

H3Africa

Wits-INDEPTH Partnership

Genomic and environmental risk factors for cardiometabolic disease in Africans

Collaborative Centre



Co-PI

Osman Sankoh

INDEPTH - International Network for the Demographic Evaluation of Populations and their Health in low and middle-income Countries



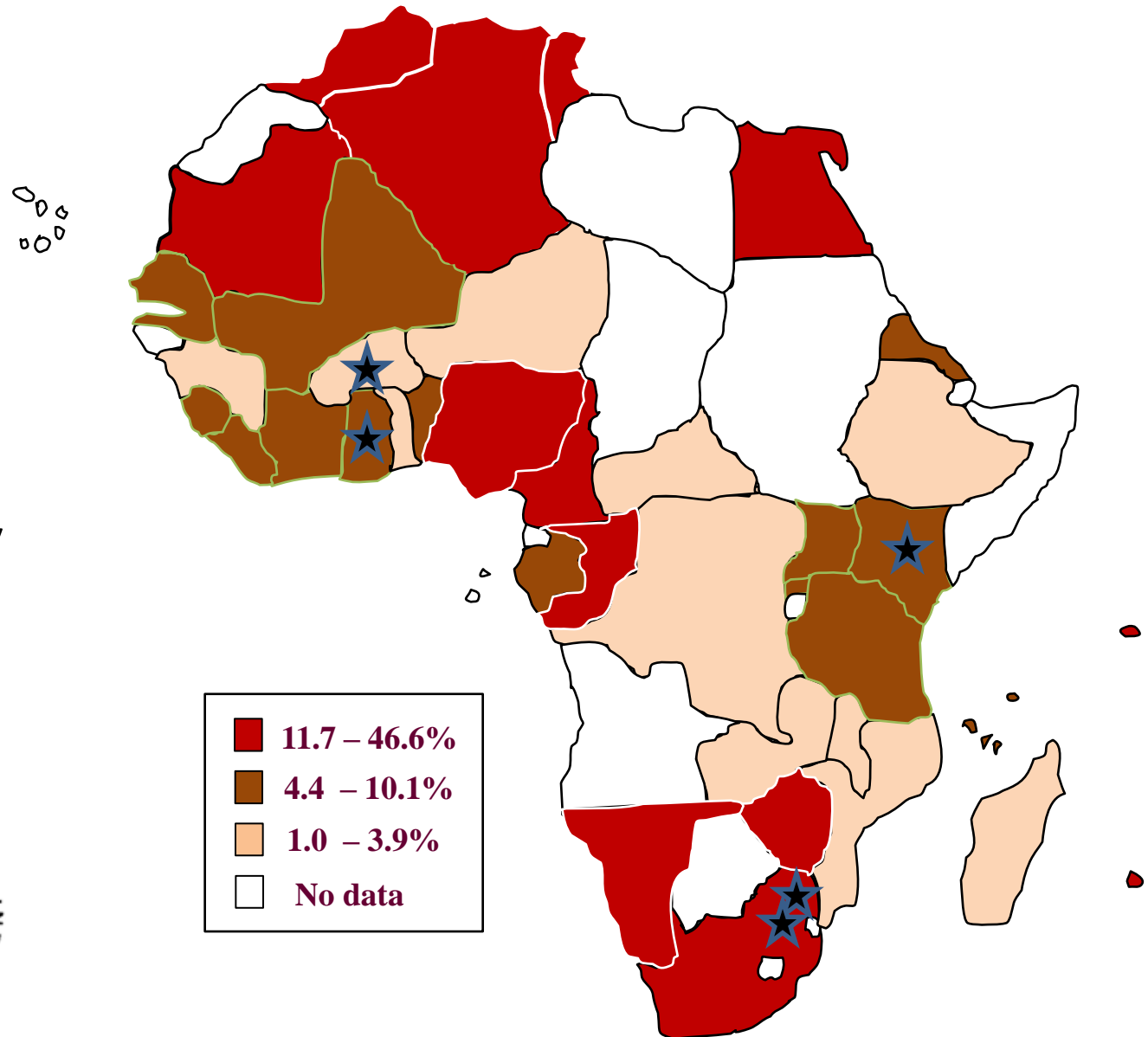
Broad aims aligned with H3Africa vision

- To **build capacity in sub-Saharan Africa for research** that leads to an understanding of, and response to, the interplay between genetic, genomic, epigenetic and environmental risk factors for obesity and associated cardiometabolic diseases
- To **develop sustainable capability and infrastructure** for the use of molecular technologies to understand patterns of disease and to inform management and prevention strategies



Prevalence of female obesity in Africa

Positive correlation between obesity and T2D and hypertension

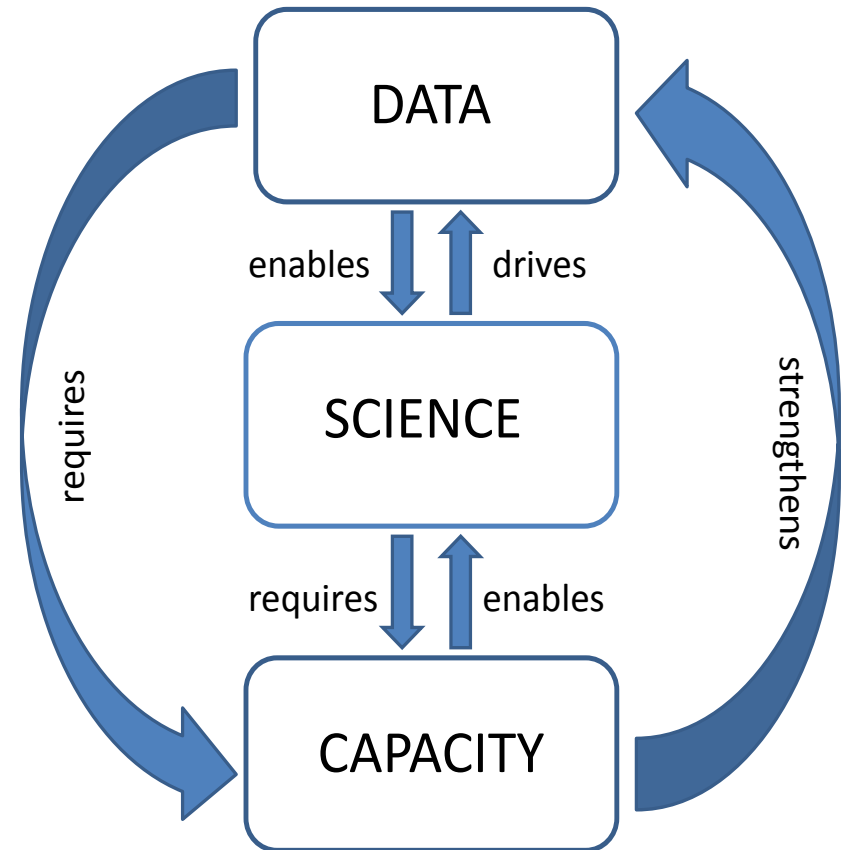


Prevalence of obesity and related disorders in females in Soweto

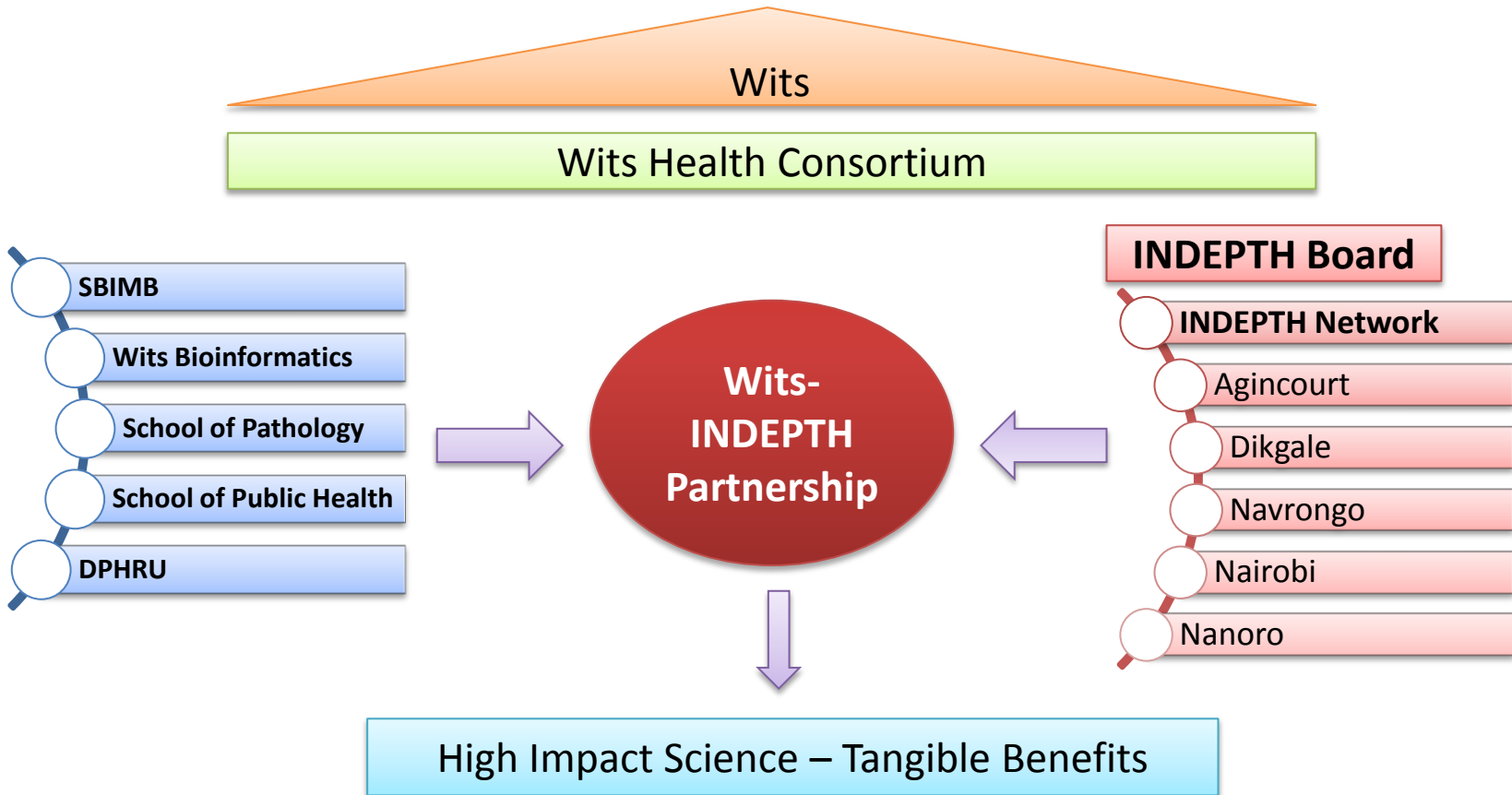
Variable	Levels (% or mean SD)
Age (with range)	42.0 8.5 (18 - 84)
BMI (with range)	30.5 6.7 (16.2 – 58.8)
Prevalence of obesity (BMI \geq 30)	50.1 %
Prevalence of severe obesity (BMI \geq 35)	23.0 %
Prevalence of waist circumference \geq 80cm	69.3 %
Prevalence of diabetes (glucose $>$ 7mM)	14.3 %
Prevalence of IFG (glucose \geq 5.6, \leq 7mM)	20.2 %
Prevalence of metabolic syndrome (harmonised guidelines)	42.1 %

Wits-INDEPTH Partnership

- Strong collaborative links
- Relevant research
- Complementary endeavor
- Inclusivity and excellence
- Capacity development
 - Training (staff and students)
- Research output
 - Knowledge generation
 - Publications
 - Influencing policy



Participant overview



Wits strengths

- Population Genetics
- Longitudinal cohort
- Bioinformatics
- Molecular genetics
- Cardiometabolic disease research
 - Basic and clinical
- Public Health Research





The INDEPTH Network of Health and Demographic Surveillance Systems *founded 1998, constituted 2002*

Osman Sankoh
Executive
Director of
INDEPTH



**Informing global efforts to
improve the health and
wellbeing of low and middle-
income populations**

Stephen Tollman
Principal Scientist

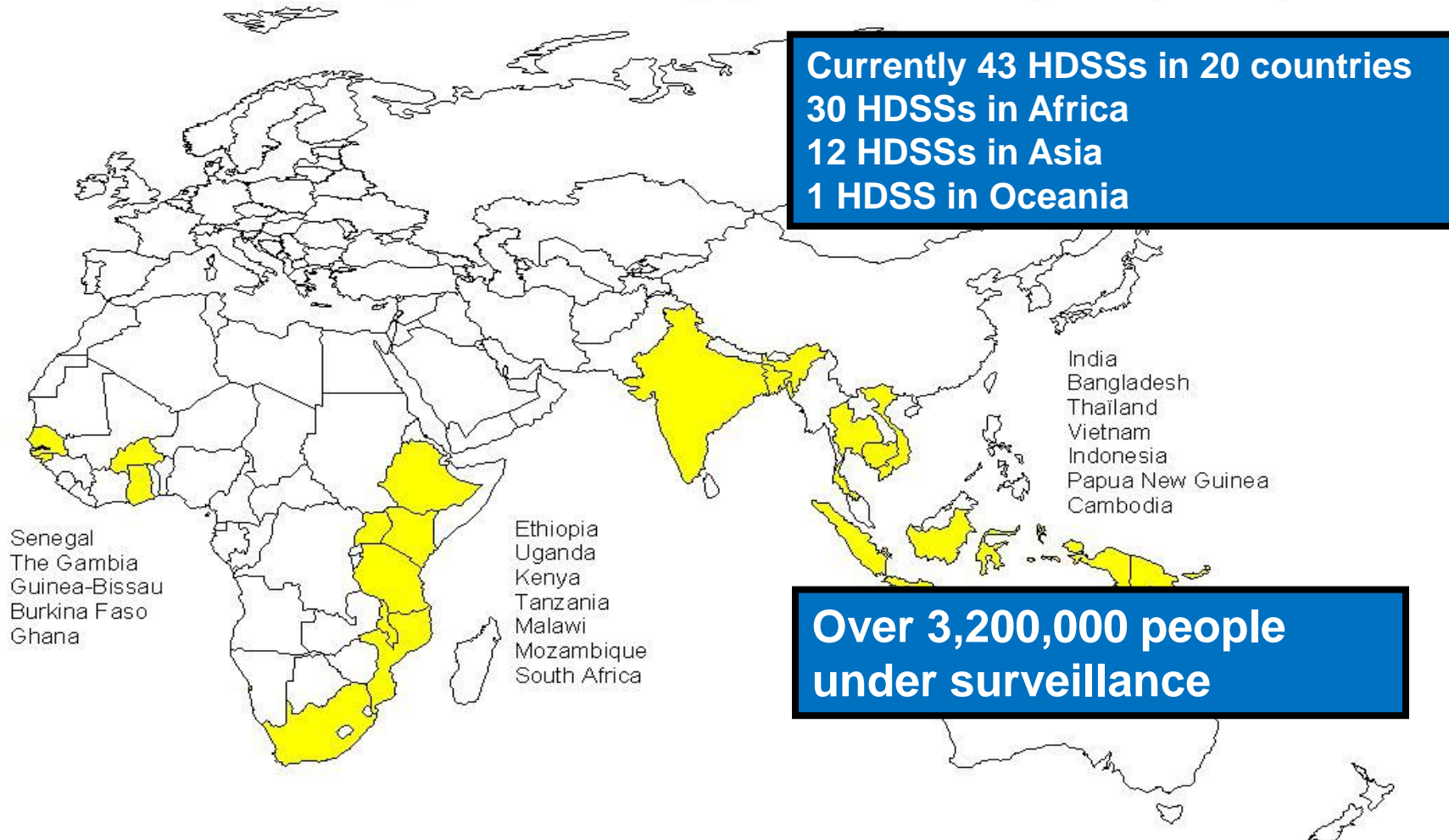


Kathleen Kahn
Board Member

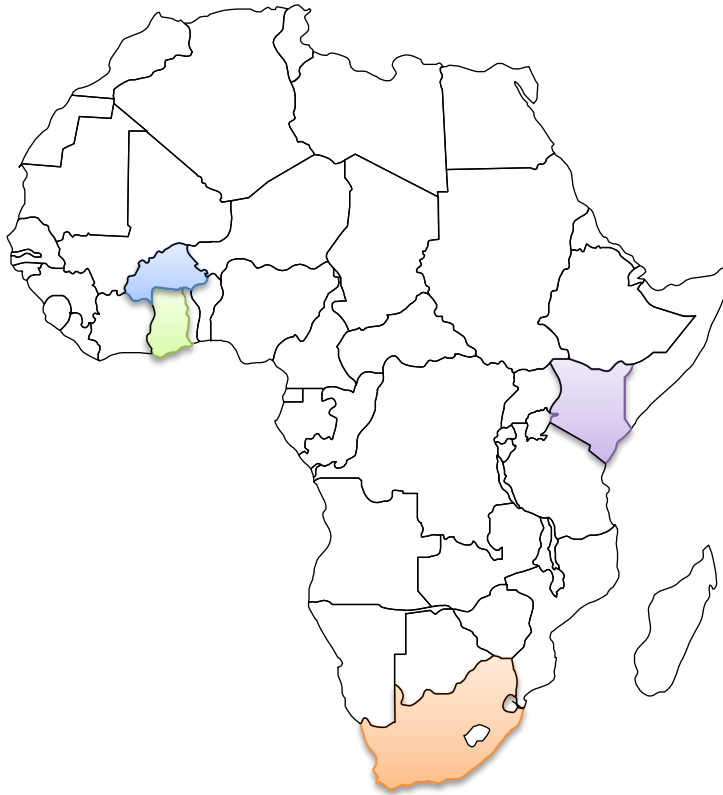




Low- and Middle-Income Countries with INDEPTH member centres Running Health and Demographic Surveillance Systems (HDSSs)



Where in Africa?



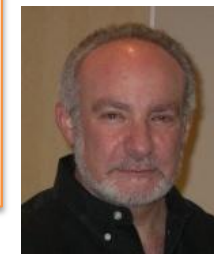
Ghana, Navrongo (Rural)
Abraham Oduro

Burkina Faso, Nanoro (Rural)
Halidou Tinto

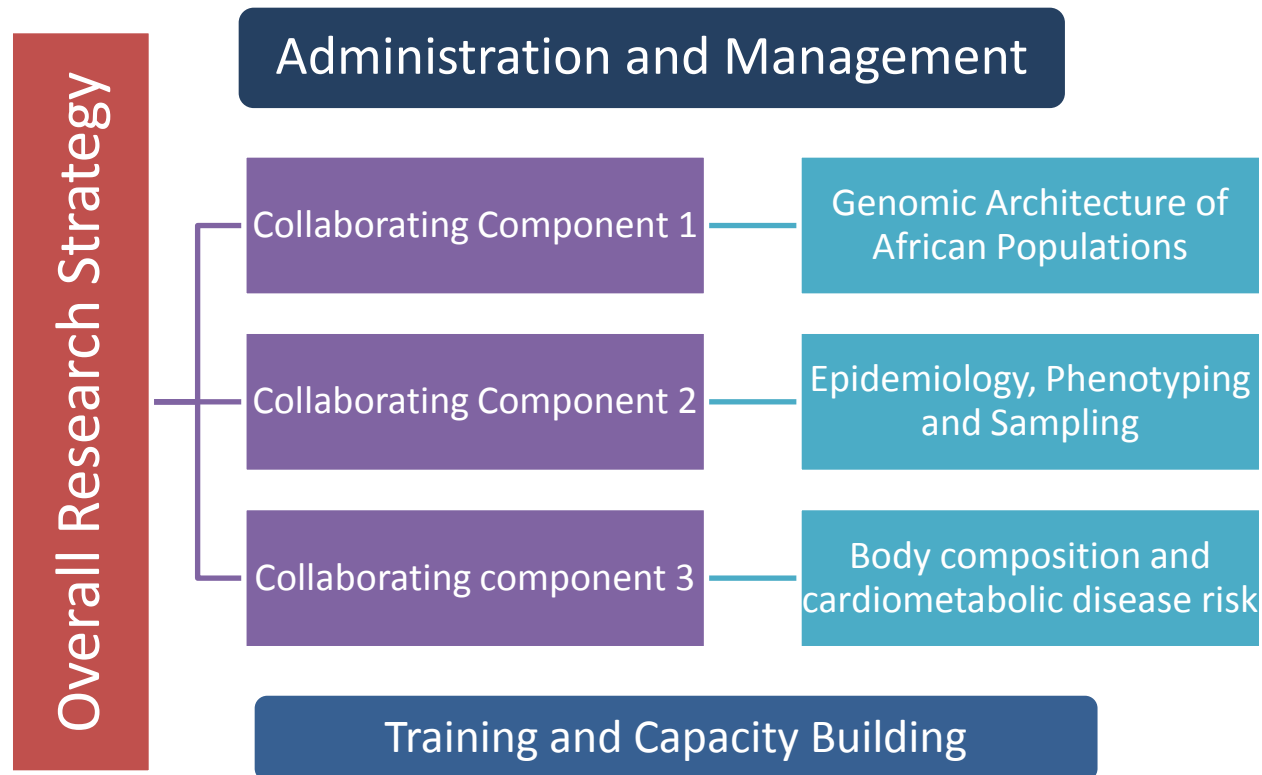
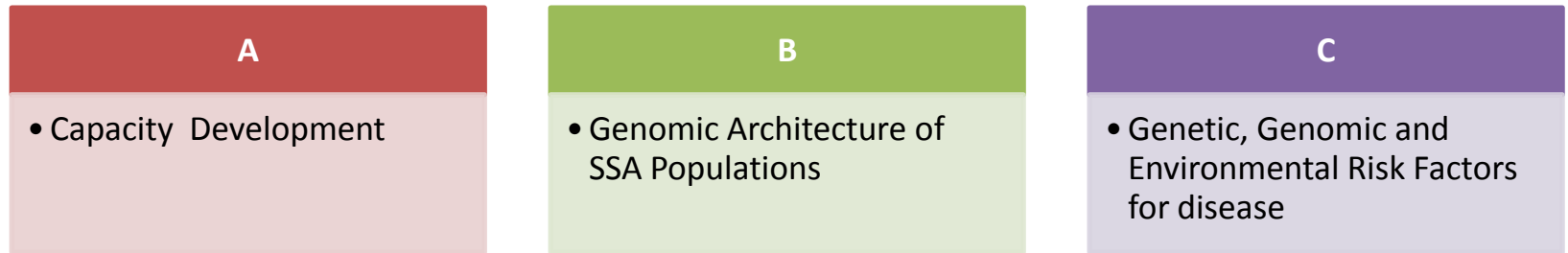
Kenya, Nairobi (Urban)
Catherine Kyobutungi

South Africa, Soweto (Urban)
Shane Norris

South Africa, Agincourt &
Dikgale (Rural)
**Stephen Tollman and
Marianne Alberts**



Themes of the Collaborative Centre



Collaborating Component 1

Aims:

- To examine the genetic structure of participating sub-Saharan African populations
- To identify the role of contributing factors to shaping the gene pool
- To use genetic data in conjunction with data from other disciplines to help to unravel the history of these African populations

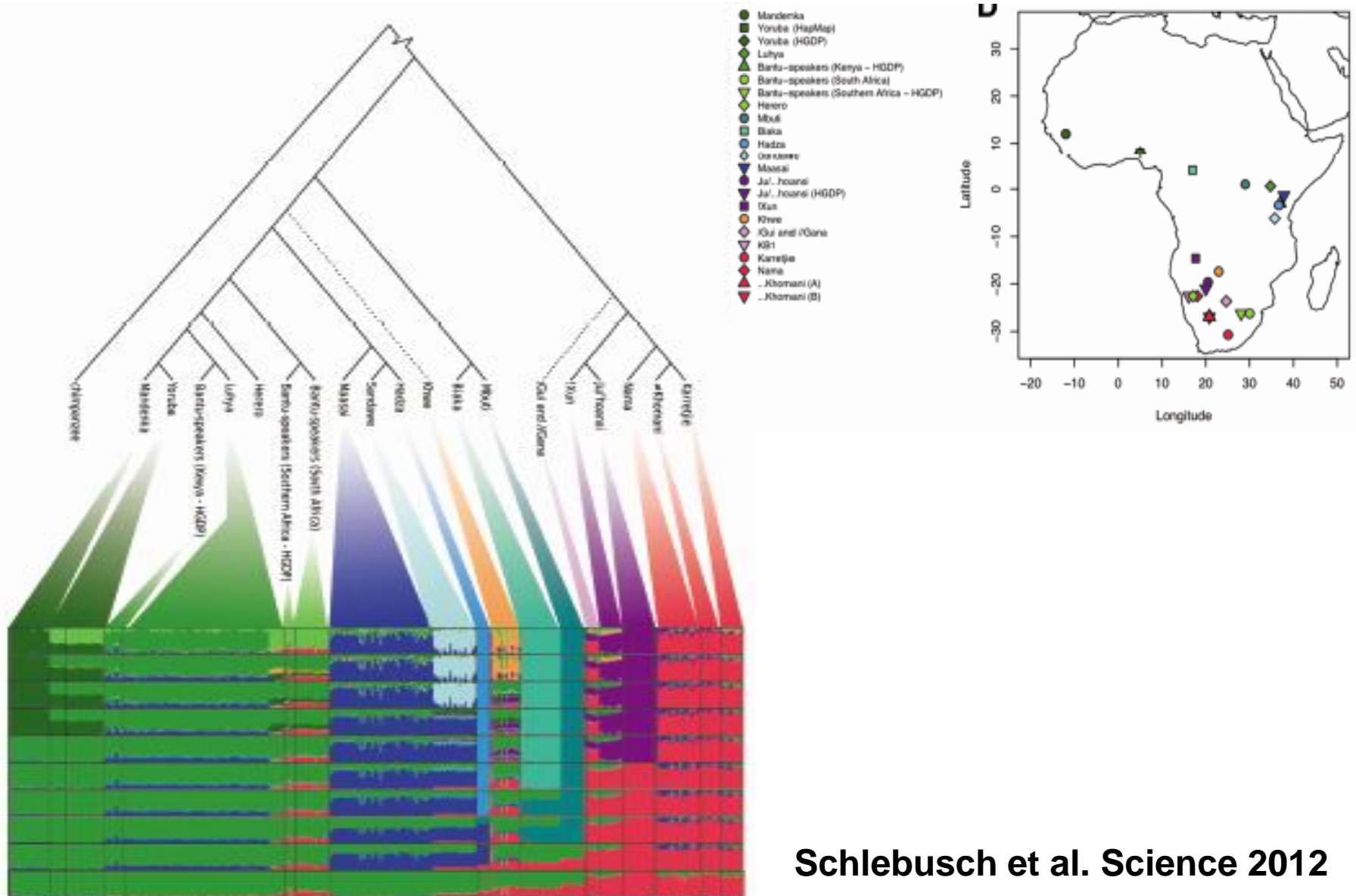
Genomic Architecture of African Populations



6 ethnolinguistic groups
100 unrelated individuals
30 family trios



Genetic structure in sub-Saharan Africa



Schlebusch et al. Science 2012

Collaborating Component 2

Epidemiology, Phenotyping and Sampling



Aim

Harmonised phenotype data collection capacity across the centres to collect **body composition data**, and to lay the foundation for **future cardiometabolic studies**

Phenotype & genomic study

- 2000 samples per collection site (n=10000)
- 40-60 years; 50/50 female/male



Phenotype data

Minimum measures across all sites

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

Enriched measures in 3 sites

- Soweto
 - Cardiometabolic risk markers
 - DXA whole body composition
 - Funded
- 2 HDSS centres (Agincourt & Navrongo)
 - Cardiometabolic risk markers
 - NIH PO1 application

Autopure LS

- Automated DNA purification
- Up to 10ml blood
- Yields up to 350 µg from 10 ml
- Good quality DNA for long term storage
- Processing of 8 or 16 samples per batch



Collaborating Component 3

Genetic and environmental contributions to body composition



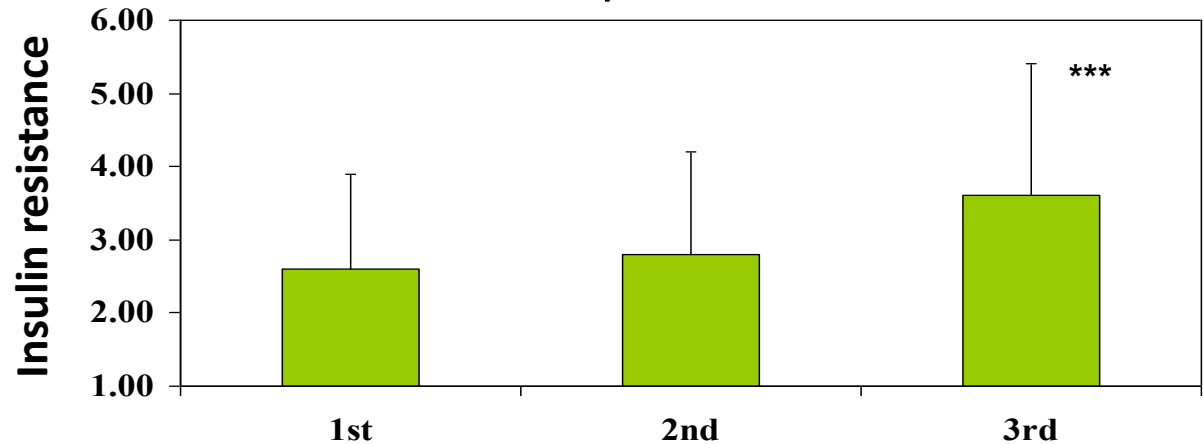
AIMS:

1. To identify genetic factors that influence **body fat distribution**: Pilot study in **urban Soweto** group with enriched phenotype data
2. **Genome wide** association study across west, east and southern Africa to examine **genetic and environmental contributions to body composition** and risk for cardiometabolic disease

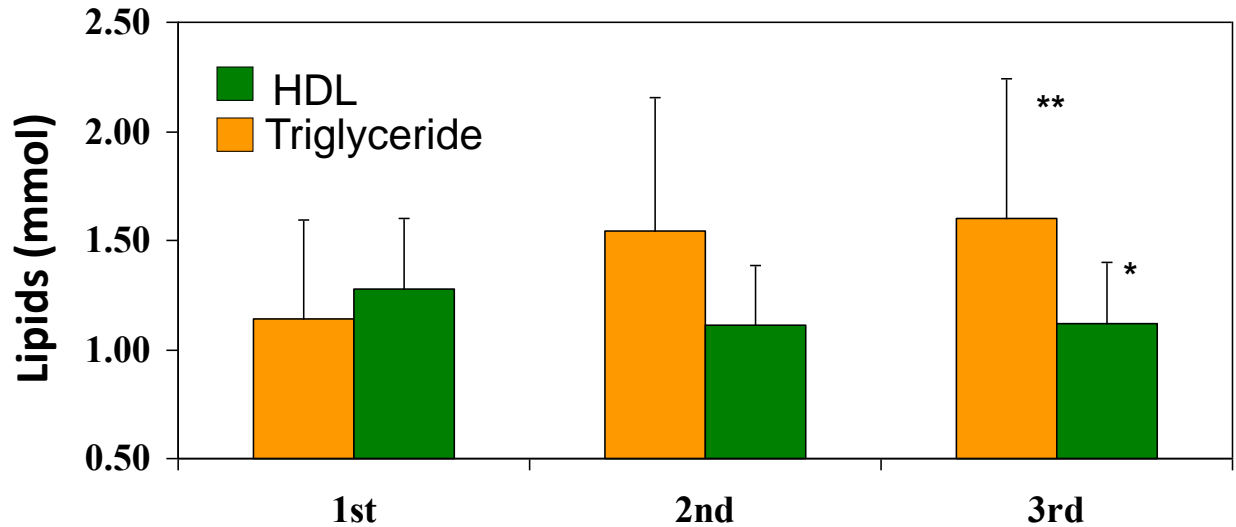


Abdominal obesity and cardiometabolic risk in an urban South Africa population

Waist-to-hip ratio tertiles



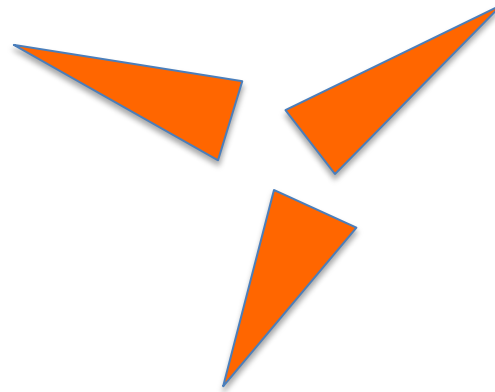
Mean BMI
equivalent across
groups



Education and Training



Research
preparation



Analysis &
interpretation



Capacity building

Activities

- Short courses
- Research exchange/mentorship
- Participation in established courses
- Training internships



Short courses

- Data management
- Phenotyping
- Laboratory practice
 - DNA extraction and PCR
- Ethics
- Bioinformatics & Statistical genomics
- Epidemiology
- Epigenetics
- Writing (grants and manuscripts)

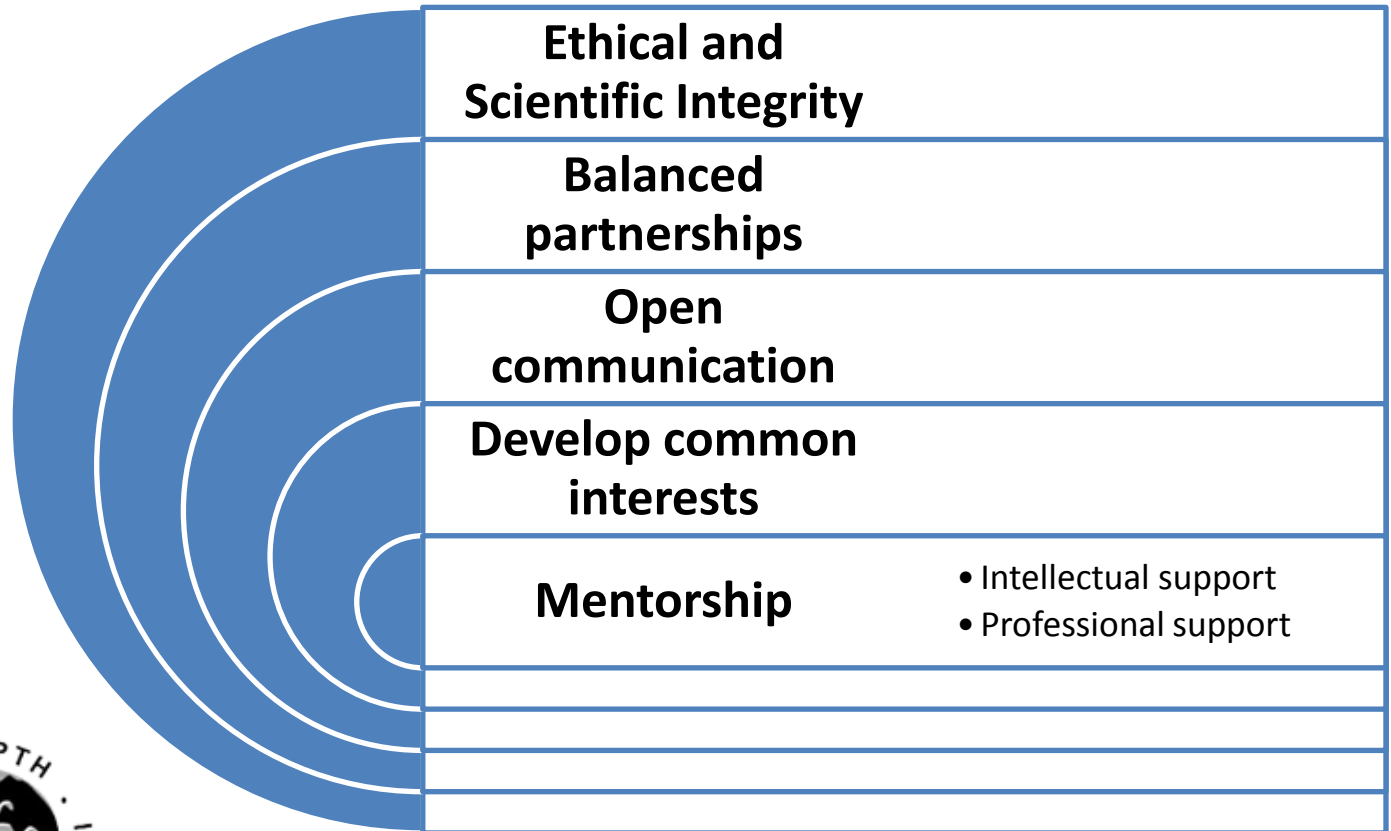


Bioinformatics Network: Joint node ZA North (Wits, University of Pretoria and University of the Free State)

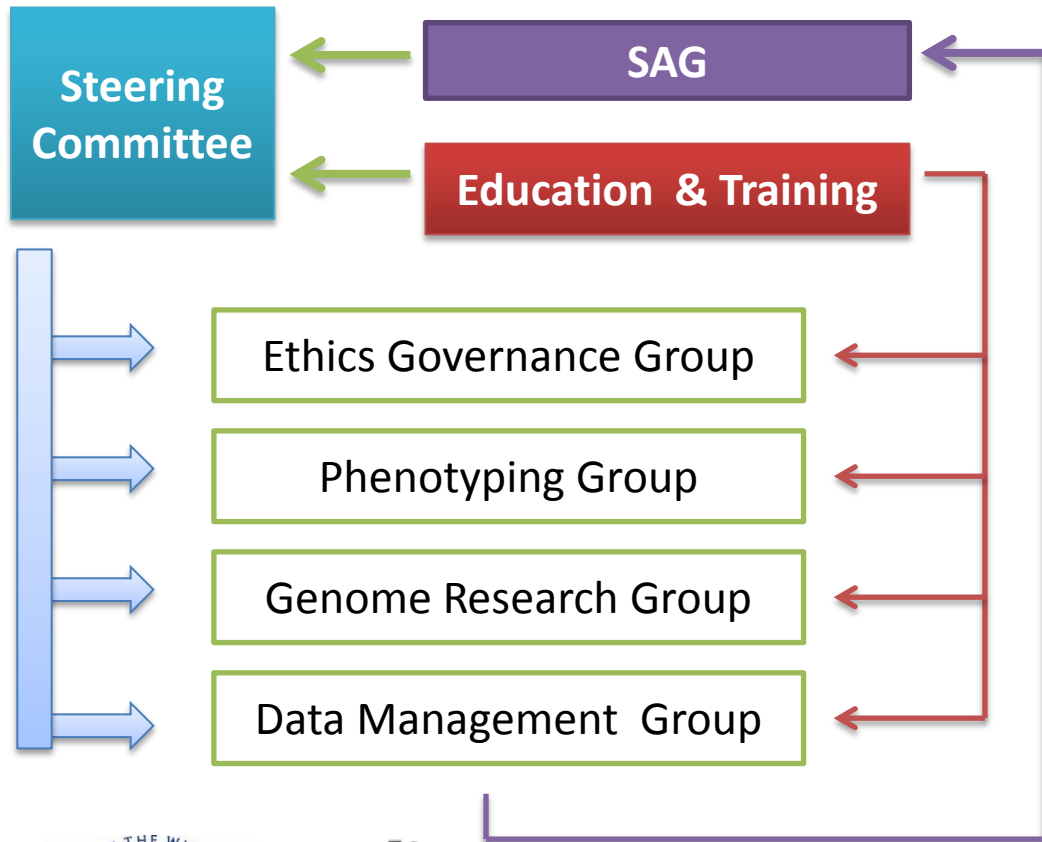
Training needs and expertise

	Wits	Bristol	Harvard	Newcastle	U Penn	Penn State	INDEPTH	Others
Epidemiology								
Phenotyping								
Data management								
Statistical genomics								
DNA extraction								
Lab management								
Bioinformatics								
GWAS								
Epigenetics								
Translational medicine								

Management Philosophy



Management Structure



Standardisation

- **Centralized and distributed**
 - Phenotyping equipment
 - DNA extraction and storage
 - Computer servers and data management
- **INDEPTH Centers**
 - Field work
 - Phenotyping
 - Data management
 - Financial management
 - Sample storage



Timelines

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





World Health Organization

wellcome trust



NATIONAL HEALTH LABORATORY SERVICE

THE ROCKEFELLER FOUNDATION

HEALTH Media NETWORK

