

RHEUMATIC HEART DISEASE IN UGANDA: RESEARCH TO CLINICAL PRACTICE

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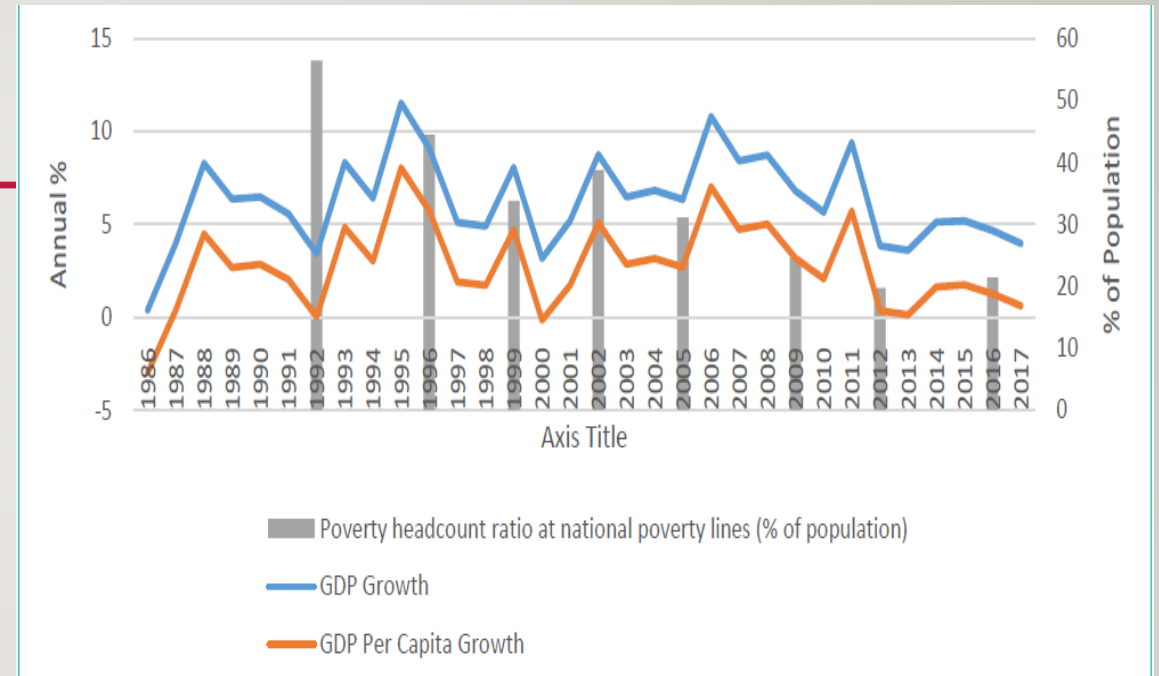


ACKNOWLEDGEMENTS

- Partners: UHI, CNHS, GOLI, RHEACH
- Colleagues at UHI:
- Emmy Okello, Isaac Sinabulya
- Nurses
- Support groups
- RHD Patients

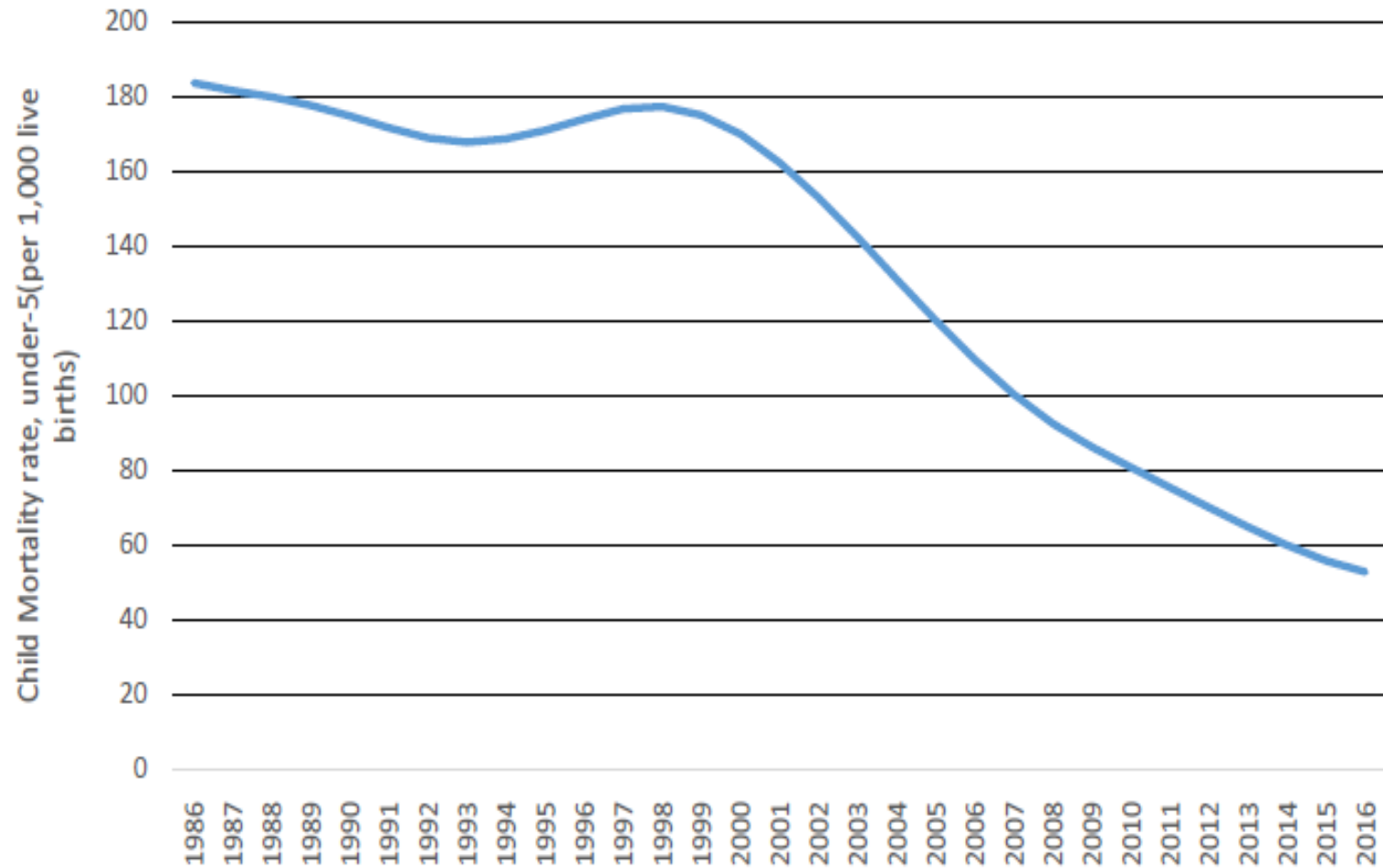


UGANDA



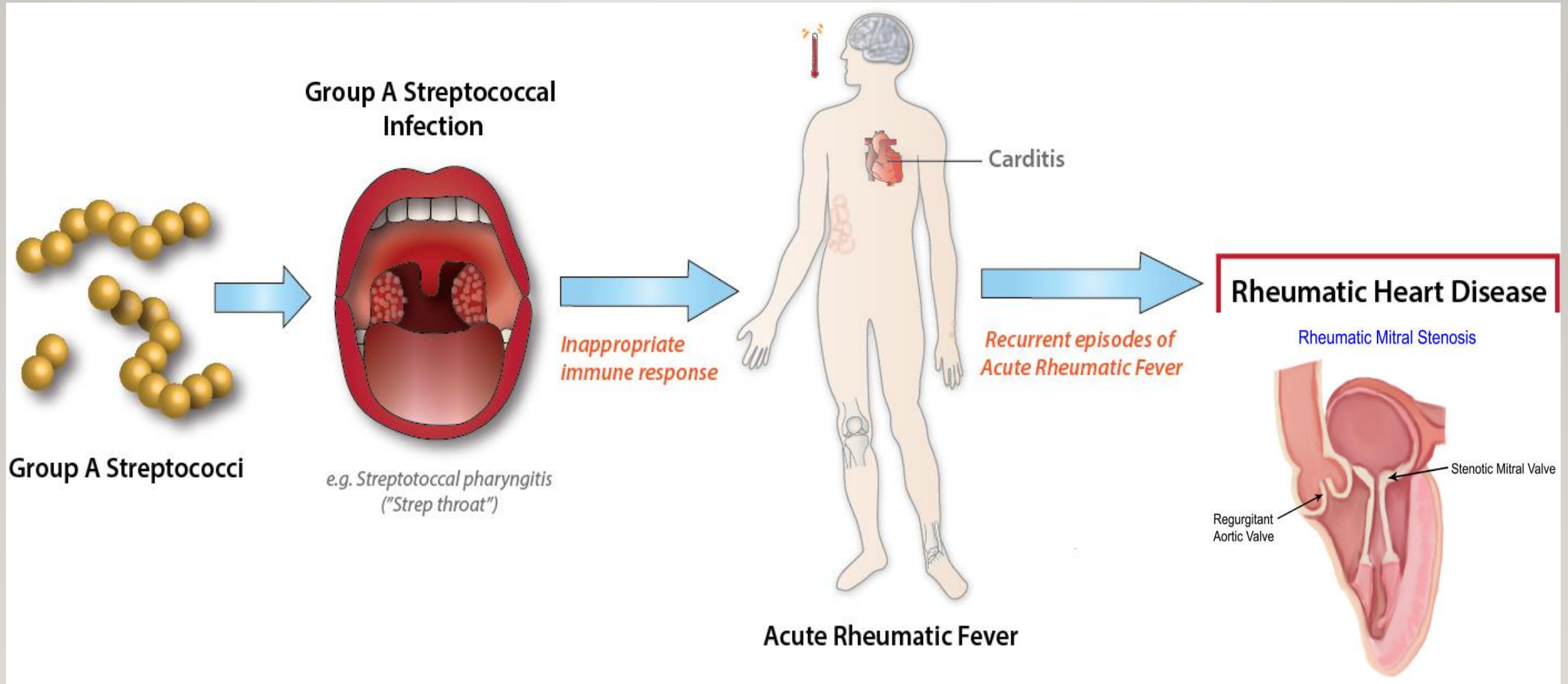
- Estimated Population 44 Million
- Population Growth Rate 3.03%
- Total Fertility Rate 5.4 per woman
- Poverty Prevalence of 21.4%
- GDP Per Capita \$706 (2017)

UGANDA ECONOMIC/HEALTH INDICATORS



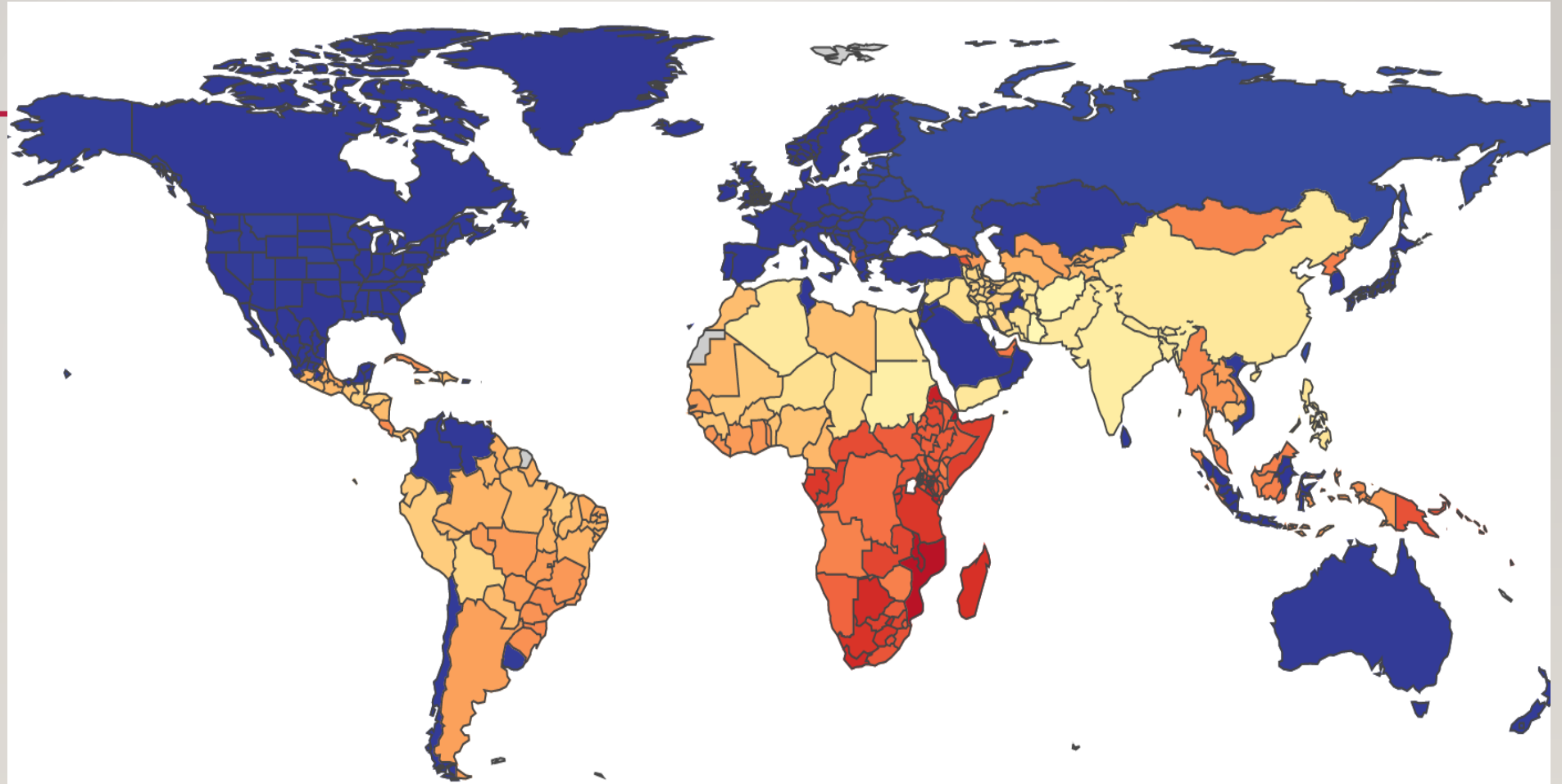
- Under-5 Mortality Rate 43 per 1,000 live births
- 54.7% of the population <18 years
- 33.4% Aged 6-17 years
- 75.2% of population <30 years
- Dependency ratio of 103%
- No National Health Insurance

NATURAL HISTORY OF RHD

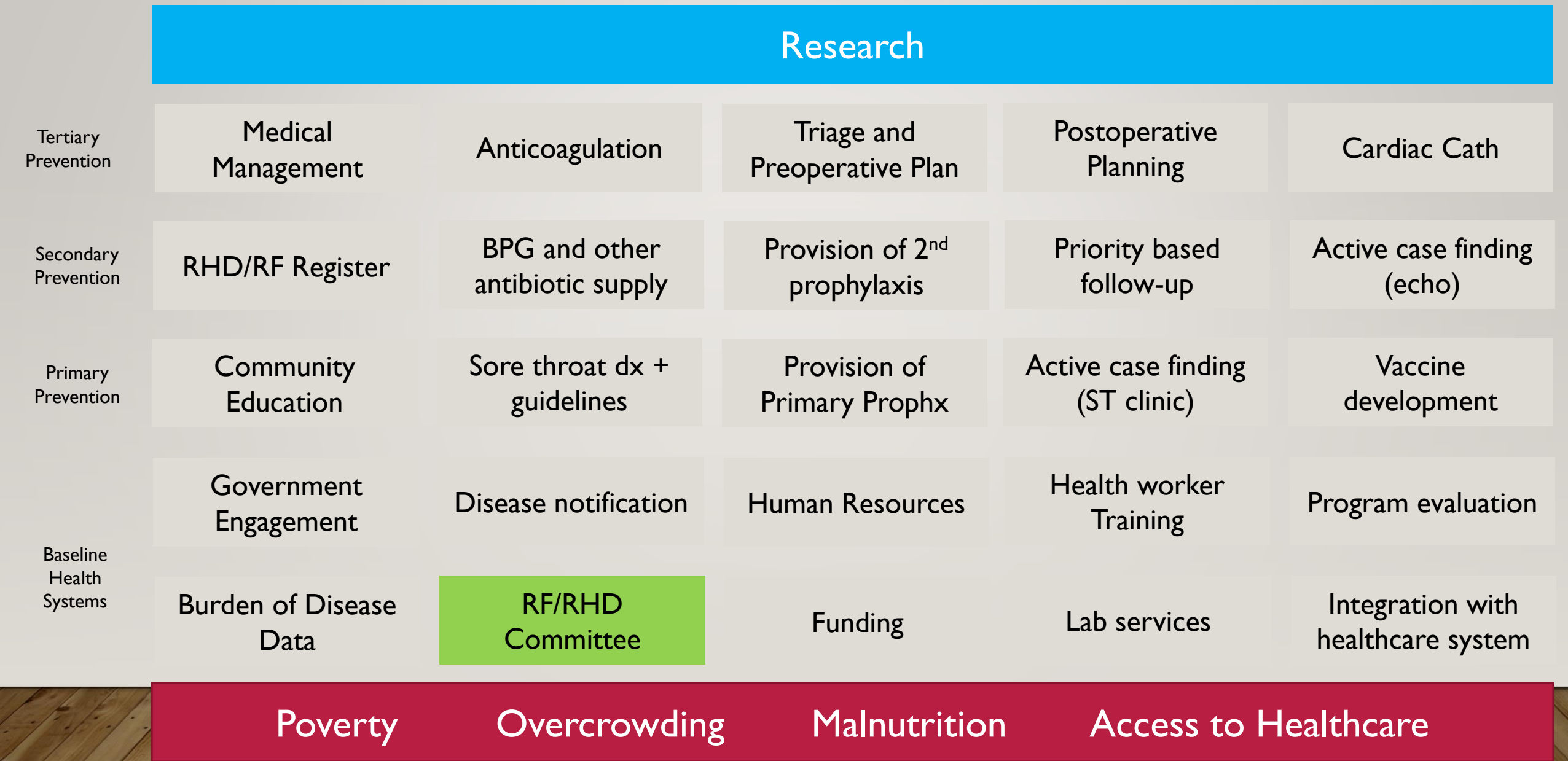


Global burden of RHD, 2017

- >39 million persons living with RHD
- 80% in LMIC



TIPS CONCEPTUAL FRAMEWORK



REFOCUSING ON RHEUMATIC HEART DISEASE

2010 and beyond

- Research begins to quantify what is felt by frontline healthcare providers across Uganda
- UHI develops a paper RHD registry UHI
- UHI makes a conscious decision to refocus on reducing the national burden of RHD
- RF/RHD committee formed within UHI

DISEASE BURDEN

Echocardiography Screening for Rheumatic Heart Disease in Ugandan Schoolchildren

Andrea Beaton, MD; Emmy Okello, MD; Peter Lwabi, MD; Charles Mondo, MD;
Robert McCarter, ScD; Craig Sable, MD

- 4,869 Kampala School children aged 5-16 years underwent echo screening
- 2.7% had abnormal echo cardiograms
- Prevalence of 1.5% of RHD (72/4869 cases)
- 98% involvement of Mitral valve
- Lower socioeconomic groups had more prevalence of RHD and More advanced disease

Beaton et al, 2010

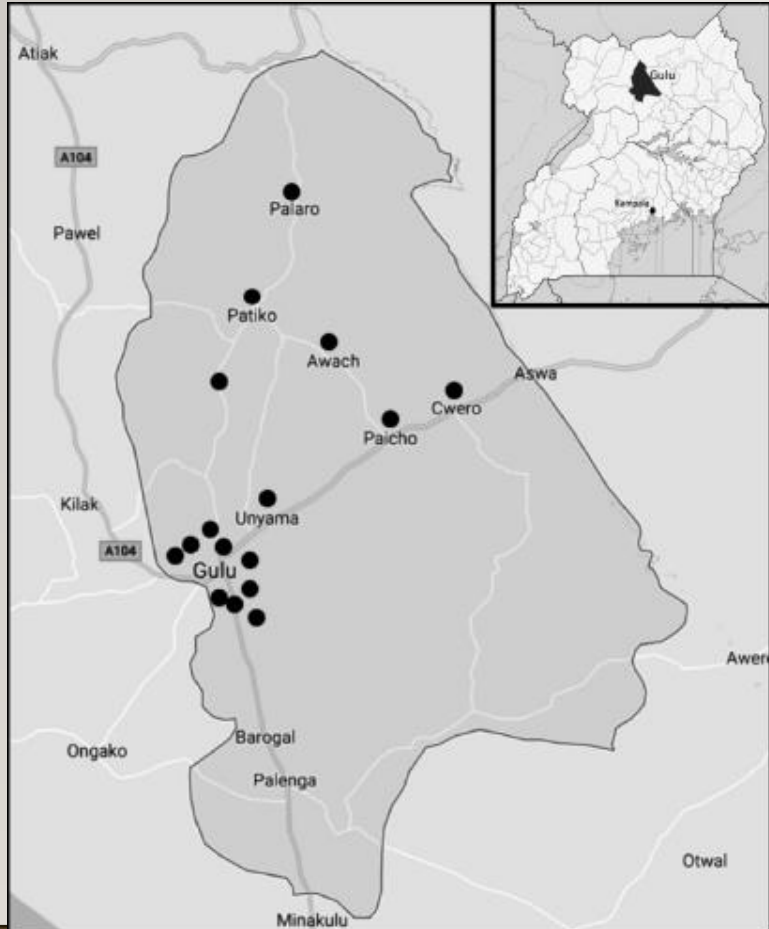
BURDEN OF RHEUMATIC HEART DISEASE: SCHOOL CHILDREN

- Over 15,000 children screened in Kampala (central), Mbarara (West), and Gulu (North) Districts
- **Pooled RHD prevalence 2.97%** (95% CI 2.70-3.24%) for latent RHD (echo detected)
- 2/3 borderline and 1/3 definite (screening vs. active case finding)
- **Upto 150,000 school age children have definite RHD**
- Some regional variability
 - Kampala 1.5% Vs Gulu 3.7%

(Beaton, 2012, Beaton 2014, Weinberg 2015)



BURDEN OF RHEUMATIC HEART DISEASE: COMMUNITY STUDY IN GULU



- 480 households screened (aged 5-50)
- 2,453 echocardiograms performed
- 2.5% children (37/1472) with RHD
- 2.3% adults (23/981) with RHD
- RHD prevalence of 13 per 1000 persons aged 5-60 years
- Prevalence increases with age, peaking at 16-20 years
- *Scheel et al, 2018*

BURDEN OF RHEUMATIC HEART DISEASE: PREGNANCY OUTCOMES



- Prospective Screening echo in 3506 women, routine ANC, 2 rural HCIIIs and 1 regional referral hospital over 24 months; Heart disease present in 58
- 17 per 1000 women with heart disease; 15 per 1000 of these (>85%) RHD
- Only 2 (3.4%) women had prior diagnosis
- CV complications occurred in 51% of women with heart disease, most commonly heart failure
- Only 1 maternal death – “best case” scenario, access to diagnosis, cardio-obstetrical consultation and care
- Population percent attributable risk of heart disease on maternal mortality 11%; fetal mortality 1.1% and Neonatal mortality 6%

Beaton et al, 2018

GENETICS OF RHD IN UGANDA

Okello et al. *BMC Cardiovascular Disorders* 2014, **14**:28
<http://www.biomedcentral.com/1471-2261/14/28>



RESEARCH ARTICLE

Open Access

Rheumatic heart disease in Uganda: the association between MHC class II HLA DR alleles and disease: a case control study

Emmy Okello^{1,2*}, Andrea Beaton³, Charles K Mondo¹, Paul Kruszká⁴, Noah Kiwanuka⁵, Richard Odoi-Adome⁶ and Juergen Freers¹

- 199 subjects; 96 RHD cases vs 103 controls aged 5-60 years
- HLA typing done and HLA-DR frequency comparison between cases and controls
- HLA-DR II associated with increased risk of RHD (OR=331, $P < 0.001$, $P_c < 0.001$)
- HLA-DR I decreased risk of RHD (OR 0.42, $P = 0.01$, $P_c = 0.09$)

Okello et al, 2014

INCREASED FAMILIAL RISK

RESEARCH ARTICLE

Targeted Echocardiographic Screening for Latent Rheumatic Heart Disease in Northern Uganda: Evaluating Familial Risk Following Identification of an Index Case

Twalib Aliku¹, Craig Sable², Amy Scheel², Alison Tompsett², Peter Lwabi³, Emmy Okello^{3,4}, Robert McCarter⁵, Marshall Summar⁶, Andrea Beaton^{2*}

¹ School of Medicine, Gulu University, Gulu, Uganda, ² Division of Cardiology, Children's National Health System, Washington, District of Columbia, United States of America, ³ Uganda Heart Institute, Kampala, Uganda, ⁴ School of Medicine, Makerere University, Kampala, Uganda, ⁵ Division of Biostatistics and Informatics, Children's National Health System, Washington, District of Columbia, United States of America, ⁶ Division of Genetics and Metabolism, Children's National Health System, Washington, District of Columbia, United States of America



- All first degree relatives ≥ 5 years
60 RHD cases/67 RHD negative controls
- 455/668 (68%) relatives screened
- Definite RHD more common among
siblings of RHD positive cases
- RHD positive cases were 4.5 times more
likely to have a sibling with RHD

Aliku et al, 2016

BURDEN OF RHEUMATIC HEART DISEASE: PRESENTATION AT TERTIARY CENTRE

1. Poor Health System infrastructure for early diagnosis and Referral
2. Patients present late with advanced RHD
 - 85% of patient with advanced RHD
 - 75% meet criteria for surgical or catheter-based intervention

Zhang et al, 2015

CLINICAL PRESENTATION

80

CARDIOVASCULAR JOURNAL OF AFRICA • Vol 24, No 3, April 2013

CVAFRICA

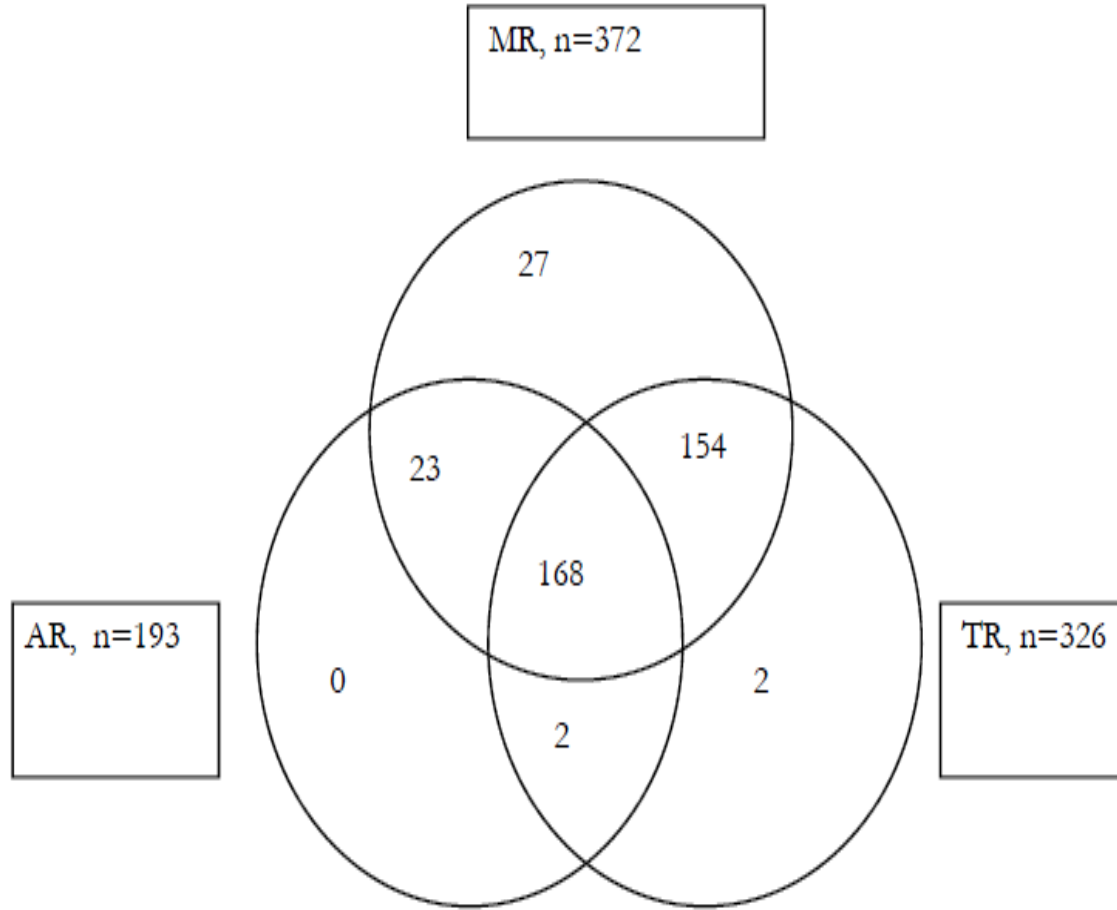
Cardiovascular complications in newly diagnosed rheumatic heart disease patients at Mulago Hospital, Uganda

EMMY OKELLO, ZHANG WANZHU, CHARLES MUSOKE, ALIKU TWALIB, BARBARA KAKANDE, PETER LWABI, NYAKOOJO B WILSON, CHARLES K MONDO, R ODOI-ADOME, JUERGEN FREERS

- 309 Patients aged 15-60 years
- Newly diagnosed RHD
- Complications such as CHF, PAH, Atrial Fibrillation, ARF recurrence, infective endocarditis, stroke
- Complications present in 49% (152/309)
- Heart failure: 46.9%, Atrial fibrillation 13.9%

Okello et al, 2013

Paediatric RHD at tertiary care



- 3503 abnormal echo reports of children < 15 years from 2007-2011 At UHI
- CHD in 2,677;
- 826 had Acquired Heart Disease; RHD=376 (45.5%), DCMP 22.4%, Pericarditis 8.8%, EMF 7.1%
- MR in 98.9%, severe in 73%
- Mitral stenosis in 10.6%

Lubega et al, 2013

MEDICAL MANAGEMENT

Okello et al. *BMC Cardiovascular Disorders* (2017) 17:20
DOI 10.1186/s12872-016-0451-8

BMC Cardiovascular Disorders

RESEARCH ARTICLE

Open Access



Rheumatic heart disease in Uganda: predictors of morbidity and mortality one year after presentation

Emmy Okello^{1,2,5*}, Chris T. Longenecker³, Andrea Beaton⁴, Moses R. Kamya² and Peter Lwabi¹

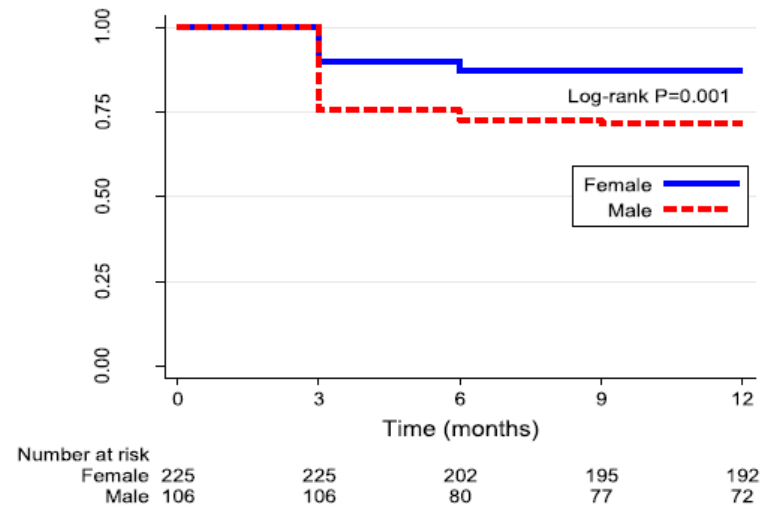


Fig. 2 Kaplan- Meier curve for mortality within one year of initial presentation with rheumatic heart disease

- 449 subjects aged 4-60 years followed at least for one year
- High one year Mortality 17.8%
- Most deaths within first three months of initial Presentation
- Predictors of mortality: Poor penicillin adherence, Heart failure, Advanced Disease (LVEDd>55mm)

Okello et al, 2013

BPG ADHERENCE

124

CARDIOVASCULAR JOURNAL OF AFRICA • Vol 24, No 4, May 2013 **CVAFRICA**

Benzathine penicillin adherence for secondary prophylaxis among patients affected with rheumatic heart disease attending Mulago Hospital

CHARLES MUSOKE, CHARLES KIIZA MONDO, EMMY OKELLO, WANZHU ZHANG, BARBARA KAKANDE, WILSON NYAKOOJO, JUERGEN FREERS

- 95 Patients (Aged 5-60 years) followed up for 6 months
- $\geq 80\%$ Adherence: 54%
- Higher educational status and residence near health facilities favor good adherence
- Painful injections listed as main reason for none adherence
- *Musoke et al, 2013*

Quantifying and Addressing GAS

- Overall GAS Carriage of 15.9% (95% CI 12.8-19.5%),
- Pilot data shows 60% of children had at least 1 sore throat over 4 weeks, 41% of kids had a GAS pharyngitis
- Mild presentation (mean pain score 2.2)
- Consideration of reintroduction of pharyngitis into the IMCI
- AFROStrep: Collaborative multicenter study aimed at understanding the clinical, microbiological, epidemiological, and molecular characteristics of GAS in Africa

Beaton et al, 2019



Table 3: Susceptibility rates of GAS Causing Acute Sore Throat^{14, 16}				
ANTIBIOTICS	MEAN VALUES ± SD	Resistant (%)	Indeterminate (%)	Susceptible (%)
B-lactams (mm)				
Penicillin G	30.0 ± 2.7	0	0	68 (100%)
Ceftriaxone	27.3 ± 2.5	2 (2.9%)	2 (2.9%)	64 (94.1%)
Macrolides (mm)				
Erythromycin	23.4 ± 3.8	2 (2.9%)	6 (8.8%)	60 (88.2%)
Glycopeptides (mm)				
Vancomycin	18.9 ± 1.2	1 (1.5%)	0	67 (98.5%)
Phenicol (mm)				
Chloramphenicol	23.1 ± 2.3	6 (8.8%)	2 (2.9%)	60 (88.2%)
Cyclines (mm)				
Tetracycline	19.5 ± 5.7	23 (33.8%)	10 (14.7%)	35 (51.5%)
Fluoroquinolones (mm)				
Ofloxacin	18.9 ± 2.5	0	3 (4.4%)	65 (95.6%)
Sulfonamides (ug/mL)				
Sulfamethoxazole/trimethoprim	0.065 ± 0.079	0	0	68 (100%)

Beaton, 2019

ANTICOAGULATION / INR MONITORING



- INR monitoring at UHI, Gulu, and Mbarara sites
- Point of care testing with training of healthcare staff to adjust medication
- Currently >50 patients being actively monitored in these settings
- UHI enrollment site for INVICTUS – RCT looking at novel anticoagulation strategies in Rheumatic Atrial Fibrillation

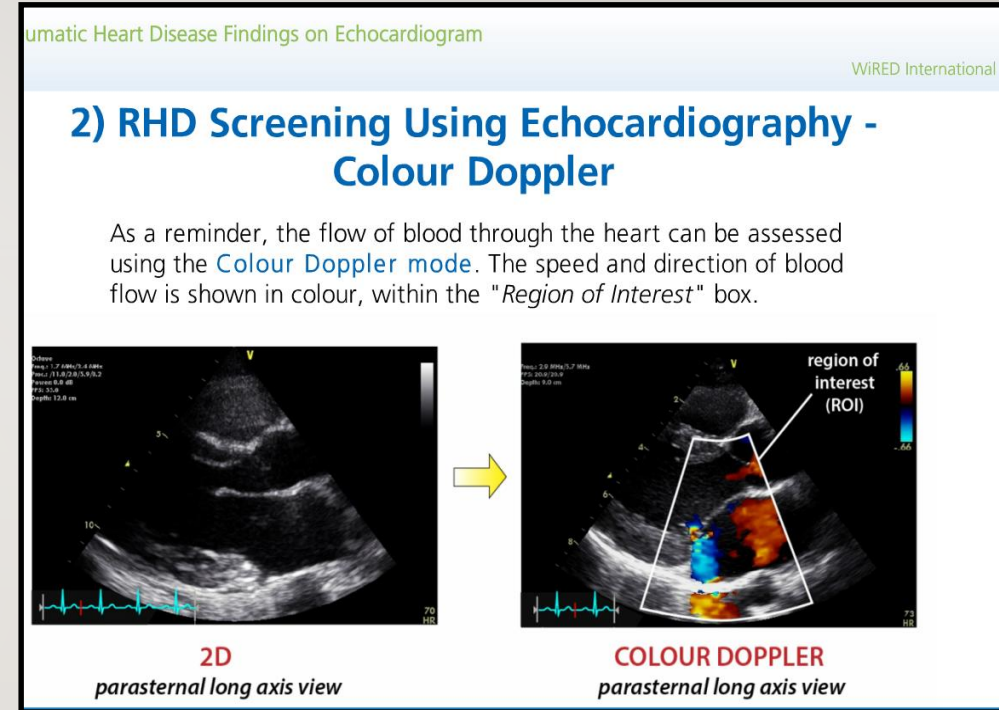
Making active case finding more practical



Handheld echo
78% sensitive
(98% definite RHD)
87% specific
(Beaton, 2014)

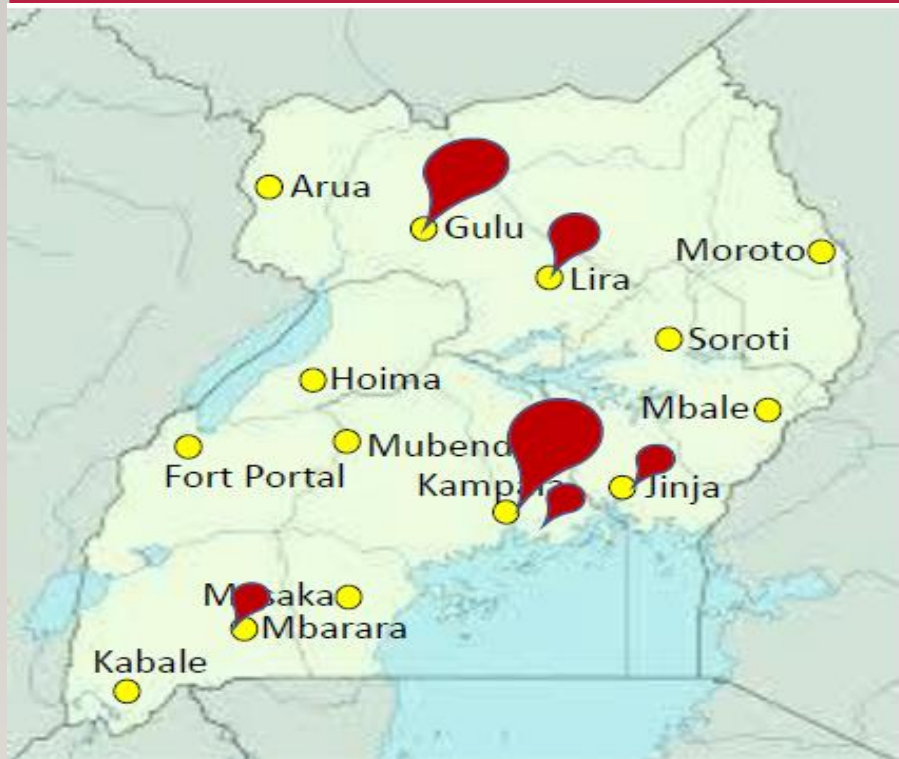


Task Shifting: Non-expert
users can
quickly and accurately
learn to screen
(Ploutz, 2015)



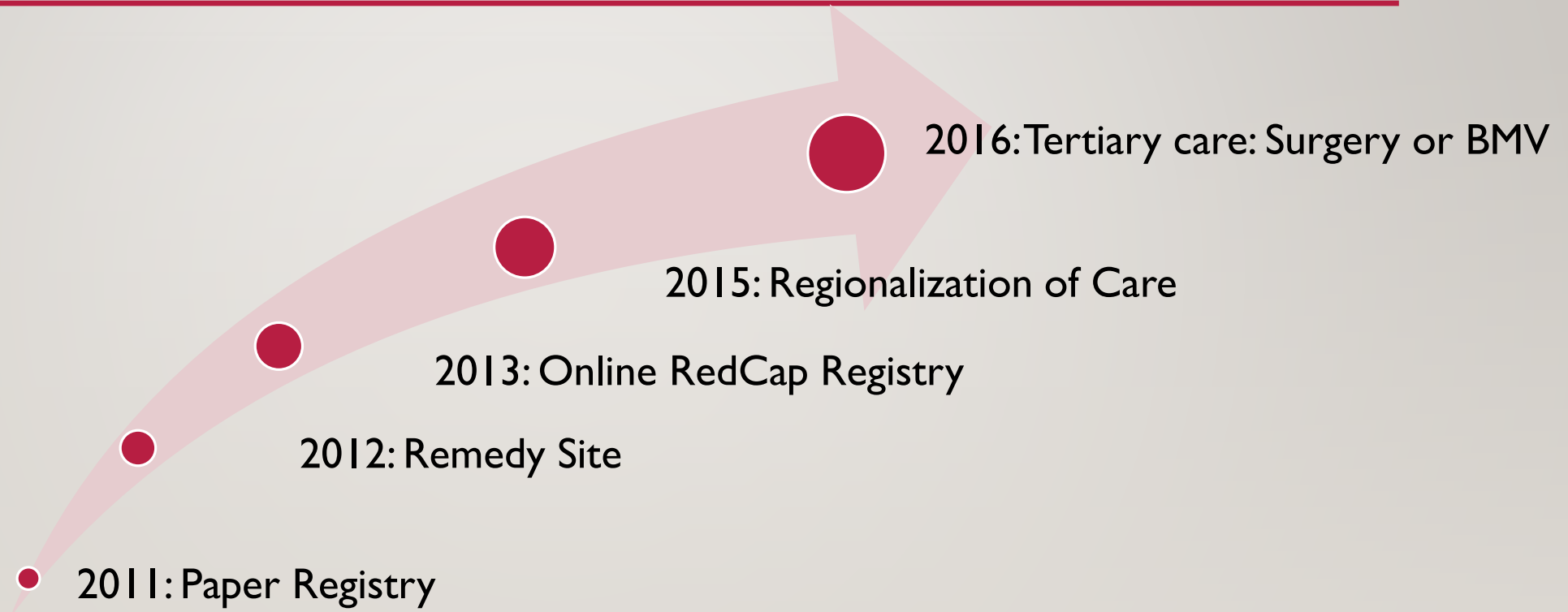
Intranet-based asynchronous
learning with limited hands on
training is effective and
reproducible
(Engelman, 2017)

CURRENT SITES OF DEDICATED RHD CARE IN UGANDA



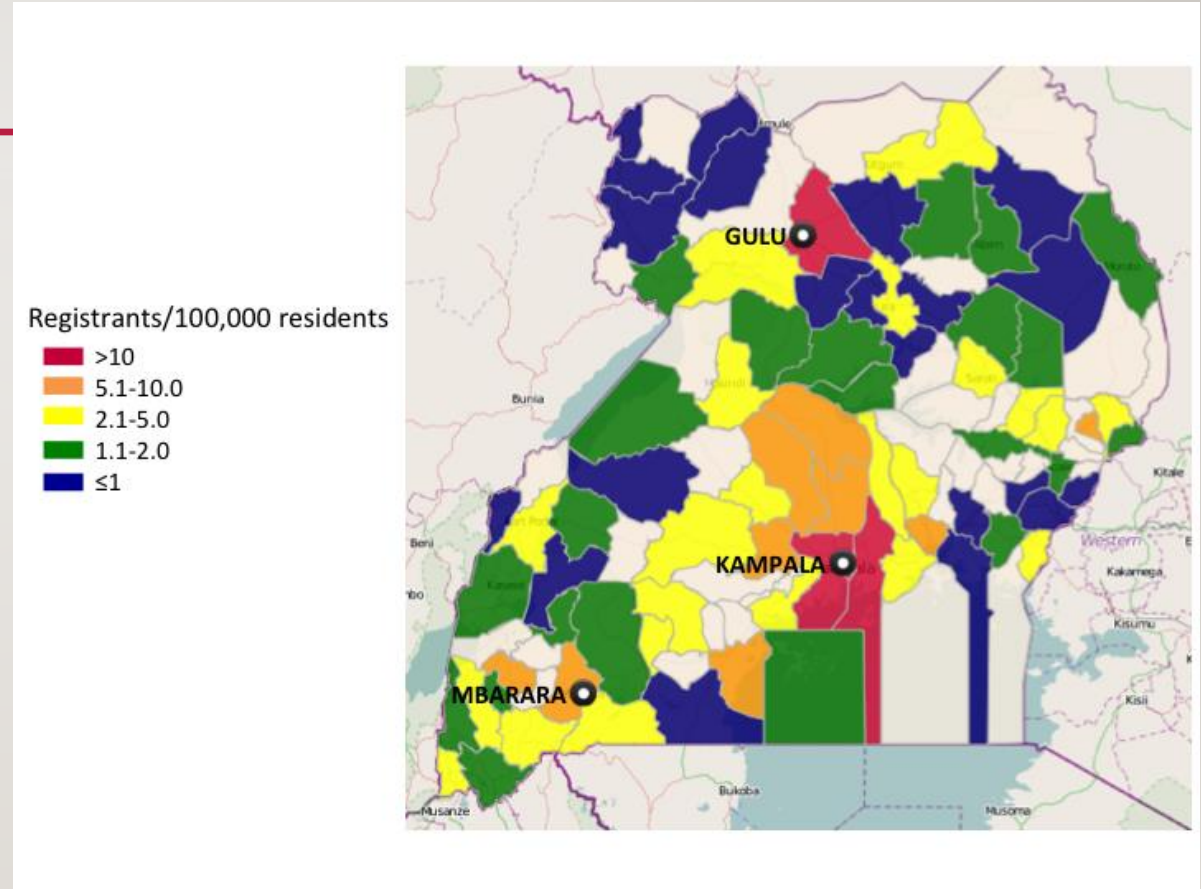
Site	Total Number Registered	Comments
Uganda Heart Institute	1488	~14 new cases per month
JCRC Lubowa	90	
Gulu	491	~12 new cases per month
Lira	166	RHD 98; ARF 68
Mbarara	115	
Jinja	19	Paper registry

PROGRESS IN RHD CARE IN UGANDA



IMPACT OF REGIONALIZATION OF CARE

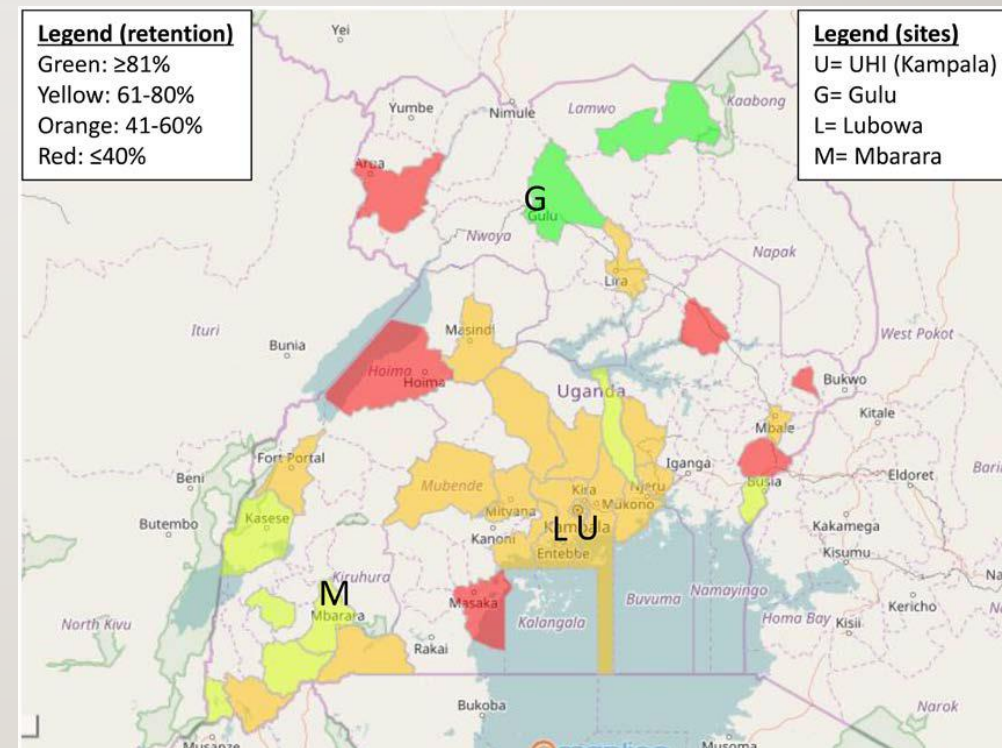
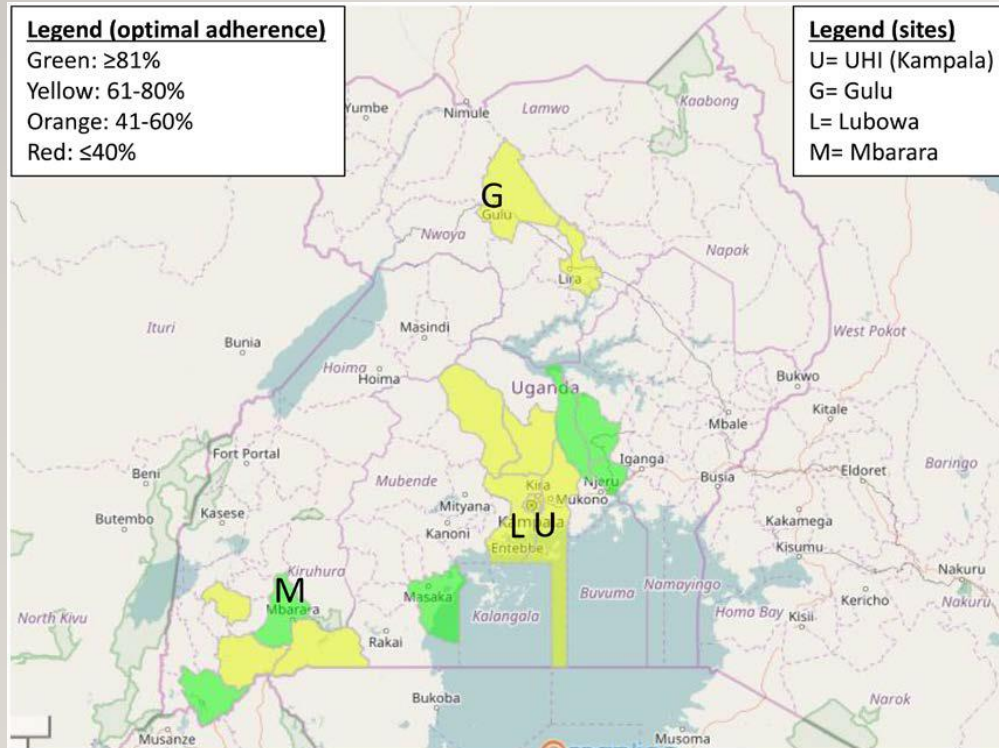
- RHD cases enrolled from almost every district
- Highest enrollment around regional centers – suggests access major determinant to diagnosis
- Case enrollment for region increased ($p < 0.01$) each time regional center established



(Okello, 2017)

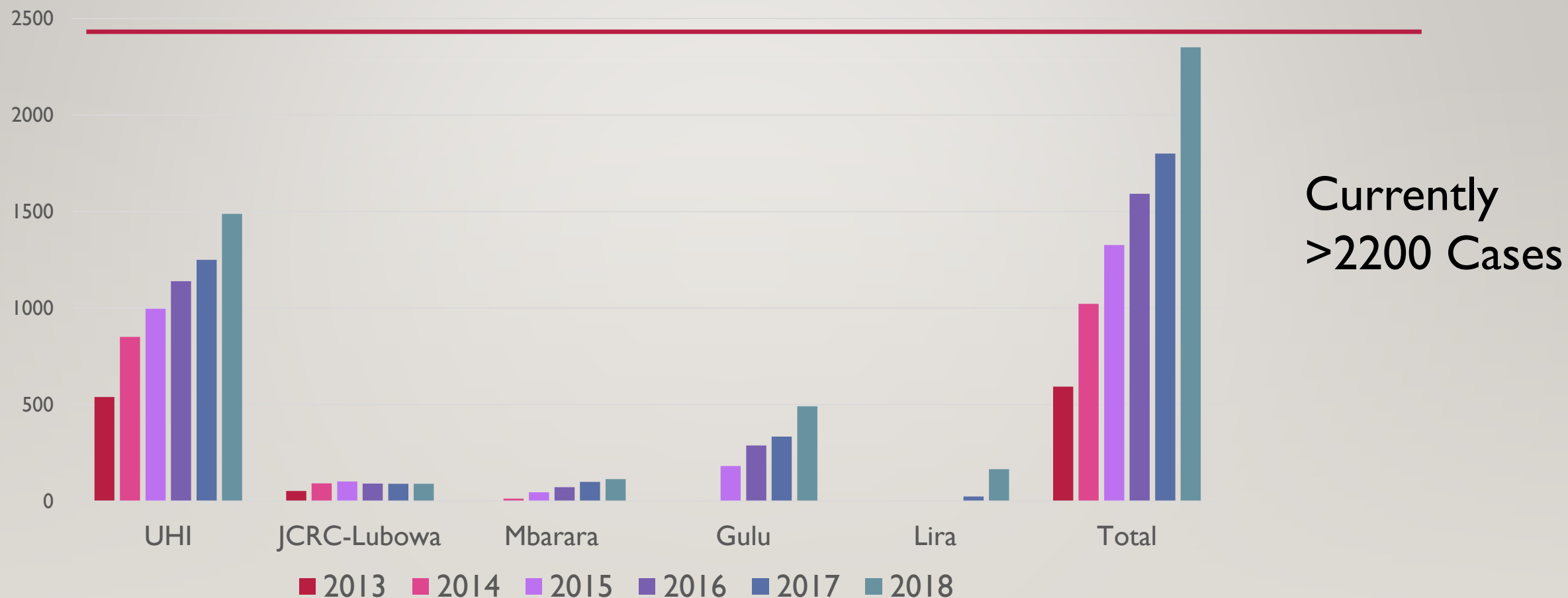
PROPORTION OF OPTIMAL BPG ADHERENCE($\geq 80\%$)

RETENTION IN CARE

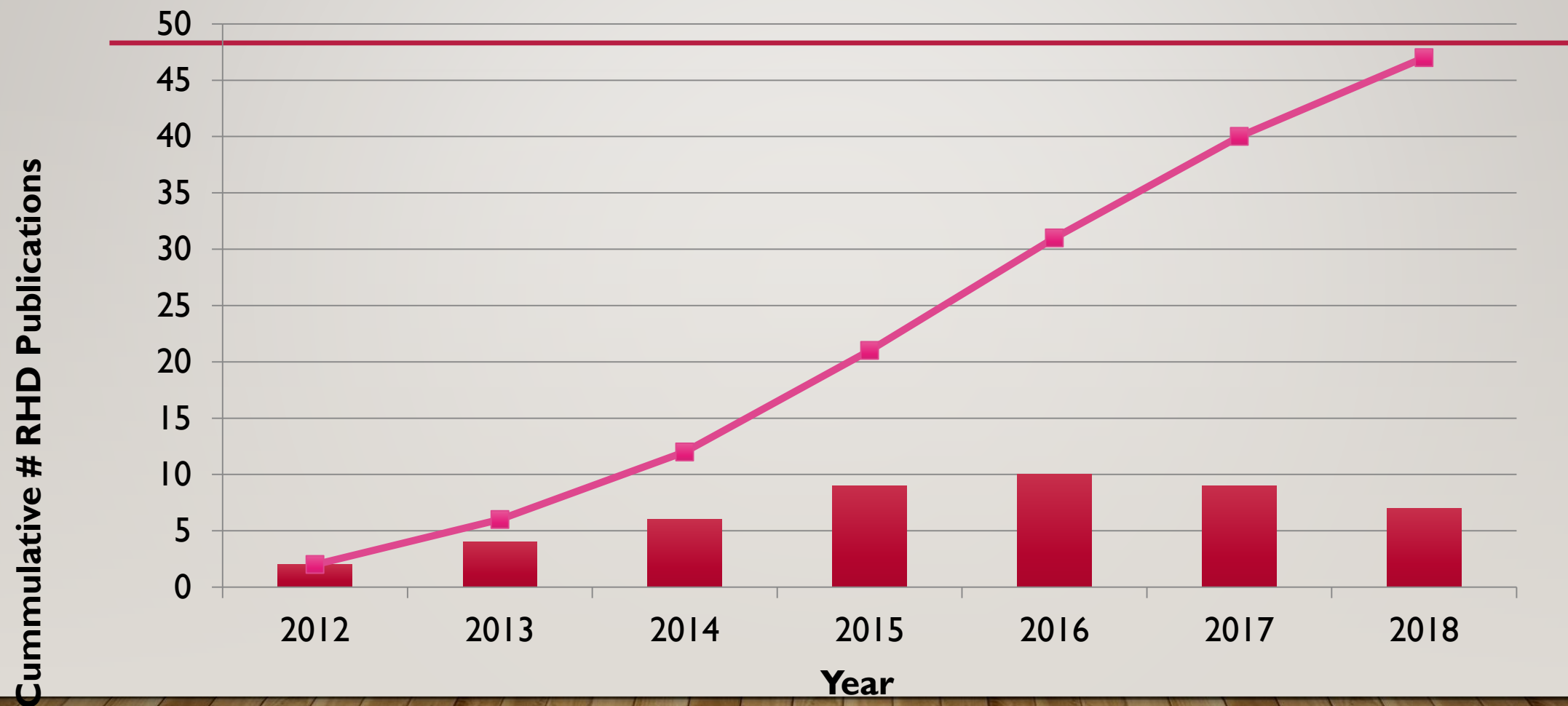


Longnecker et al, 2017

Number of RHD cases per site, 2013-2018



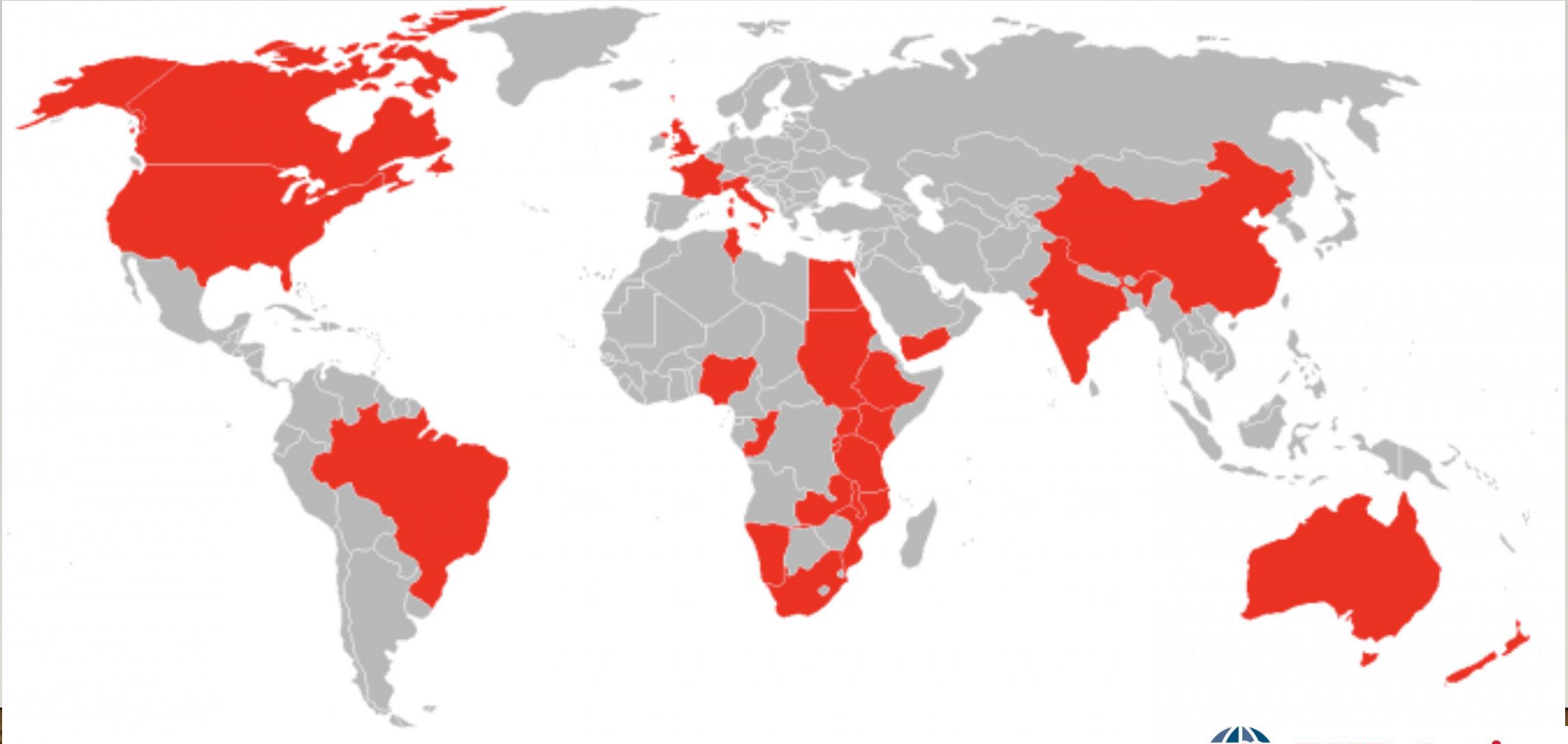
Increased Uganda Heart Institute RHD Research capacity



RHD Action

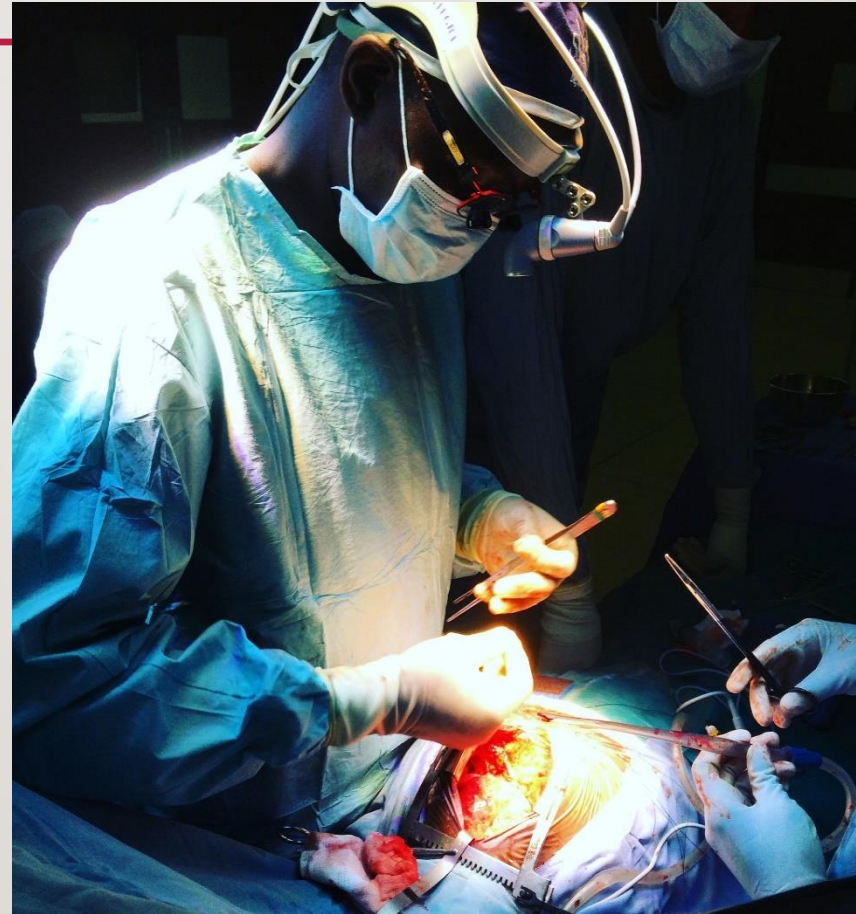
Uganda

UHI RESEARCH AND CLINICAL CARE PARTNERSHIPS



BUILDING TERTIARY CARE: VALVE SURGERY PROGRAM

- 2009: Valve surgery restarted at UHI
- Majorly limited by Costs
- ICU space limits Number of Congenital vs Adult Surgical cases



VALVE SURGERY PROGRAM



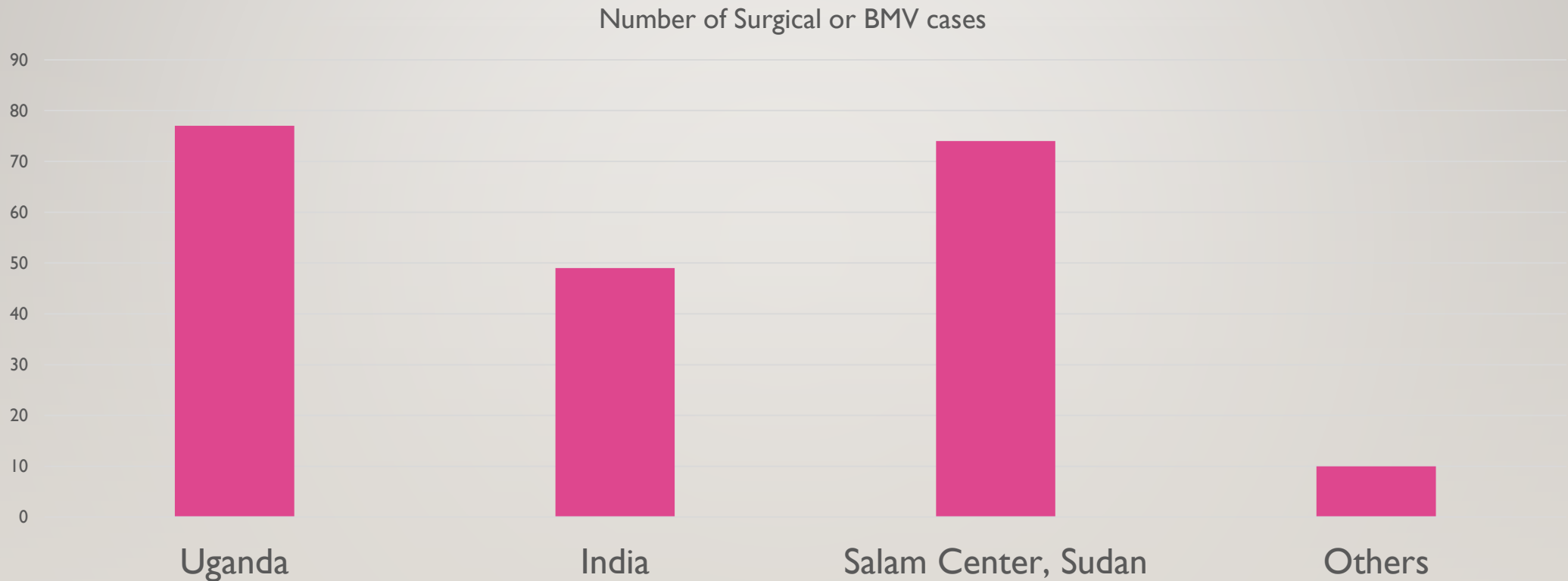
- RHD surgical camps in Past Two years
- Continue to send out cases Salam Center (Sudan) and India
- approximately 2-3 Open Heart cases per week when no visiting team

BUILDING TERTIARY CARE: BALLOON MITRAL VALVULOPLASTY

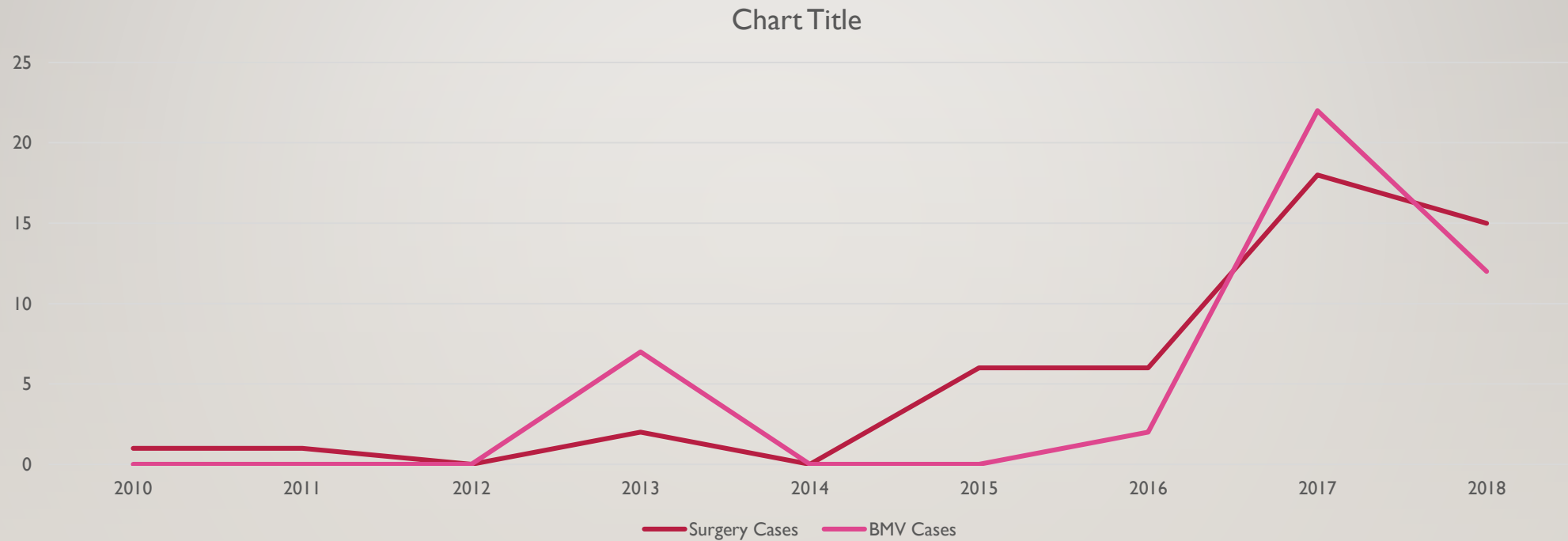


- Staff training (cath/echo guidance) at UFMG, Brazil (October, 2016)
- First independent PBMV – November 2016
- 50+ PBMV patients to date

ACCESS TO SURGERY OR BMV FOR RHD REGISTRY PATIENTS~220 SINCE 2010



PROGRESS IN RHD SURGERY AND BMV AT THE UHI OVER THE YEARS



ADDRESSING INEQUITY IN RHD CARE

- Most RHD patients come from the poorest backgrounds
- UHI and Regional Centers offer Free consultations, ECG/Echo, and Government drugs for repeat follow up appoints
- BMV subsidized to as low as \$300 or Free for patients in the RHD registry
- Free Surgeries during RHD surgical camps

BUILDING HUMAN RESOURCES

- 2010 UHI began to train cardiology fellows (18 trained in total)
- Invested in training abroad
- High retention; only 1 attrition
- Currently 6 adult cardiology, 5 pediatric cardiology and 4 Cardiac Anesthesia/critical care cardiology fellows

Cardiac Catheterization (5)

Electrophysiology (1)

Intensive Care (1)

Heart Failure (1)

Cardiovascular Surgery (2)

Cardiac ICU Nursing (5)

Cardiac Anesthesia and Critical Care / Perfusion (3)

PATIENT SUPPORT GROUPS

ADULT SUPPORT GROUP





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Short communication

The impact of a peer support group for children with rheumatic heart disease in Uganda

Amy Scheel^{a,*}, Andrea Beaton^a, Emmy Okello^b, Chris T. Longenecker^c,
Isaac Omara Otim^d, Peter Lwabi^b, Craig Sable^a, Allison R. Webel^e, Twalib Aliku^f

^a Children's National Health System, Department of Cardiology, Washington DC, USA

^b Uganda Heart Institute, Department of Cardiology, Kampala, Uganda

^c Case Western Reserve University, Department of Cardiology, Cleveland, USA

^d Lira Regional Referral Hospital, Lira, Uganda

^e Case Western Reserve University, Francis Payne Bolton School of Nursing, Cleveland, USA

^f Gulu University, Department of Pediatrics, Gulu, Uganda

Scheel et al, 2017

- 42 RHD patients aged 6-15 years on BPG, attending Monthly peer support groups
- Pre-post RHD knowledge assessment, a measure of health related quality of life (HRQOL) (PedsQLTM4.0), and a measure of social support (Hawthorne Friendship scale)
- Attending support groups resulted in increased total HRQOL scores
- Increased physical functioning, social functioning and school functioning
- Significant increases in Friendship Scale scores and RHD Knowledge scores were observed

COMMUNITY EDUCATION

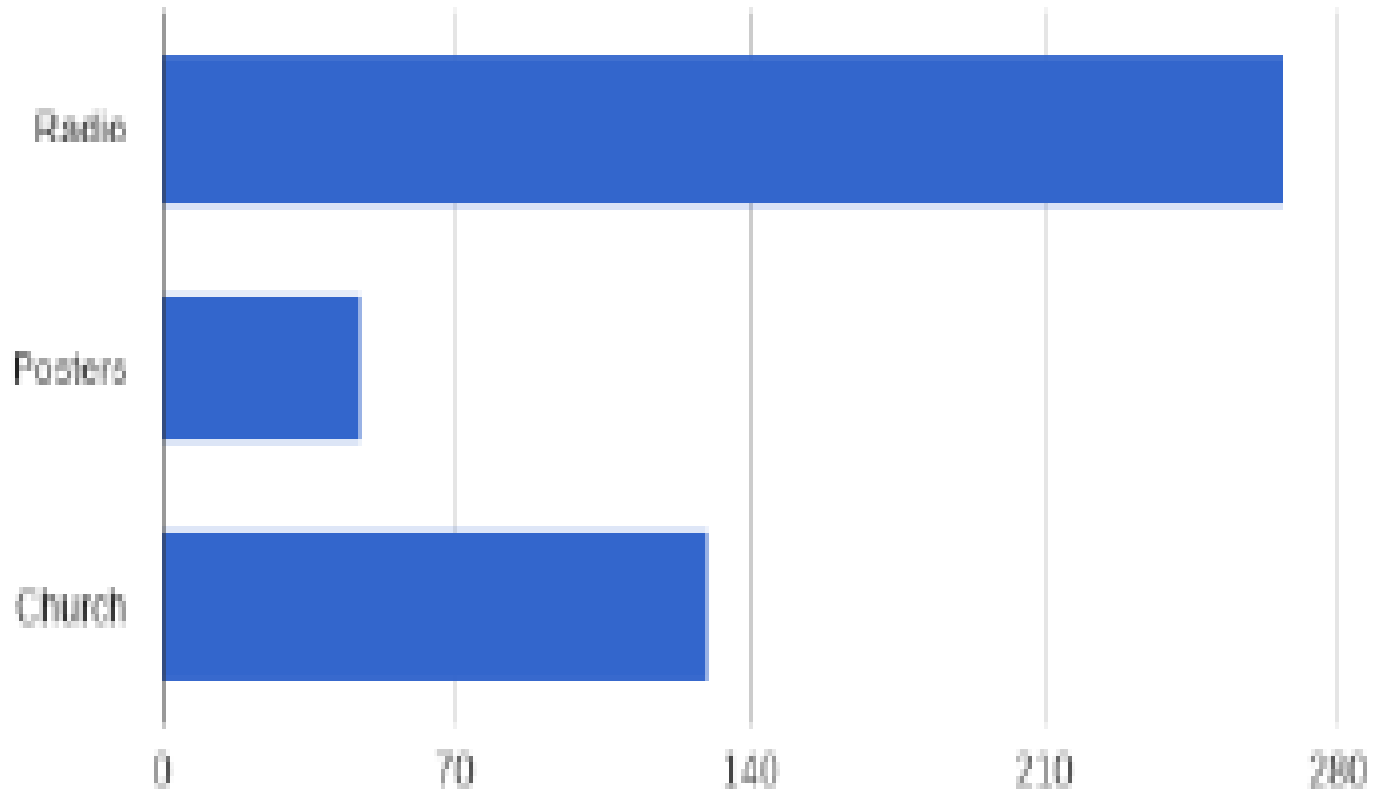


COMMUNITY SENSITIZATION

- Radio
- Posters
- Educational workshops for school teachers, health workers, Village Health Teams

COMMUNITY EDUCATION

Participants' Suggestions for Communication Methods



- In Lira over 3 months for ARF study
- 503 Community members randomly sampled
- 75% listened to radio regularly
- 51.3% (n=258) had announcements on radio, and half of these could remember at least one symptom of ARF
- Only 17% (n=87) recalled from Posters

GOVERNMENT ENGAGEMENT

1. November 2017, RHDAction event in Kampala, Uganda
2. 10 member RHD National Advisory Council – sitting within the MOH (Director General of Health Services: Chair) – goal to oversee transition to a national RHD control program
3. Uganda supported WHO RHD resolution, and Dr. Omagino (director, UHI), and MOH officials travelled to Geneva to World Health Assembly, in May, 2018



ADVOCACY: INCREASING ROLE OF PATIENT SUPPORT GROUPS



EMERGING CHALLENGES: PREGNANCY IN PATIENTS POST VALVE SURGERY



- Increasing Number of Women with RHD Operated
- Low contraceptive prevalence rate
- High Societal expectations for child bearing
- Limited health work-force experience in treating patients with Artificial valves on Warfarin

NURSE LED PRIMARY CARE



TASK SHIFTING...BECAUSE OF FEW DOCTORS

Profession	Staffing levels in Regional Referral Hospitals								
	Arua			Gulu			Lira		
	Norm	Filled	Staffing Level(%)	Norm	Filled	Staffing Level(%)	Norm	Filled	Staffing Level
Doctors	40	14	35.0	36	12	33.3	38	15	39.5
Nurse/Mid wife	116	137	118.1	169	125	74.0	60	50	83.3
Allied Health	31	22	71.0	37	27	73.0	39	24	61.5
Total	187	172	192.0	242	164	67.8	137	89	65.0

Understanding the Gap between ARF and RHD in Uganda

- Lira, Mulago, Mbarara, community sensitization, healthcare worker training
- (1) Fever + Joint Pain; (2) Carditis; (3) Chorea
- In Lira: 9 months, 279 children
- 64 children with definite ARF & 18 with ARF and likely pre-existing RHD
- Preliminary annual incidence data (only first 6 months, kids from Lira)
 - New ARF: 48 per 100,000
 - Including Recurrent ARF: 56 per 100,000
 - Poor health seeking behavior/diagnostic capacity are major barriers





GWOKO ADUNU PA LUTINO
PROTECT THE HEART OF A CHILD

Does early detection through echo screening and initiation of secondary prophylaxis improve outcomes?

- June-August, 2018, screening of 45,000+ children (5-17) in Gulu District

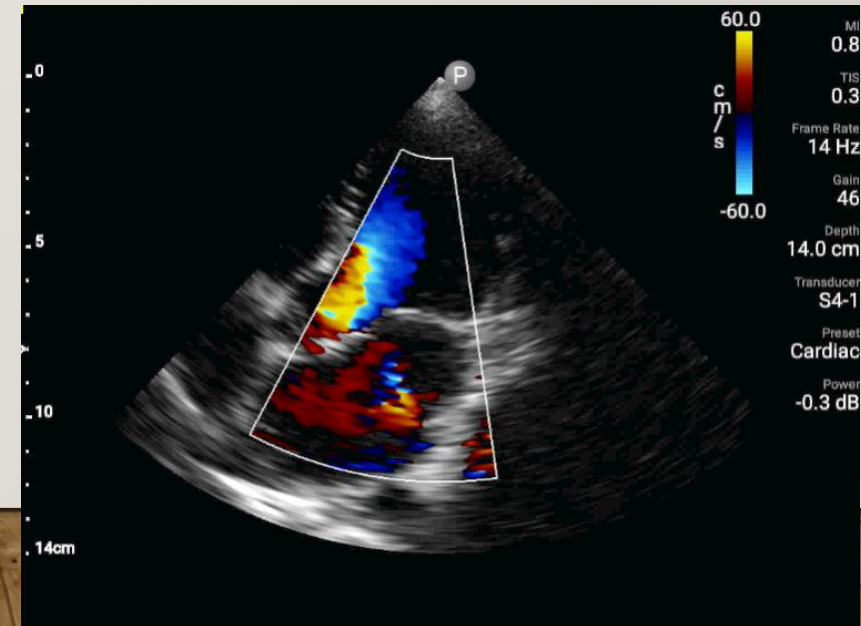
916 children with borderline and mild definite RHD to be enrolled in an RCT comparing 2 year echo-outcomes for children receiving every-4-week BPG and those not receiving prophylaxis



GULU TELEMEDICINE PILOT

- Cardiologist staffing of regional referral hospitals a critical challenge
- Nurse-led clinic with daily telemedicine consultation
- Asynchronous review – 673 pts / 10 months (370 children, 55%)
- Successful image transfer in all cases
- 385 abnormal echo; RHD, n=131 (19.5%)
- Medication initiation/adjustment: 284 patients
- Disposition
 - Outpatient : 274; Admission to Gulu: 32 (8 transferred to UHI)

assessment of feasibility, acceptability, cost, and change in outcomes



CHALLENGES AHEAD TO COVER EVERY REGION IN THE COUNTRY



Addis Ababa Communique: Recommendations FOR RHD Control In Africa

1. Establish prospective RHD registers at sentinel sites in affected member states
2. Ensure adequate supplies of high-quality benzathine penicillin
3. Guarantee universal access to reproductive health services for women with RHD and other NCDs
4. Decentralize appropriate technical expertise to the primary and district levels
5. Establish centers of excellence for cardiac surgery, which will sustainably deliver state-of-the-art surgical care,
6. Foster multi-sectoral and integrated national RHD control programmes led by the Ministry of Health,
7. Cultivate, through a strong communication framework, partnerships between the AUC

OPPORTUNITIES FOR REDUCING RHD BURDEN IN UGANDA

- School children can be empowered to report sore throat
- Over-the counter availability of antibiotics: Amoxycillin and Cotrimoxazole
- Nursing staff availability for Nurse led Care Programs
- CHWs/VHT in our Health System
- internet connectivity and mobile phone reach + hand held echo
- Widespread radio coverage for community education on RHD

THANK YOU AND VISIT UGANDA

