CAPABILITY 2009

WELCOME TO KHOKA MOYA

CAPABILITY
South African Report
Greater Sekhukhune Capability Outreach Project
(GraSCOP)

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CAPABILITY

CAPABILITY will:

- Develop an analytic framework for evidence-based genetic test evaluation including the domains; efficacy (evidence of utility in controlled settings) and effectiveness (evidence of utility in real settings).

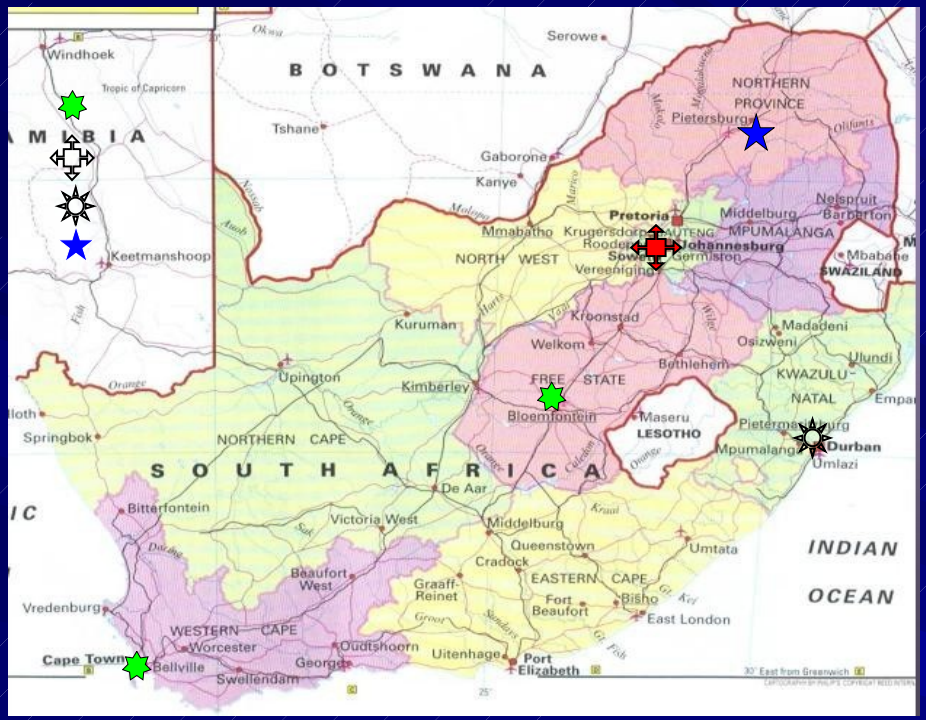
Proposed Greater Sekhukhune Capability Project

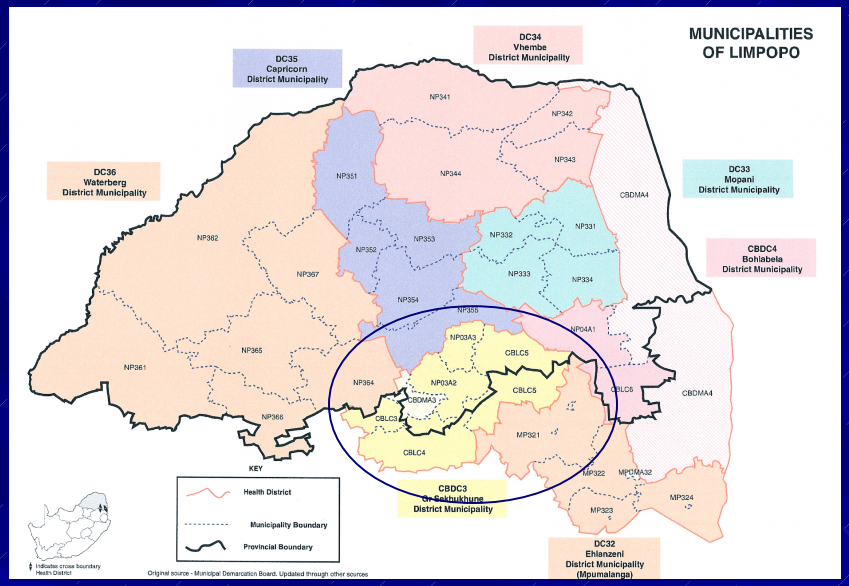
The previous outreach programme to Limpopo was instrumental in developing principle and practices for the development of clinical genetic services in SA.

This outreach should assist in furthering that process, but could be used to test the implementation and clinical utility of medical genetic tests.

NATIONAL HEALTH LABORATORY SERVICE

Greater Sekhukhune



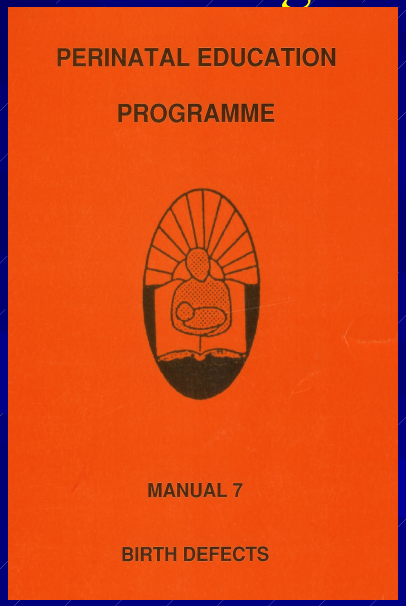


- 1 secondary care & 6 district hospitals
- 65 clinics & 4 community care centres
- ~18 400 annual births

Proposed Greater Sekhukhune Capability Project

Further evaluation of the Medical Genetic Education Programme

Basis of postgraduate nursing education programme In S Africa



Funded by MOD & produced in association with SAIDA

- ✓Improves genetic knowledge & skills
- •Need to assess if improves clinical practice
- •Use the clinical diagnosis of Down syndrome to assess if practice is improved
- ✓Use LIMPOPO to introduce MGEP by tele-teaching

Medical Genetics Education Programme Greater Sekhukhune

MGEP Part I

- First course had 20 nurses & 2 medical officers
- 5 participants could not attend all the contact days- will complete MGEP I in next course & write exam
- 13/17 (77%) passed the course examinations (pass mark ≥80%)
- Second MGEP I course is in progress

MGEP Part II

- Best 30 participants will attend this 5 day practical clinical and counselling course

Medical Genetics Education Programme Tele-teaching MGEP Part I in Limpopo

Funded by March of Dimes

- Tele-teaching from Pretoria to 4 sites in Limpopo undertaken
- Each site had an on-site nurse previously trained in medical genetics supporting the participants
- These supporting nurses had received training for their role
- 29 nurses received MGEP Part I training
- 25 (86%) passed the exit examination

St Rita's Hospital Outreach Clinics

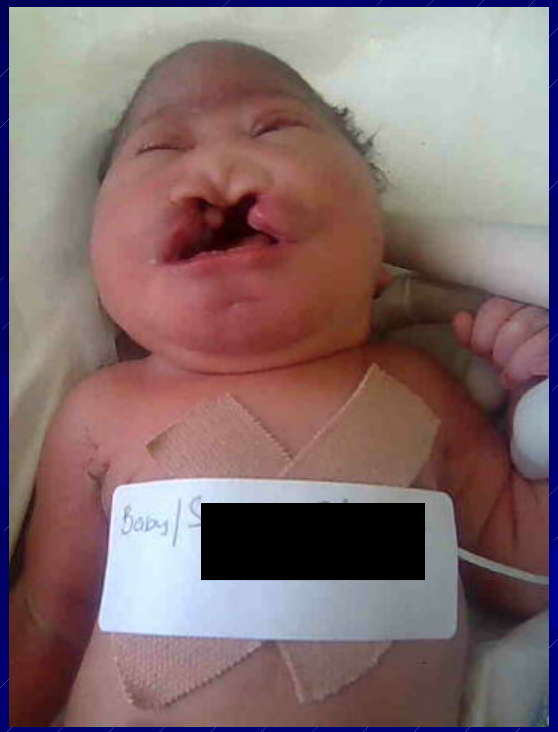
5 outreach visits to hospital to date

28 patients seen

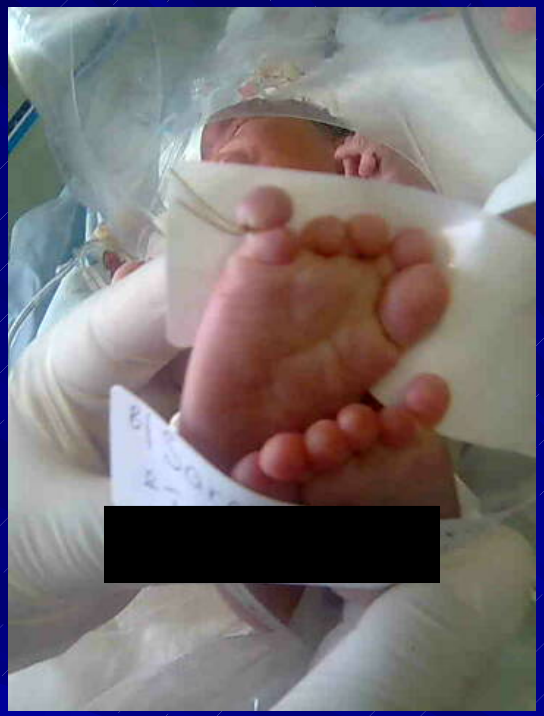
Patients seen include those with:

Myotonia congenita, an undescribed AD pigmentary abnormality, Noonan syndrome, OI, Down syndrome, trisomies 13 and 18, undiagnosed patients with dysmorphic features and dev delay, microcephaly, macrocephaly, hyrocephalus, limb defects, amniotic band sequence, sublingual cyst, and ambiguous genitalia

GraSCOP birth defect cellphone/photo project- the first patient



Clinical diagnosis
Trisomy 13
Specimen of skin sent to lab for QF-PCR
Rx. Palliative care
Babe died shortly after birth.
Mother to be counselled at next outreach visit



- Mother's consent obtained
- Clinical photos taken with cellphone & MMSed to department
- Clinical details faxed. On NDoH notification forms.
- Tentative clinical diagnosis, recommended investigations & Rx discussed with medical officer & faxed to hospital
- Mother & babe referred to the next clinical genetics outreach clinic at hospital

Cytogenetic laboratory at NHLS & University of the Witwatersrand

2006

- 2439 specimens received
  12 qualified cytogeneticists

2007

- 3193 specimens received
  9 qualified cytogeneticists

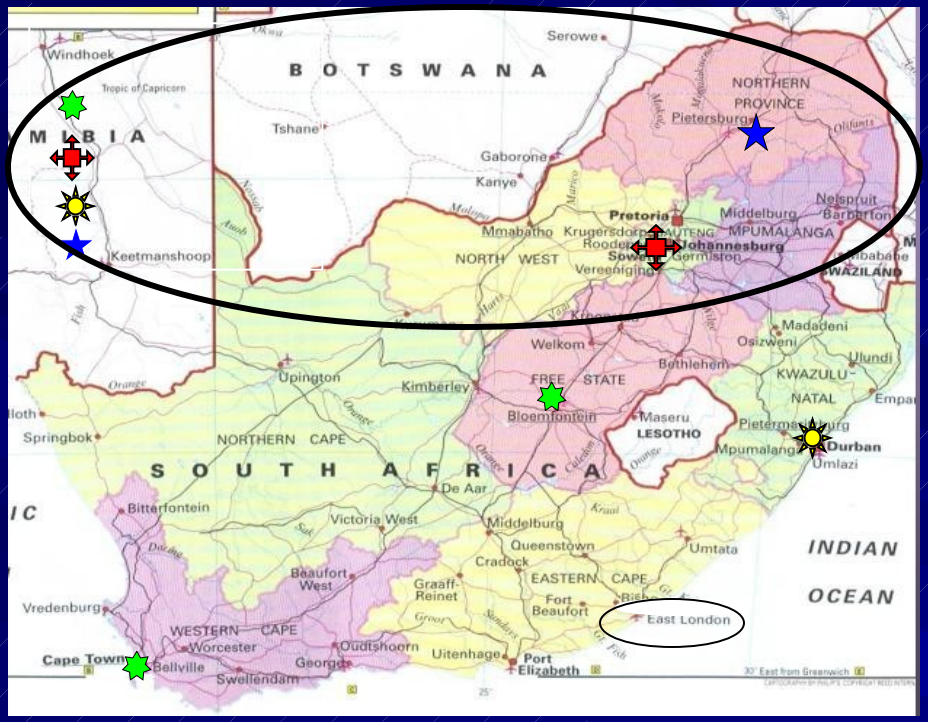
2008

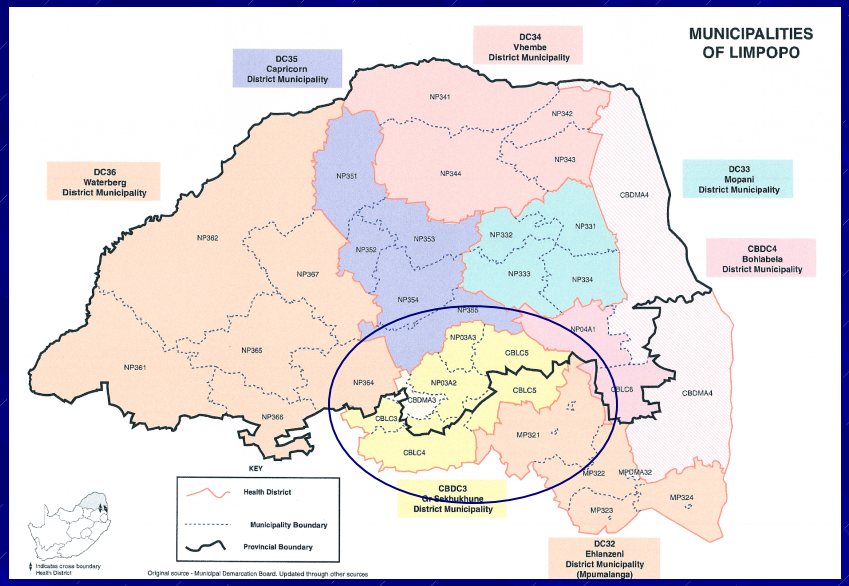
- 3227 specimens received
  6 qualified cytogeneticists

➢ QF-PCR for AMA prenatal diagnosis & postnatal diagnosis of trisomies 13, 18 and Down syndrome initiated

Cytogeneticist- ‘a disappearing breed’

Genetic testing for Down syndrome, trisomies 13 &18 with QF-PCR



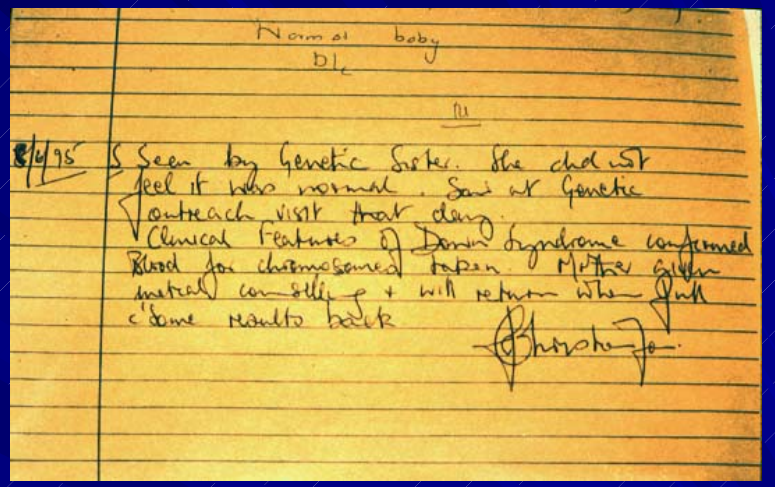


- Initially the consideration was for QF-PCR testing for DS to be undertaken with specimens from Greater Sekhukhune. On request of the paediatricians in the Province the use of QF-PCR was extended to Limpopo Province
- Because of the staffing situation in the cytogenetic laboratory all specimens received with a diagnosis of trisomy 13, 18 & DS are now analysed by QF-PCR
- The laboratory receives specimens from the 4 northern provinces of South Africa, East London in the Eastern Province, Botswana and Namiba

Genetic testing for Down syndrome- The S African scenario

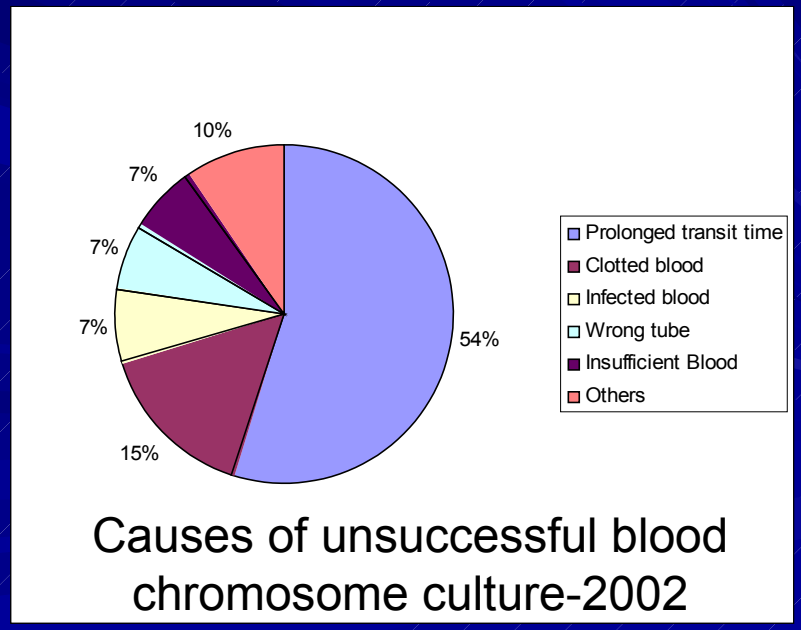
Postnatal clinical practice

- 16% DS infants diagnosed in neonatal period
- <50% DS infants diagnosed before 6 months of age



NHLS Laboratory (Jan 2007-May 2008)

- 653 specimens with DS diagnosis diagnosed with chromosome analysis
- 12% failed culture
- 33% normal chromosomes
- 1% other diagnosis
- 54% DS karyotype
- DS- 95% Trisomy 21
  - 3.6% Translocations
  - 1.4% Mosaics

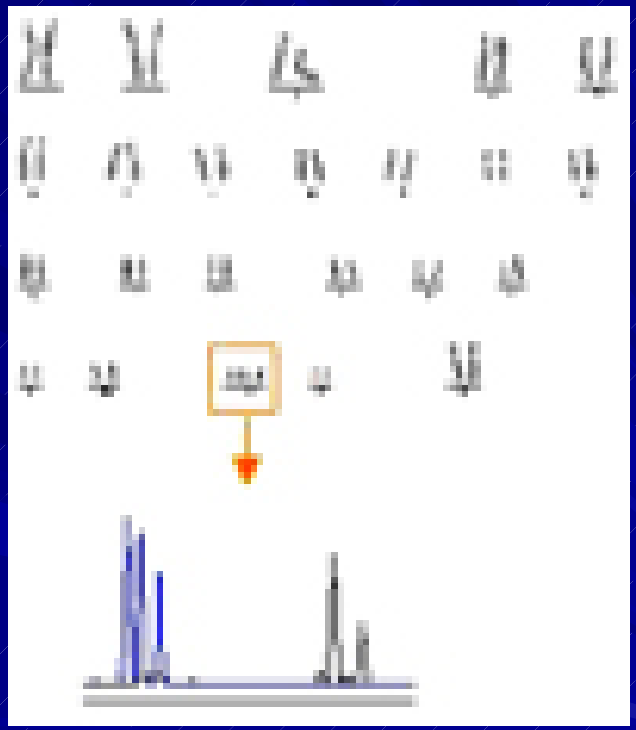


Causes of unsuccessful blood chromosome culture-2002

Genetic testing for Down syndrome with QF-PCR
July 2008- February 2009

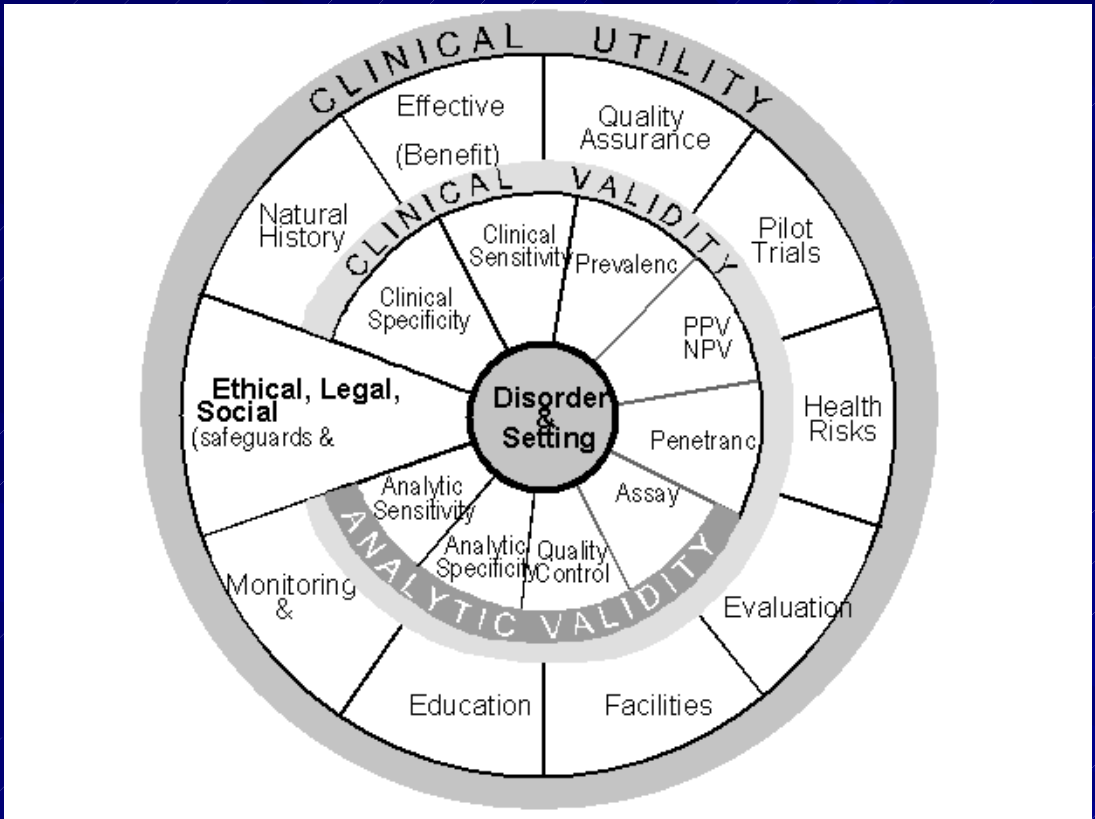
July 2008-February 2009

- 223 requests for DS diagnosis Done by QF-PCR
- 143 (64%) DS diagnoses confirmed by QF-PCR
- 80 (36%) of requests for DS diagnosis not confirmed by QF-PCR



QF-PCR diagnosis of Down syndrome

The ACCE Evaluation Process for Genetic Testing



- **Analytical validity** of a genetic test defines its ability to measure accurately and reliably the genotype of interest.
- **Clinical validity** of a genetic test defines its ability to detect or predict the presence or absence of the phenotype, clinical disease or predisposition to disease.

- **Clinical utility of a genetic test refers to the likelihood that the test will lead to an improved outcome.**
- **Ethical, legal and social issues of a genetic test.**

Other genetic testing with QF-PCR
July 2008- February 2009*

Trisomy 13 & 18

Trisomy 13- 19 confirmed diagnoses

Trisomy 18- 15 confirmed diagnoses

QF-PCR done on specimens unsuitable for chromosomal analysis

Down syndrome confirmed- 30 confirmed diagnoses

Result with 2 cell lines- 1(chromosome analysis requested)

Normal male/female- 176

Genetic testing with QF-PCR

July 2008- February 2009

Specimens tested

Down syndrome requested- 223 (51%)

Other - 211 (49%)

Total - 434 (100%)

Abnormal results

Down syndrome

Tested for DS - 143 (33%)

Tested for other reason - 30 (7%)

Trisomy 13 & 18 - 34 (8%)

Other - 1

Total - 207 (48%)

Postnatal genetic testing with QF-PCR
July 2008- February 2009*

The question is do we now decide to continue testing with QF-PCR as is currently done?

Or

Do we only use QF-PCR to only test for a specific postnatal diagnosis?

e.g. DS, Trisomies 13, & 18

Prenatal genetic testing for AMA syndrome- The S African scenario

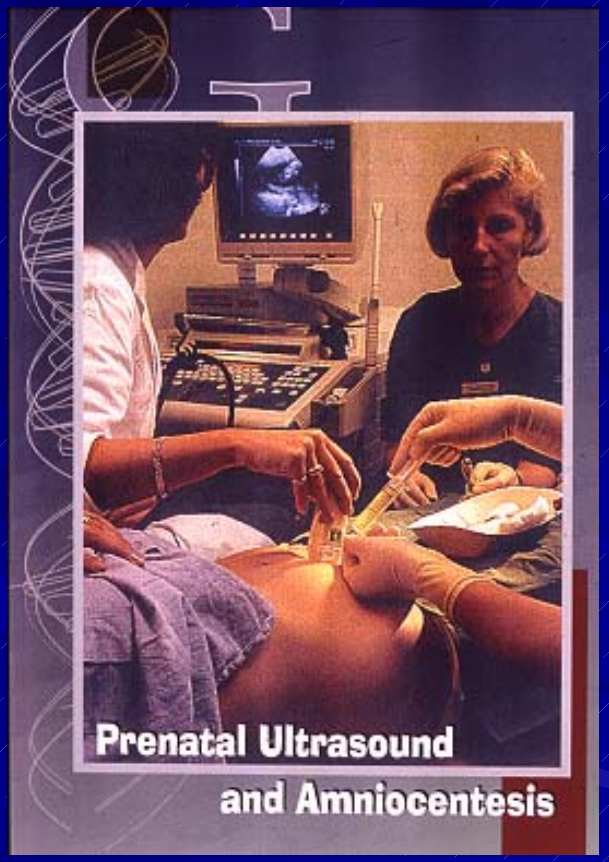
Prenatal DS diagnosis in SA

- ~170 000 women of AMA delivered in 2005
- 1221 amniocenteses for AMA performed nationally in the public service sector in 2005
- Reasons- the high cost of the test

  - failure of PHC to apply ANC protocols

  -? ↑Risk of HIV to fetus

  -? Other reasons



Prenatal diagnosis with QF-PCR

	January 2008-February 2009
Normal result	341(85.5%)
Abnormal results	56(14.5%)
• Trisomy 21	26
• Trisomy 18	14
• Trisomy 13	4
• Turner syndrome	5
• Kleinefelters	4
• Triploid	2
• Trisomy X	1
• Unable to get an result	2(0.5%)
TOTAL	399

Genetic testing with QF-PCR

2008- 2009

Using QF-PCR reduce the monthly workload in the cytogenetics laboratory by

33.8%

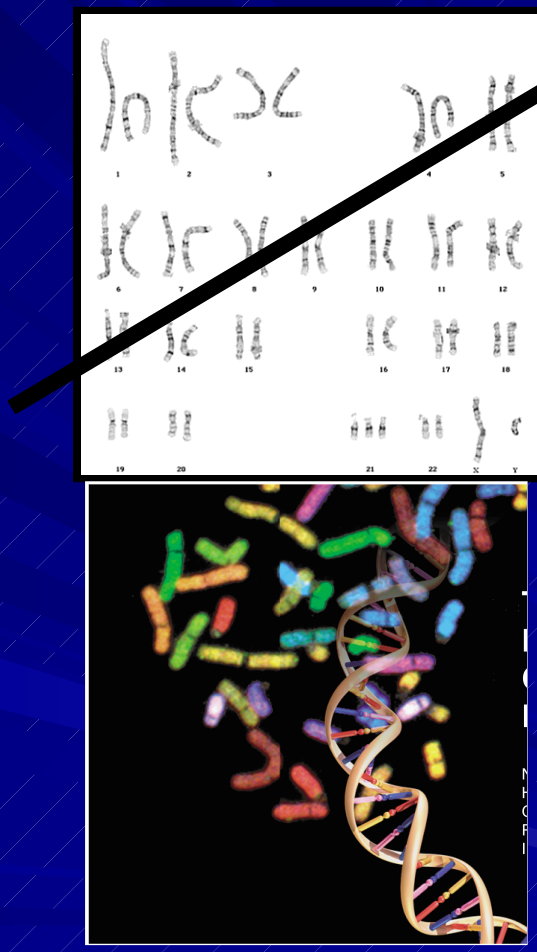
Proposed Greater Sekhukhune Capability Outreach Project

In developing future laboratory diagnostic testing for South Africa the future appears to lie in applying DNA based tests as soon and widely as possible.

The goal of this process is to develop a diagnostic laboratory service that complements the clinical service available, and is

'better, cheaper, faster…'

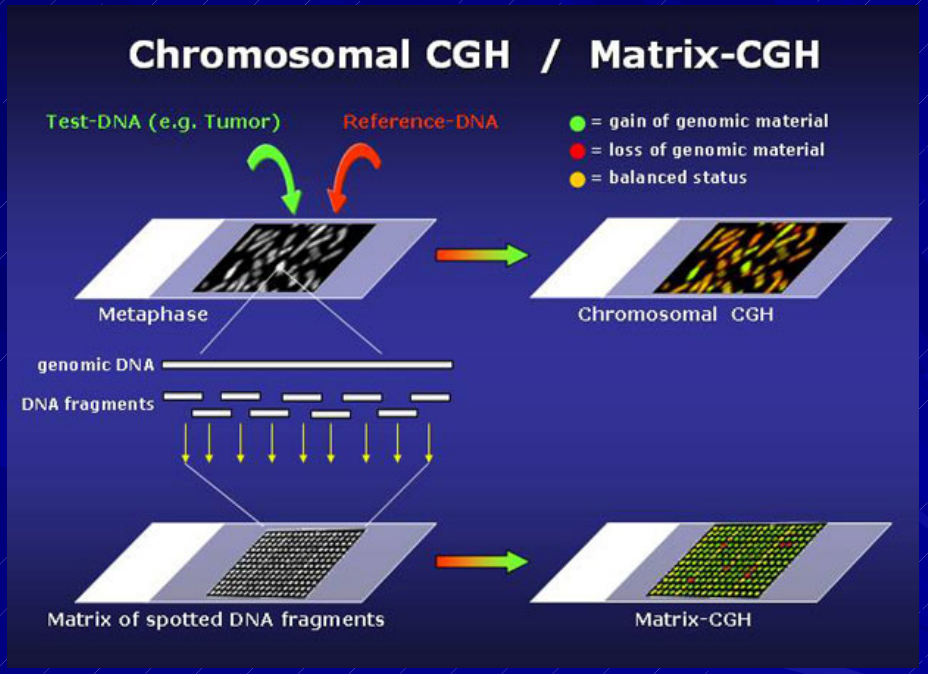
The application of QF-PCR for the pre-natal diagnosis in AMA women and postnatal diagnosis of Down syndrome appears to be appropriate for the S African situation.



The future- DNA based diagnostic testing

DNA-based testing

The application of other and new DNA-based diagnostic techniques in countries with limited resources seems to hold promise for the future



Conclusion

At the conclusion of the CAPABILITY programme we hope to have achieved:

- the training of >40 nurses & doctors in Greater Sekhukhune in basic clinical genetics (dysmorphic diagnosis, counselling & psychosocial support)
- Support for these practitioners and their patients with outreach clinics for which we will seek funds to continue
- Extend to other hospitals & leave in place the cellphone/photo programme to support ongoing care for children with birth defects
- the knowledge & insight to convince colleagues nationally to accept QF-PCR for the laboratory diagnosis of AMA & Down syndrome (+trisomies 13 &18) postnatally
- To use knowledge & insight gained in the programme to develop protocols applicable for the use in our circumstances for other DNA-based tests, including CGH microarray