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Rheumatic Heart Disease Treatment Cascade in Uganda

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Abstract

Background—Rheumatic heart disease (RHD) is a leading cause of premature death and disability in low-income countries; however, few receive optimal benzathine penicillin G (BPG) therapy to prevent disease progression. We aimed to comprehensively describe the treatment cascade for RHD in Uganda in order to identify appropriate targets for intervention.

Methods and Results—Using data from the Uganda RHD Registry (n=1,504), we identified the proportion of patients in the following care categories: (1) diagnosed and alive as of June 1, 2016, (2) retained in care, (3) appropriately prescribed BPG, and (4) optimally adherent to BPG (>80% of prescribed doses). We used logistic regression to investigate factors associated with retention and optimal adherence. Overall, median (IQR) age was 23 (15–38) years; 69% were female; and 82% had clinical RHD. Median follow-up time was 2.4 (0.9–4.0) years. Retention in care was the most significant barrier to achieving optimal BPG adherence with only 56.9% (95% CI 54.1–59.7%) of living subjects having attended clinic in the prior 56 weeks. Among those retained in care, however, we observed high rates of BPG prescription [91.6% (95% CI 89.1–93.5%)] and optimal adherence (91.4% [95% CI 88.7–93.5]). Younger age, latent disease status, and access to care at a regional center were the strongest independent predictors of retention and optimal adherence.

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Conclusions—Our study suggests that improving retention in care—possibly by decentralizing RHD services—would have the greatest impact on uptake of antibiotic prophylaxis among patients with RHD in Uganda.

Despite increased awareness and advocacy in recent years, rheumatic heart disease (RHD) continues to cause substantial disability and premature death among children and young adults in medically-underserved populations around the world[1, 2]. This preventable disease is characterized by heart valve dysfunction that results from recurrent group A streptococcal infection and acute rheumatic fever (ARF). Secondary prevention of ARF with benzathine penicillin G (BPG) injections slows progression of RHD severity and reduces mortality[3–5]. Community-based disease registry programs may help ensure compliance with injections but unfortunately have not been widely adopted[6].

Uganda is a low-income East African country of 40 million; half are <15 years old and 16% are urban[7]. Uganda ranks 163rd of 188 countries in Human Development Index[8] and adult HIV prevalence is 6.5% (10th highest in the world)[7]. In 2013, the Uganda Heart Institute, Makerere University, the Joint Clinical Research Center, Case Western Reserve University, and Children's National Health System formed a collaboration to improve RHD care in Uganda. The collaboration supported a regionalized national registry program that sought to leverage existing HIV infrastructure when possible and to employ tools and "lessons learned" from the scale up of HIV care.

One potential tool to be adapted is the HIV treatment cascade model, which examines discrete and sequential stages necessary to achieve virologic control: HIV testing, knowledge of HIV status, linkage to care, retention/engagement in care, prescription of anti-retroviral therapy (ART), and viral load suppression. The HIV treatment cascade has become a central tool for measuring uptake of HIV care components and informing policy for the UNAIDS 90-90-90 initiative: 90% of persons living with HIV being diagnosed and aware of their status, 90% of those diagnosed with HIV being on ART, and 90% of those on ART being virally-suppressed[9].

The treatment cascade concept may help improve RHD care since successful management of chronic RHD faces similar sequential obstacles as in HIV: diagnosis and referral, attendance at regular clinic visits, anti-microbial prescription, and longitudinal adherence. The RHD treatment cascade has not been comprehensively described, except for preliminary findings from our group[10]. The aims of this study were to describe the treatment cascade among all patients enrolled in the Uganda RHD Registry and to explore clinical and demographic predictors of retention in care and adherence to BPG prophylaxis.

Methods

The Uganda RHD Registry enrolls patients with RHD presenting for clinical care or through echocardiographic screening studies at four regional sites [Uganda Heart Institute (UHI) in Kampala (since 2011), Lubowa (2013), Mbarara (2014), and Gulu (2015)]. The purpose of the registry is to improve clinical care and epidemiologic surveillance of RHD in Uganda. Forms are originally completed on paper and then data is entered into a RedCap platform[11]. The registry is approved by the Institutional Review Boards of Makerere University School

of Medicine (Kampala, Uganda), the Uganda National Council for Science and Technology, and University Hospitals Cleveland Medical Center (Cleveland, OH, USA). All participants older than 18 provide written informed consent. Written parental consent and participant assent are obtained for those younger than 18. This current analysis includes participants enrolled through June 1st, 2016.

Disease categories

Clinicians classified participants at the enrollment visit into the following disease categories:

A. Acute rheumatic fever (ARF)—defined according to applicable Jones Criteria at the time of diagnosis[12, 13] but without evidence of chronic valvular heart disease.

B. Clinical RHD—defined as patients presenting to clinical attention with symptoms or signs (i.e. murmur) and echocardiographic findings compatible with RHD

C. Definite latent RHD—identified through echocardiographic screening studies

D. Borderline latent RHD—identified through echocardiographic screening studies

We defined definite and borderline categories according to the 2012 World Heart Federation guidelines for the diagnosis of latent RHD by echocardiographic screening[14].

Treatment cascade categories

We then classified participants into the following sequential treatment cascade categories based on their status as of the audit date, June 1st, 2016. Study nurses and staff attempted to document vital status for all participants by telephone contact with participants or family members. Up to three mobile phone numbers are kept on record for all participants to coordinate care and document health status.

A. Alive—defined as those without documentation of death. Documentation of death was considered through September 1, 2016, provided that the date of death recorded was on or prior to June 1, 2016. If participants died during the observation period, they were excluded from the subsequent categories.

B. Retained in care—defined as all living patients (from any disease category) with at least one in-person clinic visit in the past 56 weeks [52 weeks + 4 week grace period for those patients (particularly borderline RHD patients in more remote areas) who might only follow-up once yearly].

C. Prescribed BPG—defined as all retained participants who had been given a prescription for monthly BPG at last recorded follow-up. Outcomes of “prescribed” and “adherent” excluded those with borderline disease, since our program guidelines do not recommend antibiotic prophylaxis for this group and WHF guidelines offer no recommendation. Those prescribed oral antibiotics in lieu of BPG were counted as “not prescribed”, since the standard of care is intramuscular BPG, which has been shown to be superior to oral penicillin in clinical trials.[14]

D. Adherent to BPG—defined as all prescribed participants who had received ≥80% of prescribed BPG doses in the last 12 months [excluding n=8 missing data (1.4% of prescribed)]. The ≥80% definition is widely used as a key performance indicator of adherence[15] and was associated with decreased mortality in a previous study from our group[5]. Adherence was assessed at the most recent follow-up visit using signed administration cards.

Covariates

Participants and/or their caregivers self-reported demographic and socioeconomic covariates at the baseline visit, including age (continuous, and categorized 0–15, 15–25, 25–40, and >40 years), gender, clinic site, distance to nearest health center (km), household number, highest completed education level of participant or participant's most educated parent if <18 years of age (< or ≥ secondary school), and employment status of participant or participant's caregiver (yes/no). Study staff used medical records to obtain clinical covariates including New York Heart Association (NYHA) class, medical comorbidity (history of decompensated heart failure, stroke, atrial fibrillation, endocarditis, HIV), and history of valve surgery (repair or replacement). Missingness for these covariates was generally <5%, except for distance to nearest health center (9.1%) and NHYA class (11%).

Statistical analysis

We first described characteristics of the overall registry population and separately by treatment cascade category as median (interquartile range) for continuous variables and number (%) for categorical variables. We compared subjects who had died to those who were alive using t-tests and Wilcoxon rank-sum tests for continuous variables and Fisher's exact tests for categorical variables. Treatment cascade categories were the outcomes of interest for all analyses.

In the primary analysis and all pre-specified sub-group analyses, we described the total patient number in each treatment cascade category and the proportion (95% CI) of the parent category. As noted above, we excluded borderline RHD participants from the prescribed and adherent categories. We compared differences in the proportion of (A) retained and (B) adherent participants by sub-group using chi-squared or Fisher's exact tests as appropriate. For the HIV+ subgroup, we performed additional descriptive analyses of immune status and ART use.

We then performed district-level analysis of (A) retention and (B) adherence based on the home address of study participants. For these analyses, we included all subjects with clinical RHD from districts with at least five participants in the denominator. Latent RHD and ARF were excluded due to significant geographic selection bias.

Finally, we constructed unadjusted and multivariable adjusted logistic regression models to explore the association of clinical and demographic variables with the outcomes of (A) retention and (B) adherence. We first examined the entire study population alive at the audit date, and then separately examined clinical RHD participants only. Baseline covariates were used since time-updated measures were not available. In unadjusted analyses, we examined the association of each candidate variable with the outcome of interest. Then for

multivariable model selection, we began by forcing categorical age, gender, and disease category into the model. Clinic site was not used in the overall model due to multi-collinearity with disease status, but was used in the clinical RHD models in place of disease category. Additional covariates were selected into the final model using forward selection with retention at $p < 0.1$. We calculated the AUROC for each model, and used the Hosmer-Lemeshow test to assess goodness of fit. Sensitivity analyses were performed as follows: (1) excluding from the retention models all participants who were enrolled within 90 days of the audit date and (2) excluding from the adherence models all participants who were initially prescribed BPG injections within 90 days of the audit date.

All analyses were performed using STATA 14.2 (StataCorp; College Station, TX, USA) and a p-value of <0.05 was considered statistically significant.

Results

As of June 1, 2016, the Uganda RHD registry consisted of 1504 participants whose characteristics are described in Table 1. Participants with clinical RHD comprised >80% of the study population, whereas ARF represented less than 1%. Age and gender were similar across all treatment cascade categories. Most participants lived within two kilometers of a health center and over half had (or had caregivers with) limited education (completed < secondary school). Among those with clinical RHD, advanced disease and history of morbid complications was common. Median (IQR) follow-up time was 2.4 (0.9–4.0) years and differed by clinic site (median 35 months at UHI vs. 27 months at Lubowa vs. 12 months at Mbarara vs. 9 months at Gulu; $p<0.001$ for each regional site vs. UHI). Approximately 18% (n=273) of the population died prior to the audit date and were excluded from analyses of the treatment cascade. Patients who died were older (mean age 31 vs. 27 years, $p<0.001$), lived farther from the nearest health center (median distance 3 vs. 2 km, $p=0.002$), were more likely to have clinical RHD (97 vs. 78%, $p<0.001$), and more likely to receive care at the UHI (91 vs. 68%, $p<0.001$). Twenty-one subjects (1.4%) had transferred follow-up care between study sites prior to the audit date. Nine retained subjects were taking oral antibiotics and thus not categorized as “prescribed”, and only two of these were doing so because of documented penicillin allergy.

Retention in care was a more significant barrier along the treatment cascade than was prescription of or adherence to BPG injections (Figure 1). Overall, 56.9% (95% CI 54.1–59.7) of living subjects were retained in care, compared to 91.6% (89.1–93.5) prescription of BPG to eligible subjects and 91.4% (88.7–93.5) optimal adherence to BPG. Retention varied substantially by subgroup (Figure 2). Although there were no significant differences by gender, those with clinical RHD were less likely to be retained compared to those in other categories (χ^2 $p<0.001$). Among those with clinical RHD, participants with higher NYHA class were more likely to be retained (χ^2 $p=0.022$). Adherence was similar across all subgroups (Figure 3; all $p>0.2$). Heat maps of retention and adherence rates by district in displayed in Figures 4 and 5. Supplemental Table 1 shows retention and adherence rates by region.

The treatment cascade was similar among HIV+ patients compared to the total population (Supplemental Figure 1). Overall, 91% of all registry subjects were aware of their HIV status. Of those with known HIV status, 62 were confirmed HIV+ (4.5 % total; 5.5% of women vs. 2.4% of men, p= 0.012 for gender comparison). Patients with HIV were not more likely to have died compared to those without HIV (p=0.309). Median (IQR) age was 41 (31–46), with only 6 patients being less than 25 years old and 2 being less than 15 years old. The median (IQR) CD4+ count at enrollment was 365 (237–608) cells/ml and CD4+ at diagnosis was 230 (112–374) cells/ml. Forty-eight participants (77% of HIV+) had documented antiretroviral treatment (ART) status, and 90% (95% CI 77–96%) of these participants were on ART.

Predictors of retention in care are shown in Table 2 (full cohort) and Supplemental Table 2 (clinical RHD only). Among all living subjects in the full cohort, younger age, latent disease status, closer distance to health center, being employed (or having an employed caregiver), and having more advanced education were associated with higher odds of retention. Among clinical RHD participants, the effect of age and employment were attenuated after adjustment for other factors, and the strongest predictor of retention was whether the participant was enrolled at one of the three regional centers (vs. UHI). Other variables associated with higher retention among clinical RHD participants were closer distance to the nearest health center and more advanced education. As in the subgroup analysis above, higher NYHA class was associated with improved retention in unadjusted analyses. This relationship was somewhat attenuated after adjustment for possible confounders; however, those with mild symptoms (NYHA II) were more likely to be retained compared to those with little to no symptoms (NYHA I). Although HIV infection was also associated with borderline higher retention in unadjusted analyses (p=0.058), this was attenuated after multivariable adjustment and not kept in the final model.

Predictors of adherence to BPG are shown in Table 3 and Supplemental Table 3. Younger age was again independently associated with better adherence among all retained subjects in the full cohort, but the effect was not statistically significant in the clinical RHD subgroup. Latent disease status and limited education were associated with better adherence after adjustment for age and other confounders in the full cohort. In the clinical RHD subgroup, limited education was associated with better adherence and history of prior valve surgery was associated with worse adherence.

Sensitivity analyses were performed to determine the influence of short follow-up time on retention and adherence data. When patients enrolled within 90 days of the audit date were excluded, results of the overall treatment cascade were similar (Supplemental Figure 2). In the retention model, similar associations were seen except that the odds ratio for latent disease increased substantially [OR 25.4 (95% CI 7.9–82.1) and OR 11.0 (95% CI 4.3–28.2) for definite and borderline categories, respectively], and the AUROC also increased from 0.717 (95% CI 0.686–0.747) to 0.750 (95% CI 0.729–0.780). When patients starting prophylaxis within 90 days of the audit date were excluded from the adherence model, results were very similar except the association with latent disease was no longer statistically significant [OR 0.59 (95% CI 0.31–1.13), p=0.111].

Discussion

This novel approach to assessing the quality of care for RHD patients in Uganda reveals that retention in care is the most significant barrier to achieving optimal BPG adherence, which can prevent ARF recurrence, progression of RHD, and death[3–6]. We observed high rates of adherence among those retained in care, consistent with the HIV literature[16] suggesting that medication adherence per se is not a significant problem for RHD patients in Africa. We have previously reported on the treatment cascade early after the RHD registry was adopted[10] and for children with latent RHD in Gulu who participated in echocardiographic screening studies[17]. Here, we extend our analysis to the entire Uganda RHD registry with nearly 2.5 years of median follow-up time and report on independent predictors of retention and adherence.

Mortality, retention, and BPG adherence in our study were similar to the overall Global Rheumatic Heart Disease registry (REMEDY)[4, 18], which enrolled patients with clinical RHD from predominantly low-income south and east African countries and contained a population with similar demographics and functional status. Of note, the global study had a more lenient definition of retention: one repeat visit anytime within the two-year study (vs. 56 weeks in our study). Our estimates of adherence were additionally biased downward by categorizing oral antibiotic use as non-adherent (although there were only nine of these subjects) and by only using objective documentation of adherence rather than self-report.

The proportions of patients within each component of the RHD treatment cascade were also similar to analogous outcomes from the CDC HIV care continuum[19], which were below 90-90-90 initiative goals. Progress is being made, but more improvement in HIV care is needed to reach these goals. In sub-Saharan Africa, approximately 51% of people living with HIV were on ART in 2015, compared to about 21% in 2010[20]. Retention is a critical factor, with a recent meta-analysis estimating that only 65% of Africans starting ART are retained in care at least 36 months[21].

Interestingly, our data support prior reports of a negative correlation between HIV infection and RHD, although the treatment cascade outcomes were similar regardless of HIV status. The prevalence of HIV in our cohort (4.5% overall, <1% age 15–24) was significantly lower than the general population of Uganda (7.4% overall, 3.7% age 15–24).[20] Conversely, an echocardiographic screening study by our group[22] found that the prevalence of RHD in a cohort of HIV-infected children was less than the general population of school-aged children in Kampala[2,3]. Children with HIV may have more engagement with the health system, leading to better surveillance for and treatment of GAS pharyngitis. Other proposed mechanisms include the antimicrobial and anti-inflammatory effects of cotrimoxazole prophylaxis[21]. Larger prospective studies are needed to confirm the role of these possible mechanisms.

Significant barriers to care utilization exist in sub-Saharan Africa, including lack of transportation, poor roads/infrastructure, poverty, limited education/literacy, weather during rainy season, scheduling conflicts, drug stock-outs, and poor provider awareness or communication of health problems. Our study demonstrated that living farther away from

local and regional health care centers is a barrier to retention, as reflected in the multivariable model and the geographic heat map of retention rates. Since our analysis adjusted for distance to nearest health center, improved retention at regional sites is also likely attributable to more staff, funding, and ancillary resources per-capita dedicated to tracking patients—resulting from our initiative to decentralize RHD care. For example, HIV counselors have been repurposed to improve retention and adherence for RHD patients at the Lubowa site. Similarly, the HIV literature has demonstrated poorer retention with larger clinic size[23] and with care in higher tiers of the health system[24], further supporting the need for decentralized services. Although our heat map of retention and adherence rates suggests geographic disparities in the treatment cascade, our study was limited by the number of patients coming from more remote districts. As our national registry program is rolled out to additional regional centers and more patients are enrolled from rural districts, we will be able to conduct a more robust analysis of geographic disparities in RHD care in Uganda.

Younger age was independently associated with better retention and adherence in our study. The effect of age on adherence may be influenced by strong linkages between RHD clinics and schools where echocardiographic screening was performed. For example, in Gulu, there is an active pediatric support group and dedicated clinical resources aimed at keeping children engaged in follow-up care[25]. The age effect was also seen, however, in a previous report from the UHI[5]. These findings contrast with the HIV literature since a large multi-center African study suggested that ART adherence improves with age[26].

Patients and caregivers managing HIV or RHD face a similar bottleneck: retention in care. Thus, policy makers working to improve RHD control should focus on this step in the cascade. Since there are no tested interventions known to improve treatment cascade metrics for RHD in Africa, initial efforts might focus on strategies proven to work for HIV care. Specific interventions that appear to be most effective in HIV include weekly SMS reminders, treatment supporters, and enhanced counseling[27]. A large meta-analysis has also highlighted the benefits of decentralizing care and task shifting, demonstrating a more favorable effect for community-based vs. clinic-based ART programs on engagement in care in low- and middle-income countries[28]. Although both community- and clinic-based interventions demonstrated similar effects on adherence, virologic suppression, and mortality in this meta-analysis, interim data from the contemporary SEARCH study in east Africa suggest that community-based testing and treatment may lead to even greater improvements in ART coverage and viral suppression that meet 90-90-90 goals[29]. RHD control programs typically receive limited funding due to competing public health priorities, so cost-effectiveness and local sustainability are important. We recommend decentralizing services and adapting interventions like those above to support RHD care, focusing on patients most at risk for poor treatment cascade outcomes.

Strengths of this study include the large, extensively characterized sample size from Kampala and multiple regional centers and the relatively low proportion of incomplete or missing data. The study also has several limitations. Due to multi-collinearity resulting from certain sites having a high proportion of latent RHD patients enrolled from echocardiographic screening studies, the independent effects of disease category and clinic site could not be fully explored. Second, availability of time-updated clinical variables such

as NYHA status would have strengthened the analysis. Third, although we made repeated attempts to contact those who were lost to follow-up, some of these may have died or transferred care causing misclassification. For example, a large meta-analysis found that 24% of HIV+ subjects lost to follow-up had self-transferred care and 34% had died[30]. Fourth, it is possible that differences in follow-up time at the UHI vs. regional centers may explain some of our findings regarding decentralized care, which should be clarified in subsequent analyses of the registry with longer follow-up. Finally, because Uganda has benefited from targeted interventions to improve RHD care, our results may not be generalizable to other countries with even less investment in RHD.

Conclusions

Based on this analysis of the RHD treatment cascade, the greatest opportunity to improve the uptake of adequate antibiotic prophylaxis in patients would be improving retention in longitudinal care. Demographic variables and clinical site influenced retention and BPG adherence more than clinical variables. Future studies should test the implementation of interventions to improve retention among those at highest risk, including decentralization of RHD care and BPG prophylaxis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is Known?

- The burden of disability and premature death from rheumatic heart disease is highest among low-income countries, where health systems are ill-equipped to care for chronic non-communicable diseases.
- Secondary prophylaxis injections of Benzathine penicillin G slows progression of rheumatic heart disease and reduces mortality, but poor adherence over time is common in sub-Saharan African countries.
- The treatment cascade model has been used effectively to evaluate HIV/AIDS control programs worldwide but may also be applicable to other chronic diseases that face similar obstacles to care.

What the Study Adds?

- This large study of over 1,500 patients from a national rheumatic heart disease registry in Uganda highlights that efforts to improve uptake of penicillin prophylaxis for RHD should focus on retaining patients in care.
- Younger age, latent (vs. clinically symptomatic) disease, and close access to care at local health centers and regional centers of excellence were the strongest independent predictors of retention in care and adherence to penicillin.

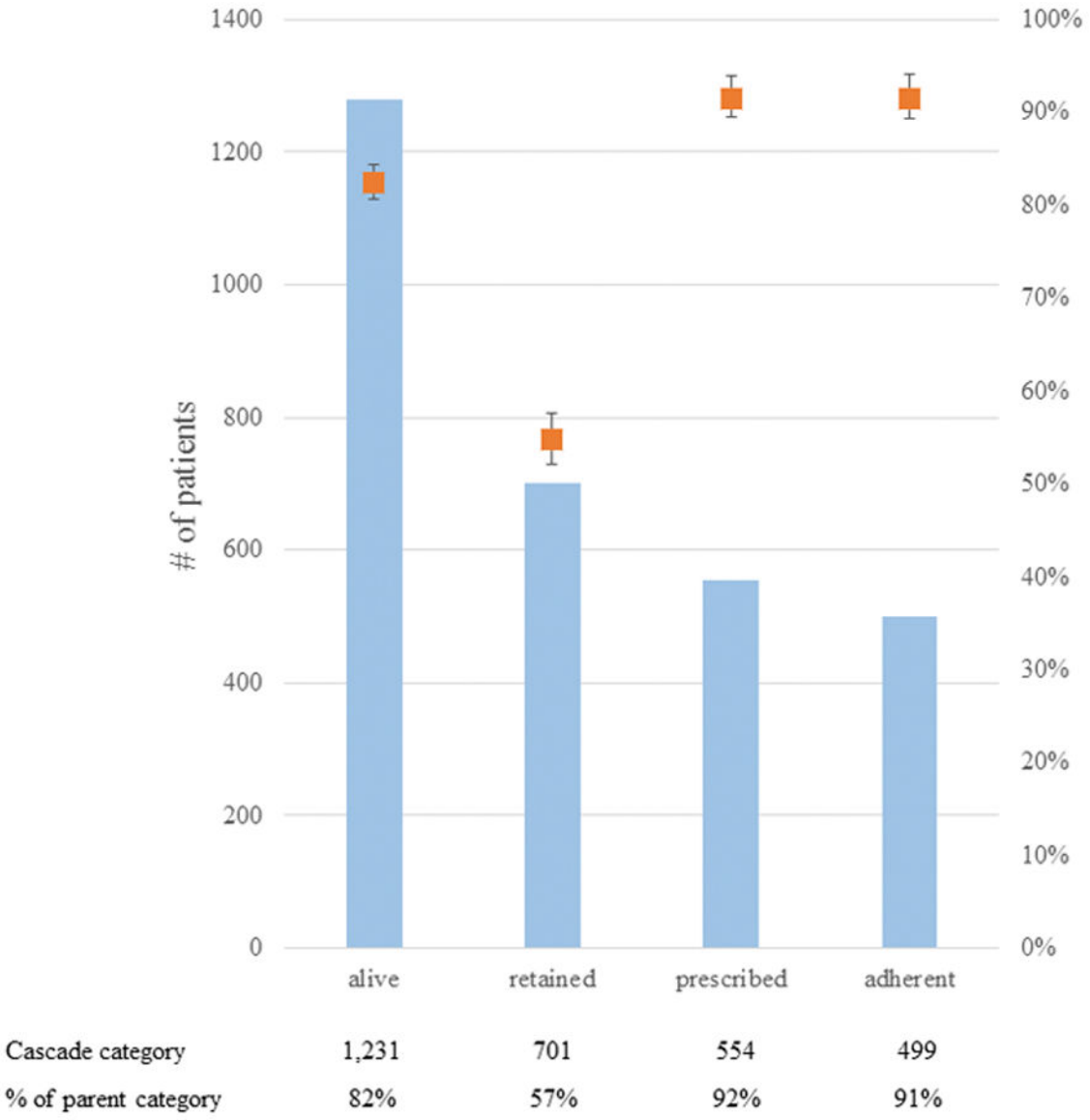

Figure 1. Overall treatment cascade for patients enrolled in the Uganda RHD registry

The left axis and blue bars indicate the number of patients in each outcome category of the treatment cascade, while the right axis and orange points indicate the percentage of patients as a proportion of the parent (prior) category. Error bars reflect the 95% confidence interval. All patients in the registry were included to assess outcomes of “alive” and “retained”, but patients with borderline RHD were excluded from assessing the outcomes of “prescribed” and “adherent”.

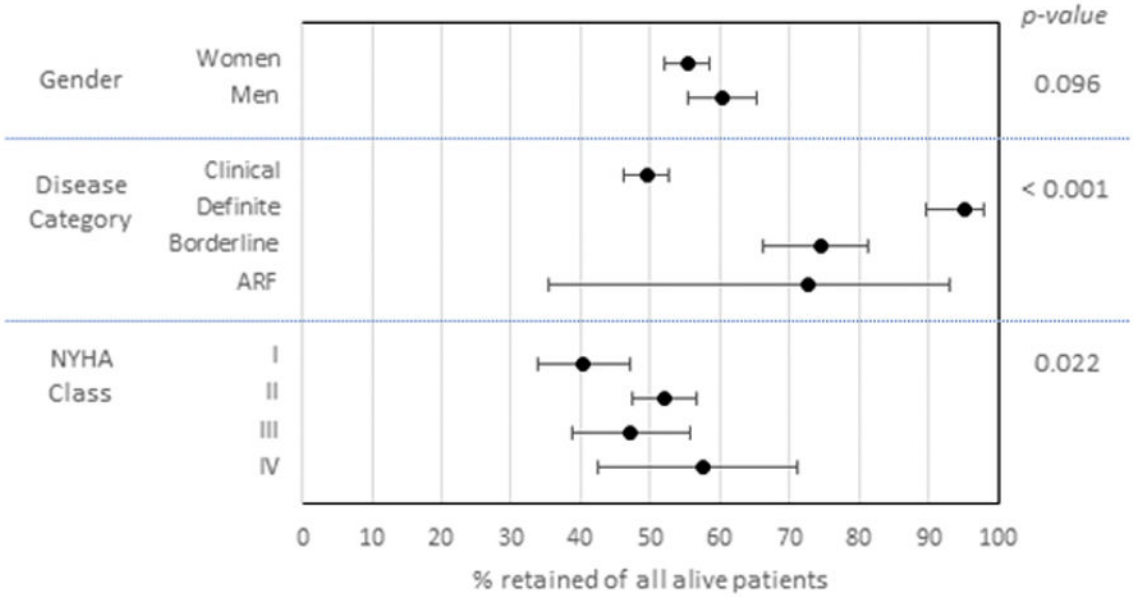

Figure 2. Subgroup analysis of patient retention

Point estimates represent the percentage of participants retained in care of all those participants who were alive at the end of the observation period. Error bars reflect 95% confidence intervals. Chi-squared p-value is shown on the right.

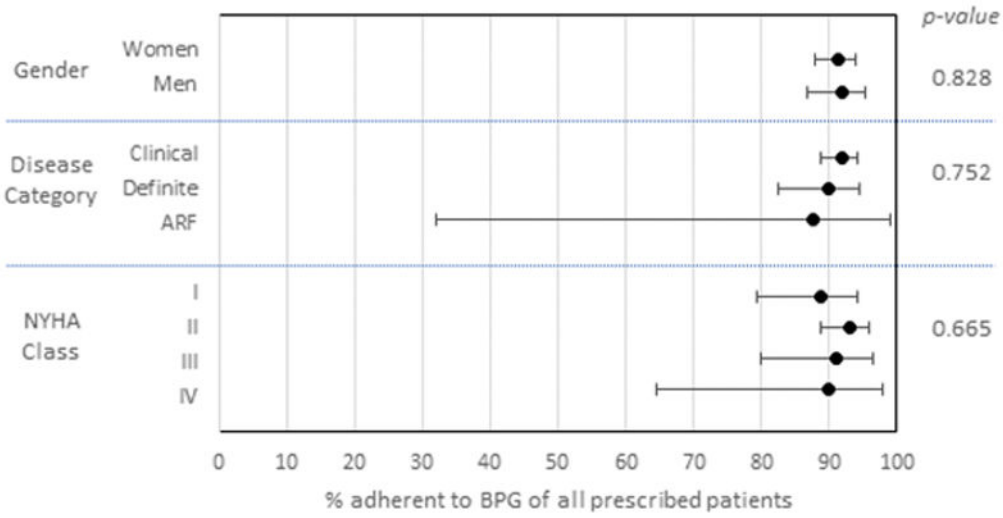

Figure 3. Subgroup analysis of adherence to prescriptions of prophylactic BPG injections

Point estimates represent the percentage of participants who were prescribed BPG who were optimally adherent (>80% of prescribed injections). Error bars reflect 95% confidence intervals. Chi-squared p-value is shown on the right.

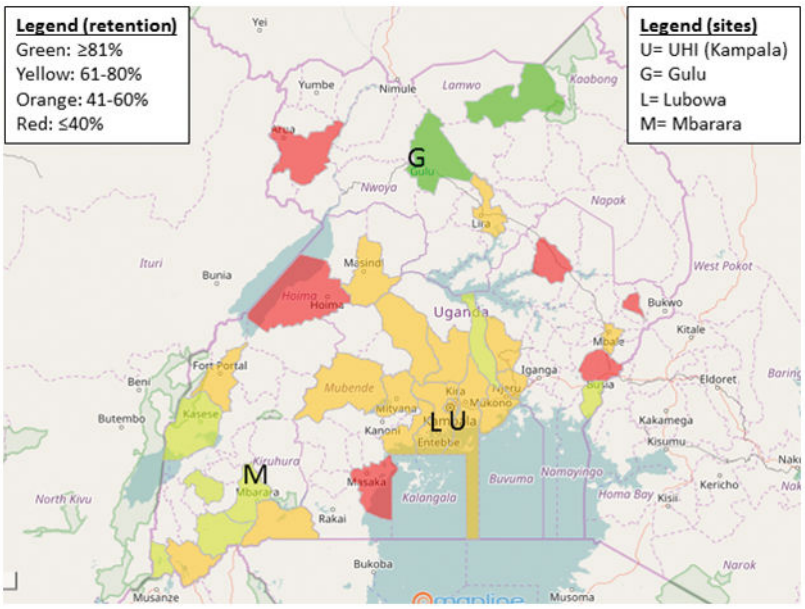

Figure 4. Heat map of retention by district

Color coding represents the proportion of patients retained in care. Only districts reporting at least five patients alive at the end of the study were included in this analysis. For reference, the locations of the clinic sites are shown.

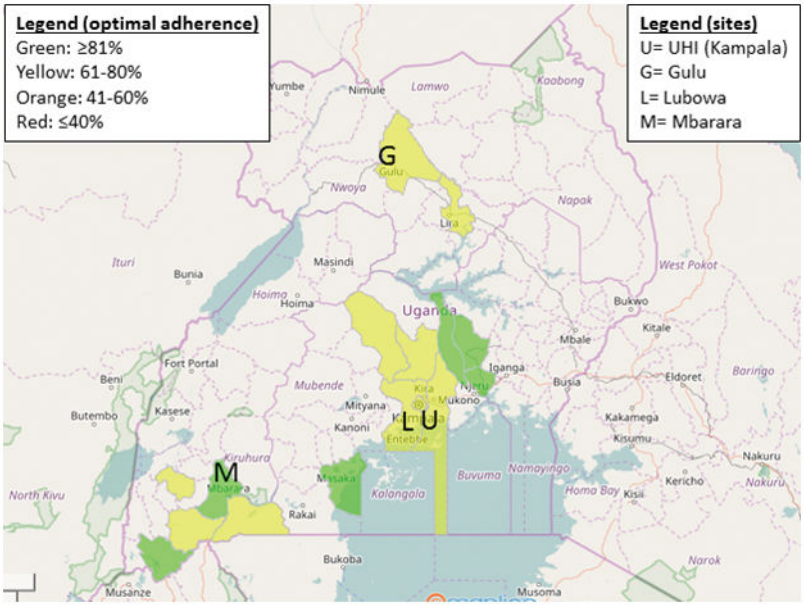

Figure 5. Heat map of optimal BPG adherence by district

Color coding represents the proportion of patients optimally adherent (>80% of prescribed doses received). Only districts reporting at least five patients prescribed BPG were included in this analysis. The locations of the clinic sites are shown with letters.

Table 1

Characteristics of the study population overall and separately by treatment cascade category.

Total Population	**Overall (N=1504)**	**Alive (N=1231)**	**Retained (N=701)**	**Prescribed (n=554)**	**Adherent (n=499)**
Disease Category					
ARF	12 (1%)	11 (1%)	8 (1%)	8 (1%)	7 (1%)
Clinical RHD	1232 (82%)	966 (78%)	478 (68%)	437 (79%)	394 (79%)
Latent Definite	129 (8%)	125 (10%)	119 (17%)	109 (20%)	98 (20%)
Latent Borderline	131 (9%)	129 (11%)	96 (14%)	n/a	n/a
Age	23 (15–38)	22 (15–37)	17 (14–33)	19 (14–35)	19 (14–33)
Female	69%	70%	68%	68%	68%
Socioeconomic factors					
Nearest health center (km)	2 (1–5)	2 (1–5)	2 (1–4)	2 (1–4)	2 (1–4)
Household number	6 (4–8)	6 (4–8)	6 (4–8)	6 (4–8)	6 (4–8)
Employed	25%	28%	32%	28%	27%
Limited Education	54%	53%	51%	52%	53%
Clinical Site					
UHI	72%	68%	53%	60%	61%
Lubowa	6%	7%	12%	7%	7%
Mbarara	5%	4%	6%	7%	6%
Gulu	17%	21%	29%	26%	26%
Clinical RHD Only	**Overall** N=1254	**Alive** N=988	**Retained** N=478	**Prescribed** N=437	**Adherent** N=394
NYHA Class					
I	22%	25%	21%	21%	21%
II	50%	54%	57%	57%	59%
III	19%	16%	15%	16%	15%
IV	9%	5%	7%	6%	5%
Medical Comorbidity					
Decompensated HF	27%	23%	24%	24%	24%
Stroke	3.7%	3.6%	4.0%	4.2%	4.4%

Total Population	Overall (N=1504)	Alive (N=1231)	Retained (N=701)	Prescribed (n=554)	Adherent (n=499)
Atrial Fibrillation	5.8%	5.7%	7.0%	7.2%	7.4%
Endocarditis	1.1%	1.0%	1.3%	1.4%	1.0%
HIV	4.5%	4.8%	5.3%	5.1%	5.4%
Prior Valve Surgery					
Valve repair	1.3%	1.5%	1.1%	1.2%	1.3%
Valve replacement	3.2%	3.4%	4.1%	3.5%	2.6%

Data are presented as median (IQR) or % of column]. RHD, rheumatic heart disease; NYHA, New York Heart Association Class; HF, heart failure; HIV, human immunodeficiency virus.

Table 2

Association of demographic variables with retention in care among all living subjects (n=1,231).

	Unadjusted		Multivariable	
	OR (95%CI)	**p**	**OR (95% CI)**	**p**
Age				
0–15 years	REF		REF	
15–25 years	**0.49 (0.36–0.68)**	**<0.001**	**0.56 (0.38–0.82)**	**0.003**
25–40 years	**0.38 (0.27–0.54)**	**<0.001**	**0.49 (0.32–0.75)**	**0.001**
>40 years	**0.32 (0.23–0.44)**	**<0.001**	**0.46 (0.30–0.70)**	**<0.001**
Female (vs male)	0.81 (0.63–1.04)	0.096	0.99 (0.74–1.34)	0.964
Disease category				
Clinical	REF		REF	
Latent Definite	**20.2 (8.8–46.4)**	**<0.001**	**14.3 (6.1–33.5)**	**<0.001**
Latent Borderline	**2.97 (1.96–4.50)**	**<0.001**	**2.30 (1.40–3.78)**	**0.001**
Acute Rheumatic Fever	2.72 (0.72–10.3)	0.141	2.76 (0.54–14.1)	0.224
Distance to the nearest health centre (per km)	**0.91 (0.88–0.94)**	**<0.001**	**0.94 (0.91–0.98)**	**0.001**
Household size (per person)	**0.96 (0.93–0.99)**	**0.038**	--	--
Employed or Employed Caregiver (vs. not)	**1.6 (1.2–2.1)**	**<0.001**	**1.42 (1.03–1.96)**	**0.030**
Limited Education (vs. more advanced education)	0.84 (0.67–1.05)	0.130	**0.69 (0.53–0.92)**	**0.011**

Bold print represents p<0.05. Hosmer-Lemeshow test for goodness of fit (p=0.89). AUROC curve 0.717 (95%CI 0.686–0.747).

Table 3

Association of demographic variables with optimal adherence to penicillin among subjects retained in care excluding borderline disease (n=597).

	Unadjusted		Multivariable	
	OR (95%CI)	**p**	**OR (95% CI)**	**p**
Age				
0–15 years	REF		REF	
15–25 years	1.14 (0.59–2.23)	0.695	1.26 (0.63–2.51)	0.515
25–40 years	**0.47 (0.25–0.86)**	**0.014**	**0.42 (0.21–0.85)**	**0.015**
>40 years	**0.51 (0.27–0.97)**	**0.040**	**0.43 (0.21–0.89)**	**0.022**
Female (vs male)	0.74 (0.45–1.21)	0.227	0.84 (0.50–1.40)	0.506
Disease category				
Clinical	REF		REF	
Latent Definite	0.90 (0.53–1.53)	0.698	**0.50 (0.26–0.93)**	**0.029**
Acute Rheumatic Fever	1.35 (0.16–11.1)	0.780	1.23 (0.14–11.0)	0.853
Distance to the nearest health centre (per km)	1.01 (0.94–1.08)	0.810	--	--
Household size (per person)	1.07 (0.99–1.16)	0.105	--	--
Employed or Employed Caregiver (vs. not)	**0.54 (0.35–0.86)**	**0.009**	--	--
Limited Education (vs. more advanced education)	**1.75 (0.12–2.74)**	**0.013**	**1.70 (1.06–2.74)**	**0.028**

Bold print represents $p<0.05$. Hosmer-Lemeshow test for goodness of fit ($p=0.75$). AUROC curve 0.651 (95% CI 0.595–0.707).