AWI-Gen
Wits-INDEPTH Partnership

Genomic and environmental risk factors for cardiometabolic disease in Africans

Collaborative Centre
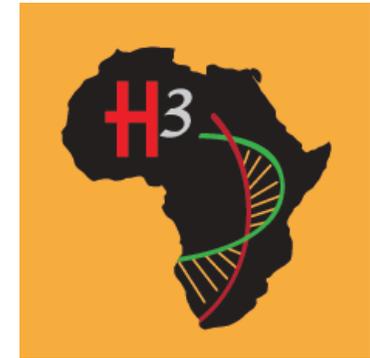
Members at this meeting:

Marianne Alberts

Nadia Carstens

Nigel Crowther

Zane Lombard

Michele Ramsay

Himla Soodyall

Ernest Tambo

Alisha Wade

Ananyo Choudhury

Daniel Achinko

Co-PI

Osman Sankoh

INDEPTH - International Network for the Demographic Evaluation of Populations and their Health in low and middle-income Countries
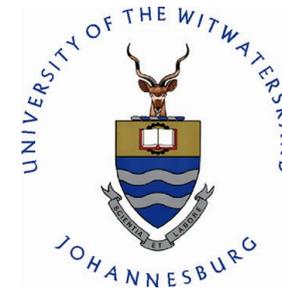
H3Africa NIH funded project

Change in obesity prevalence (1980 to 2008)

East Africa (female)
Change = 1.3% per decade (0.6, 2.0)

Southern Africa (female)
Change = 5.2% per decade (1.0, 8.9)

West Africa (female)
Change = 2.4% per decade (1.3, 3.2)

East Africa (male)
Change = 0.4% per decade (−0.2, 1.0)

Southern Africa (male)
Change = 4.3% per decade (2.1, 6.0)

West Africa (male)
Change = 1.0% per decade (0.2, 1.8)
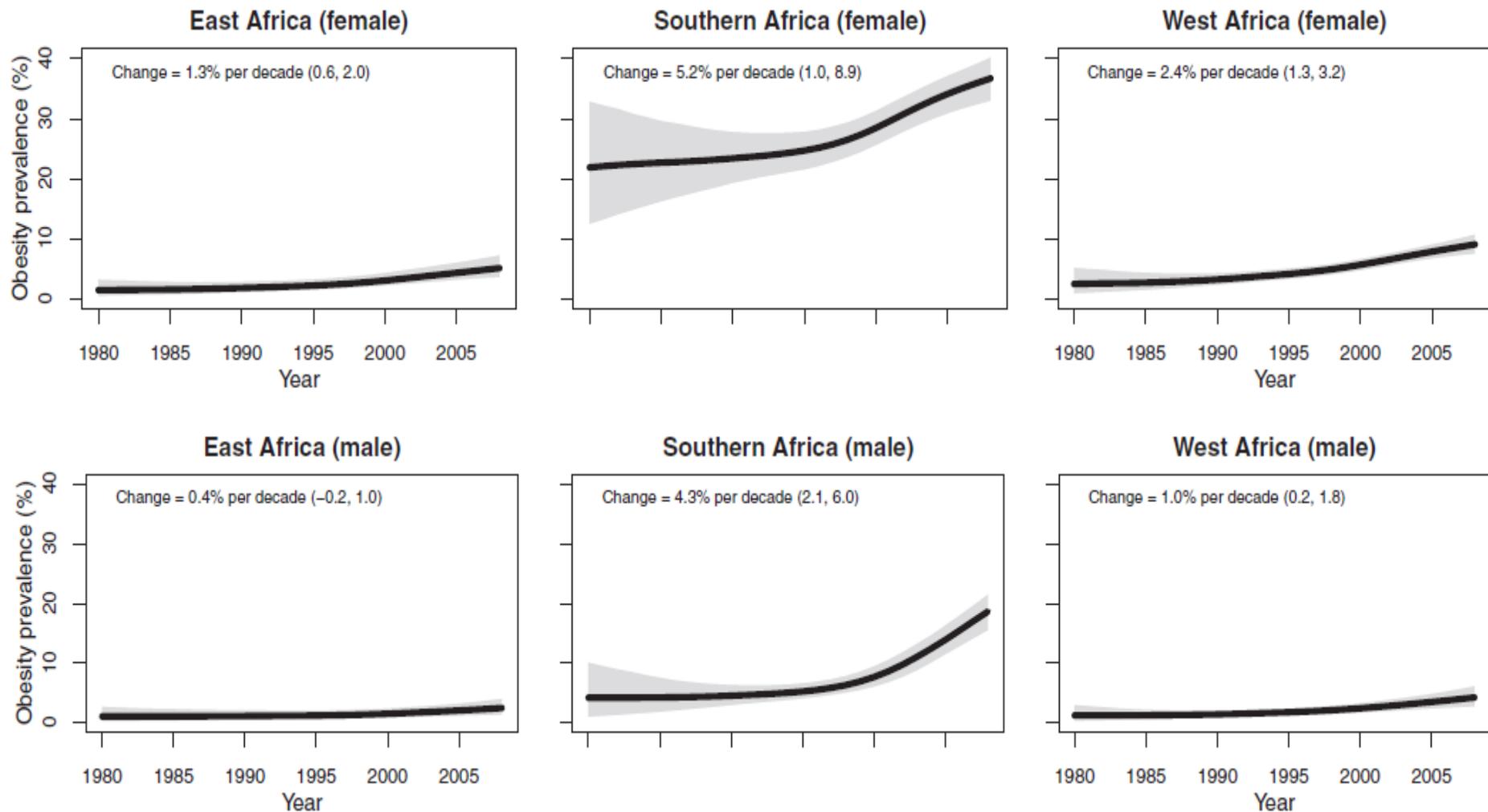
Stevens et al. Population Health Metrics 2012, 10:22
http://www.pophealthmetrics.com/content/10/1/22

Top 5 leading **risk factors** for burden of disease (DALYs) in **South Africa**
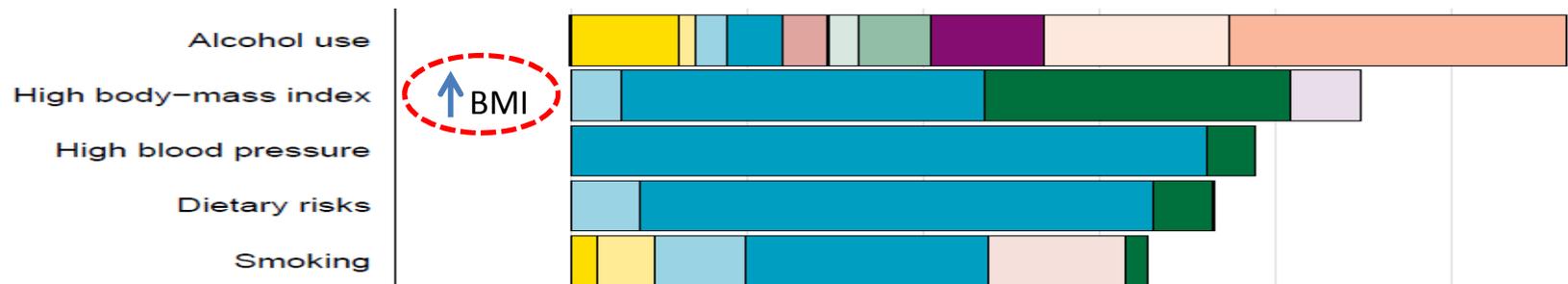
High BMI as a risk factor
Ghana 7th
Kenya 14th
Burkina Faso not in top 15

Legend:
- ★ Diabetes/urogen/blood/endo
- Mental & behavioral disorders
- Neurological disorders
- Digestive diseases
- Cirrhosis
- Chronic respiratory diseases
- ★ Cardio & circulatory diseases
- Cancer
- Other communicable
- Nutritional deficiencies
- Diarrhea/LRI/other infectious
- HIV/AIDS & tuberculosis
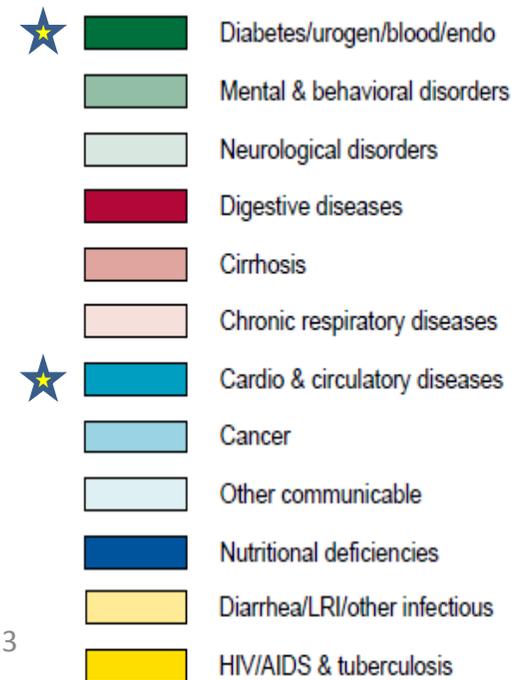
Genomic and environmental contributions to complex traits in African populations

- High genetic diversity and low LD
- Population structure
- Inter-ethnic variation
  - Global risk variants
  - Population specific risk variants
- Environments and diets
- Few studies in African populations
  - African Americans reflect predominantly west African ancestry

AWI-Gen Collaborative Center

- Wits-INDEPTH Partnership
- Project Aims
- Phenotyping & sample collection
- Data Management
- Important outcomes
- Time line

AWI-Gen overview
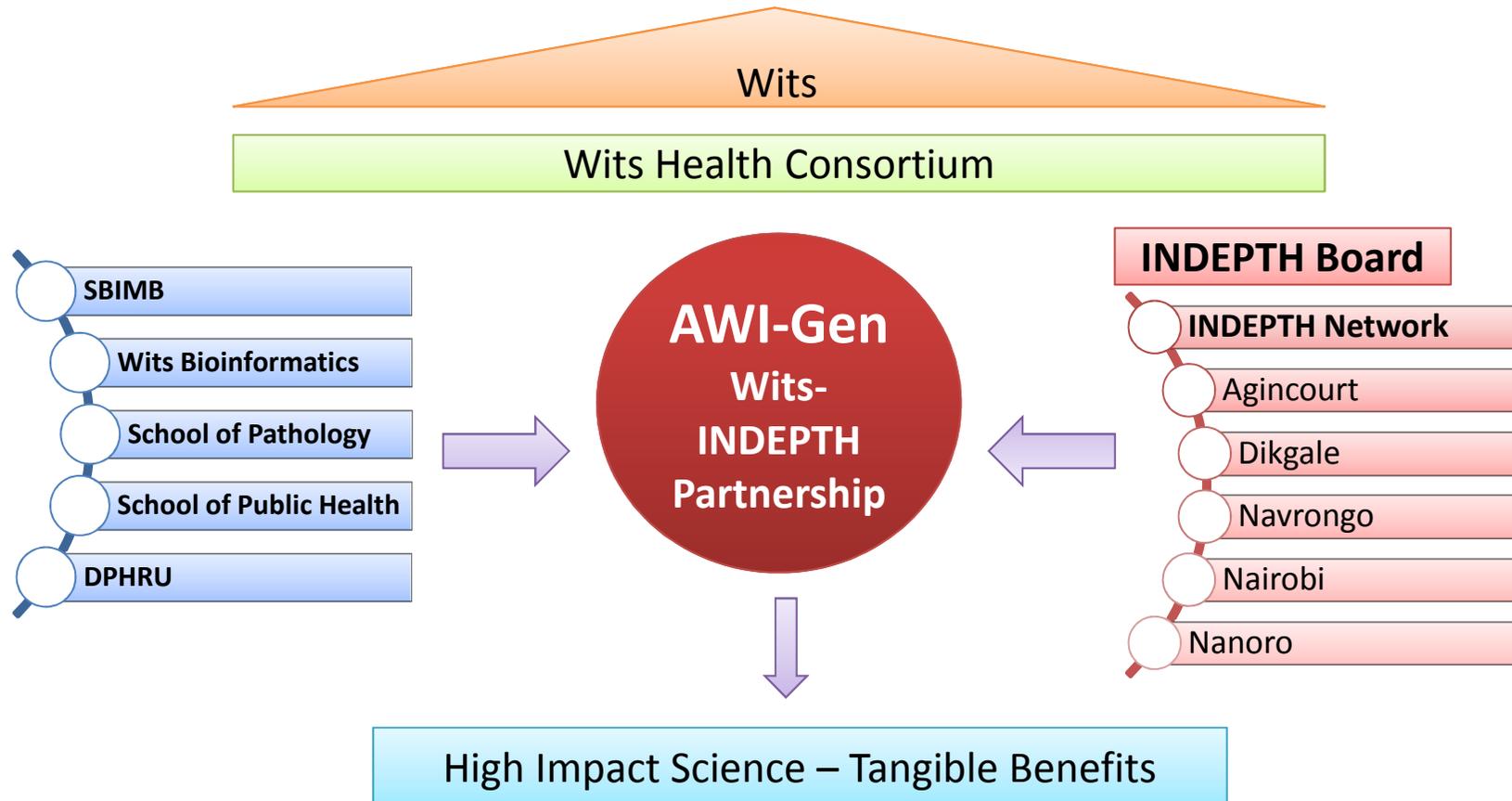
AWI-Gen
(**A**frican **W**its-**I**NDEPTH Partnership for the **Gen**omic study of body composition and cardiometabolic disease risk)
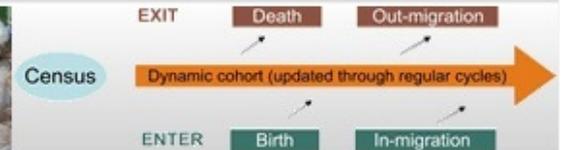
The INDEPTH Network of
Health and Demographic Surveillance Systems
founded 1998, constituted 2002

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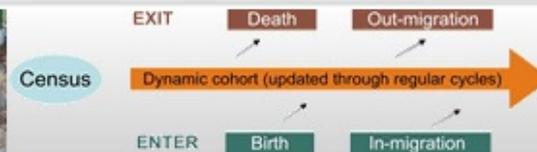
Low- and Middle-Income Countries with INDEPTH member centres
Running Health and Demographic Surveillance Systems (HDSSs)

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

India
Bangladesh
Thaïland
Vietnam
Indonesia
Papua New Guinea
Cambodia

Senegal
The Gambia
Guinea-Bissau
Burkina Faso
Ghana

Ethiopia
Uganda
Kenya
Tanzania
Malawi
Mozambique
South Africa

Over 3,200,000 people under surveillance
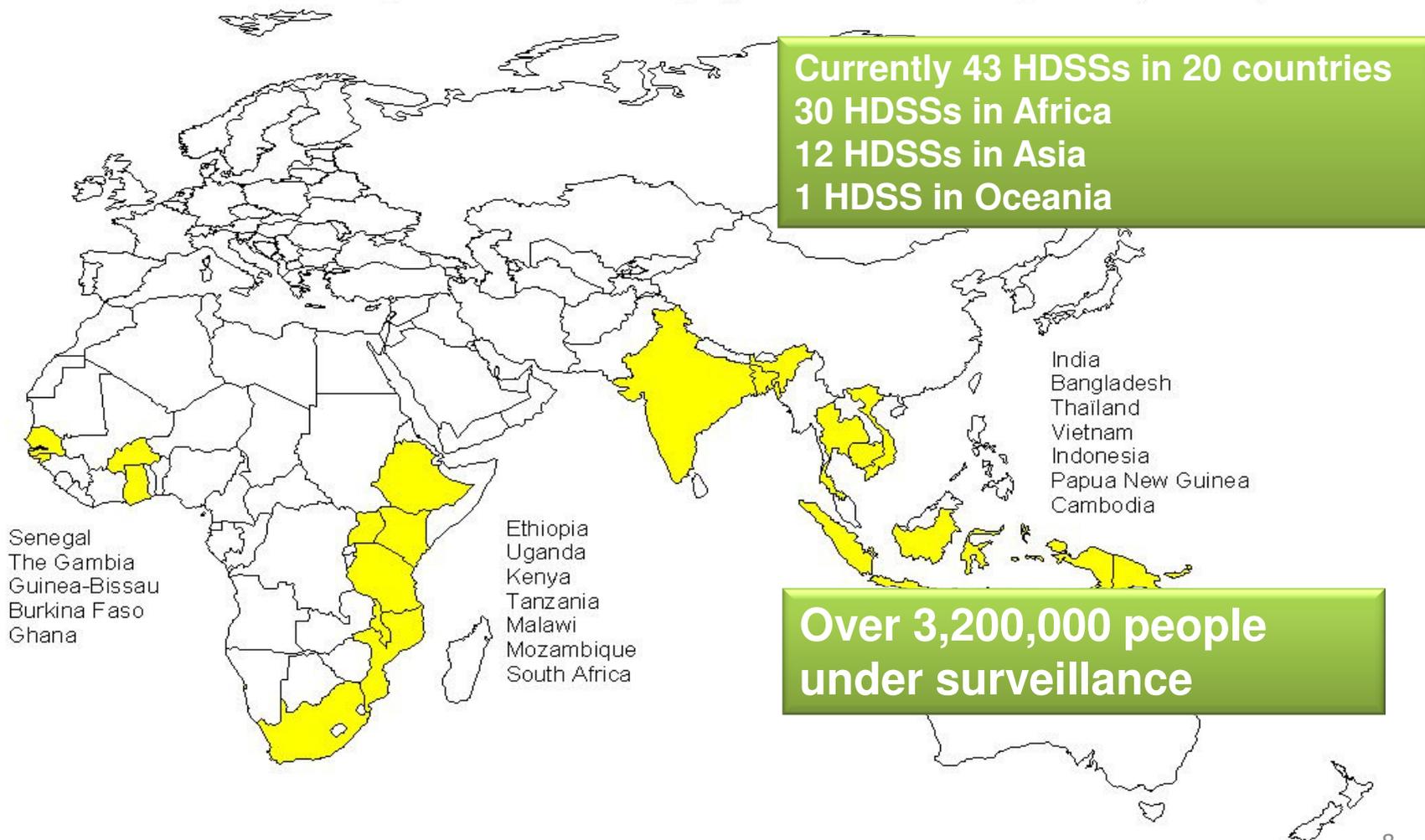
AWI-Gen study sites in Africa:
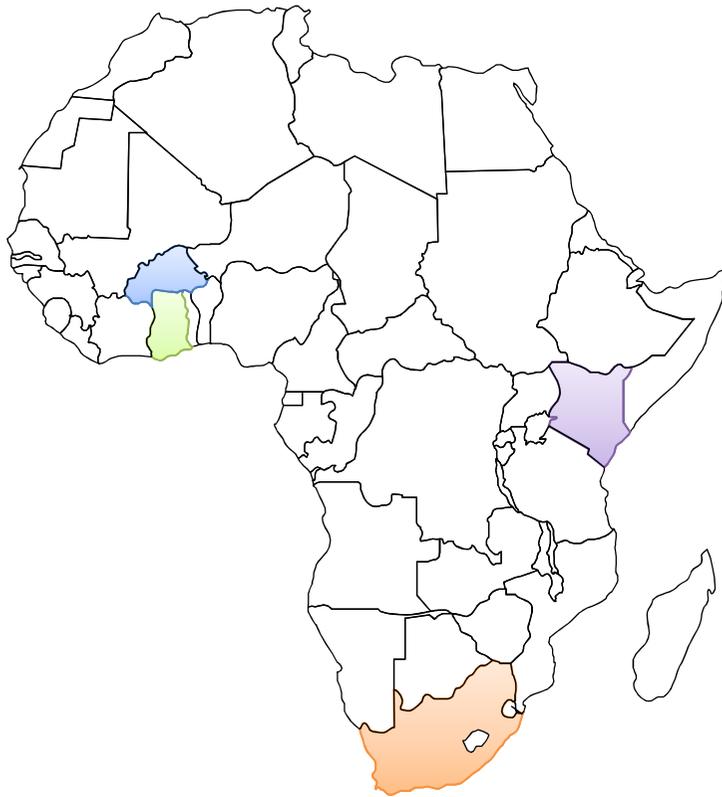
Ghana, Navrongo (Rural)
Abraham Oduro

Burkina Faso, Nanoro (Rural)
Halidou Tinto

Kenya, Nairobi (Urban)
Catherine Kyobutungi

South Africa, Soweto (Urban)
Shane Norris

South Africa, Agincourt (Rural)
Stephen Tollman

South Africa, Dikgale (Rural)
Marianne Alberts
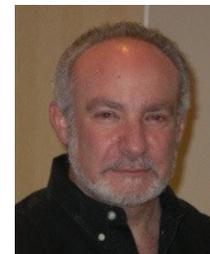
Project – Aims

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)
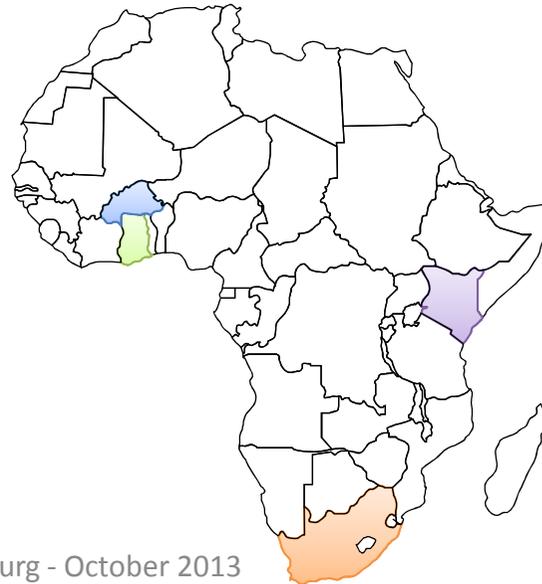
Aim 1: Pilot Project

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 related to body composition

- **Progress**
  - ~1000 females
  - 40 to 60 years
  - Phenotyped
  - Genotyped
- **Next steps**
  - Prepare DNA from next 1000 individuals for genotyping
  - Data analysis

PLoS GENETICS

The Metabochip, a Custom Genotyping Array for Genetic Studies of Metabolic, Cardiovascular, and Anthropometric Traits

August 2012 | Volume 8 | Issue 8 | e1002793

Benjamin F. Voight[1,2], Hyun Min Kang[3], Jun Ding[4], Cameron D. Palmer[1,5], Carlo Sidore[3,6,7], Peter S. Chines[8], Noël P. Burtt[1], Christian Fuchsberger[3], Yanming Li[3], Jeanette Erdmann[9], Timothy M. Frayling[10], Iris M. Heid[11,12], Anne U. Jackson[3], Toby Johnson[13], Tuomas O. Kilpeläinen[14], Cecilia M. Lindgren[15], Andrew P. Morris[15], Inga Prokopenko[15,16], Joshua C. Randall[15], Richa Saxena[1,17,18], Nicole Soranzo[19], Elizabeth K. Speliotes[1,20], Tanya M. Teslovich[3], Eleanor Wheeler[19], Jared Maguire[1], M... ...ayner[15,16,19], Neil Robertson[15,16], Kathleen Stirrups[19], W... ...Mulas[6], Ramaiah Nagaraja[4], Francesco Cucca[6,7], In... ...Loos[14], Sekar Kathiresan[1,17,22,23], Patricia B. Munroe[13], Ch... ...fe... Jo... M...

Advantages:
Cost effective
Fine mapping (previous associations)
Replication study
Rapid results
Good training opportunity

Disadvantages:
SNP choice predominantly Eurocentric
Previous associations not in African populations
Limits novel discovery

# Role of pilot project in capacity development

- PhD student – Venesa Pillay

- Soon to join: PhD student and postdoctoral fellow

- Complexity of the data - genotyping and phenotype (including biochemical markers) lends itself to multiple enquiry

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
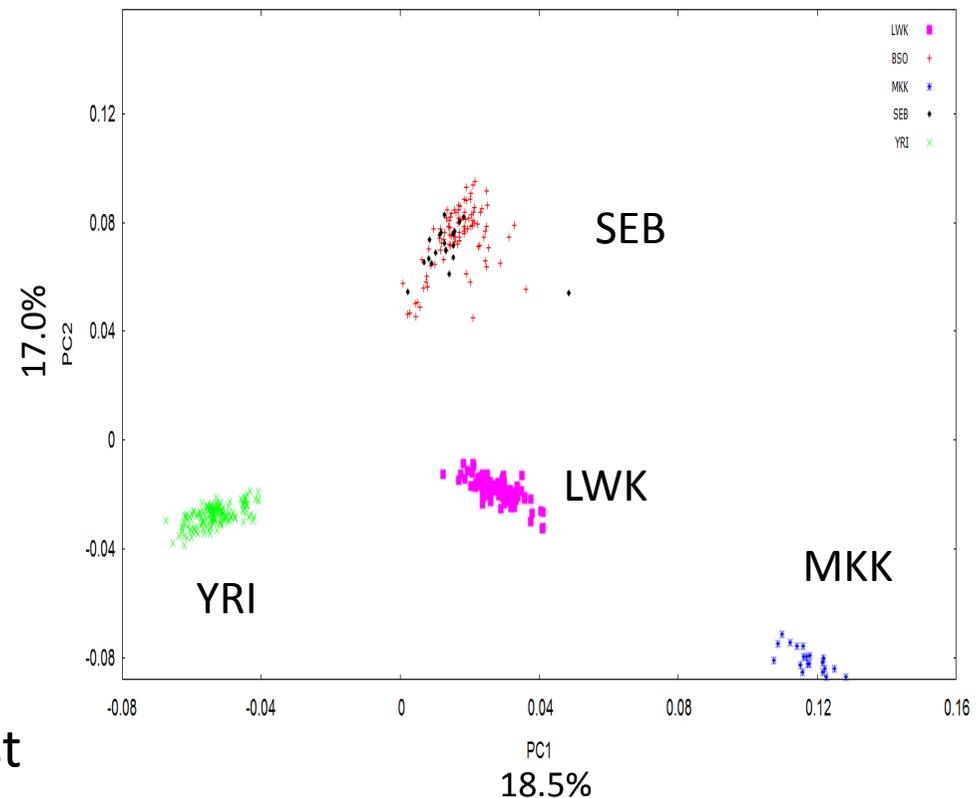
Complexity of population structure
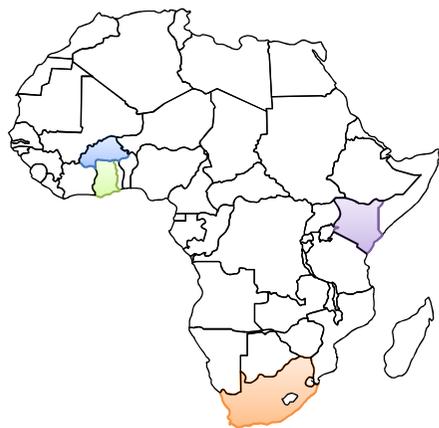
Africa
2 146 languages spoken
(30.2% of all living languages)
789 138 977 people
(12.7% of all people)

Country	No. Living languages	Indigenous languages	Immigrant languages	Population size	Diversity Index
Burkina Faso	70	68	2	10.9 M	0.768
Ghana	86	81	5	25.1M	0.835
Kenya	72	67	5	37.6M	0.928
South Africa	44	28	16	44.6M	0.874
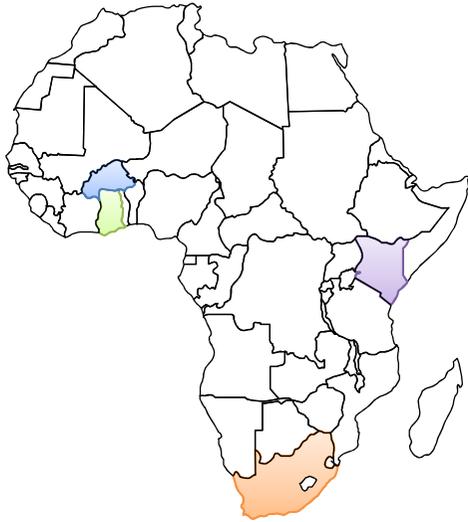
Kenya: NUHDSS

72 ethno-linguistic groups

Language divisions	NUHDSS	Kenya
Bantu	78.5	52.0
Nilotic	13.8	28.6
Cushites	6.4	8.0
Other	1.3	11.4

Ethnic Group	% NUHDSS	% Kenya
Kikuyu	29.9	17
Luhya	15.7	14
Kamba	24.6	10
Luo	12.9	10
Other	16.9	49

Catherine Kyobutungi: Nairobi Health and Demographic Surveillance System

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
  - Data Management

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 (fasting):
EDTA (DNA)
Clotted (serum - lipids)
NaF (plasma - glucose)

Added sampling:
Spot urine collections

RedCAP for AWI-Gen

Demographic Collection Data (89)

☐ General information

Demographic information
☐ • Age
• Country
• Home language*
• Ethnicity*
• Family Ethnicity*   ⭐

☐ Family Composition

Phenotypic Collection Data (231)

☐ Marital Status

☐ Education

☐ Employment

☐ Household attributes* ⭐

Substance use
☐ • Tobacco use
• Alcohol use
• Drug use

☐ General health

Infection history
☐ • Malaria
• TB

Cardiometabolic risk factors
☐ • Diabetes
• Stroke

☐ Thyroid disease

☐ Kidney disease

☐ Physical activity

☐ Sleep

Sample Data Collection (25)

☐ Anthropometric measurements

☐ Blood pressure

☐ Pulse

☐ Ultrasound measurements

⭐ Site specific data

Blood Collection Data (21)

☐ Blood collection

☐ HIV

☐ Test results

☐ Urine collection

Checklist (11)

☐ Questionnaire

☐ Anthropometric measurements

☐ Blood pressure

☐ Pulse

☐ Blood Samples

☐ Ultrasound

☐ cIMT

☐ HIV test

☐ Urine sample

☐ Travel reimbursement

☐ Quality Controller ID

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
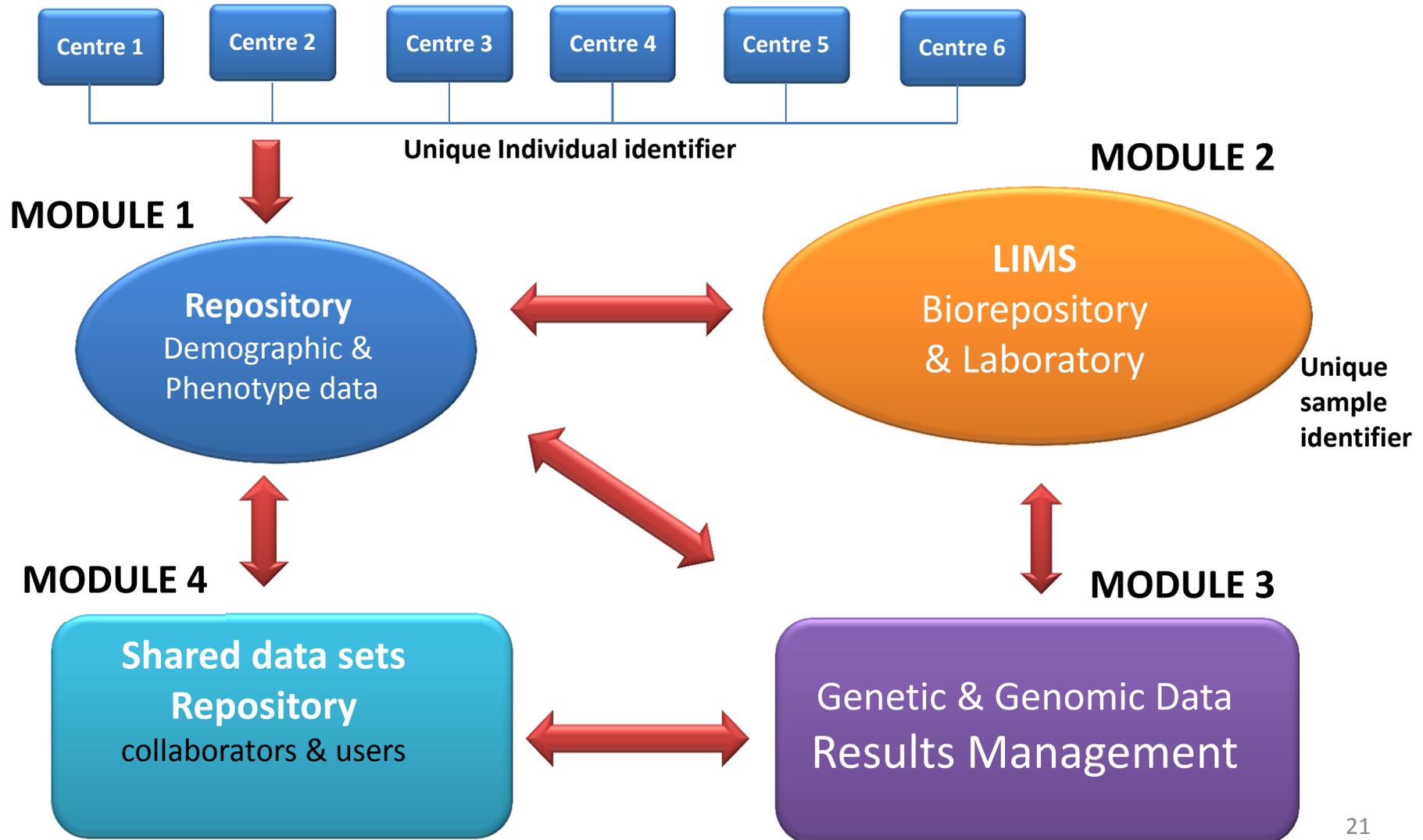
AWI-Gen Data Management Workshop
July 2013

Summary of Connectivity and Storage Capacity

Site	Speed*	Reliability	Storage capacity
Nairobi	8MBps	99%	1.4 TB
Nanoro	1MBps	Back up system	300 GB +
Navrongo	1MBps	98%	730 GB
Agincourt	4MBps	96%	5 TB
Dikgale	45MBps	95%	30 TB
Soweto	94MBps	99%	300 GB +

Important outcomes

- **Capacity development**
  - PhD students, postdocs, scientists
  - Epidemiology, population genetics, genomics, bioinformatics
- **Phenotype and blood profiles**
  - Means and ranges for African populations
- **New knowledge**
  - African population diversity
    - African variation enhanced chip (cost effective)
    - African population structure
  - Pilot study
    - Replication data, Longitudinal analysis, Training
  - Main study

Timeline (Aug 2012 – July 2017)

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			🟩	🟩	🟩

Acknowledgements

- ## Wits

Michele Ramsay	Nigel Crowther
Himla Soodyall	Zane Lombard
Shane Norris	Kathleen Khan
Stephen Tollman	Cassandra Soo
Alisha Wade	Ananyo Choudhury
Nadia Carstens	Venesa Pillay

- ## INDEPTH

Osman Sankoh	Halidou Tinto
Kathleen Kahn	Hermann Sorgho
Stephen Tollman	Marianne Alberts
Abraham Oduro	Catherine Kyobutungi
Godfred Agongo	Kate Theron