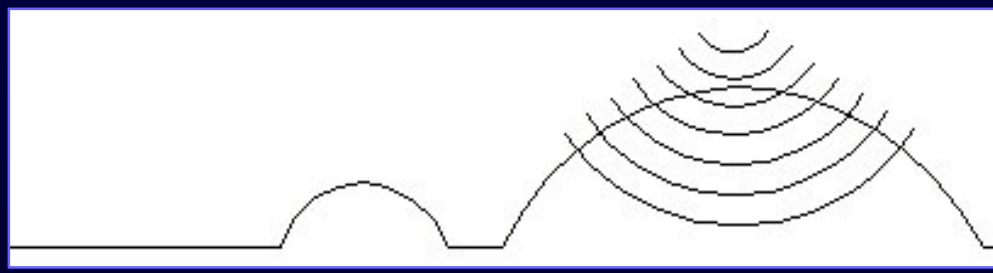
The prenatal diagnosis of chromosomal abnormalities in a resource-poor setting



Lut Geerts

Tygerberg O&G US Unit

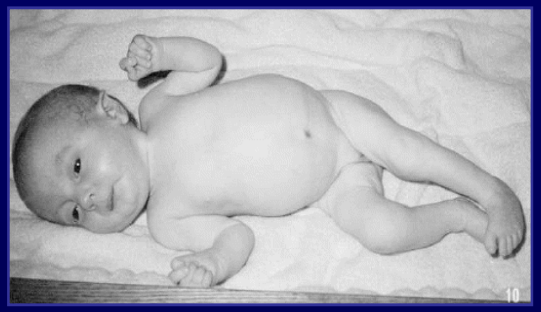
Congenital anomalies - PNM

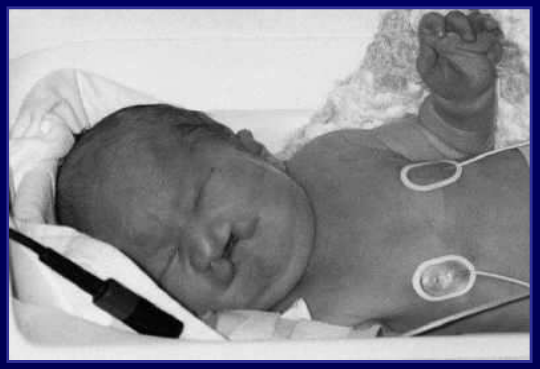
5th cause of PNM (UK 3rd)

- 1983: 7.9%
- 1996: 9.2%
- 2007: 11.4%

2nd cause of NNM: 17.2%

Chromosomal abnormalities





- Most common abnormality
- PND creates options:
  - Legal TOP
  - Prepare for birth

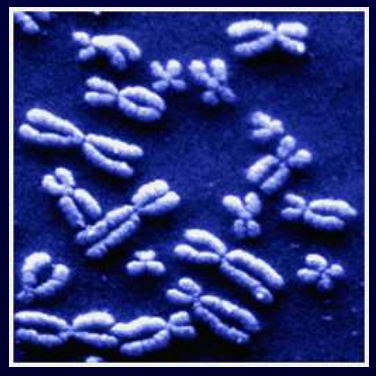
Screening – Public sector

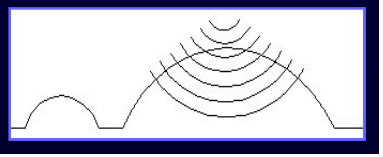
- **Mainly maternal age**
  Variable, arbitrary cut-off

"We cannot afford more….."

Laboratory cost is HIGH!

50 karyotypes = annual sonographer salary





Screening - Public sector

- Expanding ultrasound service
- Value for aneuploidy detection? Not yet evaluated

Screening - TBH

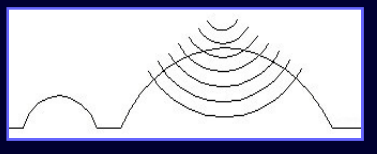
Maternal age (37)/Historical risk **11-23w**

Opportunistic risk assessment

Routine ultrasound: 11-14w and 18-23w

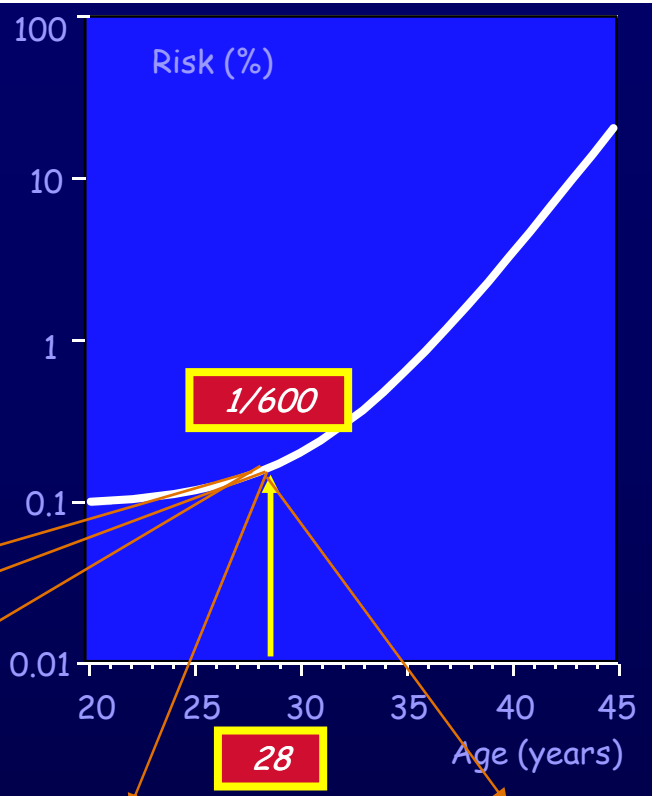
Selective ultrasound: *When clinically indicated*

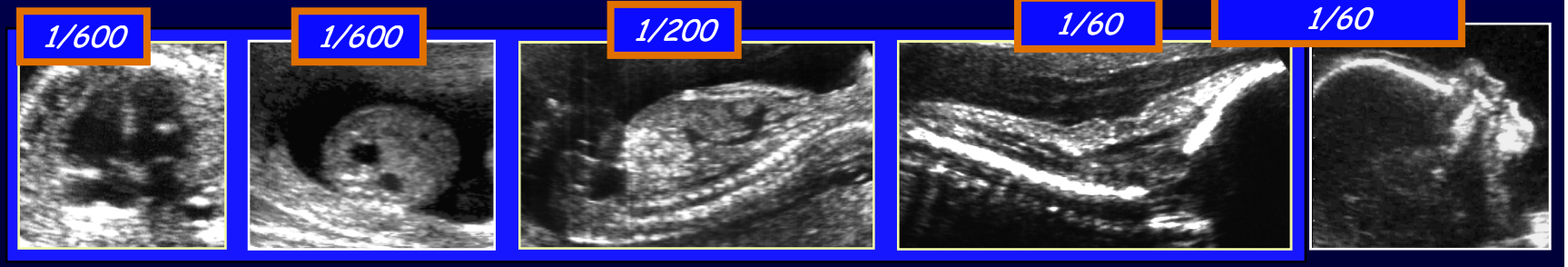
- Typical major anomalies
- High risk >1/200 after US
- Calculation with software package (FMF)



Chromosomal markers

	Normal	Tr 21	LR+	LR-	LR
Mild hydronephrosis	2.6%	17.1%	6.8	0.85	1.0
Echogenic foci	4.4%	30.3%	6.4	0.75	1.0
Short femur	5.2%	42.0%	7.9	0.62	1.5
Echogenic bowel	0.6%	17.3%	21.2	0.87	3.0
Nuchal fold >6 mm	0.6%	41.1%	53.1	0.67	10.0
Major defect	0.7%	21.4%	33.0	0.79	5.0
Short NB	2.4%	48.2%	42.8	0.40	



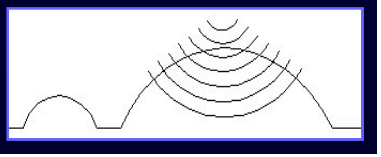


All markers absent = Risk reduction (not 14-18 weeks)

Audit @ TBH

Effectiveness of integrated US risk assessment, compared to MA alone

- Retrospective
- 3 years (2003 – 2005)
- All aneuploidies @ TBH genetic lab
- Matched with all prenatal US reports
- Results of risk assessment



TBH – Ultrasound Unit

Intermediate background risk (T21 1/333 – all 1/151)

9662 women formal scan (13.3% AMA
85% for routine karyo)

921 invasive procedures (72% for AMA)

46 Abnormal results (1:20)

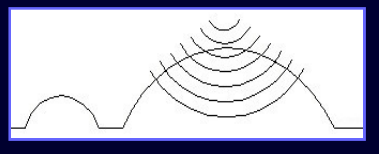
TBH – Genetics Laboratory

136 abnormal perinatal karyotypes

124 classic aneuploidies (91.2%)

114 autosomal trisomy (83.4%)

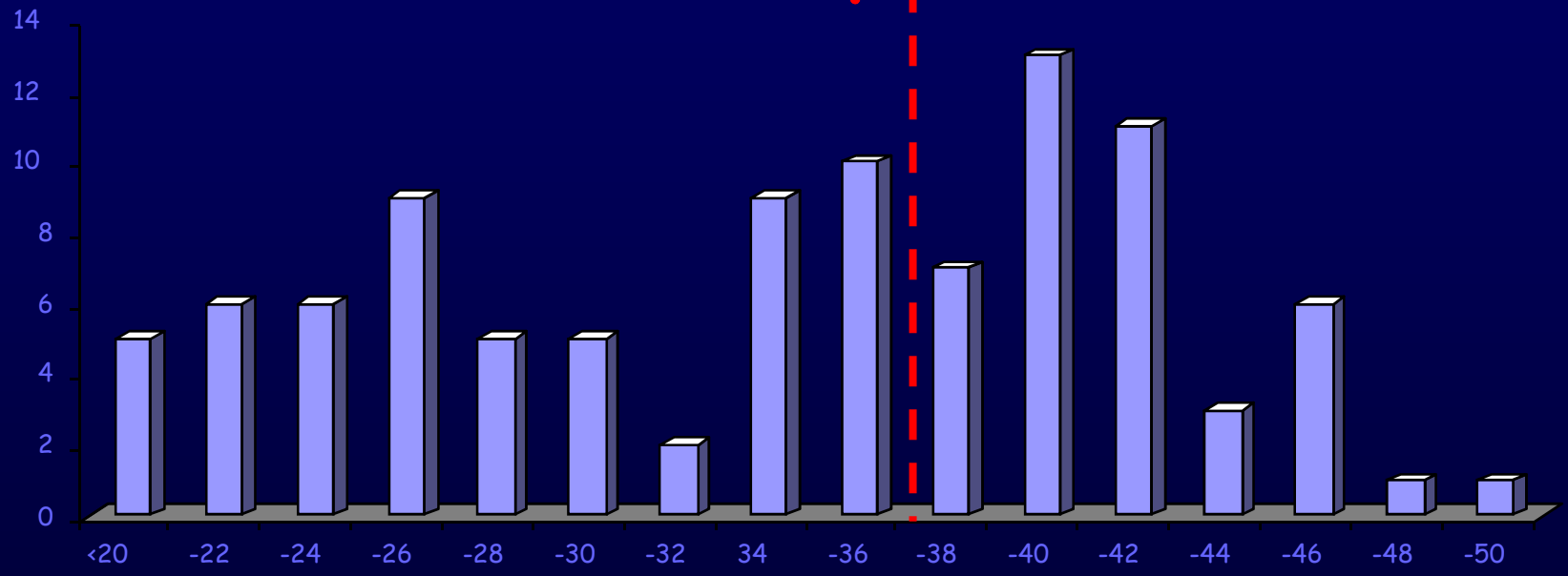
71 T21 (52.2%)



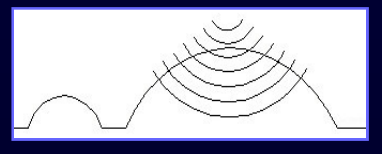
Aneuploidy ~ Maternal age

MA known in 103/135 (86/114 trisomies)

Mean 33.4±8.4y – Mode 40



Missed >=37y: 56.7%

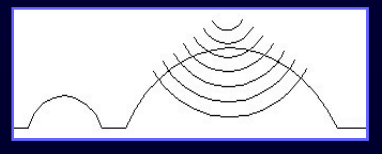


Aneuploidy ~ Maternal age

Uptake of karyotyping 52.3% (685/1310)
PPV 2.2% (29/1310)

Autosomal trisomies (screened population)

- PPV 1.9% (25/1310)
- FPR 13.4% (1285/9613)

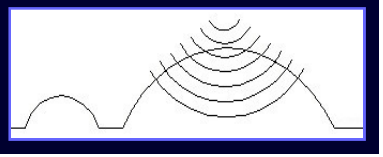


US-All abnormal karyotypes
(64/136)

9 nl US	HR 6	
12 markers only	HR 11	(8 young)
43 structural abnl	HR 42	(23 young)

92% High Risk result (59/64) (31 young)

73% PND (43/59)



US-All abnormal karyotypes

Normal US (9)

- Only 4 severe – 2 <24w

  2 T21 (16w, 37w), 1 T13 (late), 1 del (4p) (early)

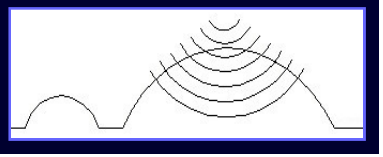
- 5 not severe

Abnormal US (55) (31 young)

ALL severe

27 T21, 13 T18, 6 T13, 2 Triploidy, 2 Turner's
Unbalanced rearrangements

P<0.0001

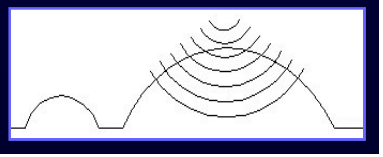


US – Autosomal Trisomies (49/114)

4 nl US	HR 2	
10 markers only	HR 9	(6 young)
35 structural abnl	HR 35	(16 young)
12 "minor"		*(5 young)*

3/49 not suspected

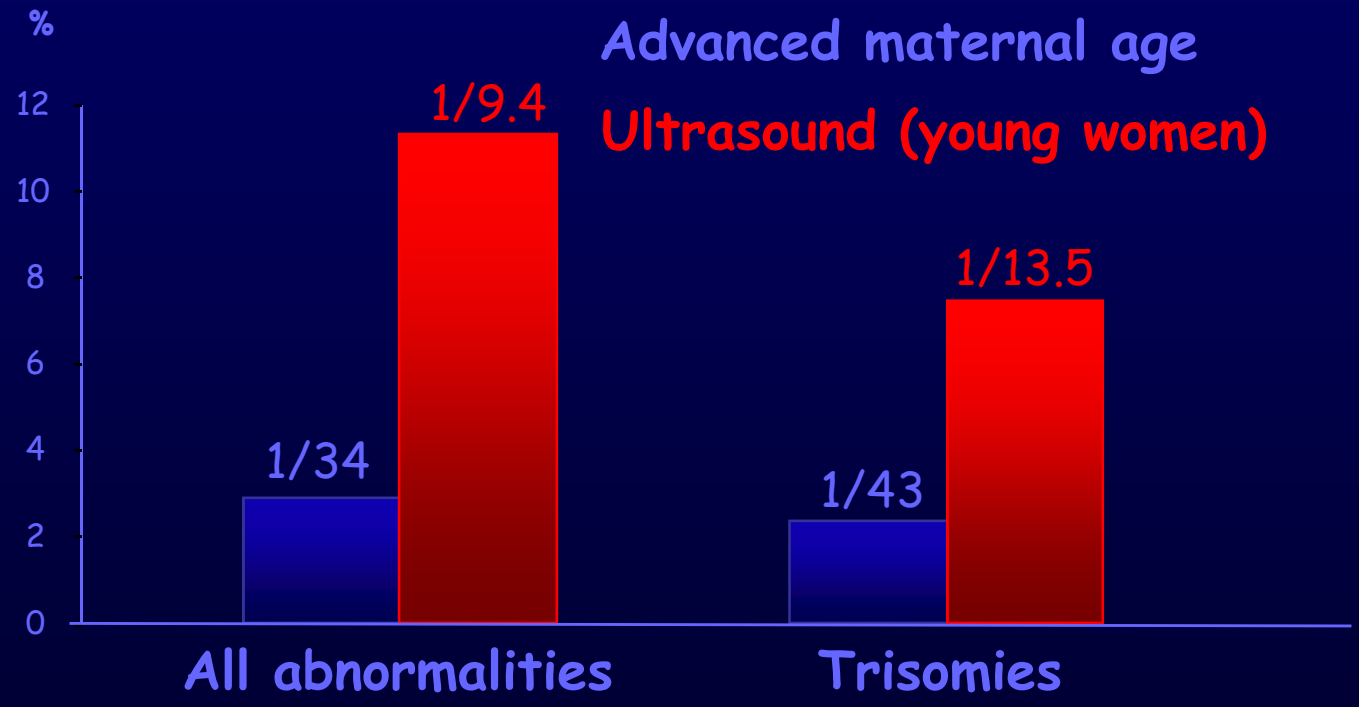
- T21, 39y, small NT, echogenic focus, risk<1/300
- T21, young, 28 weeks, bleeding placenta praevia
- T13, young, 27weeks, bleeding placenta praevia



AMA - US risk assessment

Efficiency

Prenatal samples with abnormal result



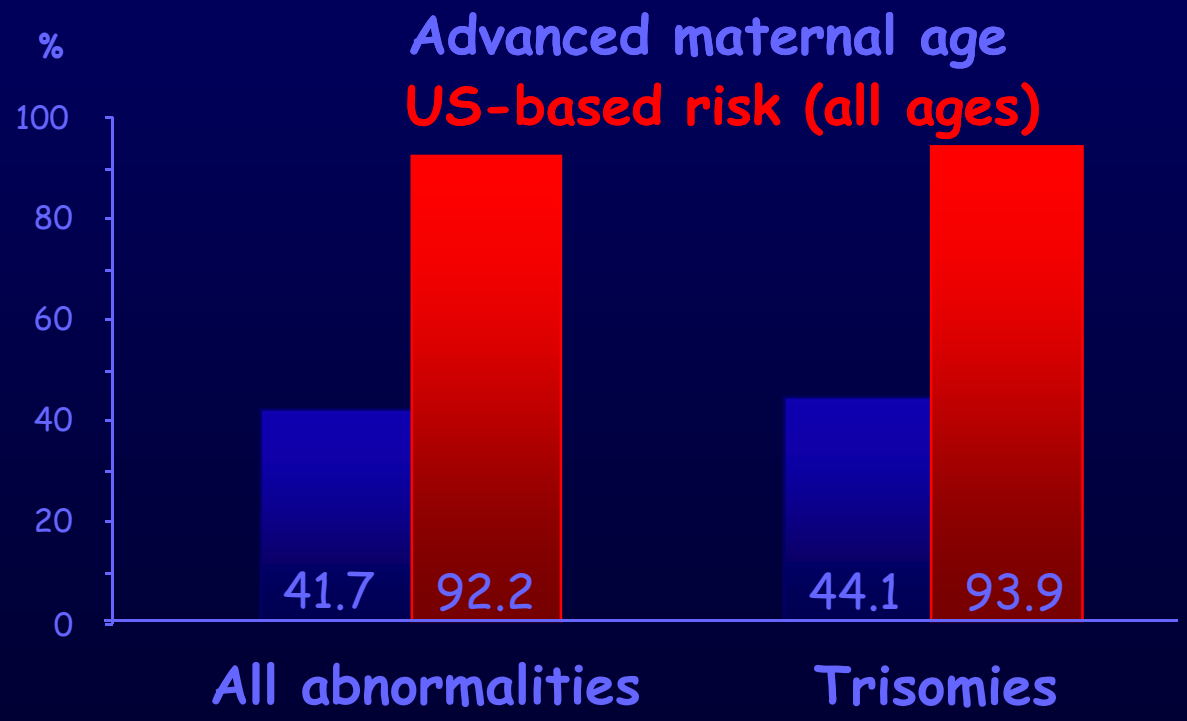
p<0.0001

If karyotyping restricted to US-risk>1/200
Potentially 2/3 reduction in AMA amnios

AMA - US risk assessment

Efficacy

Detection Rate (%)



P < 0.0001

Overall "prenatal detection"

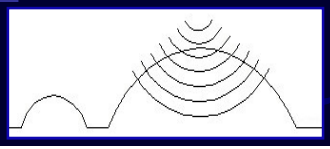
43% (59/136)

Overall prenatal confirmation

33% *(Private 27%)*

Postnatally diagnosed autosomal trisomy

- 3/81 "missed" on US
- 13/81 suspected on US
  (TOP, too late or refused PND)
- **65/81 no US screening!**



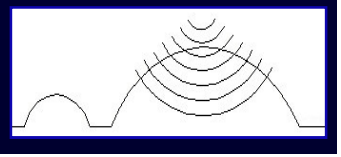
Conclusions

US based risk assessment superior to AMA
Efficacy and Efficiency

US screening more than doubled PND

(add 26 cases in young women; 8 markers only + 5 "minor")

Further improvement in aneuploidy detection requires wider access to US screening



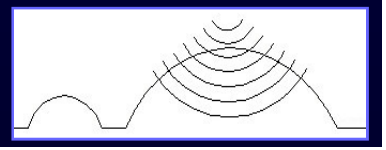
Improved exposure to screening

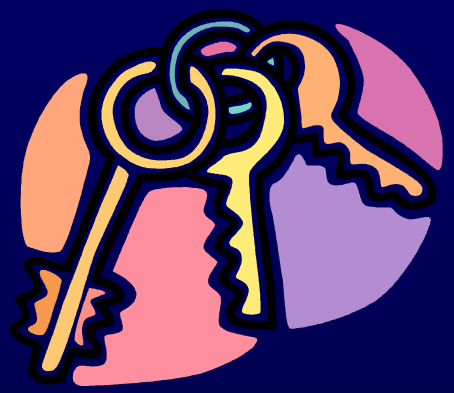
- Educate community + Staff
- Sonographer-based routine US in primary care

  Improved skills strong markers *(NT, AVSD, NB, Vemeg, Fists)*

Funding?

- AMA referral for RISK assessment
  (not routine amnio)





Equitable access to the most efficient and effective PND service

+ many other advantages.....

Thank you