may have a lower failure rate for obese patients compared with other tests.

Abbott also offer Generation Plus (not processed in Australia), which also assesses for microdeletions. This test is NOT recommended for routine care, prior to requesting this test patients should have significant counselling as the risk of false positives is substantially higher, it should not be offered without specialist indication and counselling at a consultant level.

Repromed offer the NEST screening test http://nestscreen.com.au/about/ , processed in Adelaide. This uses massively parallel sequencing, they report a failure rate of <0.1%

All women with a test failure (regardless of provider) should be considered high risk for aneuploidy and offered invasive testing. Some women with a failed Harmony test may consider a NEST or Generation test, however proceeding to a second test may delay an invasive procedure and subsequent diagnosis of aneuploidy.

All women with a high risk result on NIPT need diagnostic confirmation with either amniocentesis or CVS.

Counselling points:

- NIPT is a screening test, not a diagnostic test. All cfDNA tests have false positive results and therefore any positive/high risk result must be confirmed with invasive testing (amniocentesis or CVS).
- NIPT offers parents the choice to find out the sex and can investigate for sex chromosome abnormality (screening for sex chromosome anomalies has a higher false positive rate than for T21/T18).

- Obese patients and those conceiving with IVF are more likely to have a test failure; however women with an aneuploid fetus are also more likely to have a test failure. All women with a test failure should be advised this places them at high risk for aneuploidy and they should be advised to have an invasive test.
- All women who have either an amniocentesis or NIPT should have a registrar or consultant appointment two weeks later to discuss the result. This appointment could be booked at Modbury hospital unless the patient has transport/geographical issues with attending Modbury.

Based on the above flowchart:
SAMSAS Risk <1:500 – reassure, routine ANC.

Anyone with a SAMSAS risk >1:500, structural anomaly on US or NT >3mm should be referred for registrar/consultant counselling in ANC.

SAMSAS Risk 1:250 – 1:500 – advise of availability of cfDNA and cost associated. Patients that decline cfDNA but are concerned re aneuploidy risk – consider amniocentesis with associated risks.

SAMSAS Risk 1:50 – 1:250 – advise of availability and cost of cfDNA, also offer invasive testing.

SAMSAS Risk >1:50 or structural anomaly on US or NT >3.5mm – offer invasive test (if NT >3.5mm or structural anomaly consider microarray). Women with a NT >3mm or those with structural anomaly should also be referred for early tertiary morphology US +/- foetal ECHO.

In patients requiring an amniocentesis, FISH can be utilized in patients at a particularly high risk of Trisomy 21 or Tri 18 (> 1/50), or in patients undergoing amniocentesis at a more advanced gestation (> 18 weeks) invasive test. These cots will be covered by the hospital. If the FISH is just on the patient's request – write on form **'invoice patient'.**

Two weeks after NIPT/amniocentesis patients should have a Registrar/Consultant ANC appointment to discuss the results and ongoing management as required. Those with a thickened NT or low PAPP-A need further investigation as per above, even with normal karyotype.

Monitoring and Auditing

We will monitor for any clinical errors through the SLS system. Any failure to adequately provide counselling or arrange follow-up will be reported through SLS. Any adverse clinical outcomes will be monitored and presented through our perinatal morbidity and mortality meeting.

Hand Hygiene

The 5 moments of hand hygiene are to be complied with by all staff at all times as per Policy Directive, Hand Hygiene, Infection Prevention and Control, SA Health.

Patient ID

Staff must identify the patient at the beginning of a care episode and at each patient intervention using the 3 mandatory identifiers; 1. Medical Record Number, 2. Name and 3. Date of birth.

Because of the non-transferability of the Medical Record Number across health care services, an additional patient identifier should be used such as address or Medicare number during inter-hospital patient transfers.

See the SA Health Policy Directive, Patient Identification, Patient Identification Guideline and NALHN OWI01168 Patient Identification Procedure for further information.

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Consent

All Procedures involving the provision of medical treatment to a patient must be undertaken in accordance with the Consent to Medical Treatment and Palliative Care Act 1995.

Work Health Safety

The responsible manager must ensure all workers who undertake this Procedure receive adequate information, training, supervision and support. Staff following this Procedure have a duty of care for taking reasonable steps to protect their own health and safety and not adversely affecting another person while at work. Further information is available from the NALHN Work Health and Safety Services intranet.

Standards

National Safety and Quality Health Service Standards

Standard 1 Governance for Safety and Quality in Health Service Organisations	Standard 2 Partnering with Consumers	Standard 3 Preventing & Controlling Healthcare associated infections	Standard 4 Medication Safety	Standard 5 Patient Identification & Policy Matching	Standard 6 Clinical Handover	Standard 7 Blood and Blood Products	Standard 8 Preventing & Managing Pressure Injuries	Standard 9 Recognising & Responding to Clinical Deterioration	Standard 10 Preventing Falls & Harm from Falls
☒	☒	☐	☐	☒	☐	☐	☐	☐	☐

☐ **Australian Aged Care Quality Agency – Accreditation Standards**

☐ **Quality of Care Principles 2014**

Risks

Risk Matrix

Rating	Risk
Low	There is a current risk that we are not identifying a number of foetus' with aneuploidy in early pregnancy and this procedure will reduce this risk of missing foetal anomalies

Legislation

Search legislation at: ComLaw Home and South Australian Legislation

N/A

SA Health Policy Directives/Procedures and external references and best practice Procedures

Clearly identify SA Health Policy Directives / Procedures relating to the document. Search these documents at: A - Z directives and Procedures: SA Health

Hui L, Hyett J, Noninvasive prenatal testing for trisomy 21: Challenges for implementation in Australia, ANZJOG 2013

RANZCOG Guideline "Prenatal screening and diagnosis of chromosomal and genetic conditions in the foetus in pregnancy" Accessed 10/5/18

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NALHN Policies/Procedures/Guidelines/Forms/Consumer Information sheets (NALHNPPG)

See RANZCOG patient information sheet - https://www.ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Patient%20information/Prenatal-Screening-for-Chromosomal-and-Genetic-Conditions.pdf?ext=.pdf

Definitions and Acronyms

NT = nuchal thickness

SAMSAS – South Australian Maternal Serum Antenatal Screening

cfDNA – cell free DNA

NIPT – non invasive prenatal testing

Key Word Search

NIPT, cfDNA, aneuploidy, first trimester screening, trisomy

Issues/comments

If you have any issues or comments in relation to this Procedure, please contact the Sponsor.

Procedure Sponsor

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Version control

This Procedure Supersedes Document Number/s: Enter PPG number or N/A ☒

Title of Document/s Superseded: Enter title here

Version	Effective from	Effective to	Change summary
1.0	04/2018	04/2021	New Procedure

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ADMINISTRATION USE ONLY

Division Approval
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Chief Operating Officer Approval for Organisation-Wide Procedures
Clinical/Corporate Governance Committee Date:
Name:
Date: