

*Awareness ♦ Surveillance ♦ Advocacy ♦ Prevention*

---

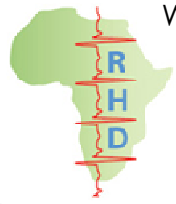
**A.S.A.P.** Rheumatic Fever &  
Rheumatic Heart Disease

# RHDGen Progress Report

Chishala Chishala  
Mayosi Research Group

# Goals

- Recruit 2,500 cases of RHD and 3,500 non-RHD ethnically-matched adult controls;
- Conduct a case-control GWAS
  - by genotyping 5 million single nucleotide polymorphisms (SNPs) in 1,500 RHD cases and 1,500 controls;
- Replication of findings in a further 1,000 cases and 2000 parental controls (Trio Study);
- Train 16 scientists/clinicians in genomics and ethics at masters, doctoral and post-doctoral levels;
- Address ethical, legal and social issues that are relevant to Africa.

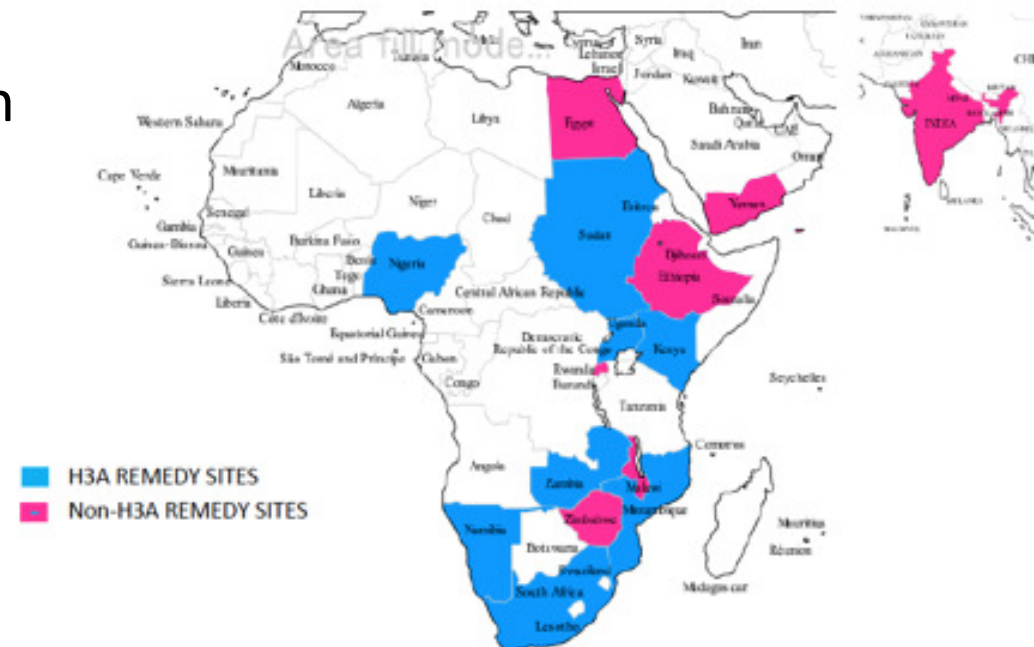


Wellcome H3Africa  
RHDGen Network

[www.RHDAfrica.org](http://www.RHDAfrica.org)

# Sampling Framework

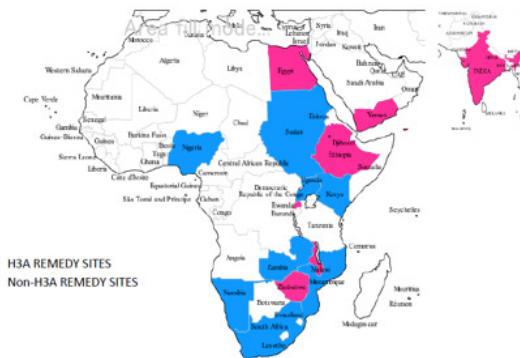
- RHD cases from hospitals in 8 sub-Saharan countries
- Controls: Mostly community-based



Appendix: The map shows in colour the 15 African and non-African countries with collaborative centres in the REMEDY study. The blue countries are participating in the RHDGen Network, and the pink countries are not participants in the RHDGen Network.

# Experimental design

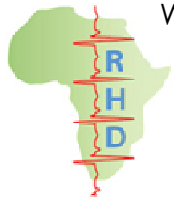
- Phase 1: GWAS of 1500 cases and 1500 controls to discover SNPs associated with susceptibility and resistance to RHD (i.e., the Discovery Cohort)
- Phase 2: family-based GWAS of an independent set of 1000 trios to replicate the findings of the first phase (i.e., the Replication Cohort)
- Phase 3: combined case-control study of 2500 cases and 2500 controls or pseudo-controls derived from the first two phases in order to discover genetic variants of modest effect and confirm the findings of the first two phases (i.e., the Meta-analysis).



Appendix: The map shows in colour the 15 African and non-African countries with collaborative centres in the REMEDY study. The blue countries are participating in the RHDGen Network, and the pink countries are not participants in the RHDGen Network.

# Recruitment Sites

Site	Principal Investigator	Status	Date of Initiation
101 - Cape Town	Bongani Mayosi	Recruiting	Oct 2013
201 - Zambia	John Musuku	Recruiting	Sep 2014
301 - Namibia	Chris Hugo-Haman	Recruiting	Oct 2014
401 - Nigeria	Fidelia Bode-Thomas	Recruiting	Sep 2014
501 - Mozambique	Ana Mocumbi	Final stage contract	?May 2015
601 - Kenya	Steve Ogendo	Recruiting	Feb 2015
701 - Sudan	Ahmed El-Sayed	Recruiting	Feb 2015
801 - Uganda	Charles Mondo	Ethics approved	May 2015

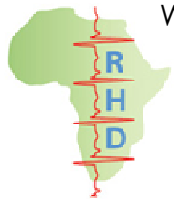


Wellcome H3Africa  
RHDGen Network

[www.RHDAfrica.org](http://www.RHDAfrica.org)

# Recruitment

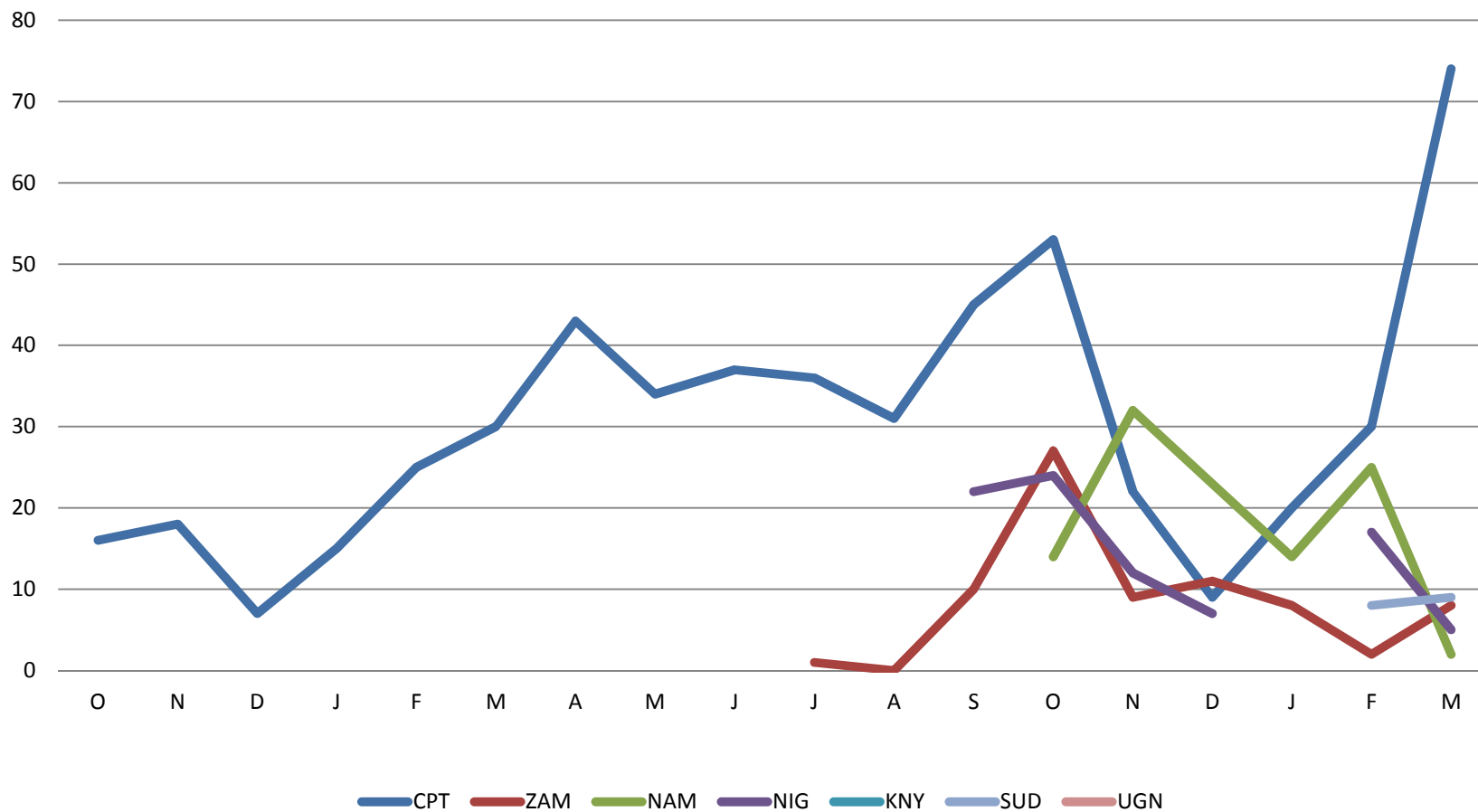
Site	Cases	Controls
Cape Town	676	735
Zambia	92	0
Namibia	145	0
Nigeria	69	64
Kenya	50	0
Sudan	44	0
<b>Total</b>	<b>1076</b>	<b>800</b>
Trios	35 across 4 sites	



Wellcome H3Africa  
RHDGen Network

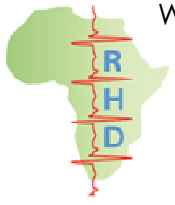
# Monthly Case Recruitment

[www.RHDAfrica.org](http://www.RHDAfrica.org)





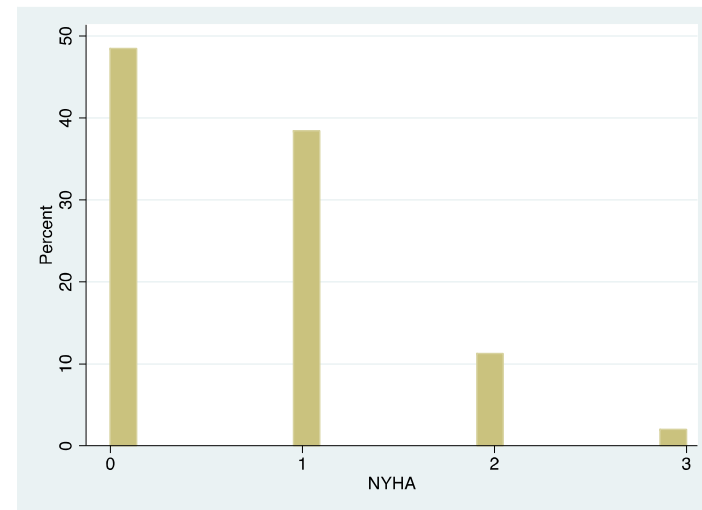
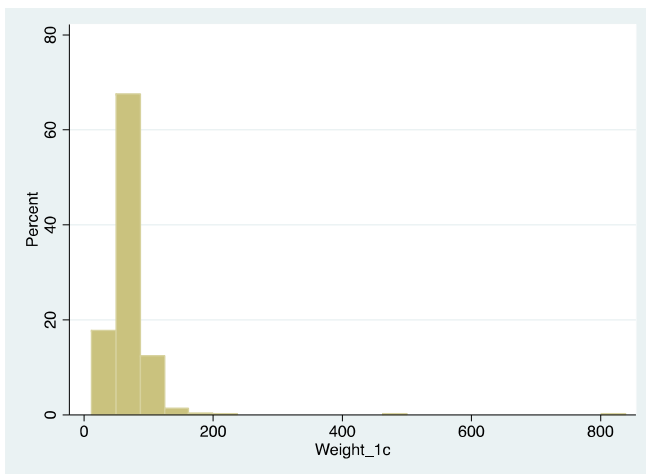
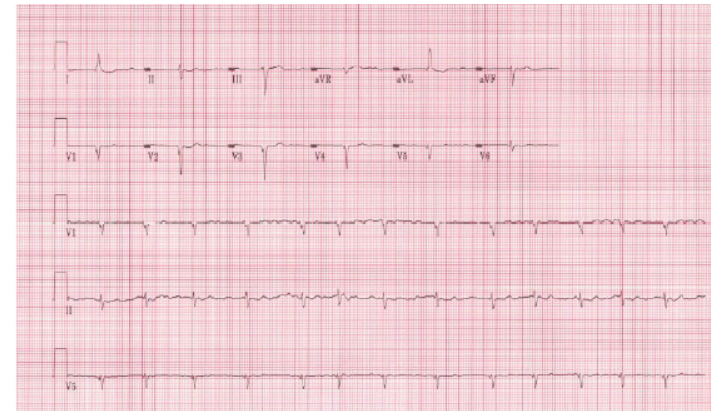
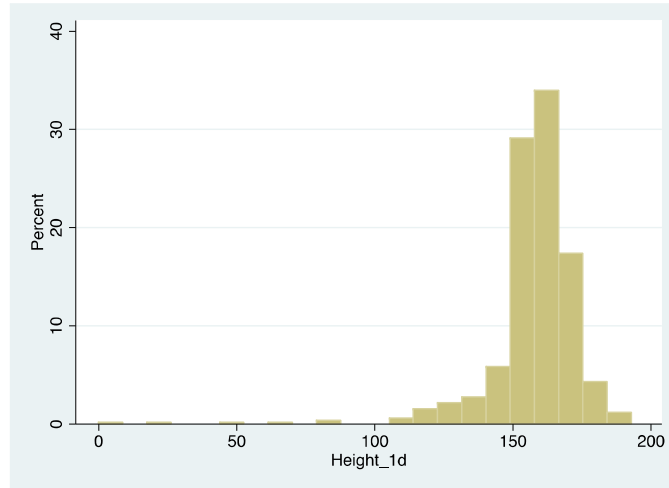


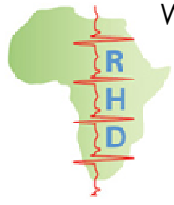


Wellcome H3Africa  
RHDGen Network

# Phenotype

[www.RHDAfrica.org](http://www.RHDAfrica.org)





Wellcome H3Africa  
RHDGen Network

[www.RHDAfrica.org](http://www.RHDAfrica.org)

# Pilot phase

- DNA Extraction: 1,670 specimens
- 1,094 specimens sent for first GWAS analysis to Guillaume Pare (McMaster) in April 2015
- 2.5 M Illumina chip
- Challenges:
  - Sample couriering
  - QA issues
  - QC issues



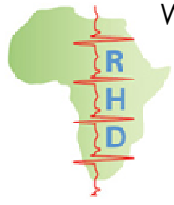


[www.RHDAfrica.org](http://www.RHDAfrica.org)

# RHDGen Health Scholars' Programme

- Appointments :
  - 1 x Postdoctoral Fellow (Zambia)
  - 2 x MSc studentships in empirical ethics awarded (Malawi / Cameroon)
  - 2 x MSc studentships in molecular genetics awarded (Kenya / Zimbabwe)
  - 1 x PhD studentship in molecular genetics awarded (Burundi)
  - O/S: PhD studentships in statistical genetics (x 1), and bioinformatics (x1)
- 7 x MMed Fellows appointed:
  - 1 x each recruiting centre (outside SA)



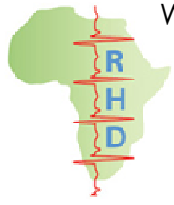


Wellcome H3Africa  
RHDGen Network

[www.RHDAfrica.org](http://www.RHDAfrica.org)

# Challenges

- Delayed site initiation
  - October 2013 to ?May 2015
  - Ethics approval delay
  - Admin problems including financial issues
  - Infrastructure

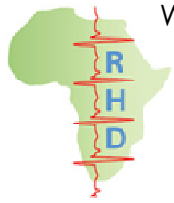


Wellcome H3Africa  
RHDGen Network

[www.RHDAfrica.org](http://www.RHDAfrica.org)

# Challenges

- Recruitment
  - Small number of fully active sites
  - Site specific challenges e.g small patient pool, distance from hospitals, loss to follow up
  - Trios are not as many as initially thought:
    - e.g Nakita found only 22 out of 500 at Cape Town alone. May well have to revise the target to only 200 trios.
  - REMEDY: n=1,500: currently only 26% of these have been enrolled



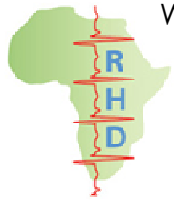
# Challenges

www.RHDAfrica.org

• Re

Based on actual numbers of CRFs in RHDGen Dbase			
Site	No of pts in REMEDY	Recruited into RHDGen	%
101 - Cape Town	489	276	56
201 - Zambia	127	35	28
301 - Namibia	277	49	18
401 - Nigeria	143	44	31
501 - Mozambique	42		
601 - Kenya	305	4	1
701 - Sudan	185	5	3
<b>Totals</b>	<b>1568</b>	<b>413</b>	<b>26</b>

*Potential Enrollees > 1,000*

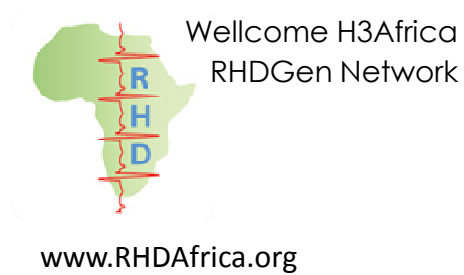


Wellcome H3Africa  
RHDGen Network

[www.RHDAfrica.org](http://www.RHDAfrica.org)

# Challenges

- Recruitment
  - REMEDY: n=1,500: currently only 26% of these have been enrolled
  - Small number of fully active sites
  - Site specific challenges e.g. small patient pool, distance from hospitals, loss to follow up
  - Trios are not as many as initially thought. Nakita example where only 22 out of 500 at Cape Town alone. May well have to revise the target to only 200 trios.



# Challenges

- Possible solutions:
  - All sites should be fully active
  - Outreach/Partnerships
  - REMEDY

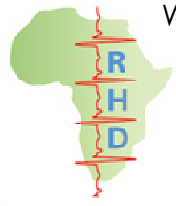




[www.RHDAfrica.org](http://www.RHDAfrica.org)

# MMED Meeting

- Recruitment review
- Science aspects to be discussed within postgraduate projects as part of RHDGen
- Come up with innovative methods (collectively) to improve recruitment to meet the (new) recruitment target date of June 2016.



Wellcome H3Africa  
RHDGen Network

[www.RHDAfrica.org](http://www.RHDAfrica.org)

# Community Engagement Activities

- Heldeberg college  
Health Awareness Week –  
opportunity to highlight RHD  
and the importance of sore  
throat management
- RHD day during NDOH  
Rheumatic Fever Week 2014 –  
patient report-back.

