Evaluation of non-invasive prenatal testing within antenatal screening

- the findings so far

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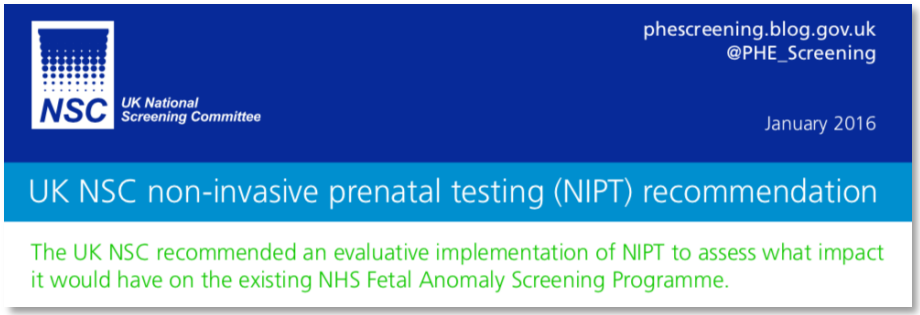
Clinical Forum, 27th May, 2022

Overview of the talk

- Rationale for NIPT in Scotland
- What is non-invasive prenatal testing (NIPT)
- Referral criteria
- Findings from NHS Wales
- Scottish data so far
- Opportunities for NIPT

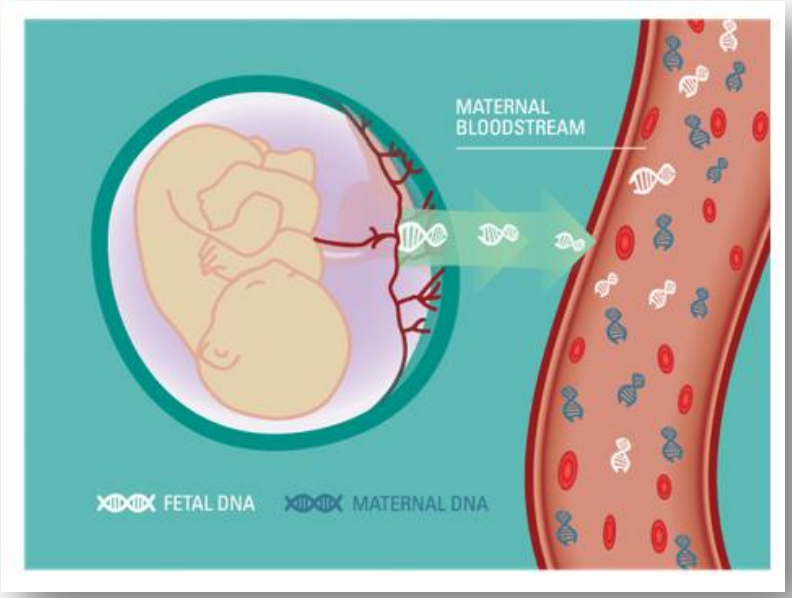
Establishing NIPT in Scotland



- National Pregnancy Screening Programme in Scotland included a 3-year evaluation of NIPT
- Offered as a second-line screening test for pregnancies identified as higher chance of Down's syndrome, Edward's syndrome and Patau's syndrome from first-line screening
- Expanded to include **both** singleton and twin pregnancies
- Illumina VeriSeqNIPT solution identified through NSS Procurement
- NIPT went live on 28th Sep 2020.
- NIPT evaluations launched in NHS Wales (April 2018) and NHS England (June 2021).

NIPT using cell-free DNA

- cfDNA mixture of maternal and “fetal”
- Fetal DNA arises from placental trophoblast cells
- 10 weeks +
- Fetal fraction 2-20%
- High sensitivity and specificity for common aneuploidies (>99%)
- High uptake and subsequent reduction in invasive procedures



Test performance metrics

VeriSeq NIPT Solution v2 – Singleton Pregnancies

	T21	T18	T13
Sensitivity	>99.9%	>99.9%	>99.9%
Specificity	99.9%	99.9%	99.9%

VeriSeq NIPT Solution v2 – Twin Pregnancies

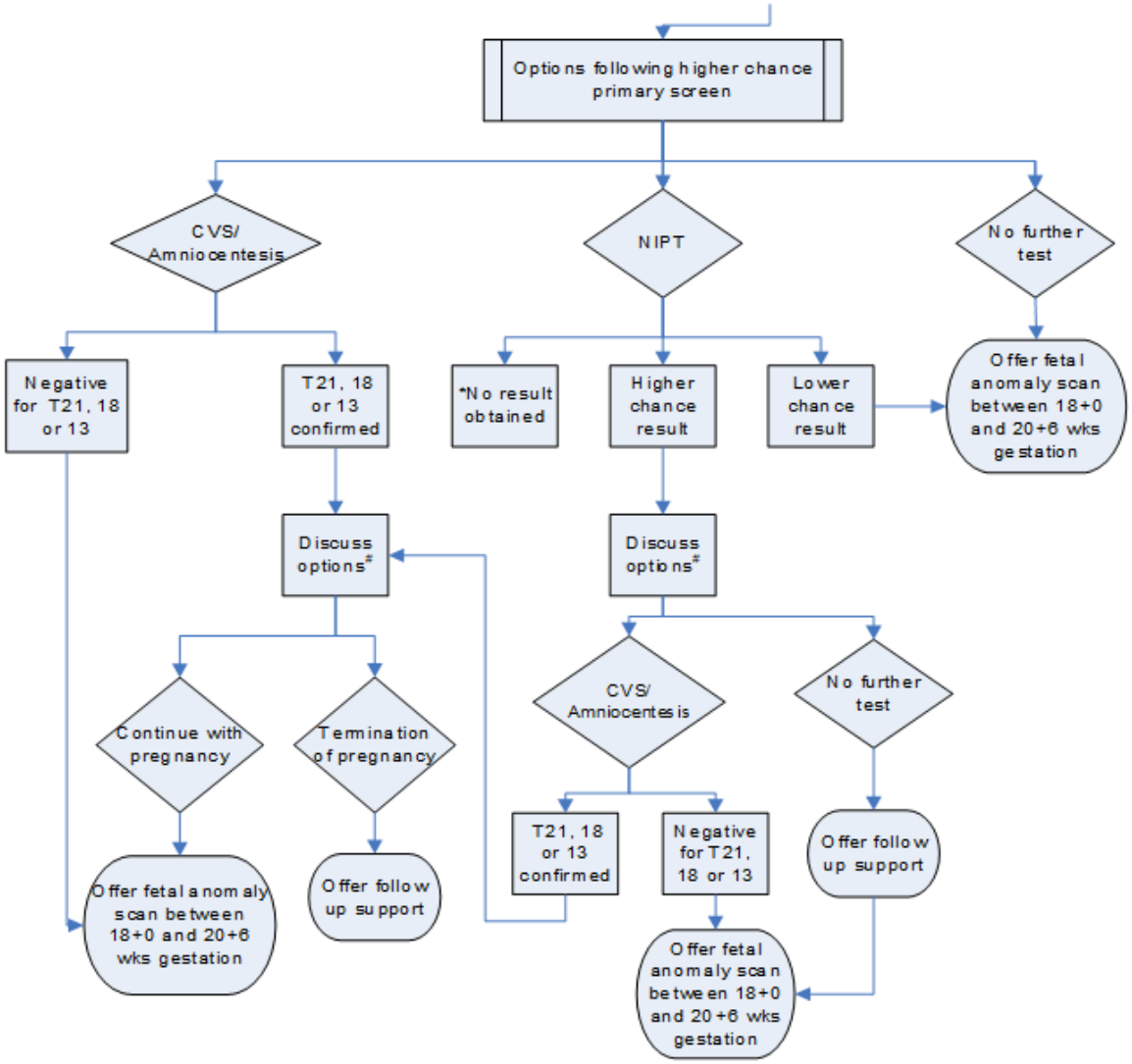
	T21	T18	T13
Sensitivity	96.4%	95.7%	93.6%
Specificity	99.9%	>99.9%	>99.9%

Failure rate

1.2% of samples failed QC on first pass.

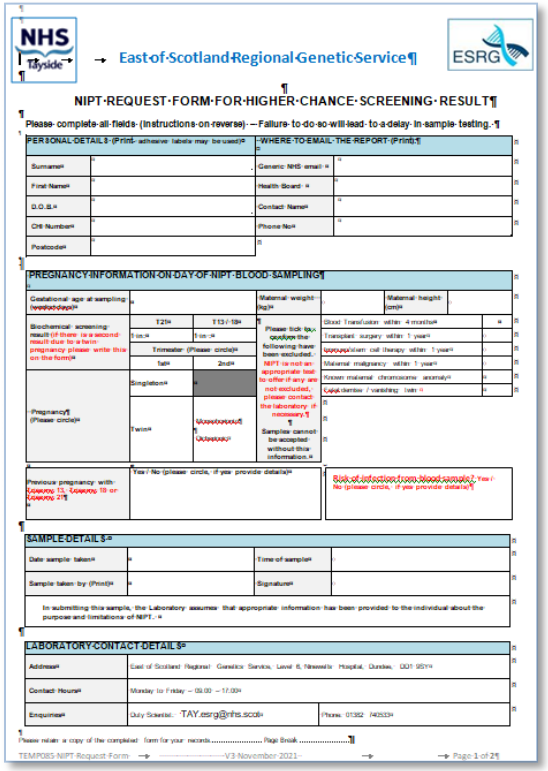
Antenatal Screening Pathway

NHS National Services Scotland



Acceptance criteria for NIPT

Appropriate	Inappropriate
Higher chance (≤ 1:150) of T21, T13/T18 from serum screening	No participation in national screening pathway
Previous trisomy (T13,T18 or T21)	Abnormal early pregnancy scan
Missed 1st / 2nd trimester serum screening	Evidence of vanished twin
	Maternal blood transfusion/transplant surgery/malignancy
	Known maternal chromosome anomaly
	Fetal sexing



NHS Tayside → East of Scotland Regional Genetic Service ESRG

NIPT REQUEST FORM FOR HIGHER CHANCE SCREENING RESULT

Please complete all fields (instructions on reverse) – Failure to do so will lead to a delay in sample testing.

PERSONAL DETAILS (Print- adhesive labels may be used)

WHERE TO EMAIL THE REPORT (Print)

Surname | Generic NHS email | First Name | Health Board | D.O.B. | Contact Name | CHI Number | Phone No | Postcode

PREGNANCY INFORMATION ON DAY OF NIPT BLOOD SAMPLING

Gestational age at sampling (weeks/days) | Maternal weight (kg) | Maternal height (cm)

Biochemical screening result (if there is a second result due to a twin pregnancy please write this on the form) | T21 risk | T13 / T18 risk | Trimester (Please circle) 1st 2nd | Singleton | Twin | Pregnancy (Please circle)

Please tick (✓) or circle the following have been excluded. NIPT is not an appropriate test to offer if any are not excluded, please contact the laboratory if necessary.

Blood Transfusion within 4 months | Transplant surgery within 1 year | Stem cell therapy within 1 year | Maternal malignancy within 1 year | Known maternal chromosome anomaly | Early demise / vanishing twin

Samples cannot be accepted without this information.

Previous pregnancy with trisomy 13, trisomy 18 or trisomy 21 | Yes / No (please circle, if yes provide details)

Risk of infection from blood sample? Yes / No (please circle, if yes provide details)

SAMPLE DETAILS

Date sample taken | Time of sample | Sample taken by (Print) | Signature

In submitting this sample, the Laboratory assumes that appropriate information has been provided to the individual about the purpose and limitations of NIPT.

LABORATORY CONTACT DETAILS

Address: East of Scotland Regional Genetics Service, Level 6, Ninewells Hospital, Dundee, DD1 9SY

Contact Hours: Monday to Friday – 09.00 – 17.00

Enquiries: Duty Scientist. TAY.esrg@nhs.scot Phone: 01382 740334

Please retain a copy of the completed form for your records ..... Regd Briak .....

TEMPOBS-NIPT-Request Form → V3 November 2021 → Page 1 of 2

Key findings from NHS Wales

	n (%)
Higher chance screening ≤ 1:150	1273
1st trimester	1015 (79.7%)
2nd trimester	258 (20.3%)
Women choosing NIPT following high-chance	1073 (84.3%)
SPR	72 (6.7%)
Specificity	100%
Low chance NIPT requesting invasive	0%
Failed NIPT	11 (1%)

- 30-month evaluation period (average 42.4/month)
- Singleton pregnancies
- Mean reporting time of 6.25 calendar days
- Approx **9-fold** reduction in invasive procedures following implementation of NIPT
- No significant impact on live birth rate for Down's syndrome

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ORIGINAL ARTICLE

PRENATAL DIAGNOSIS WILEY

Implementation of non-invasive prenatal testing within a national UK antenatal screening programme: Impact on women's choices

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Funding information
Public Health Wales

Abstract

Objective: To evaluate the implementation of non-invasive prenatal testing (NIPT) on pregnant women's choices in a national NHS antenatal screening programme for Down's syndrome, Edwards' syndrome and Patau's syndrome.

Method: An observational study of all pregnant women with a singleton pregnancy and higher chance (≤1:150) combined or quadruple screening result from 30 April 2018 to 25 September 2020 in Wales, UK. Pregnant women's journey through the pathway was determined including uptake of NIPT, performance of NIPT in a non-research setting and invasive procedures performed.

Results: Of the 1273 women with a higher chance initial screening, 1073 (84%) chose NIPT contingent test, 174 (14%) no further testing and 26 (2%) invasive procedure. There were 1001 (93%) low chance NIPT results; 11 (1%) failed results and 61 (6%) high chance results. Average annual incidence of 27 invasive procedures undertaken compared to 229 pre-NIPT implementation, a nearly ninefold reduction. Down's syndrome annual live birth rate remained unchanged across the implementation period.

Discussion: This study demonstrates that NIPT contingent screening was highly acceptable to women with a resulting reduction in invasive procedures performed.

Conclusion: The high uptake of NIPT in NHS antenatal screening pathway conditions should inform planning for other national screening programmes.

Key points

What is already known about this topic?

- Non-invasive prenatal testing (NIPT) is considered a highly accurate contingent screening test for Down's syndrome, Edwards' syndrome and Patau's syndrome in pregnancy.
- In 2015 UK National Screening Committee recommended that the offer of NIPT should be introduced into UK antenatal screening using an evaluative implementation approach.
- Wales was the first UK country to implement the offer of NIPT within a national antenatal screening programme in 2018.

What does this study add?

- NIPT as a contingent screening test was highly acceptable to women with the majority (84%) opting for NIPT following an initial higher chance screening test.

Scottish data – 12 months

- Period from 1/4/21 to 31/3/22 (12 months)
- NIPT data submitted quarterly to PHS
- Collated with pregnancy outcome data (CARDRISS, MOTSCAG)

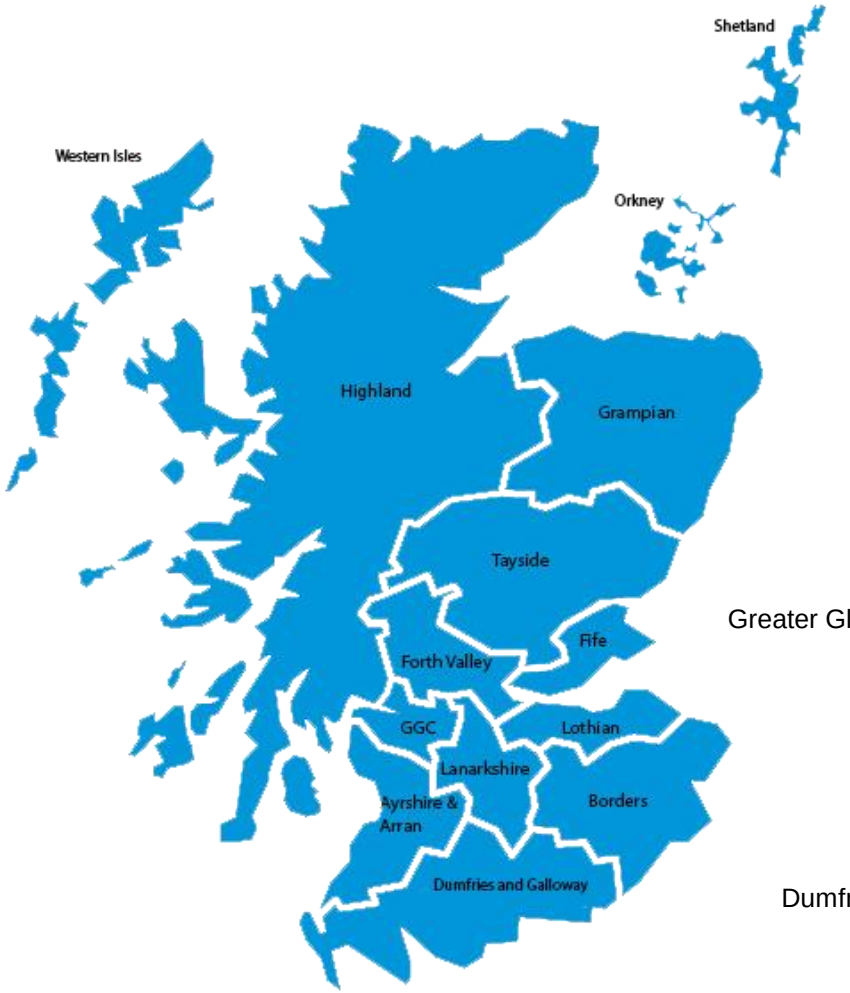
	n (%)
Higher chance referrals	1031
Singleton	1017 (98.6%)
Twin	14 (1.4%)
1st Trimester	774 (75.1%)
2nd Trimester	232 (22.5%)
No info	25 (2.4%)
SPR – High Chance from NIPT	79 (7.7%)
NIPT Failed (after repeat blood)	4 (0.4%)
Samples rejected (failure to meet criteria)	16 (1.5%)

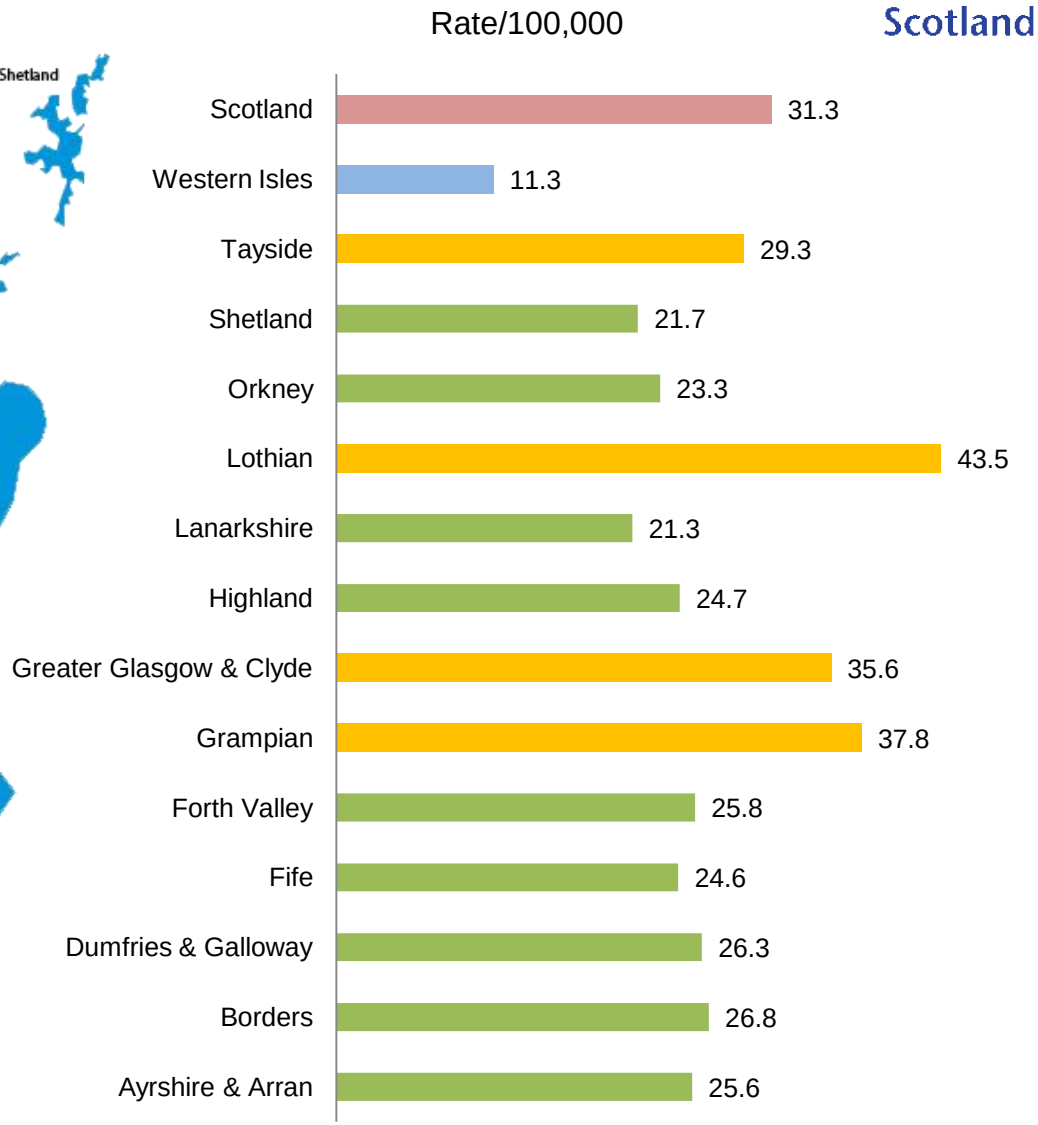
- Average of 87 referrals/month
- 98.6% of reports issued within 7 calendar days
- Mean reporting time of 5.3 calendar days

Other referrals

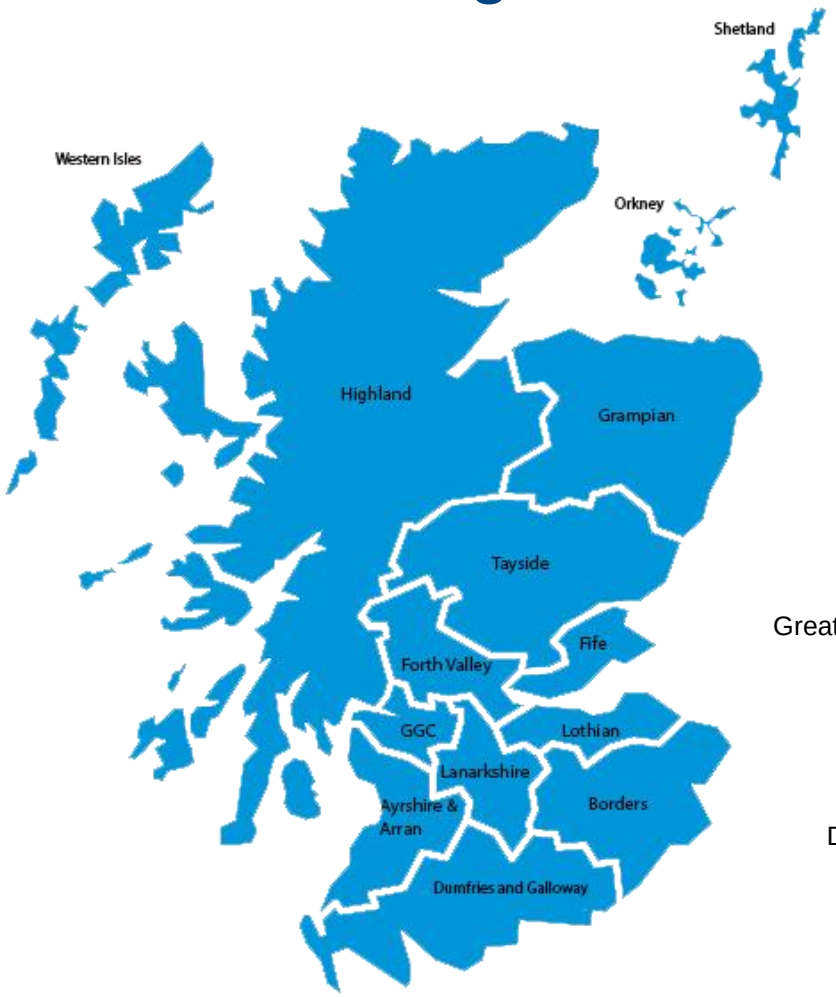
Previous Trisomy	n (%)	Missed Screening	n (%)
Singleton	125 (96.9%)	Singleton	4 (100%)
Twin	4 (3.1%)		
SPR	3 (2.3%)	SPR	0
T21	1		
T18	1		
T13	1		
Failed	1 (0.8%)	Failed	0
Not tested	3 (2.3%)		
Unsuitable	2 (1.5%)		
Previous Turners	1 (0.75%)		

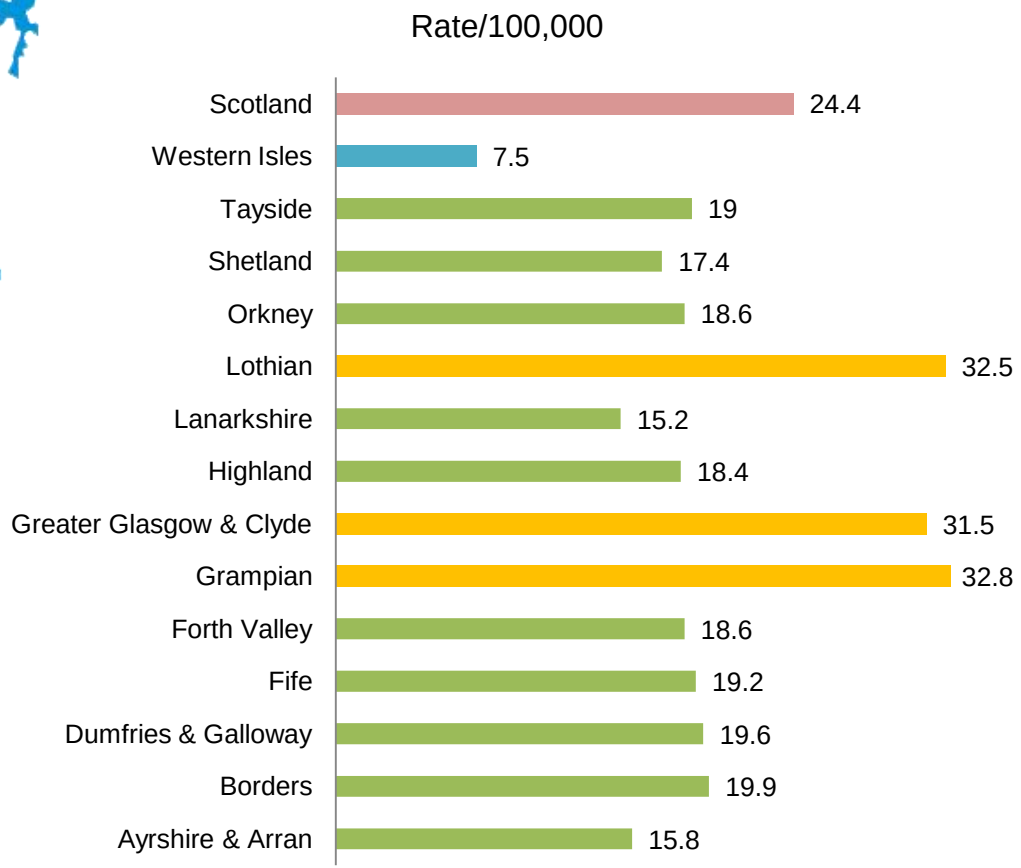
Referral Rates for NIPT



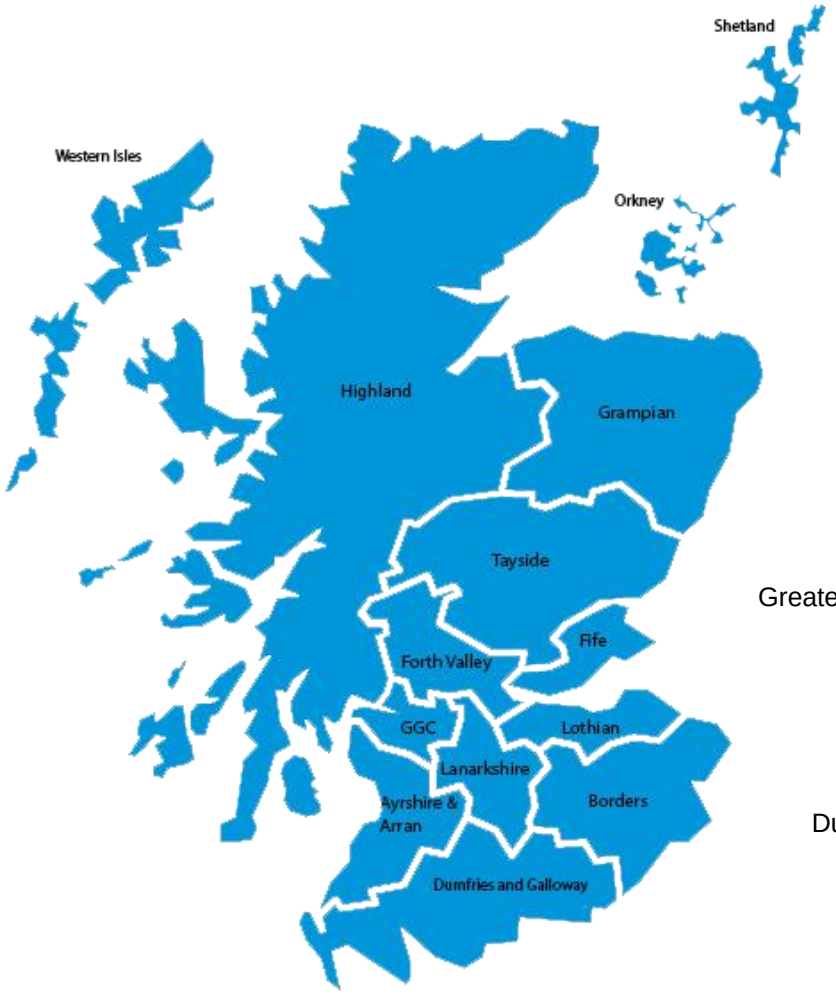


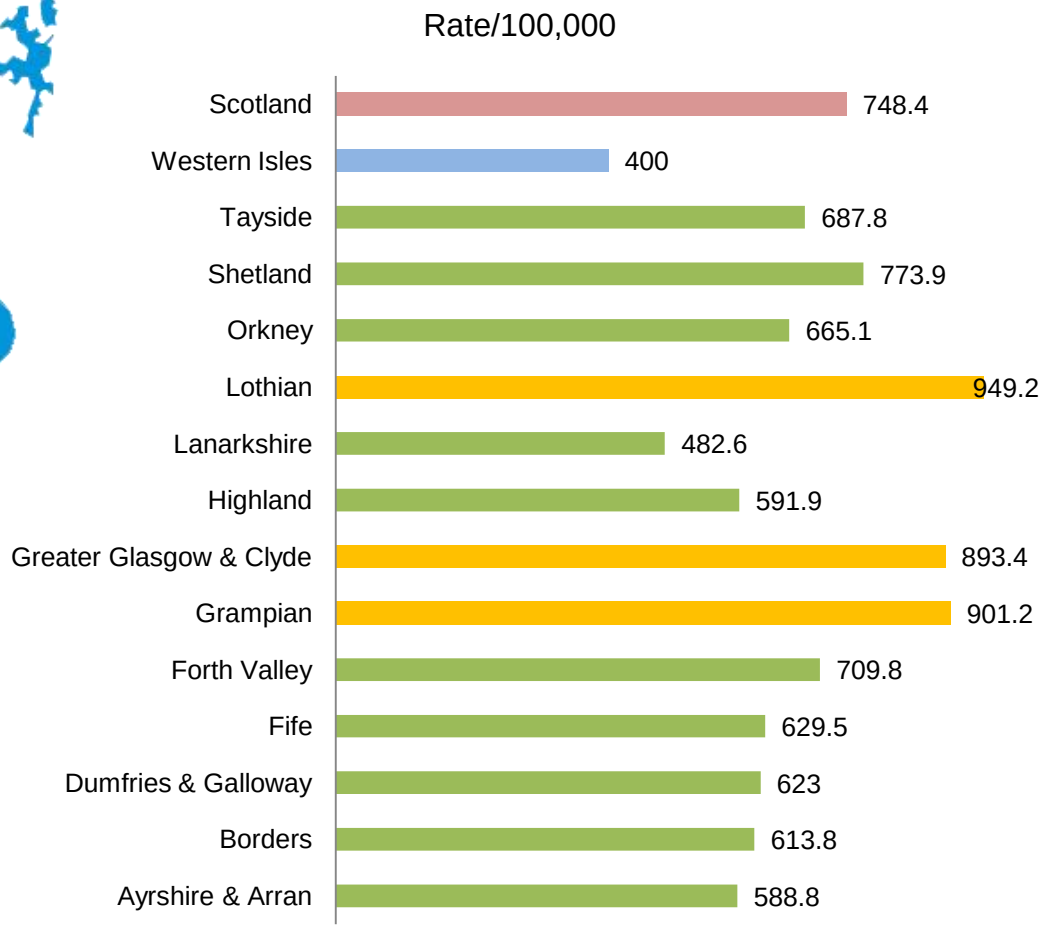
Higher Chance results – 1st & 2nd Trimester serum screening





Referrals for 1st & 2nd trimester serum screening





Opportunities for using NIPT

Approximately 32% of available wells on Veriseq-NIPT solution contain blanks
This capacity could be used to run clinically useful tests and reduce cost/referral for NIPT

- Abnormal scans/increased NT – evaluation of genome-wide NIPT to identify atypical chromosomal anomalies
- Fetal sexing
- ?

Acknowledgments

- Special thanks to the NIPT Team in Dundee

- Dr Lorna Rashid for serum screening data