



AWI-Gen

Wits – INDEPTH Partnership

Genomic and environmental risk
factors for cardiometabolic disease
in Africans

Collaborative Centre



World Bank – Change in burden of disease (1990 to 2010)

WEST AFRICA

HIV/AIDS	483%
Road Injury	112%
Malaria	79%
Cirrhosis	74%
Sickle Cell	66%

NORTH AFRICA AND MIDDLE EAST

Diabetes	94%
Low back pain	74%
Major depressive disorder	63%
Road injury	36%
Ischaemic heart disease	37%

EAST AFRICA

HIV/AIDS	178%
Neonatal sepsis	26%
Neonatal encephalopathy	29%
Preterm birth complications	10%
TB	5%

CENTRAL AFRICA

HIV/AIDS	240%
Malaria	61%
TB	57%
Neonatal encephalopathy	56%
Meningitis	53%

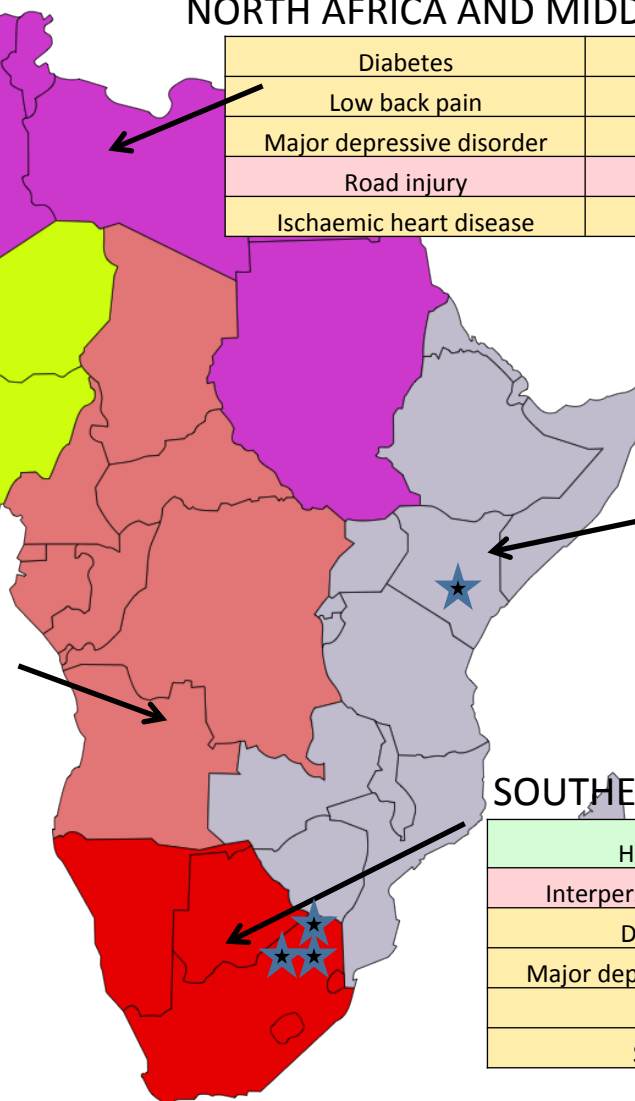
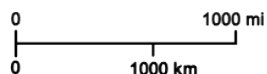
SOUTHERN AFRICA

HIV/AIDS	1065%
Interpersonal Violence	79%
Diabetes	99%
Major depressive disorder	47%
COPD	38%
Stroke	33%

COMMUNICABLE

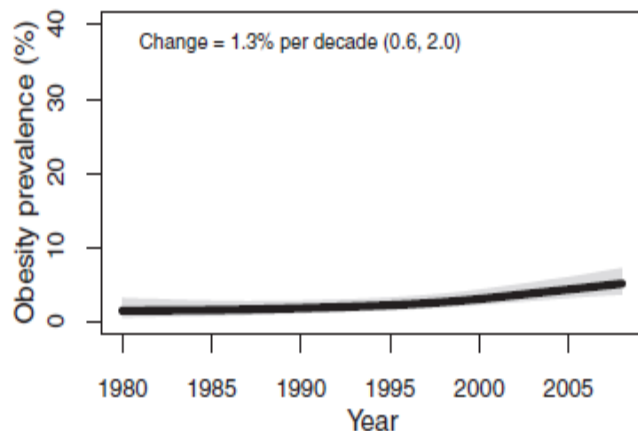
NON-COMMUNICABLE

ACCIDENTAL

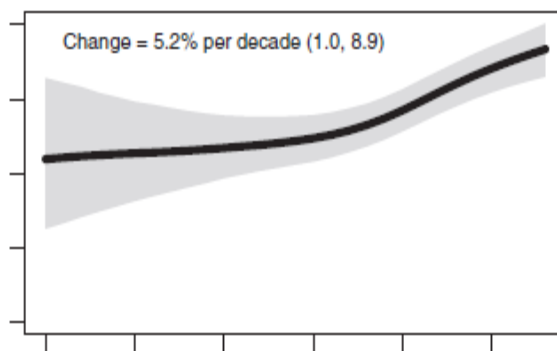


Change in obesity (1980 to 2008)

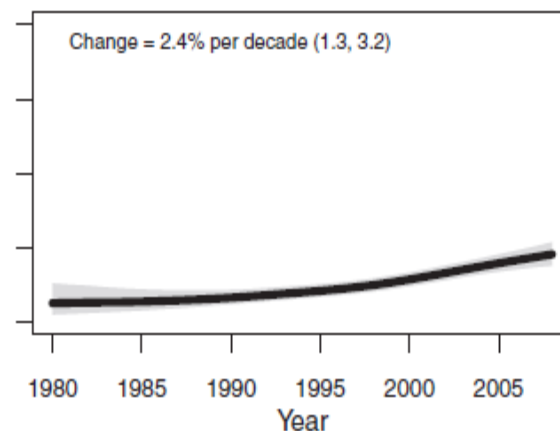
East Africa (female)



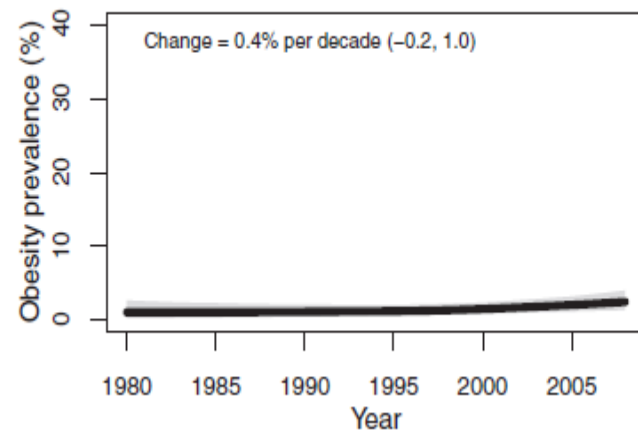
Southern Africa (female)



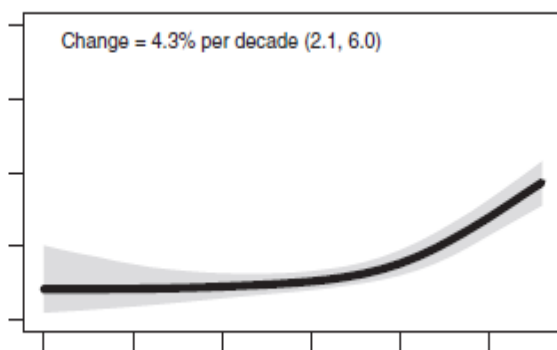
West Africa (female)



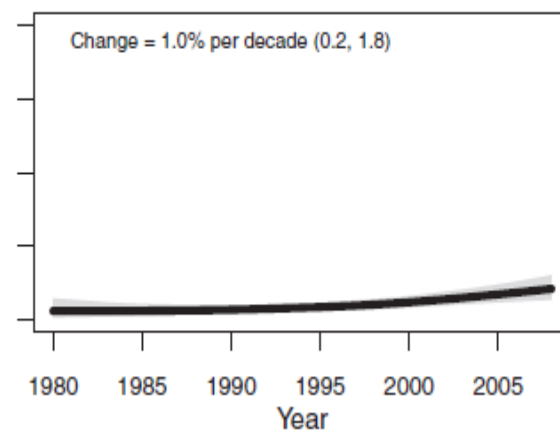
East Africa (male)



Southern Africa (male)

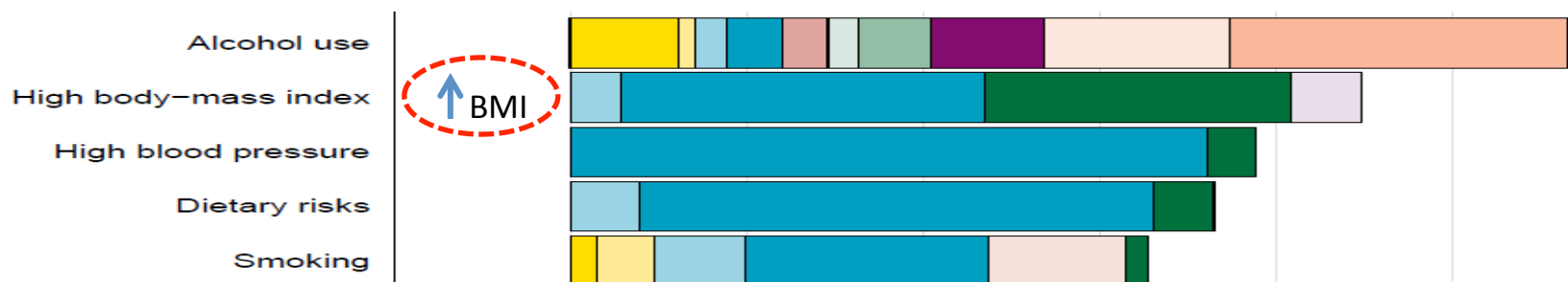


West Africa (male)



Stevens et al. Population Health Metrics 2012, 10:22
<http://www.pophealthmetrics.com/content/10/1/22>

Top 5 leading **risk factors** for burden of disease (DALYs) in South Africa

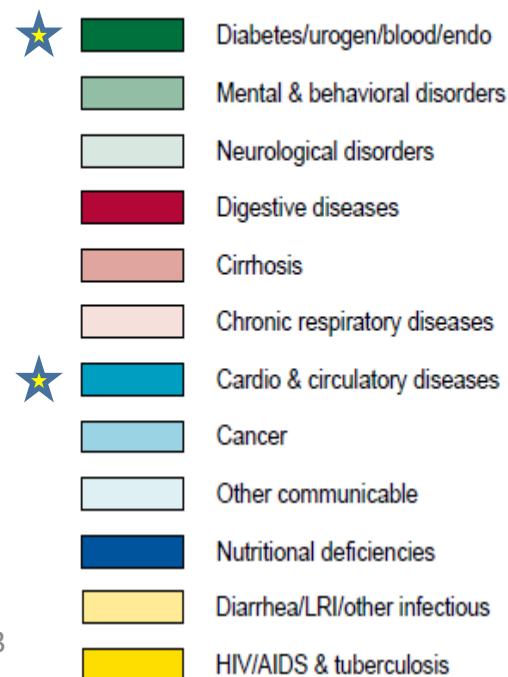


High BMI as a risk factor

Ghana 7th

Kenya 14th

Burkina Faso not in top 15



AWI-Gen - Outline

- Projects
- Management
- Ethics
- Phenotyping
- Data Management
- Training
- Challenges
- Progress



Project – Aims

1. Pilot Project – Soweto (~2000 individuals)
2. Population structure and genome architecture
3. Genetic and environmental contributions to body composition across six Centres in Africa (~12 000 individuals)



Aim 1: Pilot Project

Urban Soweto study

- Study design
 - Population sample
 - Age 40 to 60 yrs
 - Male & Female
 - Body composition phenotype
- Platform
 - Candidate gene/region assessment
 - Metabochip
- Analysis
 - Correlations with quantitative traits

• Progress

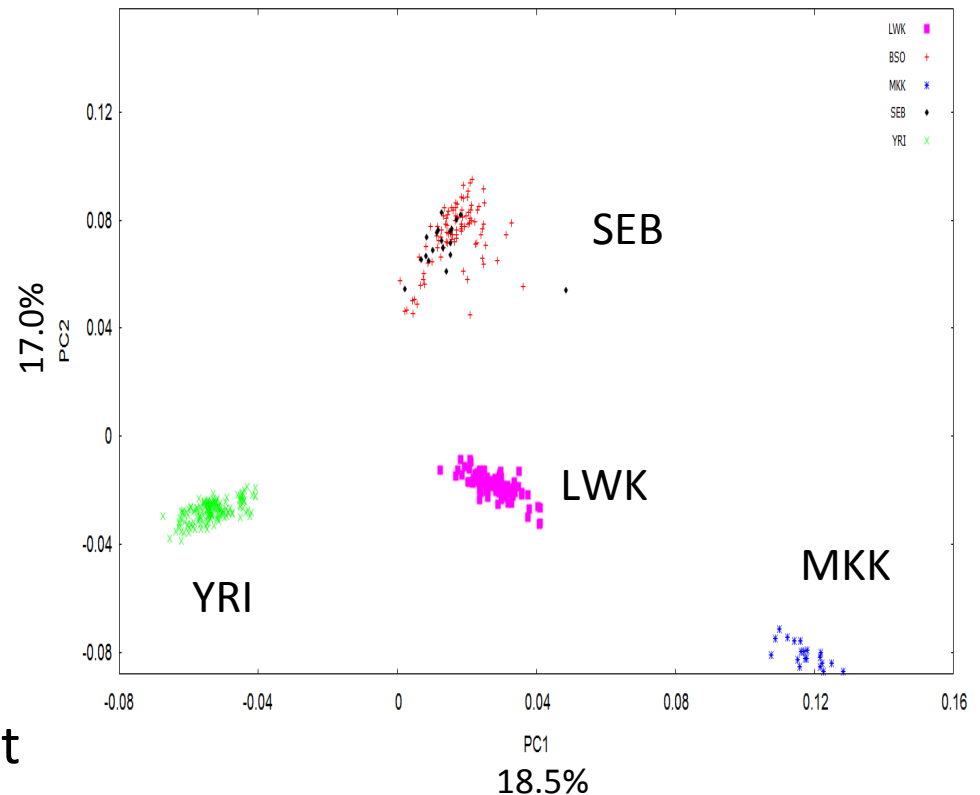
- ~1000 females
- 40 to 60 years
- phenotyped
- DNA normalized
- Sent to service provider for genotyping

• Next steps

- Prospective phenotyping of ~1000 males
- Sample collection
- DNA extraction & normalisation
- Genotyping & data QC
- Data analysis & interpretation

Aim 2: Population structure and genomic architecture

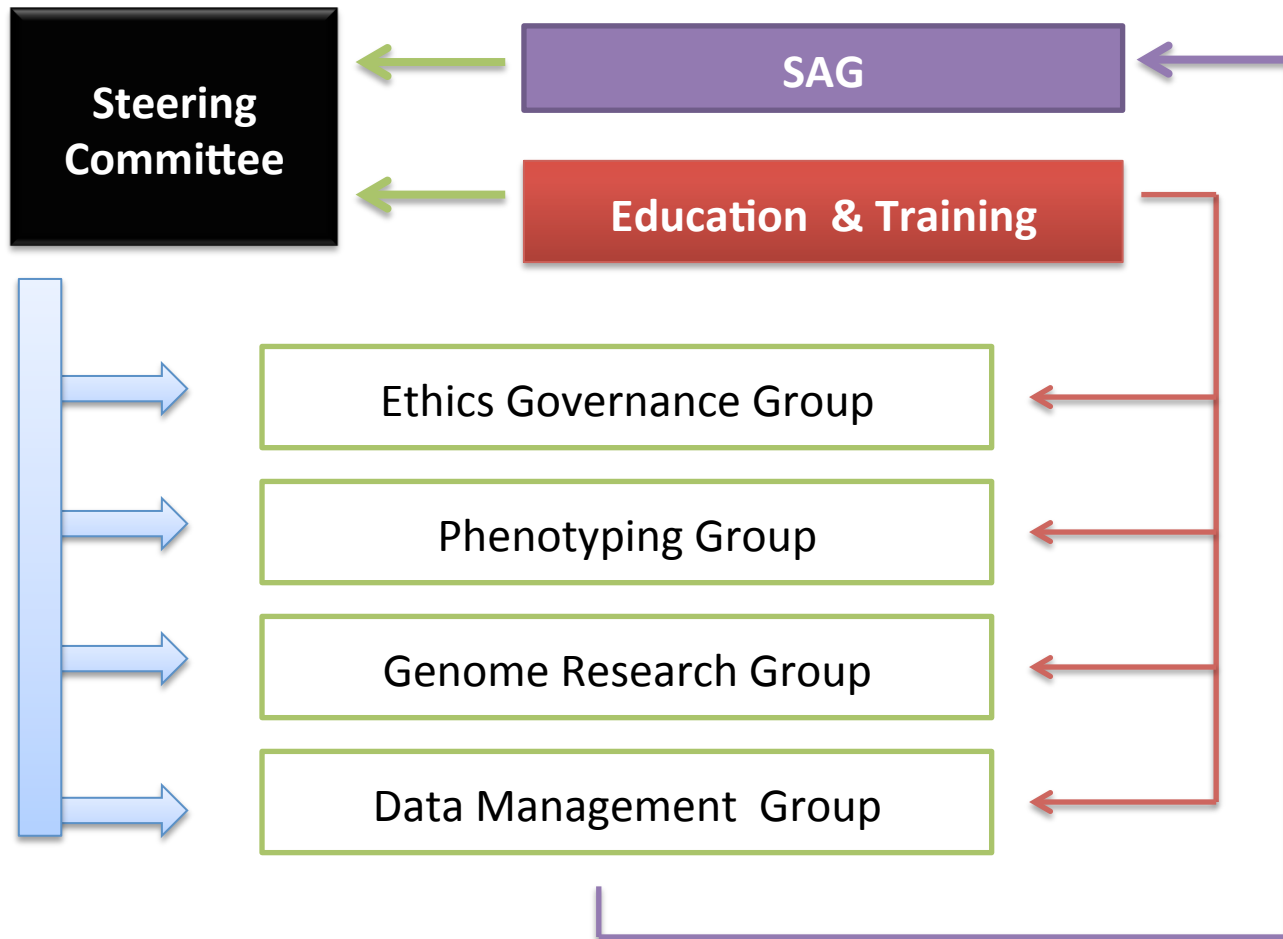
- Study design
 - 30 unrelated trios
 - 40 unrelated individuals
- Genotyping Platform
 - uncertain
- Outcome
 - HapMap equivalent for each population
 - Common variant allele frequencies
- Challenge
 - Which populations to test



Aim 3: . Genetic and environmental contributions to body composition

- Standardised phenotype questionnaire
- Instructions & SOPs
- Equipment purchase
 - Stadiometers
 - Scales
 - Ultrasound machines
- Training
- Field roll out
 - Staggered to ensure QA
 - Years 2, 3 & 4
 - Phenotyping
 - Blood sampling
- Data (demography & phenotype)
 - Collection
 - Central Data Management

Management



Financial Management – WHC/INDEPTH - Project Manager and Administrator

Ethics approval for the study

- Wits Ethics Approval (Soweto and Agincourt)
 - Project
 - Two informed consent forms
 - MTA
- Dikgale (South Africa)
- Navrongo (Ghana)
- Nanoro (Burkina Faso)
- Nairobi (Kenya)

Ethics Workshop – December 2012

Ethics Review Board members



Objective: To discuss ethical issues related to genomic science in African communities

Phenotype & Sample collection

Funded

- Demographic information
 - Home language & self-reported ethnicity
 - Medical & health histories
 - Living conditions (SES)
- Body composition
 - Height & Weight
 - Blood pressure
 - Waist & hip circumference
 - Ultrasound subcutaneous & visceral fat

Not funded

- Glucose
- Lipids

Blood samples:







10ml EDTA (DNA)

15ml Clotted (serum - lipids)


5ml NaF (plasma - glucose)

Body composition and HIV infection

In a population sample of 2000 individuals.....

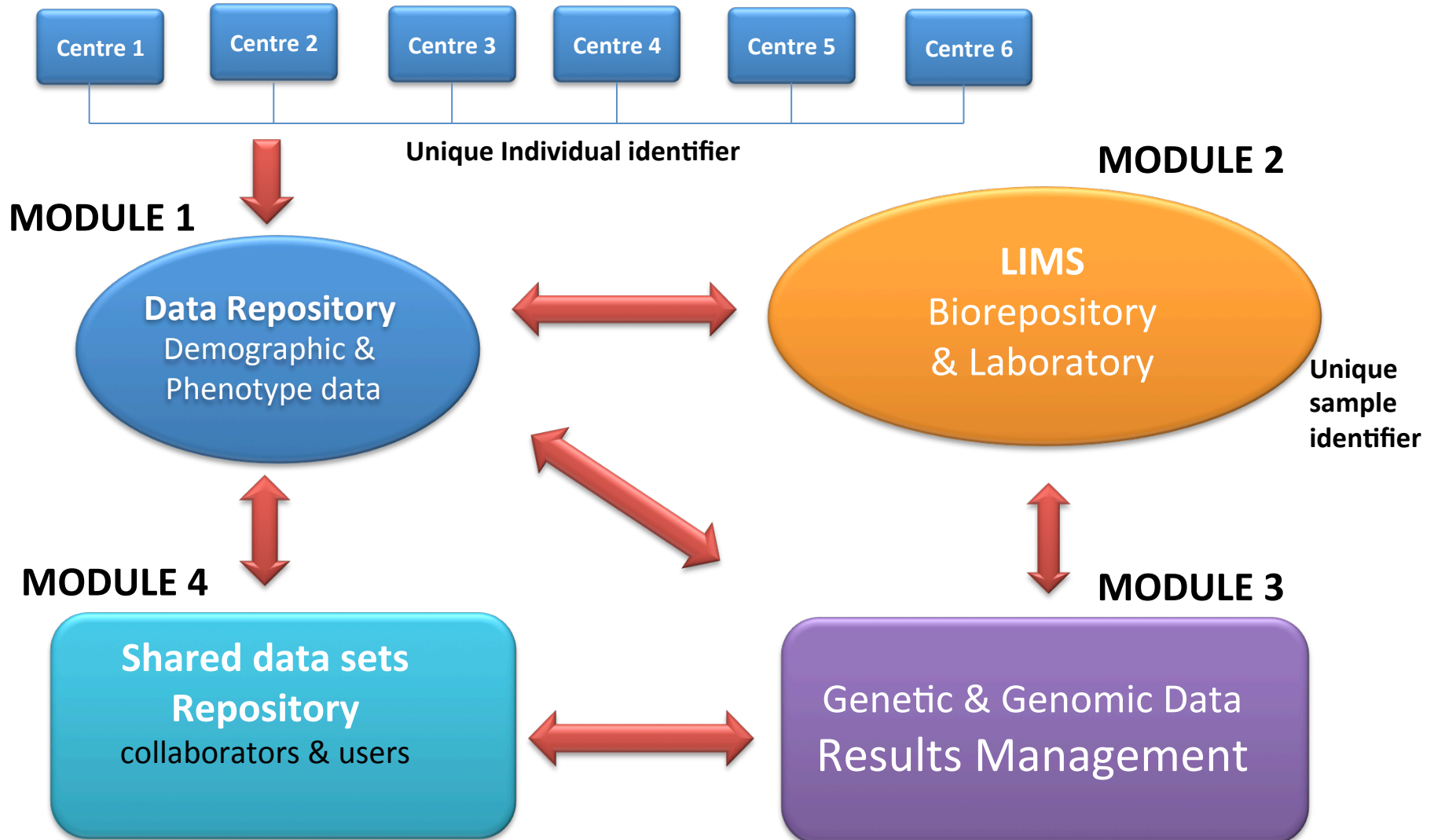
	Agincourt	Dikgale	Nairobi	Nanoro	Navrongo	Soweto
Expected number HIV infected individuals	462 	274 	248 	22 	30 	304 

 Based on regional averages

 Based on country average



Data Management



Training

Objective: Capacity development

- Assessing needs
- Bringing international partners on board
- Timing of training workshops
- AWI-Gen specific training
 - Data management workshop
 - Phenotyping workshop
- External training opportunities
 - Wellcome Trust courses
 - BioNet courses

Challenges

- Effective communication given poor internet connectivity across African countries (keeping everyone onboard)
- Standardisation across Centres
- Coordinating training activities
- Structure of African populations in study
- Funding & Financial management of the project
- Employing experienced senior scientists

Progress

- Management structure
- Ethics approval
- Phenotyping questionnaire
- Data Management Framework
- Pilot project



Timeline

ACTIVITY	YEAR 1	YEAR 2	YEAR 3	YEAR 4	YEAR 5
Training and capacity development					
African genome structure					
Phenotyping and sampling for Cohorts					
Obesity and body composition pilot study – urban South Africa					
Genome association study – west, east and south Africa					