IMPLEMENTATION EFFECTIVENESS OF HIV SELF-TESTING AND PREFERENCES FOR HIV TESTING IN UGANDA

by

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(Under the Direction of CHRISTOPHER C WHALEN)

ABSTRACT

Background

Knowledge of one's HIV status is a critical step in the cascade of HIV care and prevention. Despite being available, many people at risk of HIV cannot access these services due to low uptake of HIV testing. Unsupervised HIV self-testing (HST) has potential to increase knowledge of HIV status; however, its accuracy is unknown. The main objectives were to determine the accuracy of HST and user preferences for HIV testing in Uganda.

Methods

We conducted a conjoint survey and performed a non-blinded, randomized controlled, non-inferiority trial of unsupervised compared with supervised HST among high-risk fisherfolk in three fishing communities in Uganda between July and September 2013. The study enrolled 246 participants and randomized them in a 1:1 ratio to unsupervised HST or provider-supervised HST. The primary outcome was difference in assay sensitivity and specificity, assessed with one sided Wald's asymptotic test for non-inferiority with a -15% non-inferiority margin in the intent to treat and per-protocol analyses. Conjoint analyses using a hierarchical Bayes model were used to estimate utilities for HIV testing attributes. Utilities were used to simulate and estimate the

shares of preference of 2 scenarios including an oral self HIV test, with price added as a key attribute.

Results

In an intent-to-treat analysis, the HST sensitivity was 90% in the unsupervised arm and 100% among the provider-supervised, yielding a difference 0f -10% (90% CI: -21%, 1%); non-inferiority was not shown. In a per protocol analysis, the difference in sensitivity was -5.6% (90% CI: -14.4, 3.3%) and did show non-inferiority. Relative importance of HIV test attribute was highest for timeliness and accuracy (30.2%), price (29.7%) and counseling (17.5%) respectively. Given no costs of service, an oral home based self-test had the largest share of preference (24.5%), twice that of the rapid testing done at a public clinic. The share of preference drops to 9.9% when a $2 fee is included.

Conclusion

Unsupervised HST is feasible in rural Africa and may be non-inferior to provider-supervised HST. Highly accurate HST with oral tests and immediate results offered at no fee with counseling support could increase HIV test uptake.

INDEX WORDS: Unsupervised, HIV Testing, Accuracy, Randomized, Implementation, Conjoint Analysis, Preferences

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A Dissertation Submitted to the Graduate Faculty of The University of Georgia in Partial Fulfillment of the Requirements for the Degree

DOCTOR OF PUBLIC HEALTH

ATHENS, GEORGIA

2013

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DEDICATION

This work is dedicated to those in the fight against the deadly HIV/AIDS epidemic along with its associated co-morbidities throughout the world.

To those we have lost, and to those we must save.

ACKNOWLEDGEMENTS

Am so grateful to my wife Maureen Asiimwe, and boys Arinda, Atwine and Aine for the support they have provided to me thus far. I have surely taxed your endurance heavily during this period. Thank you so much, I love you all!

We would like to thank our research assistants Ahimbisibwe Regan, Orishaba Carol, Tumusiime Obed and Ms Merabu. Many thanks go to my colleague Dr Juliet Sekandi, for the ideas shared and shaped over time. Dr Noah Kiwanuka guided me through the field residency training, and shaped my field-based clinical trial skills. We received very useful comments from members of the departmental Epidemiology in Action research working group led by Christopher Whalen, including Doctors Amara E Ezeamama and James Oloya.

I would like to appreciate my senior colleagues Ruanne V Barnabas, Andrew Mujugira and Connie Celum from the University of Washington in Seattle, for their expert field guidance and mentorship. Our gratitude extends to the staff of Kabwohe Clinical Research Center, Uganda led by Elioda Tumwesigye for being the host institution for this study project. We thank our study participants in the fishing villages so much for volunteering and providing us this data.

My doctoral studies in the USA were all supported by the NIH Fogarty International Center AIDS International Training and Research Program (TW 000011-24), PI – Christopher C Whalen, to whom am most sincerely and eternally grateful.

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CHAPTER 1

INTRODUCTION

Public Health Significance

Access to almost all HIV preventive services is determined by knowledge of one's current HIV status. HIV testing is the entry mechanism into a whole world of HIV care, management and prevention options. Knowledge of one's HIV status is therefore a critical step in the cascade of HIV care. It may result in a series of actions that may reduce one's risky sexual behaviors as well as allow the individual access HIV medical care and treatment. Despite the positive strides made in the field of HIV care and prevention, several people still cannot access these services simply because they have not tested for HIV. The recent new developments in HIV prevention considered game changers that include pre-exposure prophylaxis (PrEP) (Baeten et al., 2012) and treatment for prevention (Cohen et al., 2011) cannot have any significant impact unless all persons with HIV have been identified by testing, and linked to HIV care, treatment and prevention services. These new effective preventive strategies both require the use of anti-retroviral drugs therapy (ART) or anti-virals (ARV's). Hence they depend on knowledge of one's HIV status even more, as suboptimal exposure to ARV's may result if persons of unknown HIV status are included in such programs.

In a recent stakeholder engagement regarding the new ART HIV prevention methods like PrEP, people's willingness and ability to take long-term prophylactic medications and to frequently get tested for HIV were raised as major challenges (Wheelock et al., 2012). This will require the availability of HIV tests that are accessible and provide accurate results in a short

time. Despite the critical role of HIV testing, many national HIV Counseling and Testing (HCT) programs including that of Uganda have not been able to even cover half of their at risk populations (J. K. B. Matovu & Makumbi, 2007).

In Uganda, HIV testing has been done traditionally using 4 key strategies – facility based HCT, mobile outreach HCT, lab-based HCT and home based door-door HCT (MOH, 2003). Facility based HCT is provided by health workers or trained community owned resource person's (CORP's) at a health facility or any locality designated as such. Mobile HCT outreaches are conducted by specialized field teams from various Government or Non-Governmental Organizations (NGOs), usually in hard-reach or remote areas. Home based HCT involves trained teams of health providers working with CORPs to visit people's homes from door-door, offering them opportunities of conducting rapid tests for HIV.

For traditional HIV testing methods, access is associated with barriers like stigma, disclosure issues, poor male involvement as well as long distances to health facilities (Bajunirwe & Muzoora, 2005; Emmanuel Mugisha, van Rensburg, & Potgieter, 2010; E. Mugisha, van Rensburg, & Potgieter, 2011). These factors have hindered access to HIV care and support for many in the hardest hit communities in Africa. Facility based HCT has not kept up with the demand, creating several missed opportunities for linkage to care (Wanyenze et al., 2011). In Uganda, household member and door-door HIV testing strategies were able to reach the majority of previously untested individuals (>90% of all clients) (Menzies, 2009). Home based door-door HIV testing played a key role in reducing stigma, particularly in rural and some urban community settings of Uganda (Nuwaha, Kasasa, Wana, Muganzi, & Tumwesigye, 2012a; Sekandi et al., 2011). However, home based HIV testing may not be desirable for persons who may still be uncomfortable being tested by people known to them. Despite its efficiency, home

based door-door HIV testing is also labor intensive and requires vast resources that may not be available or sustainable in the long term. Disclosure and privacy concerns may also limit the scale up of such programs to reach entire communities.

Novel and efficient approaches like self-administered oral HIV testing have a potential to reach even more clients of previously unknown HIV status (Spielberg, Levine, & Weaver, 2004). Self-administered oral HIV testing has the potential to be of greater convenience, decreased stigma, heightened privacy and has been shown to be feasible in some African community settings (Choko et al., 2011). Since 2007, validation of HIV self-testing (HST) with an oral HIV test kit has been done successfully in settings of low developed countries like Malawi, Zimbabwe and India respectively (Choko et al., 2011; Pant Pai et al., 2007; Pascoe et al., 2009). To date, HIV self-testing has not been undertaken as a major HIV testing strategy by any of these national programs. Part of the concerns have related to the validity of the results in field settings (Campbell & Klein, 2006). In a literature review on HST in high income settings, accuracy of the oral HIV tests when supervised by clinicians is close to 99.9% but drops to 92.9% when used unsupervised or self-tested (Pant Pai et al., 2013). Till recently (July 2012) the oral HIV test kit was not approved by the US Food and Drug Administration (FDA) for home use until more favorable data on accuracy from wider programs was provided (McNeil, 2012). Approval for over the counter use will potentially increase access to HIV testing and hopefully entry into care.

It is unclear whether HST stimulates appropriate follow-up behavior, particularly in the case of self-administered, un-supervised oral HIV testing. Previous studies on other self-administered medical tests showed that respondents who had performed a self-test seemed to base their follow-up behavior on the result of the test (Ickenroth et al., 2010). After receipt of non-normal results, most self-testers sought medical care. Despite its potential, it is also not

clear how much HST will improve on the linkage to care, particularly in Ugandan settings. In a study that assessed linkage to care in well facilitated emergency departments in the USA, nearly half of their patients were not successfully linked to care within 30 days of an HIV diagnosis, though 80% of patients were ultimately linked to care within 1 year of the initial HIV diagnosis (Rothman et al., 2012). This was partially due to the costs linked to the HIV care to be received. In Africa, clients do not link quickly into care as a study in Rwanda showed, less than half of patients were not enrolled into care within 90 days of an HIV diagnosis (Kayigamba et al., 2012). The strategy used in HIV detection as well as availability of point of care CD4 testing (for ART eligibility) improves this linkage significantly (Jani et al., 2011).

Given this background, there are several but related questions this study will attempt to answer. These include but are not limited to:

1. Is self-administered HIV self-testing (HST) feasible among high risk yet hard to reach populations?
2. How accurate is self-administered un-supervised oral home HST in a population of lay users (including first time HIV testers) in Uganda compared to the current standard of care?
3. Is self-administered oral home HST testing a preferable HIV testing strategy as compared to the existing modes of HIV testing?
4. How does uptake and preference of self-administered oral HST differ by gender? Is it a potentially more successful strategy of reaching out to the males in particular?

Study Goal

The goal of this study is to increase access to HIV Testing by demonstrating the feasibility, accuracy and implementation effectiveness of self-administered (HST) compared to

the standard health worker (provider-administered) HIV testing methods using different delivery strategies in field settings of Uganda.

Specific Objectives

1. To determine the accuracy of self-administered HST in field settings in Uganda.

We hypothesized that the accuracy of unsupervised, self-administered HST done by lay users was non-inferior to provider-supervised, self-administered HST among high risk communities in Uganda.

2. To evaluate the respondent's preferences for HIV testing strategies in Uganda.

We hypothesize that based on differences in HIV test attributes like accuracy, timeliness, price, mode of HIV testing and sample collection, location, anonymity, privacy and confidentiality; respondents will prefer those test strategies that maximize their utility.

Study Justification

HIV self-testing has the potential to increase the privacy and confidentiality desired by many clients involved in HIV testing programs used by different strategies that target health facilities (Facility-based HCT), outreaches (mobile clinic HCT) as well as in the home (home-based testing, HBHCT) (Colfax et al., 2002). It may also contribute to increasing the number of first-time testers, as well as males who have not tested as much using current strategies. HST with Oraquick ® has a high positive predictive value in high prevalence settings (Pant Pai et al., 2012). If successfully used in high prevalence settings of sub-Saharan Africa, this strategy may result in a higher number of patients rapidly assessed for ART eligibility. The summary of few available data on access to and retention in care indicates substantial losses of patients between HIV testing and ART eligibility assessment, particularly among those in whom HIV test results

are not provided on the same day or time of testing (Rosen & Fox, 2011). HST also has a potential to be utilized repeatedly by clients (repeat testers), particularly those who feel that they have greater exposures or risks of acquiring the infection, as seen among fishing communities in Africa. However it is plausible that un-supervised HST use by lay users will be error prone and therefore be of lower accuracy than conventional testing methods. Use of un-supervised HIV self-test kits may also be abused by the locals, particularly those that may have disputes or domestic quarrels. It is also not clear how preferable such self-tests will be if available as options for HIV testing in rural settings of a high-risk population in Africa.

The extent to which the public health benefits of HIV self-testing can be realized after implementation is unknown, especially in community settings away from health facilities. This particular study will examine whether HIV tests done independently and anonymously (the oral HIV self-tests) in Ugandan community settings are accurate, and can increase the numbers of persons tested by eluding these barriers. The study will also examine user preferences for HIV testing including provider administered mobile or facility based standard HCT in field community settings.

CHAPTER 2

REVIEW OF THE LITERATURE: MANUSCRIPT 1 & 2

Background

Fairly early in the HIV epidemic, it was recognized that HIV testing had a key role in both identification of new cases of the disease as well as a preventive biomedical intervention. A large meta-analysis of 27 studies conducted between 1985 -1997 with outcome data on behavior before and after HIV testing determined that HCT is an effective secondary HIV prevention strategy since persons identified as positive subsequently reduced their sexual risk behavior (Weinhardt, Carey, Johnson, & Bickham, 1999). Compared to individuals who did not receive HCT, persons who were HIV negative did not modify their risk behavior, a finding that has been consistent with more recent studies (Kilian et al., 1999; Kirungi et al., 2006). The rationale for diagnostic testing gradually evolved, from clinical confirmation of suspected HIV disease to the potential for prevention and care afforded by knowing one's HIV status (Branson, 2000). HCT has now become increasingly important for HIV prevention due to recent advances in ART based HIV prevention (Table 1.1).

Recently, a series of randomized studies have been published that have generated new body evidence showing the promise of anti-retroviral therapy based HIV prevention. ARVs are used as topical or oral pre-exposure prophylaxis (PrEP) (Baeten et al., 2012; Grant et al., 2010; Thigpen et al., 2012), topically as vaginal/rectal microbicides (Abdool Karim et al., 2010), and for prevention of mother to child transmission (MTCT) (Guay et al., 1999). The discovery of several broadly neutralizing antibodies has also raised hopes for the development and production

of an effective HIV vaccine (Walker, 2009). For most of these interventions, first time and repeat HCT will be vital for both accesses to these programs, prevention of resistance, as well as for monitoring and evaluating their effectiveness in HIV prevention. HCT as a preventive strategy has been faced with several barriers that have limited universal access to other HIV preventive services.

Table 1.1: Potential intervention target and approaches for biomedical prevention of HIV

Target	Biomedical Intervention	Evidence
Microbial & Cellular Level		
HIV Viral Load	ART for prevention	RCT
	Pre-exposure prophylaxis (PrEP)	RCT
	Post-exposure prophylaxis (PEP)	Case-Control
	ART for Infected partner	RCT
	Microbicides	RCT
Co-infections	Prevention and Treatment	
	Genital Herpes	RCT
Host Defenses	Vaccines	RCT
	Male Circumcision	RCT
Individual & Local Community Level		
Sexual Behavior & Networks	Risk reduction approaches	
	Voluntary HIV counseling & Testing (VCT)	RCT
	Barrier Methods	Prospective
	Non-barrier methods	Cohorts

Barriers to Uptake of HIV Counseling and Testing

Expanding HIV testing requires a better understanding of the determinants to its uptake, particularly in sub-Saharan Africa where the epidemic is still raging. Previous studies have examined and identified determinants of HIV testing in various African countries and contexts (Cremin, Cauchemez, Garnett, & Gregson, 2012; Gage & Ali, 2005; Jean, Anglaret, Moh, Lert, & Dray-Spira, 2012; Koku, 2011; Ostermann et al., 2011; Sambisa, Curtis, & Mishra, 2010; Sherr et al., 2007; Wringe et al., 2008). These determinants can be enabling for HCT uptake or

barriers to HCT uptake depending on the community or population studied. Determinants related to access to HCT, self-administered testing (HST) and linkage to care remain highly variable, and largely misunderstood in resource limited settings. Access to HCT and patient confidentiality increased with initiatives like home-based HCT approaches (Njau, Watt, Ostermann, Manongi, & Sikkema, 2012; Tumwesigye, Wana, Kasasa, Muganzi, & Nuwaha, 2010). Risky sexual behaviors as well as stigma and discrimination were also shown to reduce significantly in these home-based HIV testing programs (Nuwaha, Kasasa, Wana, Muganzi, & Tumwesigye, 2012b). Inter-related structural and contextual factors like HCT program coverage, availability of adequate funding and health infrastructure indirectly affect the penetrance of HCT programs in sub-Saharan Africa, and in Uganda specifically. These can be enabling for HCT service provision where optimal. According to experts at the World Health Organization, these contextual factors have to be addressed by affected nations in order to significantly increase the uptake and coverage of HIV testing (WHO) (2007).

A demographic health survey (DHS) done in the west African nation of Cote d'Ivoire identified barriers associated with HCT done within the past 2 years to include being male, low socio-economic status, low HIV related knowledge and being employed (Jean et al., 2012). These findings are typical of many settings in sub-Saharan Africa where HIV prevalence is high. Higher socio-economic status and education have been consistent with a positive association with HIV testing across studies (Cremin et al., 2012; Gage & Ali, 2005; J. K. Matovu et al., 2005). Association with other individual characteristics including sexual behavior, knowledge and attitudes towards HIV/AIDS have been reported more inconsistently (Müller et al., 1992). This may imply that these associations vary according to epidemiological or social contexts, and perhaps gender especially in Uganda where partner consent for HIV testing is important (Homsy

et al., 2007). Determinants of HIV testing may also differ according to the HIV test strategy used, either as client initiated (VCT) or provider initiated opt-in or opt-out HIV testing approaches recommended by the World Health Organization ((WHO), 2007). Most studies do not account for the test strategy, and few have evaluated the feasibility of oral self-administered HIV testing in Africa (Choko et al., 2011; Pascoe et al., 2009; Zachary et al., 2012), with none in Uganda.

Despite these barriers, communities particularly those in rural areas have shown increased interest in having increased access to HIV testing programs, even if conducted by trusted community health workers (Kipp, Kabagambe, & Konde-Lule, 2002). A large randomized community-based intervention to increase HIV testing and case detection involving 16,129 people aged 16-32 years in Tanzania, Zimbabwe and Thailand respectively (NIMH Project Accept, HPTN 043) indicated a higher uptake of the community based intervention (CBHCT) compared to the standard of care - standard clinic based HCT (Sweat et al., 2011). Uptake of HIV testing was the secondary endpoint. They noted lower HIV case detection among 28% of repeat testers at CBVCT level, indicative of some behavioral reinforcement and potential prevention effect of a combination initiative. The authors claim this was based on self-report given that this was a program done in very rural areas in the three countries where HIV testing services were limited to the study program area. No other biomedical prevention methods were used in this study, like condoms and medical male circumcision.

Critical and effective biomedical HIV prevention methods with efficacy above 50% have a high potential to impact the population level HIV incidence (Table 1.2). Those with efficacy below 50% may need to be combined with other behavioral interventions, or other biomedical interventions to improve the overall protective effect against HIV. They are still vital,

particularly an HIV vaccine (therapeutic or preventive). Effective biomedical prevention modalities all require knowledge of HIV status to begin with.

Table 1.2: Efficacy of Key Biomedical HIV Prevention Strategies from Randomized Clinical Trials

Intervention	Study	Effect Size, % (95% CI)
ART	HPTN 052, Africa, Asia, Americas(Cohen et al., 2011)	96 (73 – 99)
PrEP	Partners PrEP Uganda, Kenya(Baeten et al., 2012)	73 (49 – 85)
PrEP	PrEP for Heterosexual Men and Women, Botswana(Thigpen et al., 2012)	63 (21 – 84)
Circumcision	MMC, Orange Farm SA, Rakai, Kisumu(Auvert et al., 2005; Bailey et al., 2007; Ronald H. Gray et al., 2007)	54 (33 – 66)
STI Treatment	STI Treatment; Mwanza, Tanzania(Hugonnet et al., 2002)	42 (21 – 58)
Microbicides	Microbicide Trial, CAPRISA 004, South Africa(Abdool Karim et al., 2010)	39 (6 – 60)
HIV Vaccine	RV 144 Vaccine Trial, Thailand(Rerks-Ngarm et al., 2009)	31 (1 – 51)

By and large, the literature was generally void of completed combination prevention studies of HIV biomedical prevention modalities, using the UNAIDS definition. However, several expert reviews and panels recommended them as the way forward, given that no single biomedical HIV prevention tool has been so successful in its entirety (De Cock, Jaffe, & Curran, 2011; Dieffenbach & Fauci, 2011; Hammer, 2011; Kurth, Celum, Baeten, Vermund, & Wasserheit, 2011). A large community randomized trial to assess the feasibility of a community-level HIV test, linkage to care, plus treat strategy in the United States (U.S.) is currently enrolling (HPTN065, 2010). This study involves several randomization levels at individual, site and the community; as well as biomedical, behavioral and structural interventions that will examine feasibility and effectiveness outcomes.

Despite the enormous logistical and efficacy challenges, there have been calls for scale-up of combination prevention interventions, beginning with HIV testing (Kurth et al., 2011). Due

to the time that elapses before results of conventional lab-based HIV tests are available, providing patients or clients with their test results can be cumbersome and resource intensive for screening programs. Subsequently, rapid tests were developed to reduce the test-result wait time. They have been used successfully in various screening programs across Africa. However, positive rapid HIV test results are preliminary and must be confirmed using external positive and negative controls before the diagnosis of HIV infection is established (Greenwald, Burstein, Pincus, & Branson, 2006). However their use in screening programs has been successful due to the cheap cost, fairly high accuracy when used by trained personnel and a quick turnaround time (for results). Questions regarding the validity of rapid tests remain, particularly if used unsupervised in populations of varying prevalence of the disease.

Validity of HIV Self-Testing (HST)

Rapid HIV tests (defined as HIV tests that provide results within 20-60 minutes) were first approved by the US Food and Drug Administration (FDA) in 2002, specifically the OraQuick® Rapid HIV-1 Antibody Test (OraSure Technologies, Inc., Bethlehem, Pennsylvania). This was approved for use by trained personnel as a point-of-care test to aid in the diagnosis of infection with human immunodeficiency virus type 1 (HIV-1). Subsequently, various types and brands of rapid tests have been approved and used in various serial and parallel test algorithms by several countries affected by the HIV epidemic. These tests used whole blood specimens from finger pricks, as well as oral fluid with fairly good validity as indicated in post-marketing surveillance done between 2004 and 2005 (Wesolowski et al., 2006). During this period, 135,724 whole blood and 26,066 oral fluid rapid tests respectively were conducted. The median health department whole blood OraQuick sensitivity was 99.98% (range: 99.73-100%) and Positive

Predictive Value (PPV) was 99.24% (range: 66.67-100%); the median oral fluid specificity was 99.89% (range: 99.44-100%) and PPV was 90.00% (range: 50.00-100%). Another study conducted by CDC evaluating the performance of OraQuick® rapid tests for whole-blood and oral fluid established that slightly more false-positive and false-negative results occurred with oral fluid samples than with whole blood, but performance with both specimen types was similar to, or better than, that of conventional lab based Enzyme Immuno Assays (EIAs) (Delaney et al., 2006). Use of oral swabs for HIV testing with lower specificity may have implications for countries with low HIV prevalence.

In the United States, the Food and Drug Administration (FDA) approved the first HIV self-testing kit in 1996 (Ganguli, Bassett, Dong, & Walensky, 2009). However, the test was only indicated for use clinically along with other tests due to concerns on its validity. This diagnostic technology improved over time resulting in the recent FDA approval for the over the counter HIV In-Home oral self-test kit (Food and Drug Administration, 2012). In-Home HIV tests are less sensitive than current HIV blood tests in clinical settings; particularly HIV-1/2 enzyme immunoassays (EIA) with confirmatory western blot testing. Sensitivity and specificity of Oraquick® in-home unobserved self-administered HIV tests determined in a large phase III trial of 5,662 people (80% of whom were at risk of HIV) tested concurrently with the gold standard blood tests was 92.9% and 99.9% respectively (OraSure Technologies, 2012). The test identified 106 positive out of 114 patients with a positive test on blood testing; and gave a negative result in 5,384 of 5,385 patients with a negative result on blood testing. Hence a positive in-home test result is likely to be truly positive, but a negative result is not as reliably truly negative. With the fairly low sensitivity, false negatives may occur particularly in the window period early in HIV infection. However, since the predictive value of the test depends on the prevalence of the

disease in the population being tested as well as the patients' pre-test probability of disease at the time of testing, the utility of the oral self-administered test is likely to be high as a screening test in Uganda where the general population prevalence is high. The test may also be useful in screening high-risk groups like fisherfolk with its qualities of anonymity and privacy (Kissling et al., 2005).

Several studies have been done in clinical settings to validate supervised use of the HIV oral self-test, specifically the OraQuick® InHome HIV1/II test as well as related oral rapid tests for HIV. Below is a summary of the findings (Table 1.3).

Table 1.3: Sensitivity of Oral HIV testing

Study	Sample Size (N)	Country	Sensitivity (95% CI)
Pant Pai et al. (2007)	450	India	100 (98 -100)
Pascoe et al. (2009)	591	Zimbabwe	100 (97.9 – 100)
Choko et al. (2011)	260	Malawi	99.2 (97 – 100)
Ng et al. (2012)	994	Singapore	97.4 (95.1 – 99.7)
Zachary et al. (2012)	4,458	Zambia	98.7 (97.5 – 99.4)

All the above were cross-sectional studies where use of the test was supervised. The Indian study was conducted among hospital patients. For most of the studies above, specificity was high, mostly close to 100%. Other blood-based rapid HIV test kits whose interpretation of positive bands is also subjective, were found to have low specificity and predictive values of 94.1% and 74% respectively in a large validation study conducted in Rakai, Uganda (Ronald H Gray et al., 2007). Due to this, most rapid assays including the oral home self-test will require confirmation using a more specific test, like an enzyme immune-assay (EIA) or western-blot. This could also be for quality control if used in large screening programs. Due to some of these concerns, the self-administered oral test has also been suggested to play a limited role as an alternative to HIV screening in professional settings in developed countries (Paltiel & Walensky,

2012). Among developing countries like Uganda where access to professional settings and facilitation are limited, the role of self-testing may be more positive in increasing uptake and coverage of HIV testing.

By and large, rapid HIV tests have fairly high accuracy comparable to standard lab based tests that makes them useful for screening large populations, particularly in high HIV prevalence settings in Africa. Self-testing has the potential to increase uptake, however feasibility may differ from setting to setting. More evidence is needed in this area, particularly to determine whether the new technologies can work in unsupervised field settings of Uganda.

Preferences for HIV testing

Scaling-up of health services has two facets- one is 'extending the availability of cost-effective interventions' to the population (coverage) and the other is 'increasing the level of demand' for these services (uptake) (Pokhrel, 2006). Despite improved supply of HIV health care services in low-income countries in the recent past, their uptake continues to be lower than anticipated. According to the 2006 Uganda Demographic Health Survey (UDHS) report, only one-quarter of women (25%) and one-fifth of men (21%) aged 15-49 have ever been tested for HIV and received their results (Uganda Bureau of Statistics, 2007). This has made it difficult to scale-up those interventions which are not only cost-effective from supply perspectives but that might have substantial impacts on improving the health status of these countries. Understanding demand-side barriers that hamper uptake is therefore critically important.

One of the ways of understanding uptake is to analyze individual preferences. The extent of patients or clients preferences in medical decision making has been traditionally minimal, particularly in Uganda where most HIV programs are heavily subsidized by the Ugandan

Government (Ministry of Health, MOH) and relevant development partners like the US Centers of Disease Control & Prevention (CDC), United States Agency for International Development (USAID), the US Presidential Emergency Plan For AIDS Relief (PEPFAR) as well as other related sub-partners and multilateral organizations. Subsequently, community participation, uptake and sustainability of many HIV programs has become a significant challenge, even as funding for these has not increased in the past decade (Geng et al., 2010). Greater involvement of patients and communities in choosing their health services has been advocated for, particularly in those nations with predominantly public funded health programs (Florin & Dixon, 2004). Elicitation of patients and community values and preferences represents a key step in enhancement of benefits of HIV testing service provision.

Understanding how patients (clients) perceive the benefits of a service or program features and their tolerance for possible risks requires a valid and reliable measurement method. Stated Choice (SC) methods, also called Discrete Choice Experiments (DCEs) or Conjoint Analysis are reportedly the most valid and reliable for quantifying patient preferences (Maddala, Phillips, & Reed Johnson, 2003; M. Ryan et al., 2001). The discrete choice experiment was developed as a survey method of data collection and analysis to elicit and study patient or community preferences to a good or service, which could include HIV testing services. These methods are used to study consumer product or service preference and simulate consumer choice. SC methods recognize that products have value because of their characteristics (or attributes). People have preferences for each attribute and are willing to accept tradeoffs among different attributes. SC analysis examines these trade-offs to assess the weight people assign to various service attributes. Analysts have used SC methods to quantify preferences for a variety of market and non-market goods and services e.g. health care (Mandy Ryan & Farrar, 2000),

medical programs and interventions (J. Hall, Viney, Haas, & Louviere, 2004), immunization participation rates (Jane Hall et al., 2002), vaccine acceptance programs (S. J. Lee, Newman, Comulada, Cunningham, & Duan, 2012), pharmaceutical treatment programs (M. Ryan & Gerard, 2003) and even HIV testing (Phillips, Maddala, & Johnson, 2002). In the latter study, the first of its kind to evaluate preferences for HIV testing using SC methods, the authors surveyed 365 respondents from 4 publicly funded HIV testing locations in San Francisco, CA, USA and were able to show that based on what they valued, their respondents were willing to pay additional fees for immediate, highly accurate results.

Summary and Gaps in Knowledge

Since most countries and communities differ in the way they have responded to HIV testing, it is clear from the above studies that self-administered testing will be received positively in low resource settings of Africa. Fairly high acceptability of HCT has been documented in Uganda, however given the cost of the tests and diminishing donor funding for HIV programs, it isn't clear whether clients in sub-Saharan Africa will be in position to purchase HIV tests, more so HIV self-tests outside of subsidized HIV program settings. From the studies cited above, it was not clear whether unsupervised HST can produce accurate results from lay users in the general population. Most studies do not assess consumer preference for HIV test strategy, hence there is no data on whether self-testing could be preferable to the existing modes of testing, more so in Uganda.

CHAPTER 3

METHODS

This section provides a summary of the methodology and procedures used in both studies described in sections 4 and 5.

Study Design

We utilized two different epidemiological study designs to answer the main objectives of this study. We conducted an individually randomized, non-inferiority effectiveness study, with an embedded preference cross-sectional survey among population-weighted HIV-1 at-risk individuals in three fishing communities around Lake Edward, western Uganda (Figure 3.1).

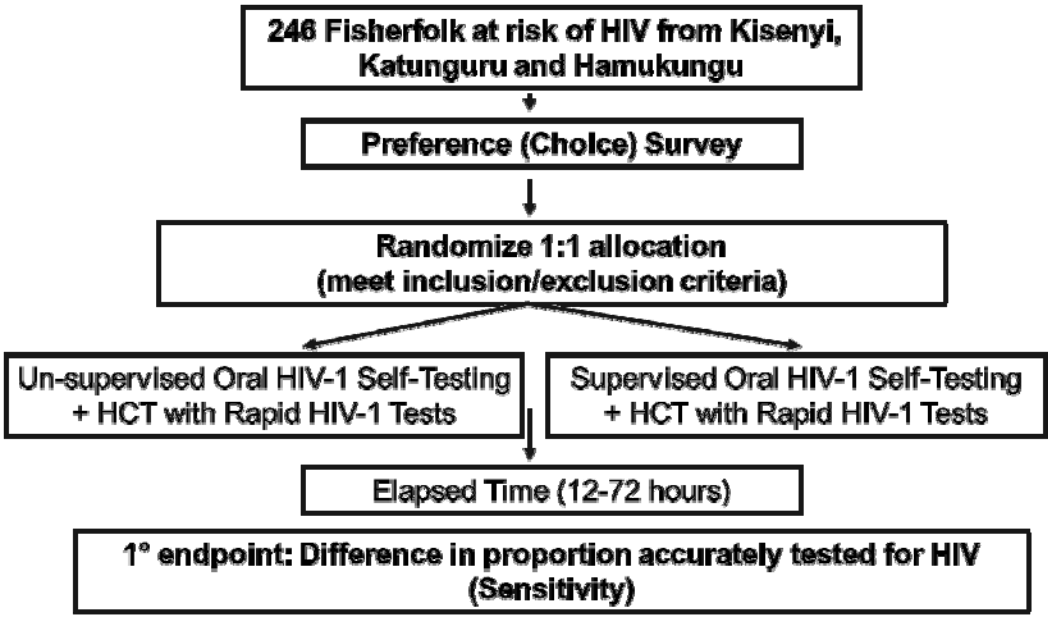


Figure 3.1: Overall Study Design

Each at-risk individual who agreed to participate in the study was surveyed on their HIV test preferences before being randomized using concealed allocation to one of two HIV testing arms:

un-supervised HST followed by rapid HIV testing OR supervised HST (also followed by rapid HIV testing) for confirmation.

Study Population

The studies were conducted in three large fishing communities that live around the landing sites of *Kisenyi*, *Katunguru* and *Hamukungu* fishing villages in Rubirizi and Kasese districts of Uganda respectively (Figure 3.2).

Figure 3.2: Study Areas in South-Western Uganda

Kisenyi fishing village lies on the shores of Lake Edward, whereas *Hamukungu* lies on the shores of Lake George. *Katunguru* village is in between the two; along a channel that connects the two lakes. The *Katunguru* fishing village is also located close to a major highway that crosses through this region to the western part of Uganda and onwards to the Democratic Republic of the

Congo (DRC). These villages are remote and fairly isolated from each other. Some members of these communities participated in a community wide home based HIV testing program in 2004 - 2007 and are familiar with some of the strategies of HIV testing available in Uganda (Tumwesigye et al., 2010). These communities also showed existence of several risk factors for HIV, with a high burden of HIV infection. These communities also lie in the area several HIV discordant couples were recruited to participate in the *gates funded(BMGF)* partners PrEP trial that was recently concluded at Kabwohe Clinical Research Center, KCRC (Baeten et al., 2012). Our study recruited 246 HIV high risk persons aged 18 to 49 years at enrolment, resident or working in these fishing communities that satisfied the study eligibility criteria described below.

Inclusion and Exclusion Criteria

We included individuals who met the following criteria: Those who had 18 to 49 completed years of age at enrollment; capable and willing to provide written informed consent for participation and HIV testing (literacy was not required); resident or working in the study community for at least 3 months prior to study enrolment; willing to undertake HIV testing, receive results and also provide a blood sample; able and willing to provide adequate locator information for immediate tracking purposes by the study staff within 12 - 72 hours of the study.

Being at risk of HIV infection was defined by at least one of the following characteristics: Reported symptoms of Sexually Transmitted Infections (STI) in the previous 3 months; unprotected sexual intercourse with more than one partner and/or new partners in the past 3 months; is a commercial sex worker or had sexual intercourse with a commercial sex worker in the past 3 months and being in a discordant relationship (partner is HIV infected).

We excluded individuals who reported no sexual activity in the previous 3 months and those with a known HIV status (or reported to have had an HIV test within the previous 12 months).

Sample Size Determination

The sample size was calculated to detect non-inferiority at 95% sensitivity of self-testing in the provider supervised HIV self-testing arm with a non-inferiority margin of - 15%, a 10% significance, and 95% power. A total sample of 220 participants was calculated, although we enrolled an adjusted sample of 246 participants giving us greater than 95% power to detect non-inferiority, defined as a difference in sensitivity of – 15% using a one-sided asymptotic wald test. The non-inferiority limit was conservatively set at -15%, guided by summarized findings of the few studies that examined accuracy of self-tests among lay users in field settings (Napierala Mavedzenge, Baggaley, & Corbett, 2013).

HIV testing programs in Uganda are supported through donor funding, mainly the US Presidential Emergency Plan For AIDS Relief (PEPFAR, 2010), as well as contributions from tax incomes (for the Uganda Ministry of Health). Hence the opportunity cost is the alternative use of these taxes or donor funds for HIV programming. We will be interested in *ex post* preferences; hence users of the HIV tests (the goods/services) are appropriate for determination of preference data. Therefore for this DCE study, all members of the general population who consented to take part in this study before randomization were all eligible and appropriate to be surveyed. We determined that the minimum sample size determined for the randomized component above (N=246) was sufficient enough to generate valid and reliable model estimates of choice.

Participant Recruitment and Data Collection

The study proposal was presented to the Community Advisory Board of Kabwohe Clinical Research Centre (KCRC) as the major stakeholders of community based research in the study area. Thereafter all community owned resource persons (CORP's) in the chosen fishing communities were informed of the study and opportunity for HIV screening through existing village-based community sensitization and mobilization meetings. Interested potential participants could access the study camp set up in central or strategic locations in their communities where more study information was provided and study procedures done systematically (Table 3.1).

Table 3.1: Summary of Study Procedures

	S	E
ADMINISTRATIVE AND REGULATORY PROCEDURES		
Obtain informed consent	X	X
Apply inclusion/exclusion criteria	X	X
Collect/update locator information	X	X
DEMOGRAPHIC AND PREFERENCE DATA COLLECTION		
Collect demographic information (Baseline Questionnaire)	X	X
Administer HIV-Test Questionnaire		X
Conduct Preference Surveys		X
COUNSELING		
Provide HIV-1 pre and post-test counseling		X
Risk reduction counseling and condom promotion	X	X
Referral for care if test positive		X
CLINICAL PROCEDURES		
Conduct HIV tests, provide HIV-1 test results		X
STI syndromic assessment and referral (where necessary)		X
LABORATORY PROCEDURES		
HIV-1 serology (rapid tests and, if positive, Western Blot)		X

S – Screening E – Enrollment

Face to face interviews were used to collect the effectiveness trial data, whereas the preference survey was computer administered, with the researcher reading the information with the participant from choice sets predetermined on questionnaires uploaded onto the computer.

Human Subject's Considerations

All participants were provided with information that participation was voluntary. After signing the consent document, consenting participants were given a copy of the consent form/information sheet translated in local language used in the communities (Runyankore). Participants had the right to refuse to participate or to withdraw from the study at any time without loss of any services or benefits. All study information was kept strictly confidential under locked filing cabinets and password protected database files that were only accessed by the Principal Investigator. Case record forms (CRFs) were kept with only participant identification numbers. The identifier page was detached from the CRFs.

The risks of the OraQuick® In-Home HIV self -test arise primarily from false negative and false positive test results. One false negative result would be expected to occur out of approximately every 12 test results in HIV infected individuals. This could potentially delay an individual's access to medical treatment and may falsely reassure an individual about engaging in risky behavior. Lack of awareness of an HIV infection may put others at risk for disease transmission. It is estimated that one false positive test result would be expected out of every 5,000 test results in uninfected individuals. False positive test results can also cause unnecessary emotional distress. To reduce these risks to our participants, the oral HIV test was followed by confirmatory HIV testing for ALL participants.

There was no compensation provided for participating in this study. The study was reviewed and approved by the National AIDS Research Committee (NARC) Institutional Review Board (IRB) of the Uganda National Council for Science and Technology (UNCST), approval ID number HS 1409. This study also underwent expedited review and approval by the University of Georgia IRB.

CHAPTER 4

ACCURACY OF UN-SUPERVISED VERSUS PROVIDER-SUPERVISED SELF-ADMINISTERED HIV TESTING IN UGANDA: A RANDOMIZED IMPLEMENTATION TRIAL[1]

[1] Stephen Asiimwe, James Oloya, Xiao Song, Christopher C Whalen. Submitted to *AIDS and Behavior*, 10/31/2013.

Abstract

Unsupervised HIV self-testing (HST) has potential to increase knowledge of HIV status; however, its accuracy is unknown. To estimate the accuracy of unsupervised HST in field settings in Uganda, we performed a non-blinded, randomized controlled, non-inferiority trial of unsupervised compared with supervised HST among high-risk fisherfolk in three fishing communities in Uganda between July and September 2013. The study enrolled 246 participants and randomized them in a 1:1 ratio to unsupervised HST or provider-supervised HST. In an intent-to-treat analysis, the HST sensitivity was 90% in the unsupervised arm and 100% among the provider-supervised, yielding a difference 0f -10% (90% CI: -21%, 1%); non-inferiority was not shown. In a per protocol analysis, the difference in sensitivity was -5.6% (90% CI: -14.4, 3.3%) and did show non-inferiority. We conclude that unsupervised HST is feasible in rural Africa and may be non-inferior to provider-supervised HST.

Introduction

Knowledge of one's HIV status is a critical step in the path toward HIV prevention and care. Despite the advances made in the field of HIV prevention and care, many people cannot access these services because they are unaware of their HIV serostatus. In sub-Saharan Africa, it has been an estimated that 36% of people have never been tested for HIV (UNAIDS, 2013). Uganda is reported among the countries where lack of knowledge of HIV status is the limiting factor to getting people into prevention and care programs (UNAIDS, 2013). Traditionally, HIV counseling and testing (HCT) has been administered by health care providers in the clinic, home-based and mobile HCT outreaches. The effectiveness of these strategies has been hampered by barriers like the lack of privacy, stigma, disclosure issues, poor male involvement, as well as long distances to health facilities (Bajunirwe & Muzoora, 2005; Emmanuel Mugisha et al., 2010; Wanyenze et al., 2011).

A more effective response to the global HIV epidemic necessitates alternative and multiple strategies to improve on knowledge of HIV serostatus. Novel and efficient approaches like oral HIV Self-Testing (HST) provides promising alternatives to clinic and provider-based HIV screening programs. Self-testing has the potential to reach more clients of previously unknown HIV status (Choko et al., 2011; Spielberg et al., 2004).

Although oral self-testing has been promising in some settings, its effectiveness has not yet been established, especially in the setting of developing countries with high HIV prevalence. Studies conducted among health workers in Kenya (Kalibala S, 2011) and an urban population in Malawi (Choko et al., 2011) found HST feasible, but the accuracy of HST among lay users remains a concern (Napierala Mavedzenge et al., 2013). This concern is especially acute in field

settings in rural populations where lay persons lack familiarity with medical devices (Lemke & Mendonca, 2013). Despite its potential, the accuracy of self-testing in un-supervised, field conditions in a high HIV risk population is unknown.

To estimate the accuracy of un-supervised, self-administered oral HIV self-testing in field settings, we performed a non-blinded, randomized controlled, non-inferiority trial among high-risk fisherfolk in three fishing communities in Uganda.

Methods

Study Participants

The study was conducted between July 10 and September 13, 2013 in three fishing communities around Lake Edward, western Uganda. Research assistants screened local residents who presented to the research camp for HIV testing. These individuals were eligible for the study if they were between 18-49 years, at high risk for acquiring HIV infection, and lived or worked in the study community for at least 3 months prior to enrollment. High risk for HIV infection was defined as sexually active clients with: a history of unprotected sexual intercourse with one or more partners, new sex partners in the past 3 months, symptoms of sexually transmitted infections (STIs) in the same period, commercial sex activity, or being in a known HIV discordant partnership. We excluded clients who did not report sexual activity (in the past 3 months) or did not consent to HIV testing and provision of blood samples for HIV confirmation. All participating clients provided written, informed consent and received adequate pre and post-test HIV counseling and referral services.

Randomization

Eligible participants were randomly assigned to one of two testing groups (Figure 4.1): unsupervised oral HST followed by rapid HIV testing OR provider-supervised oral HST followed by rapid HIV testing. Randomization was stratified by fishing village and done with a 1:1 ratio. The random allocation schedule was computer-generated using *Stata® version 11*. The individualized assignment code sheets were placed in opaque, individualized, sealed envelopes, which were stacked in batches of random blocks with uneven block sizes not exceeding 8 assignments. At the time of enrollment, each participant would select a sealed envelope in consecutive order and open it to reveal the testing assignment. Because of the nature of HIV testing, study participants and study personnel could not be blinded to the intervention. However, steps were taken to reduce reporting bias by ensuring that the interviewers were unaware of the HIV testing results at the time of the exit interviews and by blinding the laboratory staff to the viral and molecular endpoints.

Study Procedures

All enrolled participants received pre-test HIV counseling and a brief, 10 minute demonstration of how to use the oral self HIV test kit. In the provider-supervised oral HST arm, research staff (i.e., the provider) supervised the participant performing the oral HIV self-testing in the research clinic; once this test was completed and the client had recorded the result, a confirmatory HIV test was performed along with an exit interview. In the unsupervised HST arm, clients performed the oral HIV self-testing in private without supervision from the provider. Participants were asked to conduct the self-test at home (or in a convenient private location), develop and read the results guided by the illustrated instructions, and then return to the researcher within 12 - 72 hours for a confirmatory rapid HIV assay and an exit interview.

Subjects who completed the unsupervised oral HST were asked to interpret and record their results as one of three outcomes: may have HIV/preliminary positive; don't have HIV/preliminary negative; and test not working/invalid.

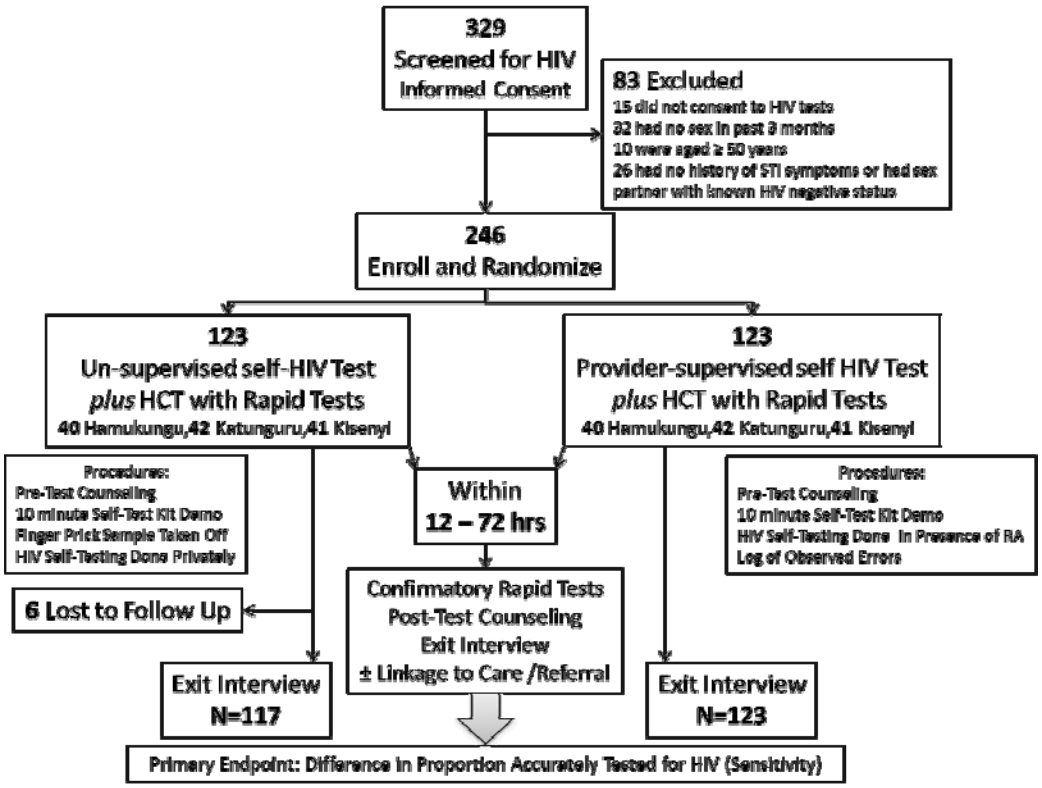


Figure 4.1: Enrollment and Randomization

The oral HIV self-testing was done using the *OraQuick® lnHome Rapid HIV-1/2 Antibody Test* (orasure technologies) self-test kit according to manufacturer's instructions. Clinic-based HIV testing was done using a serial algorithm of rapid HIV assays that is standard of care and approved by the Ugandan Ministry of Health. The algorithm included *Determine* (Abbot Laboratories), *STAT-PAK* (Chembio Diagnostic Systems Inc) and *Unigold* (Trinity Biotech plc) as tie breaker (Galiwango et al., 2013). For quality control, all HIV seropositives and 10% of HIV seronegative samples were retested with Western Blot and HIV p24 ELISA at

the MBN Molecular Laboratory in Kampala. Proper pre and posttest counseling was provided to all study volunteers so that they understood that ALL positive oral HIV test results will be subject to confirmation, both in the field and at the MBN molecular reference laboratory.

Research assistants were trained on the specific procedures included in this protocol. As part of assuring quality of HIV testing, we assessed inter-rater reliability of the three research assistants using known HIV seropositive and seronegative samples. The Cohens kappa statistic estimated to evaluate the reliability of test administration across the research assistants was high (κ=0.989, p = 0.00).

The exit questionnaire was administered after all testing was done. It assessed some secondary study outcomes such as performance errors, requests for help, and linkage to care.

Study Outcomes

The primary outcome was the difference in accuracy of HST, comparing the unsupervised testing to the provider-supervised HIV testing. Accuracy in this analysis is defined as the sensitivity of the diagnostic test. We estimated the sensitivity, specificity as well as positive and negative likelihood ratios, comparing the oral HIV self-test to the current Uganda National standard of HIV screening (rapid HIV testing in such field conditions).

Secondary outcomes included difference in accuracy among first time and repeat HIV testers; the observed and reported error rates; proportions who requested for extra help with the test beyond the standard pre-test demonstration; return for test result revalidation and exit interviews; and finally linkage to HIV prevention, treatment and care services. We determined the above secondary outcomes as our measures of implementation effectiveness of oral self HIV

testing compared to the standard of care (rapid provider administered testing) conducted in field conditions of Uganda.

Statistical analysis

We used a one-sided design to test non-inferiority between groups; specifically to test the hypothesis that the accuracy of unsupervised self-administered HIV testing is objectively non-inferior to that of provider administered testing in field settings of Uganda. To reduce variability between subjects, conditional tests were employed to evaluate the differences in accuracy between the new and standard diagnostic procedures since tests conducted on the same subjects are correlated.

The sample size was calculated to detect non-inferiority at 95% accuracy of self-testing in the provider supervised HIV self-testing arm with a non-inferiority margin of - 15%, a 10% significance, and 95% power. A total sample of 220 participants was calculated, although we enrolled an adjusted sample of 246 participants giving us >95% power to detect non-inferiority, defined as a difference in sensitivity of – 15% using a one-sided Wald asymptotic test. The non-inferiority limit was conservatively set at -15%, guided by summarized findings of the few studies that examined accuracy of self-tests among lay users in field settings (Napierala Mavedzenge et al., 2013). Data were entered (after consistency checks and cleaning) into a Microsoft Access (version 2010) database using Epi-Info™ 7, then exported to Stata® (version 11) and SAS® (version 9.3) for analyses.

The primary analysis was by intention to treat (ITT), including all participants in their randomized group. We assumed that the clients who had oral HST and didn't return for re-validation of their results were HIV negative. For the analysis of the primary study outcome, we compared the differences in the sensitivity and specificity within individuals between the two

arms. Sensitivity was defined as the conditional probability that the oral HST was positive given that the standard rapid HIV test algorithm was also positive. Specificity was defined as the conditional probability that the oral HST was negative given that by the standard rapid HIV test algorithm was also negative. A one sided Wald asymptotic test was used to assess for non-inferiority. The confidence interval for the difference was based on the Wald asymptotic method, at an alpha level of 0.05 corresponding to 90% confidence limits. Because 6 participants from the self-administered arm failed to return to report results and complete an exit interview, we performed a per-protocol analysis in which the data from these participants were removed from the analysis.

No compensation or incentives were provided for participating in this study. This trial was approved and registered by the University of Georgia IRB, the Uganda National AIDS/HIV Research Ethics Committee (NARC) and the Uganda National Council of Science and Technology (UNCST) respectively, ID number HS 1409.

Results

Of 329 screened participants, 246 (74.5%) were enrolled, with 83 ineligible on basis of consent, age, and low risk for HIV (Figure 4.1). The two study groups were similar in terms of age, sex, marital status, education, monthly income, HIV transmission risk, and previous testing for HIV (Table 4.1). The study population was predominantly male, currently married or married in the past, and had less than primary school education. Less than half of the participants had tested for HIV in the past 12 months, but nearly 80% had tested at some point in the past. The group had evidence of high risk behaviors. Most participants did not have a regular sex partner and did not use condoms. Over half had signs of STI within the past 3 months.

Table 4.1: Baseline Characteristics of Study Participants by Study Arm

Participant Characteristics	Unsupervised Oral Self HIV Test N=123	Provider Supervised Oral Self HIV Test N= 123	p-value	Total, N (%)
Sex – no. (%)				
Male	64 (52.1)	77 (62.6)	0.1217	141 (57.3)
Female	59 (47.9)	46 (37.4)		105 (42.7)
Age (Median IQR)	28 (23-32)	27 (22-32)	0.2865	28 (23 – 32)
Marital Status – no. (%)				
Never Married	20 (16.3)	28 (22.8)	0.1322	48 (19.5)
Currently Married	63 (51.2)	68 (55.3)		131 (53.3)
Ever Married	40 (32.5)	27 (21.9)		67 (27.2)
Education - no. (%)				
No Education	78 (63.4)	63 (51.2)	0.1142	141 (57.3)
Primary Complete	15 (12.2)	24 (19.5)		39 (15.9)
Lower Secondary	17 (13.8)	26 (21.1)		43 (17.5)
Post-Secondary	13 (10.6)	10 (8.1)		23 (9.4)
Monthly Income (USD§, Median IQR)	23.6 (7.9 – 59.0)	35.4 (11.8 – 59.0)	0.2362	31.5 (17.9 – 59.0)
HIV Transmission Risk Factor				
Non Regular Sex Partner (n, %)				
None	74 (60.7)	79 (64.2)	0.4209	53 (62.4)
1	38 (31.2)	30 (24.4)		68 (27.8)
> 1	10 (8.2)	14 (11.4)		24 (9.8)
Condom Use with non-regular sex partners (n/N, %)				
0	30 (69.8)	34 (84.9)	0.3542	64 (76.2)
≥ 1	13 (30.2)	7 (17.1)		20 (23.8)
Sexually Transmitted Infection in past 3 mo				
Present	68 (55.3)	70 (56.9)	0.7972	138 (56.1)
Absent	55 (44.7)	53 (43.1)		108 (43.9)
Circumcision Status (Men Only, N=141; no/total number, %)				
Circumcised	36/65 (55.4)	49/76 (64.5)		85/141 (60.3)
Non-Circumcised	29/65 (44.6)	27/76 (35.5)	0.2276	56/141 (39.7)
HIV Test in past 12 Months (n, %)				
Yes	58 (47.9)	49 (39.8)	0.2025	107 (43.9)
No	63 (52.1)	74 (60.2)		137 (56.2)
HIV Test Preference of Rapid Test (n, %)				
Finger Prick Sample	18 (14.6)	16 (13.0)	0.729δ	34 (13.8)
Oral (Mouth) Sample	63 (51.2)	72 (58.5)		135 (54.9)
Blood Sample (Venipuncture)	39 (31.7)	33 (26.8)		72 (29.3)
Urine Sample	3 (2.4)	2 (1.6)		5 (2.0)
Would You Buy Oral-Self HIV Test Kit if Locally Available?				
Definitely Yes	84 (68.3)	95 (77.2)	0.466δ	179 (72.8)
Probably Yes	30 (24.4)	21 (17.1)		51 (20.7)
Maybe	5 (4.1)	2 (1.6)		7 (2.9)
Probably Not	3 (2.4)	3 (2.4)		6 (2.4)
Definitely Not	1 (0.8)	2 (1.6)		3 (1.2)
At What Cost Would You Find It Affordable?				
USD (Median, IQR)	1.9 (0.8 – 1.9)	1.9 (1.2 – 3.9)	0.8562	1.9 (0.8 – 3.9)

δ - Fishers exact 2-sided test. § - 1USD ($) is equivalent to 2,543 Uganda Shillings (UGX), September 2013

All participants perceived themselves at risk for HIV infection with 57 (46.3%) reported high-risk, 32 (26.0%) medium risk, 22 (17.9%) low risk, and 12 (9.8%) perceived themselves at no risk for HIV acquisition at all. There were no differences in HIV risk perception across study arms (p=0.276).

Table 4.2: Diagnostic Accuracy of Oral Self-HIV Testing (Rapid HIV Testing as Gold Standard)

Participant Characteristics	Unsupervised Oral Self HIV Test N=123	Provider Supervised Oral Self HIV Test N= 123	P value	Total N (%)
HIV Test Results				
Oral Self HIV Test[¶] (n=240)				
Positive	18 (15.4)	13 (10.6)	0.2945[δ]	31 (12.9)
Negative	98 (83.8)	109 (88.6)		207 (86.3)
Indeterminate	1(0.8)	1 (0.8)		2 (0.8)
Rapid HIV Testing				
Positive	20 (16.3)	13 (10.6)	0.2615	33 (13.4)
Negative	103 (83.7)	110 (89.4)		213 (86.6)
Indeterminate	-	-		-

δ - Fishers exact 2-sided test. ¶ - 6 participants had no results

Sensitivity: (31/33)100 = 93.9% (78.4 - 98.9)

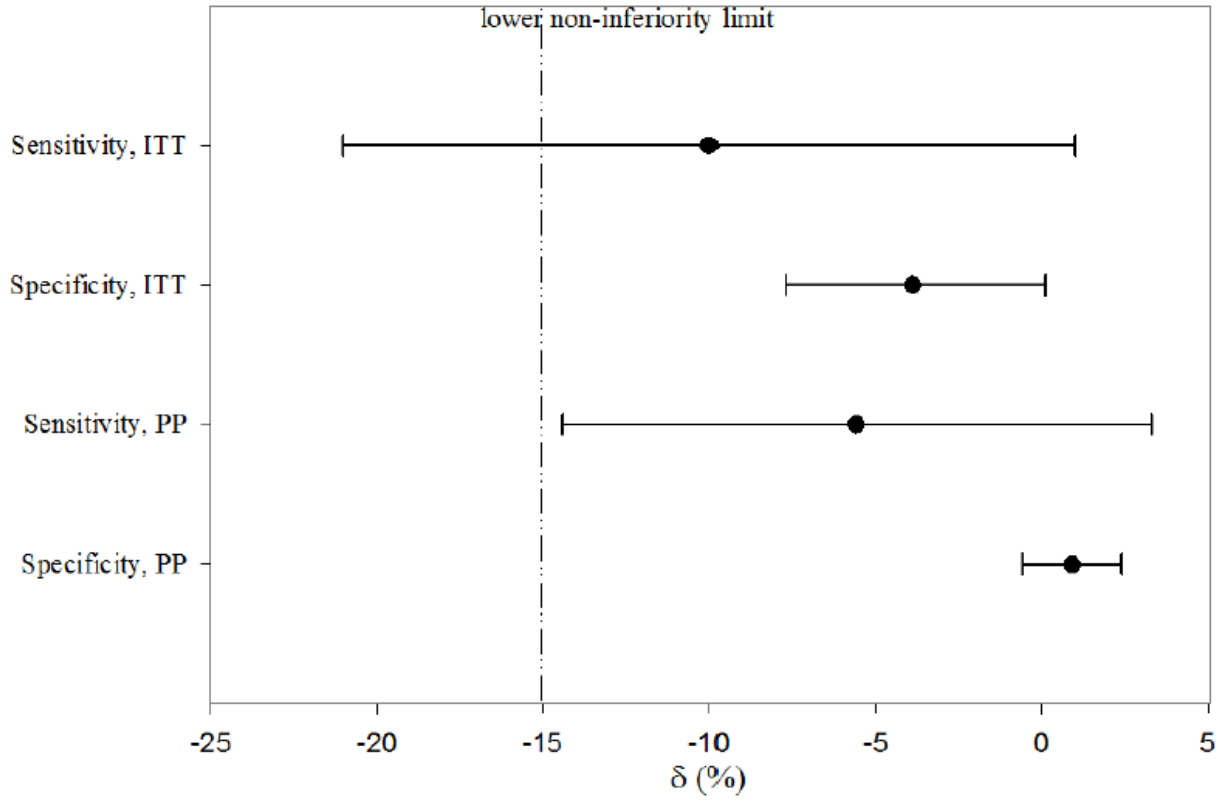
Specificity: (207/213)100 = 97.2% (93.9 – 98.9)

Positive Likelihood Ratio: 100 (25.1 – 398.5)

Negative Likelihood Ratio: 0.06 (0.02 – 0.23)

All 246 HIV tests conducted were included in the primary intent to treat (ITT) analysis (Figure 4.2). Overall, using the oral HIV self-test, 18 participants (15.4%) tested positive for HIV infection in the self-administered arm whereas 13 tested positive (10.6%) in the provider-supervised arm. Using the rapid HIV test algorithm, 20 participants (16.3%) tested positive for HIV infection in the self-administered arm whereas 13 tested positive (10.6) in the provider-

supervised arm. The sensitivity and specificity of the oral HIV self-test was 93.9% and 97.1%, respectively, in the self-administered arm (Figure 4.2), whereas the sensitivity and specificity were 100% and 99.1%, respectively, in the provider supervised arm. The prevalence of HIV infection did not differ by study arm (p = 0.26).



	Unsupervised Self-Test % (95% CI)	Supervised Self-Test % (95% CI)	Difference % (90% CI)
Sensitivity, ITT	90.0 (68.3, 98.8)	100 (75.3, 100)	-10 (-21, 1)
Specificity, ITT	95.2 (89.0, 98.4)	99.1 (95.0, 99.9)	-3.9 (-7.7, 0.1)
Sensitivity, PP	94.4 (72.9, 99.9)	100 (75.3, 100)	-5.6 (-14.4, 3.3)
Specificity, PP	100 (96.3, 100)	99.1 (95.0, 99.9)	0.9 (-0.6, 2.4)
ITT – intention-to-treat; PP – per protocol. Differences assessed with Wald Asymptotic test, non-inferiority limit of -15%, equivalence bounds (-15% to 15%)			

Figure 4.2. Implementation effectiveness measures of HIV self-testing in Uganda, 2013 by study arm, using a serial rapid HIV algorithm as the gold standard

The absolute difference in sensitivity was 10% between the two study arms. The null hypothesis that the difference in accuracy between arms was greater than or equal to the lower

equivalence margin was rejected (p=0.0001); however, the lower one sided 90% confidence limit fell below the lower equivalence boundary of -15% (Figure 4.2). Therefore, we were unable to show non–inferiority of unsupervised HST when using the oral HIV test kit. During the study, 6 participants failed to return to report self-test results; based on the confirmatory test sample, 1 of these 6 was HIV seropositive. In a per protocol analysis that excludes these 6 participants, the difference in sensitivity between the two arms was 5.6%, lower than the 10% observed in the ITT analysis. Moreover, the lower limit of the 90% confidence interval was -14%, indicating that the unsupervised oral HST was not inferior to the provider administered oral test.

Accuracy (sensitivity of HST) among the 53 first time testers was high (100%) and not different across study arms (Table 4.3). Participants in the unsupervised arm were less likely to return for test revalidation and exit interview (p=0.038). No errors were reported on exit interview for self-testers, however errors were observed almost one fifth of participants in the provider-supervised arm (24 participants, 19.5%). The errors observed most often were incorrect swabbing of the upper and lower gums for a suitable mucosal exudate sample (12, 9.8%), touching the flat pad (6, 4.9%), and spills of developer fluid (5, 4.1%). Overall, most participants (181, 75.4%) reported that the oral HST was very easy to conduct, and strongly agreed that they would recommend it to a friend or family member (159, 66.5%). However, among unsupervised testers, at least 29 (23.6%) found some form of additional help necessary, mostly with using a timer (15, 12.2%). Among the provider-supervised arm, a higher number of participants (51, 41.5%) requested some form of help when testing. The majority in this arm (27, 21.9%) were also unable to use a timer. Differences in request for help were not statistically significant across arms. All participants found HIV to be seropositive were referred for care and treatment.

However, only 25 out of the 33 (75.7%) HIV positives identified were able to provide samples for CD4 test to facilitate quick uptake into care programs.

Discussion

In this un-blinded, randomized, non-inferiority trial of unsupervised self-administered oral HIV testing, we found that the sensitivity of unsupervised oral HST was satisfactory, 90%, but we could not demonstrate non-inferiority when compared to provider-supervised oral HST in a conservative intention-to-treat analysis. The absolute difference in test sensitivity between the two arms was large (10%) and the lower boundary of the 90% confidence limit fell below the pre-stated -15% non-inferiority margin. In the per protocol analysis, however, the difference in test sensitivity was reduced (5.6%), and we were able to demonstrate non-inferiority.

Although these findings do not provide convincing evidence that individuals from an African rural setting can accurately test themselves without the supervision of a health care provider, the preponderance of evidence from this study supports the use of unsupervised HST. In both the conservative ITT and per protocol analysis, the point estimate of difference in test sensitivity between the two study arms fell within the pre-specified boundary of non-inferiority. The wide confidence intervals in the ITT analysis suggest that a larger sample size would have provided greater precision to the estimate and allowed us to conclude non-inferiority. The test sensitivity with unsupervised HST was very good, identifying 90% or more HIV-infected persons. Finally, our findings were close to the 91.7% sensitivity claimed by the oral test kit manufacturers (OraSure Technologies, 2012).

Although our finding is promising, the observed sensitivity of oral HIV testing falls below what has been previously reported. In an urban community setting in Malawi, the

Table 4.3: Implementation Effectiveness Measures for Self HIV Testing in Uganda

Secondary Outcomes	Unsupervised Oral Self HIV Test N=123	Provider Supervised Oral Self HIV Test N=123	Proportion Difference (%) (Exact, 90% CI)	Total (Overall)	p-value
Sensitivity (n/N, %)					
First Time Testers	6/6 (100)	7/7 (100)	0	53 (21.5)	-
Repeat Testers (>12mths)	12/13 (92.3)	6/6 (100)	-7.7 (-37.7 – 38.8)	193 (78.5)	0.6635
Return Rate (Test Validation and Exit Interview) (N, %)	117 (95.1)	123 (100)	-4.9 (-10.5 – 0.6)	240 (95.8)	0.0382
Help Requested[§] (N, %)	29 (23.6)	51(41.5)	-17.9 (-29.7 – 5.5)	240 (95.8)	0.1708
Observed Performance Error Rate (N, %)	(N/A)	24 (19.5)	-	123 (50)	-
Linkage to Care[β]					
CD4 Cell Counts (N; Median, IQR)					
Total (Median, IQR)	N=16; 418 (127 -672)	N=9; 551 (387 – 822)	-	N=25; 452 (348 – 810)	0.1374
Among Clients CD4 <=500	N=10; 251 (68 – 410)	N=4; 369 (328 – 439)		N=14; 349 (101 – 410)	0.0596

§- At least some form of help found necessary or help actually requested. β - All 33 HIV positives referred for HIV care and treatment. CD4 Samples derived from 25 consenting participants.

sensitivity of the test was 99.2% (Choko et al., 2011). In a clinical setting in Singapore, the sensitivity was estimated to be 97.4% (Ng et al., 2012). Previous studies that have assessed accuracy of oral HIV testing in comparison to blood based tests have shown that oral tests perform very well with accuracy close to 100% (Delaney et al., 2006; Pant Pai et al., 2012; Pascoe et al., 2009; Wesolowski et al., 2006). Since we found that the sensitivity of HST improved to 100% when clients were supervised, we believe that higher accuracy can be achieved once individuals are sufficiently trained.

Two other findings may affect the widespread use of unsupervised oral HST. First, we observed a high error rate when participants performed the oral test in the clinic. If we assume that these same errors are occurring when self-testing is performed unsupervised, then these errors may have affected our estimate of sensitivity. Again, greater attention to training before testing may be needed to optimize the use of the oral kits. Second, we observed that 5% of our participants in the unsupervised test arm did not return to report the test result or complete the exit interview. Of concern, one of these individuals was HIV seropositive. Because of the confidential manner in which the tests were performed, the study health providers were not able to track this individual. Further education and counseling may be needed to motivate individuals who self-test outside of the clinic setting to return for appropriate counseling and care. Overall, most participants who tested HIV seropositive were linked to care, thereby indicating the potential value of this type of rapid testing.

The strengths of this study lie in the randomization, which minimized potential confounding effects between testing groups. The study was set in a high prevalence, rural area of Africa where many individuals with undiagnosed HIV infection reside. It provides insights into the potential value of oral HIV self-testing and provides guidance on how to improve upon test

performance in the field. Among the weaknesses of this study, differences in proportion may be affected by the underlying test response rate in the control group. In our study, this wasn't an issue because we achieved 100% response (all persons) in the control arm. Because sensitivity and specificity depend on the selected diagnostic thresholds of a test method, they have to be considered simultaneously as outcome indices (Lu, Jin, & Genant, 2003). We therefore report both sensitivity and specificity as measures of accuracy. The tests used in this trial will not detect acute HIV infection because they are antibody tests; so it is possible any participant with acute HIV infection would be missed, even with our confirmatory test. We could not adequately measure acceptability as the HIV testing experience was high (few first time testers). Because of this we also did not objectively assess disclosure.

In conclusion, our study showed that unsupervised HST is feasible and can achieve high sensitivity and specificity for HIV infection, even in a rural setting among individuals at high risk for HIV infection. Although we did not show non-inferiority of unsupervised HST, we believe that improved counseling and training prior to unsupervised HST would enhance the test accuracy. Our findings provide evidence that unsupervised oral HST should be evaluated further as a way to improve access to HIV testing and open new paths to care in an African rural setting.

CHAPTER 5

USER PREFERENCE'S FOR HIV TESTING IN UGANDA: A CONJOINT ANALYSIS[2]

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Abstract

Background: Knowledge of one's HIV status is a critical step in the cascade of HIV care and prevention. Many people at risk of HIV cannot access these services due to low uptake of HIV Testing despite availability. We used conjoint analysis to inform and estimate relative preferences for HIV testing, as well as estimate and simulate the probability of HIV test uptake in Uganda using the stated preferences.

Methods: We conducted a discrete choice experiment (DCE) by surveying 246 high-risk fisherfolk from western Uganda. We defined five important attributes of HIV tests and their levels (mode of HIV test and specimen collection method, location of HIV test service, price, availability of counseling services, timeliness and accuracy). A fractional factorial design was used to develop scenarios that consisted of combinations of attribute levels. Respondents were asked 10 questions about whether they would choose between 5 alternatives each, including 'none' based on these scenarios.

We used conjoint analysis, a method used to measure economic preferences (utilities). A multinomial conditional logit and hierarchical Bayes model were used to estimate utilities for HIV testing attributes. Price will be included as a key attribute to enable indirect estimation of shares of preference given different costs of the service.

Results: Out of the 2,214 random choices presented, oral self HIV testing using oral swab had the highest utility within the mode of testing attribute. A home-based location, zero prices, talking to a counselor with access to immediate and accurate results all had the highest utility within attribute respectively. Mean Importance in informing respondent preferences for HIV testing was highest with timeliness and accuracy (30.2%), price (29.7%) and counseling (17.5%) attributes

respectively. Compared to persons who had never tested, previous HIV testers had a higher mean attribute importance scores for mode of HIV test (12.1% vs. 10%, p=0.04) and test location (11.5% v. 9.1%, p=0.02) respectively. Mean attribute utility scores for oral HST were significantly higher for women compared to men, although importance scores were no different by age, sex and income. Given no costs of service, an oral home based self-test had the largest share of preference (24.5%), twice that of the rapid testing done at a public clinic. The share of preference drops to 9.9% when a $2 fee is included.

Conclusion: HIV test timeliness and accuracy, price and counseling availability are the main factors that are important in determining individual preferences for HIV testing in a high-risk community of fisherfolk in Uganda. An oral HIV self-test with highly accurate and immediate results offered at no fee with counseling support could increase HIV test uptake.

Introduction

Scaling-up of health services has two facets: 'extending the availability of cost-effective interventions' to the population (coverage) and 'increasing the level of demand' for these services (uptake) (Pokhrel, 2006). Despite improved supply of HIV health care services in low-income countries in the recent past, their uptake continues to be lower than anticipated. According to the 2006 Uganda Demographic Health Survey (UDHS) report, one-quarter of women (25%) and one-fifth of men (21%) age 15-49 have ever been tested for HIV and received their results in Uganda (Uganda Bureau of Statistics, 2007). This has made it difficult to scale-up those interventions which are not only cost-effective from supply perspectives but have substantial impacts on improving the health status of these countries.

Understanding demand-side barriers is therefore critically important. One of the ways of understanding uptake is to analyze individual preferences. The extent of patient or clients preferences in medical decision making has been traditionally minimal, particularly in Uganda where most HIV programs are heavily subsidized by the Ugandan Government (Ministry of Health, MOH) and relevant development partners like the US Centers of Disease Control & Prevention (CDC), United States Agency for International Development (USAID), the US Presidential Emergency Plan For AIDS Relief (PEPFAR) as well as other related sub-partners and multilateral organizations. Subsequently, community participation, uptake and sustainability of many HIV programs has become a significant challenge, even as funding for these has not increased in the past decade (Geng et al., 2010).

Greater involvement of patients and communities in choosing their health services has been advocated for, particularly in those nations with predominantly public funded health

programs (Florin & Dixon, 2004). Elicitation of patients and community values and preferences represents a key step in enhancement of benefits of HIV testing service provision.

Understanding how patients (clients) perceive the benefits of a service or program features and their tolerance for possible risks requires a valid and reliable measurement method. Stated Choice (SC) methods, also called Discrete Choice Experiments (DCEs) or Conjoint Analysis are reportedly the most valid and reliable for quantifying patient preferences (Maddala et al., 2003; M. Ryan et al., 2001). The discrete choice experiment was developed as a survey method of data collection and analysis to elicit and study patient or community preferences to a good or service, which could include HIV testing services. These methods are used to study consumer product or service preference and simulate consumer choice. SC methods recognize that products have value because of their characteristics (or attributes). People have preferences for each attribute and are willing to accept tradeoffs among different attributes. SC analysis examines these trade-offs to assess the weight people assign to various service attributes. Analysts have used SC methods to quantify preferences for a variety of market and non-market goods and services e.g. health care (Mandy Ryan & Farrar, 2000), medical programs and interventions (J. Hall et al., 2004), immunization participation rates (Jane Hall et al., 2002), pharmaceutical treatment programs (M. Ryan & Gerard, 2003) and even HIV testing (S.-J. Lee, Brooks, Bolan, & Flynn, 2013; Phillips et al., 2002).

The specific objectives of our study were to evaluate the respondent's preferences for HIV testing methods and to simulate the HIV test consumer choices of high-risk fisherfolk in Uganda.

We hypothesized that based on differences in HIV test attributes like accuracy, price, anonymity, privacy and confidentiality; respondents may prefer HIV tests and testing strategy that maximizes the utility derived from the testing service respectively.

Methods

Study Design

We conducted a discrete choice experiment (DCE) or preference survey among 246 fisherfolk at high-risk of HIV from three fishing villages on the shores of Lake Edward in western Uganda. This survey was nested in a randomized trial for the implementation effectiveness of unsupervised versus supervised HIV self-testing (HST). The study was conducted between July 10 and September 13, 2013 in three fishing communities around Lake Edward, western Uganda. Research assistants screened local residents who presented to the research camp for HIV testing. These individuals were eligible for the study if they were between 18-49 years, at high risk for acquiring HIV infection (defined by a history of unprotected sexual intercourse within the previous 3 months, having sex with a non-regular partner, involvement in commercial sex work or reported symptoms of a sexually transmitted infection within the same period), and lived or worked in the study community for at least 3 months prior to enrollment. Participants were surveyed before being tested for HIV using oral self-tests and rapid confirmatory tests respectively.

Conceptual Framework

A discrete choice experiment using choice surveys was conducted among all participants to elicit for HIV test preferences and predicting uptake. The DCE is an attribute-based survey

method for valuing benefits. It is consistent with Lancaster's characteristics theory of demand (Lancaster, 1966): that consumers have preferences for and derive utility from underlying attributes, rather than goods per se. DCE's are consistent with welfare and consumer theory (Luce & Tukey, 1964). Conjoint Analyses have been determined to be feasible tools to help prioritize innovations for implementation (Farley, Thompson, Hanbury, & Chambers, 2013). From DCE's, utility estimates can be derived. A utility is a measure of relative desirability or worth. When estimating utility values, every attribute level is assigned a utility (also referred to as a part worth). The higher the utility, the more desirable the attribute level is in relative terms. Levels that have high utilities have a large positive impact on influencing respondents to choose HIV service packages.

Individuals were assumed to derive utility from the underlying attributes of the HIV testing modality rather than the HIV test service itself. In DCEs, individuals are asked to choose between different scenarios (e.g. HIV test scenario X, scenario Y or neither) which describe different services with different levels of attributes. The different scenarios in this study were developed using standard methods and explained below. To determine preferences, responses were analyzed using regression techniques to establish the relative importance of the different attributes of the different HIV testing methods currently available in Uganda, the tradeoffs between them, the overall utility and importance scores for different configurations of the HIV testing services and the simulated shares of preference for different configurations.

Survey Procedure

In real life scenarios, patients and clients choose between various services and products for their health care. We used the same approach to present clear discrete choices among the

attributes and levels of different HIV testing strategies currently available in Uganda, along with the more recent oral HIV testing. Since most of the choices presented had been consumed by the clients in one way or another (in community programs in the past), we do not anticipate a high hypothetical bias to arise in the responses. Since, in real life the patients or respondents do not mandatorily have to have an HIV test (voluntary), among the options to select we allowed respondents to opt out (choose none) or choose the status quo available in Uganda.

Steps in Survey Development

Defining Attributes and Assigning Levels

To inform attributes and levels for the DCE, information was derived from literature review of empirical studies and systematic reviews of HIV testing conducted in sub-Saharan Africa (Bwambale, Ssali, Byaruhanga, Kalyango, & Karamagi, 2008; Hardon et al., 2012; Jean et al., 2012; J. K. B. Matovu & Makumbi, 2007; Nuwaha, Kabatesi, Muganwa, & Whalen, 2002). Most of these studies examined the attitudes and preferences of HIV testing in this environment, using attitude based surveys with Likert scales. Based on the above studies, we defined important attributes of an HIV test that inform client's choice of HIV testing service (Table 5.1). These attributes were identified as type and location where test is done, the cost (price) of the test, the mode of sample collection, availability of pre and post-test counseling, timeliness and accuracy, as well as privacy/anonymity.

Modes of HIV test and specimen collection attributes were combined due to inherent linkage and to avoid illogical combinations. Previous studies have shown these levels to be plausible, clinically relevant and include currently available alternatives in the field settings of Africa. Within the modes of HIV testing services, the key alternatives to be evaluated were:

Provider-administered rapid HIV testing (the current standard of care), provider-administered oral HIV testing, oral HIV self-testing, lab-based HIV testing and no HIV testing respectively.

Table 5.1: Attributes and Levels for HIV Testing

Attributes(Factors)	Levels	Variable in Eq. (i)	Parameters
Mode of HIV Test and Specimen Collection	Rapid HIV Test by Finger Prick	Rapid	β_1
	Oral Self HIV Test by Oral swab	Oral Self	β_2
	Provider administered HIV Test by Oral swab	Provider	β_3
	Lab based HIV tests by venipuncture	Lab	β_4
Location of HIV testing	Public Clinic	Public	B_5
	Private Clinic	Private	β_6
	Mobile Outreach	Mobile	β_7
	Home	Home	β_8
Price$^{\delta}$ of the test	$0 (Free)	Cost1	B_9
	$2 (5,000 Ush)	Cost2	β_{10}
	$4 (10,000 Ush)	Cost3	β_{11}
Counseling	Talk to counselor	Counsel	β_{12}
	No Counseling	No Counseling	β_{13}
Timeliness/Accuracy	Immediate, almost always accurate	Time1	β_{14}
	Results 1-2 wks, almost always accurate	Time2	β_{15}

δ Average 2012 prices from National Medical Stores (NMS) Price List

Determining Choice Sets and Obtaining Preference Data

The final design employed five alternative discrete choice concepts with a (none) option in each set of choice tasks, as some individuals may choose not to prefer any HIV test scenario given the alternatives available (Figure 5.1). Nine random and 1 fixed (hold-out) choice tasks were created for each survey version. The fixed task was to be used as a proximal indication of validity, measured by the utilities' ability to predict choices not used in their estimation and also evaluate the reliability of the survey responses between individuals, like consistency checks (stability of preferences). The four concepts for the fixed task had 2 scenarios reflecting the current standard (HIV testing) in the public and private sector (Free or priced rapid HCT, done with access to counseling and immediate results). The other two concepts in the fixed task has 2

scenarios in which an oral self-test is available (also in public/private sectors). Consistency and reliability checks within individual were not done. Respondents were randomized to receive the combinations in any one of 28 survey versions. We had 2 restrictions (prohibitions) in the design. Lab-based HIV testing was restricted not to appear with a home based location as well as have immediate results respectively in any choice task. From the CBC design efficiency testing, preliminary standard error estimates of utilities (with synthetic data using aggregate modeling) indicated a strong design with low standard errors of parameter estimates (all less than 0.05). The random tasks of this design were generated using the balanced overlap method which allows some level of overlap of levels within choice tasks without too much loss of independence (orthogonality).

Pilot Testing

The choice sets generated above were pilot tested with 20 respondents to determine the completion rates, suitability and understanding. Pilot testing enabled us to determine that the key terms used in each of the attributes and levels could be well explained in lay language understandable to the participants. Ten choice tasks per respondent were determined to be sufficient for fielding, and could be completed within 20 to 30 minutes. Compared to paper and pencil surveying, we determined that a computer assisted survey was feasible in field settings, and used them for the main survey.

Statistical Analysis

Estimation of part-worth utilities (unique utility values for each variable)

Choices made in discrete choice experiments are analyzed based on random utility theory (RUT) (Lancaster, 1966; McFadden, 1973), which basically posits that the utility (U) for

individual i conditional on choice j can be decomposed into an explainable or systematic component Vij and a non-explainable or random component εij (Equation (i) below)

$$U_{ij} = V_{ij} + \varepsilon_{ij} \text{ , } j=1,\ldots J. \text{ ----------Equation (i)}$$

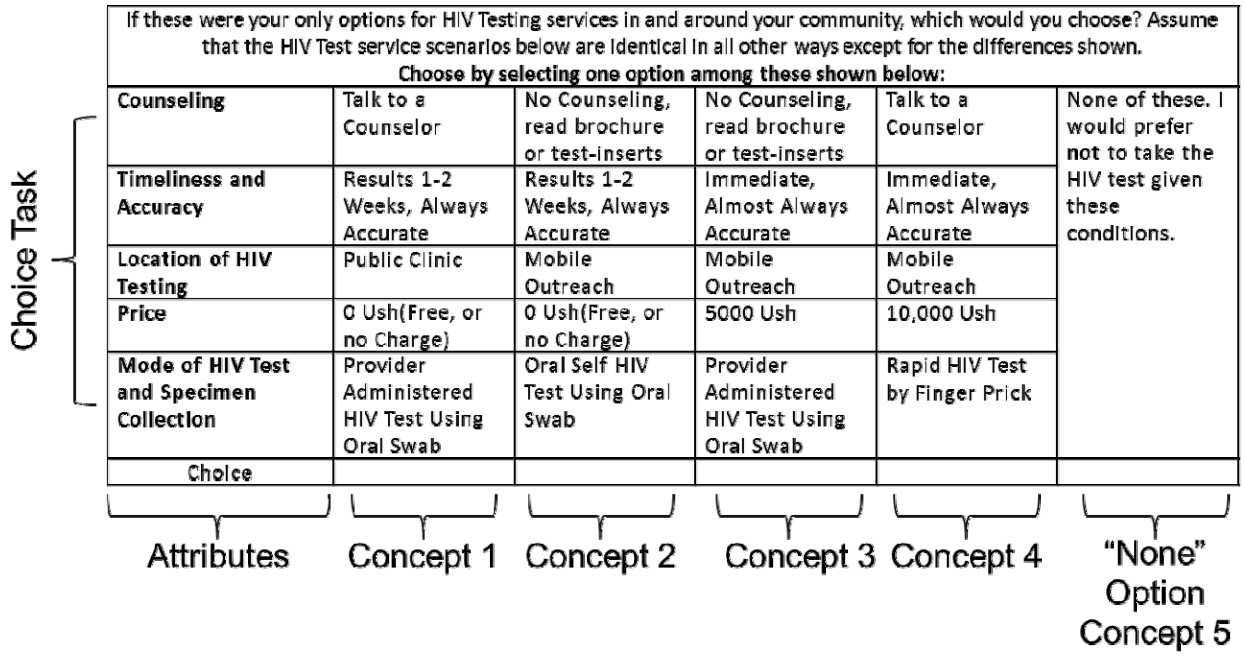


Figure 5.1: Survey Choice Set (Sample)

The random components are due to unobservable or unobserved attributes, unobserved preference variation, and specification and or measurement error. This may also be due to inherent variability within and between individuals.

The systematic component is a function of attributes of the HIV test/HIV testing service as well as the characteristics of individual choosers modeled as follows

$$V_{ij} = X_{ij}\beta + Z_i\gamma \text{ ----------Equation (ii)}$$

Xij is the vector of attributes, including price and quality of the HIV test j as viewed by individual i, and Zi is a vector of characteristics of individual i, and β and γ are vectors of coefficients to be estimated.

Since utility is a latent, unobserved quantity; we observe only indicators of utility, namely choices. We will assume a respondent chooses option i if, and only if, it's utility is higher than the utility of any other option in the set of j alternatives. We estimated an Indirect Utility Function, IUF (Equation (iii) below) using a Hierarchical Bayes (HB) model rather than a conditional aggregate logit regression model using *Sawtooth*™ software. This was done in order to capture the heterogeneity in the data and improve the precision of individual utility estimates. The logit model, done at the lower level in the HB model would pool or combine all respondent preferences and estimate a single set of effects (utilities) to fit the total sample, assuming homogeneity.

$$
\begin{aligned}
Uij = {} & \beta 0 \\
& + \beta 1\ \text{Rapid} + \beta 2\ \text{Oral Self} + \beta 3\ \text{Provider} + \beta 4\ \text{Lab (Type of test \& sample)} \\
& + \beta 5\ \text{Public} + \beta 6\ \text{Private} + \beta 7\ \text{Mobile} + \beta 8\ \text{Home (Location of Testing Service)} \\
& + \beta 9\ \text{Cost1} + \beta 10\ \text{Cost2} + \beta 11\ \text{Cost3 (Price of Test)} \\
& + \beta 12\ \text{Counseling} + \beta 13\ \text{No Counseling (Counseling)} \\
& + \beta 14\ \text{Time1} + \beta 15\ \text{Time2 (Timeliness/Accuracy)} \quad \text{----------} \quad \text{(iii)}
\end{aligned}
$$

Personal characteristics do not appear in equation (iii) because they do not vary between choice sets within each individual. Effects coding (1, 0, -1) coding was used for all attributes. This was to avoid the correlation of alternatives and intercepts by minimizing collinearity in the matrices used for estimation. When using effects coding parameter estimates sum to zero within an attribute, whereby the parameter estimate for the base category is equal to the negative sum of the parameter estimate for all other categories of that variable. In an effects-coded model the intercept is a reflection of other attributes not included in the model and statistical significance is

evaluated relative to the mean effect, which is normalized at zero, rather than relative to the omitted category.

Hierarchical Bayes Model:

We fitted the data using hierarchical bayes (HB) estimation, which is a hierarchical (sequential) logit model (Arora & Huber, 2001). At the upper (population) level, we assumed that individuals were distributed in multivariate normal distribution, with means and covariance's to be estimated. At the lower (individual) level, we assumed that each individual's answers (choices) conformed to a separate logit model. When estimating betas or part worth's, we estimated the population means and covariance's as well as the betas or part worth's of each individual. Information about the population means and covariance's strengthens our estimation of individual results for each respondent. The estimation ran 20,000 iterations before assuming convergence, and then run another 20,000 for a total of 40,000 iterations. Convergence was adequate, assessed by using trace plots. Only a main effects model was estimated with covariates included (Age, Sex, average monthly Income and history of an HIV test in the past 12 months).

Attribute Relative Importance

Importance of an attribute was defined as its weight or the maximum influence it can have on a product or service choice, given the range of levels in the study. This relative importance was defined by how much difference each attribute could have in the total utility of the service or product. This difference (maximum minus minimum) was expressed as a percentage. The relative importance of each attribute was estimated using the average individual utility values from the hierarchical model described above.

We evaluated whether attribute mean relative importance was related to a personal characteristic of the individual, specifically sex (male/female) and history of HIV testing. This was assessed by conducting t-tests of the mean relative importance values estimated from the hierarchical Bayes model. Specific characteristics of interest included sex (Male vs. Female) and HIV Test History (Ever tested vs. Never). We also assessed for differences in the mean relative importance values by age (<= 28 years or >28 years) and Income (<=$31.5 vs. >$31.5) across all attribute levels. The cut-offs used corresponded to the median values for age and income for this sample of participants.

Shares of Preference

The benefit (utility) from any defined HIV test service, represented by V, was characterized by combinations of attribute levels. Different combinations were used to generate a given benefit score, which was then used to calculate the predicted uptake (share of preference) for a defined HIV testing service combination. The probability of uptake, P, was defined as the ratio of the exponentiated benefit (utility) from the chosen HIV test service option to the sum of the exponentiated utilities of all the possible HIV testing service options, including not testing for HIV (doing nothing); whose utility was assumed to be zero.

P_i = exp (Vi)/ summation j=1 to N exp (Vj).

Considering five alternatives (A, B, C, D, E) in a choice set:

$$P_A = \exp(U_A) \;/\; [\exp(U_A)+\exp(U_B)+\exp(U_C)+\exp(U_D)+\exp(U_E)]$$

where: P_A = "Probability of choosing alternative A"

U_A = Total utility for alternative A, etc.

We used the utilities estimated from the main effects HB model above assuming no interactions to estimate these shares of preference for the scenarios described below.

Simulation of Client Choices for HIV Testing

From a provider perspective (the Ugandan health ministry), we used the estimated individual utility values to evaluate the shares of preference of some HIV service packages that may be offered and compared these to the current locally available service packages (Free Rapid HIV Testing offered at Public Facilities, Mobile Outreaches and Home Based programs). The method used for simulation was the share of preference method, which uses the logit rule explained above to estimate shares.

We further examined the uptake and price sensitivity of an oral self-tests offered in a service package at a nominal fee of $2 in the various locations where HIV testing is done. The simulation also examined any differences by sex. Our assumptions were that each respondent chooses the service product he/she considers to have the highest utility; that all individuals will select and purchase an HIV testing service product among those offered; that aggregate respondent probabilities represent shares of choice, shares of preference or market share; that there will be equal availability (service products to be distributed equally) among the sample/population and all respondents are aware of all available options; that no stock outs are present or will arise and that the service products have had an equal time on the market (long range equilibrium) respectively.

Scenario I – In this scenario we created 6 service packages, all offered at no charge ($0), with counseling available and immediate, accurate results. Three packages use the rapid HIV test offered at a mobile outreach, public clinic and home based location respectively. These represent

the standard of care currently in Uganda. Three new service packages used the oral self HIV test offered at a mobile outreach, public clinic and home based location respectively.

Scenario II – In this scenario we created 6 service packages, 3 of them at a nominal price of $2, with counseling available and immediate, accurate results. Three packages at no cost use the rapid HIV test offered at a mobile outreach, public clinic and home based location respectively. These represent the standard of care currently in Uganda. Three new service packages priced at $2 each use the oral self HIV test offered at a mobile outreach, public clinic and home based location respectively.

All analyses above were performed using Sawtooth™, STATA™ and SAS™ statistical software packages.

Testing Validity of Estimates

We used consistency with theoretical predictions to evaluate the validity of our predicted estimates. In particular, the expectation was that the higher price, the lower the utility. The sign and significance of parameter estimates was explored in view of this expectation.

We also used the hold-out (fixed) choice task to examine the validity of our utility estimates. Specifically, we used the hold-out task to determine shares of preference of 4 conceptual HIV test service packages. We then compared our fixed task findings with the shares of preference derived from the utility values estimated from the random choice tasks provided to all the respondents.

Results

Our survey had a total of 246 predominantly male (57.3%) respondents. Most of our participants were young adults, with a median age, interquartile range (IQR) of 28 years (23-32) with most having at least one risk factor for HIV. Most of them - 141 (57.3), had little or no education with a low median monthly income of $31.5, IQR ($17.9- $59.0). Most, 193(78.5%) had ever tested for HIV at some point in their past, with less than half (43.9%) reporting having tested in the past 12 months.

Table 5.2: Average Utility Values (Hierarchical Bayes Estimation)

Average Level Utilities (Zero Centered)	Average Utilities[§] (SE)	Adjusted[*] Average Utilities (SE)
Mode of HIV Test and Specimen Collection		
Rapid HIV Test by Finger Prick	-15.73 (23.34)	-13.85 (25.0)
Oral Self HIV Test Using Oral Swab	10.50 (22.17)	11.42 (24.0)
Provider Administered HIV Test Using Oral Swab	9.51 (22.30)	10.17 (23.2)
Lab-based HIV Test e.g. ELISA Using Venipuncture	-4.28 (25.33)	-7.74 (31.1)
Location of HIV Testing		
Public Clinic	1.96 (23.18)	2.52 (24.1)
Private Clinic	-7.99 (24.25)	-7.99 (24.2)
Mobile Outreach	-2.31 (24.00)	-2.86 (24.5)
Home Based	8.34 (26.48)	8.33 (26.7)
Price		
$ 0	72.47 (55.39)	71.59 (55.7)
$ 2	-10.33 (23.84)	-10.35 (24.3)
$ 4	-62.14 (42.04)	-61.24 (41.8)
Counseling		
Talk to a Counselor	41.21 (34.67)	40.30 (34.4)
No Counseling, read brochure or test-inserts	-41.21 (34.67)	-40.30 (34.4)
Timeliness and Accuracy		
Immediate, Almost Always Accurate	71.64 (40.35)	70.16 (39.9)
Results 1-2 Weeks, Always Accurate	-71.64 (40.35)	-70.16 (39.9)
None	-99.09 (160.99)	-103.56 (166.3)

§ Generic Main Effects Hierarchical Bayes (HB) Model * HB Model with Covariates (Age, Sex, Monthly Income and HIV Test History). Average Root Likelihood (RLH) = 0.568 (Generic HB Model), improves to 0.620 (HB Model with Covariates)

Overall, there were 2,214 observations to represent the various random choices presented to the 246 participants. When the five attributes were presented, the generic HB model showed

that within mode of HIV test and specimen collection attribute, oral HIV self-testing using an oral swab the highest (positive) utility followed closely by provider administered HIV tests using oral swabs (Table 5.2). The results are presented with utilities on the larger-scaled "zero centered diffs" to normalize the scale across the respondents so that some respondents don't have greater effects on the final results than others. Home based location, payment of $0, talking to a counselor, and immediate accurate results had the highest positive utility values within the respective levels of the various attributes. The standard errors of all estimates were fairly small. The magnitude and directionality of the utility values remained unchanged even with covariates included in the model.

The HB model with covariates had an improved fit (increase in the average root likelihood) and is therefore the model that represents our final main findings. From the average utilities estimated, oral self HIV testing had the highest utility value within the modes of testing and specimen collection levels presented. Home based location as well as testing at public clinics had positive average utility values. All forms of payment for HIV testing had low (negative) average utility values. Talking to a counselor retained its positive utility along with receipt of timely and accurate results.

We used the estimated covariance estimates to derive the average non-rescaled (raw) utility values for each covariate by level of HIV test attribute (Table A3 – Appendix). Overall, the covariates did not significantly alter the average utility values by level of HIV test attribute; however they narrowed the standard errors in comparison to the generic HB model, indicating a better fit. For sex, the utility of oral self HIV testing using oral swab was much higher for females than males, holding other covariates constant.

Table 5.3: Mean Differences in Utility Estimates, by Sex (Hierarchical Bayes Model)§

Variable (Attribute), Level	Males	Females	p-value*
Mode of HIV Test and Specimen Collection			
Rapid HIV Test by Finger Prick	-17.8	-8.5	0.0034
Oral Self HIV Test Using Oral Swab	3.7	21.8	**<0.0001**
Provider Administered HIV Test Using Oral Swab	8.4	12.5	0.1729
Lab-based HIV Test e.g. ELISA Using Venipuncture	5.7	-25.7	**<0.0001**
Location of HIV Testing			
Public Clinic	1.33	4.1	0.3641
Private Clinic	-5.3	-11.6	**0.0408**
Mobile Outreach	-3.3	-2.3	0.7338
Home Based	7.3	9.8	0.4691
Price			
$0	67.3	77.4	0.1581
$2	-8.0	-13.5	0.0832
$4	-59.2	-63.9	0.3828
Counseling			
Talk to a Counselor	42.9	36.6	0.1562
No Counseling, read brochure or test-inserts	-42.9	-36.6	0.1562
Timeliness and Accuracy			
Immediate, Almost Always Accurate	70.1	70.1	0.9704
Results 1-2 Weeks, Always Accurate	-70.1	-70.1	0.9704

§ - Hierarchical Bayes Model with Age, Monthly Income and HIV Test History * p-value for two sample t-test

The mean difference in utility scores was significantly different by sex for particular attribute levels (Table 5.3). Females had significantly higher mean utility scores for oral HIV self-testing compared to men, and significantly lower mean utility scores for lab-based testing. Females had significantly lower mean utility scores for testing from private clinics compared to men.

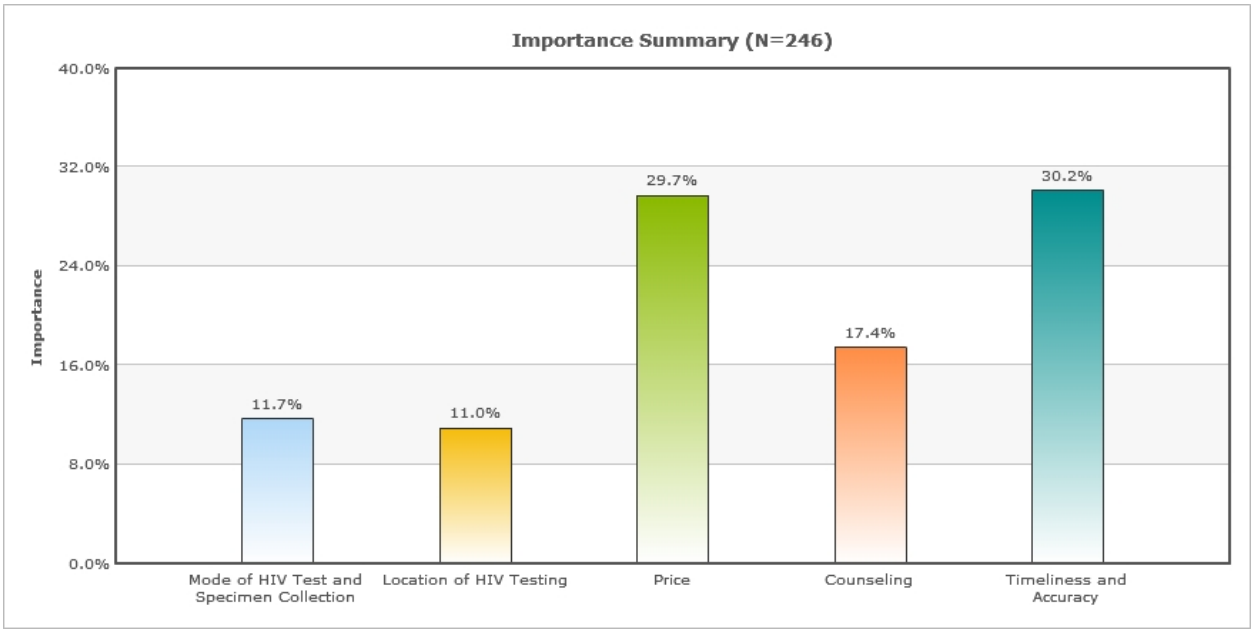


Figure 5.2: Attribute Relative Importance

Timeliness and accuracy had the highest average relative importance score among attributes (30.2%), followed by price (29.7%) and counseling (17.45%) respectively (Figure 5.2). Differences in importance were not significantly different by gender, though females considered timeliness and accuracy of results as well as price of slightly higher importance than men. No differences in the mean percent attribute relative importance score was observed by sex for all attributes (Table 5.4). However, significant differences in the mean score for relative importance of attribute were observed among those who had never had an HIV test compared to previous testers, more specifically with the mode of HIV test and specimen collection, as well as location of HIV testing. Both attributes were of higher relative importance to 'previous testers' in informing their utility for HIV testing. The mean score for relative importance of timeliness and accuracy was higher for 'never testers' compared to 'previous testers' and marginally significant.

Of all the new service products assembled in scenario I, oral HIV self-tests had a higher share of preference compared to rapid HIV tests (Table 5.5). Oral HIV self-testing done in a home-based setting/location had the highest share of preference, more than twice the local standard of care for HIV testing (rapid testing at a public clinic). Rapid testing at a mobile outreach setting had the lowest share of preference (Figure 5.3). When price is introduced into some of the service

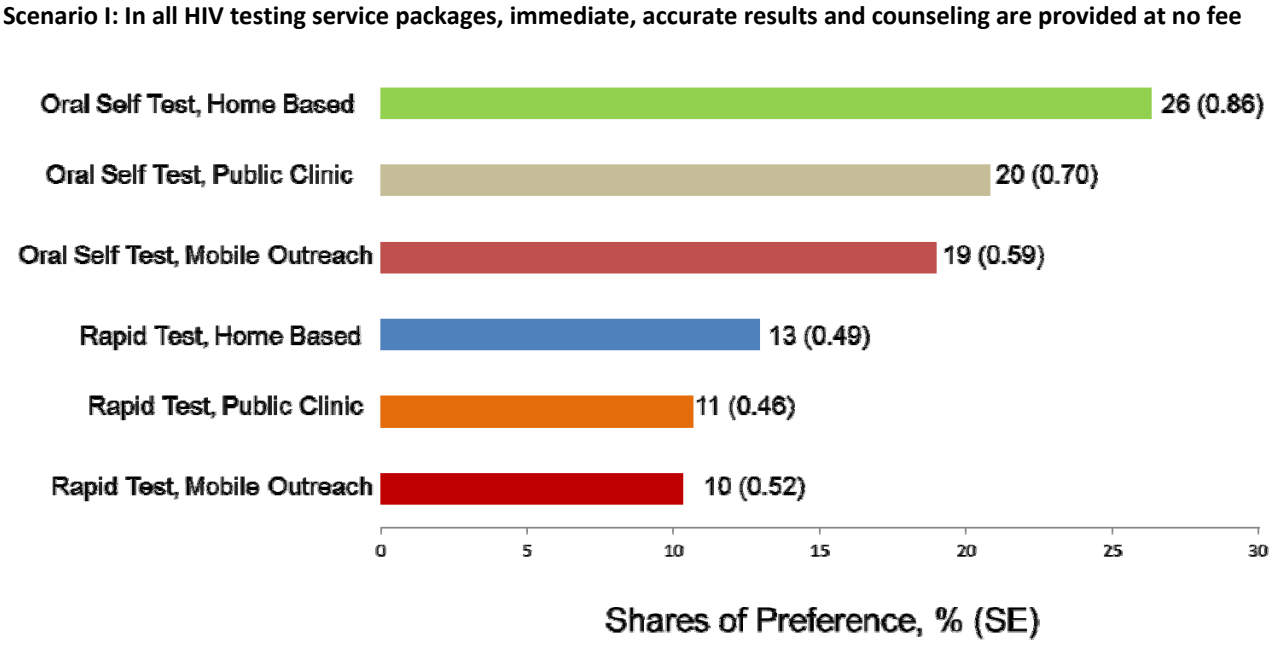


Figure 5.3: Simulation of Shares of Preference of No Cost Oral Self-Test Packages Compared to Current Standard of Care for HIV Testing in Uganda (Rapid Tests)

Table 5.4: Difference's in the Mean Attribute Relative Importance (%), by Key Demographics

Characteristic/Attribute	N	Mode of HIV Test and Specimen Collection	Location of HIV Testing	Price	Counseling	Timeliness and Accuracy
Age						
≤ 28 years	132	11.25	10.98	28.32	18.47	30.98
> 28 years	114	12.17	10.93	31.39	16.27	29.24
p-value*		0.2767	0.9558	0.1092	0.1749	0.300
Sex						
Male	141	11.72	10.80	29.76	18.09	29.63
Female	105	11.62	11.17	29.71	16.59	30.91
p-value*		0.8987	0.6730	0.98	0.3606	0.452
Income						
≤ $ 30.5	129	11.37	11.18	15.77	17.24	30.30
> $ 30.5	117	12.01	10.71	14.14	17.67	30.04
p-value*		0.4465	0.5914	0.8649	0.7922	0.8745
HIV Testing History						
Ever Tested for HIV	193	12.13	11.48	29.45	17.58	29.37
Never Tested for HIV	53	10.04	9.06	30.81	16.97	33.13
p-value*		0.0401	0.0245	0.5597	0.7557	0.0643
Mean Relative Importance, SE (%) **§**	246	11.68, 6.57	10.96, 6.92	29.74, 14.96	17.45, 12.63	30.18, 13.08
Mean Relative Importance, SE (%) **δ**		12.71, 6.92	11.17, 7.03	29.44, 14.92	17.07, 12.55	29.59, 12.92

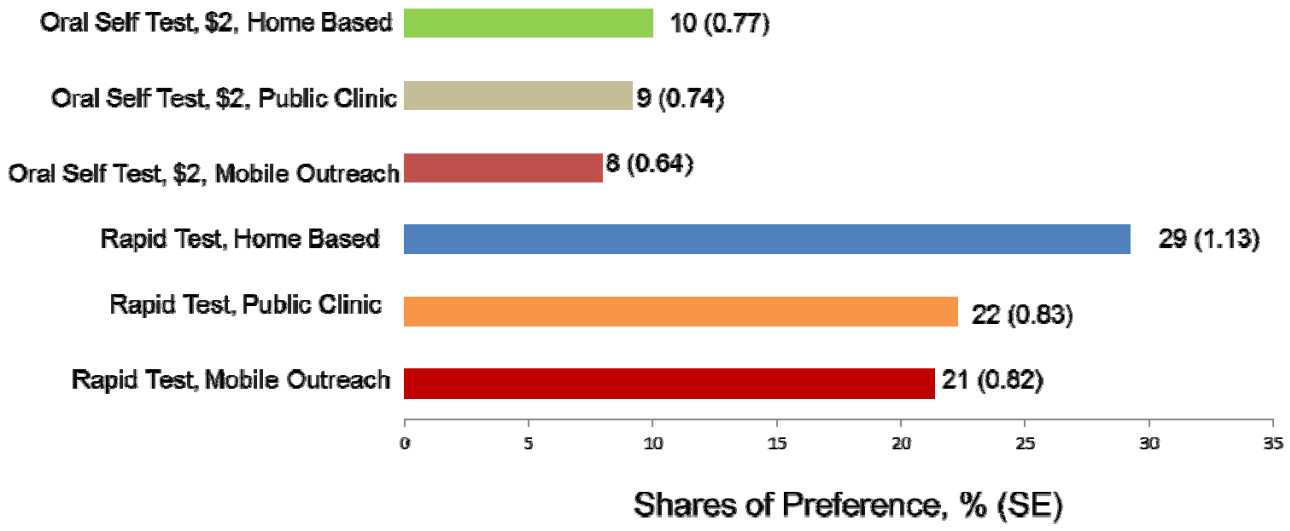
§ - Generic HB Model δ – HB Model with Covariates (Age, Sex, Monthly Income and HIV Test History) * p-value for a two sample t-test

Table 5.5: Simulation of Shares of Preference Based on a Scenario I and II, N=246

Product Package	Shares of Preference (%)	SE (%)	95% CI
Scenario I[§]			
Rapid Test, Mobile Outreach	11.20	0.45	10.30 - 12.09
Rapid Test, Public Clinic	11.64	0.42	10.82 - 12.46
Rapid Test, Home Based	13.74	0.44	12.87 - 14.61
Oral Self-Test, Mobile Outreach	18.83	0.50	17.85 - 19.81
Oral Self-Test, Public Clinic	20.10	0.58	18.96 - 21.24
Oral Self-Test, Home Based	24.50	0.71	23.10 - 25.89
Scenario II[*]			
Rapid Test, $0, Mobile Outreach	21.40	0.83	19.77 - 23.03
Rapid Test, $0, Public Clinic	22.41	0.85	20.75 - 24.06
Rapid Test, $0, Home Based	29.23	1.13	27.01 - 31.44
Oral Self-Test, $2, Mobile Outreach	7.86	0.65	6.59 - 9.12
Oral Self-Test, $2, Public Clinic	9.16	0.76	7.67 - 10.64
Oral Self-Test, $2, Home Based	9.95	0.78	8.42 - 11.48

Utility estimates derived from Hierarchical Bayes Model. § In all HIV testing service packages, immediate, accurate results and counseling are provided at no fee ($0), * Oral Self-Tests are priced at $2, accurate immediate results and counseling is provided.

packages as in scenario 2, the shares of preference of oral self-tests drops markedly, regardless of location (Figure 5.4). In this scenario rapid tests conducted within home-based programs take the largest share of preference at 29.2%. These shares of preference are sustained and largely unchanged even by sex.



Scenario II: Three, $2 Self HIV testing service packages available. In all HIV testing service packages, immediate, accurate results and counseling are provided at no fee

Figure 5.4: Simulation of Shares of Preference of Priced Oral HIV Self-Testing Packages Compared to Current Standard of Care for HIV Testing in Uganda(Rapid HIV Testing)

Discussion

Our study identified three key factors that inform the choice of an HIV test among this rural high-risk community. These were timeliness and accuracy, counseling and price respectively. From our findings, the ideal HIV test strategy to increase uptake of HIV testing in this community was identified to be an immediate and accurate oral test using oral swabs done in a home-based location offered at no cost with access to counseling. Our findings were confirmed in the simulation where the share of preferences for oral self-testing in a home based setting were twice those of the existing standard of care (Rapid testing from public facility at no cost), given that in both strategies immediate, accurate results and counseling are provided.

This finding of preference for oral testing at home is consistent with a recent study examining willingness to test for HIV among a US population of men who have sex with men(MSM), where a home test also fulfilled key attributes – timeliness and accuracy and home based location(S.-J. Lee et al., 2013). The high utility for oral HST seem to be driven by women, since we also found significantly higher mean utility values for oral HST among women in comparison to men. However the overall mean importance score for mode of HIV testing was not significantly different by sex.

Surprisingly, our rural-based study participants considered timeliness and accuracy of the test most important in forming their utility for HIV test (30.2%). Most HIV rapid testing is done within 30 minutes and results available immediately. Like other rapid tests, the oral self-testing can be accomplished within that time (20 to 40 minutes). However, the accuracy of the recently FDA approved in-home oral self-test (*OraQuick*®) home test has an estimated 91.7% sensitivity, meaning that about 1 in 12 people who have HIV infection will receive a negative test result

(Food and Drug Administration, 2012). False negatives have also been reported when comparing the oral test to blood test results respectively (Delaney et al., 2006). The predictive values however are likely to be high especially when used in a high prevalence setting. Therefore, the use of oral testing and interpretation of the results needs to be approached cautiously in field settings.

Our participants had a high utility for in-person counseling, contrary to another conjoint study done in publically funded test centers in Los Angeles California (Phillips et al., 2002). Individualized counseling has been shown to be effective for HIV and STD reduction (Kamb, Fishbein, Douglas, Jr, & et al., 1998) and has been part of standard HCT programs over the past decade. Recent evidence however shows no added benefit for STD prevention (Metcalf et al., 2005; Metsch, Feaster, Gooden, & et al., 2013). Our findings show that talking to a counselor is deemed essential by this rural community where support structures for guidance and follow-up care are minimal. The manufacturers of the new *OraQuick*® oral home self-test kit set up a US based toll-free 24/7 support center to address this. Our findings underscore the importance of setting up a relevant local mechanism of counseling support depending on the settings if the self-testing strategy is to be adopted.

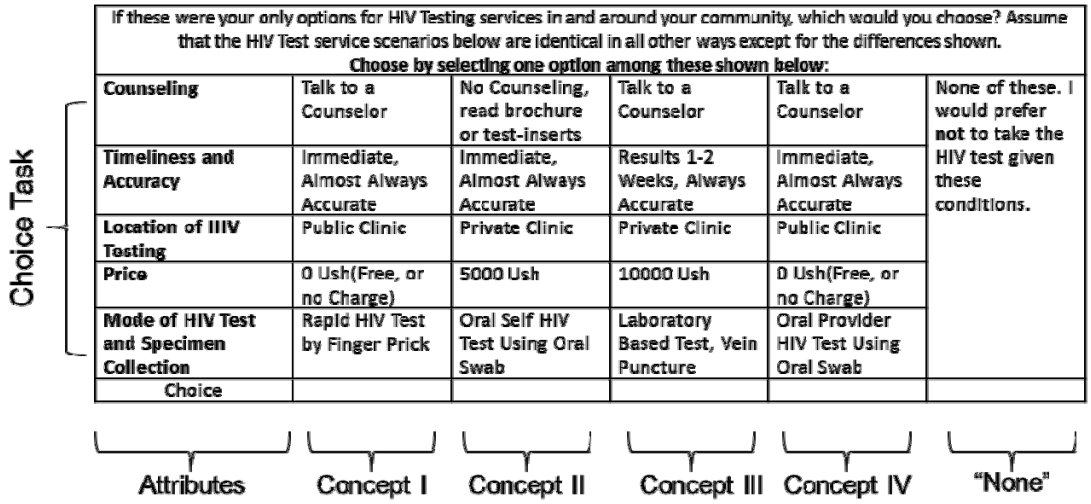
Payment for HIV tests was one of the very important attributes determining choice of HIV test. Of concern, the utility of any test package with a cost attached was relatively low, consistent with other studies. The costs presented to participants in this study was the current (2012) cost prices of HIV rapid tests by the National Medical Stores (NMS) annual price list (Ministry of Health, 2012). However, the actual retail cost of an oral self-test is likely to be much higher as reported in the United States, at ($40) per kit. From our findings, it is clear that any increase in price, even at $2 for the package reduces the utility of oral testing significantly

(Figure 5). In fact the existing rapid testing (home-based or even at public or mobile outreaches) gets higher shares of preference in that scenario. In this study, most participants, 179 (72.7%) reported that they would definitely purchase an oral HIV self-test kit when available on the local market, at a median (IQR) price of $1.9 ($1.2 - $3.9). This finding supports the claim that costing oral tests highly may deter uptake among the rural poor and attract a predominantly affluent clientele composed of persons at low risk for HIV infection (the "worried well" and new sexual partners) as well as persons with very recent (and therefore undetectable) high-risk exposures (Campbell & Klein, 2006; Paltiel & Walensky, 2012). However, self-testing is still among the key strategies that can reach HIV positives earlier and contribute to increasing uptake if incorporated into community HIV testing and counseling (HTC) programs (Suthar et al., 2013).

The location where HIV testing is done may influence the uptake and frequency of HIV testing. Our study identified higher preference for locations that minimize the necessity to travel, like home-based, public facilities and mobile outreaches respectively. This finding is plausible considering that long distances to care facilities are a critical barrier for HIV testing (Larsson et al., 2012). Private locations had the least utility, probably in part due to the costs of care usually associated with the care provided.

We examined the internal validity of our data by comparing the frequencies that selected concepts of the fixed task with the predicted (simulated) shares of preference from the overall random tasks respectively (Figure 5.5). The differences corresponded to the mean absolute and squared errors respectively. The utility values estimated from the covariate HB model were used to predict the shares of preference for the fixed task. The shares of preference were predicted fairly accurately across all HIV test service concepts. The mean absolute error was quite small (less than 4%) with the mean square error at 16%. Our results showed strong consistency with

theoretical predictions, given the direction and magnitude of the utility values estimated, particularly for the price attribute.



Product	Shares of Preference, SE (%)				
	Fixed Task	Simulated	Error (%)	Absolute Error	Square Error
Concept I	24.35 (2.65)	30.85 (1.03)	-6.50	6.50	42.25
Concept II	5.31 (1.42)	3.69 (0.61)	1.62	1.62	2.62
Concept III	3.87 (1.16)	3.55 (0.82)	0.32	0.32	0.10
Concept IV	66.59 (2.91)	61.91 (1.35)	4.68	4.68	21.9
				MAE = 3.28	MSE = 16.72

Figure 5.5: Vaidation of Utility Values:Fixed vs. Simulated Shares of Preference

MAE – Mean Absolute Error MSE – Mean Square Error

To our knowledge, this may be the first study to add value to the numerous attitudes based surveys and provided in-depth understanding of valuations that drive such populations seeking HIV testing services. Unlike previous conjoint studies, our study derived these utilities from a community of previously untested fisherfolk at high-risk of HIV representing the general population. Our study assessed the utility of oral swabs and self-tests as these are likely to be increasingly used in the near future. The utility measures may be limited by the fact that HIV

testing is not purely a private good and may be influenced by other extraneous factors not assessed in this study. However, we examined realistic scenarios including the *none* option, to represent those who despite all service options may not desire to trade. Being computer assisted, the survey administration did not take more cognitive effort compared to paper based versions. Our findings were consistent with the theoretical predictions. Our assumptions for the simulation may not have been realistic in these settings, considering the current logistical challenges of maintaining adequate stocks of HIV tests for HIV test programs. However these results are meaningful in relative context in as far as choice of HIV test services in Uganda are concerned.

Conclusion

Our study showed that HIV test timeliness and accuracy, counseling and the price of the test are the main factors that are important in determining individual preferences for HIV testing in a high-risk community of fisherfolk in Uganda. An oral HIV self-test with highly accurate and immediate results offered at no fee with counseling support could increase HIV test uptake.

CHAPTER 6

SYNTHESIS

Key Findings

To our knowledge, our study is the first to provide empirical evidence on balancing the potential benefits of accessing HIV testing services using self-testing as the main strategy; with the unknown potential risks of errors, misuse and misinterpretation. This balance has been a subject of wide debate and speculation, more so within the general population located in areas with a high HIV burden, limited resources and education.

On evaluating the accuracy of unsupervised HIV self-testing, we found that its accuracy was satisfactorily high, with an overall sensitivity of 90% compared to the current standard of care in field settings of Uganda. This accuracy was non different among males compared to females, or by any other demographic characteristics. The accuracy improved significantly when its use was supervised, although the difference was large enough not to demonstrate non-inferiority to the rapid tests currently in use. Non-inferiority was not demonstrated definitively, using a conservative non-inferiority limit. However the test performance improved among those who actually used it and was non-inferior in its measure of specificity. HIV self-testing will be useful in these settings once potential users are trained better in its use.

Among the implementation effectiveness measures, our study observed a fairly high error rate among the supervised users of the self-test, confirming concerns that have been raised previously. Although these errors may not significantly affect the performance of the test, they have the potential to limit the overall effectiveness of the self-testing strategy at community level

if not addressed, assuming that a similar proportion of errors occurred among the unobserved or unsupervised users of the HIV self-test. Most individuals who erred in timing the test did so because they suddenly discovered that they lacked a timing device, like a watch or clock at a point when they had already began testing. Others were so curious and excited and ended up incorrectly swabbing their oral mucosa having not followed the illustrated instructions well. Some of these can be addressed by modifying the behavior or improving the knowledge base of potential users, or by finding innovative ways to provide timing devices or demonstrations on using the test kits.

We also discovered that close to 5% of individuals conducting HST did not return for follow-up and revalidation of their findings. This underscores that among HST users a substantial number may not link to care, or remain with invalid findings (if their test was poorly conducted or read).

From our initial analysis, it is clear that HST is a feasible strategy and can be used to improve access (and thereby coverage) to HIV testing in these settings.

In our analysis of preference data, we found that timeliness and accuracy have the highest relative importance score, followed by HIV test price and counseling respectively. Individuals placed high a high utility on tests that were immediate and provided highly accurate results. Most of our participants were sensitive to the price of the test, despite more than 70% declaring that they would purchase an HIV self-test-kit if commercially available. This indicates that if priced right, several individuals are ready to subsidize their own costs of taking an HIV test, thereby giving them the anonymity and privacy they desire in taking HIV testing as they could purchase it whenever they want it for immediate or subsequent use.

Being able to access the services of a trained counselor was among the top three attributes with highest relative score of importance in preference for HIV tests. This finding underscores the value participants attach to the ability of conveying the test results and explanation of their significance, a role traditionally done by a counselor. Unfortunately self-test kits only come with illustrations and some phone contacts if this service is needed. This needs to be evaluated further, as it is clear that these aides may not be effective in rural settings. An appropriate modality of offering counseling needs to be designed and optimized for the successful use and or roll-out of HST as a key strategy to improve uptake of HIV testing.

Our study also found no differences in the mean relative importance scores by age, sex or income. However, significant differences were found in the mean utility scores for oral self-testing; with females having significantly higher scores. Our study also showed significant differences by HIV testing history, with the first time testers having comparatively significantly low mean importance scores for mode of testing and location of testing. There was no difference in mean importance score for price, counseling and accuracy among previous testers and first-time testers. This finding could indicate that previous testers are highly motivated to test, given their higher utility values to HIV test attributes in general compared to those who have never taken the test. Compared to men, the uptake of HST may be more successful among women; however this hypothesis requires further evaluation.

Using the utility scores generated from individual choices, our study showed the superiority of an HIV test service package that includes and oral test conducted in a home based setting to the current standard of care, assuming it is also provided at no cost. When introduced at a cost its share of preference drop significantly.

In summary, our study found that HIV self-testing is feasible but sub-optimal for use in field settings of Uganda. More evaluation needs to be done to optimize HST in order to improve its implementation effectiveness.

Policy and Practice Recommendations

Our findings are important in meeting the policy and practitioner needs of stakeholders in low resource settings that need to increase access and uptake of HIV testing programs. Our findings will be critical in five key policy areas.

Regulation

Use of un-regulated HIV self-testing has already been reported in several areas hardest hit by the epidemic, including Uganda (Natukunda, 2013). This study provides evidence that can be used for development of a regulatory framework of quality diagnostics for HIV, more so for providers that may need to review their testing algorithms in light of these findings. Key factors that may impact procedural and design controls for a more effective HST roll-out have been highlighted by our analysis. These include the major attributes of HIV testing highlighted above. HST may need to be well supervised by practitioners until it has been optimized for wider field use.

Priority Populations

Like other HIV testing strategies, HST may not work for all the masses but may need to be prioritized to meet the needs of most at risk persons (MARPS). Among these groups, our study highlights the utility of HST use among fisherfolk, a group of individuals with one of the highest burden of HIV in Uganda (Kissling et al., 2005). Our findings show the feasibility and

acceptability and accuracy of HST in this priority population, and its implementation effectiveness measures that can guide targeted interventions for this population. Our findings are also suggestive that the uptake of HST may be better among women, given their significantly higher mean utility scores in comparison to men.

Access, Affordability and Logistics

This is a critical policy and practice area in the field of HIV testing. Many programs have had logistical nightmares maintaining adequate logistics for testing, with several stock-outs of HIV test logistics reported. Our study provides cost information that can be used to estimate willingness to pay, as well as the incremental cost effectiveness measures for such interventions.

Combination Prevention

Our study has ably demonstrated the response of lay persons to current HCT strategies used as a precursor to combination prevention approaches. The relative importance of attributes and variations in preferences identified in this study provide health care professionals and policy makers a better understanding of the expectations of high-risk persons for HIV testing.

Social and Ethical Issues

This study provides some insights into some of the potential social and ethical issues of HST. Counseling was found to be of high relative importance in the overall utility of an HIV test; however our study did not examine alternative models that can minimally be provided to respondents. Findings from this study also shed light on the potential for human error using HIV self-tests, a concern that has to be addressed if the tests are to be used at a wider scale in resource limited settings. Guidance and education on how to minimize these errors will be critical. Like

most other rapid tests, the performance of rapid HST is imperfect especially during sero-conversion. Therefore guidance for users who test HIV seronegative with HST is crucial, more so for individuals with high or repeated exposure to HIV. Linkage to care and support is a crucial policy area, considering that counseling and referral for first time testers is not assured after HST.

Limitations and Alternate Approaches

Our analysis of accuracy in this context was limited by the ideal choice of gold standard (Rapid HIV Testing). When compared to the true gold standard (Western Blot) test results, the rapid tests had lower sensitivity and specificity of 96.8%; 95% CI: (83.3 – 99.9%) and 94.7%; 95%CI: (73.9 – 99.9%) respectively (Table A1, Appendix A). The accuracy of oral HST was even much lower in comparison to Western Blot, as the sensitivity and specificity was 93.6% and 94.4% respectively. This may have artificially overestimated our findings on accuracy. Due to the high cost of confirmatory tests and practical considerations, not all clients would have had Western Blot confirmatory tests done. Given that 93.9% (31/33) of the participants who tested seropositive on the screening test (using rapid HIV test algorithm) had their disease verified using the gold standard test, while only 8.9% (19/213) of the participants who tested seronegative on the screening test had their disease verified, our ordinary estimates of sensitivity and specificity would have been subject to partial verification bias if Western Blot was used as the gold standard (Pepe & Alonzo, 2001). This bias was eliminated in our study since all participants had Rapid HIV testing, including the six individuals who did not return for HST revalidation. Despite the shortcomings of the serial Rapid Test Algorithm, it was practical for field evaluation of the effectiveness of oral HST considering that it is the current standard of care

for HCT in Uganda. The Western Blot results indicated very high quality of the field tests conducted in this study.

We found two individuals with indeterminate results, however equal among both groups as there was 1 indeterminate in both the supervised and unsupervised arms of the study. Both were confirmed to be HIV negative and considered as such in the ITT and PP analysis. By assuming that all 6 persons who did not return as HIV negative for the ITT analysis gave us a conservative estimate of the sensitivity and specificity of unsupervised HST without significantly biasing our findings. Only 1 among these was ultimately confirmed as HIV positive. The assumption reduced our estimate of sensitivity from 94.7% in the per-protocol analysis to the 90% reported in the ITT analysis; but slightly increased our estimate of specificity from 94.9% reported for the ITT analysis to 95.1% determined in the PP analysis respectively.

Random utility models have good measurement properties for the values individuals attach to their choices. However, they provide limited insight into the cognitive process that informs those values (Hawkins et al., 2013). More qualitative studies need to be done to evaluate the utility of HST, particularly as regards to the individual needs or thoughts for counseling while using a home based HIV self-test kit. The assumptions made for the simulations may not be met in the real market, however they provide useful clues to what the preferences may be when these service packages come to life in the near future. Our utility models were built and reported according to the good conjoint research practice checklist developed by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) (Bridges et al., 2011).

Future Research

In light of our findings, new hypotheses on the utility of HST as a strategy to increase access and uptake to HCT have been generated that will need to be evaluated further. There is need for longitudinal studies to follow-up participants and assess the true outcomes of HST, specifically the HIV serostatus, given that it may not detect HIV infection during the acute sero-conversion phase of HIV (false negatives). Despite the false negative rate being so low, the precision of the true measure of HST accuracy can be improved once individuals are followed-up with continual and repeated testing.

Our study did not evaluate any population-level risk factors or benefits of expanding HIV testing through HST. Although we didn't find evidence of preference of HST within segments of our study participants, or by any covariate data, there is need to understand the motivation behind conducting a self-test in order to know if this strategy may work better for particular sub-groups of the population.

Counseling was identified among the key attributes informing the utility of an HIV test. There is need to determine alternative models of counseling that can be done seamlessly with an HST strategy, or the determination of the minimum information sufficient to conduct unsupervised HST in such rural high-risk populations.

The true cost and cost effectiveness of HST interventions in these populations needs to be clearly understood if this strategy is to be applied to any part of these population.

Conclusion

In light of the performance of existing strategies of HIV counseling and testing, our study has shown that HIV self-testing has sub-optimal accuracy. We have shown that un-supervised

HST has high accuracy among lay users, and may be non-inferior to rapid HIV testing conducted in field settings. Our findings have demonstrated that HST is a feasible approach to increase the access to HCT, and subsequently its uptake in order to bring many into HIV care and prevention programs. Individuals most prefer oral tests conducted at no cost in home based settings, with rapid, accurate results that can be provided with access to a counselor.

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APPENDIX

A – QUALITY ASSURANCE – HIV CONFIRMATORY RESULTS

Table A1: Quality Assurance Test Results

	Western Blot		Total
Index Test	Positive	Negative	
HIV Self-Test$^{\delta}$ +	29	1	30
HIV Self-Test -	2	17	19
Sub-Total	31	18	49
Rapid Test§ +	30	1	31
Rapid Test -	1	18	19
Sub-Total	31	19	50

δ – *Oraquick* In-Home HIV Test § - Serial Algorithm of *Determine*, *StatPak* and *Unigold* Rapid Tests

Sensitivity (HST) – 93.6%, 95%CI: (78.6 – 99.2); Specificity (HST) – 94.4%, 95%CI: (72.7 – 99.9)

LR+ (HST) – 16.83 (2.5 – 113.3); LR-(HST) – 0.068 (2.5 – 0.2626)

Sensitivity (Rapid Test) – 96.8%, 95%CI: (83.3 – 99.9); Specificity (Rapid Test) – 94.7%, 95%CI: (73.9 – 99.9)

LR+ (Rapid Test) – 18.39 (2.72 – 124.01); LR- (Rapid Test) – 0.034 (0.0049 – 0.235)

B –CONDITIONAL AGGREGATE LOGIT MODEL

Table A2: Utility Estimates, Multinomial Conditional Logit Regression Model (Aggregate Logit)

Variable (Attribute), Level	Coefficient	Standard Error
Mode of HIV Test and Specimen collection		
Rapid HIV Test by Finger Prick	-0.17817	0.05217
Oral Self HIV Test Using Oral Swab	0.10115	0.04921
Provider Administered HIV Test Using Oral Swab	0.15788	0.04858
Lab-based HIV Test e.g. ELISA Using Venipuncture	-0.08086	0.08391
Location of HIV Testing		
Public Clinic	0.03769	0.04712
Private Clinic	-0.12970	0.04932
Mobile Outreach	-0.01175	0.04834
Home Based	0.10376	0.04983
Price		
$0	0.91931	0.03825
$2	-0.18616	0.04052
$4	-0.73315	0.04536
Counseling		
Talk to a Counselor	0.50147	0.02879
No Counseling, read brochure or test-inserts	-0.50147	0.02879
Timeliness and Accuracy		
Immediate, Almost Always Accurate	0.81960	0.03915
Results 1-2 Weeks, Always Accurate	-0.81960	0.03915
NONE	-0.81532	0.08991

C – SATURATED HIERARCHICAL BAYES MODEL

Table A3: Utility Estimates for Covariates Run (Hierarchical Bayes Model)

Variable (Attribute), Level	Intercept[§]	Age > 28 vs. ≤ 28 yrs (ref)	Sex Male vs. Female (ref)	Income ≥$30.5 vs. ≤$30.5 (ref)	HIV Test History Ever vs. Never (ref)
Mode of HIV Test and Specimen collection					
Rapid HIV Test by Finger Prick	-0.48564	0.127414	-0.27864	0.116161	0.09618
Oral Self HIV Test Using Oral Swab	0.845651	-0.14148	-0.43491	-0.08301	-0.23254
Provider Administered HIV Test Using Oral Swab	0.277431	0.375874	-0.16441	-0.06058	-0.03389
Lab-based HIV Test e.g. ELISA Using Venipuncture	-0.63744	-0.36181	0.877956	0.02743	0.170247
Location of HIV Testing					
Public Clinic	0.461629	0.165526	-0.10762	-0.02569	-0.49081
Private Clinic	-0.32866	0.123796	0.165977	0.00209	-0.16489
Mobile Outreach	-0.06783	-0.25212	-0.01637	0.014124	0.174857
Home Based	-0.06514	-0.0372	-0.04199	0.009471	0.48084
Price					
$0	2.172155	0.584532	-0.41248	0.143232	-0.00504
$2	-0.29389	-0.18004	0.135866	0.104683	-0.14571
$4	-1.87827	-0.40449	0.276611	-0.24792	0.150746
Counseling					
Talk to a Counselor	1.252615	0.040711	0.095638	0.166163	-0.31746
No Counseling, read brochure or test-inserts	-1.252615	-0.040711	-0.09564	-0.166163	0.31746
Timeliness and Accuracy					
Immediate, Almost Always Accurate	2.29686	-0.08955	-0.08983	0.12782	-0.00165
Results 1-2 Weeks, Always Accurate	-2.29686	0.08955	0.08983	-0.12782	0.00165
NONE	-1.96686	0.261136	0.39783	-0.28565	-0.01841

§ - Mean population part-worth (utility) estimate when referent covariates are coded zero

D – CONSENT FORM

I, _____, agree to participate in a research study titled " *Implementation Effectiveness of oral self-HIV testing and preferences for HIV testing in Uganda: A randomized study* " conducted by Dr Christopher Whalen, an Investigator from the Department of Epidemiology & Biostatistics at the University of Georgia (706-542-0468) and with Dr Stephen Asiimwe, also from the Department of Epidemiology & Biostatistics, University of Georgia (706-542-8087 or 256-772-479062). I understand that my participation is voluntary. I can refuse to participate or stop taking part at anytime without giving any reason, and without penalty or loss of benefits to which I am otherwise entitled. I can ask to have all of the information about me returned to me, removed from the research records, or destroyed.

The purpose of this study is to determine the accuracy of oral self-administered HIV testing to find out if lay users can obtain valid HIV test results that are as accurate as currently available health worker or provider- administered rapid tests used in field settings in Uganda; and to determine user preferences for HIV testing. All consenting participants will be surveyed to determine their preferences for HIV testing. You will then be randomly assigned to one of two possible groups, one with a health worker(provider) collecting an oral sample and a finger-stick sample for HIV testing; or the other in which you would collect the oral sample and self-test for HIV and the health worker(provider) would collect the finger-stick sample for confirmation.

HIV is the germ that causes the disease called AIDS. The test for HIV detects the body's reaction to the virus (antibody). It does not detect the virus itself. You are not required to have the test. Your oral fluid and blood will be tested for HIV. You understand that questions regarding the oral and blood tests are not for diagnostic purposes. If you have questions about your test results you should see a physician (Doctor). Testing for HIV is voluntary. This test is being done for a research study. You should be tested only if you are well informed about the risks and benefits of testing. Please read this consent form carefully so that you can make an informed decision about having the blood test.

What the Test Means
If you test POSITIVE, you have the HIV virus. That means you can pass it to others. The test cannot tell how long a person has been infected. A positive test does not mean that you have AIDS, which is the most advanced stage of HIV infection.

If the test is NEGATIVE, you probably do not have the HIV virus. A negative test usually means that a person is not infected with HIV; however, recently infected persons can have a negative test, which becomes positive in three months after infection. This would mean that your body has not yet made antibody to fight the virus.

False results (a negative test in an infected person, or a positive result in an uninfected person) are rare. Indeterminate (unclear) results are also rare. When a test result does not seem to make sense, a repeat test or another kind of blood test is done to find out if the person is infected or not.

Procedures

This is what will happen if you decide to have the test. First, you will meet with a counselor to get more information about the risks and benefits of the test. They will explain the meaning of test results. They will teach you how to reduce the chance of spreading HIV. They will explain the dangers of HIV infection. They will take an oral swab and later a sample from your finger, with a sterile lancet. Self-administered testers will do the oral HIV testing themselves after a demonstration. An oral fluid specimen is collected by swabbing the upper and lower mucous lining along the gum line in the mouth. They will test your blood to confirm presence or absence of HIV. It will take about 20 minutes to get your test result. You will be told your result on the same day that you give an oral sample and blood to have the test. The study staff will talk with you about the meaning of your result and how you feel about it. Sometimes HIV tests are not clearly positive but also not negative. In that case, we will do more tests until we know the result for sure. If the test result is positive, you will learn how to notify anyone with whom you have sex, and how to get services for yourself.

Risk and Benefits

The lancet used to draw blood for the test may cause discomfort. A bruise may form where the lancet enters the skin, and if you get a bruise, it usually goes away within a week. Learning the test results may cause stress, anxiety and depression for people being tested and for their partners. You might be tempted to have unsafe sex if the result is negative. This would increase your risk of becoming infected with HIV. It is possible that you may feel nervous about the information you are going to give us and concerned about any links between this information and your name or identity.

The benefits of being tested are personal. Test results may help diagnose a medical problem, guide your health care, help you follow strategies to improve your health, and may help you avoid transmitting HIV to other people. If you are worried about AIDS, you might feel better if you have a negative test. Sometimes knowing that the test is positive can relieve stress. You may want to know your test results before you have sex with a new partner. There may be other benefits of testing that we don't know about now.

Confidentiality

Your HIV antibody test result must be held in the strictest confidence, and no identifying information of any kind will be released to any other person or agency without your specific written permission. No publication or public discussion of the testing will contain information that could identify you.

Other Information

We will tell you the results of the test in person. If you test positive, we will encourage you to notify your sexual partners. The investigator or his representative can answer all your questions about this study. If you have any additional questions, you can ask them now, or contact a study representative at the telephone number on this form.

VOLUNTEER'S STATEMENT

The benefits and risk about HIV testing on the preceding page has been explained to me, and I willingly agree to participate. I have had an opportunity to ask questions. I have been told that if I have future questions about the research, I can ask one of the investigators listed above.

No reimbursements will be provided for participation in this study.

No individually-identifiable information about me, or provided by me during the research, will be shared with others without my written permission, except if it is necessary to protect my welfare (for example, if I were injured and need physician care) or if required by law. I will be assigned an identifying number and this number will be used on all of the questionnaires I fill out.

The investigator will answer any further questions about the research, now or during the course of the project.

I understand that I am agreeing by my signature on this form to take part in this research project and understand that I will receive a signed copy of this consent form for my records.

_____	_____	
Name of Researcher	**Signature**	**Date**

Telephone: _____

Email: _____

_____	_____	
Name of Participant	**Signature**	**Date**

_____	_____	
Witness Name (Print)	**Witness Signature**	**Date**

Please sign both copies, keep one and return one to the researcher.

Additional questions or problems regarding your rights as a research participant should be addressed to The Chairperson, Institutional Review Board, University of Georgia, 629 Boyd Graduate Studies Research Center, Athens, Georgia 30602; Telephone (706) 542-3199; E-Mail Address IRB@uga.edu

And the Chairperson, HIV/AIDS Research Committee (ARC) Institutional Review Board, Dr Katongole Mbidde (Tel: 041 – 320 631) or the HIV/AIDS Research Committee Secretariat at Uganda National Council for Science and Technology Nasser Road, Kampala; on Telephone 041-705 500.

E – SAMPLE CHOICE SET

If these were your only options for HIV Testing services in and around your community, which one would you choose? Assume that the HIV Test service scenarios below are identical in all other ways except for the differences shown.
Choose by selecting **one** option among these shown below:
(2 of 10)

Mode of HIV Test and Specimen Collection	**Provider Administered HIV Test Using Oral Swab**	**Rapid HIV Test by Finger Prick**	**Rapid HIV Test by Finger Prick**	**Oral Self HIV Test Using Oral Swab**	
Location of HIV Testing	**Mobile Outreach**	**Private Clinic**	**Home Based**	**Private Clinic**	**None of these. I would prefer not to take the HIV test given these conditions.**
Counseling	**No Counseling, read brochure or test-inserts**	**No Counseling, read brochure or test-inserts**	**Talk to a Counselor**	**Talk to a Counselor**	
Price	**10,000 Ush**	**5000 Ush**	**5000 Ush**	**0 Ush(Free, Subsidized or no Charge)**	
Timeliness and Accuracy	**Immediate, Almost Always Accurate**	**Results 1-2 Weeks, Always Accurate**	**Immediate, Almost Always Accurate**	**Immediate, Almost Always Accurate**	
	○	○	○	○	○

D - 7, T - HIVPrefStdy_Random2

Uganda National Council for Science and Technology

UNCST

National HIV/AIDS Research Committee

ARC 137 **May 23rd 2013**

Dr. Stephen Asiimwe
Principal Investigator
Kabwohe Clinical Research Center
Bushenyi

Category of review:
[**X**] Initial review
[ ] Continuing review
[ ] Amendment
[ ] Reactivation
[ ] SAEs

In the matter concerning the continuing review of a research project entitled, **"Implementation Effectiveness Of Oral Self-HIV testing and Preferences for HIV testing in Uganda: A Randomized Study"**

The National HIV/AIDS Research Committee (NARC) at its 136th meeting held on April 26th 2013 reviewed the above study and raised comments, your responses in a letter dated May 3rd 2013 have been reviewed and found to be satisfactory.

In this respect, the NARC's **APPROVAL** of the study is granted and shall be valid until **April 26, 2014**. The approval granted includes all materials submitted to the NARC for review.

Please note that the annual report and the request for renewal where applicable, should be submitted two months before expiry date of approval.

Also note that any problems of a serious nature related to the execution of the research protocol should be promptly reported to the NARC, and any changes to the research protocol should not be implemented without NARC's approval except when necessary to eliminate apparent immediate hazards to the research participant(s).

You are required to register the research protocol with the Uganda National Council for Science and Technology (UNCST) for final clearance to undertake the study in Uganda.

Signed .....
Dr. Joseph Ochieng, Vice Chair NARC

cc: Executive Secretary, UNCST

NATIONAL HIV/AIDS RES. COMMITTEE
APPROVED
VALID UNTIL
26 APR 2014
P. O. BOX 6884 KAMPALA
UGANDA

LOCATION/CORRESPONDENCE

Plot 6 Kimera Road, Ntinda
P. O. Box 6884
KAMPALA, UGANDA

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EMAIL: info@uncst.go.ug
WEBSITE: http://www.uncst.go.ug

G – RESEARCH CLEARANCE (UGANDA)

THE REPUBLIC OF UGANDA

OFFICE OF THE PRESIDENT

PARLIAMENT BUILDING P.O.BOX 7168 KAMPALA. TELEPHONES: 254881/6, / 343934, 343926, 343943, 233717, 344026, 230048, FAX: 235459/256143
Email: secretary@op.go.ug. Website: www.officeofthepresident.go.ug

ADM 154/212/01

July 25, 2013

The Resident District Commissioner, Sheema District
The Resident District Commissioner, Bushenyi District
The Resident District Commissioner, Kasese District
The Resident District Commissioner, Rubirizi District

This is to introduce to you **Asiimwe Stephen** Researcher who will be carrying out a research entitled **"Implementation effectiveness of oral self-HIV testing and preferences for HIV testing in Uganda: A randomized study"** for a period of **05 (five) months** in your district.

He has undergone the necessary clearance to carry out the said project.

Please render him the necessary assistance.

By copy of this letter **Asiimwe Stephen** is requested to report to the Resident District Commissioners of the above districts before proceeding with the Research.

Alenga Rose
FOR: SECRETARY, OFFICE OF THE PRESIDENT

Copy to: Asiimwe Stephen

H – NATIONAL APPROVAL (UGANDA)

Uganda National Council for Science and Technology

(Established by Act of Parliament of the Republic of Uganda)

05/08/2013

Our Ref: HS 1409

Dr. Stephen Asiimwe
Kabwohe Clinical Research Centre
Bushenyi

Re: Research Approval: **Implementation Effectiveness of Oral-self HIV Testing and Preferences for HIV testing in Uganda: A Randomized Pilot Study**

I am pleased to inform you that on **06/06/2013**, the Uganda National Council for Science and Technology (UNCST) approved the above referenced research project. The Approval of the research project is for the period of **06/06/2013** to **06/06/2014**.

Your research registration number with the UNCST is **HS 1409**. Please, cite this number in all your future correspondences with UNCST in respect of the above research project.

As Principal Investigator of the research project, you are responsible for fulfilling the following requirements of approval:

1. All co-investigators must be kept informed of the status of the research.
2. Changes, amendments, and addenda to the research protocol or the consent form (where applicable) must be submitted to the designated local Institutional Review Committee (IRC) or Lead Agency for re-review and approval **prior** to the activation of the changes. UNCST must be notified of the approved changes within five working days.
3. For clinical trials, all serious adverse events must be reported promptly to the designated local IRC for review with copies to the National Drug Authority.
4. Unanticipated problems involving risks to research subjects/participants or other must be reported promptly to the UNCST. New information that becomes available which could change the risk/benefit ratio must be submitted promptly for UNCST review.
5. Only approved study procedures are to be implemented. The UNCST may conduct impromptu audits of all study records.
6. A progress report must be submitted electronically to UNCST within four weeks after every 12 months. Failure to do so may result in termination of the research project.

Below is a list of documents approved with this application:

	Document Title	Language	Version	Version Date
1	Research proposal	English	N/A	30th Jan 2013

Yours sincerely,

Jane Nabbuto
for: Executive Secretary
UGANDA NATIONAL COUNCIL FOR SCIENCE AND TECHNOLOGY

cc Chair, National HIV/AIDS Research Committee IRC, UNCST, Kampala

LOCATION/CORRESPONDENCE

Plot 6 Kimera Road, Ntinda
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KAMPALA, UGANDA

COMMUNICATION

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EMAIL: info@uncst.go.ug
WEBSITE: http://www.uncst.go.ug

I - UNIVERSITY OF GEORGIA IRB APPROVAL

The University of Georgia

Office of The Vice President for Research
DHHS Assurance ID No. : FWA00003901

Institutional Review Board
Human Subjects Office
612 Boyd GSRC
Athens, Georgia 30602-7411
(706) 542-3199
Fax: (706) 542-3360
www.ovpr.uga.edu/hso

APPROVAL FORM

Date Proposal Received: 2013-01-10 **Project Number:** 2013-10551-0

Name	Title	Dept/Phone	Address	Email
Dr. Christopher Whalen	PI	Epidemiology and Biostatistics N132 Coverdell Center	706-227-4736	cewhalen@uga.edu
Dr. Stephen Asiimwe	CO	Epidemiology and Biostatistics		asiimwes@uga.edu

Title of Study: Implementation Effectiveness of oral self-HIV testing and preferences for HIV testing in Uganda: A randomized study

45 CFR 46 Category: Expedite 2a, 3, 7

Parameters:
This study will also receive review and approval from National HIV/AIDS Research Committee (NARC): PI will submit a copy of NARC IRB approval when this becomes available;
Approved for Institutions with Authorization Letters on File;

Change(s) Required for Approval:
Receipt of final version of instruments;
Revised Application;
Revised Consent Document (s);

Approved : 2013-04-10 Begin date : 2013-04-10 Expiration date : 2014-04-09

NOTE: Any research conducted before the approval date or after the end data collection date shown above is not covered by IRB approval, and cannot be retroactively approved.

Number Assigned by Sponsored Programs: **Funding Agency:**

Your human subjects study has been approved.

Please be aware that it is your responsibility to inform the IRB:
. . . of any adverse events or unanticipated risks to the subjects or others within 24 to 72 hours;
. . . of any significant changes or additions to your study and obtain approval of them before they are put into effect;
. . . that you need to extend the approval period beyond the expiration date shown above;
. . . that you have completed your data collection as approved, within the approval period shown above, so that your file may be closed.

For additional information regarding your responsibilities as an investigtor refer to the IRB Guidelines.
Use the attached Researcher Request Form for requesting renewals, changes, or closures.
Keep this original approval form for your records.

Chairperson or Designee,
Institutional Review Board