Title: Evolving failures in the delivery of HIV care: Lessons from a Ugandan meningitis cohort 2006-2016

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Running title: HIV care failures in Ugandans with AIDS

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Summary: A growing proportion of Ugandans presenting with AIDS and meningitis are receiving but failing antiretroviral therapy. The "treatment gap" is narrowing, yet populations are still at risk of AIDS and death because investments in HIV care post-ART initiation remain insufficient.

Abstract:

Background: Investments in HIV care in sub-Saharan Africa have increased the number of people aware of their status and receiving antiretroviral therapy (ART), yet HIV/AIDS mortality remains high.

Methods: We performed retrospective analysis of three sequential prospective cohorts of HIV-infected Ugandan adults presenting with AIDS and meningitis from 2006-2009, 2010-2012 and 2013-2016. Participants were categorized as: 1) unknown HIV status; 2) known HIV+ without ART; 3) known HIV+ with previous ART. We further categorized 2006 and 2013 cohort participants by duration of HIV-status knowledge and of ART receipt.

Results: We screened 1353 persons with suspected meningitis. *Cryptococcus* was the most common pathogen (63%). Over the decade we observed an absolute increase of 37% in HIV status knowledge and 59% in antecedent ART receipt at screening. 2006 cohort participants were new/recent HIV diagnoses (65%) or known HIV+ but not receiving ART (35%). Many 2013 cohort participants were new/recent HIV diagnoses (34%) and known HIV+ with <1 month ART (20%), but a significant proportion were receiving ART 1-4 months (11%) and >4 months (30%). 4% discontinued ART. From 2010 to 2016, meningitis cases per month increased by 33%.

Conclusions: While improved HIV screening and ART access remain much-needed interventions in resource-limited settings, greater investment in viral suppression and opportunistic infection care among the growing HIV-infected population receiving ART is essential to reducing ongoing AIDS mortality.

Introduction:

The HIV care continuum is the process by which an HIV-infected individual progresses from initial HIV diagnosis to the end goal of viral suppression—a process that occurs simultaneously with HIV disease progression until reversed by effective ART.[1] The continuum consists of a series of states in which an individual can exist: 0) unknown HIV status, 1) known HIV status, 2) linked into regular care, 3) receiving ART and 4) virologically suppressed.[2-4] An HIV-infected population's distribution within this continuum has important implications for HIV mortality and for the trajectory of the epidemic.[5] The past decade has seen major efforts to scale up HIV care services with a global investment larger than that for any other disease in history.[6] In Uganda, these efforts have significantly improved HIV status awareness and ART coverage.[7] By 2015, an estimated 57% of the 1.5 million Ugandans living with HIV were receiving ART.[7]

Yet, despite this progress in Uganda, the rate of new infections remains high and, although absolute HIV-associated deaths in decreased by an estimated 58% from 2005 to 2015, HIV is still the leading cause of death in adults with UNAIDS estimating 28,000 AIDS-related deaths in 2015.[7] These trends are largely mirrored in sub-Saharan Africa as a whole.[7] Data on the HIV status knowledge and ART coverage among persons developing AIDS in Uganda and much of sub-Saharan Africa over the past decade and presently is lacking. Without this evidence, decisions about prioritizing HIV investments cannot respond to the needs of the subset of HIV-infected individuals most likely to transmit the virus and to die of AIDS-related infections. *Cryptococcus neoformans* accounts for 15-20% of AIDS-related deaths worldwide, is the most common cause of adult meningitis in Africa, and is a sentinel event marking advanced HIV progression to AIDS and high risk of death.[8-11] Early HIV diagnosis, effective ART, and screening for cryptococcal antigen among late presenters are cost-saving interventions that prevent cryptococcal meningitis.[12-14] Among HIV-infected persons receiving ART, cryptococcal meningitis indicates ART failure, and evidence from South Africa suggests a high incidence of cryptococcal meningitis may persist even with improvements in ART access.[15]

We describe characteristics of HIV care that led to AIDS progression and risk of death among HIV-infected Ugandans presenting with meningitis, and we assess how the HIV care history of this key HIV-infected population has shifted over this decade of massive HIV care scale-up. We conclude by calling for a re-evaluation of HIV investment priorities to keep up with the evolving needs of HIV-infected Ugandans and sub-Saharan Africans.

Methods:

We performed a retrospective analysis of three sequential prospective cohorts of HIV-infected adults presenting with suspected meningitis and consenting to receive a lumbar puncture at two public hospitals in Uganda: Mulago National Referral Hospital in Kampala and Mbarara Regional Referral Hospital in Mbarara. Our 2006 cohort included patients from May 2006 to Sept 2009[16,17] and our 2010 cohort included screened patients from November 2010 to December 2012.[9,18] The 2013 cohort included screened patients from August 2013 to April 2016, with an institutional review board (IRB)-imposed six-month gap in screening from September 2014 to February 2015.[19]

In each cohort, we interviewed patients to assess knowledge of HIV status and any previous ART receipt. In the 2006 cohort, we screened all persons with meningitis but interviewed a subset of patients with cryptococcal meningitis who survived hospitalization at their time of entry into outpatient HIV clinic. Cryptococcal meningitis was defined as a positive cerebrospinal fluid (CSF) culture, India ink, or cryptococcal antigen. The 2010 cohort screened patients at time of hospital presentation for the Cryptococcal Optimal ART Timing (COAT) trial, which was an ART strategy trial of timing of ART initiation.[18] While there was no ART exclusion to being screened when presenting with suspected meningitis, the clinical trial exclusion criterion of previous ART receipt may have subtly biased the patients who were screened.. In the 2013 cohort, we further documented initial HIV diagnosis date and the duration of ART in all participants who were eventually alert and oriented. Participants who did not regain normal mental status prior to death were unable to provide detailed HIV history and ART duration.

All participants, or their surrogates, provided written informed consent and all relevant IRBs in Uganda and Minnesota approved the prospective cohorts in 2006, 2010, and 2013.

Upon receiving a lumbar puncture, we categorized participants as: 1) new HIV diagnosis, 2) known HIV diagnosis without previous ART, and 3) known HIV with previous ART. We compared the proportion in each cohort to describe trends in HIV screening and ART access from 2006-2016 in persons who developed AIDS. For the subset of participants of the 2006 cohort and the 2013 cohort who were able to provide more detailed information, we categorized HIV history into groups based on immediate history prior to in-hospital meningitis screening and review of prescribed outpatient medications, including the last ART refill date. Participants were categorized as:

1) New/recent HIV diagnosis: HIV status known <1 month prior
2) Known HIV with <1 mo ART: HIV status known >1 month but receiving ART <1 month or not receiving ART prior
3) Stopped ART: Started ART but discontinued >1 month prior
4) 1-4 months ART: Receiving continuous ART for 1-4 months prior
5) ART virologic failure: Receiving continuous ART for >4 months prior

Statistical analysis was done in a descriptive fashion and tested for difference between the three cohorts using the chi square test and the Kruskal-Wallis test. Analysis was done using Stata version 13.1 (Stata Corp, College Station, Texas).

Role of the funding source:

Funding sources had no role in the collection, analysis and interpretation of data, in the writing of this paper, or in the decision to submit for publication. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results:

We screened 1353 persons with suspected meningitis from 2006 to 2016 including 262 in the 2006-2009 cohort, 469 in the 2010-2012 cohort and 622 in the 2013-2016 cohort (Table 1). Participant

age increased significantly from the 2006 cohort to the 2013 cohort (median 34 years, IQR 29-39 vs. median 35 years, IQR 30-42 respectively, $P<0.008$). Proportion of women in the cohorts differed significantly, with 42% women in the 2006 cohort, 48% in 2010 and a decrease to 38% in 2013 ($P=0.01$). Prior to 2013 *Cryptococcus* was isolated in 57% (420/731) of patients, bacterial meningitis was diagnosed in 1.6%, and 23% were found to have aseptic or viral meningitis, with the remainder unknown.[9] In the 2013 cohort, cryptococcal meningitis was diagnosed in 71% (439/620) using first fingerstick cryptococcal antigen LFA screening followed by CSF analysis, and *Mycobacterium tuberculosis* was isolated in cerebrospinal fluid of 3% (n=18) of a cohort subset (n=107) tested by Xpert MTB/RIF assay (Cepheid, Sunnydale, CA) and mycobacterial growth indicator tube culture.[20]

Baseline CD4 counts were low, and we observed no significant difference between cohorts over time. In the 2013 cohort, participants diagnosed with cryptococcal meningitis had lower CD4 counts than those with other forms of meningitis (15 vs 89 cells/μL, $p<.001$). The absolute number of patients presenting with meningitis to these two public hospitals increased from 18 per month in 2010-2012 to 24 per month in 2013-2016 (33% increase; 95%CI, 18-50%, $p<0.001$).

We observed a major increase in HIV status knowledge at time of hospital presentation from 56% (40/71) in the 2006 cohort to 93% (578/622) in the 2013 cohort ($p<0.001$) (Figure 1). We observed a large increase in antecedent ART receipt at time of in-hospital screening as well, from 0% in the 2006 cohort to 59% (366/622) in the 2013 cohort ($p<0.001$). A subset of 71 participants in the 2006 cohort and 426 participants in the 2013 cohort were interviewed to establish date of previous HIV diagnosis and date of ART initiation, if any. Participants in the 2006 cohort subset had far shorter duration of known HIV status (median 17 days, IQR 0-79 days) than participants in the 2013 cohort (median 134 days, IQR 10 days - 38 months), and 34% (146/446) of the 2013 cohort subset had received >4 months of continuous ART.

In the 2006 cohort subset with more detailed HIV care information (n=71), we categorized 65% (46/71) as new/recent HIV diagnosis and the remaining 35% (25/71) as known HIV with <1 month ART (Figure 2). Among the 2013 cohort subset (n=426) we categorized 34% (143/426) as new/recent HIV

diagnosis, 20% (86/426) as known HIV with <1 month ART, 4% (15/426) as having stopped ART, 11% (47/426) as 1-4 months ART and 30% (128/426) as ART virologic failure. Of the 2013 cohort subset, 2% (7/426) could not provide dates and were categorized as unknown. Of the 2013 cohort subset, 30% were categorized as ART failure with a median ART receipt of 35 months (IQR 12-71 months).

Discussion:

Despite increased HIV screening and ART access in Uganda, HIV-associated infections such as cryptococcal meningitis have not disappeared. Indeed, our screening indicates the absolute number of persons presenting with cryptococcal meningitis increased from 2010 to 2016. In the decade from 2006 to 2016, we observe significant changes in HIV care history among such persons presenting with AIDS and meningitis to the public hospitals where we screened. Our point-of-screening assessment of HIV status knowledge and ART receipt showed large increases in HIV screening and ART receipt prior to participants' presentation with AIDS and, among the interviewed subsets of our 2006 and 2013 cohorts, we observe a major shift towards the later stages of the HIV care continuum, mirroring trends in the general population.[7] The decreased proportion of women presenting with meningitis in the most recent cohort is likely associated with efforts to prevent mother-to-child transmission and expanded ART access therein through the Option B+ program (of lifelong ART). The increased representation of men among persons presenting with AIDS indicates the current need for interventions to prevent AIDS progression in men.

Data from our 2006 cohort indicate the most-needed interventions at that time were HIV screening and ART initiation, and the improvements in HIV status knowledge and ART receipt indicate these interventions were made with relative success over the decade. A push for ART access at Ugandan public clinics from 2010-2013 was likely responsible for the substantial improvement in ART receipt after an earlier increase in HIV screening seen in screened participants[21]. However, our data from the recent 2013 cohort indicate a significant current need for investment in the tools required for HIV-infected individuals to reach and maintain viral suppression, which is the ultimate goal of the HIV care

continuum. Most disturbing are the 30% of the 2013 cohort subset in the ART failure category who presented with AIDS and high risk of death after receiving more than four months of continuous ART, for whom median ART receipt was 34 months. Immediately prior to presentation with AIDS, this group was receiving ART for sufficient duration to reverse AIDS progression, yet at the time of our screening these individuals had clearly not been virally suppressed for some time.

HIV policy and financing is most effective when it can respond to the current needs of the HIV-infected population. Unfortunately, high HIV burden is often accompanied by weak health systems with poor reporting—making it difficult to identify the needs of the subset of HIV-infected individuals developing AIDS. Our screened cohorts are a substitute for this lack of timely information in a key population at high risk of AIDS-related death, and our observations can promote policy changes with the goal of reducing the number of HIV-infected individuals who enter this high-risk group. In our recent 2013 cohort subset, 34% of participants were categorized as recent HIV diagnosis, a major decline from the 2006 cohort's 65% but still significant to warrant prioritization of HIV screening interventions in Uganda and specific interventions for late presenters, such as baseline CD4 testing to gauge the degree of immunosuppression and opportunistic infection care in order to reduce deaths.

However, our 2013 cohort's ART failure group, at 30%, was nearly as significant. This observation underscores the critical need for investment in virologic monitoring, access to newer generation antiretrovirals and patient support to ensure individuals receiving ART achieve virologic suppression, instead of failing treatment and developing AIDS. Policymakers and HIV financers should be concerned that this group will continue to grow as more of the HIV-infected population is diagnosed with HIV and receives ART. Our 2013 cohort's known HIV with <1mo ART group (20%) and 1-4 months ART group (11%) also illustrate the importance of continued ART scale-up in Uganda. Only 4% of 2013 the cohort subset had started but stopped ART, indicating that ART program default is not a common event immediately prior to AIDS hospital presentation. Of note, the most common reason cited for discontinuing ART in this group was adverse medication effects.

Cryptococcal meningitis was by far the most common pathogen directly responsible for hospital presentation in our screened patients. Unlike many opportunistic infections, cryptococcosis can be diagnosed with point-of-care cryptococcal antigen lateral flow assay (Immy, Norman, Oklahoma) in any locale. Regarding meningitis in particular, our data indicate investment in cryptococcal antigen screening and preemptive antifungal therapy for early, disseminated cryptococcal infection is another much-needed step to reduce this frequent cause of AIDS-related death. Participants in the known HIV with <1 mo ART, 1-4 months ART, and ART failure categories, (together 61% of the 2013 cohort subset) could have been eligible for this cost-effective intervention.[12,13]

This study has several limitations. Our point-of-screening assessment of HIV status knowledge and any ART receipt was a blunt tool that relied on participant self-reporting and medication review. However, previous HIV diagnoses and ART receipt were sufficient to categorize participants into the broad HIV care categories used to identify system failures and areas of improvement. The size of our 2006 interviewed cohort subset was small due to limited resources, but the experiences were consistent with the time period of persons presenting late with opportunistic infections and unknown HIV status. Our 2010 cohort's focus on predominantly ART-naïve participants likely yields a slight underestimation of ART coverage among individuals with AIDS in the middle of the decade.

The large size of the 2013-2016 cohort allows for a comprehensive assessment of the current situation among persons presenting with AIDS-related opportunistic infections of the central nervous system. Our assessment of patients failing ART leaves important questions unanswered and requiring further exploration, especially given that 30% were receiving >4 months of continuous ART. From our data, we cannot infer the relative contributions toward ART failure from program factors, patient factors, or if primary ART resistance was present. However, our data indicate that an area of growing priority for preventing AIDS deaths is achieving and maintaining viral suppression in persons receiving ART. The observed trends and current HIV care needs identified in Uganda likely are generalizable to other sub-Saharan African settings.

Contributors

DRB, DBM, JR, and AGF, participated in the study concept and design. JR, DAW, AM, KT, AS, RR, LN, and CM participated in acquisition of data. KHH, MR, DRB, AGF, and BMM participated in statistical analysis. AGF, DRB, and KHH participated in interpretation of data. AGF, DRB, and JR participated in initial manuscript drafting. DRB, AGF, and DBM participated in critical revisions for intellectual content. DRB, DBM, and PRB participated in obtaining funding. DAW, PRB participated in administrative, technical or material support.

Declaration of interests

We declare no competing interests

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References

1. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med.* 2011; 365(6): 493-505.

2. Greenberg AE, Hader SL, Masur H, Young AT, Skillicorn J, Dieffenbach CW. Fighting HIV/AIDS in Washington, D.C. *Health Aff (Millwood).* 2009; 28(6): 1677-1687.

3. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis.* 2011; 52(6): 793-800.

4. Lesko CR, Edwards JK, Moore RD, Lau B. A longitudinal, HIV care continuum: 10-year restricted mean time in each care continuum stage after enrollment in care, by history of IDU. *AIDS.* 2016; 30(14): 2227-2234.

5. Sharma M, Ying R, Tarr G, Barnabas R. Systematic review and meta-analysis of community and facility-based HIV testing to address linkage to care gaps in sub-Saharan Africa. *Nature.* 2015; 528(7580): S77-85.

6. Vermund SH. Massive benefits of antiretroviral therapy in Africa. *J Infect Dis.* 2014; 209(4): 483-485.

7. UNAIDS. AIDSInfo: Coverage of people receiving ART. 2017; http://aidsinfo.unaids.org/. Accessed 20 March, 2017.

8. Park BJ, Wannemuehler KA, Marston BJ, Govender N, Pappas PG, Chiller TM. Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. *AIDS.* 2009; 23(4): 525-530.

9. Rajasingham R, Rhein J, Klammer K, et al. Epidemiology of meningitis in an HIV-infected Ugandan cohort. *Am J Trop Med Hyg.* 2015; 92(2): 274-279.

10. Jarvis JN, Meintjes G, Williams A, Brown Y, Crede T, Harrison TS. Adult meningitis in a setting of high HIV and TB prevalence: findings from 4961 suspected cases. *BMC Infect Dis.* 2010; 10: 67.

11. Durski KN, Kuntz KM, Yasukawa K, Virnig BA, Meya DB, Boulware DR. Cost-effective diagnostic checklists for meningitis in resource-limited settings. *J Acquir Immune Defic Syndr.* 2013; 63(3): e101-108.

12. Meya DB, Manabe YC, Castelnuovo B, et al. Cost-effectiveness of serum cryptococcal antigen screening to prevent deaths among HIV-infected persons with a CD4+ cell count < or = 100 cells/microL who start HIV therapy in resource-limited settings. *Clin Infect Dis.* 2010; 51(4): 448-455.

13. Mfinanga S, Chanda D, Kivuyo SL, et al. Cryptococcal meningitis screening and community-based early adherence support in people with advanced HIV infection starting antiretroviral therapy in Tanzania and Zambia: an open-label, randomised controlled trial. *Lancet.* 2015; 385(9983): 2173-2182.

14. World Health Organization. Rapid advice: Diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children. 2011; www.who.int/hiv/pub/cryptococcal_disease2011. Accessed 1 Nov, 2015.

15. National Institute for Communicable Diseases. GERMS-South Africa Annual Report 2014. 2014; www.nicd.ac.za/?page=publications&id=196. Accessed Dec 1, 2015.

16. Kambugu A, Meya DB, Rhein J, et al. Outcomes of cryptococcal meningitis in Uganda before and after the availability of highly active antiretroviral therapy. *Clin Infect Dis.* 2008; 46(11): 1694-1701.

17. Boulware DR, Meya DB, Bergemann TL, et al. Clinical features and serum biomarkers in HIV immune reconstitution inflammatory syndrome after cryptococcal meningitis: a prospective cohort study. *PLoS Med.* 2010; 7(12): e1000384.

18. Boulware DR, Meya DB, Muzoora C, et al. Timing of antiretroviral therapy after diagnosis of cryptococcal meningitis. *N Engl J Med.* 2014; 370(26): 2487-2498.

19. Rhein J, Morawski BM, Hullsiek KH, et al. Efficacy of adjunctive sertraline for the treatment of HIV-associated cryptococcal meningitis: an open-label dose-ranging study. *Lancet Infect Dis.* 2016; 16(7): 809-818.

20. Bahr NC, Tugume L, Rajasingham R, et al. Improved diagnostic sensitivity for tuberculous meningitis with Xpert((R)) MTB/RIF of centrifuged CSF. *Int J Tuberc Lung Dis.* 2015; 19(10): 1209-1215.

21. *2015 Annual Report.* Makerere University College of Health Sciences, Kampala, Uganda: Infectious Diseases Institute;2015.

Table 1: **Baseline characteristics and HIV history of HIV-infected meningitis patients 2006-2016**

Baseline characteristics at hospital presentation	**2006 Cohort (N=262)**	**2010 Cohort (N=469)**	**2013 Cohort (N=622)**	***P*-value, test for difference**
Age in years, median (IQR)	34 (29-39)	34 (29-40)	35 (30-42)	0.008*
Women (%)	109 (42%)	223 (48%)	239 (38%)	0.01C
CD4 count cells/μL, median (IQR, 90th percentile)	20 (7-40, 77)	19 (9-70, 107)	10 (8-73, 173)	0.17*
Aware of HIV status, n (%)	40 (56%) [1]	411 (88%)	578 (93%)	<0.001C
Receiving/ever received ART, n (%)	0 (0%) [1]	10% (estimate)	366 (59%)	<0.001 C
Cryptococcal meningitis, n (%)	160 (61%)	260 (55%)	439 (71%)	<0.001 C
Incident meningitis cases per month of active screening	N/A [2]	18.0	24.0	<0.001
HIV history prior to hospital presentation [3]	**N=71**		**N=426**	
HIV status known <1 month	46 (65%)	N/A	143 (34%)	<0.001
HIV status known >1 month but receiving ART <1 month or none	25 (35%)		86 (20%)	
Started but stopped ART >1 month prior	0 (0%)	N/A	15 (4%)	
Receiving continuous ART 1-4 months	0 (0%)	N/A	47 (11%)	
Receiving continuous ART >4 months	0 (0%)	N/A	128 (30%)	
Unknown	0 (0%)		7 (2%)	
Total	71 (100%)		426 (100%)	

[1] Denominator n=71

[2] In 2006-2009, all persons with suspected meningitis were not enrolled due to limited resources.

[3]Among persons alert and oriented to interview. In 2006-2009, limited to persons with diagnosed cryptococcal meningitis.

* Kruskal-Wallis

** Nonparametric test for trend across ordered groups

C Chi^2

Figure Legends:

Figure 1. Significant changes in HIV care were observed over the decade. The 32% absolute improvement in HIV status knowledge at time of meningitis presentation from the 2006 cohort to the 2010 cohort indicates significantly increased HIV screening during this time. An estimated 10% of the 2010-2012 persons with meningitis were presenting on ART. Improvements in ART access have occurred over time. During 2013-2016, 59% are receiving ART among those presenting with AIDS-related opportunistic infections involving the central nervous system

Figure 2. Meningitis patients exhibited a changing experience with HIV care over the decade. Whereas HIV screening and ART initiation were key interventions needed in 2006-2009, our 2013-2016 cohort's experience indicates the increasing need for interventions to prevent or address ART failure as well as pre-ART cryptococcal antigen screening.

Figure 1.

HIV status knowledge and history of ART receipt among Ugandan AIDS patients at time of in-hospital meningitis screening 2006-2016 (n=1162)

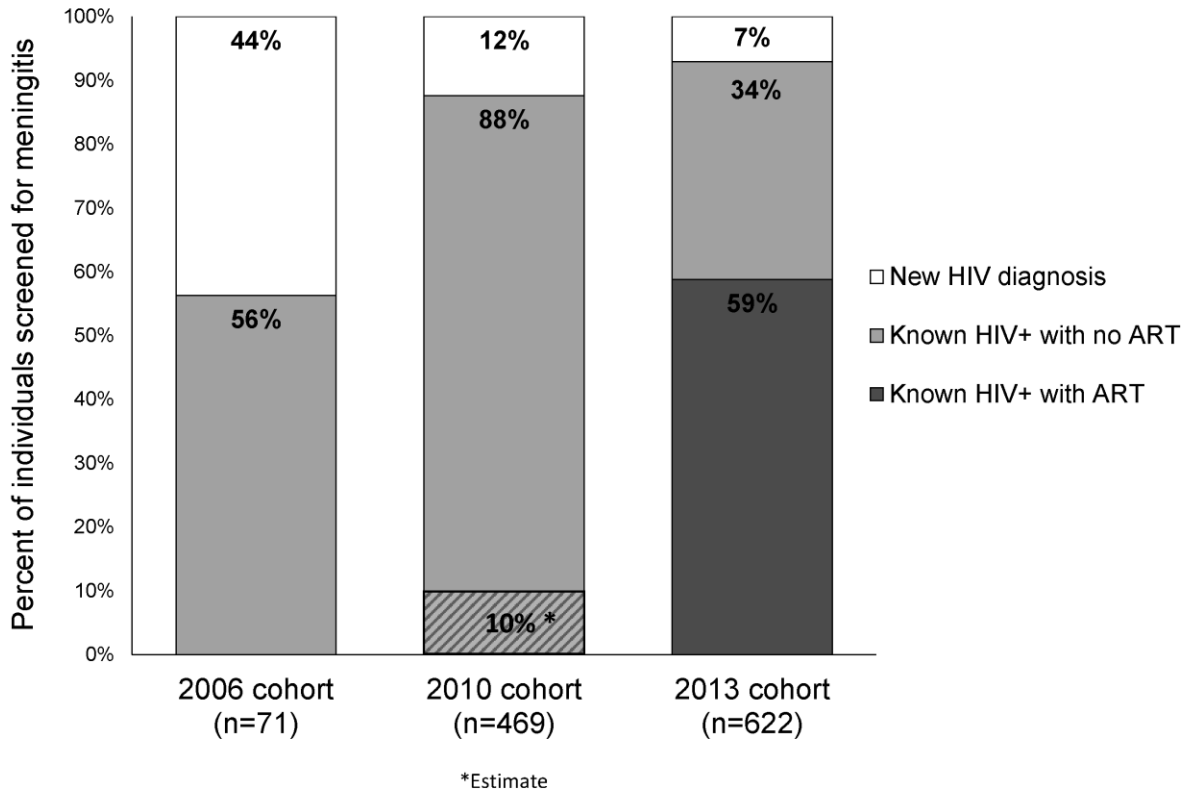

Figure 2.

HIV care history of Ugandan AIDS patients presenting to hospital with meningitis 2006-2009 (n=71) and 2013-2016 (n=426)