AWI-Gen

Africa Wits-INDEPTH Partnership for Genomic Reseach

Strengthening genomic studies of cardiometabolic diseases in Africa – the AWI-Gen experience

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

SDIMB SYDNEY BRENNER INSTITUTE FOR MOLECULAR BIOSCIENCE

H3

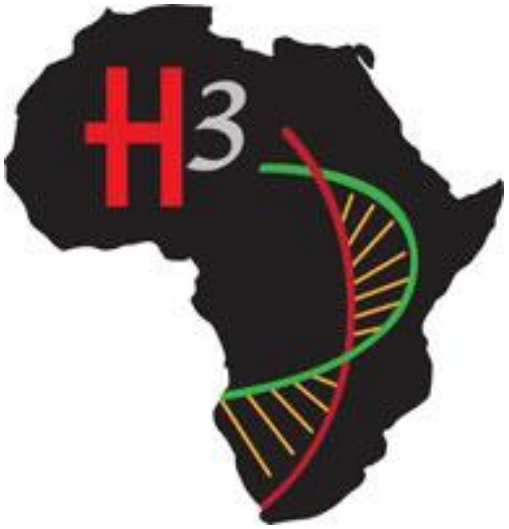
NATIONAL INSTITUTES OF HEALTH

INDEPTH

Human Heredity and Health in Africa

Inaugural H3Africa meeting
Addis Ababa - October 2012

Human Heredity and Health in Africa

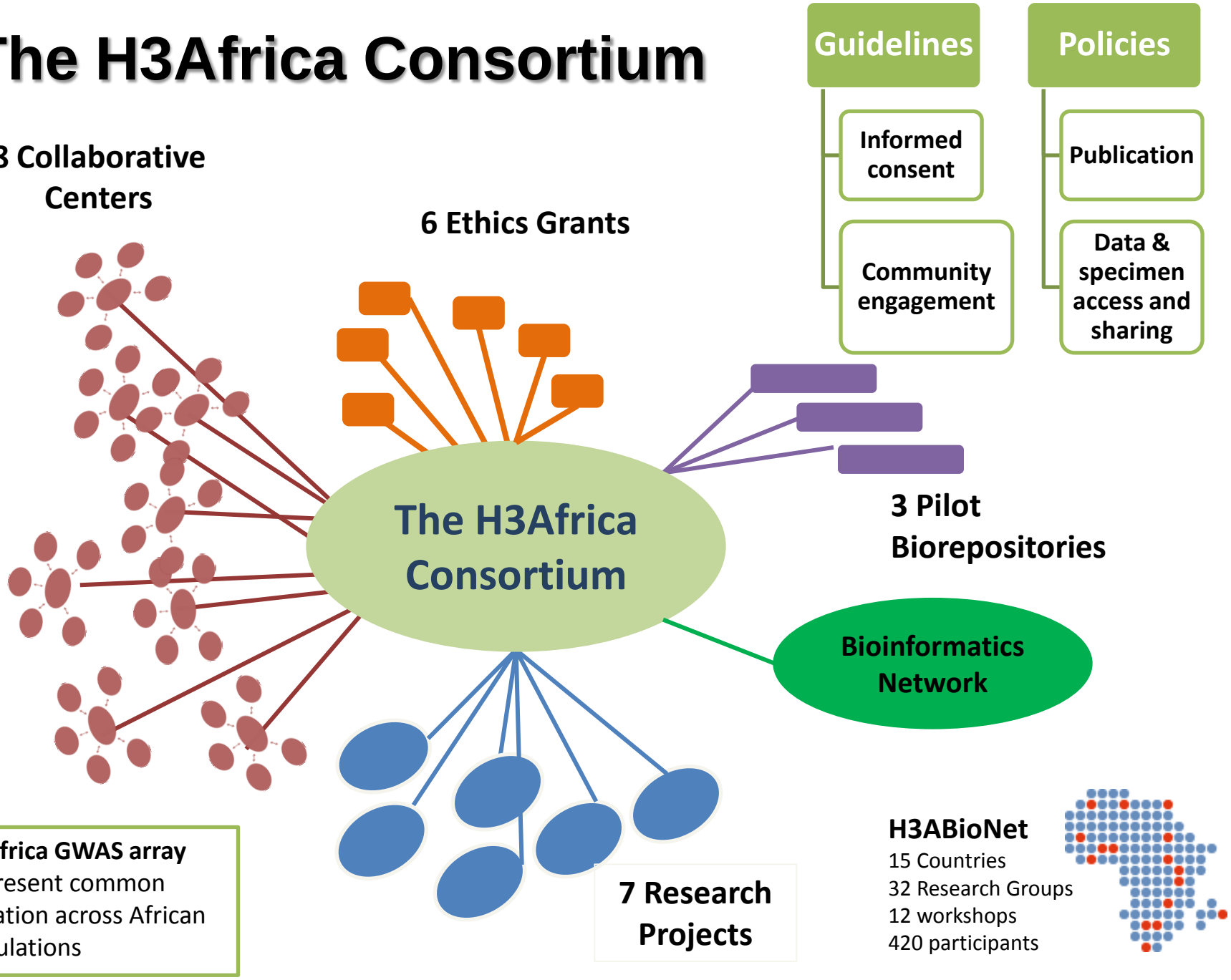


"To facilitate an Africa-based contemporary research approach to the study of genomics and environmental determinants of common diseases with the goal of improving the health of African populations"

1. Study genomic and environmental determinants of disease
2. Develop capacity for genomic research in Africa (teaching and training)
3. Develop an ethical, legal and social framework for genomic studies

www.h3africa.org

The H3Africa Consortium



National Institutes of Health
Wellcome Trust H3Africa Research Network

H3Africa Footprint 2014

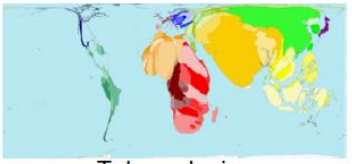
RESEARCH CAPACITY

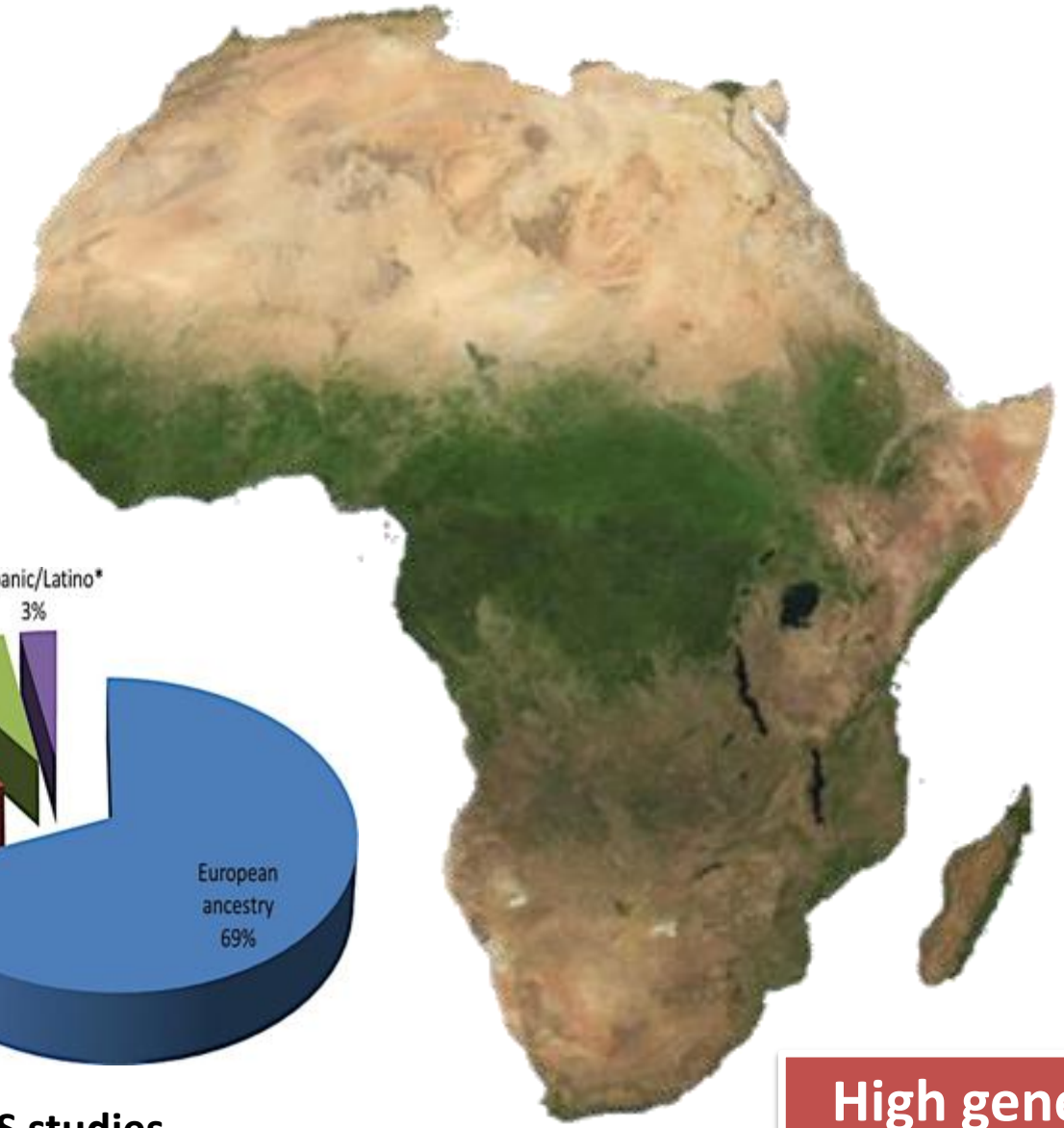
Enabling the genomic revolution in Africa

H3Africa is developing capacity for health-related genomics research in Africa

By **The H3Africa Consortium*†**

Science (June 2014)
344 (6190):1347-8



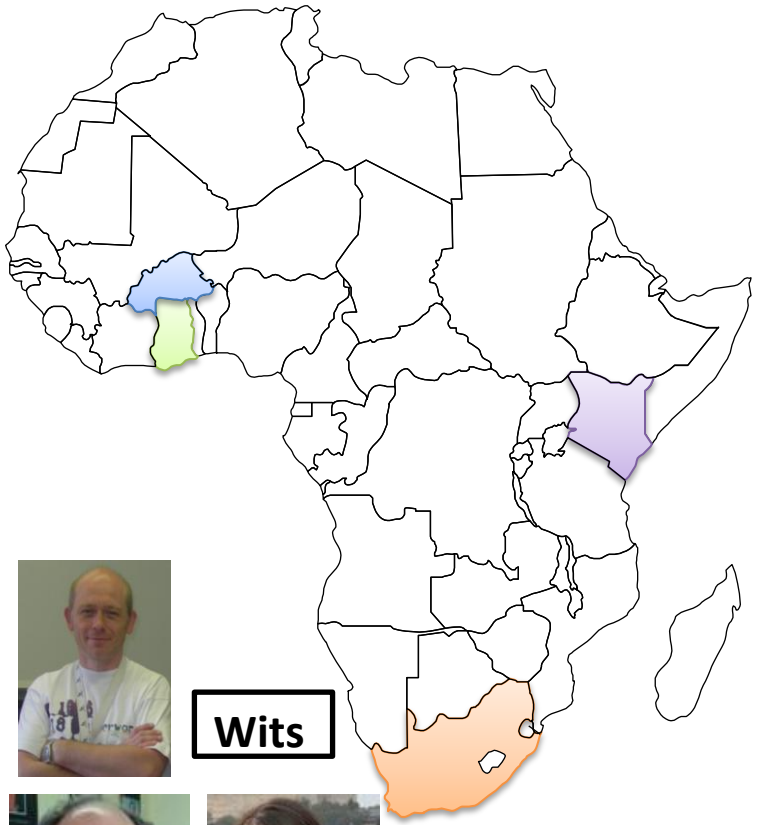


GWAS studies

Increase in NCD deaths in Africa

High genetic diversity

AWI-Gen team & 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





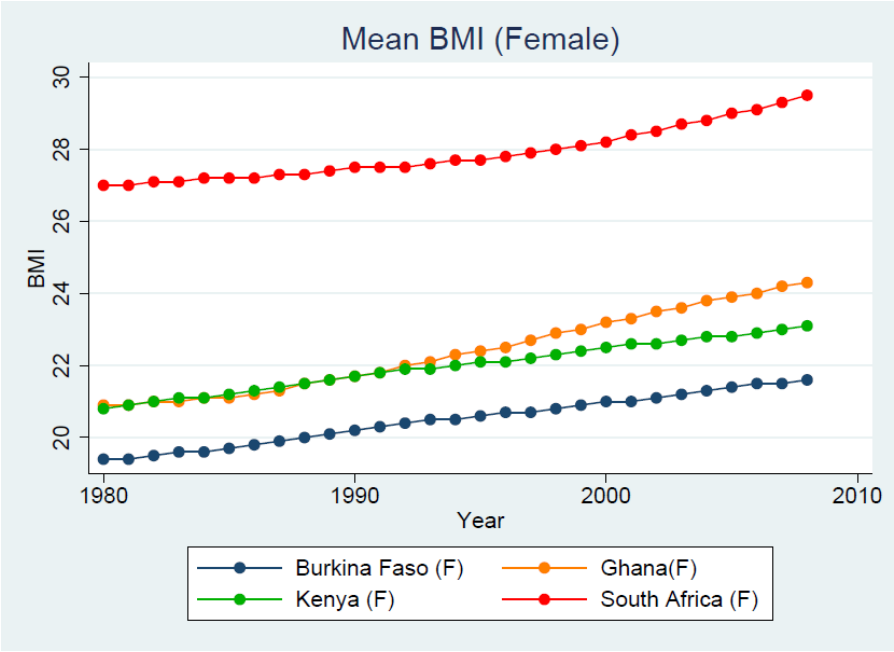


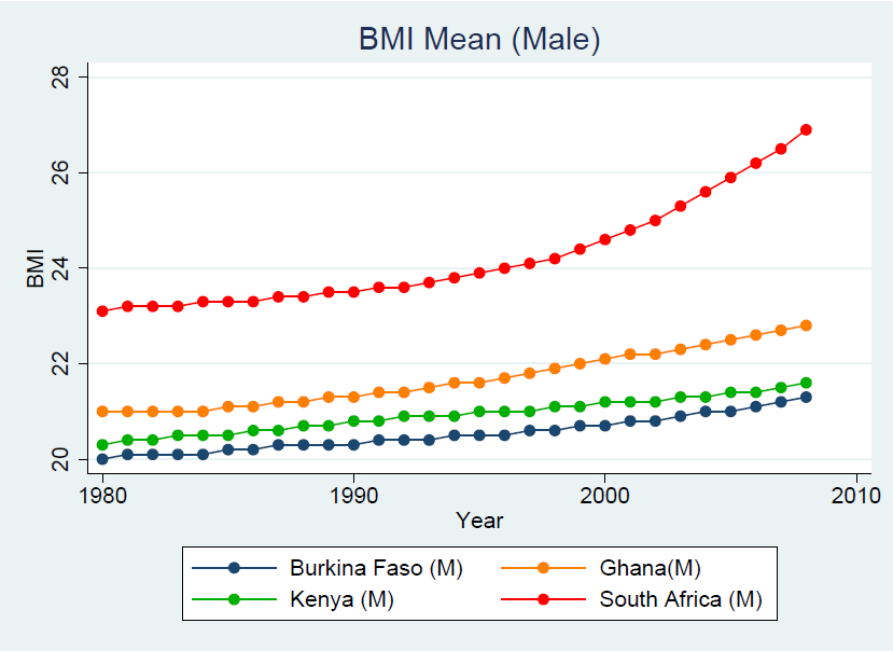

Wits






BMI in Countries from AWI-Gen Study

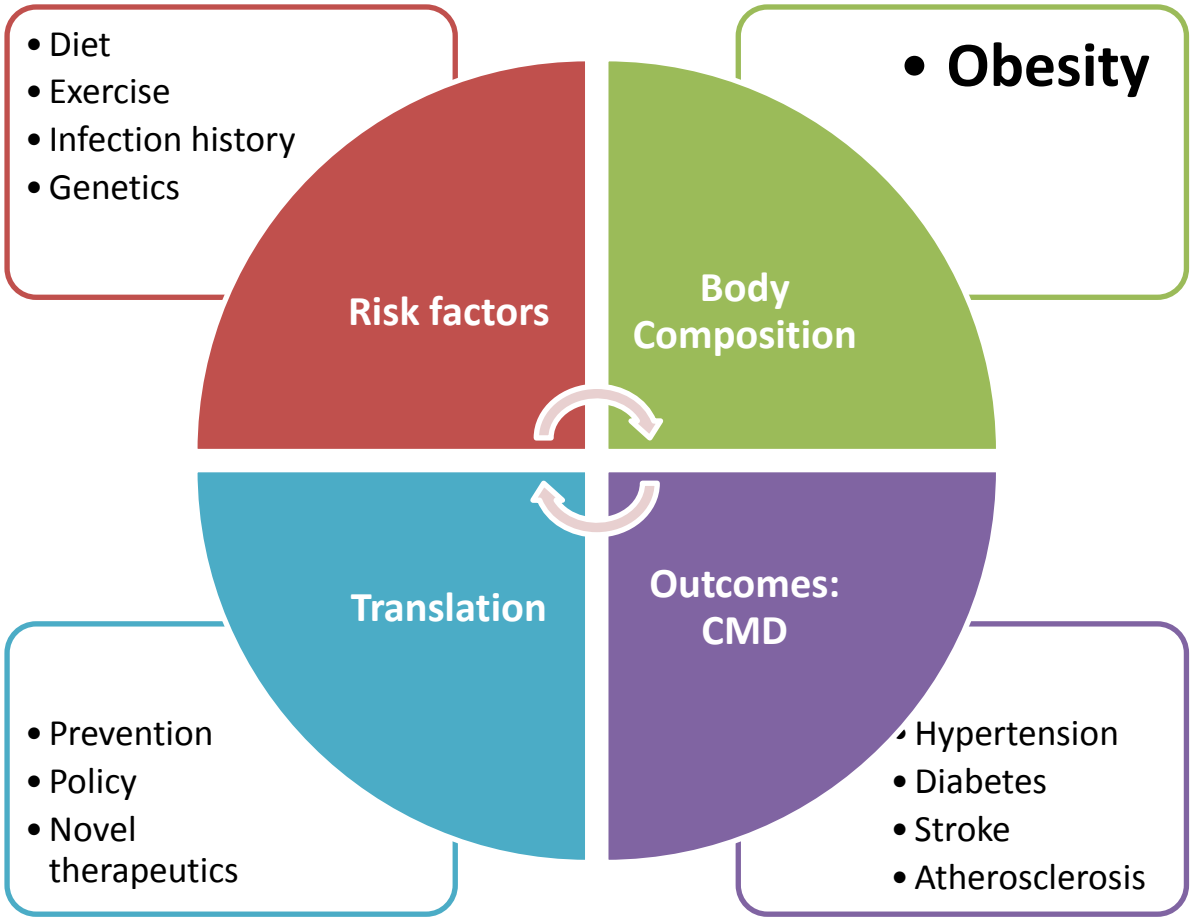




Data from - http://www1.imperial.ac.uk/medicine/globalmetabolics/

Graphs: Carol Liu

AWI-Gen Conceptual Framework



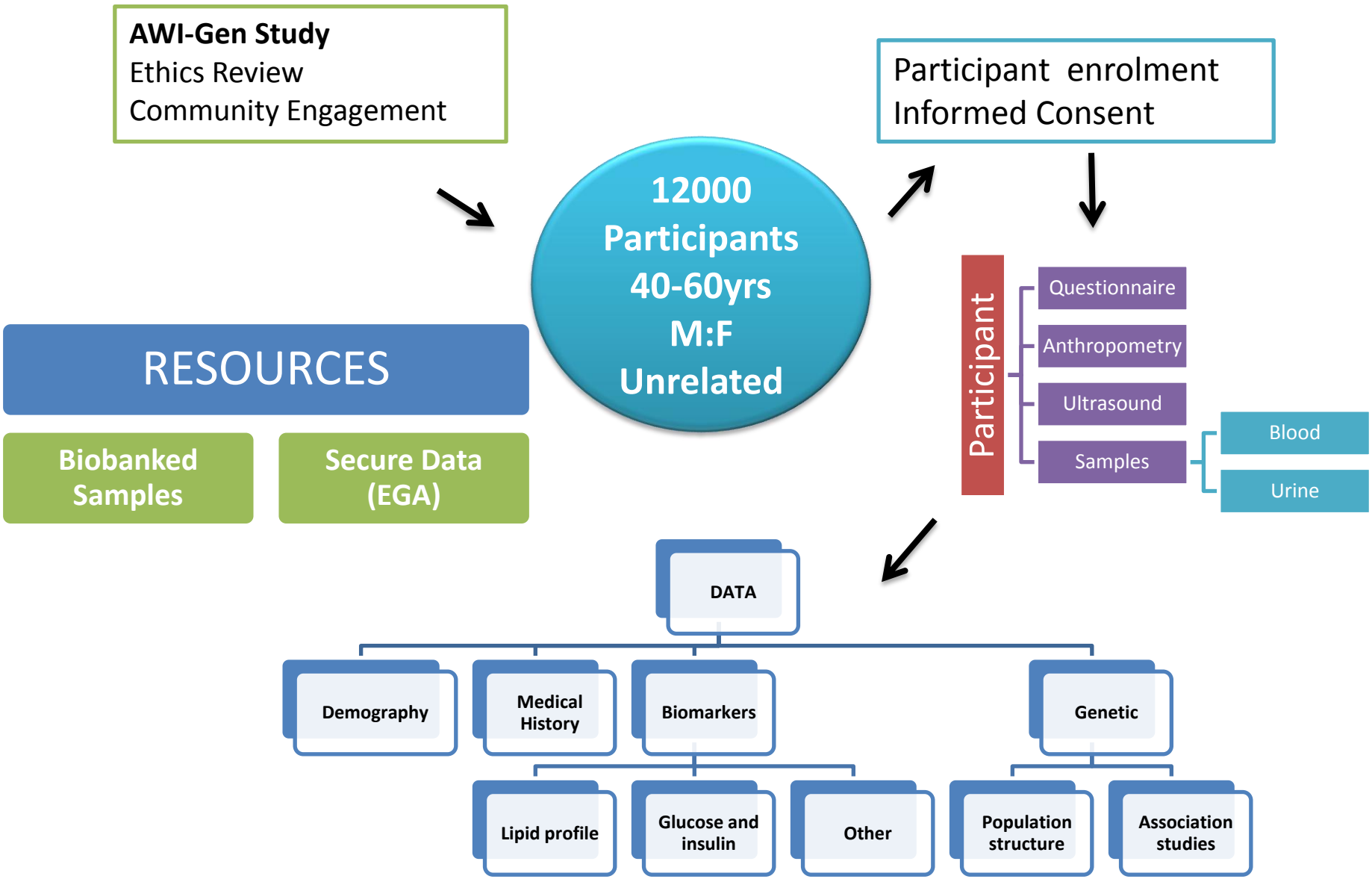
AWI-Gen Aims

1. Building capacity for genomic research
2. Population structure and genome architecture
3. Genomic and environmental contributions to body composition and CMD diseases across six Centres in Africa (GWAS with ~12 000 individuals)

Flagship Project: Metabochip study

AWI-Gen workshop October 2015

AWI-Gen Trait Association Study at glance




SPARK
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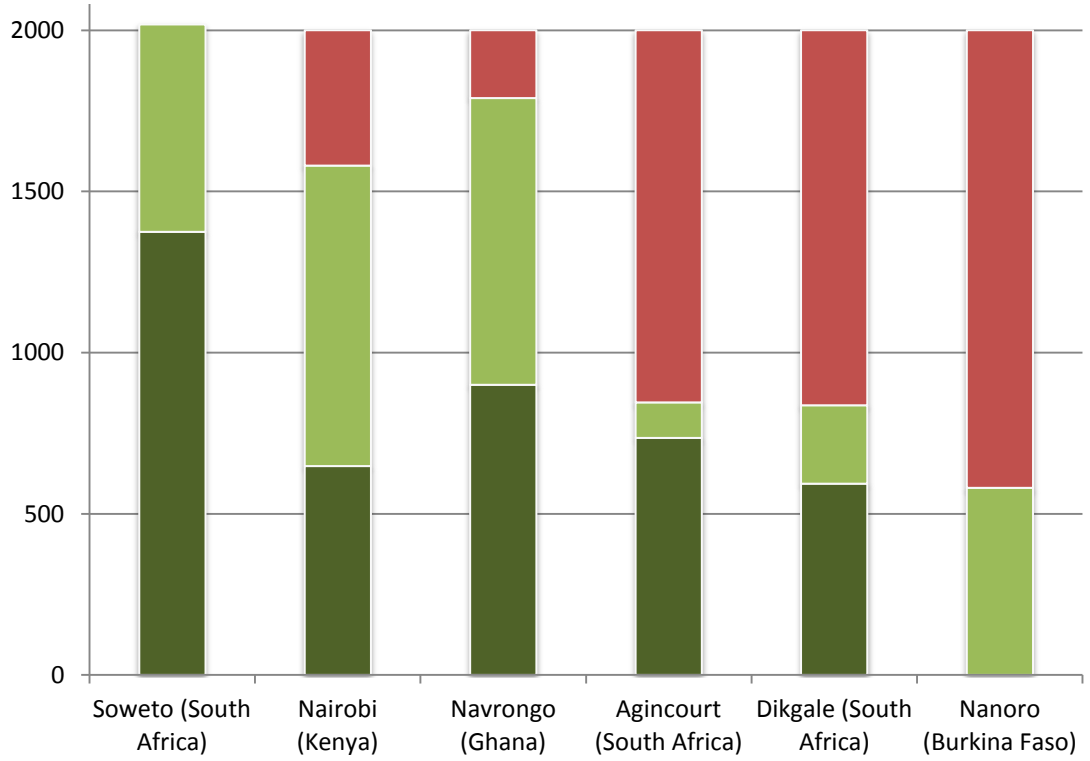
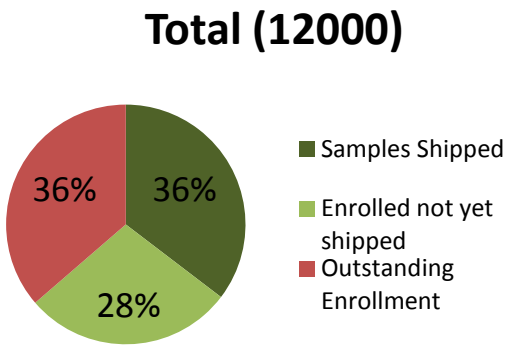
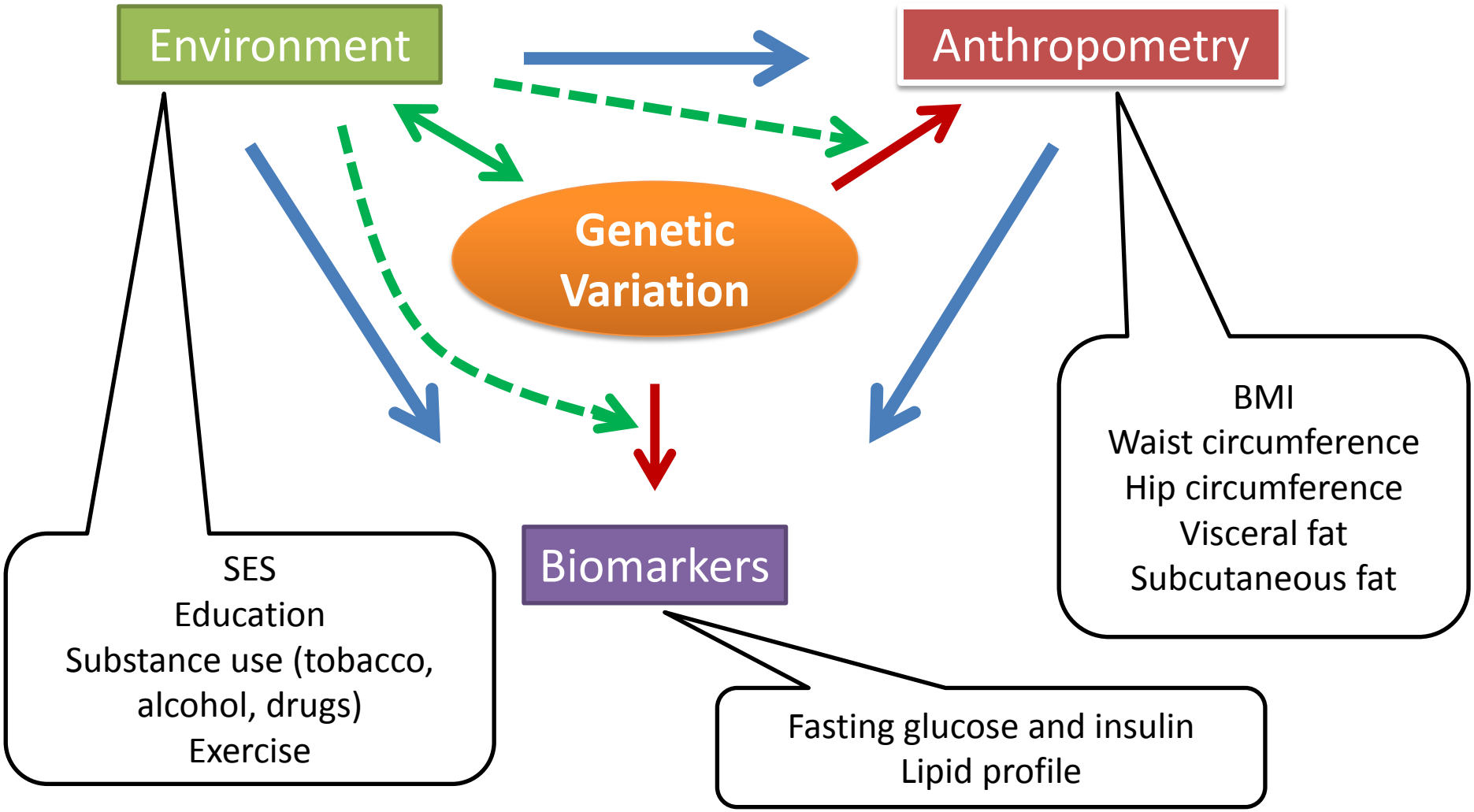
Participant Recruitment

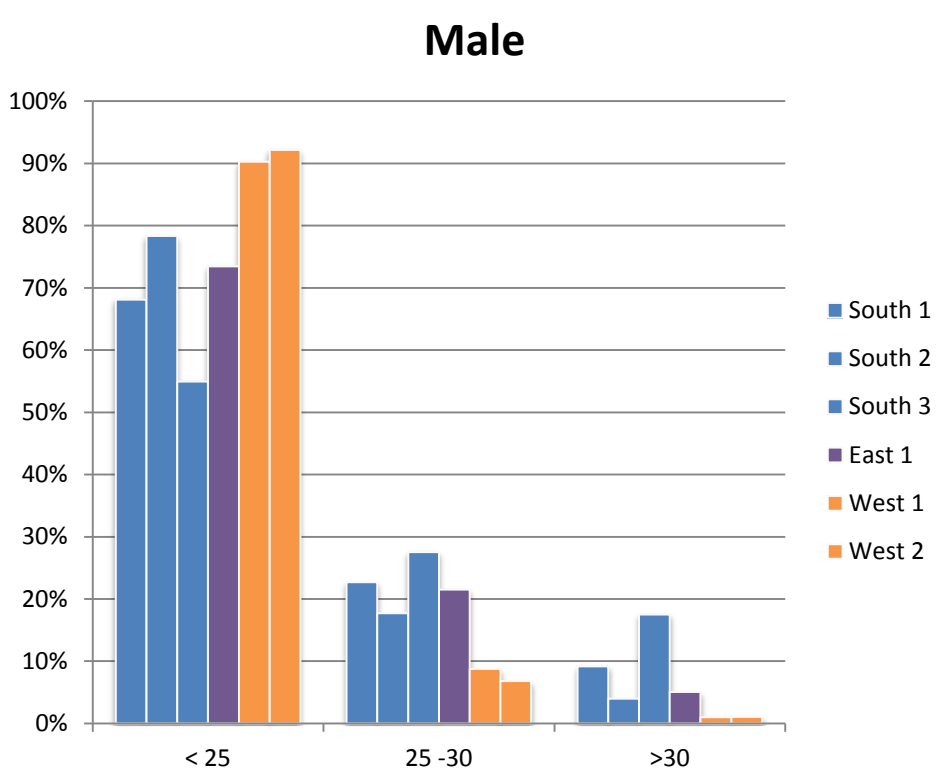


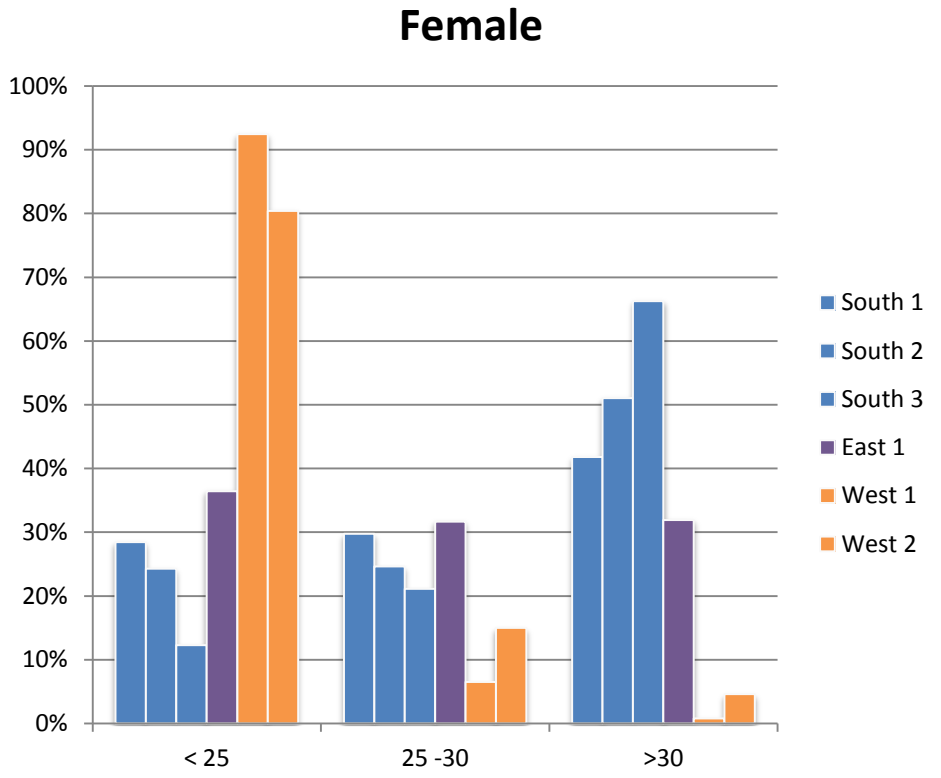


Baseline data and preliminary analysis



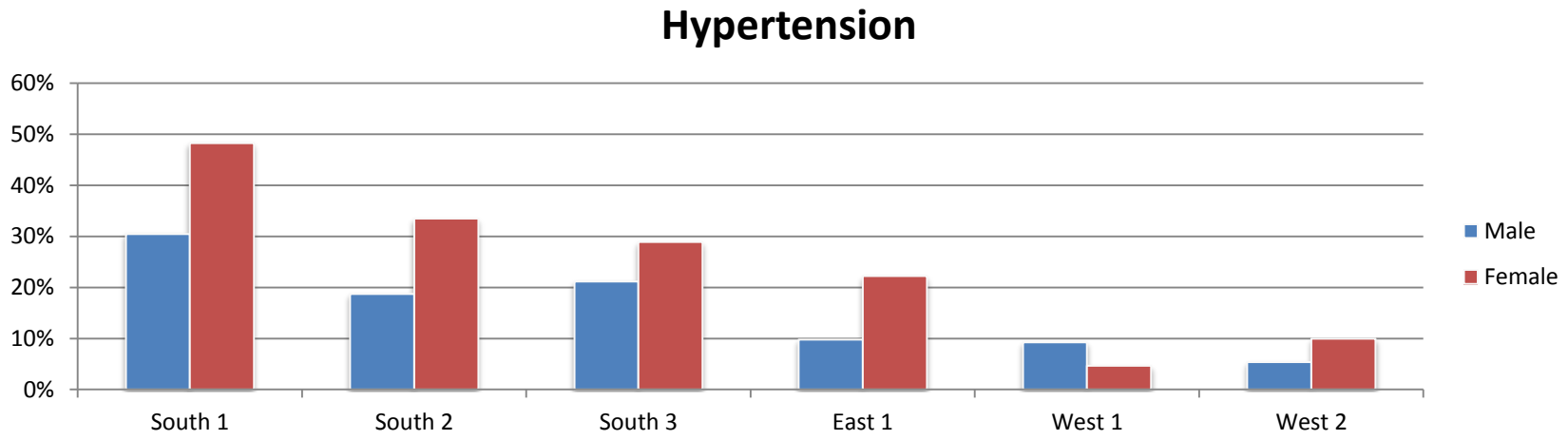
Preliminary Analysis: BMI



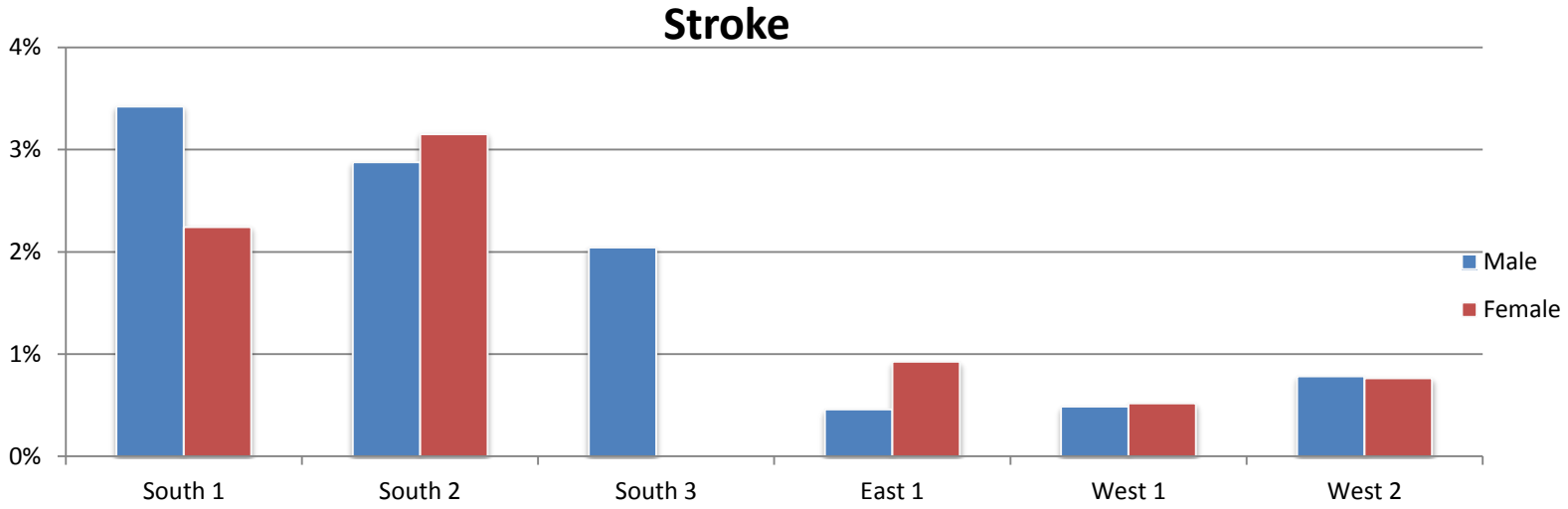


		Male		Female	
Site	n	Mean	SD	Mean	SD
South 1	845	23.6	4.9	29.2	6.7
South 2	837	21.7	4.3	30.8	8.0
South 3	2018	24.9	5.7	33.2	5.7
East 1	1580	22.8	3.8	27.5	6.0
West 1	580	21.1	3.0	20.5	3.0
West 2	1790	21.0	3.0	22.4	3.8

Preliminary Analysis: Self-reported CVD



Numbers	845	837	2018	1580	580	1790



Flagship Project

The Metabochip as a tool to identify genetic markers of obesity risk in the South African black population

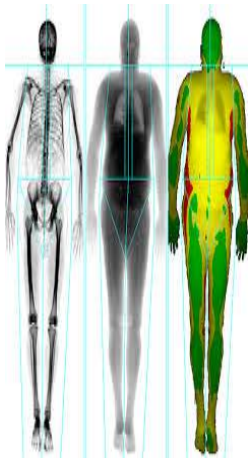
Venesa Pillay – PhD Student

Supervisors: Z Lombard, N Crowther, H Soodyall

Female caregivers
n = 1033
Median age 41.8 yrs

DPHRU
MRC/Wits Developmental Pathways for Health Research Unit

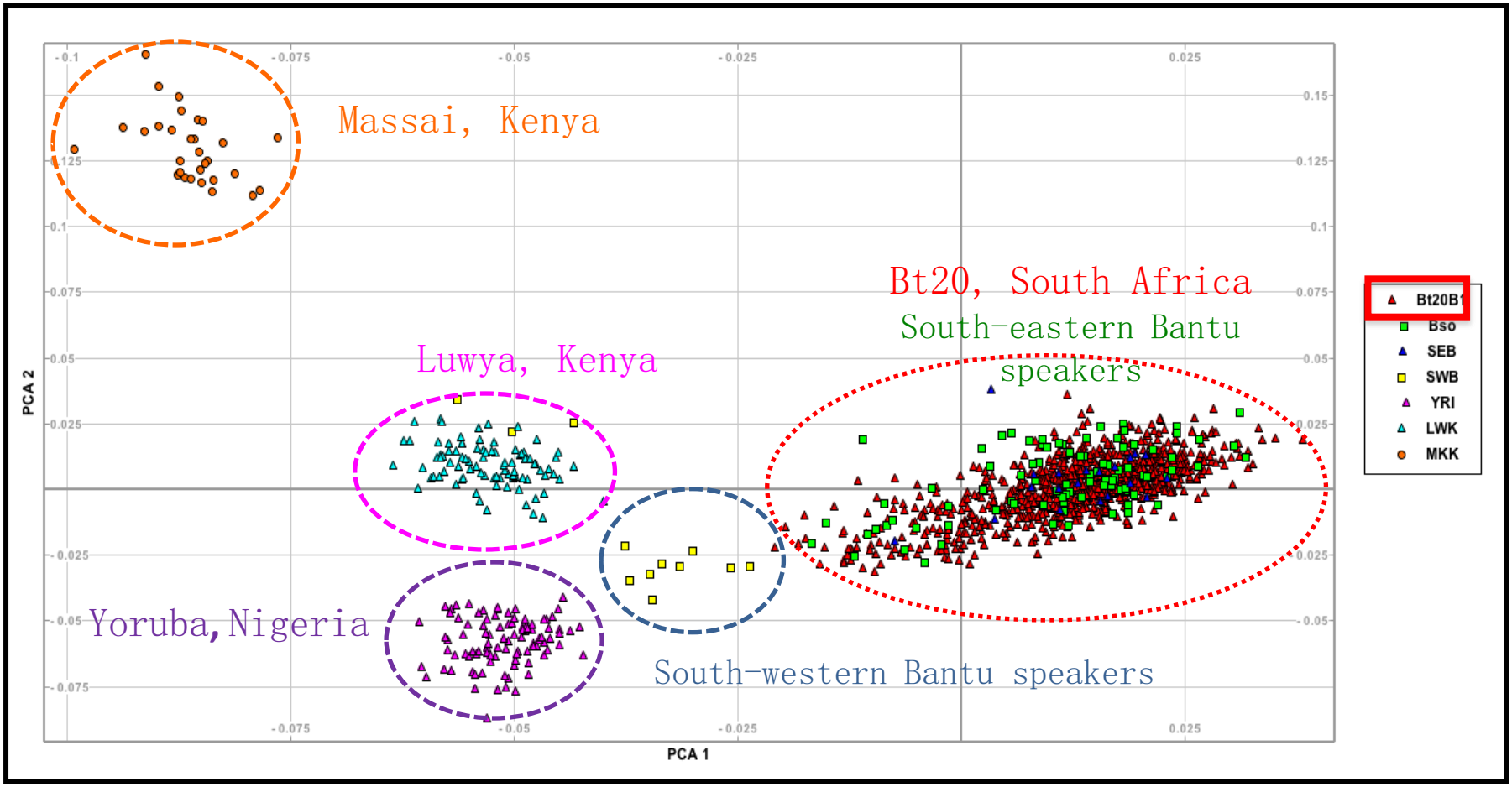
Birth to Twenty



Genotyping – UC Davis Genome Center (USA)
QC: SNPs and samples

Association with **anthropometric** and **body composition measures** using ***linear regression*** *(adjustment for covariates)*
PLINK software (vs. 1.9) and GCTA (vs. 1.24.4)

Population stratification



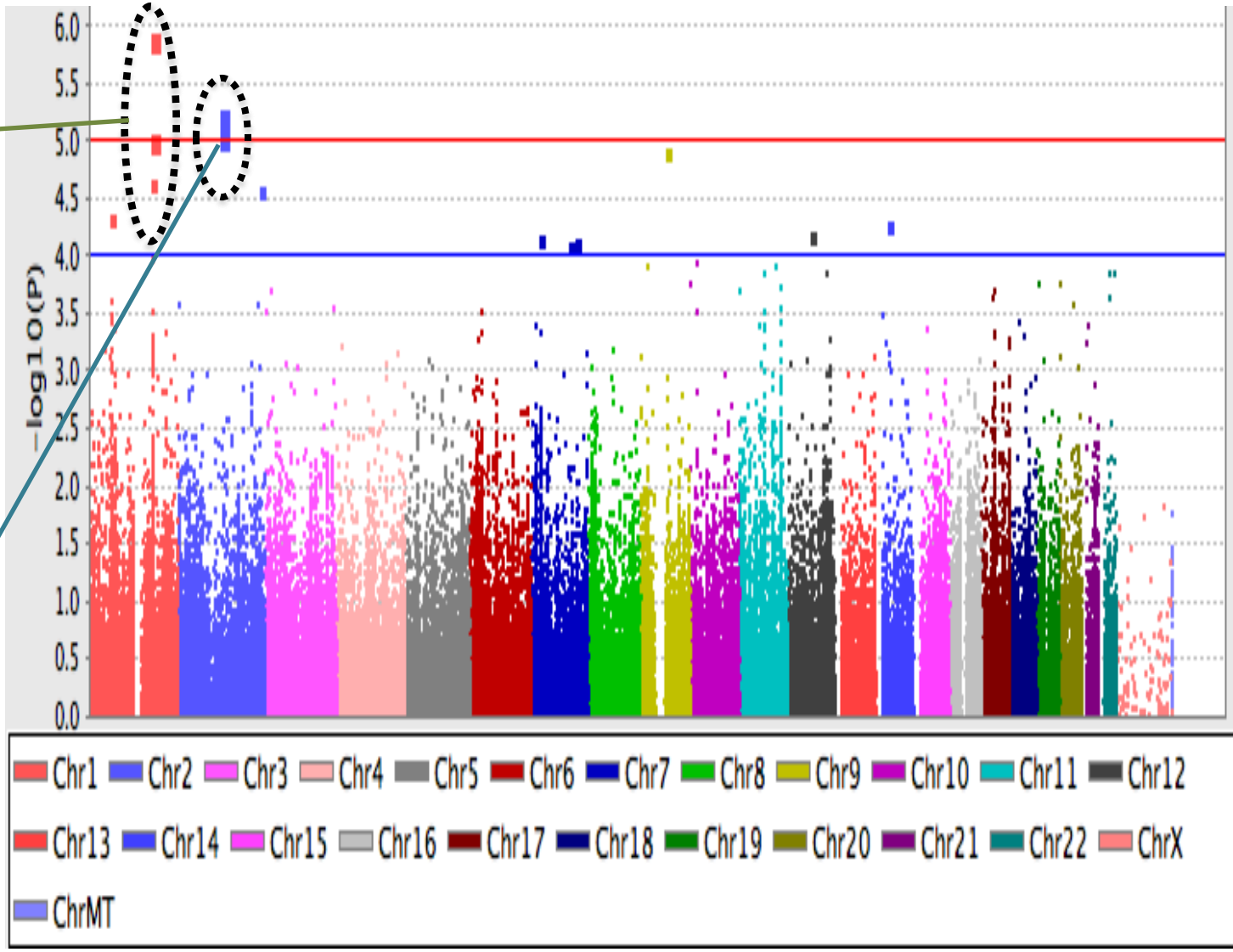
Association with total fat mass

rs6425446 *SEC16B*
Universal risk locus for BMI

Effect (β) = 2.32kg fat mass

CNTNAP5
GWAS Catalogue not associated with body composition

Effect (β) = -5.2kg fat mass



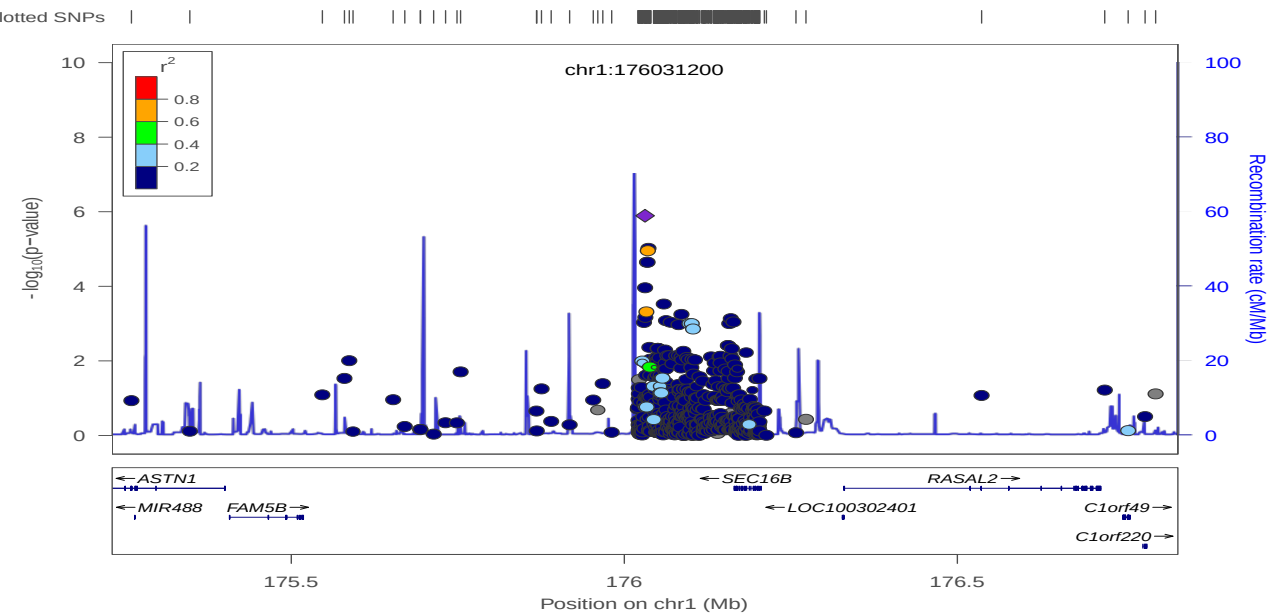
SEC16B

1. *SEC16B* associated SNPs show association with BMI in European, Asian and African American populations
2. Mouse model: Allele - Sec16b$^{tm1a(KOMP)Wtsi}$

   Association: body weight, cholesterol levels

   HDL differences show sex specific effect

rs6425446 – downstream of *SEC16B*



LD relative to YRI HapMap data

Timeline

Aug 2015 to Feb 2016

Activity		1a	1b	2a	2b	3a	3b	4a	4b	5a	5b
Training and capacity development											
Questionnaire, phenotyping, sample collection, shipping	Soweto										
	Navrongo										
	Nanoro										
	Nairobi										
	Dikgale										
	Agincourt										
African population structure											
Flagship project Soweto											
Epidemiology papers											
GWAS study											
Data analysis and publications											

Year 1a – Aug 2012 to Jan 2013
Year 1b – Feb 2013 to July 2013

July 2017

H3Africa Timeline for Phase 2

Next call for NIH proposals

May-July 2016

Submission of Proposals October-Dec 2016

Award of proposals

Aug-Dec 2017

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wellcome trust

Acknowledgements

Wits

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Himla Soodyall
Kathleen Khan
Nadia Carstens
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Nigel Crowther
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Shane Norris
Stephen Tollman
Cassandra Soo
Venesa Pillai

INDEPTH

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

….and all the scientists, clinicians, fieldworkers and participants!