First Trimester Screening & NIPT – What Do You Need to Know?

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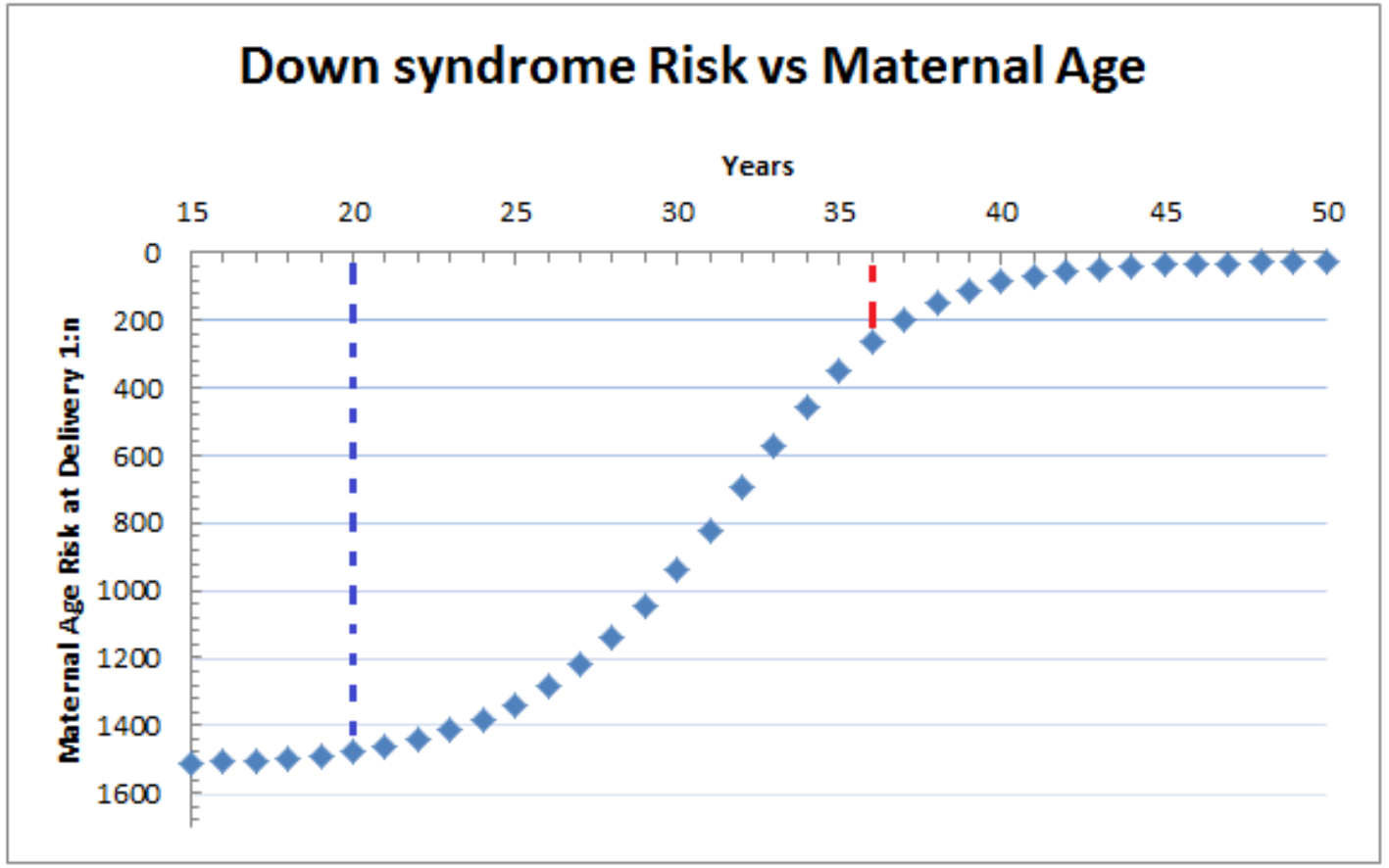
(WITH THANKS TO DR TRISTAN HARDY AND THE SAMSAS TEAM)

Available screening

- First trimester screen – good negative predictive value
  - Combined, biochemistry only
- Nuchal translucency ultrasound – includes anatomy screen and NB
- Second trimester screen
  - Still useful for a late booker
- Non invasive prenatal testing – good negative and positive predictive value
  - Harmony
  - NEST
  - NEST +
- Morphology ultrasound
- Carrier Screening and pre-eclampsia screening – may discuss later

First trimester screen

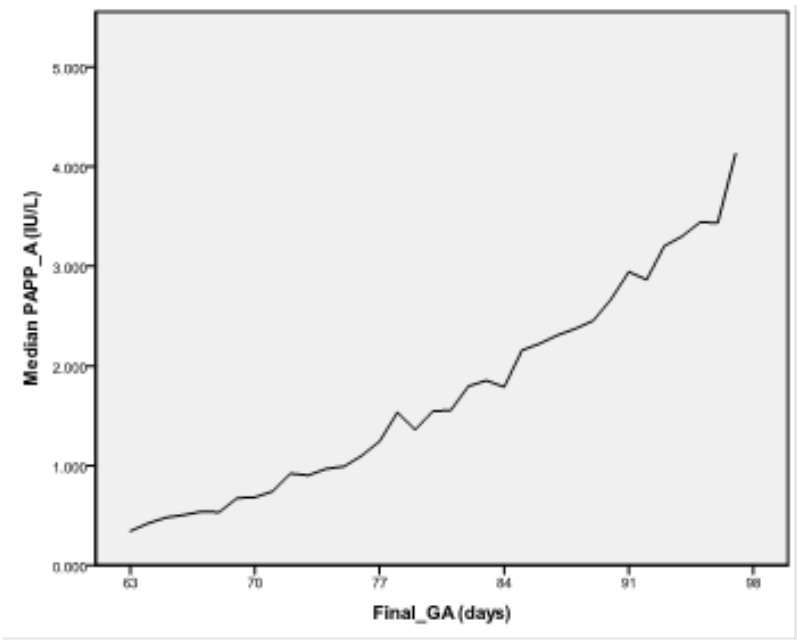
- SAMSAS bloods from 9 weeks – 13+6 weeks
  - Sensitive around 10 week mark
- NT ultrasound at 11-13+6
  - Sensitive around 12 week mark
- Risk cut off 1:250
  - About the T21 risk of a 35 yo
- Things to remember in low risk screen
  - NT cut of 3.5mm
    - May be an indicator of other problems, cardiac, anaemia, infection for example
  - Papp-A <0.35 MoM
    - May be an indicator for placental issues, PET, IUGR for example

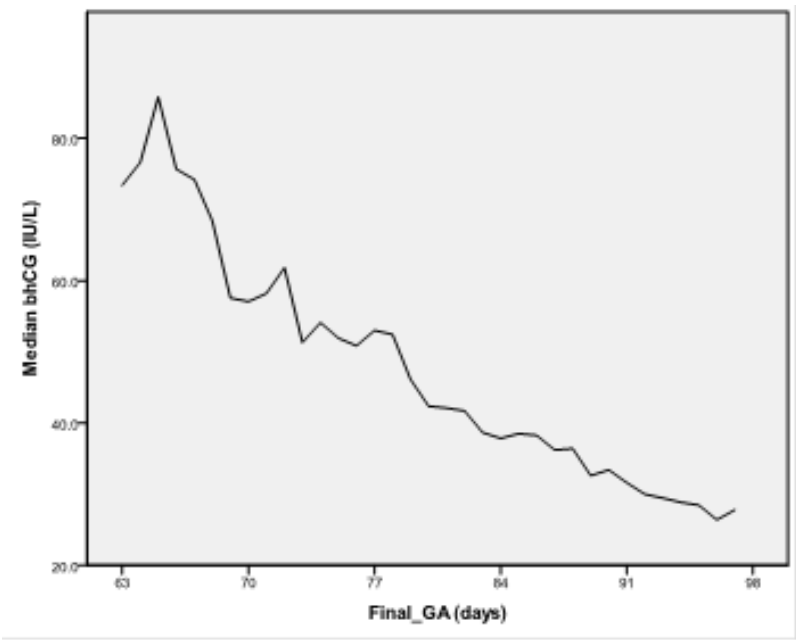

Down syndrome Risk vs Maternal Age
Years
15
20
25
30
35
40
45
50
Maternal Age Risk at Delivery 1:n
0
200
400
600
800
1000
1200
1400
1600

Things that affect the first trimester screen

- Maternal weight
  - High weight affects the risk, will usually lower a high risk result
- T1DM
  - affects the PappA
- Previously affected pregnancy
  - Some quotes as high as 1:100 recurrence, need to factor in
- Ethnicity
  - PappA MoM different in for example the African population
- Egg age, whether donor or own

Analyte concentration changes in 1st trimester.

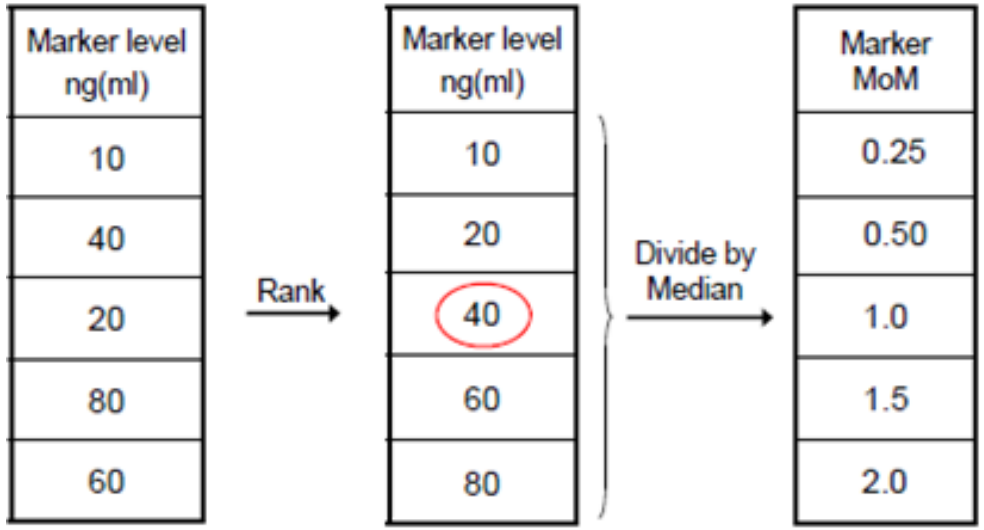




Relationship between the median concentration of PAPPA (left) and free ßhCG (right) as measured in maternal serum with increasing gestational age (GA) in normal first trimester pregnancy. Data obtained from SAMSAS program screening, total of 11330 cases.

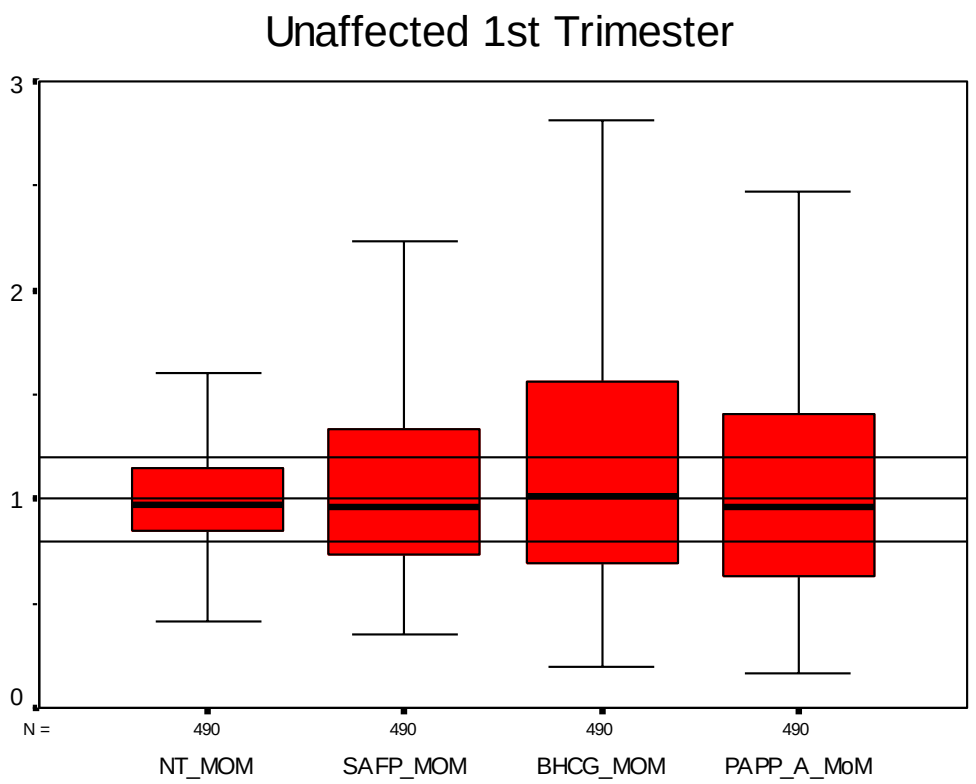
What is a MoM?

- Multiple of the population Median
- Why use MoM?
- Removes scale by converting values to a multiple of the analyte median (50th centile)
- 1MoM is equivalent to the 50th centile



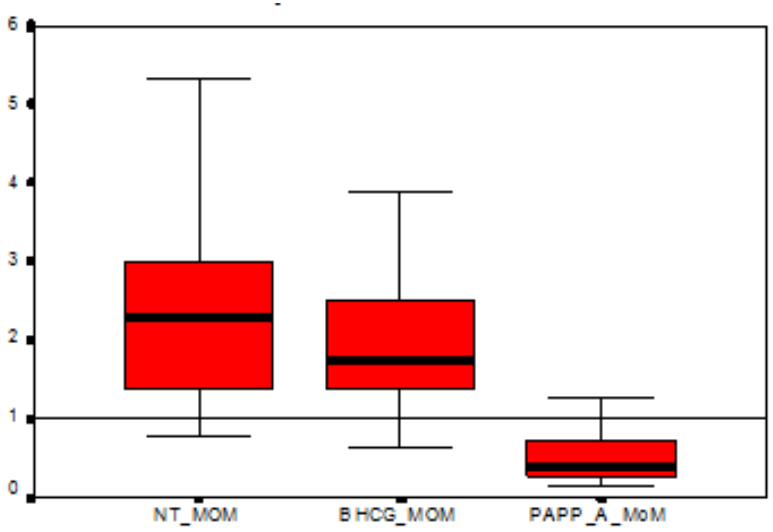
Bestwick, J, Intensive Course Screening for Down's syndrome. Wolfson Institute of Preventative Medicine. 2011

SAMSAS

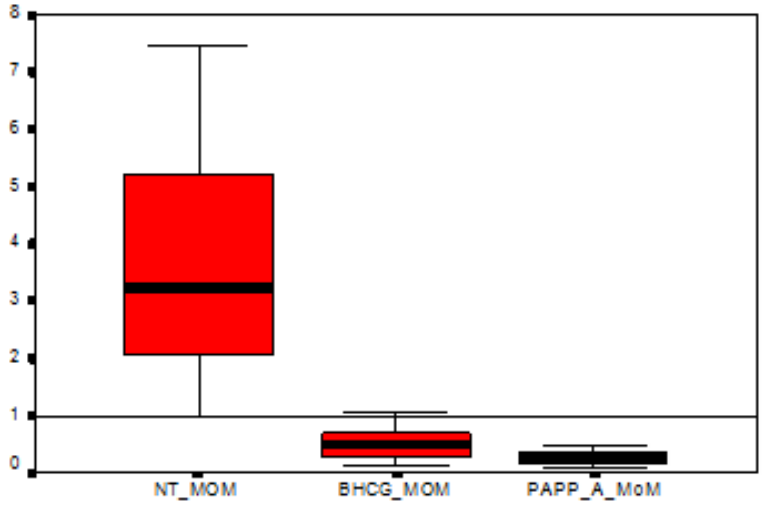

Unaffected 1st Trimester
3
2
1
0
N =
490
490
490
490
NT_MOM
SAFP_MOM
BHCG_MOM
PAPP_A_MoM

SAMSAS

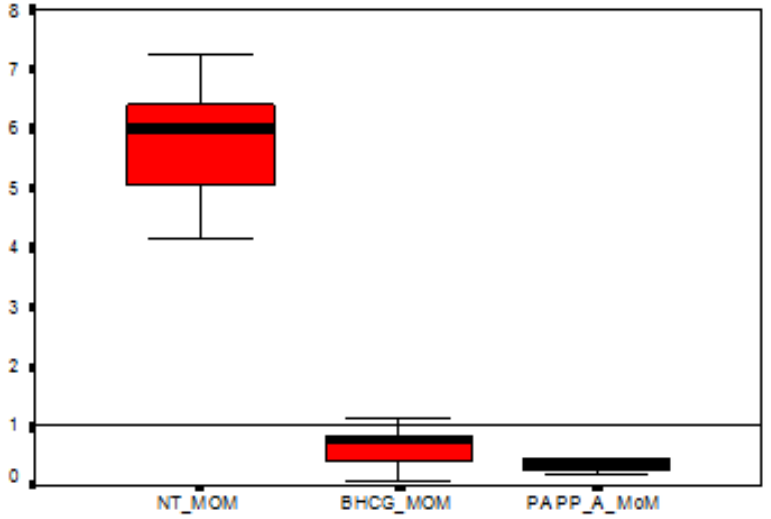
Trisomy 21-1st Trimester



Trisomy 18 -1st Trimester



Turner syndrome- 1st Trimester



	NT	PappA	HCG
T21	↑	↓	↑
T13	↑	↓	↓
T18	↑	↓	↓
Turners	↑↑	↓	↓

What to do?

- If low PappA
  - Add Uterine Artery Dopplers to the morph scan
  - If abnormal → refer to tertiary hospital for consideration of management and timing of further surveillance
- If high NT
  - Refer to tertiary centre for discussion of invasive testing and and infective screens
- If risk > 1:100
  - Refer to teritary center for discussion of invasive screen
- If risk 1:100 < 1:1000, discuss NIPT
- Any anatomical abnormalities on NT scan
  - refer to tertiary centre for second opinion scan and consideration if invasive screening

NEST vs Harmony

- Both are NIPT
- Both massively sequence DNA in parallel shotgun fashion
- Each relies on a "default normally chromosomal" mother
- Each about the same cost
- Both similar sensitivities and specificities
- NEST uses a "check all chromosomes" approach
- Harmony uses a "targeted approach" to the high risk chromosomes
- NEST can deliver a result at a lower fetal fraction
- Harmony available at more locations
- NEST collection centre can test for PLGF as part of PET screen

Possible concerns with extended panels

- One practice in NSW – over one year, 2 labs; PPV 1/17 for the non standard aneuploides

- https://www.abc.net.au/news/2021-02-16/doctors-push-better-education-some-prenatal-genetic-screening/13156408?utm_medium=content_shared&utm_source=abc_news_amp&utm_campaign=abc_news_amp&utm_content=mail&fbclid=IwAR1wNYwZiTOB0W6xjjnnyhIQazSUzBJWUOBox5kUlHOKzeXunRAM1KzpfLI