

SOUTH AUSTRALIAN MATERNAL SERUM ANTENATAL SCREENING (SAMSAS[®]) PROGRAM

www.wch.sa.gov.au/samsas.html



“providing obstetric support”

Robert Cocciolone,

Head, Antenatal Screening,
Department of Genetic Medicine, WCH



Government of South Australia
Children, Youth and Women's
Health Service

SOUTH AUSTRALIAN MATERNAL SERUM ANTENATAL SCREENING (SAMSAS[©]) PROGRAM

Longest running program in Australia,

-1978 Neural Tube Defect (NTD) screening

-1990/91 Down syndrome & other pregnancy pathologies(15-20wks).

- June 2001 First Trimester Down syndrome screening (10-14wks).

**Develop and manage own software and algorithms,
with one of the largest databases in Australia.**

Services SA, TAS & NT.

Offer Screening service support to PMH in WA

Integrated with Neonatal Screening database.

Electronic access to Cytogenetic and Ultrasound reports.

Access to WCH pregnancy outcome data.

SAMSAS audits published in the SA Birth Defects Register Report.

MSS is offered as a program with access to pre & post test information, counselling and diagnostic services – cvs, amnio & ultrasound.

Pre Test Information



Pre-test information for parents about

**Screening for
Neural Tube Defects and
Down Syndrome**

Information from the South Australian Maternal Serum Screening
Department of Chemical Pathology
Women's and Children's Hospital, North Adelaide 5008

Post Test Information



Information for parents from the South
Australian Maternal Serum Antenatal
Screening (SAMSSA) Programme

**"increased risk of
Down syndrome"**

What does it mean?



Information for Parents

**"increased risk of
Neural Tube Defect"**

what does it mean?

Information from the South Australian Maternal Serum Screening
Department of Chemical Pathology
Women's and Children's Hospital, North Adelaide 5008

Information for
Health Professionals
about Maternal Serum Screening

www.wch.sa.gov.au/samsas.html

SAMSAS[©]

Biochemical Markers;

2nd Trimester

AFP

free β hCG

uE3

1st Trimester

free β hCG

Papp-A

Other Markers;

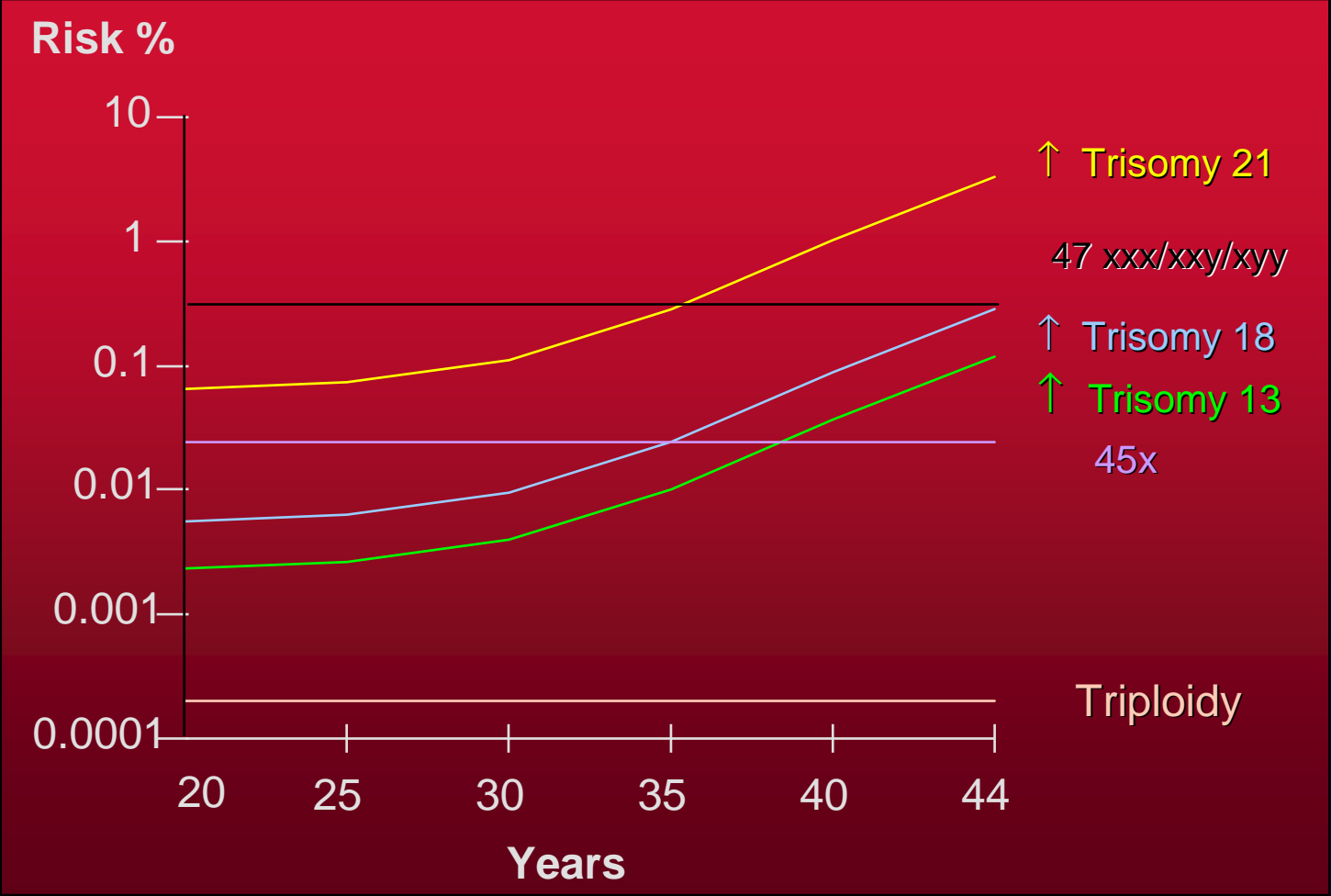
Nuchal Translucency

← Maternal age →

← Gestational age →

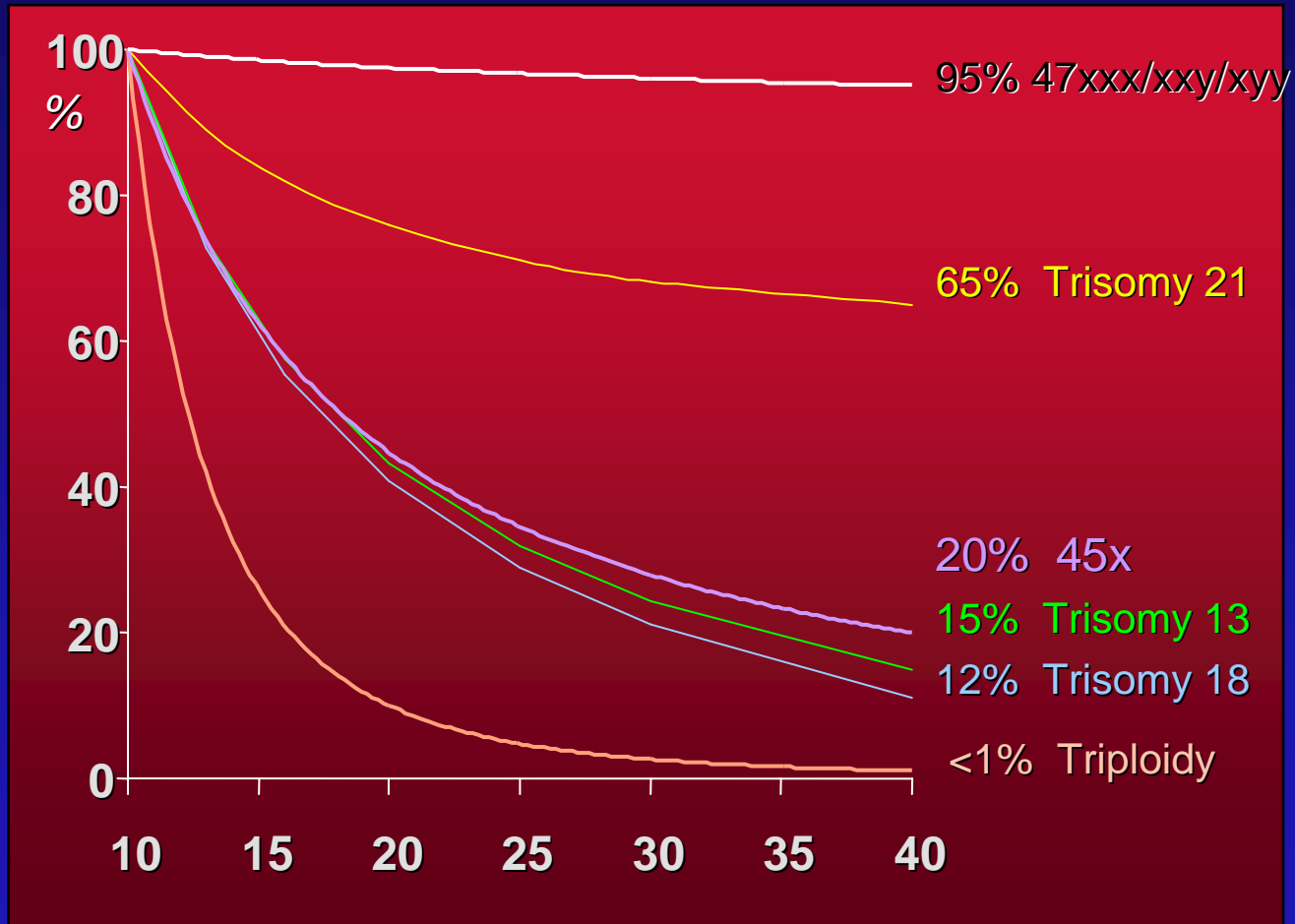
← Maternal weight →

Background Risk of Aneuploidy vs Maternal Age



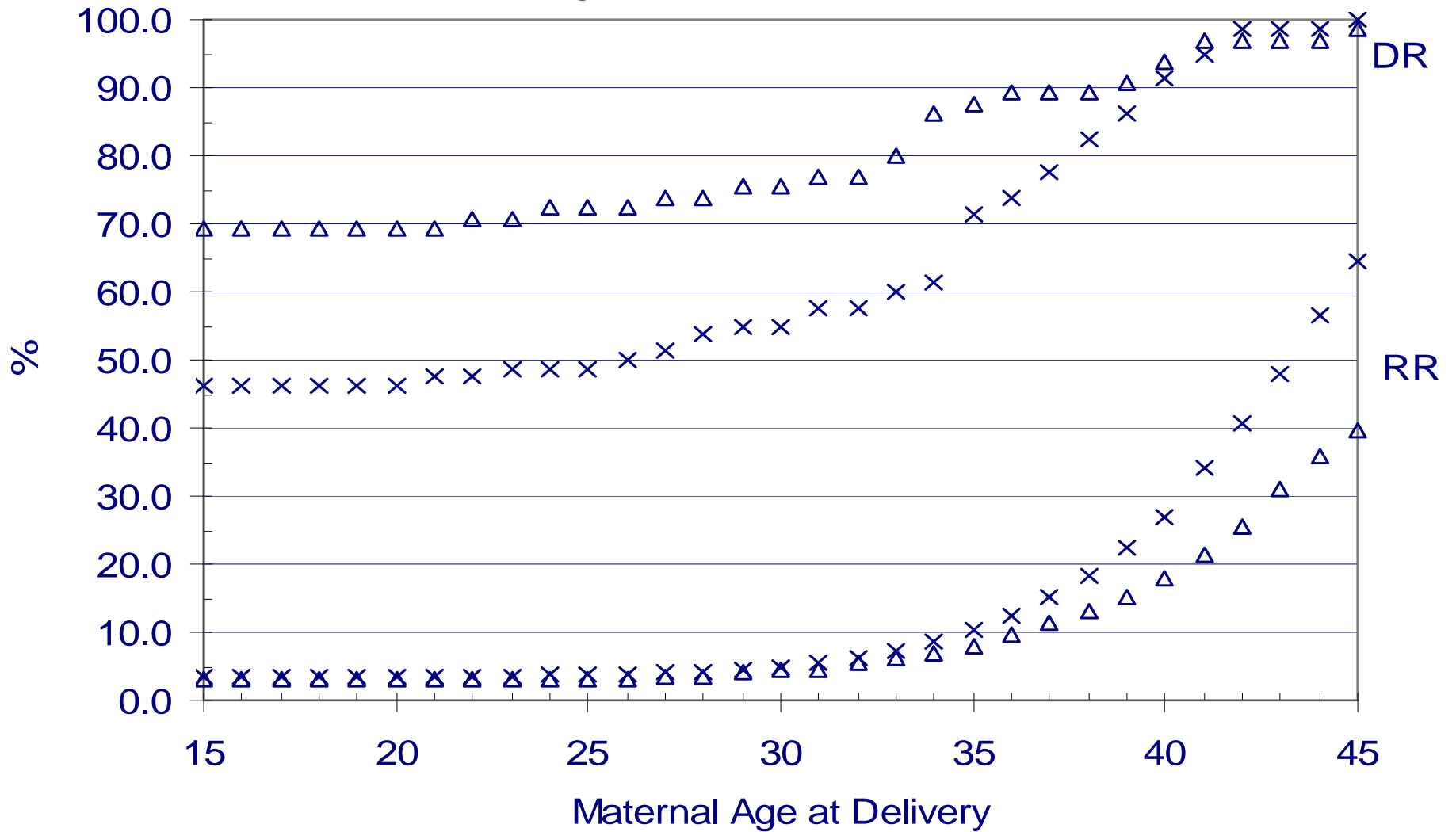
Snijders et al 1995

Background Risk of Aneuploidy ↓ with GA



Snijders et al 1995 Nicolaidis et al., The 11-14-week scan, London 1999

Age Specific Performance Comparison of 1st and 2nd Trimester Screening. Maternal Age vs Recall and Detection



× %RR 2nd × %DR 2nd △ %RR 1st △ %DR 1st

SAMSAS[©]

	Maternal Age Screening alone	Second trimester biochemical screening	First trimester combined screening
Amniocenteses performed per case detected	250	40	20
Fetal loss per case of Down syndrome detected	1 : 1	1 : 5	1 : 10

Wald NJ, Rodeck C, Hackshaw AK, Walters J, Chitty L, Mackinson AM. First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study (SURUSS). Health Technol Assess 2003; 7(11):1-77

Marker Levels Change Significantly with Gestation

Measured levels are converted to Multiples Of the Population Median or **MoM** values.

Reference is therefore 1 MoM

beta hCG at 10 wks GA

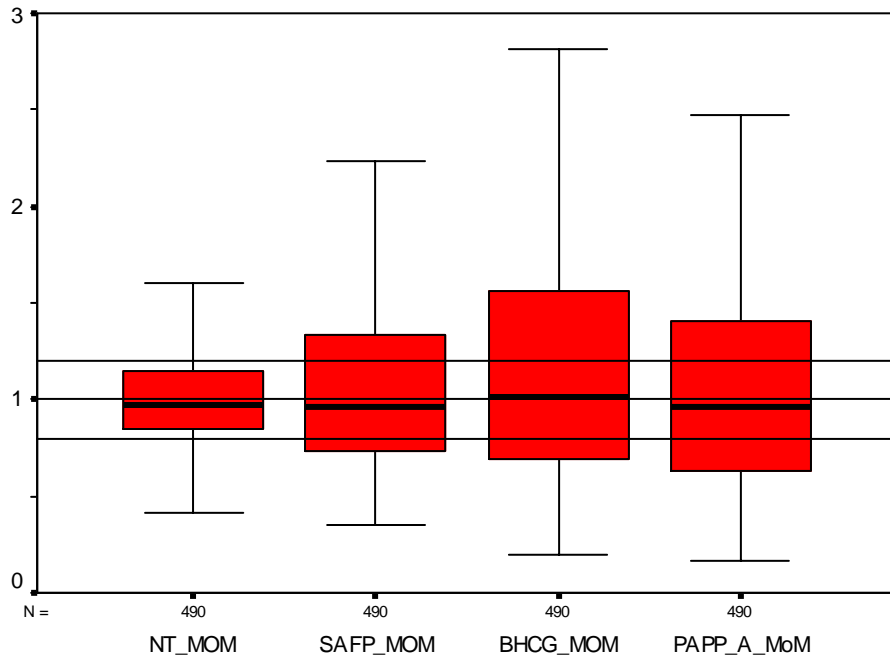
Patient $\frac{120 \text{ IU/L}}{60 \text{ IU/L}} = 2 \text{ multiples}$

Median 60 IU/L

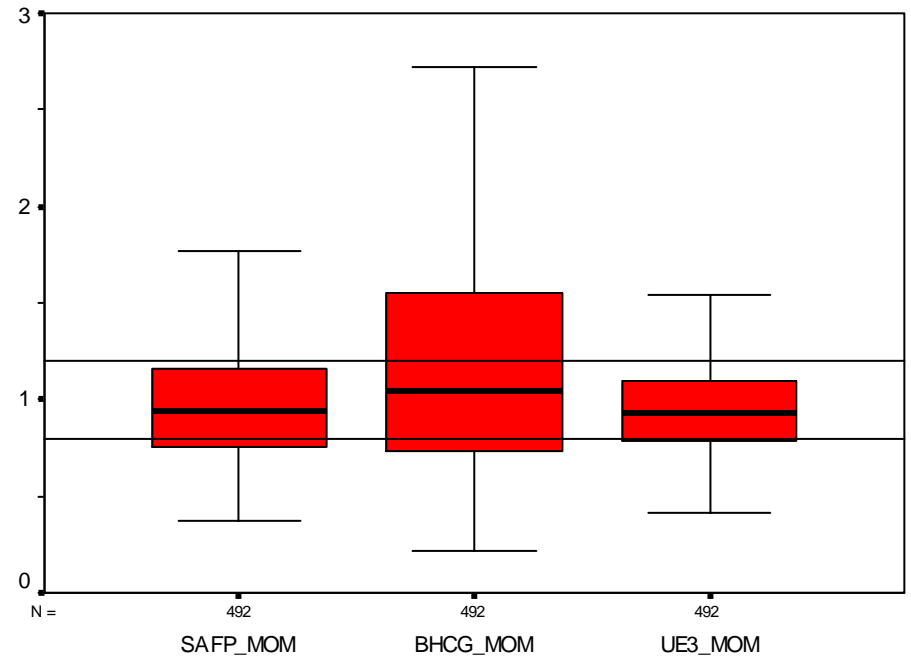
MoMs are independent of gestational age and concentration Units

LogMoM values are used in calculations as they exhibit a Gaussian distribution (Mean +/- SD)

Unaffected 1st Trimester



Unaffected 2nd Trimester



RISKS

1. **Open Neural Tube Defects (NTD)**
 2. **Down syndrome**
 3. **Other**
-

NTD

2nd Trimester

↑ **AFP ≥ 2 MoM**

Independent of Maternal Age

Morphology scan

~ 1/30 will have a NTD

Down syndrome

1st & 2nd Trimester

↑ **Risk ≥ 1 in 300**

Age Dependent

CVS / Amnio

~ 1/20 or 1/40 will have DS

Other Not NTD & Not DS: **AFP < 2 MoM & DS risk is < 1 in 300**

But

Biochemical results fall outside the Normal expected.

NTD

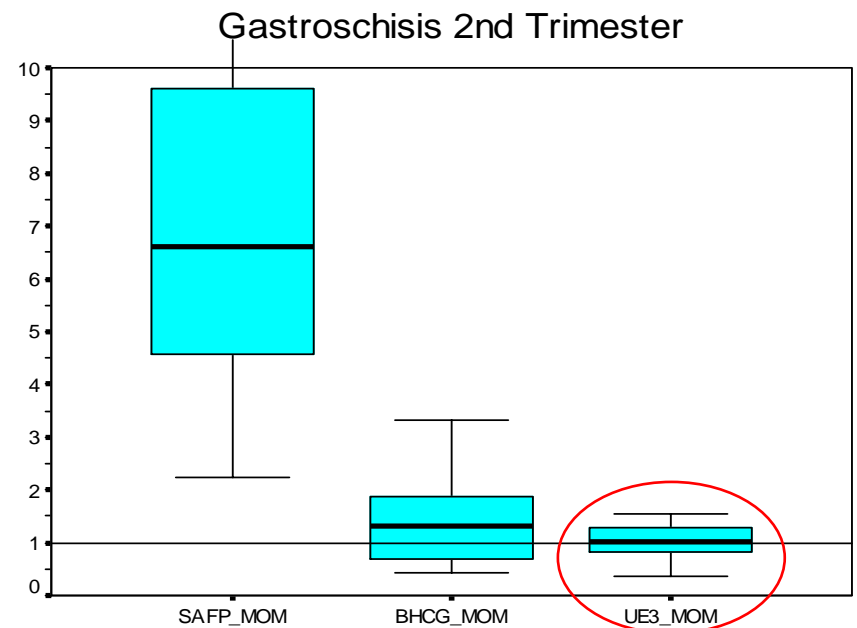
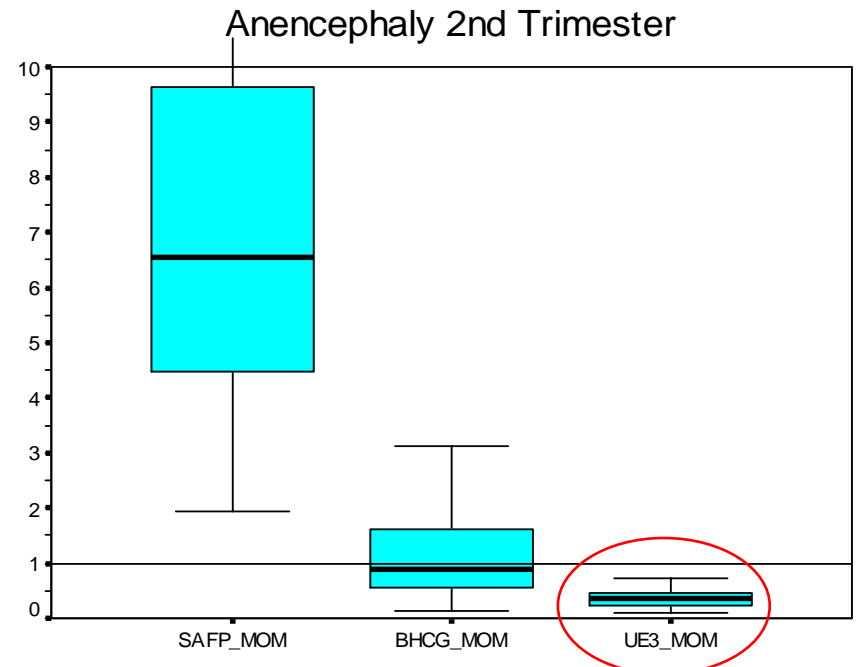
A review of SAMSAS pregnancies screened N = 67,965.

1,976 or 2.9% had a raised AFP > 2 MoM.

Conditions found in the raised AFP group.

NTD	61 (1 in 32)	32 anencephaly 27 meningomyelocele 2 encephalocele
Other Fetal Anomalies	19 (1 in 104)	5 exomphalocele 9 gastroschisis 2 triploidy 2 trisomy 13 1 Turner syndrome
FDIU	48 (1 in 41)	Fetal death at time of screen
Other Pregnancy Complications subsequent to maternal serum screen.	75 (1 in 26)	Missed Abortion, PROM, stillbirth, other fetal demise.
Unsuspected Twins	47 (1 in 42)	
TOTAL ANOMALIES IN RAISED AFP GROUP	250 (1 in 8)	

NAD in 1726/1976 or 87.4% with raised maternal serum AFP.



Down syndrome

A review of SAMSAS pregnancies screened N = 65,328.

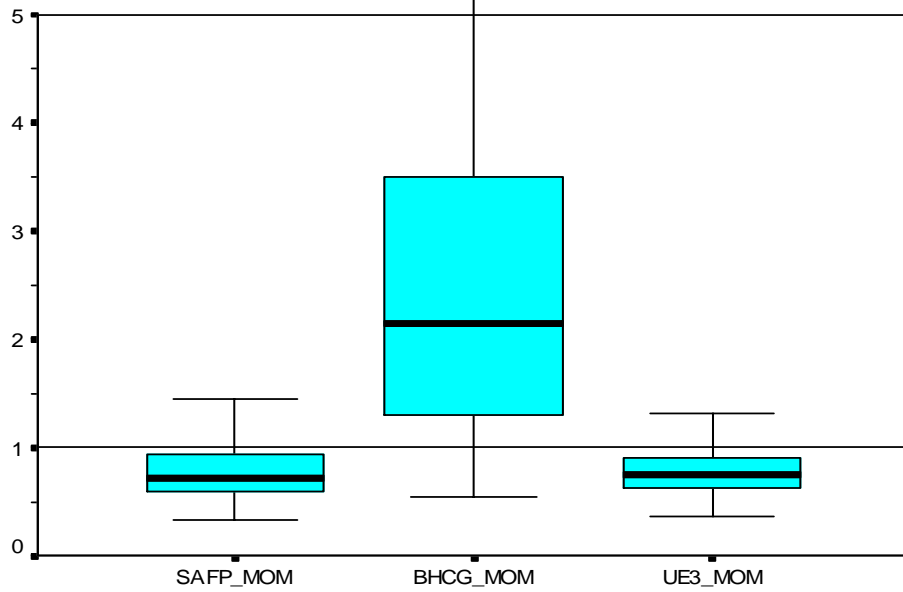
3,481 or 5.3 % were reported at increased risk for Down syndrome.

Conditions found in the increased risk group.

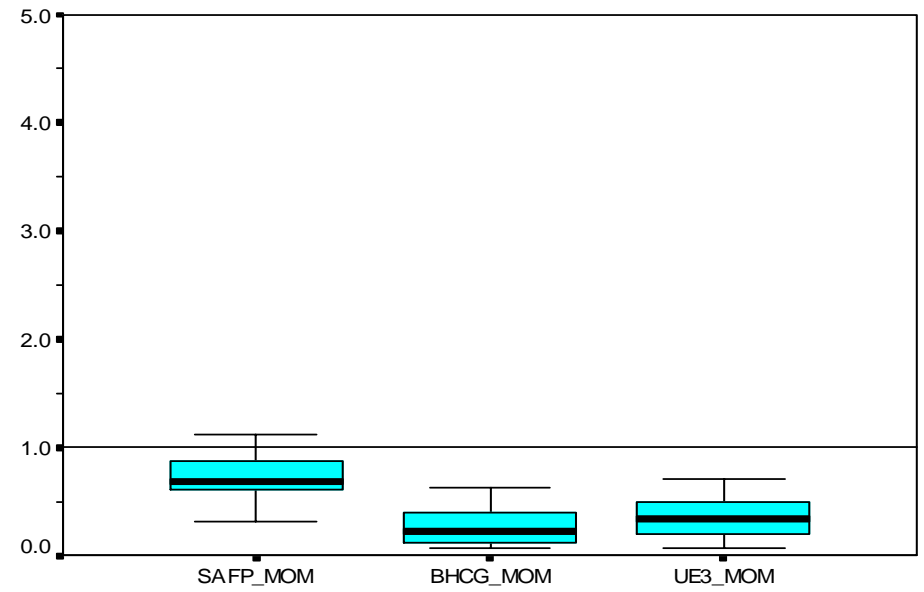
Down syndrome	84 (1 in 41)
T18, T13, Triploidy	9 (1 in 386)
Male & Female Sex Chromosome Abnormalities	12 (1 in 290)
Unbalanced & balanced <i>de novo</i> karyotypes	4 (1 in 870)
Balanced Translocations or inversions	17 (1 in 204)
TOTAL ANOMALIES in increased risk group	126 (1 in 28)

NAD in 3355/3481 or 96.4% with an increased risk report.

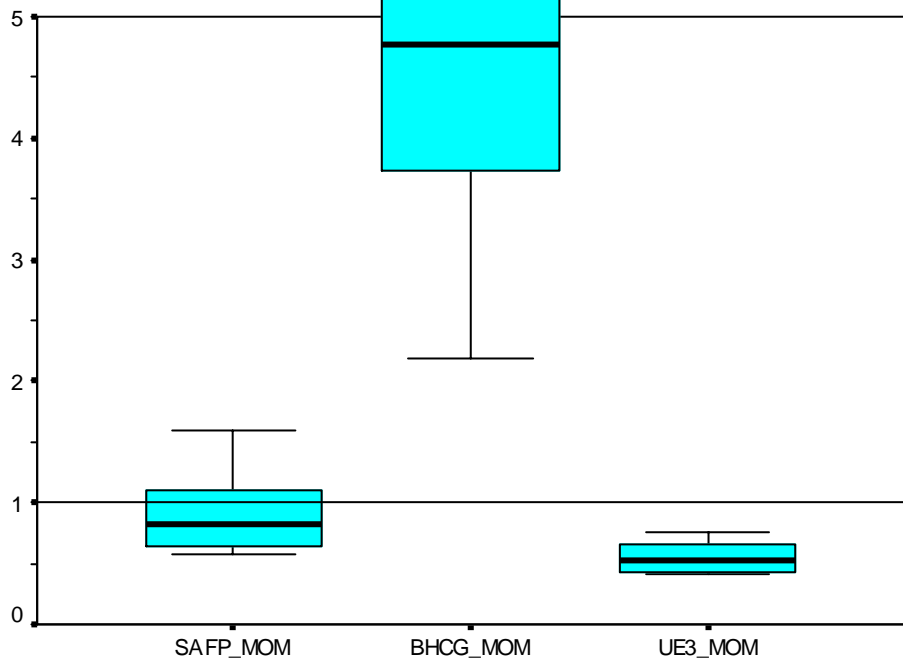
(GA Overestimate) T21 2nd Trimester



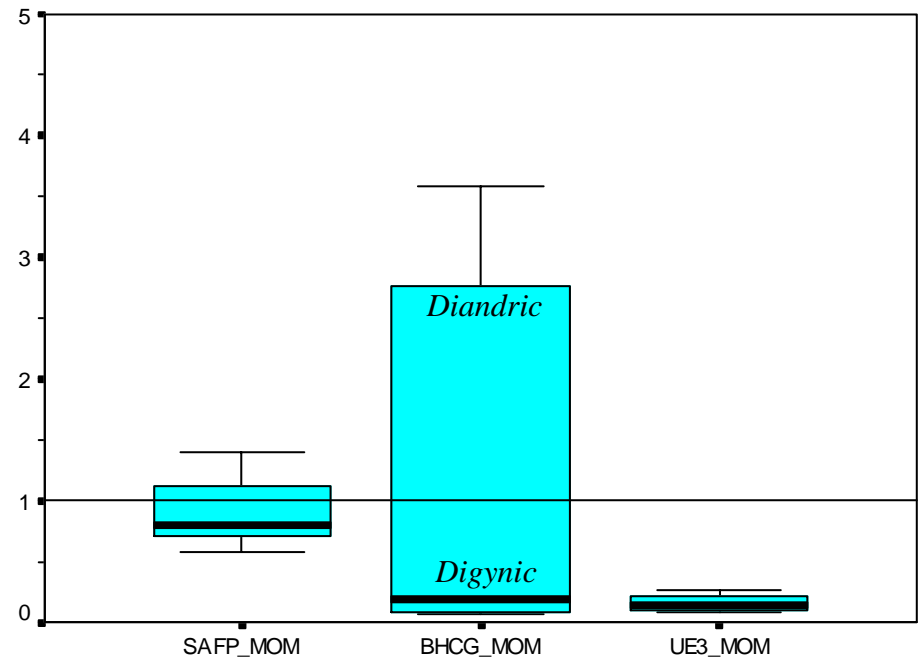
T18 2nd Trimester



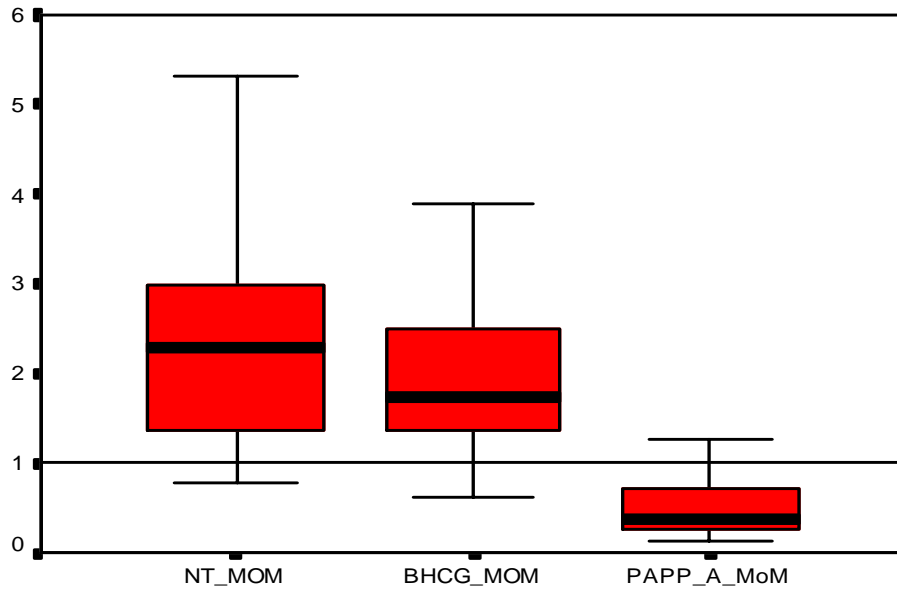
Turners 2nd Trimester



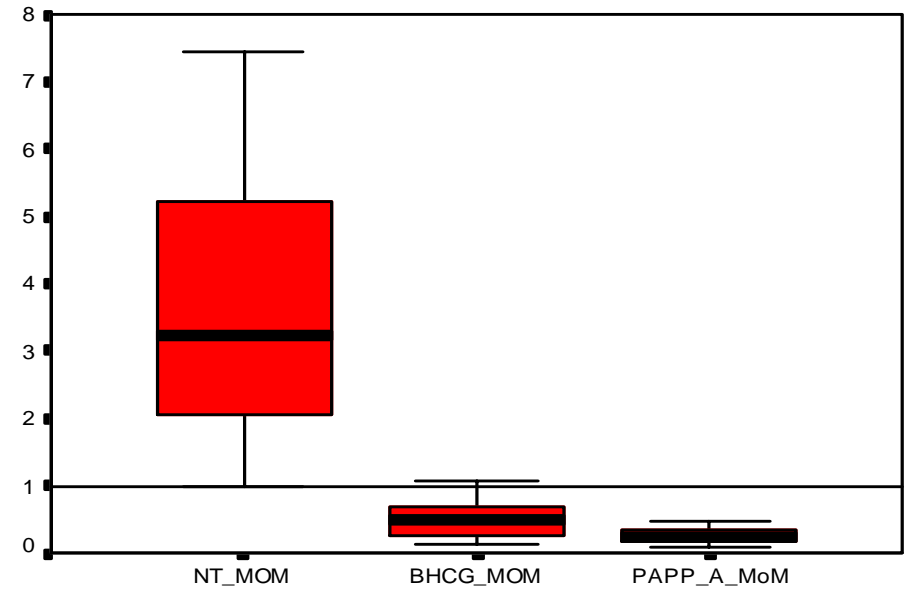
Triploidy 2nd Trimester



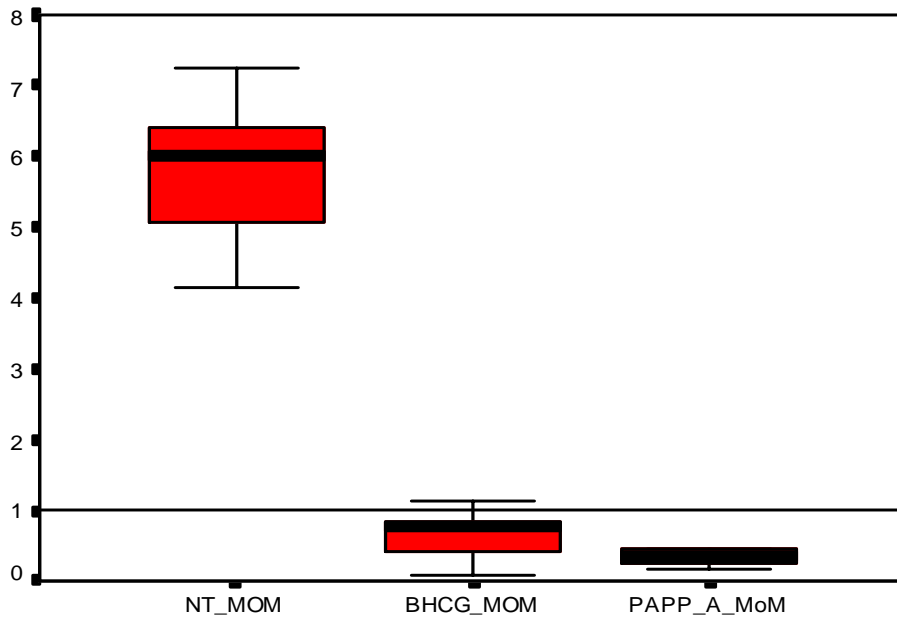
Down syndrome First Trimester



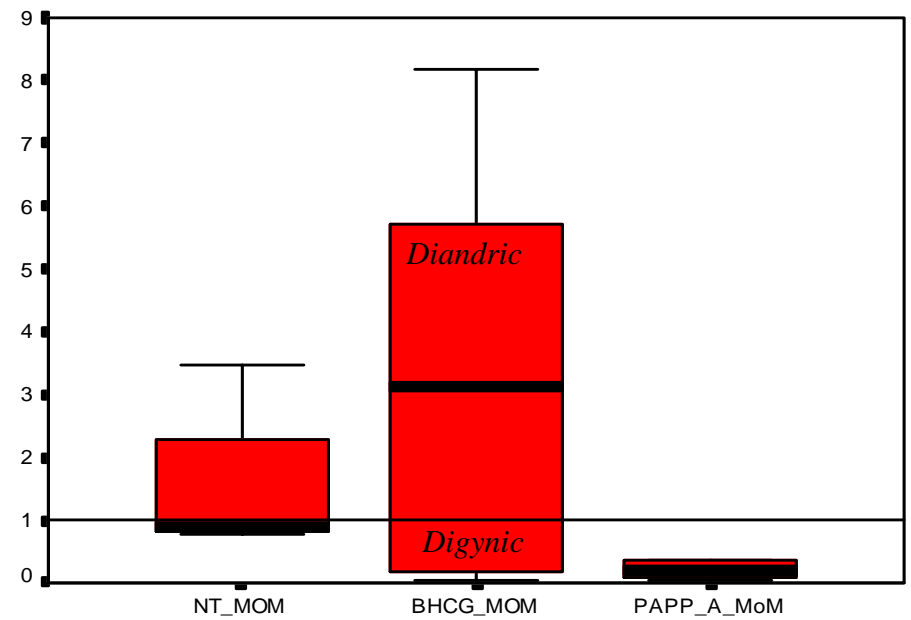
Trisomy 18 First Trimester



Turners syndrome First Trimester



Triploidy First Trimester



~thus far~

	Marker	Condition
↑	AFP	Congenital Abnormality/Twins/Non Viability
↓	AFP	Aneuploidy
↑	Beta hCG	Aneuploidy
↓	Beta hCG	Aneuploidy
↓	UE3	Aneuploidy
↓	Papp-A	Aneuploidy

Not NTD & Not Downs Profiles

SAMSAS screened pregnancies N=62,563

1st Trimester N= 26,914

Profile

Non Downs

N= 206 (0.77%)

2nd Trimester N= 35,649

Profile

Not NTD Not Downs

N= 123 (0.35%)

Total N = 329 (0.53%)

OUTCOMES

NOT KNOWN

N = 25 (7.6%)

NORMAL

N = 103 (31.3%)

FETAL DEATH

N = 171 (52%)

ABNORMAL

N = 30 (9.1%)

9 x Triploidy, 9 x T18

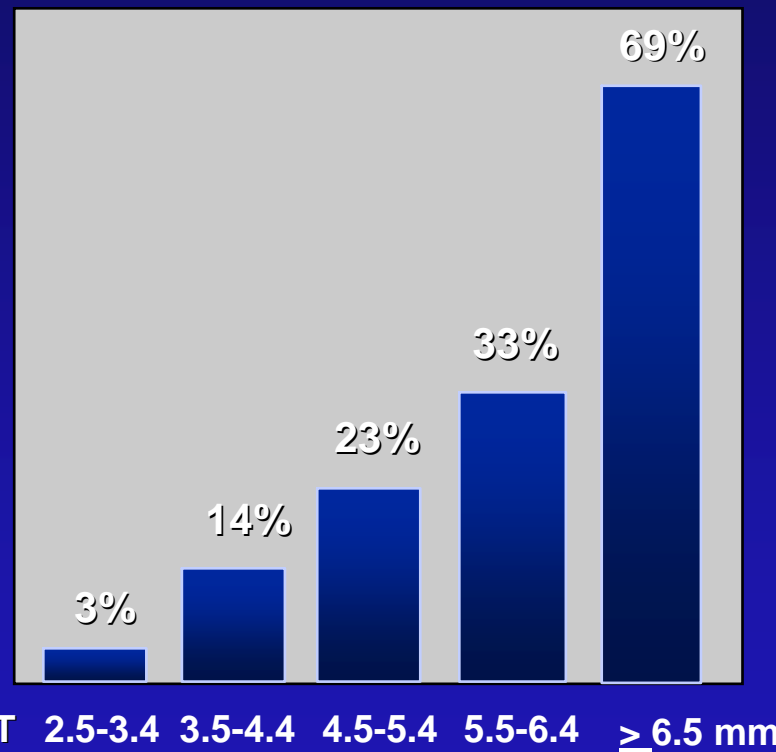
3 x T15, 3 x Anenceph. 1st Tr

2 x Turners, 2 x Mult. Abn.

2 x Metabolic

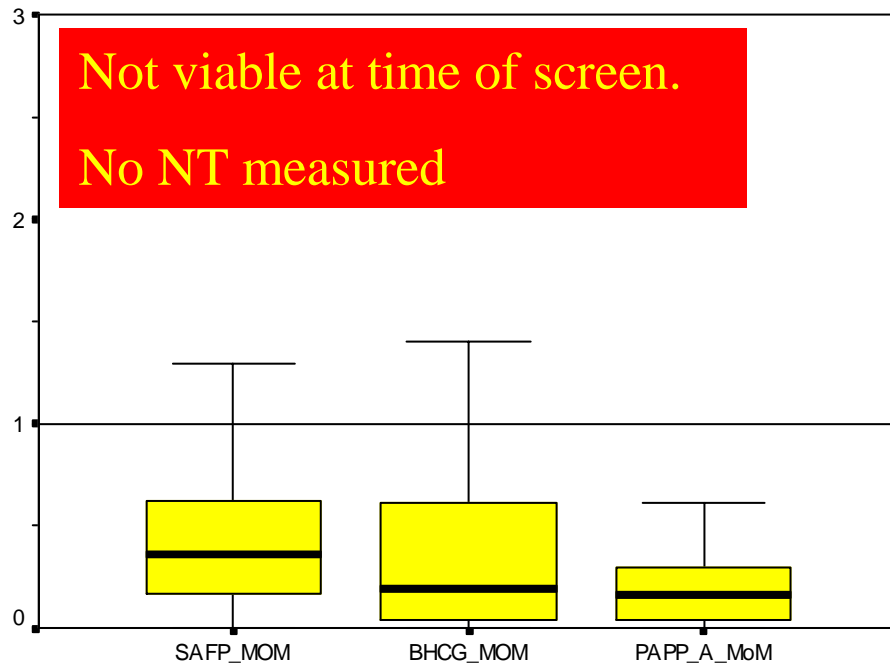
Frequency of death and/or major anomaly in fetuses with an increased nuchal translucency and a normal karyotype

Death or major anomaly



Nicolaides KH. Fetal nuchal translucency. Am J Obstet Gynecol 2004

1st Trimester ? Fail

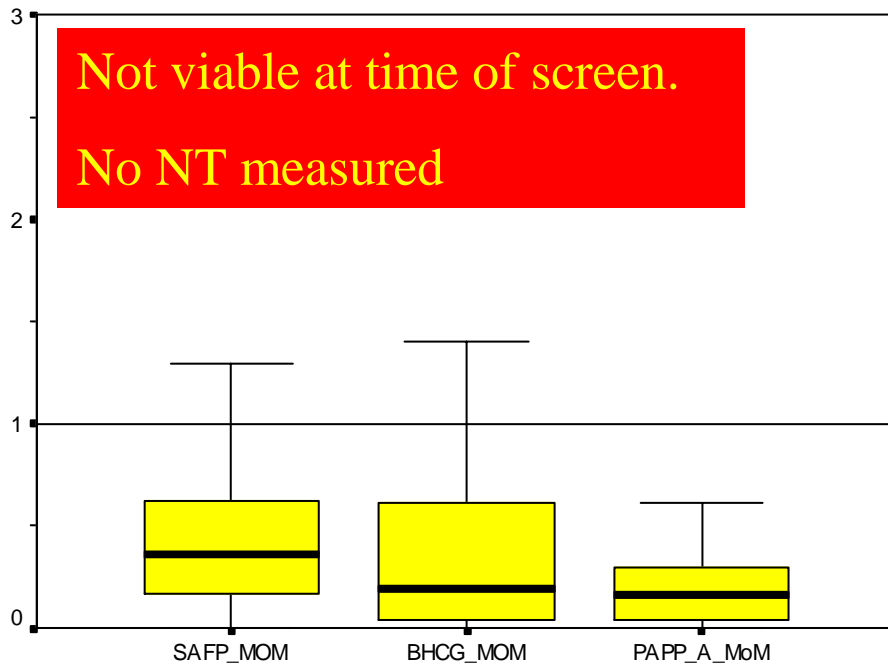


- N= 149
- Not Known= 4
- Normal= 2 (Obese~no NT)
- Fetal Death= 137
- Abnormal= 6 (1xTriploidy,2xXO,2xT15,1xAnencephaly)

•**Anomalies Found 143/145**

•**Odds 1/1 (98.6%)**

1st Trimester ? Fail

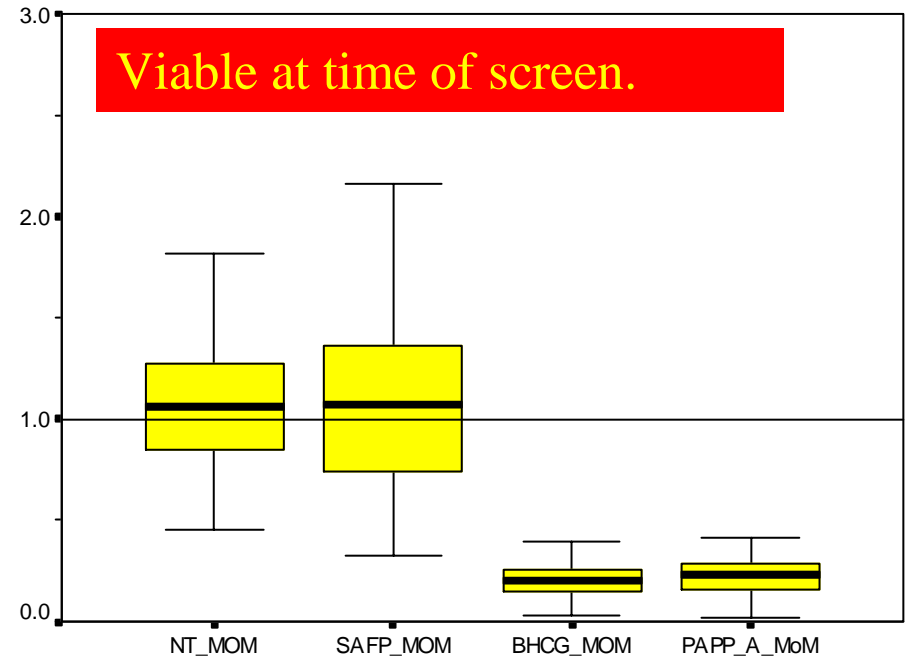


- N= 149
- Not Known= 4
- Normal= 2 (Obese~no NT)
- Fetal Death= 137
- Abnormal= 6 (1xTriploidy,2xXO,2xT15,1xAnencephaly)

•Anomalies Found 143/145

•Odds 1/1 (98.6%)

1st Trimester Not Downs

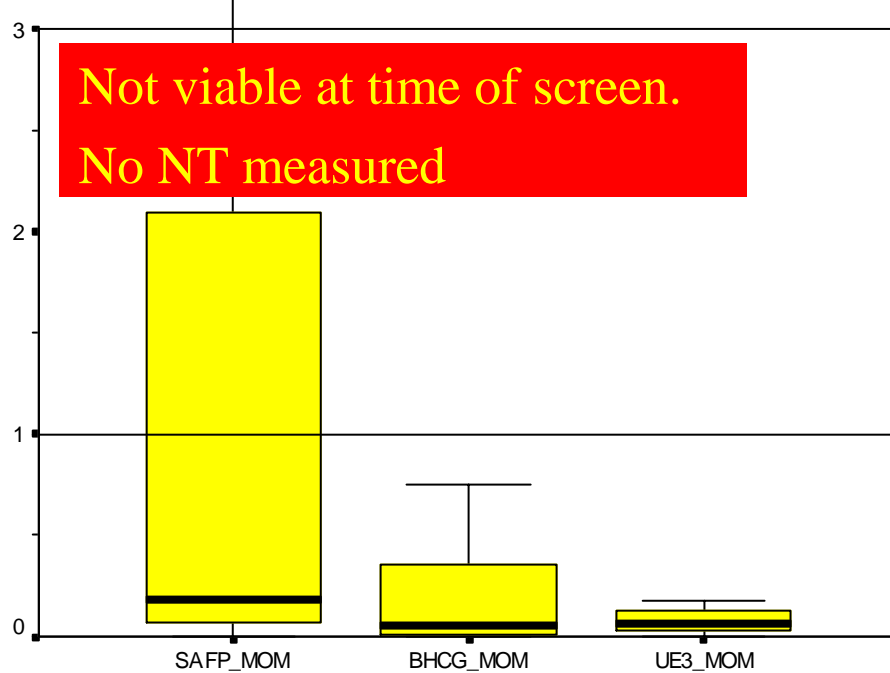


- N= 57
- Not Known= 7
- Normal= 39
- Fetal Death= 3
- Abnormal= 8 (4xTriploidy,1xT18,1xOther,1xAnencephaly,1xRenal)

•Anomalies Found 11/50

•Odds 1/4.5 (22%)

2nd Trimester ? Fail

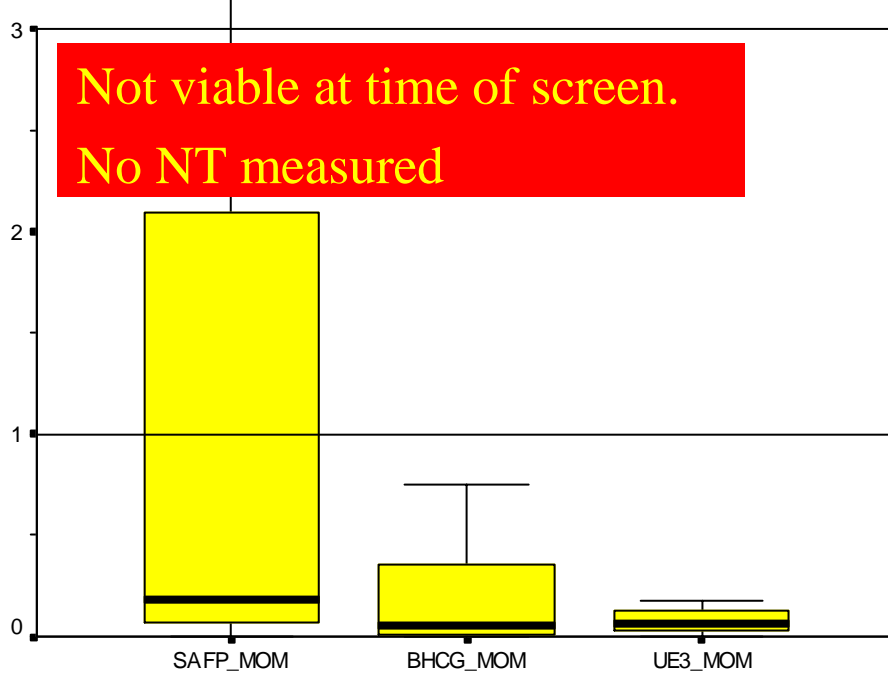


- N= 24
- Not Known= 2
- Normal= 0
- Fetal Death= 18
- Abnormal= 4 (2xT18,1xAnencephaly,1xMultiple Con. Abn.)

•**Anomalies Found 22/22**

•**Odds 1/1 (100%)**

2nd Trimester ? Fail

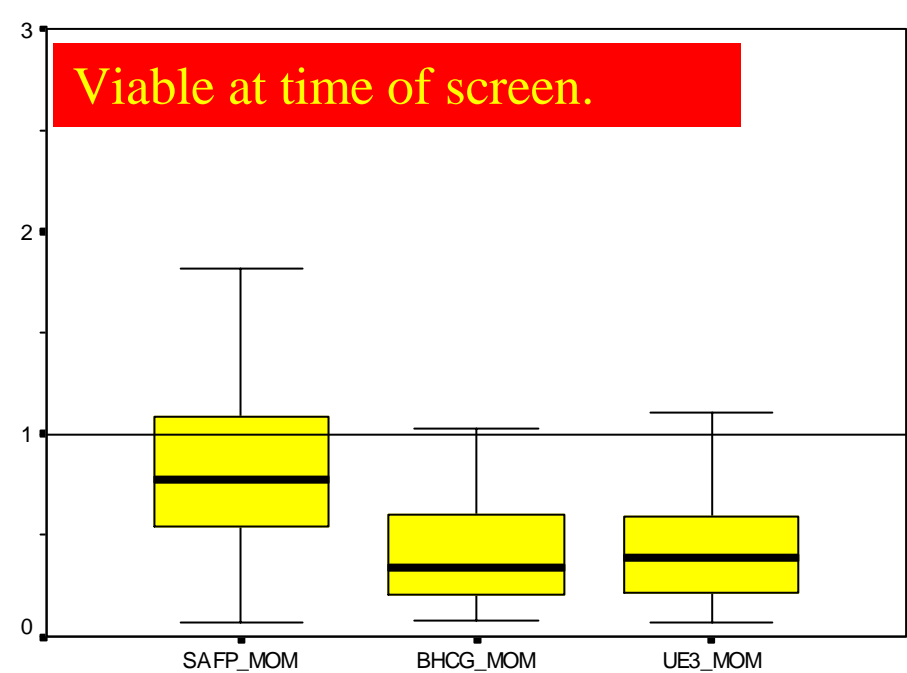


- N= 24
- Not Known= 2
- Normal= 0
- Fetal Death= 18
- Abnormal= 4 (2xT18,1xAnencephaly,1xMultiple Con. Abn.)

•**Anomalies Found 22/22**

•**Odds 1/1 (100%)**

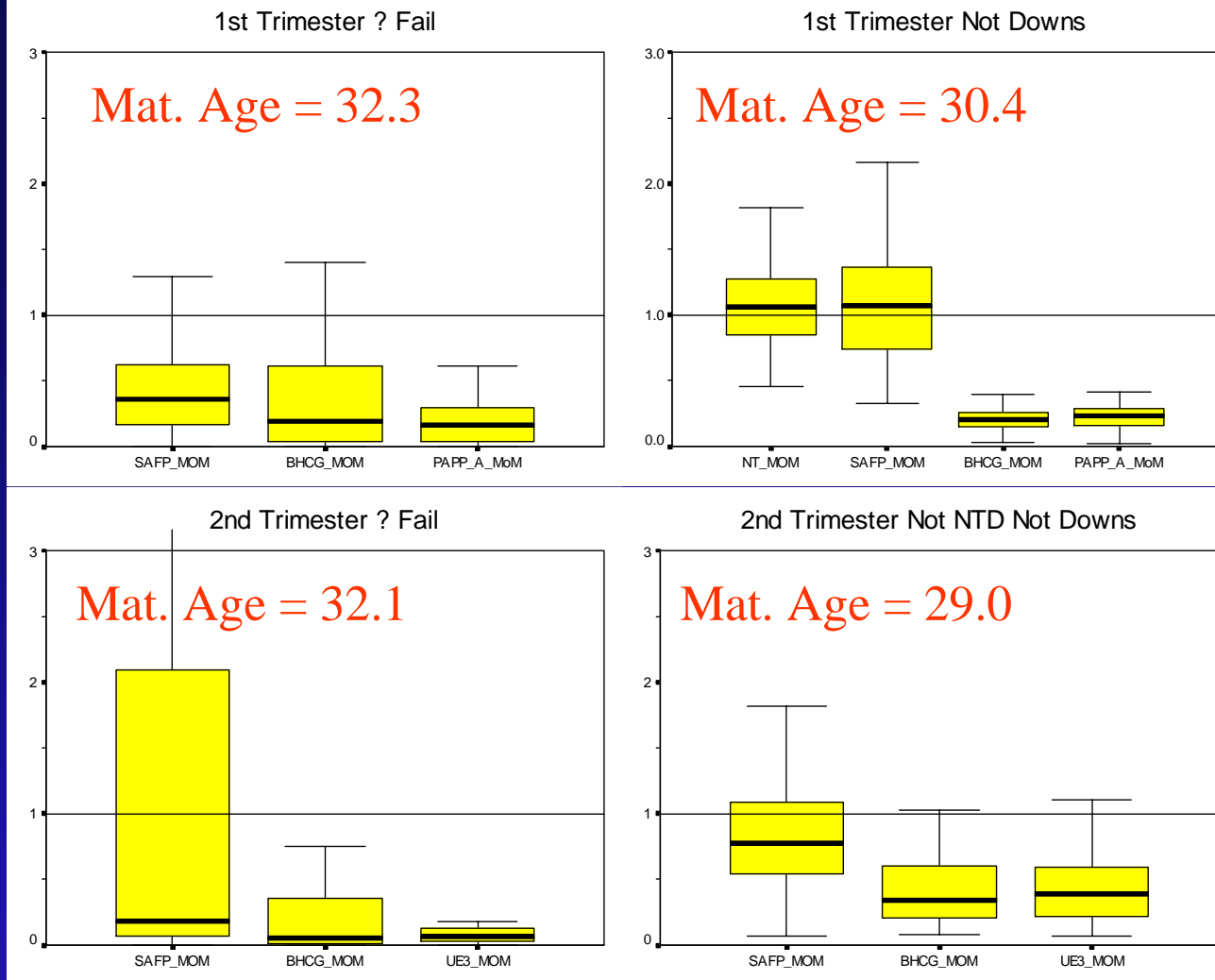
2nd Trimester Not NTD Not Downs



- N= 99
- Not Known= 12
- Normal= 62
- Fetal Death= 13
- Abnormal= 12 (4xTrip.,6xT18,1xMultiple Con. Abn.,1xMetabolic)

•**Anomalies Found 25/87**

•**Odds 1/3.5 (28.6%)**



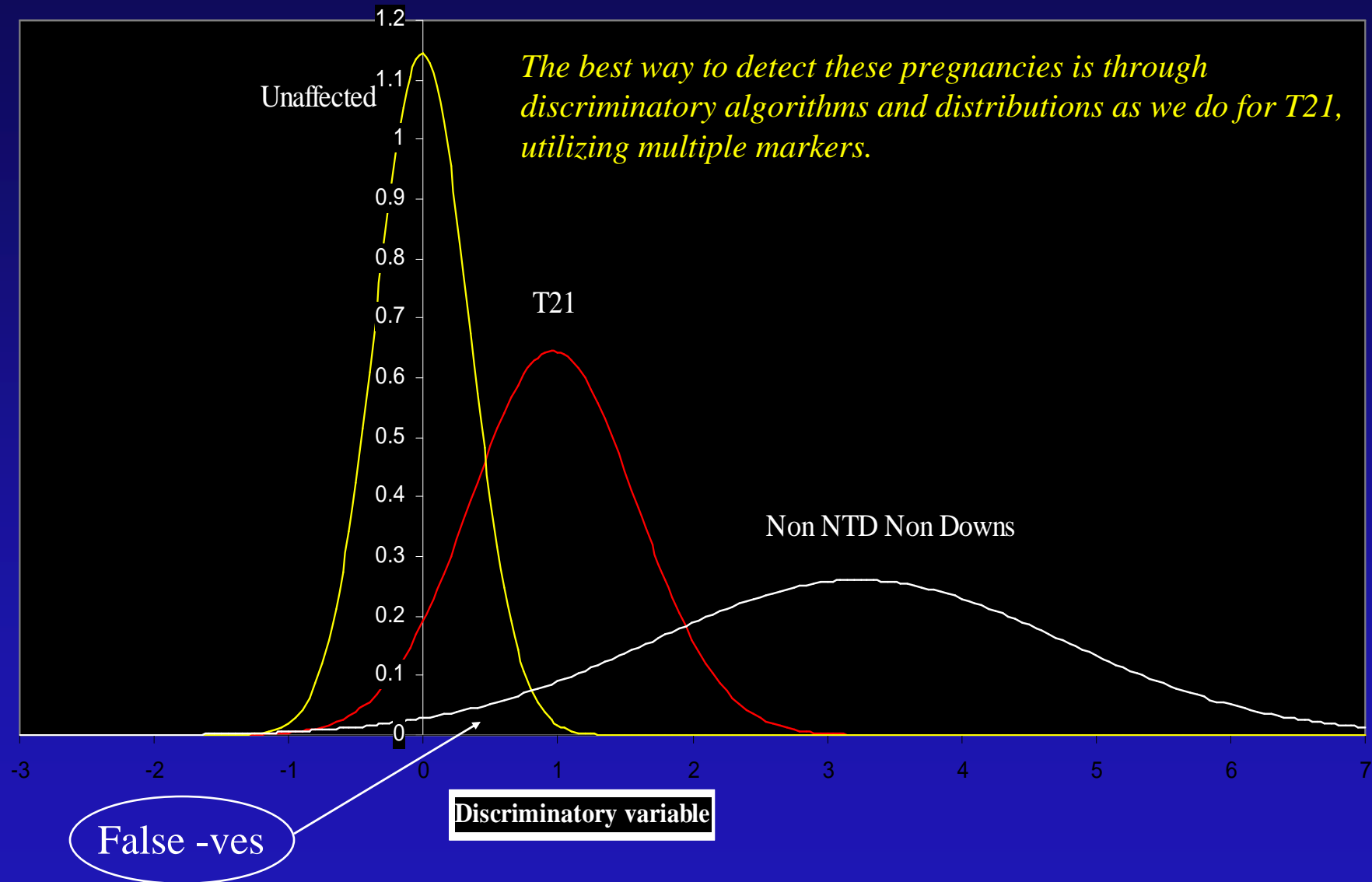
Maternal Age in Failed groups was sig. older $P < 0.05$.

This comparison suggests an association between early pregnancy loss and maternal age.

	Marker	Condition	Significant Levels
↑	AFP	Congenital Abnormality/Twins/Non Viability	≥ 2 MoM
↓	AFP	Aneuploidy/Non Viability	≤ 0.5 MoM
↑	Beta hCG	Aneuploidy/Non Viability	≥ 2 MoM
↓	Beta hCG	Aneuploidy/Non Viability	≤ 0.5 MoM
↓	UE3	Aneuploidy/Non Viability	≤ 0.5 MoM
↓	Papp-A	Aneuploidy/Non Viability	≤ 0.5 MoM

~rule of thumb~ ≤ 0.5 MoM or ≥ 2 MoM means likely poor outcome

SAMSAS T21 & Non NTD Non Downs distributions



**Pregnancy Outcome Unit
Epidemiology Branch
Department of Health Adelaide**

<http://www.dh.sa.gov.au/pehs/pregnancyoutcome.htm>

- Perinatal Mortality Rate for SA in 2003 was 0.99% of all Births ($\geq 400\text{g}/20\text{wks}$)

Exclude Deaths due to:

1. Infection
2. Antepartum Haemorrhage
3. Haemolytic Disease
4. Maternal Disease
5. Birth Trauma & Intrapartum Asphyxia

Include Deaths due to:

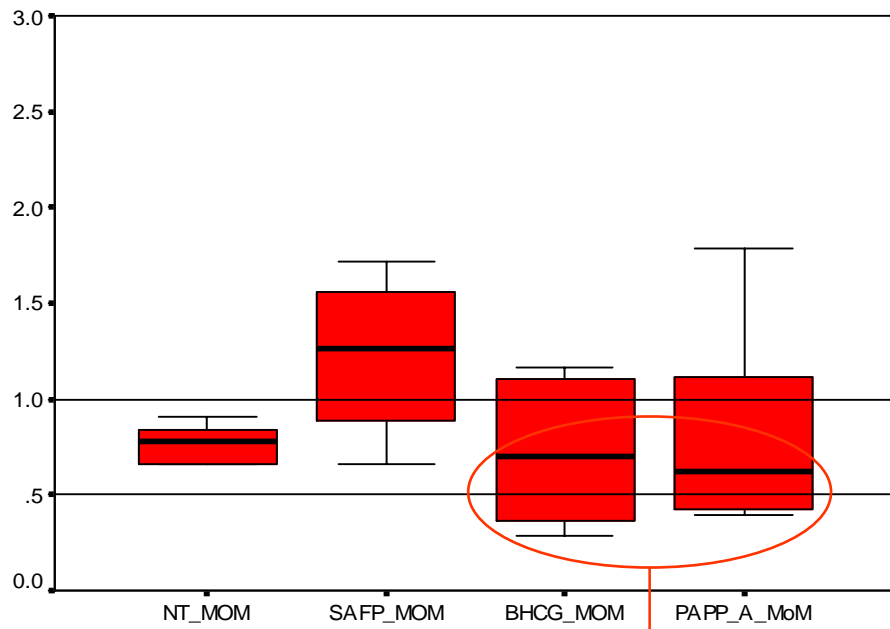
1. Spontaneous Preterm $<37\text{wks}$
2. IUGR
3. Unexplained IUD
4. Hypertension/Pre-eclampsia
5. Fetal Abnormality

Corrected Mortality Rate = 0.73%

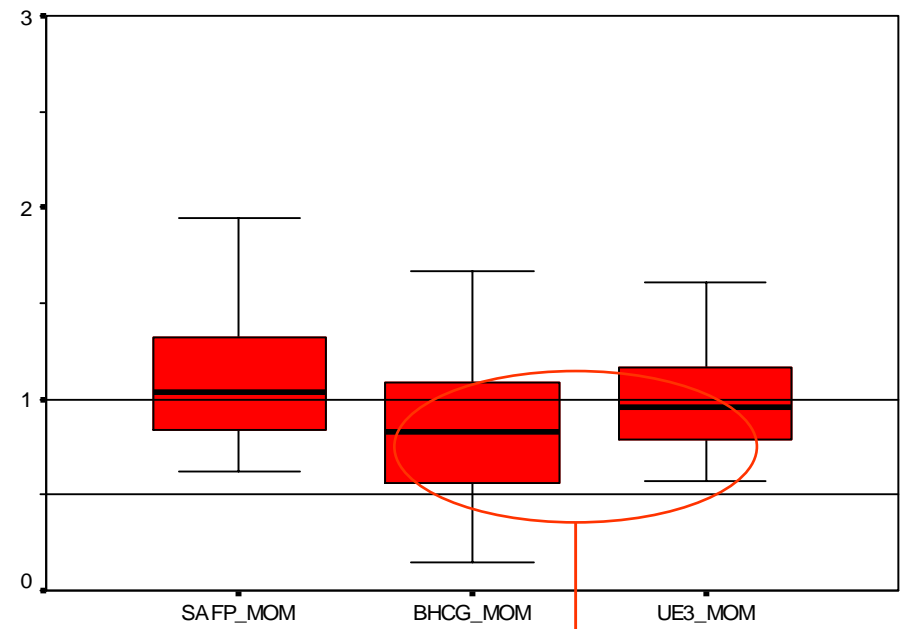
SAMSAS Recall Rate = 0.53%

Differential of 0.2% = Miss Rate. Equivalent to 1/500 pregnancies.

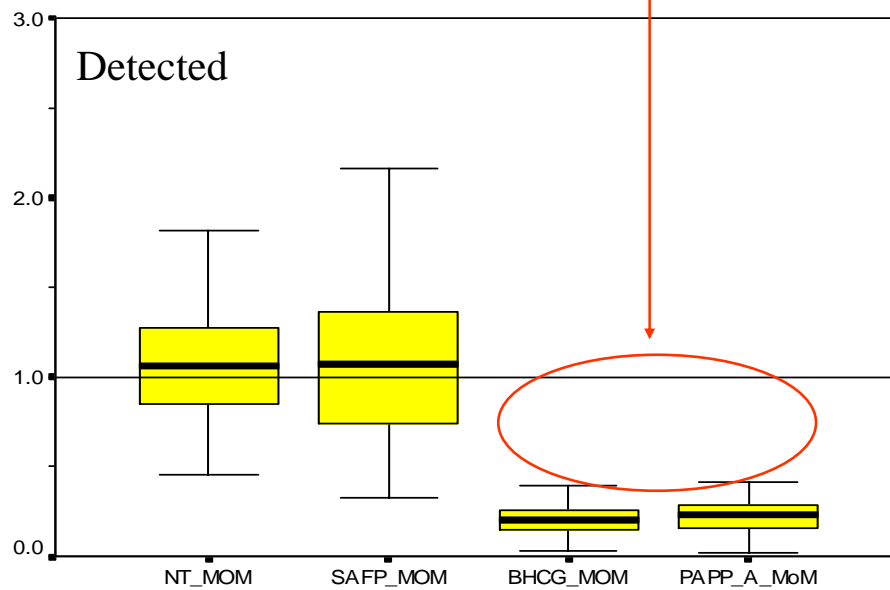
Missed 1st Trimester Fetal Deaths



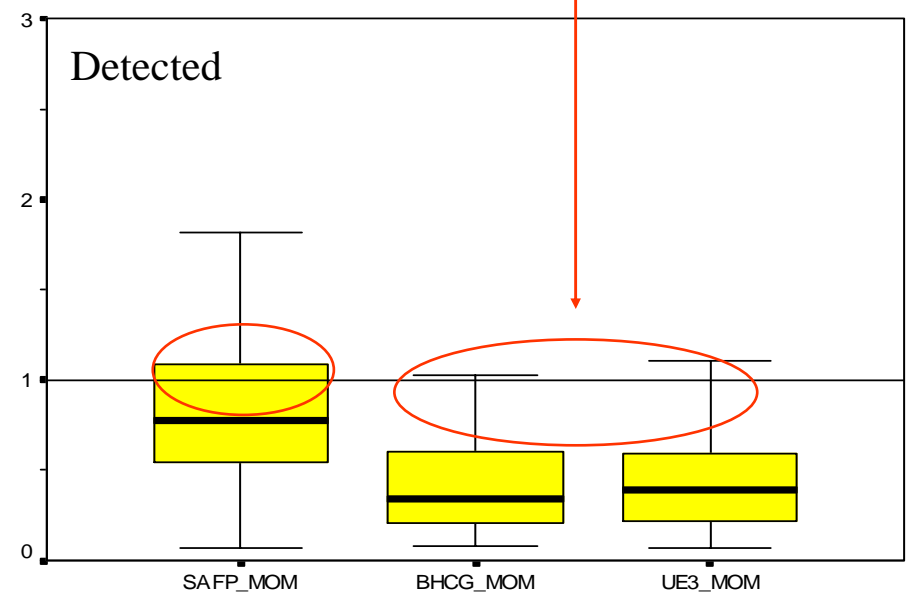
Missed 2nd Trimester Fetal Deaths



1st Trimester Not Downs



2nd Trimester Not NTD Not Downs



What does a risk report mean?

	% Recall	% Det.	ODDS Adverse Outcome	ODDS Affected	Miss Rate
2 nd Tr Raised NTD Risk	3%	>90%	1 / 8	1 / 30	1 / 10,000
2 nd Tr Raised DS Risk	5%	65%	1 / 30	1 / 40	1 / 2,500
1 st Tr Raised DS Risk	5%	90%	1 / 10	1 / 20	1 / 3,500
Not NTD Not Downs ? Viability	0.5%	75%	1 / 4		1 / 500

Reassurance of $\geq 99.8\%$ & Anomaly Risk of 2.5 – 25%



Helen Liston



Renata Bird



Diana Penhall

“providing obstetric support”

Lyn Raniolo



Chris Rothe



Leonie Thomas

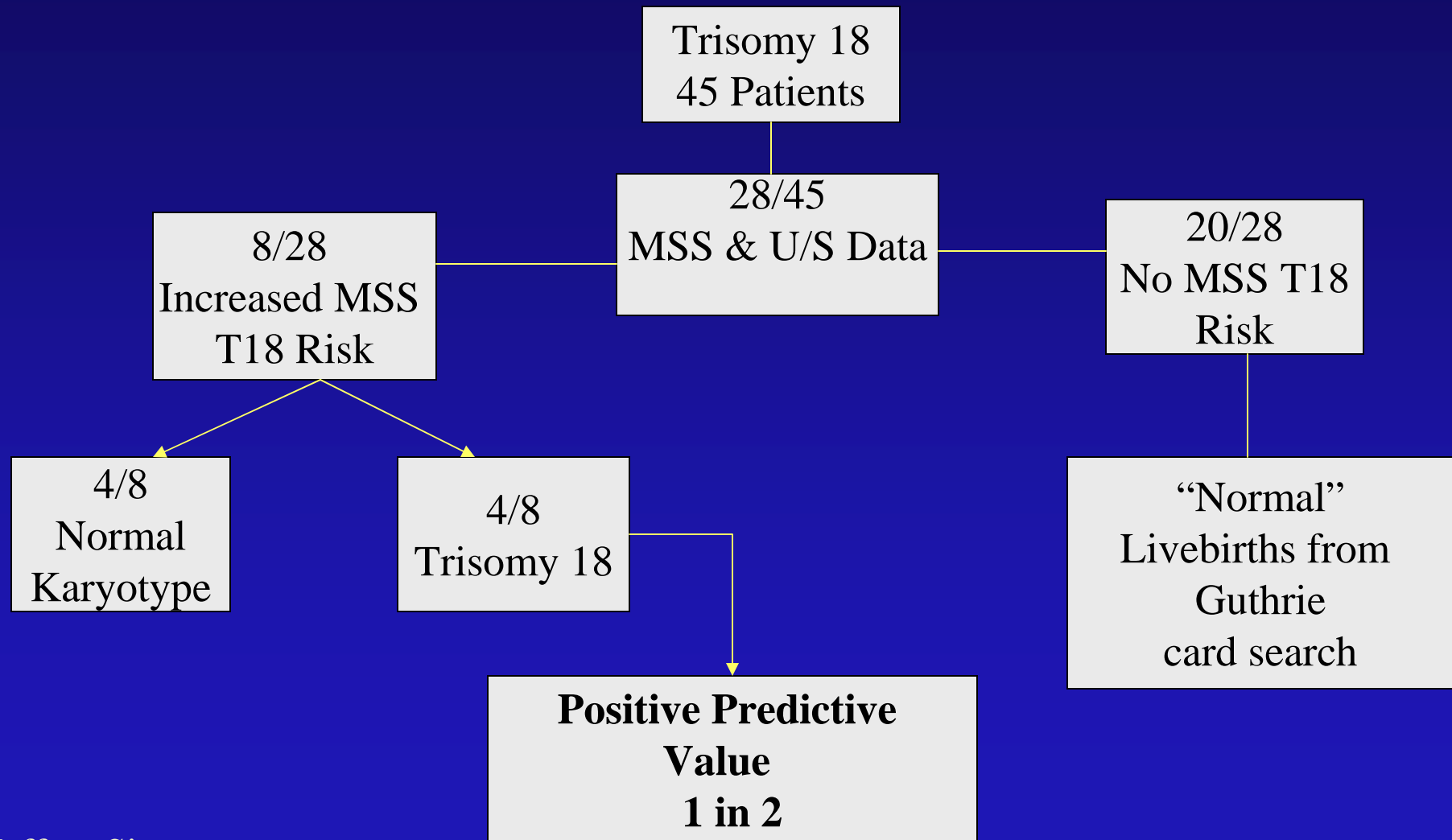


Eva Martin



Search Results

Search based on Trisomy 18 as keyword



RISKS

1. **Open Neural Tube Defects (NTD)**
2. **Down syndrome**
3. **Other (+ Edwards syndrome)**

NTD

2nd Trimester

↑ AFP ≥ 2 MoM

Independent of Maternal Age

Morphology scan

~ 1/30 will have a NTD

Down syndrome

1st & 2nd Trimester

↑ Risk ≥ 1 in 300

Age Dependent

CVS / Amnio

~ 1/20 or 1/40
will have DS

Edwards syndrome

1st & 2nd Trimester

↑ Risk ≥ 1 in 300

Age Dependent

Morphology scan

CVS / Amnio

~1/10 or 1/20

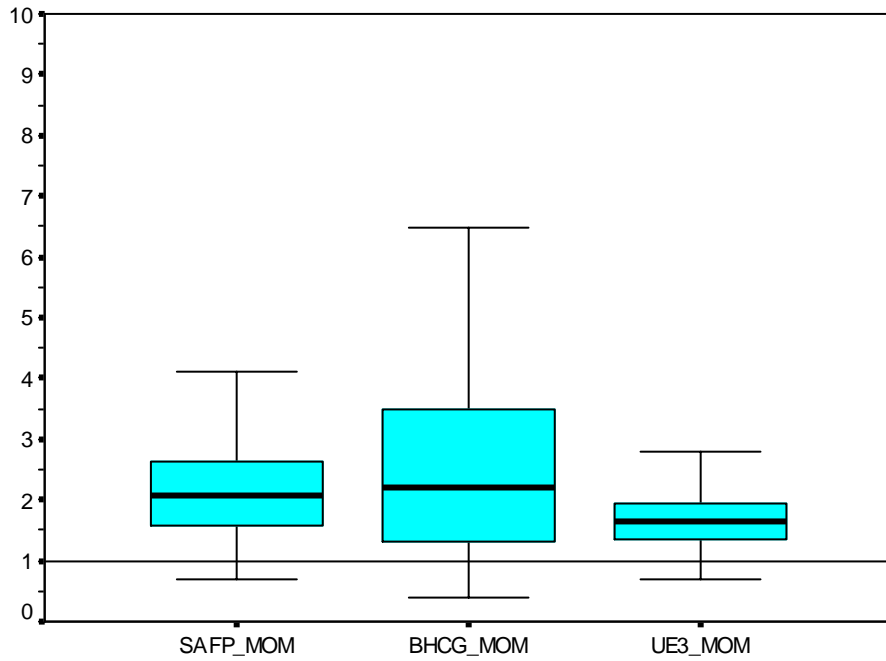
Other

Not NTD & Not DS : **AFP < 2 MoM & DS risk is < 1 in 300**

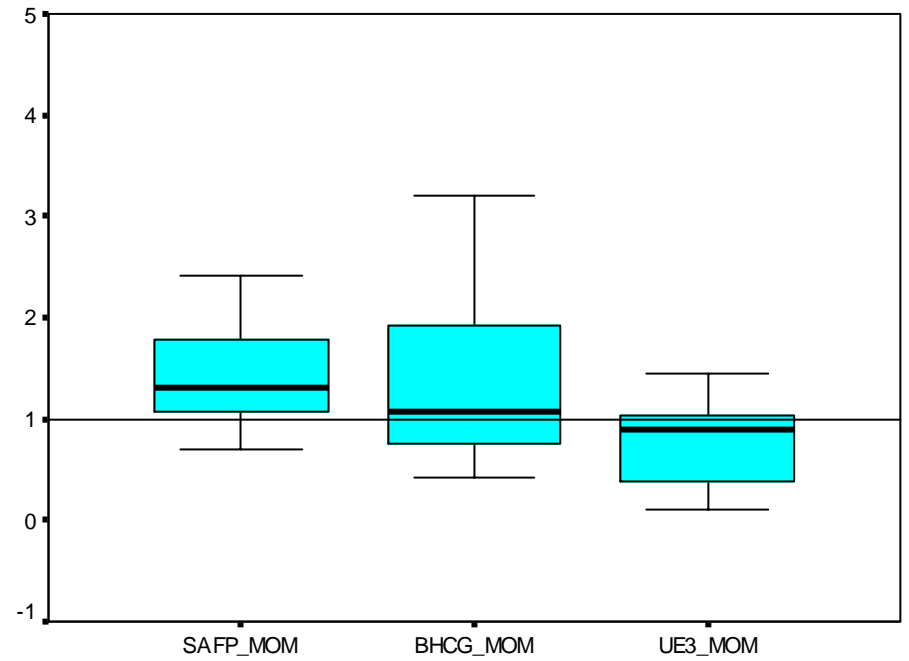
But

Biochemical results fall outside the Normal expected.

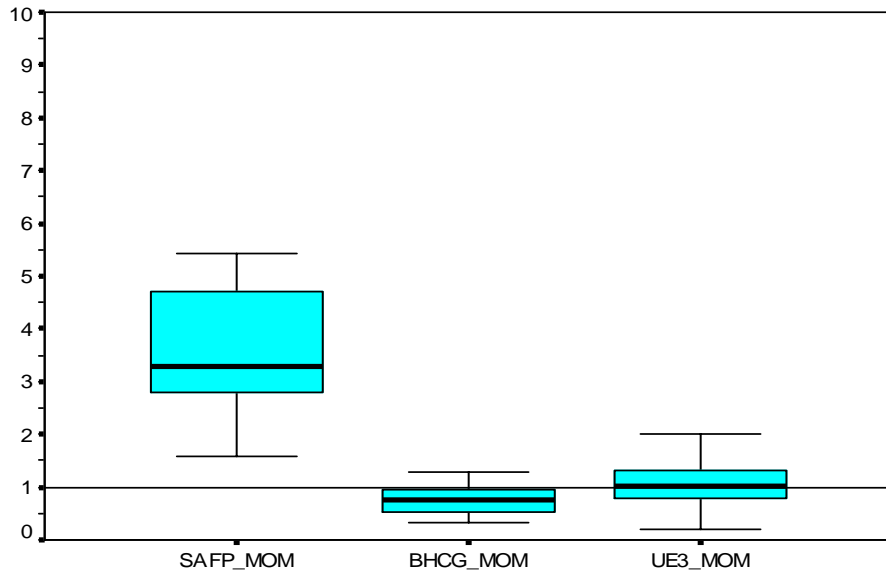
Twins 2nd Trimester



T13 2nd Trimester



Spina Bifida 2nd Trimester



Gastroschisis & Spina Bifida 2nd Trimester

