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Universal HIV testing and treatment (UTT) integrated with chronic disease screening and treatment: The SEARCH Study

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Abstract

Purpose of Review: The growing burden of untreated chronic disease among persons with HIV (PWH) threatens to reverse heath gains from ART expansion. Universal test and treat (UTT)'s population-based approach provides opportunity to jointly identify and treat HIV and other chronic diseases. This review's purpose is to describe SEARCH UTT study's integrated disease strategy and related approaches in Sub-Saharan Africa.

Recent Findings: In SEARCH 97% of adults were HIV tested, 85% were screened for hypertension and 79% for diabetes at health fairs after two years, for an additional $1.16/person. After 3 years, population-level hypertension control was 26% higher in intervention versus control communities. Other mobile/home-based multi-disease screening approaches have proven successful, but data on multi-disease care delivery are extremely limited and show little effect on clinical outcomes.

Summary: Integration of chronic disease into HIV in the UTT era is feasible and can achieve population level effects; however, optimization and implementation remain a huge unmet need.

Keywords

HIV testing; HIV treatment; non-communicable disease; hypertension; treatment as prevention

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Conflict of Interest

Gabriel Chamie, Matthew Hickey, Dalsone Kwarisiima, James Ayieko, and Moses Kamya declare that they have no conflict of interest. Diane Havlir has received nonfinancial support from Gilead Sciences.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

Introduction

Over the past two decades, access to antiretroviral therapy (ART) for people with HIV (PWH) in sub-Saharan Africa (SSA) has expanded from an initial emergency response for those with advanced HIV to the present state of universal ART for all PWH. As a result, mortality rates have dropped and PWH are living longer within health systems that provide chronic HIV care across much of SSA.[1] In addition to the health benefits for PWH, effective use of ART with viral suppression results in elimination of HIV transmission from PWH to uninfected sexual partners and reduced mother-to-child transmission.[2, 3] Despite this major public health achievement, there is increasing awareness of missed opportunities to leverage HIV testing and treatment infrastructure to address the growing burden of non-communicable diseases (NCDs), such as cardiovascular disease, across SSA.[4–7] This growing awareness comes at a time when NCDs are on the rise due to demographic transitions across SSA, influenced by rural to urban migration and changing diets among people with and without HIV infection, as well as aging populations of PWH due to rising life expectancy with increased ART access.[8] For example, over the past 20 years, the prevalence of cardiovascular disease (CVD) has tripled among PWH, with the greatest impacts in SSA.[9]

In light of the individual and public health benefits of universal HIV treatment, over the past decade, several large trials in SSA were designed and implemented to test the impact of universal HIV testing and treatment (UTT) interventions on HIV incidence and HIV-associated morbidity and mortality.[10–13] Though the UTT trials sought to maximize the potential of antiretroviral “Treatment as Prevention” (TasP) on HIV incidence, they also provided opportunities to better understand *how* to implement universal testing and treatment. Among these UTT trials, the Sustainable East Africa Research in Community Health (SEARCH) trial in rural Kenya and Uganda developed a community-wide intervention based on the PRECEDE implementation science framework[14] that was based on four key principles: 1) community engagement; 2) community-based (i.e. not clinic-based) HIV testing delivered through a multidisease approach – inclusive of both communicable and non-communicable diseases; 3) rapid ART start upon HIV diagnosis; and 4) patient-centered, flexible testing and treatment services. As such, the SEARCH community cluster-randomized trial tested the hypothesis that a community-based, multi-disease and patient-centered intervention would result in reduced HIV incidence *and* improved community health – for both PWH and those without HIV – compared to current standard of care in rural SSA.[10] In this narrative review, we review how SEARCH integrated chronic NCD screening and treatment into its UTT intervention and compare and contrast this approach to other published examples of NCD integration into HIV testing and treatment across SSA.

Multi-disease screening during universal HIV testing

Universal HIV testing to increase the proportion of PWH who are aware of their status is a critical step for maximizing the potential of universal ART eligibility and reducing onward HIV transmission. From the time of the SEARCH UTT trial’s inception and design, the SEARCH team forged partnerships with community leaders, organizations and residents to

understand local health priorities, as well as barriers and facilitators to achieving universal HIV testing in rural East Africa. Through these partnerships, community members emphasized that universal testing and treatment would only succeed if offered as part of a broader effort: a) to improve community health, rather than an HIV-focused approach that could stigmatize those accessing services and alienate community members without HIV who have chronic health problems, and b) to reduce barriers to accessing services at local clinics, which included lengthy wait and travel times, with associated costs due to accessing centralized clinic sites and time away from income generating activities.

The SEARCH team therefore designed a universal testing intervention that was a hybrid of two out-of-facility, mobile testing strategies: community health fairs and home-based testing. Universal HIV testing in SEARCH included mobilization and a rapid baseline census enumeration for communities with populations of approximately 10,000, followed by two-week multi-disease health fairs, with home-based testing for non-attendees in the four to six weeks after the health fairs.[15] Integration of universal HIV testing into multi-disease health fairs both demonstrated SEARCH's commitment to broader community health needs and provided a means for residents to cope with stigma when accessing HIV testing services: rather than being perceived as seeking HIV testing in isolation and identifying oneself as at-risk for HIV, anyone could attend at festive venues in full view of other residents to check on one's health.

Integration of universal HIV testing into multi-disease health fairs also allowed for efficiencies in community-based delivery and measurement of population-level prevalence of NCDs. At health fairs, core NCD services included screening for hypertension (HTN) and diabetes mellitus (DM) among adults.[15] Upon entry into health fairs, group pre-test counseling by trained health workers integrated education about screening for HIV, HTN and DM. A brief pre-testing questionnaire collected information regarding prior diagnoses, alcohol use, depression and anxiety, and medication use. Hypertension screening, height, and weight measures were obtained by nurses, and laboratory technicians offered integrated screening for HIV, malaria (if febrile), and DM (by random blood glucose measurement) using point-of-care diagnostics from fingerstick blood samples. Following screening, post-test counselors reviewed all results (positive or negative) individually with fair participants, provided education on NCDs as well as HIV, emotional support and counseling, and prompt referral to care at a local health center for those who screened positive (Figure). Over time, based on feedback from community members, additional NCD services were integrated into health fairs, including cervical cancer screening and family planning, and a men's health station to address questions regarding sexual health (e.g. erectile dysfunction and sexually transmitted infections) and marital or other relationship concerns. Although multi-disease screening was not integrated into home-based testing of campaign non-attendees in SEARCH, others have shown that integration of HTN, DM and lipid screening into home-based testing is feasible and acceptable.[16]

With the SEARCH multi-disease approach to integrated HIV and NCD screening, after two years in 16 intervention communities, 97% of adult, stable residents (those reporting living in their community ≥6 months of the year prior to baseline census enumeration) had been tested for HIV at health fairs and home-based testing,[17] whereas 85% and 79% had been

screened for HTN and DM respectively at multi-disease health fairs (table).[18] Qualitative data showed health fair participants were drawn by non-HIV services, and health fairs attracted those who reported prior reluctance to test for HIV as well.[18] Such high rates of screening coverage allowed for population-level measures of NCD prevalence and risk factors. For example, in the 20 SEARCH communities in Uganda that underwent baseline health fairs, the prevalence of HTN was 14% among adults attending health fairs (N=65,544) and 11% among adults living with HIV: 79% of HTN patients were previously undiagnosed, 85% were not taking medication, and 50% of previously diagnosed patients on medication had uncontrolled blood pressure.[19] High rates of integrated screening also allowed for a greater understanding of how NCDs and HIV may impact one another. For example, through baseline screening for hazardous alcohol use during brief questionnaires at health fairs and home-based testing, the negative effects of higher levels of alcohol use on HIV care outcomes, including lower population-level HIV viral suppression with increasing alcohol use at baseline prior to the SEARCH intervention, was demonstrated.[20]

Integrated screening for HIV and NCDs represented a key component of the SEARCH trial's efforts to rapidly achieve HIV testing coverage for all community members within a UTT approach. Several other approaches to integrated HIV testing and NCD screening have been published, establishing the feasibility and acceptability of integration of NCD screening into home-, mobile van-, and clinic-based HIV testing. For example, van Heerden *et al* described integration of HTN, DM, hyperlipidemia, depression and obesity screening into home-based HIV testing in KwaZulu-Natal, South Africa,[16] Govindasamy *et al* conducted integrated HTN, DM and tuberculosis symptom screening with HIV testing services offered via mobile health units in Cape Town, South Africa,[21] and Kachimanga *et al* integrated HIV, HTN and DM screening into out-patient departments in Malawi.[22] Integrated HIV/NCD screening at clinics has the advantages of centralized resources (e.g. staff, screening equipment, medical records) and on-site immediate linkage to care after a new diagnosis. However, potential advantages of community-based screening over clinic-based screening may include earlier diagnosis of both HIV and asymptomatic NCDs. Out-of-facility HIV screening approaches have been shown to identify adults at higher CD4+ cell counts compared to facility-based screening.[23] In a SEARCH pilot campaign in Southwestern Uganda, we found that feeling well was a barrier to linking to care after screening positive for HTN[24] and that greater distance from the local health center was associated with a lower likelihood of having been previously diagnosed with HTN among hypertensive adults[25] – findings that suggest community outreach identifies people with NCDs who may not otherwise seek care at health centers.

Several recent narrative and systematic reviews have described models of HIV and NCD screening integration and highlighted barriers and facilitators to integration.[26–29] Practical challenges to HIV/NCD integrated screening include disease-specific funding, siloed service delivery, and ensuring linkage and access to care, including NCD-specific medications, for the multiple diseases for which screening is offered. These challenges may be overcome by highlighting the rationale and advantages of such integrated screening approaches to international funding agencies and national governments, and within universal HIV testing infrastructure – such as the SEARCH intervention – demonstrating that the marginal costs of including HTN and DM screening are relatively low.

Multi-disease approach to HIV treatment

"Integrated" models of HIV care in Sub-Saharan Africa that diagnose and treat chronic diseases in PWH are an underutilized opportunity to pave the path to universal health access.[4] Continued reductions in morbidity and mortality in PWH will only be possible if we move beyond the critical but often singular focus of achieving viral suppression targets and address the unmet need of untreated health threats in aging and diverse populations.[5, 9] The spectrum of chronic diseases in PWH is broad and includes but is not limited to chronic hepatitis, malignancies, obesity, tobacco, hypertension, diabetes, chronic kidney disease, mental health, alcohol and substance use disorders and varies by region and population.[7, 30–36] HIV testing within or outside of health facilities presents an opportune moment to screen for some of these non-HIV chronic diseases, as discussed above. However, health gains will only be achieved when such efforts are linked to effective care delivery models.[28, 37] We use hypertension as one example of a chronic disease that is prevalent among PWH and is treated with medications that are low cost (as compared to cancers) to show that integrated care models can be implemented within a UTT setting, but that as a whole, sustainable and scalable care delivery systems are grossly understudied and require urgent attention.[38]

There is a robust literature on the epidemiology of hypertension prevalence among PWH in SSA as well as detailed and thoughtful reviews of foundational components for treatment programs.[28, 36, 37] Modelers have projected costs and cost-effectiveness for integrated HIV and hypertension care in South Africa and Kenya with scenarios that provide promising approaches for policy makers.[5] Most countries have standardized guidelines for management of hypertension derived from WHO guidelines.[39, 40] Yet, reports across multiple countries show shortfalls in essential medications and technologies, quality assurance programs, human resources and data collection systems among hypertension treatment programs,[41–43] and there are surprisingly few published reports evaluating the effectiveness and costs of an integrated HIV hypertension care model.[37, 44]

In theory, hypertension should be one of the simplest of the chronic conditions to include in an integrated HIV and multi-disease care approach. Clinical treatment algorithms for uncomplicated cases for both diseases are straightforward, and trained health care professionals (e.g. nurses) can effectively deliver care. Technology requirements are minimal; hypertension management requires a functioning sphygmomanometer. Desired but not necessary laboratory assessments are less costly for hypertension than for HIV and include blood creatinine and urine protein assessments. Patients with well-controlled hypertension and HIV can be managed with 3–6 month visit intervals.

In the SEARCH study, we used an integrated chronic care mode to treat PWH (as well as those without HIV) with a "streamlined" care that aimed to reduce patient level barriers and maximize health system efficiency.[10, 45] The model included components to reduce structural barriers to care (co-location of services, wait time, visit intervals, clinic hours), to improve relationships to clinic (providing direct access to clinicians and providing friendly and respectful service) and to enhance knowledge of HIV and other chronic diseases. Nurses

and clinical officers were trained in hypertension management and used country-standardized algorithms for treatment.

Population level hypertension screening with access to treatment in an integrated HIV and hypertension chronic care model had favorable short-term effects on hypertension control, but also showed room for improvement.[10] After three years, hypertension control among adults with prevalent hypertension was 26% higher (RR 1.26; 95%CI 1.15–1.39) in the intervention (47%) versus control (37%) communities in SEARCH. Similar trends were observed in longitudinal analysis of those with hypertension at baseline. Dual HIV viral suppression and control of hypertension among baseline HIV-infected persons with prevalent hypertension was 22% higher in the intervention (72%) versus control (59%) arm (RR 1.22; 95%CI 1.08–1.37).

A more detailed analysis of the hypertension "cascade" in a subset of 10 intervention communities in Uganda provides insight into some of the challenges encountered in the UTT model.[46] Despite near universal screening, only 45% of those diagnosed with hypertension were linked to hypertension care within 1 year. Furthermore, linkage was the same for HIV-infected and uninfected individuals, suggesting that delays in linkage persisted despite engagement in HIV care. Medication stock-outs also limited effectiveness. Treatment guidelines utilized in the SEARCH integrated care model included 12-week visit intervals for those with controlled hypertension, however scheduled follow up of less than 12 weeks due to medication stock-outs was associated with lower hypertension control (aOR 0.89; 95% CI 0.79–0.99). Limitations in linkage and in medication stock-outs provide two important targets for improving integrated HIV and hypertension treatment.

Another integrated care model described by Patel *et al* provides additional insight into challenges associated with integration of hypertension and HIV care, as well as creative solutions to address these challenges.[47] They piloted integration of hypertension treatment into two large PEPFAR-supported clinics in urban Malawi with the goal of creating a scalable model for the rest of the country. They used a health systems strengthening approach to define key areas of implementation related to policy, systems strengthening, health worker training, and monitoring/evaluation. Specific interventions included development of an HIV-specific hypertension treatment algorithm, health worker training, development of a monitoring/evaluation tool within their electronic medical record, strengthened medication supply chain, and a referral network for difficult cases. In their pilot study, they screened 29,359 people, diagnosing 11% of them with new hypertension, and initiating treatment per their standard protocol among 85% of those diagnosed. Despite this success in implementation, only 38% of those with mild hypertension and 30% of those with moderate hypertension achieved hypertension control after 6 months of treatment. This study provides important insights into implementation considerations when developing an integrated HIV and hypertension treatment program and highlights ongoing challenges in achieving blood pressure control that will need to be addressed with future study.

Ameh *et al* used an interrupted time series analysis to evaluate implementation of an integrated chronic disease management model undergoing scale up in South Africa.[48] This integrated model included health care services for HIV, tuberculosis, hypertension, diabetes,

chronic obstructive pulmonary disease, asthma, epilepsy, and mental health in primary health centers. Interventions included implementation of new care guidelines, health worker training, improved medication supply chain, and referrals for complex cases. Despite implementation of this integrated model, blood pressure control among patients with both HIV and hypertension only improved by 1% in the integrated care model compared to control clinics, with both groups achieving <50% control. The authors highlighted several implementation barriers to achieving greater blood pressure control, including siloed public health leadership, overburdening of providers, and medication stock-outs. These barriers may serve as important targets for future intervention.

Costs of integrating NCD and HIV testing

Understanding costs associated with integration of chronic disease screening and treatment into routine HIV care is essential for decision-making about implementation and scale up.[49, 50] Current noncommunicable disease costing data is largely limited to integration of screening for cardiometabolic disease into HIV screening interventions[44] with treatment integration cost estimates limited those reported from SEARCH.[51]

Several studies have assessed the cost of integrating cardiometabolic disease screening into community-based HIV testing. Reported costs for cardiometabolic screening range from $1.16 per adult screened for diabetes and hypertension in the SEARCH study in Uganda and Kenya[52] to $12.31 per adult screened for hypertension, diabetes, dyslipidemia, anemia, and obesity within the Bophelo study in Namibia.[53] During the first two years, the multi-disease screening approach in SEARCH reached 97% of adults for HIV testing,[17] 85% for hypertension and 79% for diabetes screening,[18] costing $20.5 per adult overall and $1.16 for combined diabetes and hypertension screening.[52] Patients who screened positive for any of these conditions were referred to integrated HIV-NCD clinics. The Linkages study incorporated a broad package of NCD screening (hypertension, diabetes, dyslipidemia, obesity, depression, and smoking) and linkage to care into home-based HIV testing in South Africa.[54] Among integrated HIV-NCD screening studies reported in the literature, Linkages reported the lowest overall cost, at $13.30 per adult screened. Despite overall lower costs, NCD-specific screening costs were more than triple that reported in SEARCH, at $3.95, though this cost included a broader array of NCD screening and was driven partially by the cost of lipid test strips ($1.71 per test). The Bophelo study incorporated hypertension, diabetes, dyslipidemia, anemia, and obesity screening into mobile and workplace-based HIV testing in Namibia, reporting much higher costs at $65.72 per adult overall and $12.31 per adult for NCD screening.[53] One other study evaluated mobile and home-based multi-disease screening for HIV, diabetes, and hypertension in Lesotho.[55] This study reported similar overall costs to SEARCH and Linkages of $16.68 per adult for home-based testing and $18.33 per adult for mobile testing, however NCD-specific costs were not reported.

Costs of integrating NCD and HIV treatment

The most robust costing information available is for non-integrated cardiometabolic treatment.[44] A study in Rwanda reported the average health-system costs at a public

district hospital of $73 per patient annually for hypertension, $104 for heart failure, and $151 for diabetes, including fully subsidized medication costs.[56] This study included construction costs for the clinic, clearly highlighting one anticipated area of cost savings with integration of NCD services into existing HIV treatment infrastructure. Another study in Tanzania estimated the average health-system costs of cardiometabolic treatment at $30–41 per person annually in primary health centers and $52–71 per person annually in hospitals. Inclusion of fees charged to patients for medical consultation, laboratory testing, and prescribed drugs would add $33–54 on average (range $0–167). Incremental costs to optimize cardiometabolic treatment based on WHO guidelines would further add an additional $4 for patients at low cardiovascular (CVD) risk and $71 annually for those at high CVD risk. Patient costs due to transportation and lost income were substantial in this study, suggesting that integration with pre-existing HIV care may offset some direct and indirect patient costs associated with separate visits for NCD care.[57] A study of a private health center in Nigeria where all patients were covered by community-based health insurance, and thus had no co-pays for NCD care, estimated the annual average cost of delivering hypertension care at $118 for hypertension and $263 for diabetes care.[58] Highlighting the value of integrated care models, the estimated annual cost for patients receiving both hypertension and diabetes care was $295 per patient, less than the combined cost for individual disease management. This study also modeled opportunities for cost savings, demonstrating that both reduction in the frequency of diagnostic testing to that recommended by the WHO and task shifting to nurse-led care with less frequent visits would lead to reductions in overall per-patient health-system cost by more than 40%.

In addition to health-system cost estimates for providing NCD care, several studies have provided more nuanced insight into patient-facing costs of cardiometabolic care. Patient co-pays are often substantial and frequently lead to catastrophic financial costs for patients.[59–64] High costs of private health care facilities are one driver of high out-of-pocket costs to patients. A study in Kenya reported an average annual per patient cost of $76 for hypertension treatment (range $26 for one medication to $159 for resistant hypertension), $88 for diabetes care among patients on oral medications and $214 for those requiring insulin in public facilities.[65] Costs were substantially higher for care in private facilities, where estimated out-of-pocket annual per-person costs were $679 for hypertension (range $418 for one medication to $987 for resistant hypertension), $489 for diabetes treated with oral medications, and $637 for diabetes treated with insulin. The cost of acute care or serious illness is another driver of high patient costs associated with NCD care. A pair of studies in Kenya reported high out-of-pocket healthcare costs for routine hypertension and diabetes care, with an annual average cost of $94 for hypertension care, $289 for diabetes alone, and $353 for comorbid diabetes and hypertension.[60, 63] However, the total average annual cost including urgent care and inpatient admissions was even higher ($477 for hypertension alone, $673 for diabetes alone, and $817 for co-morbid diabetes and hypertension), leading 59% of patients with hypertension, 70% of patients with diabetes, and 80% of patients with co-morbid diabetes and hypertension to report levels of expenditure that were deemed catastrophic. These and other reports of catastrophic healthcare expenditures for patients highlight the importance not only of minimizing the cost of NCD care and improving access

through integrated services, but also ensuring universal health coverage to protect patients from high costs associated with serious and unexpected illness.[59, 62, 66]

In contrast to relatively high costs of stand-alone hypertension treatment described above, the SEARCH study has estimated that hypertension can be integrated into HIV care for approximately 4% increased marginal cost in addition to the cost of HIV care, or $11 per patient per year.[51] Integration of hypertension treatment within routine HIV care and streamlining care to reduce visit frequency may also minimize the high patient-facing costs of hypertension care that has been described in non-integrated settings.

Conclusion

Impact of UTT can be maximized by multi-disease screening and linking to care strategies that identify those with HIV (ART), those at risk for HIV (prevention interventions) and those with other chronic diseases (treatment). There is a growing literature on various multi-disease screening approaches that are feasible and add modest costs to a core HIV program. The SEARCH UTT study implemented both multi-disease screening and treatment that achieved favorable population level effects on hypertension control. However overall, hypertension is only one of many chronic diseases that needs to be addressed, and there is still limited evidence on the best approaches to disease prioritization and integrated care delivery. Finally, new cost sharing models for integrated HIV-NCD care are needed and require discussion among funding agencies. Sustained momentum in the HIV response must address the growing burden of chronic diseases and needs to be a top priority in this decade.

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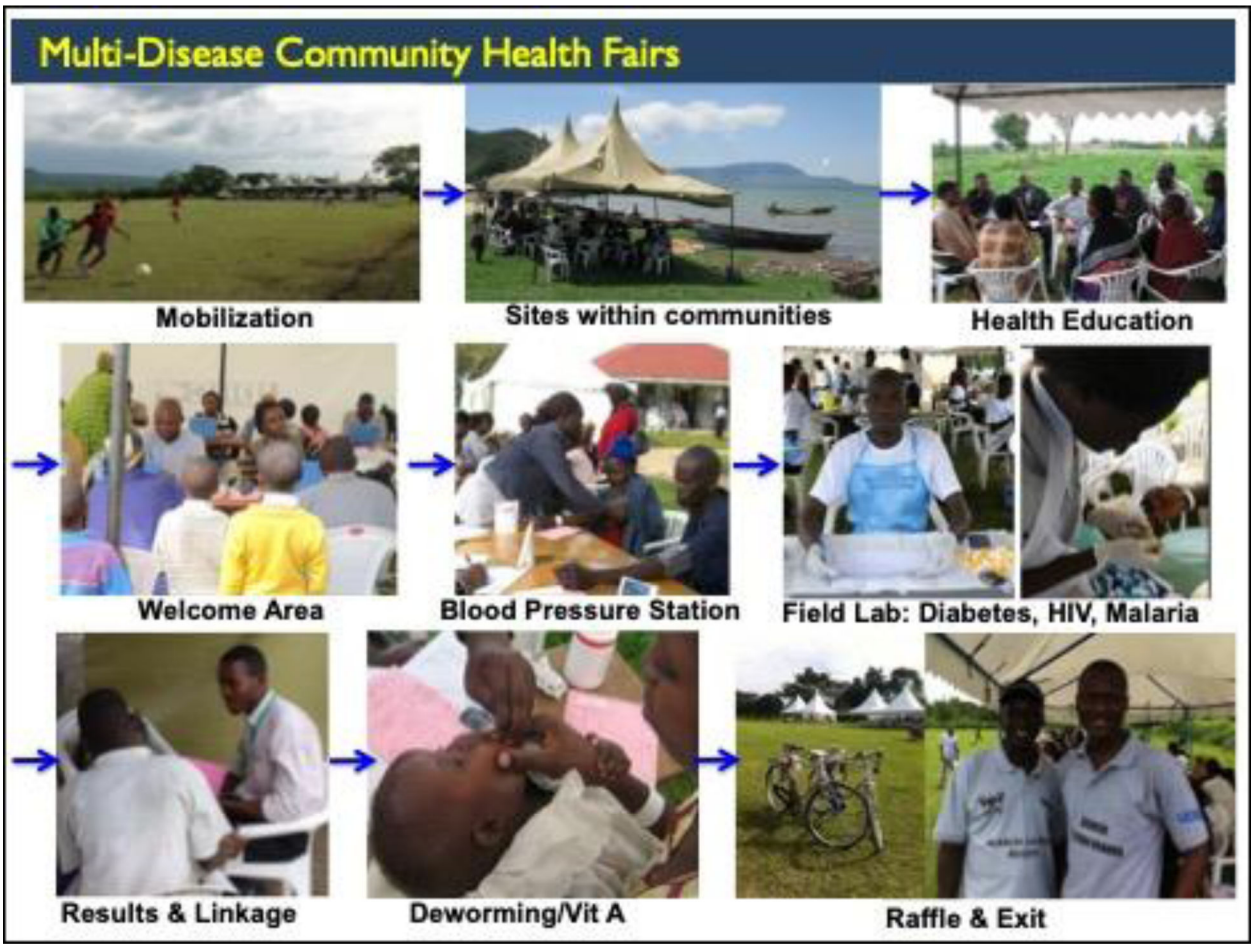

Figure.

Community health campaign participant flow for universal, integrated HIV and multi-disease screening, referral, and linkage.

Table.

3 annual multi-disease health fairs in 16 SEARCH intervention communities over 2 years

Service	Method	Population accessing services	Demand: Population uptake (%)	Population uptake (%), by sex
Hypertension Screening	Blood pressure x1 Repeated measure x2 if elevated	≥18 year-olds	57,935 /68,121 (85%)	Women:89% vs. Men:79%
Diabetes Screening	Random blood sugar	≥15 year-olds	61,283 /77,788 (79%)	Women:83% vs. Men:74%
Malaria Screening	If fever present, offer rapid diagnostic testing	All residents	**≥15:** 65,497 /77,788(84%) **<15:** 74,868/81,397(92%)	**≥15:** Women:88% vs. Men:79%
TB Screening	If cough >2 weeks, offer spot sputum fluorescence microscopy x2	≥15 year-olds; Eastern Uganda only	22,269 /25,126 (89%)	Women:90% vs. Men:86%
Urgent Care	On-site clinician to address urgent complaints	All residents	18,892 /77,788 (24%)	Women:28% vs. Men:20%