Results of NIPT confirmation testing, following invasive prenatal sampling, highlight a need for consistent NIPT provision in the NHS

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Part of the British Society for Genetic Medicine

Birmingham Women's NHS
NHS Foundation Trust

Regional Genetics Laboratory

Positive results

NIPT

harmony PRENATAL TEST
NIFTY™
MaterniT21 PLUS
genesis genetics
verifi prenatal test
percept
panorama natera prenatal screen
the IONA test
progenity
Counsyl

Lucina NIPT
West Midlands RGL

Confirmation testing

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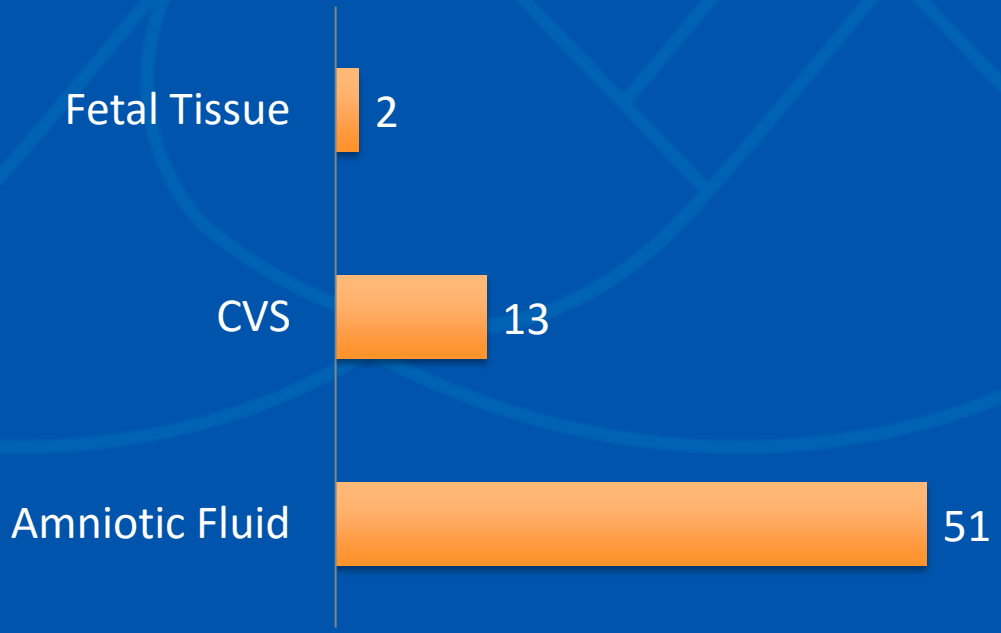
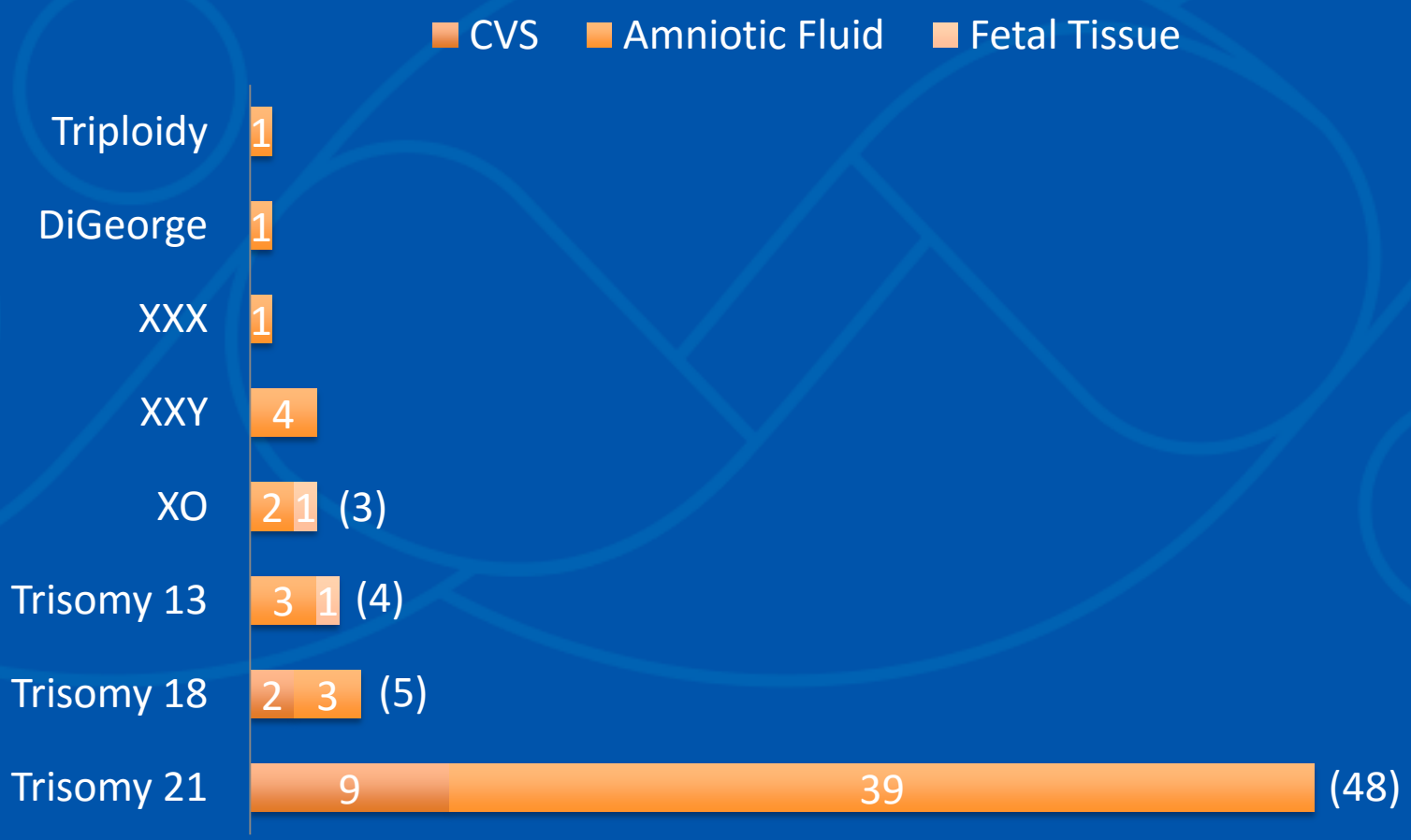
Audit of NIPT confirmations

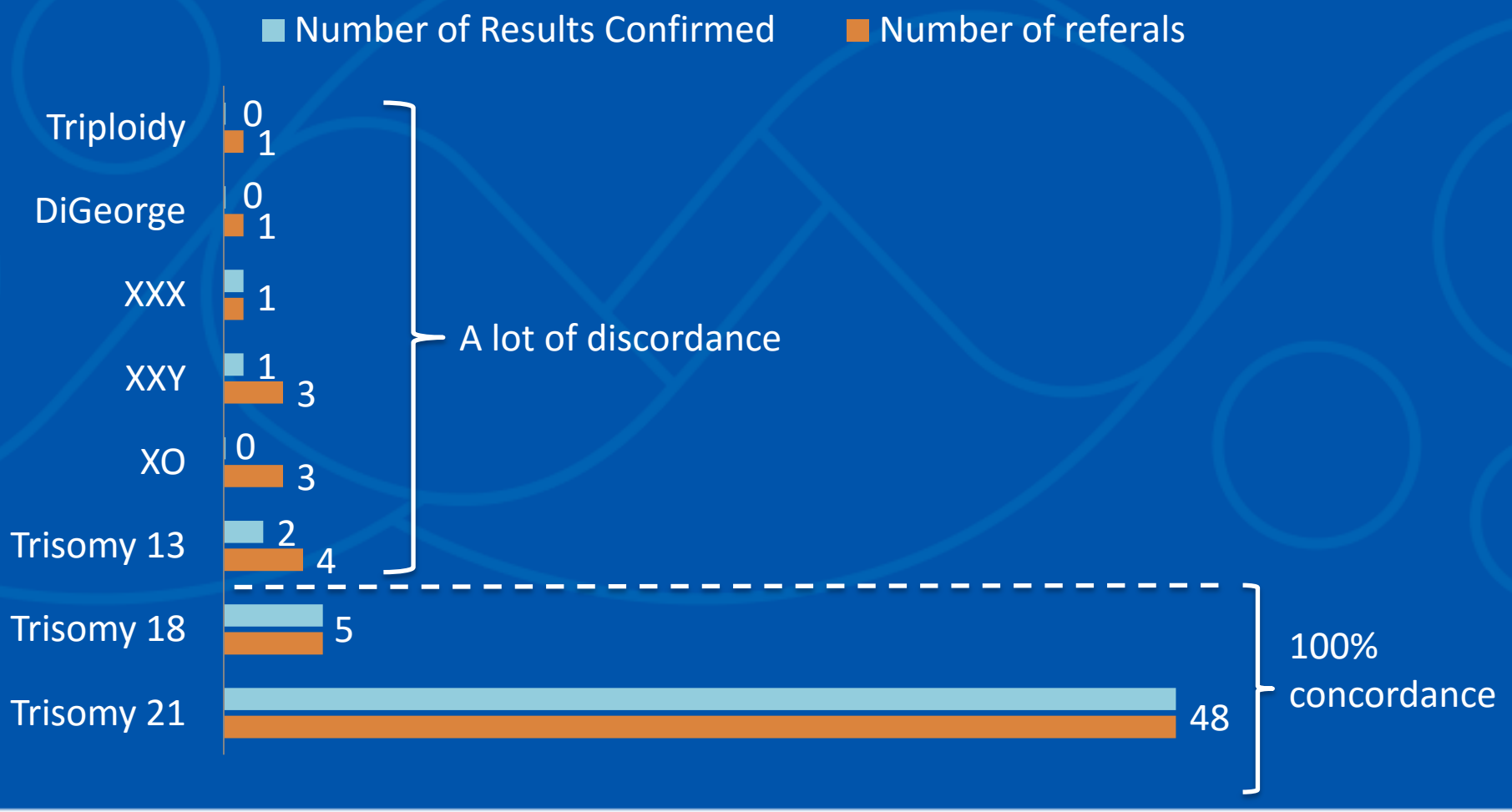
- June 2013- June 2016
- 66 diagnostic NIPT confirmation samples



Reasons for referral



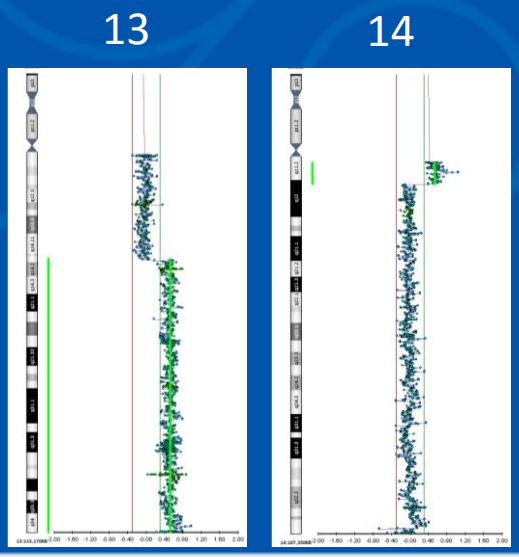
Results


Number of Results Confirmed
Number of referals
Triploidy
0
1
DiGeorge
0
1
XXX
1
1
XXY
1
3
XO
0
3
Trisomy 13
2
4
A lot of discordance
Trisomy 18
5
Trisomy 21
48
100% concordance

Trisomy 13

- 50% concordance (2/4 confirmed)
  1. Full Trisomy 13 confirmed
  2. Partial Trisomy 13
     - Fetal tissue
     - arr 13q14.3q34(46,381,711-115,092,619)x3,

       14q11.2q12(20,608,246-25,631,604)x3



Trisomy 13

- 50% discordance (2/4 not confirmed)
  1. 45% risk of trisomy 13 and no features on scan
  – Amniotic fluid, no evidence of trisomy

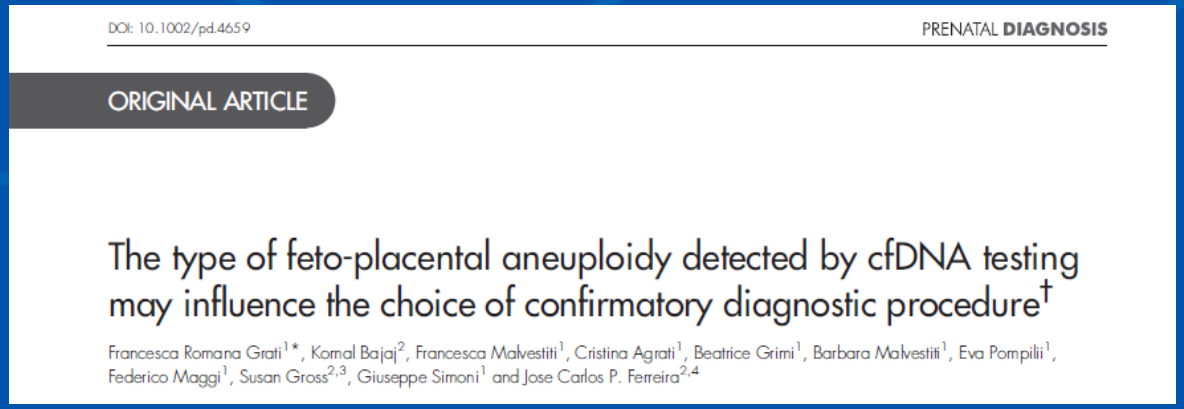
  2. CVS QF-PCR by private genetics lab in London confirmed T13
     - Report suggested amniotic fluid confirmation
       – ?Biallelic result by QF-PCR
       – No scan findings

  – AF taken by local NHS hospital and referred to our lab
  – No evidence of trisomy by QF-PCR or cytogenetics

  – Cultured CVS result from private lab also normal
  – Confined Placental Mosaicism

Methods of follow-up

- Amniotic fluid preferable
  - Prolonged patient anxiety
  - Trisomy 13 (and sex c'some abnormalities) in the absence of any scan findings, should await AF
  - Risk of CVS mosaicism and need for AF increased



DOI: 10.1002/pd.4659 PRENATAL DIAGNOSIS

ORIGINAL ARTICLE

The type of feto-placental aneuploidy detected by cfDNA testing may influence the choice of confirmatory diagnostic procedure†

Francesca Romana Grati[1]*, Komal Bajaj[2], Francesca Malvestiti[1], Cristina Agrati[1], Beatrice Grimi[1], Barbara Malvestiti[1], Eva Pompilii[1], Federico Maggi[1], Susan Gross[2,3], Giuseppe Simoni[1] and Jose Carlos P. Ferreira[2,4]

Grati et al, 2015

Turner syndrome

- 3 Turner syndrome referrals
  - No scan findings
  - 100% discordance by invasive sampling
    - CPM (frequently observed with X chromosome)
    - Maternal sex chromosome mosaicism (age related or true)…only ~10% of cfDNA is fetal (placental).
    - Vanished twin
  - ?Test when clear clinical indication only

Other sex chromosome referrals

- 4 Klinefelter syndrome referrals and 1 Triple X
  - 60% (3/ 5) discordant
    - CPM, maternal sex chromosome mosaicism, vanished twin

- 1% risk of Klinefelter!!
  - Patient anxiety +++++
    - 7th IVF cycle and first pregnancy
    - Didn't know this was something that could be identified, only wanted to exclude Downs (pre-test counselling!!!)
  - Counselling, sampling, testing (+maternal cyto)

Other referrals

- 1 DiGeorge syndrome -discordant
- 1 triploidy - discordant

- Results raise some ethical concerns
- Testing for additional conditions risks reversing expected reduction in invasive sampling that NIPT adoption promises

Conclusions

- National guidelines needed
  - NIPT testing and confirmation studies
  - Trisomy 13, 18 and 21 (XO with clinical indication)
  - Recommend AF
    - in particular for T13 without scan findings or sex chromosome aneuploidy follow-up
- National RGL study to collate audit data
  - Fiona.Togneri@bwnft.nhs.uk

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Patients and referring clinicians

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