Co-PI
Osman Sankoh

AWI-Gen
Wits-INDEPTH Partnership

Genomic and environmental risk factors for cardiometabolic disease in Africans

Collaborative Centre

Project Manager:
Ntombizodwa Mthembu

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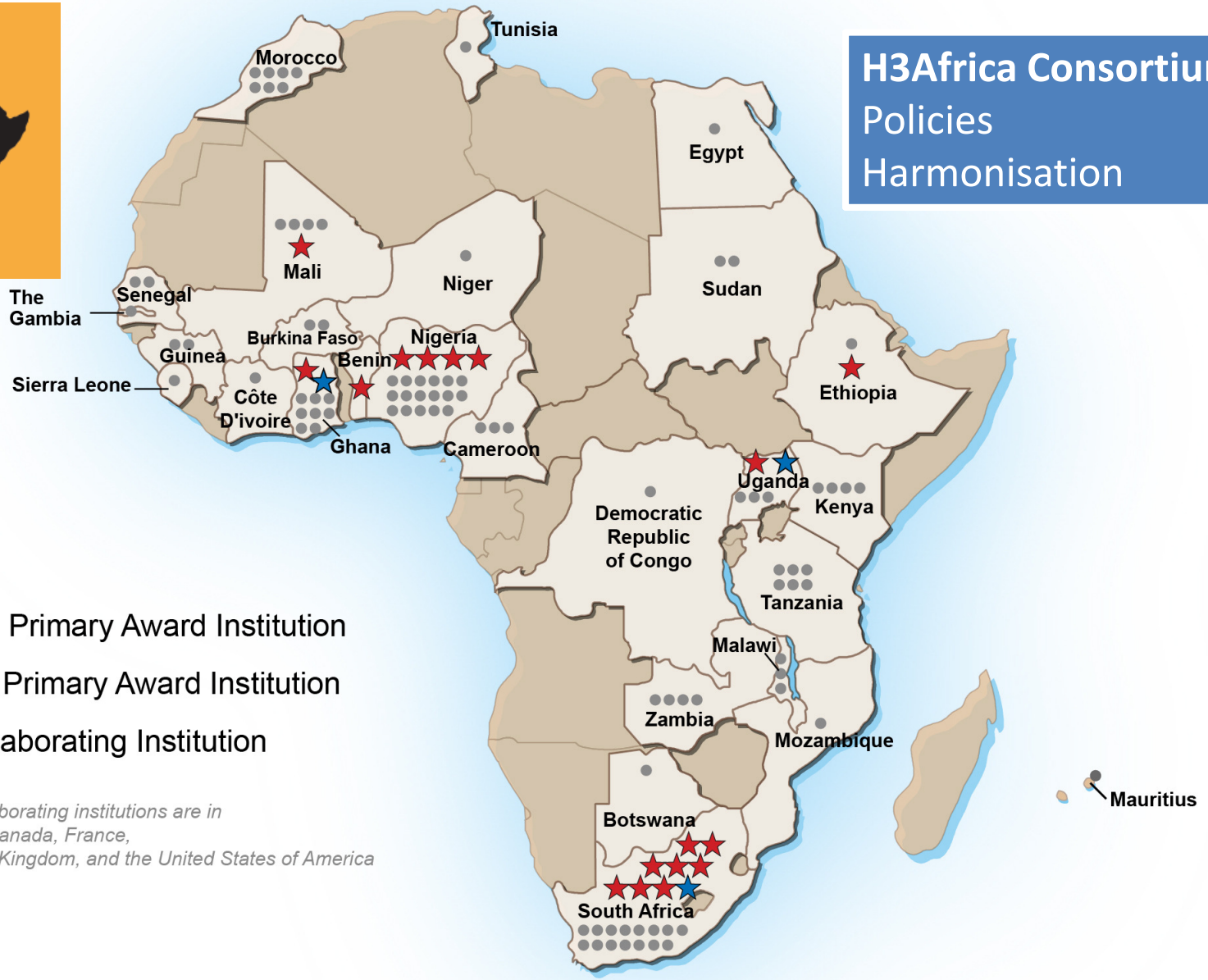
National Institutes of Health - Wellcome Trust H3Africa Research Network

H3Africa Consortium:
Policies
Harmonisation



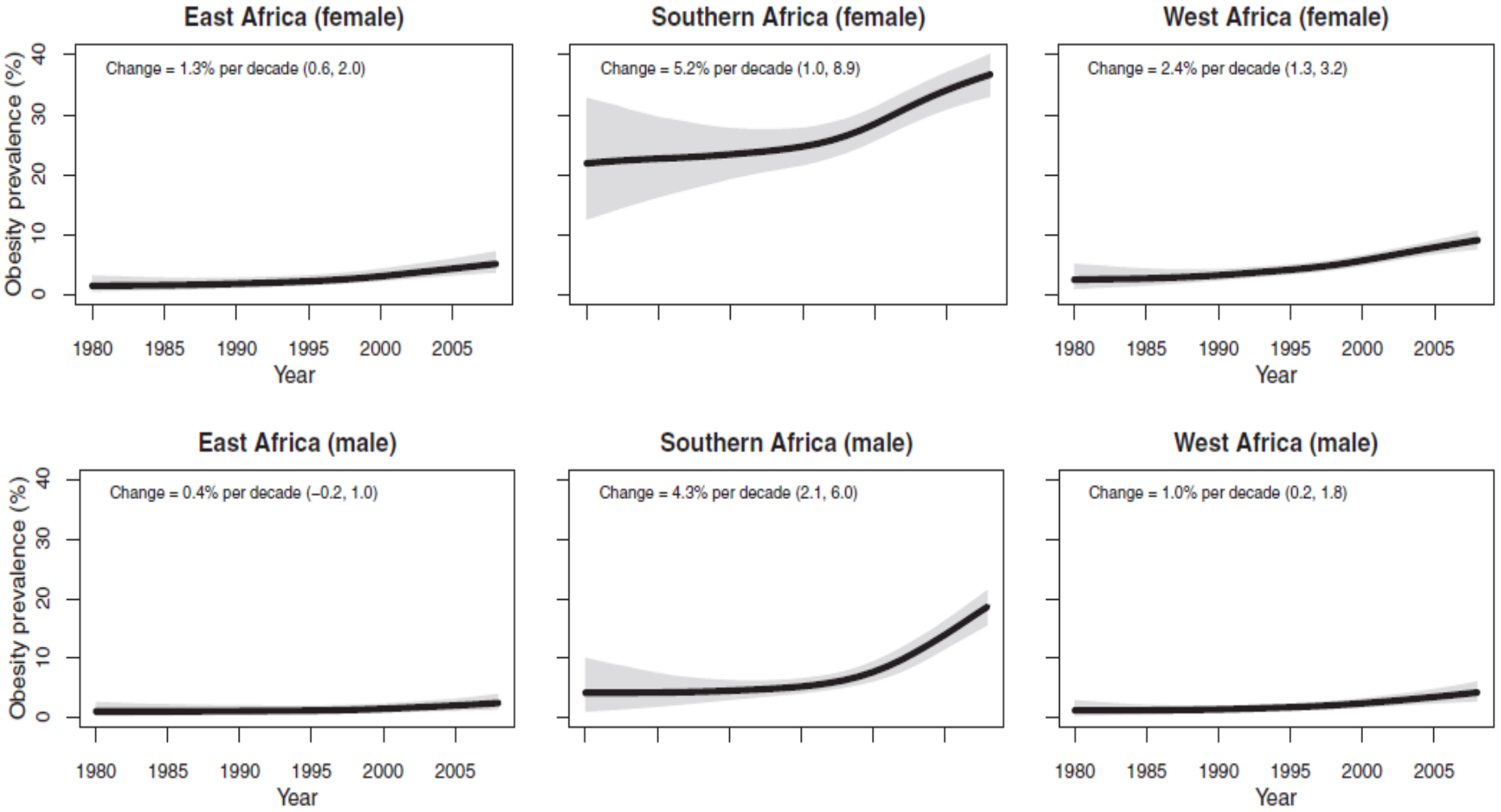
★ NIH Primary Award Institution

★ WT Primary Award Institution

• Collaborating Institution

Other collaborating institutions are in Belgium, Canada, France, the United Kingdom, and the United States of America

Change in obesity (1980 to 2008)



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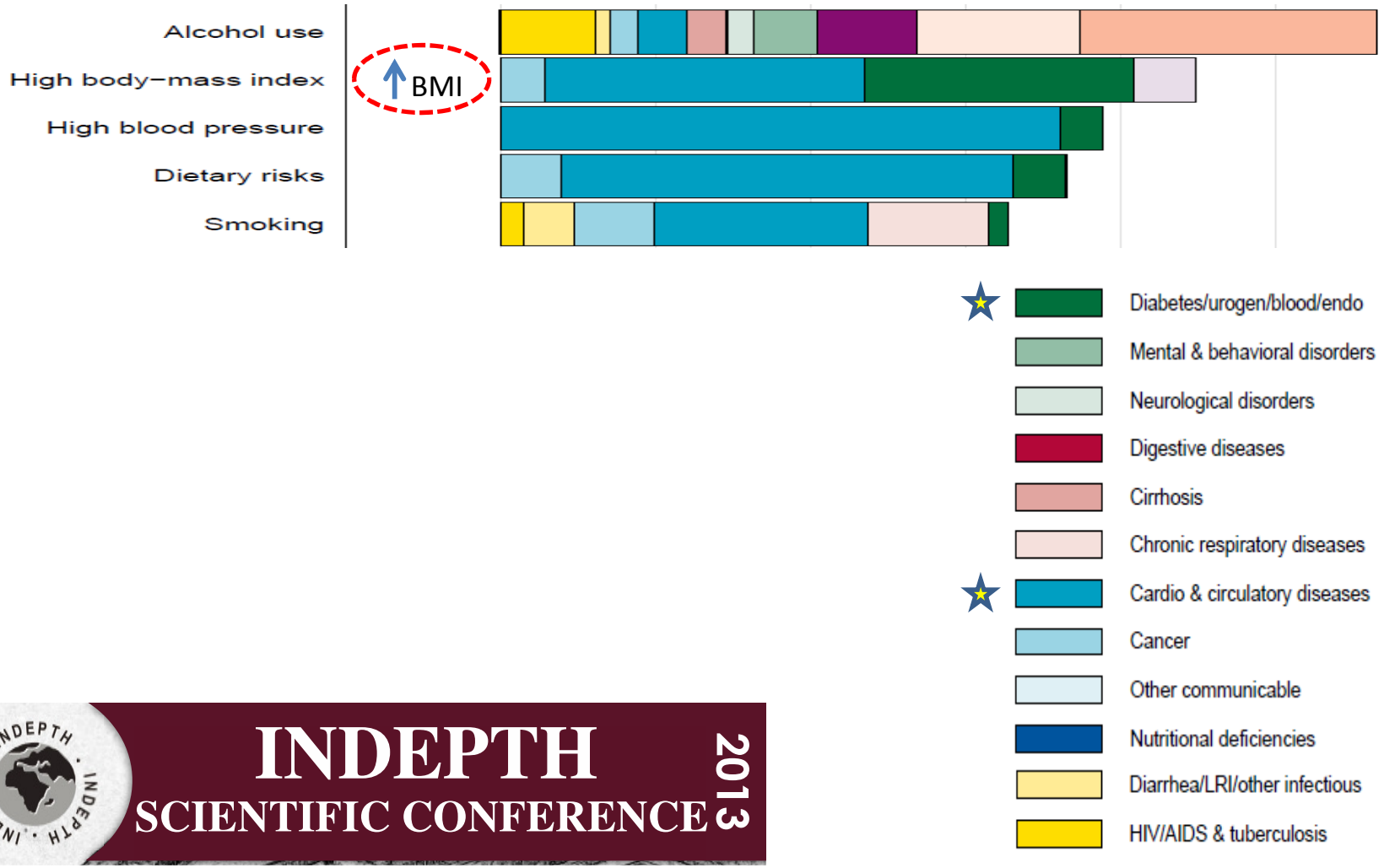
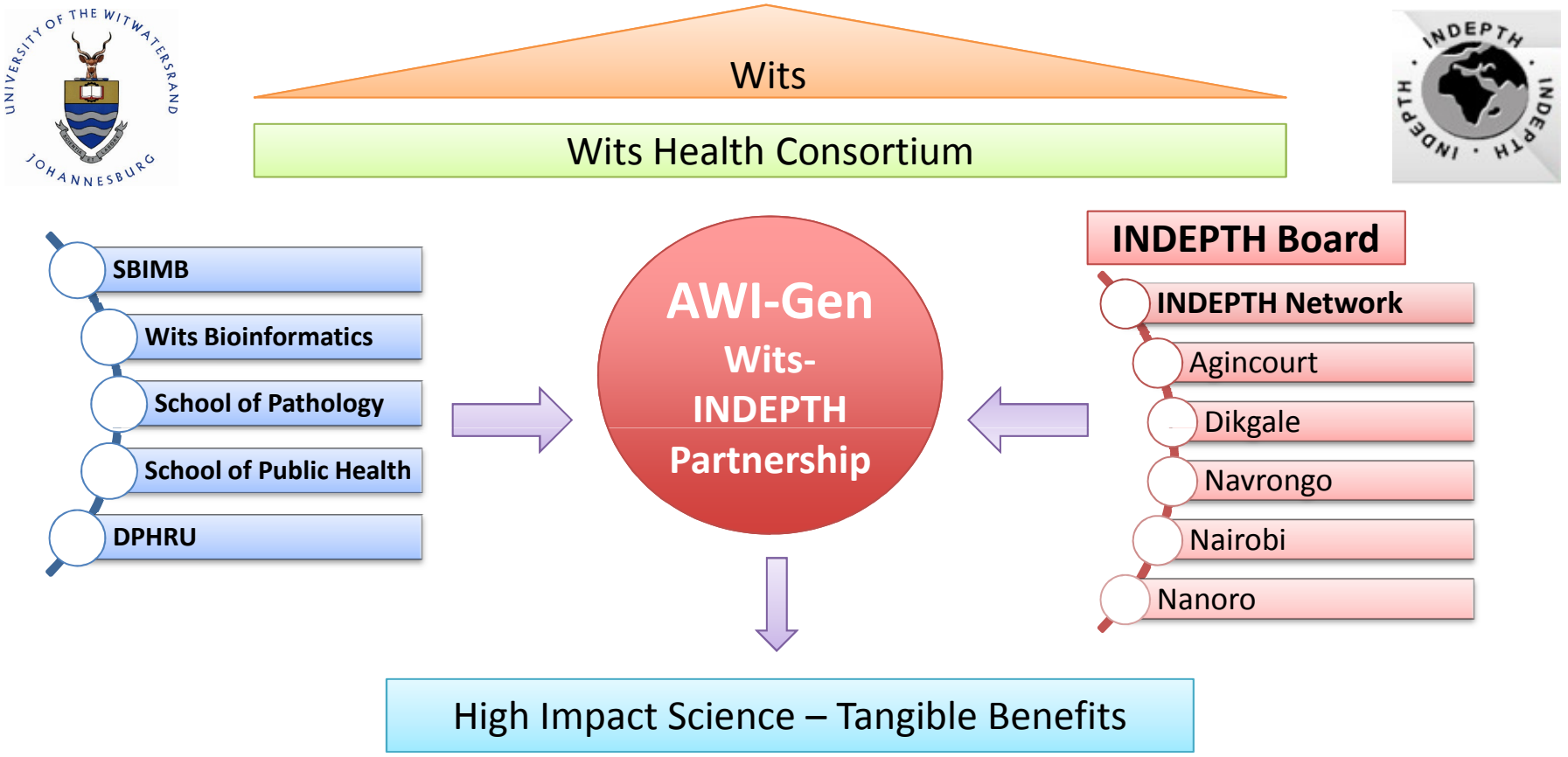
Stevens et al. Population Health Metrics 2012, 10:22
http://www.pophealthmetrics.com/content/10/1/22

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



AWI-Gen Collaborative Center overview



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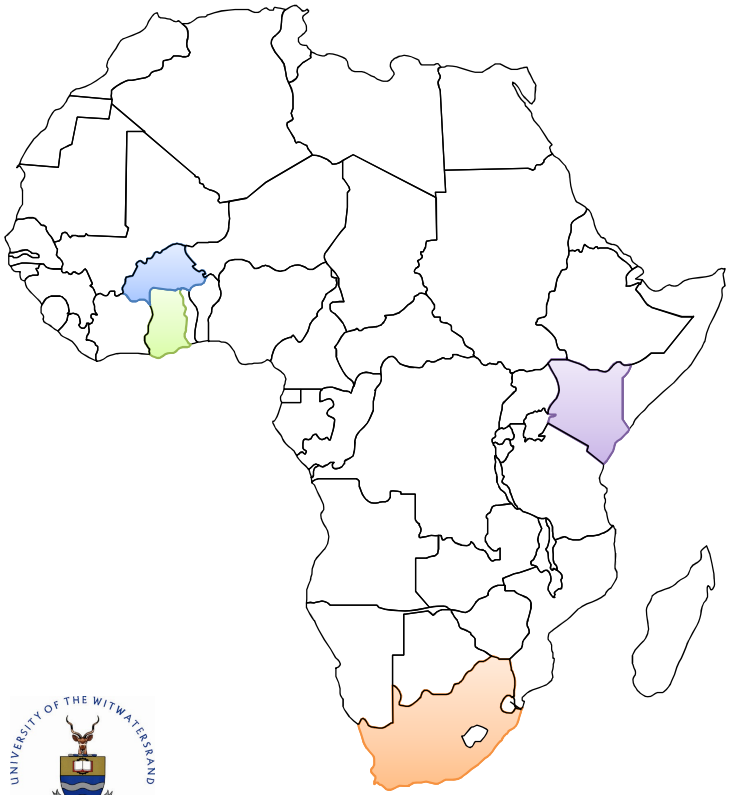
AWI-Gen study sites in Africa:



Ghana, Navrongo (Rural)
Abraham Oduro

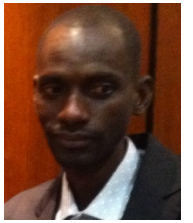
Burkina Faso, Nanoro (Rural)
Halidou Tinto

Kenya, Nairobi (Urban)
Catherine Kyobutungi

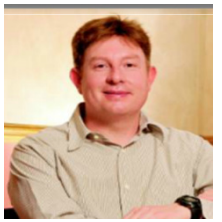
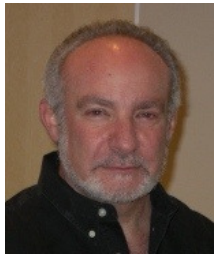
South Africa, Soweto (Urban)
Shane Norris

South Africa, Agincourt (Rural)
Stephen Tollman

South Africa, Dikgale (Rural)
Marianne Alberts

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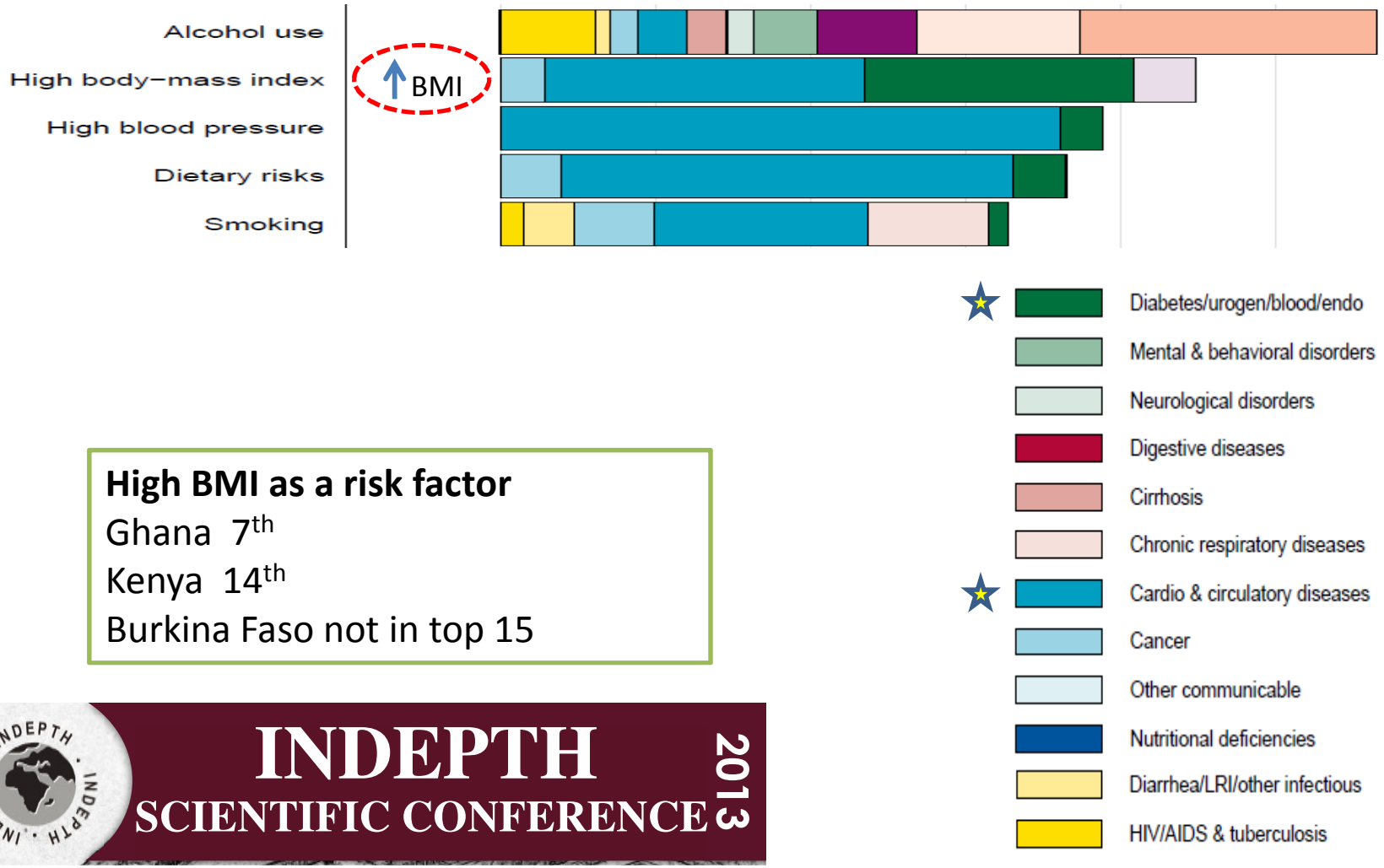
Top 5 leading **risk factors** for burden of disease (DALYs) in **South Africa**



High BMI as a risk factor
Ghana 7th
Kenya 14th
Burkina Faso not in top 15

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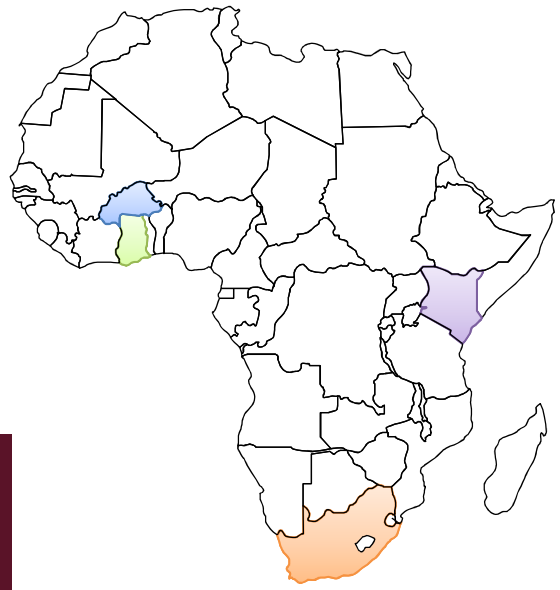
Project – Aims

1. Pilot Project – Soweto (~2000 individuals)
2. Population structure and genome architecture
3. Genomic 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
- Genomic platform
  - Metabochip
  - Candidate gene/region fine mapping
- Analysis
  - Correlations with quantitative traits related to body composition and cardiometabolic risk

- **Progress**
  - ~1000 females
  - Phenotyped
  - Genotyped
- **Next steps**
  - Preparing DNA from next 1000 individuals for genotyping
  - Bioinformatics training
  - Data analysis

OPEN ACCESS Freely available online 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[1,29], Hyun Min Kang[39], 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], Melissa Parkin[1], Simon Potter[19], N. William Rayner[15,16,19], Neil Robertson[15,16], Kathleen Stirrups[19], Wendy Winckler[1], Serena Sanna[6], Antonella Mulas[6], Ramaiah Nagaraja[4], Francesco Cucca[6,7], Inês Barroso[19,21], Panos Deloukas[19], Ruth J. F. Loos[14], Sekar Kathiresan[1,17,22,23], Patricia B. Munroe[13], Christopher Newton-Cheh[1,17,22,23], Arne Pfeufer[24,25,26], Nilesh J. Samani[27,28], Heribert Schunkert[9], Joel N. Hirschhorn[1,5,29], David Altshuler[1,17,23,29,30,31]*, Mark I. McCarthy[15,16,32]*, Gonçalo R. Abecasis[3]*, Michael Boehnke[3]*

Advantages:

- Cost effective & Rapid results
- Fine mapping (previous associations)
- Replication study
- Data provide a great training opportunity

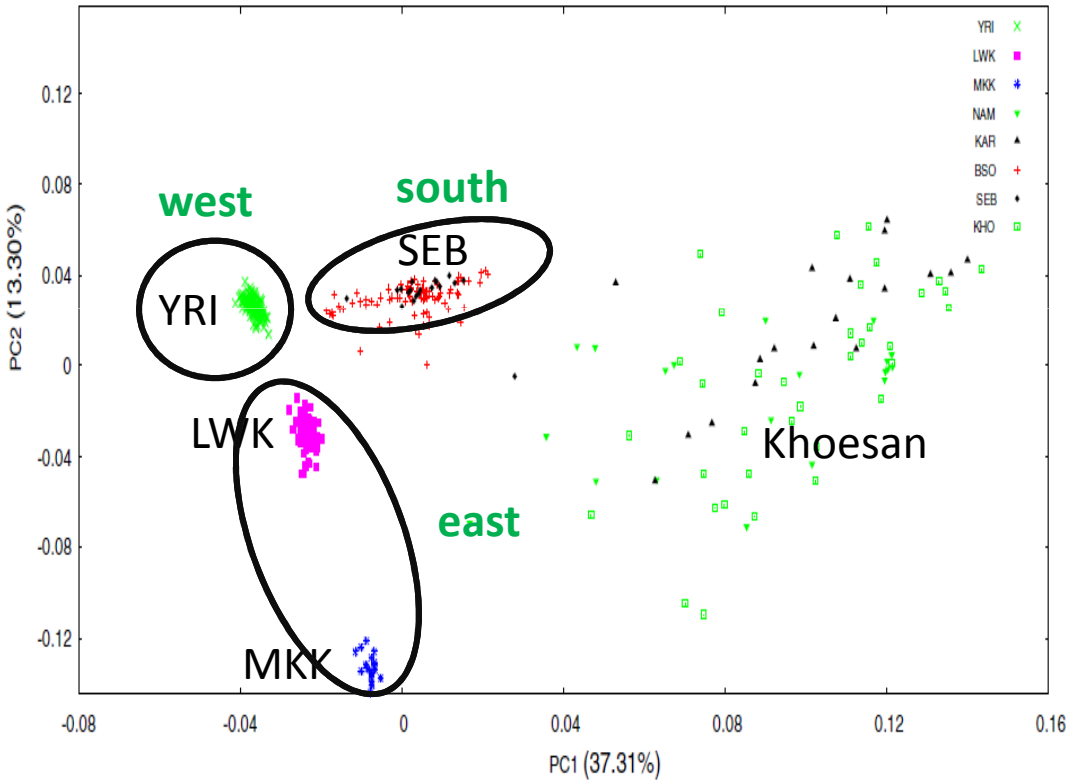
Disadvantages:

- SNP choice largely Eurocentric
- Previous associations not in African populations
- SNP choices now outdated (designed in 2009)
- Limits novel discovery

Aim 2: Population structure and genomic architecture

- AWI-Gen Study design
  - 30 unrelated trios
  - 40 unrelated individuals
- Genotyping Platform
  - Uncertain (Genome sequencing?)
- Outcome
  - HapMap equivalent for each population
  - Common variant allele frequencies
- Challenge
  - Which populations to test

African populations



PCA – ~ 460 000 SNP markers
May et al. (2013) BMC Genomics

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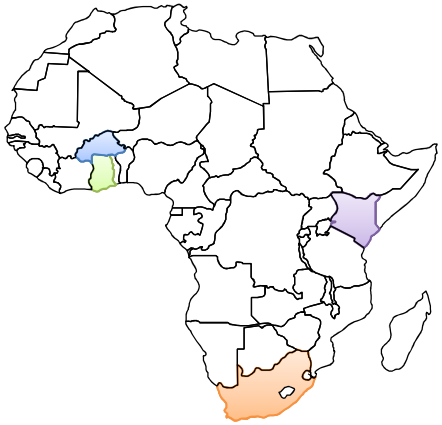
Complexity of population structure



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

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Ethnologue may be cited as: Lewis, M. Paul, Gary F. Simons, and Charles D. Fennig (eds.). 2013. *Ethnologue: Languages of the World, Seventeenth edition.* Dallas, Texas: SIL International. Online version: http://www.ethnologue.com.

Aim 3: Genetic and environmental contributions to body composition

- Ethics approval (Community engagement)
- Standardised phenotype questionnaire
- SOPs
- Central measurement equipment purchase & training
- Training in genomic science
- Staggered field roll out (QA)

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

Added sampling:
Spot urine collections

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

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Data Collection: RedCAP for AWI-Gen

Demographic Data (89)

- General Information
- Demographic information
  - Age
  - Country
  - Home language*
  - Ethnicity*
  - Family Ethnicity
- Family Composition

Phenotypic Data (231)

- Education
- Employment
- Household attributes*
- Substance use
- General health
- Infection history
- Cardiometabolic risk factors
- Thyroid disease
- Kidney disease
- Physical activity
- Sleep

Individual measurements (25)

- Anthropometric measurements
- Blood pressure
- Pulse
- Ultrasound measurements

Sample Collection (21)

- Blood collection
- HIV testing
- Urine collection

Checklist (11)

- Questionnaire
- Anthropometric measurements
- BP, pulse and ultrasound measures
- Blood Samples
- HIV test
- Urine sample
- Travel reimbursement
- Quality Controller ID

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Phenotype Harmonisation with H3Africa Consortium

AWI-Gen Data Management Workshop

July 2013

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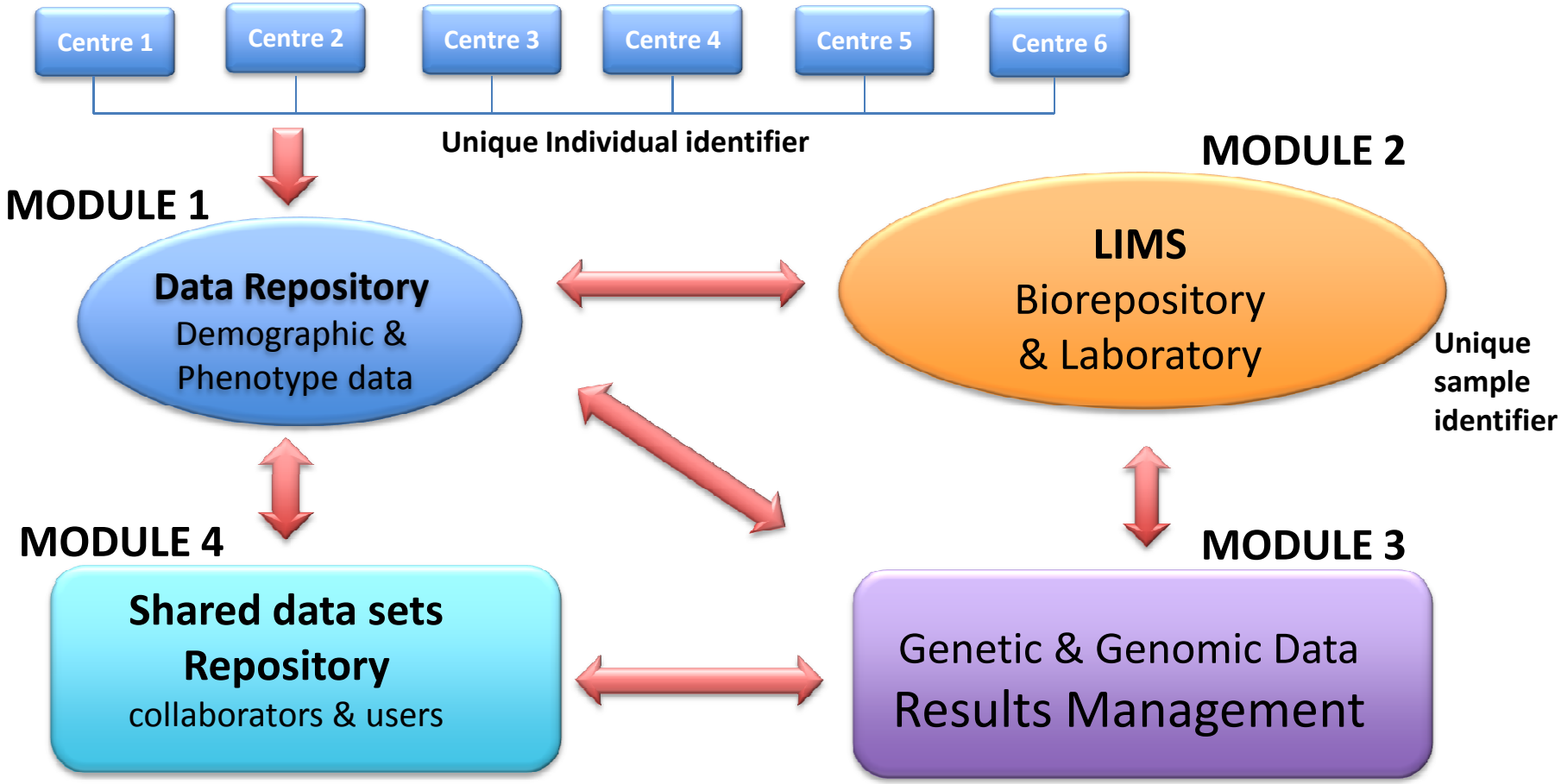
Data Management



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Timeline (Aug 2012 – July 2017)

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

Outcomes

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

Increased understanding of the role of genome variation and environmental factors in cardiometabolic risk across African populations

Acknowledgements

- Wits

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Shane Norris
Stephen Tollman
Cassandra Soo
Venesa Pillai

- INDEPTH

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