

# Increased NT with normal karyotype: Is termination justified?

Dr JBF Cilliers

Maternal – Fetal Medicine

Dept Obstetrics & Gynaecology

University of the Free State



# Introduction

- Measuring NT during the first trimester scan in combination with PAPP-A and B-HCG can predict 80 – 90% of chromosomal abnormalities
- Abnormal NT can also predict structural defects especially cardiac defects.
- It is also used as an early marker of twin-to-twin transfusion in monochorionic twins
- Furthermore some syndromes have been described to have abnormal NT's



# Incidence of chromosomal defects according to NT measurement

Nuchal translucency	Chromosomal defects
$\leq 3.4$ mm	0.33 %
3.5 – 4.4 mm	21.1 %
4.5 – 5.4 mm	33.3 %
5.5 – 6.4 mm	50.5 %
$\geq 6.5$ mm	64.5 %

Souka et al. 2001

# The dilemma!

- Parents counselled
- We measure an abnormal NT
- Karyotyping is done
- Results: NORMAL

SO WHAT NEXT?



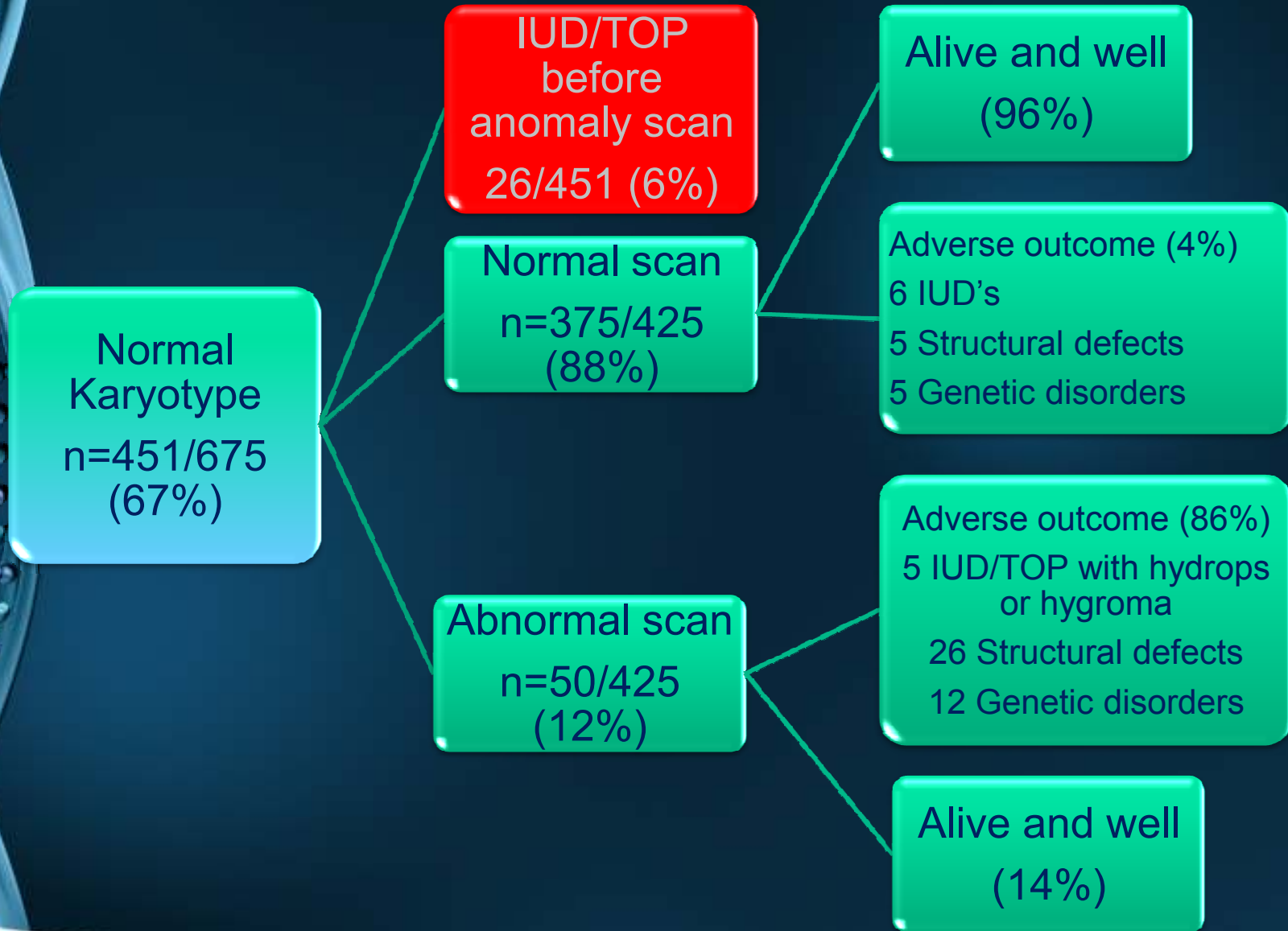


# What can we expect if karyotype is normal?

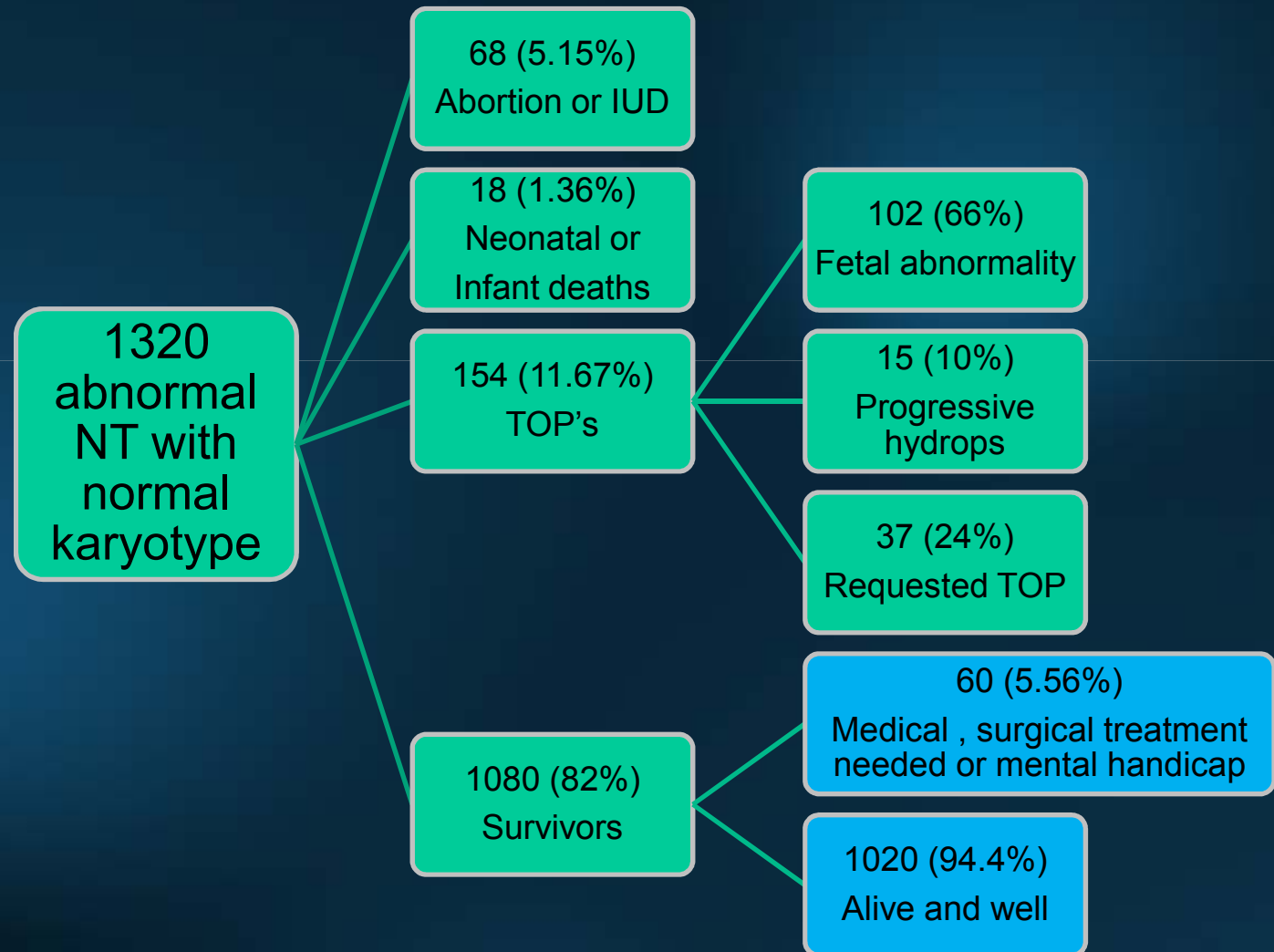
As NT increases the chance for a normal fetus decreases

NT (mm)	Live births, no defects (Bilardo et al. 2007)	Live births, no defects (Souka et al. 2001)
95 <sup>th</sup> centile – 3.4	92 %	
3.5 – 4.4	83 %	85.9 %
4.5 – 5.4	71 %	77.3 %
5.5 – 6.4	58 %	66.7 %
≥6.5	20 %	31.2 %

# Example of outcome in Bilardo et al.



# Outcome in Souka et al.






# So why the increase in NT?

## Proposed mechanisms:


- Cardiac dysfunction due to abnormalities of the heart or great arteries
- Venous congestion of the head and neck
  - Amnio rupture sequence
  - Diaphragmatic hernia
  - Narrow chest in skeletal abnormalities
- Failure of lymphatic drainage
  - Delayed development of lymphatic tissue
  - Impaired fetal movements
- Fetal anaemia or hypoproteinemia
- Altered composition of subcutaneous tissue



# Fetal abnormalities and genetic syndromes reported in association with increased NT

## Central nervous system defect

Anencephaly	Joubert syndrome
Craniosynostosis	Microcephaly
Dandy-Walker malformation	Macrocephaly
Diastematomyelia	Spina Bifida
Encephalocele	Iniencephaly
Holoprosencephaly	Trigonocephaly C
Hydrolethalus syndrome	Ventriculomegaly



# Fetal abnormalities and genetic syndromes reported in association with increased NT

## Facial defect

Agnathia/micrognathia

Facial cleft

Microphthalmia

Treacher-Collins syndrome


## Nuchal defect

Cystic hygroma

Neck lipoma

## Cardiac defect

Multiple lesions – VSD, ASD, DORV, Epstein's, AVSD etc.



# Fetal abnormalities and genetic syndromes reported in association with increased NT

## Pulmonary defect

Cystic adenomatoid malformation

Diaphragmatic hernia


Fryn syndrome

## Abdominal wall defect

Cloacal extrophy

Exomphalos

Gastrochisis




# Fetal abnormalities and genetic syndromes reported in association with increased NT

## Gastrointestinal defects

- Crohn's disease
- Duodenal atresia
- Esophageal atresia
- Small bowel obstruction

## Genitourinary defect

- Ambiguous genitalia
- Hydronephrosis
- Hypospadias
- Infantile polycystic kidneys
- Multicystic dysplastic kidneys
- Renal agenesis



# Fetal abnormalities and genetic syndromes reported in association with increased NT

## Skeletal defect

Achondrogenesis

Achondroplasia

Asphyxiating thoracic dystrophy

Campomelic dwarfism

Jarcho-Levin syndrome

Kyphoscoliosis


Limb reduction defect

Osteogenesis imperfecta

Roberts syndrome

Short rib polydactyly

VACTER association



# Fetal abnormalities and genetic syndromes reported in association with increased NT

## Fetal anemia

Blackfan-Diamond anemia

Fanconi

Parvo B19 virus infection

## Neuromuscular defect

Fetal akinesia deformation sequence

Myotonic dystrophy

Spinal muscular atrophy

## Metabolic defect

Beckwith- Weidemann syndrome

## Other

Severe development delay

Noonan syndrome



# What should our management be?

- Reassure the parents:
  - Overall adverse outcome quoted in most studies around 18%
- Follow up anatomy scan at 16 and 20 weeks (should include extensive cardiac evaluation)
- If this scan is normal, the chance of a live birth with no defects increases to **96-98%** (Adverse outcome in 2.24%)
- Adverse outcome can be expected in 18% if nuchal edema persists



# If chromosomal defects are included


- The chance of an adverse outcome, including chromosomal defects increase with nuchal translucency

<b>Nuchal Translucency (mm)</b>	<b>Adverse outcome including chromosomal abnormalities</b>
3.5 – 4.4	32%
4.5 – 5.4	49%
5.5 – 6.4	67%
≥6.5	89%



## Severe development delay

- 1.2 % if nuchal edema persists
- 0.4% if follow-up scans was normal



## What about added diagnostic techniques for genetic/developmental syndromes?

- Studies up to now has failed to show added benefit (Schou et al. 2009)

What we do know.....

Of the known 99 genetic/developmental syndromes associated with increased NT:

- Only 49 have genes identified
- Only 36 have reported mutations (400 in all)



## 5 Diseases most prominent

1. DiGeorge: 7 genes with 17 mutations
2. Noonan syndrome: 5 genes with 108 mutations
3. Smith-Lemli Opizt: 1 gene with 130 mutations
4. Congenital adrenal hyperplasia: 1 gene with 25 mutations
5. Spinal muscle atrophy: 1 gene with 1 mutation

Should we identify common syndromes in our population associated with increased NT and test for those, if testing is available?



# Conclusion

- Outcome not so poor
- With a good and thorough mid trimester scan we can identify most of the 18% that will have an adverse outcome.
- With a normal follow-up scan the outcome can be expected to be favourable in 96 – 98% of cases.
- We need to counsel our patients accordingly to let them make an informed decision.



Thank you