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

11.7 – 46.6%
4.4 – 10.1%
1.0 – 3.9%
No data

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**Prevalence of obesity and related disorders in females in Soweto**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Levels (% or mean SD)</th>
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<tbody>
<tr>
<td>Age (with range)</td>
<td>42.0 8.5 (18 - 84)</td>
</tr>
<tr>
<td>BMI (with range)</td>
<td>30.5 6.7 (16.2 – 58.8)</td>
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<tr>
<td>Prevalence of obesity (BMI ≥ 30)</td>
<td>50.1 %</td>
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<td>Prevalence of severe obesity (BMI ≥ 35)</td>
<td>23.0 %</td>
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<tr>
<td>Prevalence of waist circumference ≥ 80cm</td>
<td>69.3 %</td>
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<td>Prevalence of diabetes (glucose &gt; 7mM)</td>
<td>14.3 %</td>
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<tr>
<td>Prevalence of IFG (glucose ≥ 5.6, ≤ 7mM)</td>
<td>20.2 %</td>
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<tr>
<td>Prevalence of metabolic syndrome (harmonised guidelines)</td>
<td>42.1 %</td>
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</tbody>
</table>

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

Wits Health Consortium

SBIMB

Wits Bioinformatics

School of Pathology

School of Public Health

DPHRU

INDEPTH Board

INDEPTH Network

Agincourt

Dikgale

Navrongo

Nairobi

Nanoro

High Impact Science – Tangible Benefits
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

Stephen Tollman
Principal Scientist

Kathleen Kahn
Board Member

Informing global efforts to improve the health and wellbeing of low and middle-income populations
Over 3,200,000 people under surveillance

Currently 43 HDSSs in 20 countries
30 HDSSs in Africa
12 HDSSs in Asia
1 HDSS in Oceania
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

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Themes of the Collaborative Centre

**A**
- Capacity Development

**B**
- Genomic Architecture of SSA Populations

**C**
- Genetic, Genomic and Environmental Risk Factors for disease

**Overall Research Strategy**

- Administration and Management
  - Collaborating Component 1: Genomic Architecture of African Populations
  - Collaborating Component 2: Epidemiology, Phenotyping and Sampling
  - Collaborating Component 3: Body composition and cardiometabolic disease risk

**Training and Capacity Building**

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Collaborating Component 1

Genomic Architecture of African Populations

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

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

Mean BMI equivalent across groups

Crowther et al., *Clin Endocrinol* (2006) 64: 535-41; *p<0.05, **p<0.005, ***p<0.0005 for trend
Education and Training

Research preparation

Analysis & interpretation

Capacity building

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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

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<th></th>
<th>Wits</th>
<th>Bristol</th>
<th>Harvard</th>
<th>Newcastle</th>
<th>U Penn</th>
<th>Penn State</th>
<th>INDEPTH</th>
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<td>Data management</td>
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<td>Translational medicine</td>
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Management Philosophy

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<thead>
<tr>
<th>Ethical and Scientific Integrity</th>
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<tr>
<td>Balanced partnerships</td>
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<td>Open communication</td>
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<td>Develop common interests</td>
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<td>Mentorship</td>
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<td>• Intellectual support</td>
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<tr>
<td>• Professional support</td>
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Management Structure

- **Steering Committee**
- **SAG**
- **Education & Training**
  - Ethics Governance Group
  - Phenotyping Group
  - Genome Research Group
  - Data Management Group

**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

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**Addis Ababa**
**8-10 October 2012**
## Timelines

<table>
<thead>
<tr>
<th>ACTIVITY</th>
<th>YEAR 1</th>
<th>YEAR 2</th>
<th>YEAR 3</th>
<th>YEAR 4</th>
<th>YEAR 5</th>
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<td>Training and capacity development</td>
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<td>African genome structure</td>
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<td>Phenotyping and sampling for Cohorts</td>
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<td>Obesity and body composition study – urban South Africa</td>
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<td>Genome association study – west, east and south Africa</td>
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