Nasal Bone Screening: Introduction to Practice in Australia

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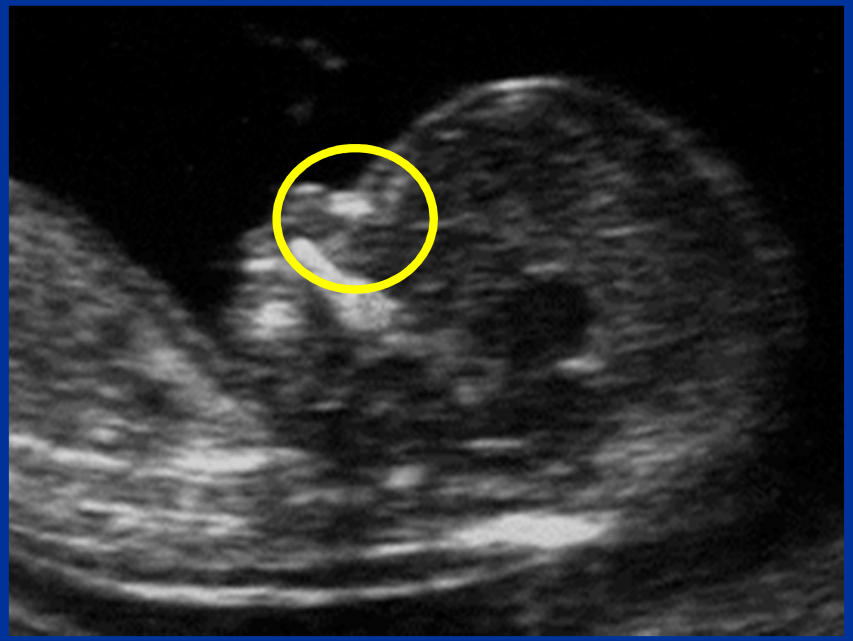
NASAL BONE

….The face is flat and the nose is small….

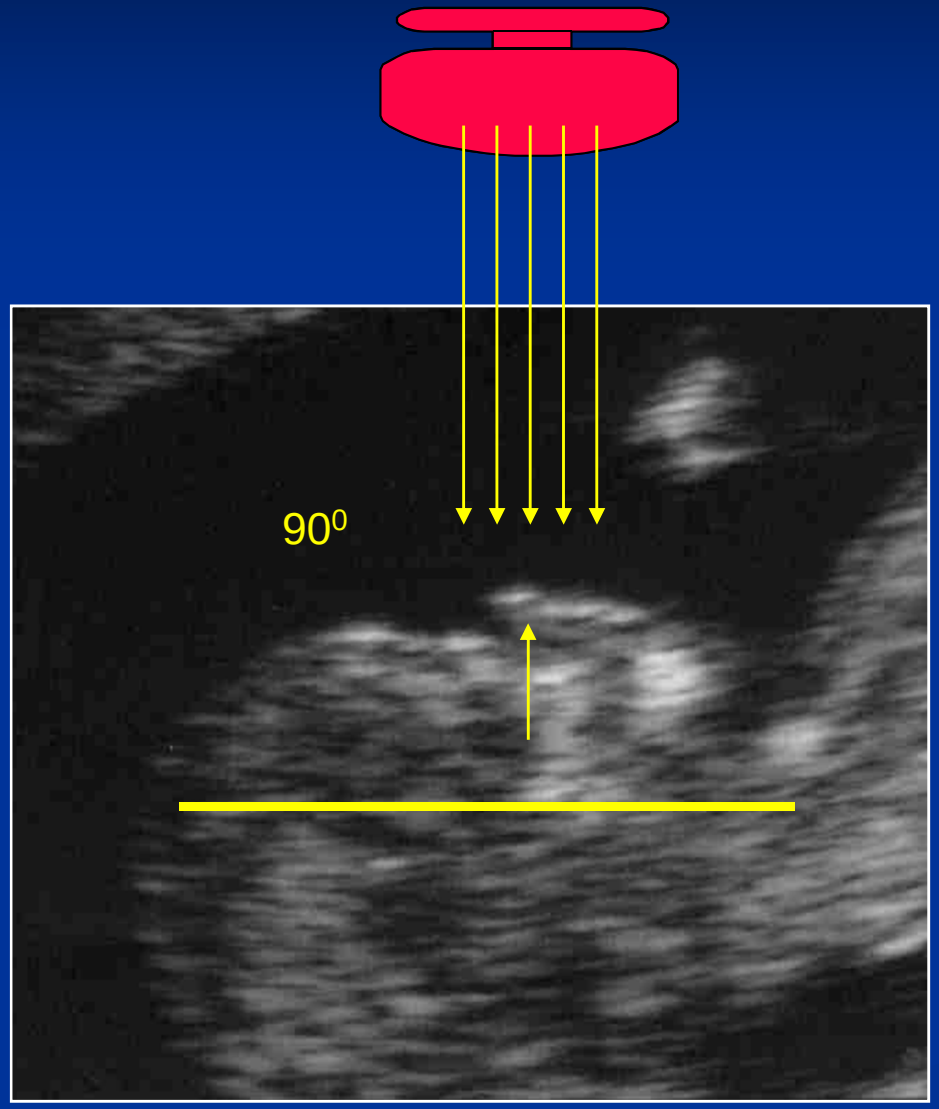
Observations on an ethnic classification of idiots. Langdon Down 1866

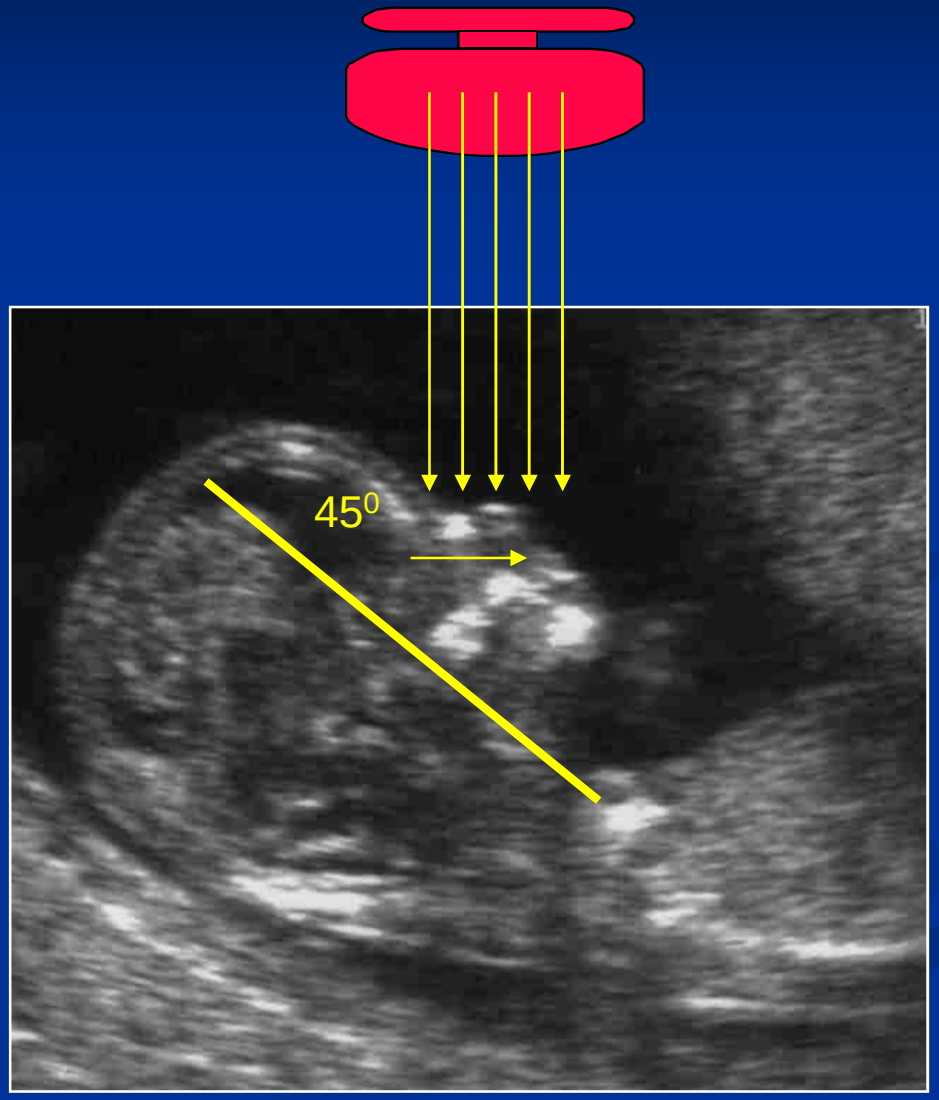
Technique for nasal bone assessment



- *Gestation 11-14 wks: CRL 45-84 mm*
- *Image size: caliper movement 0.1 mm*
- *Mid-sagital view: beam vertical to nose*
- *First line: nasal skin (bridge & nasal tip)*
- *Second line: nasal bone – cartilage*

Technique for nasal bone assessment





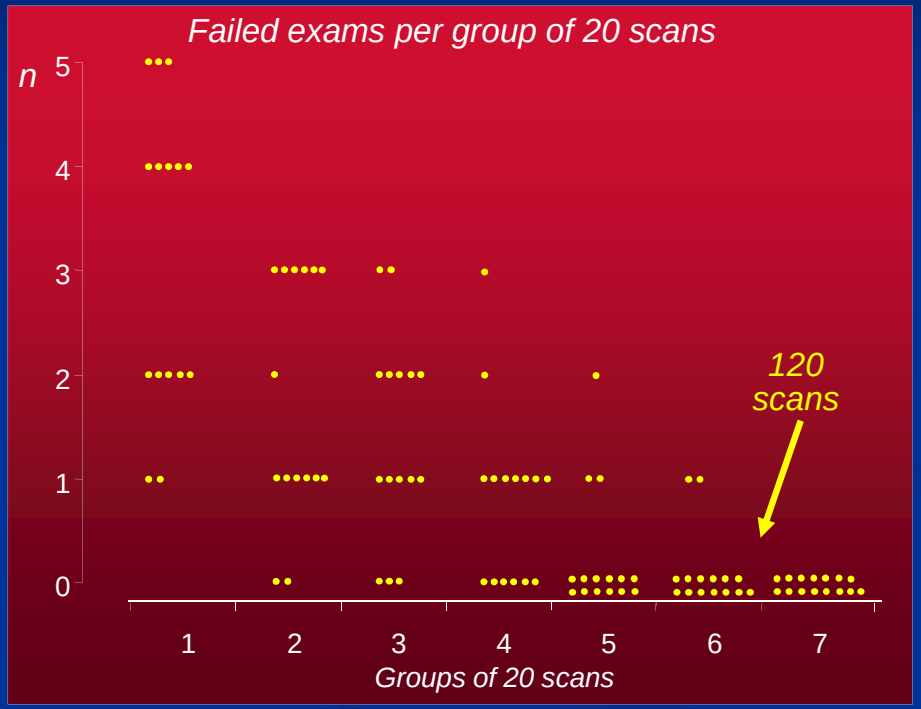
Nasal bone: importance of operator experience

- **Minimum training for experienced operators 80 scans (40 – 120)**

  Cicero et al 2003

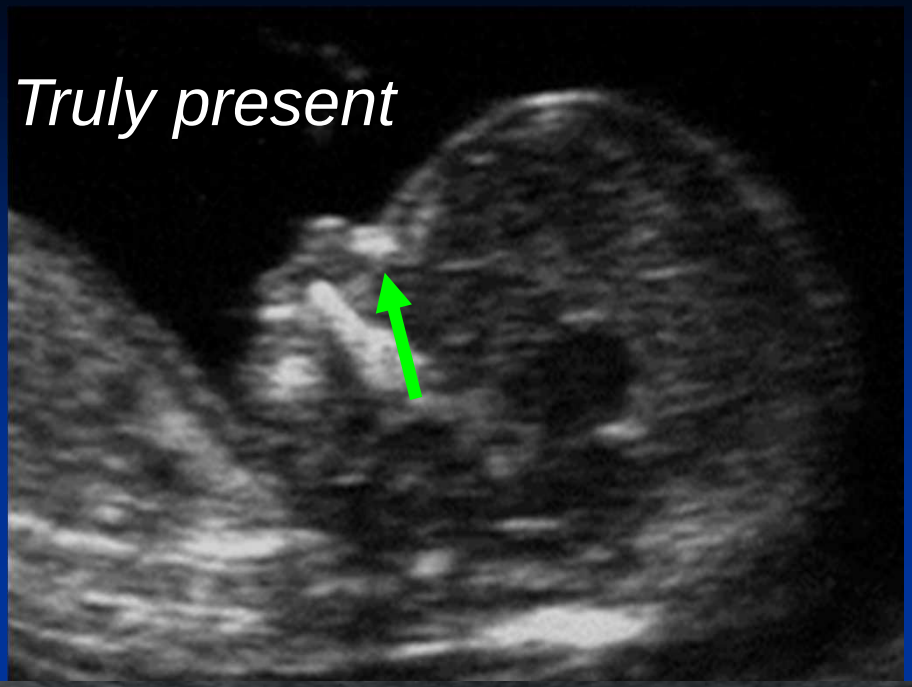
- **Adequate visualization in 94 – 97%**

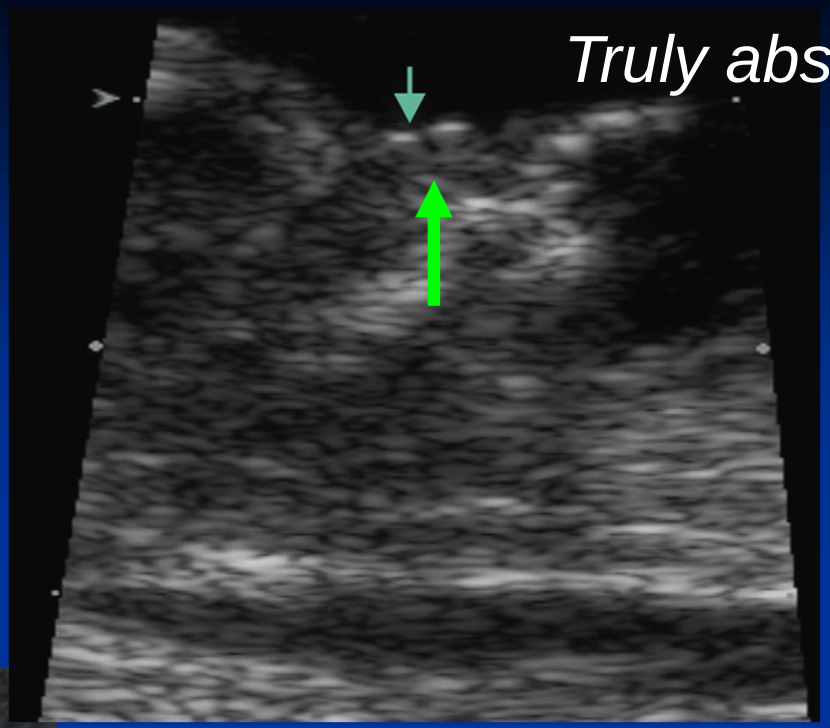
  Sonek 07, Rosen et al 2007

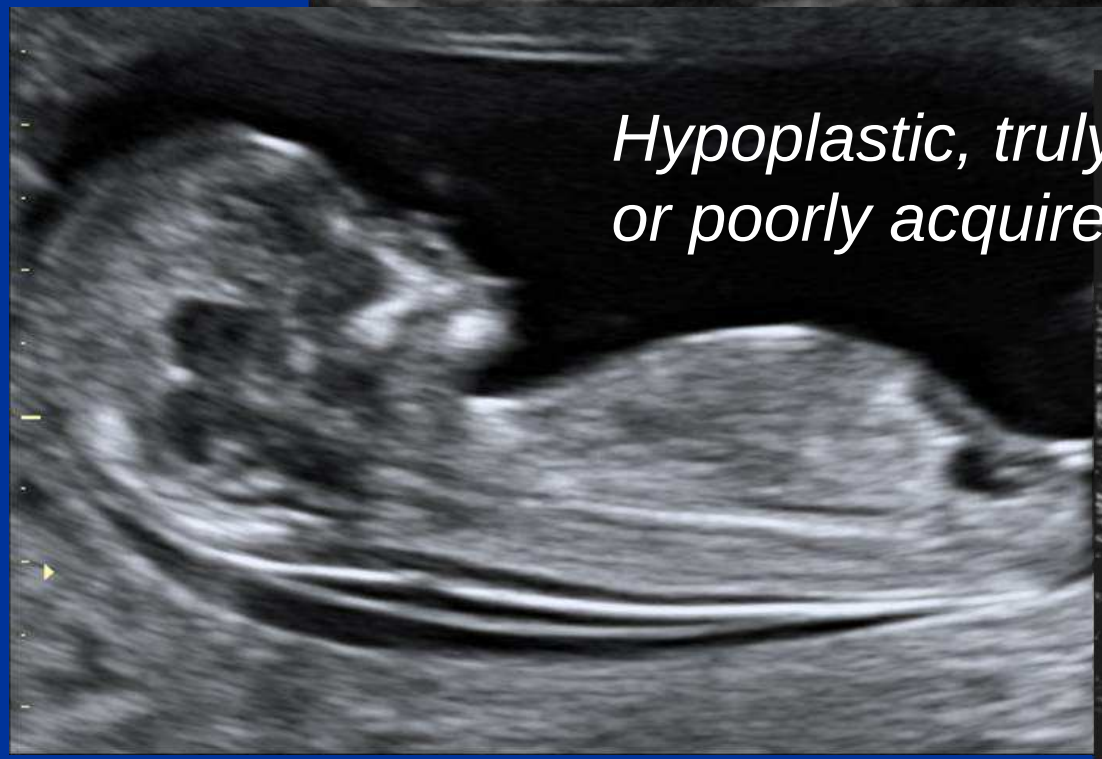


Prevalence of absent NB is increased amongst normal fetuses:

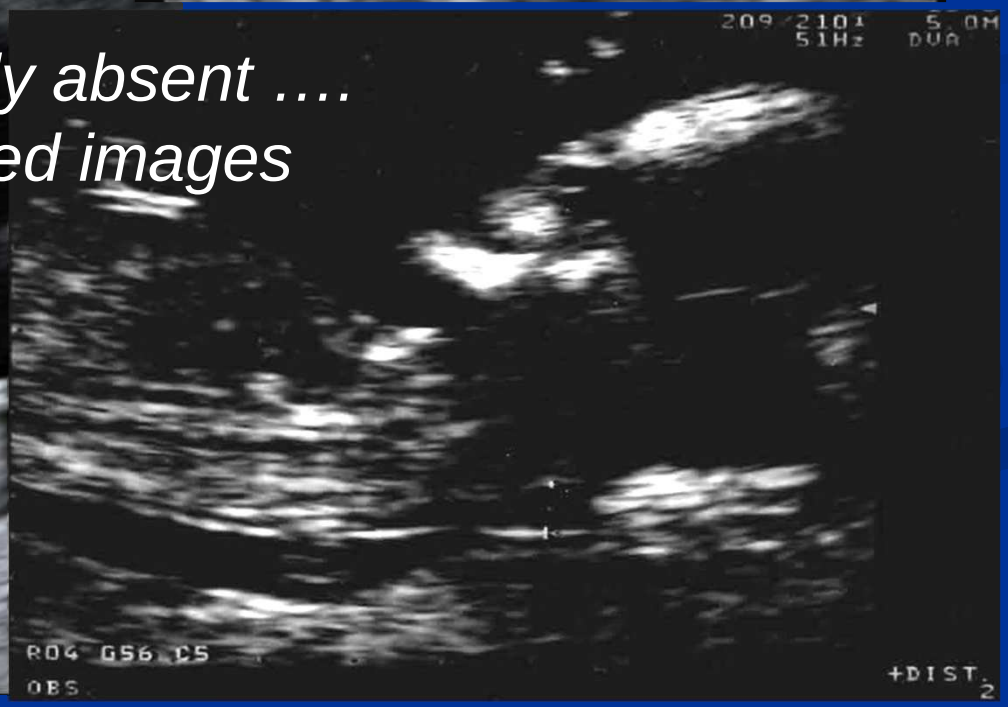
- In certain ethnic groups (Caucasian 1.2%; African 10.4%)
- In early gestation (CRL 45 – 54mm 4.6%; CRL 65 – 84m 1.4%)
- With enlarged NT (NT < 95th centile 1.8%; NT > 4.5mm 11.8%)







Hypoplastic, truly absent ….
or poorly acquired images



Absent Nasal Bone data

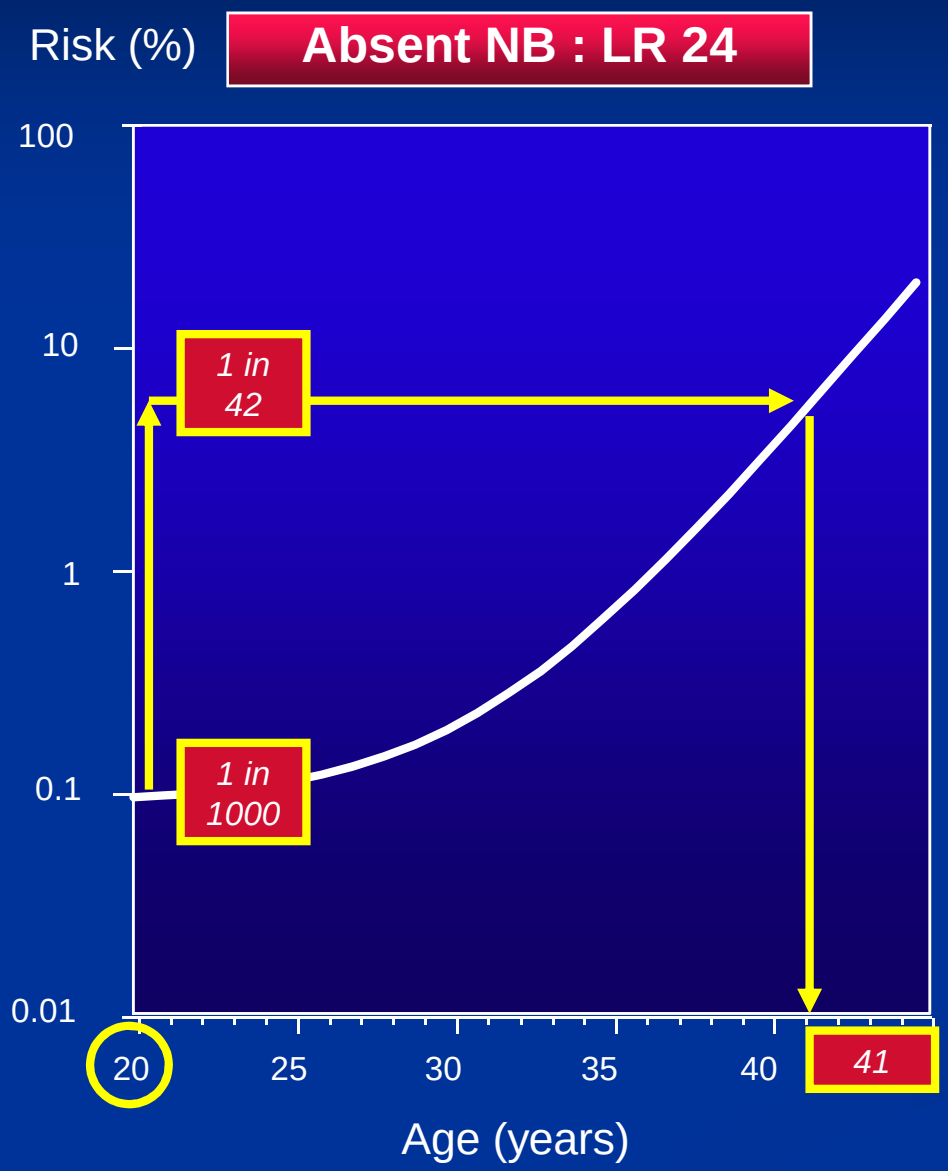
Author	Trisomy 21	Normal
Cicero 2001	43 / 59 (73%)	3 / 603 (0.5%)
Otano 2002	3 / 5 (60%)	1 / 175 (0.6%)
Zoppi 2003	19 / 27 (70%)	7 / 3463 (0.2%)
Orlandi 2003	10 /15 (67%)	10 / 1000 (1.0%)
Viora 2003	8 / 10 (80%)	24 / 1733 (1.4%)
Senat 2003	3 / 4 (75%)	4 / 944 (0.4%)
Wong 2003	2 / 3 (67%)	1 / 114 (0.9%)
Cicero 2003	162 / 242 (67%)	93 / 3358 (2.8%)
Cicero 2004	229 / 333 (69%)	129 / 5223 (2.5%)
Orlandi 2005	8 / 15 (53%)	9 / 2396 (0.4%)
Sonek 2006	282 / 412 (68%)	185 / 15048 (1.2%)
Moon 2008	8 / 15 (53%)	16 / 6456 (0.2%)
Total	**777 / 1140 (68%)**	**482 / 40513 (1.2%)**

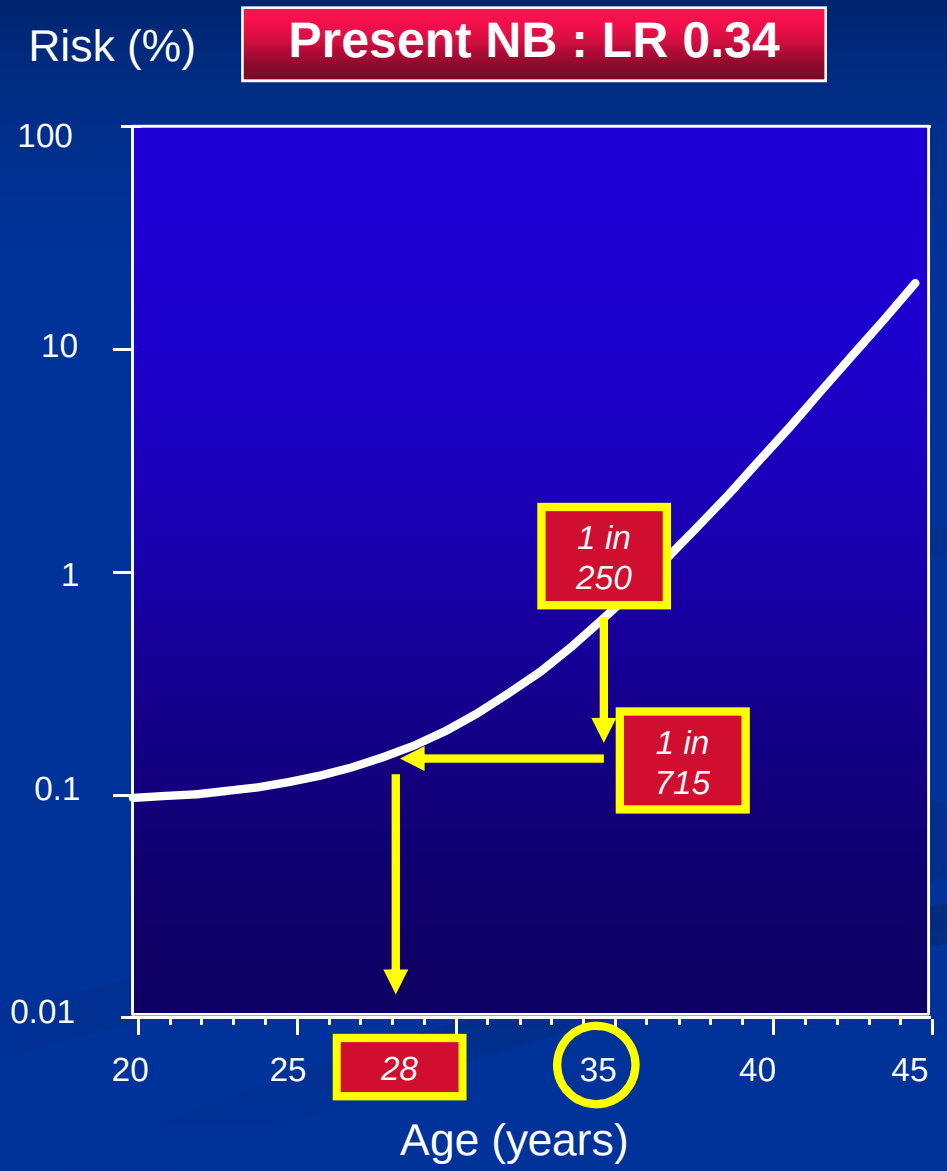
Poor protocol = very low DR
Sonek 07

De Biasio2001	*0/5*	-
Malone 2003	*0/9*	-

Absent nasal bone and screening for trisomy 21

Likelihood ratios for risk assessment





Absent nasal bone and screening for trisomy 21

Other chromosomal abnormalities

	N	*Absent nose*
Trisomy 21	**242**	**162 (67%)**
Trisomy 18	**84**	**48 (57%)**
Trisomy 13	**22**	**7 (32%)**
Turner's	**34**	**3 (9%)**
XXX or XXY	**15**	**1 (7%)**
Triploidy	**11**	**0**
Other	**22**	**3 (14%)**
Normal	**3358**	**93 (2.8%)**

Unable to examine: 41 (1%)

Cicero et al 2003

n = 3,829

Australian First Trimester Screening

- Aust Program created in 2002 – provide theoretical and practical training plus audit of centres and individual operators (image assessment and NT measurement distribution)
- Development of an image scoring method to enhance assessor agreement to ensure accuracy of audit
- Initial under-measurement of NT in Australia
- Steady improvement in performance (39% of centres reaching audit standard in 2001 –> 65% in 2006 - 8)
- It is now appropriate to introduce NB screening into routine practice

Preparation for NB screening

- A protocol of written information, MCQ examination and image audit was prepared based on the FMF criteria.
- 4 centres with large NT experience and consistently high quality audit results participated in the Nasal Bone Trial
- 40 operators participated in the education process and provided images for review

1. Clinical Review of Nasal Bone Utility

- Operators recorded the nasal bone information as:
  - clearly present
  - clearly absent
  - uncertain or
  - unexaminable
- Information NOT disclosed to the patient or the referrer.
- The NB status was later entered into the FMF program to create a new trisomy 21 risk after activating the nasal bone component of the risk algorithm.
- Neonatal information was obtained in all cases

Study Results (1)

- 1034 patients with singleton pregnancies underwent 'routine' combined NT and FTSS screening May – October 2007.
  - NB clearly absent = 9 (0.9%)
  - NB uncertain = 55 (5.3%)
  - NB unexaminable = 70 (6.8%)
  - NB clearly present = 900 (87.0%)

Study Results (2)

- 12 chromosome abnormalities identified
  - Trisomy 21 (6)
  - Trisomy 18 (2), Trisomy 13, 45X, 47XXX, 47 XXY
- Nasal bone
  - Absent: Trisomy 21 (4/6), Trisomy 18 (1/2), Trisomy 13
  - Uncertain: T21 (1/6), T18 (1/2), 45X
  - Present: T21 (1/6), XXX, XXY

Study Results (3)

	NT + FTSS	NT + FTSS + NB
High Risk	53 (5.1%)	31 (3.0%) *
DR T21	5 / 6 (83.3%)	5 / 6 (83.3%) #
DR OT	5 / 6 (83.3%)	4 / 6 (66.7%) ^

Changed risks after addition of NB information:

1 extra false positive; 23 extra true negatives

* $X^2=6.00$; p=0.014

1 fetus NB + HR -> LR; 1 fetus NB – LR -> HR

^ Fetus with XXY NB + HR -> LR

2. Review of NB image audit

- FMF (UK) require 3 nasal bone images from experienced NT operators that satisfy the qualitative categories of
  - Image magnification
  - Mid- sagittal plane
  - US beam perpendicular to the nasal bone
  - Skin line separate over nasal bridge and nasal tip
  - Nasal bone thicker and more echogenic than the overlying skin

- The addition of NB assessment to routine screening practice in Australia requires the audit process to be as rigorous as possible, because:
  - the image is more difficult to obtain than the NT
  - there is a long learning curve even for experienced operators
  - the impact of the nasal bone information on the risk algorithm is powerful
- Therefore, we undertook to assess whether a quantitative assessment of NB images was more reliable than qualitative review and could provide more meaningful feedback to operators.

Image audit study

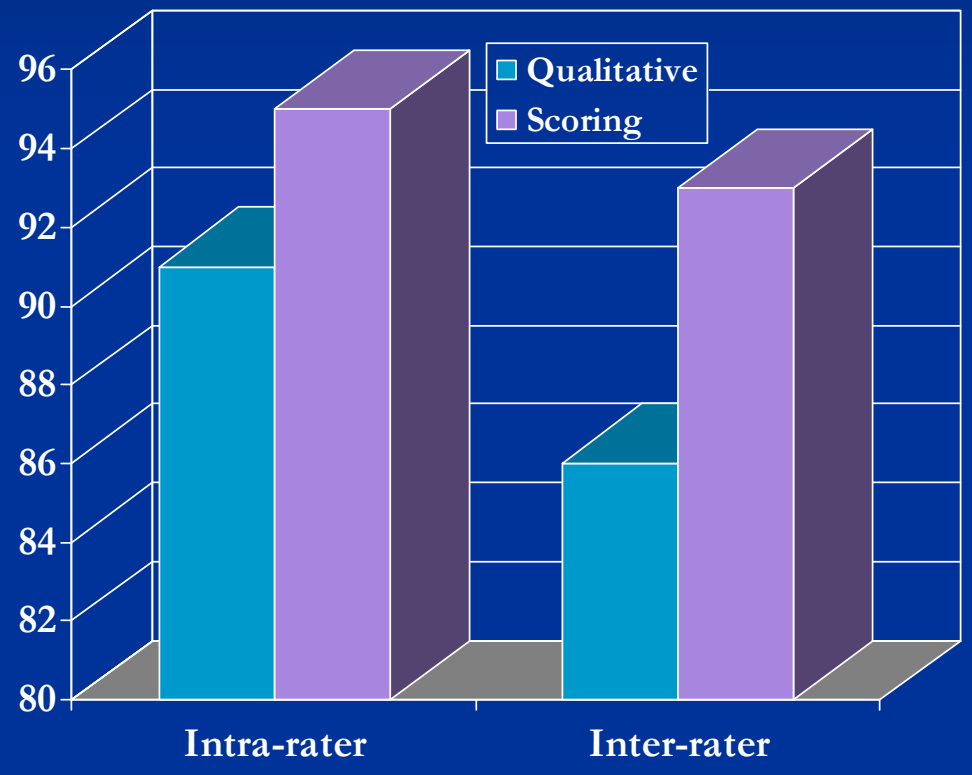
- 20 NB images were submitted by 20 experienced accredited NT operators who had completed the educational process
- 3 experienced assessors reviewed each image twice (2400 assessments) using the FMF qualitative criteria on a satisfactory / unsatisfactory basis
- A random selection of 100 images was then reviewed twice by the 3 assessors (600 assessments) using a quantitative scoring method designed by the assessors in an effort to reduce perceived subjectivity and improve agreement.

Quantitative NB image assessment

Criterion	Definition	Score
Image size	Include head, neck, upper chest	1 or 0
Image plane	Mid-sagittal (accept infraorbital segment of the maxilla as outer limit)	1 or 0
Face / head angle	45 degrees to the axis of ultrasound beam - nasal bone perpendicular to beam (accept 30-60 degrees).	1 or 0
Skin line(s)	Two separate skin lines – over the nasal bridge and, at an elevated level, over the nasal tip. - 2 clearly separate lines (gap and level) - Single line - No clear skin line separate from NB	2 or 1 or 0
Nasal bone*	Thicker / brighter than overlying skin Visible, isoechoic with overlying skin Visible, thin as overlying skin Thinner / less bright than overlying skin	2 or 1 or 1 or 0

Maximum score of 7. A score of 5 or more was considered an acceptable image

Study Results



- Intra-rater agreement: odds of discordance using image scoring was **0.48 x** that of qualitative method (p=0.01)
- Inter-rater agreement: odds of discordance using image scoring was **0.3 x** that of the qualitative method (p<0.01)

McLennan *et al* 2009 DOI:10.1002/uog.7473

Conclusions

- Nasal bone absence is a powerful marker for Down syndrome
- Introduction into Australian practices can substantially reduce the false positive rate of screening
- Introduction of this marker into 'routine' screening practice should be limited to experienced operators with a satisfactory NT audit history
- Operator accreditation will require a course of theoretical and practical training and submission of 10 images for expert review
- The image scoring method is recommended as the basis of future NB image audit.