Uptake, Acceptability, and Cost-Effectiveness of a Targeted Pediatric HIV Testing Strategy

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Abstract

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Background: Prevention of mother to child transmission of HIV (PMTCT) programs have scaled up and resulted in fewer new infant infections globally. However, children born prior to the scale up of PMTCT and early infant diagnosis (EID) systems, as well as those who are missed by the complex systems, remain undiagnosed. In the absence of treatment, pediatric HIV infection has high morbidity and mortality; prompt testing and treatment are essential. Universal testing strategies are relatively inefficient; provider-initiated testing and counseling identifies many positive children but tends to identify those children who are already symptomatic and least likely to survive even with appropriate treatment. Targeted strategies are needed to increase the efficiency of pediatric HIV case detection.

Methods: In a HIV care clinic in Nairobi, HIV-infected adults were systematically assessed to determine whether they had children of unknown HIV status ages 0-12. Eligible caregivers were referred for enrollment in the study and elected to test their children in either a home- or clinic-based setting. Uptake and yield of testing were compared before and after the systematic assessment and active referral intervention (Chapter 1). Health care workers from PMTCT, Voluntary Counseling and Testing (VCT), and HIV care clinics completed focus group discussions and a subset of caregivers completed in-depth interviews about barriers and facilitators to pediatric HIV testing. Themes were identified and compared with barriers and facilitators identified in the enrollment survey (Chapter 2). Cost-effectiveness of passive referral, active referral, and active referral plus home-based testing was estimated (Chapter 3).

Results: Chapter 1: A substantial proportion of adults in care had children of unknown status. Following implementation of active referral, the rate of pediatric HIV testing increased 3.8-fold ($p<0.001$). However, 86% of caregivers did not test their children during the intervention. HIV prevalence among 108 tested children was 7.4% and median age was 8 years (IQR: 2-11); one child was symptomatic at the time of testing. Chapter 2:

Interview and focus group data revealed barriers and facilitators that applied to three periods of the pediatric HIV testing process: concerns about the decision-making process to test, the test visit itself, and coping during the post-test period. The greatest concerns that emerged from both qualitative and quantitative sources were inaccurate information about the likelihood of child infection and prognosis, challenges with permission and disclosure with partners and children, experiences with discouraging provider attitudes, lack of clear pediatric testing guidelines around consent/assent and disclosure, insufficient staff and inappropriate space for children, concerns about privacy, and perceived costs of testing and care. Chapter 3: Uptake of testing and average costs were highest in the active referral plus home-based testing model, followed by the active referral model, with passive referral being the least costly and least effective. The incremental cost effectiveness ratio (ICER) comparing active referral plus home-based testing to active referral was $58 per child tested and $789 per HIV-infected child identified from the Ministry of Health perspective. The ICER comparing active referral to passive referral was $57 per child tested and $768 per HIV-infected child identified. The ICER comparing active to passive referral was robust to variations in cost and effectiveness in sensitivity analyses; the ICER comparing active referral plus home-based testing to active referral was not.

Conclusions: Referring HIV-infected parents in care to have their children tested revealed many untested children and significantly increased the rate of pediatric testing; prevalence of HIV was high. Despite increases in pediatric testing, most adults did not complete testing of their children. Interventions are needed to address client, provider, and clinic-level barriers to pediatric HIV testing. Assisted disclosure services for caregivers, partners, and children; small financial incentives to compensate for lost wages and transport costs; peer support groups and counseling before and after testing; in-service provider training on pediatric HIV testing; and weekend and school holiday clinic dates merit evaluation to address barriers to pediatric testing. Costs for case detection by active referral plus home-based testing and active referral alone were comparable to costs per person tested under adult and EID models; further research is needed to determine whether these models are cost-effective based on disability-adjusted life years averted.

Table of Contents

Abstract 3

INTRODUCTION 7

ACKNOWLEDGEMENTS 9

CHAPTER 1: Active referral of children of HIV-infected adults in care for testing reveals high prevalence of undiagnosed HIV 10

- INTRODUCTION: 10
- METHODS: 10
- RESULTS: 13
  - Recruitment of parents from VCT and PMTCT services 13
  - Testing uptake 13
  - Recruitment of parents from CCC 13
- DISCUSSION: 14
- CONCLUSIONS: 16
  - FIGURE 1: Panel A: Changes in uptake of pediatric HIV testing before and after introduction of active referral system. Panel B: Drop off in pediatric HIV testing cascade. 17
  - FIGURE 2: Study recruitment, referral, eligibility, enrollment, testing, and follow-up. 18

CHAPTER 2: HIV testing for older children: A mixed-methods study examining barriers and facilitators faced by caregivers and healthcare providers 19

- INTRODUCTION: 19
- METHODS: 20
- RESULTS: 22
  - Qualitative and quantitative study participant characteristics 22
  - Qualitative results 22
  - Quantitative results 36
- DISCUSSION: 37
- CONCLUSIONS: 39
  - Table 1: Sociodemographic characteristics of FGD participants 40
  - Table 2: Sociodemographic characteristics of IDI and TAC participants 40
  - Table 3: Illustrative quotes about barriers and facilitators 41
  - Table 4: Barriers, facilitators, and recommendations for pediatric HIV testing 43
  - Table 5: Prevalence of barriers and facilitators and association with testing choice 45
  - Figure 1: Conceptual model adapted from Andersen's Behavioral Model for Health Care Utilization. Barriers and facilitators hypothesized and confirmed in analysis 46
  - Figure 2: Barriers and facilitators to pediatric HIV testing from qualitative interviews and focus groups 47

CHAPTER 3: Comparison of costs and cost-effectiveness of three HIV testing models for older children of HIV-infected adults in care: passive referral, active referral, and active referral plus home-based testing 48

- INTRODUCTION 48
- METHODS 49
  - Model 49
  - Strategies 50
- RESULTS 53
- DISCUSSION 55
- CONCLUSION 57
  - Table 1: Model parameters 58
  - Table 2: Costs included in each comparator by perspective 59

Table 3: Pairwise and incremental cost-effectiveness analyses 60
Table 4: Cost per child tested and cost per positive child identified 61
Figure 1: Simplified decision tree 62
Figure 2: Tornado diagrams for one-way sensitivity analyses 63
Figure 3: ICE scatterplot comparing each pairwise comparison 64
Figure 4: Cost-effectiveness acceptability curve 65
REFERENCES 66

INTRODUCTION

Over 90% of the world's 3.2 million human immunodeficiency virus (HIV) infected children live in Africa and public health programs are expanding to treat infected children [1]. Scale-up of prevention of mother-to-child HIV transmission (PMTCT) programs in Africa has markedly decreased infant HIV infections. However, many HIV-exposed infants remained unidentified and at high risk for infection due to drop off in the PMTCT cascade and high incidence of undiagnosed and untreated maternal HIV during pregnancy/postpartum [2]. While repeat maternal testing during pregnancy and postpartum is recommended in national guidelines, it is poorly implemented; women with acute HIV infection are 3-4 times as likely to transmit to their infants, compared to chronically infected women [2]. Modeling studies suggest that acute maternal HIV infection accounts for a high and growing proportion of new infant infections [3]. Gaps in early infant diagnosis (EID) programs, including identifying HIV exposure, specimen collection and processing, and return of test results contribute to missed diagnoses [4-6]. Finally, a large group of older children who acquired HIV prior to the expansion of PMTCT coverage is undiagnosed.

UNAIDS has set ambitious 90-90-90 targets for HIV: 90% of HIV-infected people know their status, 90% linked to care, and 90% virally suppressed [7]. Children experience severe deficits in HIV testing and treatment; in Kenya, nearly 60% of HIV-infected children are undiagnosed and just 31% are on treatment [8]. In the absence of a systematic testing approach, older children may not be diagnosed until their HIV becomes symptomatic. Children diagnosed with HIV after they are ill have a poorer response to antiretroviral therapy (ART) in terms of growth, development, morbidity, and mortality [6, 9-14]. Additionally, undiagnosed adolescents who reach sexual debut prior to diagnosis are at risk of transmitting HIV to their peers [15]. Detecting HIV infection in children and adolescents prior to symptomatic disease and linking them to care has potential to decrease morbidity, mortality, and transmission.

Systems are lacking to routinely access children for HIV testing prior to symptomatic disease, and pediatric HIV case detection strategies must optimize testing uptake, prevalence, and life-years saved. While provider initiated testing and counseling (PITC) has high uptake and prevalence among those tested, it tends to

preferentially test the sickest children who are least able to benefit from ART. Universal testing through home- or mobile-testing has high uptake and is able to identify children prior to symptomatic illness, but has a low prevalence among those tested. Targeted testing for the children of HIV-infected adults has moderate uptake of testing, identifies children prior to symptomatic disease, and has high prevalence [16, 17]. Combining the uptake of home-based testing with the efficiency of targeted testing is a potential strategy to optimize pediatric HIV case detection.

Optimizing uptake of case detection strategies requires careful consideration of barriers and facilitators to testing [17]. Policy, provider, community, and individual-level interventions may alleviate barriers to testing and care. Determining the most cost-effective models for case detection is critical during a time of limited resources. This project aims to determine the uptake and yield, barriers and facilitators, and cost-effectiveness of a targeted pediatric HIV testing model.

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CHAPTER 1: Active referral of children of HIV-infected adults in care for testing reveals high prevalence of undiagnosed HIV

INTRODUCTION:

An estimated 3.3 million children worldwide are HIV infected, most of whom were born prior to scale up of prevention of mother-to-child HIV transmission (PMTCT) programs [1, 18, 19]. While PMTCT programs have resulted in marked decline in new infant HIV infections and include systems for early infant diagnosis, older children are not routinely tested and are only diagnosed when symptomatic. According to a national survey done in 2012, nearly 60% of HIV-infected children in Kenya are undiagnosed [8]. Outcomes of HIV-infected children who are diagnosed and treated when symptomatic are worse than among those who are treated prior to symptomatic disease [6, 9-14].

Routine testing of all children in the general population may be costly and inefficient due to a low overall prevalence. Conversely, provider initiated testing and counseling (PITC) is incompletely implemented and tends to preferentially test the sickest children who have advanced disease [20]. Testing children of adults attending HIV care may provide an efficient way to diagnose HIV-infected children prior to symptoms [17]. Children have typically lagged behind adults in HIV care and treatment globally, with only 24% on ART, compared to 38% of adults [1]. Recently, UNAIDS has called for 90-90-90 targets—to identify 90% of infected individuals, treat and retain 90% [7]. The first step for children to attain these goals is diagnosis. Targeted HIV testing for the children of HIV-infected parents may be a more efficient strategy for case detection [17, 21, 22].

In this study we systematically offered testing to the children of HIV-infected parents engaged in an HIV treatment program in Kenya. We determined the number of eligible children, uptake, and yield of pediatric testing under this active and targeted model.

METHODS:

Ethics statement The study was approved by the University of Washington Institutional Review Board (IRB) and the Kenyatta National Hospital (KNH)/University of Nairobi (UoN) Ethics and Research Committee. Oral informed consent was obtained from each adult participant enrolling in the study; written informed consent was

then obtained from the subset of those completing pediatric testing. Older children whose parents agreed provided written assent for the HIV test.

Study design This prospective cohort study evaluated uptake of a targeted HIV testing intervention for children. The Counseling and Testing for Children at Home (CATCH) pilot study began recruitment at Kenyatta National Hospital (KNH) in November of 2013 and completed enrollment in September of 2014. Clients were recruited and referred from the KNH Voluntary Counseling and Testing Clinic (VCT), PMTCT Clinic, and Comprehensive Care Centre (CCC). Aggregate hospital testing records from the CCC clinic were collected for the period of January 2013 to August 2014 to determine overall testing rates at the site.

Caregivers were eligible for the study if they were HIV-infected and had at least one child 12 years of age or younger of unknown HIV status. Willingness to have a child tested for HIV was not an enrollment criterion and efforts were made to enroll parents who did not want to test children for HIV. Children were considered to be of unknown HIV status if their biological mother was HIV-infected *or* if their biological mother's partner was HIV-infected but her HIV status was unknown AND either of the following criteria were met: a) the child had never been tested, b) the child had tested negative as an infant but had not had confirmatory negative testing after cessation of breastfeeding, or c) the caregiver felt unsure about the child's status and wished for the child to be tested. Caregivers were able to have any children formally in their care (either biological parent or legal guardian) tested as part of the study.

Recruitment and enrollment HIV-infected clinic attendees were evaluated by clinic staff and invited to participate in the study if they had any children of unknown HIV status $\leq$12 years. Caregivers were referred to the study regardless of their interest in testing their children. Caregivers who declined referral to the study were not contacted further. Caregivers were screened and a subset was excluded due to inappropriately assessed eligibility. At enrollment, caregivers were consented, after which a questionnaire was used to collect information about caregiver sociodemographic characteristics, adult and child HIV testing and treatment history, reasons a parent might want to have child testing, and transportation and opportunity costs. Caregivers were given the choice of having home-based, clinic-based, or no HIV testing for their children.

HIV testing and care referral Following enrollment, caregivers were asked to schedule a home or clinic HIV testing visit. Caregivers were reminded of their appointment to test their children by phone in advance. Caregivers who did not present their children for the testing visit were rescheduled by phone a maximum of 2 additional times, after which they were considered to have declined testing. Children were tested for HIV either in their home or at the CATCH-pilot clinic at KNH according to national Kenyan HIV testing guidelines [23]. Children over 18 months who had ceased breastfeeding were tested by a series of two rapid HIV serologic tests. Children under 18 months or who were recently breastfed were tested first by rapid serologic HIV test and confirmed by HIV DNA PCR test. HIV DNA PCR tests were conducted at the University of Nairobi laboratory as previously described [24].

HIV-infected children were referred to the HIV care clinic or PMTCT clinic of their caregiver's choice to begin treatment. Caregivers of HIV-infected children were re-contacted by phone or in-person appointment post-diagnosis to confirm linkage to care.

Statistical analysis

An interrupted time series analysis using Prais-Winsten regression (linear regression that models first order autocorrelation) was used to compare the mean number of children tested monthly during the period prior to the introduction of the CATCH-pilot study intervention and during the CATCH-pilot study intervention period. To assess the relative increase in proportion of children tested monthly during the pre- and during-intervention periods, a generalized linear model with a log link, normal family, and robust standard errors was used. In both models, a linear term was included to account for natural temporal trends in testing; an interaction term was considered to assess a change in slope between the pre- and during-intervention time periods. November 2013 was considered a washout period and was not included in analyses. All analyses were conducted using Stata 14 IC (StataCorp, College Station, TX). All tests were two-sided with alpha of 0.05.

RESULTS:

Recruitment of parents from VCT and PMTCT services

The referral model was evaluated in VCT, PMTCT, and CCC (HIV care programs) in a pilot period, during which time 11 adults were screened at VCT with 0 enrolled, and 508 mothers were screened in PMTCT, with 10 enrolled. Because the number of enrollees from VCT and PMTCT clinics was low, the following analyses include only the parents derived from the CCC treatment program, described below.

Testing uptake

After controlling for temporal trends and autocorrelation, on average, 10.1 more children were tested per month during the period at KNH CCC when the team implemented active referral compared to the months prior to the intervention (13.6 vs 3.5 children per month, $p<0.001$) (Figure 1, Panel A). This corresponded to a 3.8-fold increase in the proportion of children tested (RR: 3.8, 95%CI: 2.3-6.1, $p<0.001$).

Recruitment of parents from CCC

Between December 2013 and September 2014, 10,426 adults were screened at KNH CCC, of whom 8,287 had children, 3,477 (42%) had children of unknown HIV status, and 611 (7%) had children of unknown status 12 years of age or younger. Among these 611, 320 declined referral to CATCH-pilot study 12 were not screened due to staff unavailability, and 279 were screened. Among those screened, 40 were ineligible, 123 were eligible but not enrolled (of the 133 who initially declined enrollment, 10 later enrolled), and 116 enrolled (Figure 2). Among 116 HIV-infected adults enrolled, 74 (64%) completed testing for their children and had 108 children tested, of whom 8 (7.4%) were HIV-infected; median age was 8 years (IQR: 2-11) and all children linked to care (Figure 2).

Overall, after adjusting for the possibility of ineligibility among those caregivers who declined referral, 86% (95%CI: 83-89%) of eligible caregivers did not test their children with the study staff during the study period (Figure 1, Panel B). The most common reasons for being eligible but not enrolled were having children who lived far away or wanting to take their children for testing at another location (27%), wanting to return later or being in a hurry (35%), wanting to consult with/disclose to/bring their partner (20%), not being interested in a

research study (7%), or wanting testing but outside of a research setting (9%) (Figure 2). The most common reasons for ineligibility among those screened were that the caregiver was HIV-uninfected (14%), all children were too old for study criteria (>12) (49%), no children were of unknown HIV status (29%), and being enrolled in another HIV study (9%) (Figure 2).

DISCUSSION:

In this study we found that active referral for testing, identified a large number of untested older children of HIV-infected adults in care and significantly increased pediatric HIV testing rates. Pediatric HIV prevalence was 7.4%, higher than in the general population (1%) [8] and higher than would be estimated in early infant diagnosis programs with effective PMTCT (<1-3%). The active referral model did not require additional staffing at the HIV care program and could be feasibly implemented at a wide range of facilities with limited additional costs. By engaging adults in care, it is possible that children identified would promptly link to care and treatment because this is not the first HIV diagnosis in the family and others have familiarity with treatment and care; indeed, all HIV-infected children identified in this study linked to care. Targeted testing for the children of HIV-infected adults in care is a low resource, efficient, and easily scalable strategy for case detection prior to symptomatic disease.

As UNAIDS and PEPFAR both prioritize prompt diagnosis and treatment of HIV-infected children to achieve the 90-90-90 targets, innovative models to efficiently diagnose children prior to symptomatic illness are critical. Door-to-door home-based testing of all children is one approach. In prior studies of this model, there is generally high uptake of testing but relatively low HIV prevalence (1%) [8], with higher prevalence in children with risk characteristics such as orphanhood or a suspected or confirmed HIV-infected mother [22, 25, 26]. Provider initiated counseling and testing (PITC) through opt-out models also has generally high uptake and higher prevalence than door-to-door testing [27, 28]; however, children identified through PITC tend to be already ill with HIV, at which point ART confers less benefit compared to their asymptomatic peers [20, 29]. Additionally, PITC—while recommended universally in inpatient and outpatient settings in Kenya—tends to be incompletely implemented and tends to test the sickest children [30]. Upstream strategies that efficiently

identify children prior to symptomatic illness need to be scaled. In Kenya, 55% of children with HIV-infected parents have not been tested, representing an opportunity to scale up targeted testing [8].

Importantly, we identified several gaps that form the pediatric HIV testing and care cascade. Many HIV-infected adults in care (>35%) had children >12 years old who were untested. Our current study was limited to ≤12 year olds because of the lack of carefully formulated adolescent HIV testing approaches that consider issues such as who receives test results, adolescent and parental disclosure, and order of result dissemination when caregivers initiate adolescent testing. This burden of untested adolescents illustrates the critical need for better models and formative research to optimize adolescent HIV testing.

Additionally, while efficient for case detection, testing children of HIV-infected adults in care had suboptimal uptake in this study. Many adults had eligible children, but did not complete testing; in this study, parents reported wishes to test their children elsewhere, consult a partner, or take more time to consider the testing decision as reasons for not testing in the CATCH-pilot study. In previous work, it has been noted that HIV-infected caregivers face a variety of barriers to testing their children—emotional, social, structural, and organizational. Logistically, parents may find it an inconvenience to bring children for testing, due to challenges in affording transport, time off of work, or childcare [31]. Parents have reported fearing emotional suffering for their child if the child is tested—through discrimination and stigma—as well as fears of a child testing positive or dying from HIV, if infected [17, 31, 32]. Parents may not want to test children because a child seems healthy or the parent has uncertainty about the benefits of testing either before symptomatic illness or before sexual debut [31], or because the parent feels guilt or blame regarding having possibly infected the child [17, 32]. Finally, parents have reported fearing a lack of confidentiality and inadvertent disclosure of their own status as barriers to testing children and later disclosure [17, 31, 33]. Interventions that overcome logistical barriers; address the importance of testing before children become symptomatic; allay parents' fears about child suffering; address parents' guilt or blame, and provide support to cope with a child's diagnosis, care, and disclosure are needed to increase uptake of testing.

Strengths of our study included systematic collection of recruitment data, which enabled us to estimate gaps in uptake that would have been missed had we focused only on the enrolled cohort, and a large sample size. Additionally, our study tested active referral mechanisms using existing healthcare workers, reflecting “real life” effectiveness. Our study is limited in that it was not possible to confirm whether parents tested their children elsewhere during the study, or to determine the reason why parents refused referral to the study. The reasons for not testing given by parents who accepted referral but did not enroll may be different than the reasons that would be given by parents who rejected referral. Additionally, this model is limited to HIV-infected parents already engaged in care; in Kenya, 53% of HIV-infected adults are unaware of their status, and 11% of those who are diagnosed are not engaged in care [8]. Finally, this study was conducted at one urban site and results may not be generalizable.

CONCLUSIONS:

Active referral for testing the children of HIV-infected adults in care increased pediatric HIV testing 4-fold and revealed a high prevalence of pediatric HIV in this population. However, most parents with eligible children did not complete pediatric testing; other approaches are needed to assist those parents not testing their children promptly. Systems-level improvements, peer counselors, or financial incentives may be promising interventions to increase uptake of testing, and merit investigation. Many parents had older untested children outside our age range, suggesting the need for adolescent-focused testing strategies.

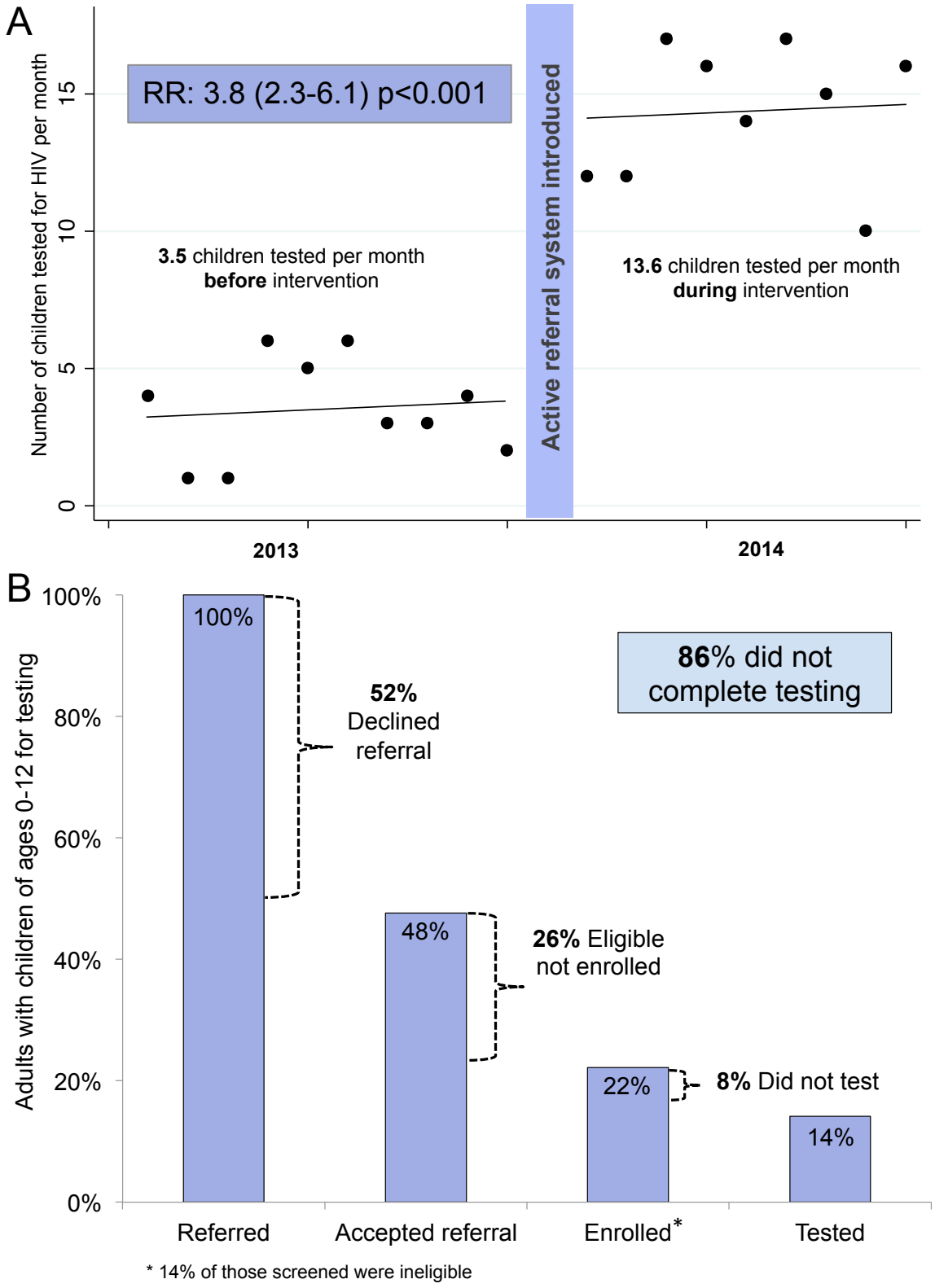

FIGURE 1: Panel A: Changes in uptake of pediatric HIV testing before and after introduction of active referral system. Panel B: Drop off in pediatric HIV testing cascade.

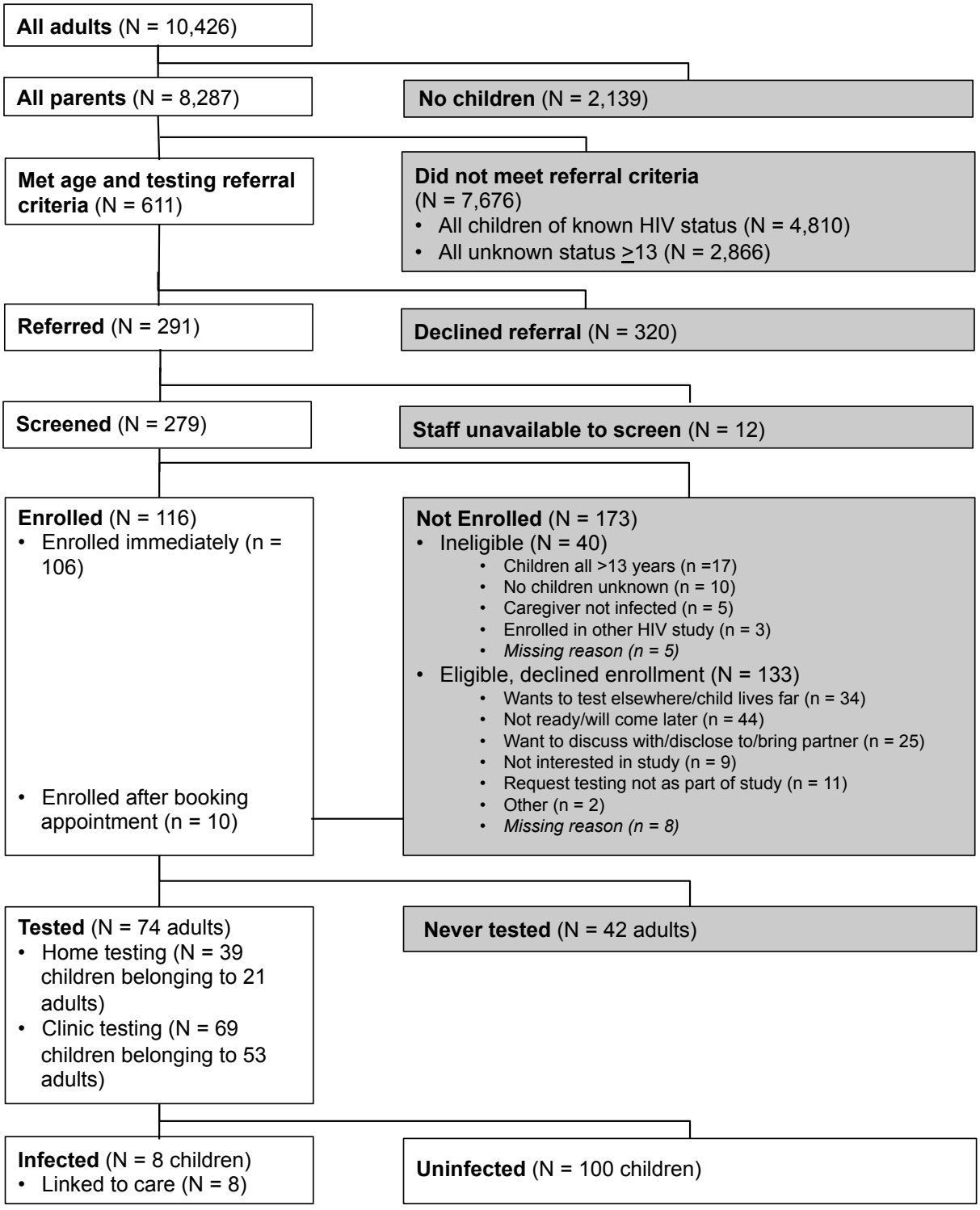

FIGURE 2: Study recruitment, referral, eligibility, enrollment, testing, and follow-up.

CHAPTER 2: HIV testing for older children: A mixed-methods study examining barriers and facilitators faced by caregivers and healthcare providers

INTRODUCTION:

Untreated pediatric HIV has an aggressive course with high mortality and morbidity; prompt testing and treatment reduce mortality and morbidity substantially, and provide long-term growth and developmental benefits [6, 9, 11-14]. The WHO has expanded its recommendations for a "test and treat" strategy for children under 10 [34], and empiric treatment may be more widely implemented in children over 10 based on findings from the START study which demonstrated benefits in adults over 18 years old [35]. However, many older children with HIV infection remain undiagnosed [8]. Pediatric HIV treatment lags adult HIV treatment, in part due to gaps in HIV diagnosis [19]. While systems to prevent and diagnose infant HIV infection have been strengthened over time, many older children were born prior to the scale-up of these programs [36]. Systems to routinely test older children for HIV prior to symptomatic illness, such as provider-initiated testing and counseling (PITC), are unevenly implemented and tend to preferentially test symptomatic children, at which point the benefits of treatment are compromised [20]. In order to achieve the 90-90-90 targets set by UNAIDS [7], substantial progress needs to be made in expanding HIV testing for older children beyond PITC.

One strategy to close this gap is to test the children of HIV-infected adults in care; this approach harnesses the efficiency of testing those children most likely to be infected [16, 17], but casts a broader net than PITC to capture children earlier in their disease. In targeted approaches adults who have learned about the benefits of HIV diagnosis, care, and ART through their own experience are offered HIV testing for their children. In HIV programs which have started using this approach it is clear that there is a substantial burden of HIV-untested children who are cared for by HIV-infected adults in care (Chapter 1).

In the CATCH-pilot study (Chapter 1), we offered pediatric HIV testing to adults in HIV Care and Treatment programs and noted increased pediatric HIV testing, however, most adults still did not bring their untested children in for testing. Understanding barriers to pediatric HIV testing experienced by caregivers and providers can help develop targeted testing approaches which are acceptable, high yield, and cost-effective. The purpose of this study was to determine barriers and facilitators to targeted pediatric HIV testing using a mixed-

methods approach. Qualitative data provides information about the wide range of possible barriers and facilitators as well as depth and detail regarding how these factors operated as barriers or facilitators. Quantitative data was used to validate and generalize results of the qualitative data, providing information about the frequency or burden of each of the hypothesized barriers and facilitators among a population of individuals considering testing their children for HIV [37].

METHODS:

Study design We utilized a mixed methods approach to evaluate barriers and facilitators to pediatric HIV testing for children of HIV-infected adults in care. Our conceptual framework adapted *Andersen's Behavioral Model for Health Services Utilization [38]*, which describes the interactions between environment, population characteristics (predisposing characteristics, enabling resources, and perceived need), health behavior outcomes, and clinical outcomes (Figure 1). The CATCH (Counseling and Testing for Children at Home) study was conducted to determine the uptake, acceptability, and cost-effectiveness of an intervention aimed at caregivers receiving HIV treatment services in Nairobi, which included the following elements: a) systematized offer of pediatric HIV testing and b) the option to test children at home or in a clinic setting (Chapter 1). Barriers and facilitators of pediatric HIV testing were assessed using a combination of standardized questionnaires and semi-structured in-depth interviews (IDI) administered to caregivers with children of unknown HIV status, and focus group discussions (FGD) with providers providing HIV testing and treatment services.

Ethics statement The study was approved by the University of Washington Institutional Review Board (IRB) and the Kenyatta National Hospital (KNH)/University of Nairobi (UoN) Ethics and Research Committee. Written informed consent was obtained from all participants in IDIs; oral informed consent was provided by FGD participants.

Recruitment and enrollment The study began recruitment at Kenyatta National Hospital (KNH) in November of 2013 and completed enrollment in September of 2014. Clients were recruited and referred from the KNH Voluntary Counseling and Testing Clinic (VCT), Prevention of mother-to-child transmission of HIV (PMTCT) Clinic, and Comprehensive Care Centre (CCC). Caregivers were defined as adult parents or guardians, and

included non-biological relationships. Caregivers were eligible for the study if they were HIV-infected and had at least one child 12 years of age or younger of unknown HIV status. Willingness to have a child tested for HIV was not an enrollment criterion and efforts were made to enroll caregivers who did not want to test children for HIV. Eligible caregivers agreeing to provide information regarding pediatric HIV testing (via standardized questionnaire) were invited to enroll in the testing acceptance cohort (TAC) and/or to complete an IDI; caregivers could complete either or both components of the study. IDI sampling was stratified to have a balance of caregivers who preferred to have their children tested by home- and clinic-based testing (HBT and CBT, respectively). Study staff recruited providers from the KNH VCT, PMTCT, and CCC clinics to participate in FGDs.

Standardized questionnaire At enrollment into the TAC and prior to child testing, a questionnaire was used to collect information about caregiver sociodemographic characteristics; caregiver and child HIV testing and treatment history; social, emotional, cultural, structural, and organizational barriers and facilitators to pediatric HIV testing; and transportation and opportunity costs. Caregivers were given the choice of whether they wanted home-based, clinic-based, or no HIV testing for their children. In this report we provide summary data for the overall TAC to evaluate individual factors identified as barriers and facilitators to testing at the KNH site; a more detailed analysis of cofactors for uptake of testing, and differences between caregivers accepting HBT and CBT will be presented elsewhere.

Qualitative data collection and analysis Interview guides were developed to explore social, emotional, cultural, structural, and organizational barriers and facilitators to child HIV testing, with themes and probes drawn from the conceptual framework. Interviews were conducted by a trained study interviewer experienced in qualitative HIV research studies, and were conducted in either English or Kiswahili according to interviewee preference. Audio recordings were translated into English by a professional translator as needed and transcribed using Microsoft Word. Transcripts were coded by three independent coders (ADW, OF, GO) using Atlas.ti using deductive coding informed by our conceptual model, and major themes were identified. The two primary coders (ADW, OF) independently coded the first set of 3 transcripts and created a comprehensive codebook together; they then independently coded the second set of 3 transcripts and reviewed application of

the codebook jointly; finally, they each acted as primary and secondary coder for the remaining 12 transcripts. All coded transcripts were reviewed by a third coder (GO) for consistency and meaning.

RESULTS:

Qualitative and quantitative study participant characteristics

Eighteen IDIs with caregivers and 3 FGDs with 7-11 providers each were completed; 116 adults were enrolled in the TAC and completed the standardized questionnaire. Characteristics of the provider and caregivers participating in the study are provided in Tables 1 and 2. Among the 27 providers participating in FGD, most were female in their late 30s with an average of 6 years working at their current clinic. In order to gather insights from multiple perspectives along the HIV testing and treatment continuum, a variety of job cadres were sampled, including nurses, social workers and lab technicians (Table 1). A majority of caregivers completing IDIs and standardized questionnaires were female. Caregivers completing IDIs were generally demographically similar to those in the TAC; most were mid-thirties, had partners, and had monthly incomes averaging $100 USD (Table 2). While efforts were made to enroll caregivers who were not interested in testing their children, none of these caregivers were willing to complete IDIs.

Qualitative results

Many hypothesized barriers and facilitators from the conceptual model emerged as themes during the qualitative interviews, as well as a few unforeseen items. These barriers and facilitators represented environmental as well as population characteristics (Figure 1). Interview data also revealed caregiver and provider concerns directed at distinct periods of the pediatric HIV testing and care process, including the ***decision-making process to test***, perceived issues with the ***testing visit*** itself, and fears regarding how they would cope in the ***post-test period*** in the event of a positive test result (Figure 2, Tables 3 & 4). Defining the barriers and facilitators at each of these necessary steps along the pathway to testing and care identify potential targets for service delivery improvement; therefore barriers and facilitators are noted below within the framework of these three periods (Figure 2).

I. Decision to test

A. Older HIV-exposed children are not considered to be likely to have HIV unless visibly symptomatic

Although a few caregivers and most providers were aware of the benefits of early HIV testing and linkage to care, overall they felt that the urgency of testing asymptomatic older children for HIV was low. Many noted a general lack of awareness that older children could be infected, tested, or treated for HIV.

A child's symptoms were a common prompt for testing, both from the view of caregivers and providers. Caregivers often felt that older children did not need to be tested for HIV because they had lived past infancy and were not visibly ill or experiencing symptoms. Others described the difficulty overcoming inertia to take action to test in the absence of an acute incident.

> *… there is no way you can stay in home and the child is not sick and you say, let me take my baby to be tested for HIV…*
>
> *IDI 11*

Some caregivers felt that children should be tested "for the child's health", generally, or for caregiver's peace of mind. One caregiver mentioned that caregivers occasionally test children as confirmation of their HIV status or their partner's HIV status. Some providers felt that children were not prioritized because vertical infection was less visible to the general public than sexual transmission. Finally, some caregivers and providers felt that child sexual abuse or early sexual debut put children at risk of infection and was a good reason to test all older children, particularly girls. Others felt that children should be tested prior to sexual debut to prevent transmission to peers.

> *…if we don't test them early enough and you know that is the stage where they are really involved in sexual practice, then we will be able to miss when they are now graduating into adulthood. So we need really to support them so that they can know their HIV status before they roll into the adulthood stage.*
>
> *VCT FGD*

Other gaps noted by caregivers were knowledge of where to get children tested; providers echoed these themes, noting that caregivers did not know that children could be tested for HIV at their clinic.

> *You know some people can have reasons like, someone doesn't know where to start and complete the whole thing, so he/she might not know if he/she goes to the hospital, how to start…*
> *IDI 8*

A minority of caregivers reported that they or others did not believe HIV existed, or had alternative explanations for a child's illness such as witchcraft. Some caregivers felt that traditional medicine or a visit to the neighborhood chemist were more appropriate care routes than HIV testing for children.

> *There is a lot of poverty and there is primitiveness… you feel that you don't have any other means, so you feel that you should give the child traditional herbs instead of taking the child to the hospital*
> *IDI 15*

A few caregivers mentioned that they would tell other caregivers about the importance of testing children early as a way of delivering educational messages in the context of a trusted relationship.

B. Complex partnership dynamics, fear of blame, and caregiver HIV disclosure underlie reluctance to test Caregivers discussed partnership dynamics extensively in the context of making a pediatric HIV testing decision, as well as in the post-test period (see Section III). Some caregivers felt that partners needed to be involved in deciding whether or not the child should be tested, while others felt it best to make that decision independently. Often, decision-making dynamics revolved around fear of disclosure and acceptance of one another's HIV statuses. Caregivers described partners being in denial about their own HIV statuses, or having perceived or confirmed discordant relationships, as a barrier to pediatric testing. Female caregivers sometimes explained that disclosing to one's partner was necessary in order to explain the need to take the child for testing or obtain partner permission to travel; women who did not feel ready to disclose their statuses to their

partners then felt unable to bring their children for testing. Some feared that even discussions about testing could bring conflict into the partnership, or could even result in violence or lack of financial support.

> *… it will be difficult because how are you going to tell him… If we have not talked about our status how are we going to talk about the status of the child?*
>
> *IDI 5*

A few caregivers noted that decision-making dynamics were different in monogamous versus polygamous relationships; female caregivers who had polygamous relationships noted that fathers had less of a right or responsibility to be involved in decision-making about child testing if they had multiple wives. However, other female caregivers reported that their male partners were the ultimate decision-makers and some explained that their husbands were superior to them.

> *You know even if I decide, he will say that he [has] to decide himself, that when he will decide to have the child tested that's when the child can be tested, but not for me to tell him that the child should be tested, so I am under him*
>
> *IDI 8*

While some felt that the caregiver who was closer to the children should decide, others felt that the caregiver with knowledge of logistics—like health insurance details—should be the one to decide. Finally, many caregivers feared relationship dissolution if they brought their children for testing, asked their partner for permission to test their children, or had a child who tested positive.

C. Other individuals influence caregiver decision to test child Caregivers noted that decision-making related to testing older children for HIV was complex and could involve many different individuals. Caregivers generally felt that while many people could be involved in decisions about taking a child to a clinic for general medical care, testing a child for HIV was unique and fewer individuals could be involved. While some caregivers felt that the decision was solely at the discretion of the caregivers (either one or both), aunts/uncles,

grandparents, neighbors, doctors, caregivers' friends, and/or teachers could also be involved, or influence primary caregivers, in the decision to test a child. One caregiver noted that in the case of caregiver neglect, the community also had a role in protecting the child.

> *You see by time the community is coming to talk, you see the parent are not taking care of the kid, it's when the community can shout at that person… Because that kid is not for you only, it is for the world.*
> *IDI 14*

Several caregivers feared involving grandparents because of the perceived threatening physical manifestations of stress and worry.

> *My parents, when it comes to testing like HIV, I don't think I can involve them… because they are old… suppose the child turns HIV positive... the blood pressure will start going up (laughing)*
> *IDI 3*

D. Accepting one's own HIV status needs to occur before caregivers can consider child testing Many caregivers reported that they could not test their children in the past because they had not accepted their own HIV status.

> *I thought that my world had come to an end and I didn't have peace and I didn't accept, and I even thought that they were lying to me because I had never experienced any problem, but now I couldn't go back to the hospital again to be tested*
> IDI 5

Some caregivers identified as having been in denial about their status, while others said that they felt their faith in their child's negative status was sufficient to protect the child.

I pray for my kid and I believe that he is ok, I choose not to take him to the hospital for testing, so faith… works. You believe that he is negative and you don't take him to the hospital…that is what I have been believing in for all those 9 years…Its only that I was told that I should come, then I said, "Let me just come". But I wouldn't have come, if there was no study, I wouldn't have come

IDI 16

E. A supportive and respectful provider attitude helps motivate caregivers to test Caregivers and providers both noted the potentially positive or negative impact that a provider's attitude could have on a caregiver's decision to test their child. While some caregivers highlighted the positive experiences of being encouraged and supported, others brought up negative experiences of being blamed, being "despised", and being chastised by providers.

Maybe if you take your child there and the healthcare providers start talking to you in a bad way, or despising you… the talk can make you angry and you might even feel that you would rather leave before you are tested and therefore such a thing can make it difficult to have the child tested, the anger

IDI 15

Additionally, caregivers noted that focusing on the outcome of a positive child during the initial testing discussion could make caregivers not want to test. Finally, providers noted that working with children and caregivers around the issue of testing requires special training and an especially blame-less and empathetic attitude.

II. Test visit

A. Guidelines and policies for testing older children require clarification and increased specificity for how to manage consent, assent, and disclosure Providers felt that one of the most challenging issues with

pediatric HIV testing was the issue of decision-making related to consent and assent, and consequently disclosure of both caregiver and child statuses to one another during the test visit itself.

> *According to practice sometimes you face challenges when the parents don't want to give consent and you can see that the child needs the test and get treatment. So it becomes a challenge on how to proceed with such a case; that is where now the policy is not coming in…*
> *CCC FGD*

Providers noted that while most caregivers give consent for child testing with good intentions for the child's care, some caregivers do not have the child's best interests in mind.

> *We… assess the reason for testing because sometimes, someone might bring a child and maybe the person is not the real parent of this child… and maybe they want to throw this child away.*
> *VCT FGD*

Providers also noted that as children became older, they asked questions related to what the HIV test was for and what the results were. Most caregivers felt that children could not keep secrets and many felt that children were too young to be told that they were to be tested for HIV. Therefore, caregivers strategized about explanations they could give to their children when bringing them to the clinic that would keep both children and partners unaware of the reason for the visit:

> *So you carry out the test and when you are done you tell the child, "weren't you having a headache yesterday?" and he/she will say "yes I was having a headache" then you will tell him/her "let's check and see if you have malaria" then you will draw his/her blood and carry out the tests. Then when he/she leaves, the child might say, because you know children don't usually keep secrets, he/she will say "I was taken to the hospital to be tested for malaria".*
> *IDI 1*

Providers often felt that children knew more about HIV—either through school or from observing their caregiver's medical care—than caregivers were aware of.

> *The children… they can be able to add one and one and get two and so they will be able to know already, our parents are already living with HIV and they have not told us.*
>
> *VCT FGD*

Providers reported that most often caregivers did not want to ask children's permission to test because they felt that asking permission through assent then required provision of test results and explanations of why the child was tested. If a child was tested because of a caregiver's infection and concerns about vertical transmission, caregivers feared inadvertent disclosure of their own status to the child.

> *I am putting myself in the shoes of this child… if the child asks 'where did I get this disease from'… how can you say, "you got it from your mother"?*
>
> *CCC FGD*

However, providers noted that despite an absence of standard practices, most providers routinely provided HIV testing and counseling (HTC) services for older children and had developed and shared knowledge with one another for how to deal with challenging situations.

B. Perceived and real costs prevent some caregivers from testing their children Caregivers repeatedly cited concerns about costs associated with testing—both perceived and real. Costs of transportation, costs of food outside of the home, costs of childcare, perceived costs of tests and treatment, and lost income or jobs due to missed work. Many caregivers echoed one participant's claim of "when I get money, I will go", suggesting that willing caregivers delay testing due to immediate lack of capital and competing financial priorities.

Just that, "I don't have money to go there"… and "I don't have time" Like maybe she is hustling for the meal for that day, so she is like… "if I go there, I will waste time, what are my children going eat in the evening?"

IDI 3

C. Providers feel clinic infrastructure and resources are not currently conducive to child testing

Providers described a variety of difficulties providing testing services for children, including concerns about infrastructure and resources. They cited concerns about insufficient staff to provide testing, long wait times that dissuade caregivers from testing and upset children, and inappropriate space—both the size of the space as well as its child-friendliness. Some suggested making clinic spaces more child-friendly for long waits, through provision of toys and snacks. Caregivers described a wide range of concerns about the test visit itself, noting that children might be disturbed by needles or the pain of the blood draw. One provider felt that limited staff was due to HIV funding being project-based, which disabled continuity of services after time-limited funds had ended. Additionally, providers felt that children needed more time for a test visit than adults.

…most of them when they come, they are bringing like three kids, they have to wait on the line… they cannot stay on the line the whole day, at times they become impatient, they cry, some of them, they get hungry on the line. So most of them, they cannot even… access health on the same day

CCC FGD

Providers described significant challenges with scheduling pediatric testing visits due to school and work schedules; many noted that services were not available at the times when caregivers were not working and children were out of school (often boarding schools). While home-based testing at non-normal times seemed to theoretically overcome some of these scheduling barriers, providers noted that finding urban homes was a barrier due to locations being either unspecific or changing without notice.

D. Home based testing might overcome some barriers, but was perceived as challenging to implement

Some caregivers advocated for testing at home, where a child might feel naturally more comfortable. However,

a few caregivers and providers had concerns about the appearance and characteristics of the testing staff; a provider noted that when they have done home-based testing in the past, they have been identified as HIV testing staff.

> *…in some areas where went you find that also they were labeled as "AIDS people", so people don't even want to be associated themselves with you. So if you are going that household you find that people either run away or decline or even hostile, so I would feel so challenged personally.*
>
> *VCT FGD*

One caregiver was concerned that his wife might feel suspicious if the tester was a young female.

> *I just want to ask whoever will come let it not be age of 35 (years) and below, because sometimes I know my wife, I know her mind, she might think that this person, there is something… Maybe she will feel that there is a relationship… she might even say the she doesn't want them to touch her children*
>
> *IDI 17*

A number of caregivers cited concerns about contaminated needles or lab mix ups giving inaccurate results both during home and clinic-testing, while providers cited infection control in the field as another challenge associated with home-testing.

> *…I went to tell my wife, she refused, she told that maybe they want to infect my children, I told her it cannot happened like that… "I am afraid because they will infect the children"… The syringe which is contaminated, a need[le] that had been used to pierce someone who is HIV positive and then infect the child, so she said, "I cannot agree to have my children tested"*
>
> *IDI 17*

E. Caregivers are concerned about privacy during the test Many caregivers were concerned about privacy and confidentiality around the testing visit itself. Some caregivers reflected on their own testing experiences in imagining what testing might be like for their children, sharing stories about switching clinics to avoid

recognition and being treated poorly by providers. A number of caregivers discussed apprehension about testing because they feared being discovered by "others". In a home-based testing setting, caregivers feared being interrupted by neighbors, particularly in settings where there was little privacy between homes; many feared inadvertent disclosure during the test visit itself.

> *Ok, there may be nosy neighbors always want to know who is that who has come to your house, they want to know, "what were they doing" So they prefer, because if they come to the hospital, these nosy neighbors won't be bugging you, "who is that who came to see you, what was he/she doing to the child". They need the privacy away from home*
>
> *IDI 6*

If children were brought to a clinic for testing, caregivers feared recognition by neighbors, friends, coworkers, or family members, who would know that children were being brought to an HIV specific clinic.

III. Post-test coping

A. Caregivers note the need for hope and support during the post-test period to cope with wide range of fears and challenging emotions The largest group of barriers to testing older children that caregivers highlighted were fears associated with post-test coping, many of which were similar to fears considered in making the decision to test (see Section I). They noted fear of abandonment, stigma, stress, emotional distress (especially for their children), ridicule, frustration, blame, "spoiling of the mind", depression, shame, and regret after testing. A number of female caregivers noted that if a child were to test positive that they would be blamed for the child's infection.

> *The other bad thing was when he asked why I did not accept my status when I was tested the first time and couldn't explain to him why I did not accept my status. And I saw some truth in it because had I*

accepted my status then I could have protected the child from getting infected, so that I remains with it alone but since I didn't accept my status, I infected someone else.

IDI 5

Many cited fear of knowing the child's status (presumably fearing it would be positive), fear of HIV as a death sentence, and fear of caregiver "shock"—the somatic manifestation of strong surprise/anger/sadness—following a positive diagnosis.

They know that HIV is for finishing, so because they know that, even the one who [knows] that she has (HIV), she doesn't want the children to be tested. What she tell herself in her mind, "my children are (HIV) positive and they are not going to be tested, because when they will be tested and they are found to be HIV positive, they will die

IDI 2

Many caregivers reflected on their own experience coping with HIV and not wanting to have their children share that experience.

Maybe you can't endure when you see your child going through what you have gone through

IDI 9

A few mentioned suicidal thoughts or ideation related to a new HIV diagnosis.

They ask you if you are prepared for it, what you will do if the child is positive, what you will do if the child is negative, they ask you such questions, those are the questions that I remember. Because I remember answering that if its positive, I will just buy rat poison and drink and die (laughing)… It's better for me but for the kid, I cannot handle it…

IDI 16

While caregivers discussed fears about their own feelings, they also highlighted fears about their children's feelings.

> *The first one, you fear because if your child discovers that she has that, she is positive and she is still young, she will not have that morale, she will feel that she is not going to live, "My life is dead."*
> *IDI 17*

A number of caregivers shared fears related to inadvertent disclosure of their status or their child's status, including fear of gossip; community, family, friend, sibling, and school stigma; isolation and being ostracized and loss of livelihood.

> *…as for the teacher maybe one day the child might make him/her angry in class, and you know he/she might not be the same teacher you had counseled with and told him/her not to do this or that. Then one day the child might be stubborn and the teacher might say, "this child is really disturbing me"… And he/she breaks the news in class so the child's classmates will start saying "don't sit close to me, you will infect me"*
> *IDI 1*

However, some caregivers had feelings of hope after testing, both for positive and negative children.

> *…you will check the child and I will get satisfaction in my heart when I leave, I wont have any problem at all.*
> *IDI 13*

> *As a parent you will have peace of mind if the children are tested… The peace of mind will come, if the children are negative, well and good, you will know how you will proceed, if they are positive, you know these children will take drugs, so you will have peace of mind*
> *IDI 11*

Additionally, a number of caregivers pointed to positive support as a strong enabling factor; many described social support from family, positive living support groups, and counselors and providers.

B. Even if caregivers complete testing, denial in the post-test period could interfere with linkage to care Providers and caregivers noted that upon receiving an HIV positive diagnosis, many caregivers would be in denial and want to repeat testing. Others noted difficulty accepting their child's status, or have partners who will not accept a child's status or providers' recommendations for treatment.

> *Yeah, so my husband was saying, "weren't they saying that she can't get well, she had not taken these medicine, she is not even sick", so he took the medicine and he threw them in the latrine. So he told me, "I don't want you to be going there, because they do say things which are not correct"…*
> *IDI 2*

C. Both caregivers and providers desire better skills for communicating with children about HIV status and care Providers and caregivers both feared having challenging conversations with children regarding the test process and test results during the test visit (see Section II) as well as during the post-test period. Providers often felt responsible for navigating disclosure of child test results; often they did not feel equipped to handle disclosure and thought twice about even performing the test.

> *…in your mind you are like if the tests turns out [HIV] positive, how do I start disclosing to this child? So it's kind of a dilemma… and kind of fear, do I want to do it or not?*
> *CCC FGD*

Both providers and caregivers had concerns about medication for children who tested positive, particularly for school aged children who might be in boarding or for children who had caregivers also on treatment.

…my wife normally say[s], taking these medicine all the time, it's something she feels disturbs her mind. So say for example the child is infected, if herself she feels that [the medication is] something that is disturbing her, I don't think the for the 3 children if they are infected, she will manage to give them that medicine, so in her mind that will be a burden.

IDI 17

Quantitative results

A total of 116 caregivers enrolled in the TAC. The frequency of caregivers reporting specific barriers and facilitators are summarized in Table 5. The frequency of barriers and facilitators supported the qualitative findings. When asked to spontaneously (unprompted) list the multiple reasons why their children had not been tested in the past, caregivers most frequently cited feeling that the child was not visibly sick (60%), not thinking that the child could be HIV-infected (47%), fearing that the child might be HIV-infected (22%), and concerns about disclosure to partner, family, or child (15%). While a wide variety of additional reasons were volunteered by participants, the frequency of these reasons was less than 10% for each. Of note, no caregivers in the TAC spontaneously explained not testing because of religious beliefs; concerns about partner or family anger, violence, or withdrawal of financial support; or lack of services or supplies at a clinic after requesting testing (Table 5).

When asked about each hypothesized barrier and facilitator to testing children, a majority of caregivers reported being concerned about the costs of transport, cost of missing work, cost of HIV care if the child was HIV-infected, ability to provide adequate nutrition and care to positive children, inadvertent disclosure of caregiver or child status, and stigma at school and in their communities. However, a majority of caregivers also reported strong trust in providers' ability to offer competent and confidential care without stigmatizing attitudes, and a majority had experienced positive support from their partner, counselor or support group in the past (Table 5).

DISCUSSION:

This mixed-methods study with providers and caregivers revealed a wide range of barriers and facilitators to pediatric HIV testing, which supported previously conducted studies and revealed some new opportunities for programmatic interventions. Barriers relevant to deciding to test included not perceiving that older children were at risk for HIV if they seemed healthy [17, 32], doubting that HIV testing had benefit prior to sexual debut [31], and not feeling ready to disclose one's own status to their children or partners [17, 31]. Barriers to completing the test visit included an absence of clear guidelines and provider unfamiliarity for testing and disclosure policies [31, 39-41] and providers' negative attitudes [17, 41]. At the clinic, long wait times and cost of transport and childcare were additional logistical barriers [41]. The main barriers noted related to the post-test period were a fear that the child would be positive and a fear of the child's death [31]. Caregivers were also hesitant to test because they wanted to protect the caregiver from blame, guilt, abandonment, and inadvertent disclosure [17, 31, 41, 42] and to protect the child from stigma, discrimination, and emotional suffering [17, 31, 32, 42].

Themes that emerged from the qualitative and quantitative data confirmed the majority of the hypothesized barriers and facilitators noted in Andersen's model with a few exceptions. Neither caregivers nor providers mentioned case management, a caregiver's age, or a caregiver's disease stage as factors that influenced testing of children. Caregivers and providers did highlight several barriers that were not hypothesized, including children living far from caregivers, gaps in health information particularly around likelihood of HIV infection, family concerns about testing children, and challenges seeking permission from one's partner for testing. These factors should be incorporated into future iterations of this model when addressing barriers to child testing. Next phases of this study will consider the influence of these barriers and facilitators on health behavior outcomes and clinical outcomes from Andersen's model, among the cohort of HIV-infected children currently being followed (Figure 1).

Interventions to address gaps in knowledge about pediatric HIV—the true probability of infection, the importance of prompt treatment, and the life-saving benefits of ART—and address fatalistic attitudes are needed (Table 4). Caregivers and providers in this study called for such educational resources and also

advocated for providers to include more hopeful language in their counseling sessions about the probability of a negative child and about the potential for children with HIV to live a long and healthy life. In-service training is needed for providers to gain and practice skills in pediatric HIV testing; this training should focus on who to test, when to test, how to take assent, how to involve child in testing visit, and how to conduct disclosure. Training models such as employing standardized patient actors allow providers the opportunity to practice skills in a safe environment with challenging case studies should be considered; this training model has been used for medical education in resource-rich settings [43-46] and resource-limited settings as well [47, 48].

Interventions to facilitate disclosure are needed to address the wide range of caregiver and provider concerns about disclosure (Table 4). Interventions that have included assisted partner disclosure as part of a comprehensive package of services to address pediatric HIV testing have achieved high uptake of testing, but are resource intensive [21]; scaling lower-cost modifications of this approach may increase testing uptake. Peer mentors—HIV-infected adults who have tested their children—have also been helpful in discussing the disclosure process with caregivers considering testing their children, and may represent opportunities for cost-effective task-shifting [49]. For children, previous work has shown that disclosure is associated with generally positive outcomes for children, and yet rates of disclosure are far behind recommended guidelines [50-53]. Interventions to guide providers and caregivers through the disclosure process are limited but have been successful where deployed [54-57]; in fact, providers in this study referenced picture books used in other studies [55] to assist in disclosure as a desired resource. Uptake of pediatric testing might be higher if disclosure interventions and peer mentors were routinely available and caregivers were exposed prior to being asked about testing their own children.

Finally, small financial incentive interventions should be tested to determine whether covering costs and lost income associated with testing increases uptake or accelerates the timeline associated with testing. Financial incentives have been successful in increasing uptake of one-time services such as adult HIV testing [58-60], but have had less success where long-term behaviors are required, such as retention in HIV care and medication adherence [61].

Our study had several strengths; it involved the viewpoints of a wide variety of providers and caregivers and collected both qualitative and quantitative data about barriers and facilitators, allowing us to triangulate our findings. Our study was limited in that caregivers who did not want to test their children were underrepresented both in our qualitative and quantitative data collection; no caregivers who did not want to test their children consented to participate in an interview and the grand majority of caregivers who did not want to test their children did not enroll in the TAC component of our study. Additionally, these results may only be generalizable to the subset of HIV-infected adults aware of their status and enrolled in care; in Kenya over half of HIV-infected adults are unaware of their status, and 11% of those who are diagnosed are not engaged in care [8]

CONCLUSIONS:

This study reveals a wide range of barriers to pediatric HIV testing with concerns about the process of deciding to test, the test experience itself, and coping in the post-test period. While barriers were numerous, caregivers and providers also identified focused changes that could be made to provider training, caregiver education, and community awareness to increase uptake of pediatric HIV testing and improve the testing process for all involved.

TABLES

Table 1: Sociodemographic characteristics of FGD participants

(N = 27)	N(%) or median(IQR)
Age	38 (33-46)
Female	19 (70)
Occupation	
Nurse	7 (26)
Counselor	6 (22)
Social Worker	3 (11)
Lab Technician	2 (7)
Clinical Officer	2 (7)
Other	7 (26)
Years at current clinic	6 (4-8)

Table 2: Sociodemographic characteristics of IDI and TAC participants

	IDI		**TAC**	
	N	n (%) or median (IQR)	N	n (%) or median (IQR)
Caregiver characteristics				
Female caregiver	17	14 (82)	116	92 (79)
Age	17	36 (31, 39)	116	36 (32, 40)
Years of education	17	14 (9, 15)	115	12 (9, 14)
Marital status	17		115	
Single (never married)		1 (6)		11 (10)
Divorced/separated		1 (6)		17 (15)
Widowed		1 (6)		16 (14)
Married monogamous		7 (41)		62 (54)
Married polygamous		4 (24)		8 (7)
Steady boyfriend		3 (18)		1 (1)
Monthly income	17	100 (70, 250)	113	100 (10, 200)
Partner characteristics				
Has partner	17	14 (82)	115	71 (62)
Partner age	14	39 (33, 46)	71	38 (35, 44)
Partner years of education	11	13 (9, 15)		12 (9, 14)

Table 3: Illustrative quotes about barriers and facilitators

DECISION TO TEST	
Information gaps in risk perception for older, asymptomatic children	To make that move is not easy… People know that HIV is real, but they try to assume, so people always wait, until it knocks, until they become sick, it's when they know it's real IDI 10
	...some people [don't] know HIV affect[s] children, they only know HIV affect big people IDI 10
	You know in the community, not many people take HIV as being real, so not many people take their children to be tested or get tested themselves IDI 9
Complex partnership dynamics -- Disclosure & permission	He usually tells me "I am alright, I know myself"… He never said he will not go for the test, he just said "I will go", sometimes he usually tells me "I don't have time", sometimes he usually tells me "I am ok, I know my status". IDI 4
	… you know I wouldn't have [told the child's status to the father] because he never knew, so if [I] start telling him that she [is] negative, he will ask "Why was she even tested?" Then he will just come with a click in his mind that this is it… IDI 16
Blame language from providers biases parents away from testing	…the way you speak to a patient, it can be a big challenge which can block the services, sometimes you can use a very rough language when you are asking somebody "have you ever been tested for HIV" and... you are asking while others are hearing, that has already blocked… VCT FGD
Supportive, respectful provider attitude motivates testing	Yes, because we stayed there for 2 hours of which he told me that he cares about me and about my health… In fact he smiled and told me, "You have the reason to live, medication, you will live, now your mind is settled, get settled, relax, feel loved, I will support you in way, anything you need, anything, because of this child"… He just gave me those positive hopes and already I have kept them to myself, if it is positive (HIV), I know how to handle it, if it is negative, I know how to handle it, you know IDI 18
TEST VISIT	
Disclosure challenging during test session -- Inadvertent disclosure of parental status	We tested him when he was 13 years old and I believe if we had tested him earlier on this boy could not have gone as far as he was with his severe infection, I am sorry he didn't make it because after…as he is saying, he asked "me I don't know women where did I get the infection from" and because I had mentioned mother to child he turned to the mother "does it mean you are HIV positive and you have never told me… We referred that boy for further management because now he was handled by psychologist, after three months when I met the mother, she told me that he refused to eat, he became depressed and he died." PMTCT FGD
Perceived costs of services	Some people fear the cost, because they feel it's costly… For the people who are very needy, maybe the transport cost, maybe they think they will charge you when you go for the tests, things like that… those are the things that people feel. IDI 16
Staffing not conducive to child testing -- Project-based HIV funding means no continuity of services	I want to say it's a national challenge, because to me in this country it's like HIV is looked at a project. That is why you hear it's a project, there is a counselor project, so when the project off, the services cut and the facility remains like there is no support, what do you do about it. VCT FGD
POST-TEST	

Fear child death, disclosure, emotional distress, stigma	How can explain? When you are there you are sweating before you even come from the house, you can't even take breakfast, then you feel butterflies I the stomach, you feel like I don't know, what if? You have so many questions in your mind. You have so many things going on in your mind, what if she is positive? Can she really be negative? You start thinking what will I do when she is positive. You have so many questions. IDI 16
	There was time I brought the child, when the child was 5 years, but when I was told to come back and collect the result I did not come back, I was like asking myself "suppose the child is positive, what will I do, how will I tell the child, suppose they start giving her the drugs, what will I tell this child that these drugs are for this condition, I said no, to hell, the child will know of her status later in life". IDI 7
Feeling of parent blame, guilt, disclosure, stigma, abandonment	Yes, I was a bit scared to get to know… Because I wouldn't want to pass this thing to an innocent child IDI 6
	… you don't want disturbance of mind…They don't want to know [their child's HIV status], it's better you stay like that… It's not a good idea, it's a bad idea, but that is what they say there. IDI 11
	There are some who are chased away from home, they chase them away, and they don't want to see them… Maybe they are the curse in the family IDI 9
Supportive messages of hope for child's life are encouraging	What made me happy was when he told me that the child will improve and is going to be ok, he even told there are so many children who are HIV positive, some of them are even in high school, so that gave me courage IDI 5
Communication with children about HIV status and care is challenging	I think sometimes it's usually a bit difficult on the part of the healthcare provider because when you test this child and it turns out to be positive and now the child now kind of asks those kinds of questions… and at some point the child now becomes rebellious towards the parent. Now you feel like you are the cause... it becomes a bit difficult ... CCC FGD

Table 4: Barriers, facilitators, and recommendations for pediatric HIV testing

	Barrier or facilitator		Recommendation
Decision to test	Information gaps & motivation to test	Unaware of prompt treatment benefits in children	Public education campaigns about benefits of early testing and treatment. Prompt all HIV-infected caregivers in care to test children with additional counseling for those who perceive their children to be low risk or alternative beliefs about HIV care
		Unaware pediatric HIV infection exists or belief that HIV is not real	
		Traditional medicine as an alternative treatment for children	
		Overcoming inertia is challenging when HIV is asymptomatic	
		Child sexual abuse or adolescent sexual debut are motivation for testing	Provider encourage adolescent HIV testing around time of sexual debut for those without risk of vertical infection
	Decision-making and partnership dynamics	Power dynamics within partnership to make decisions	Provide assisted disclosure services; invite multiple decision-makers to discuss testing children together
		Testing inspires suspicion in absence of mutual disclosure	
		Multiple individuals involved in influencing decision to test	
	Accepting one's own status as first step to testing children		Provide access to support group for caregiver
	Provider attitude	Blame language from providers biases caregivers away from testing; Positive, encouraging language from providers improves testing	Provide in-service training for existing providers on pediatric HIV testing especially. Focus on consent, assent, disclosure, and practicing hopeful, encouraging language around HIV testing noting the comparatively low probability of a child testing positive
Test visit	Guideline and policy gaps for consent/assent and disclosure	Guidelines intended for adults, not pediatrics	
		Consent, assent, disclosure processes unclear in complex situations	
		Inadvertent disclosure of caregiver status	
	Perceived & real costs	Perceived costs of services	Provide information about free nature of services. Consider small financial incentives to cover costs of lost wages, transport, and childcare
		Competing financial priorities	
	Staffing, space, scheduling	Scheduling around school holidays and caregiver work schedules is challenging	Provide weekend clinic dates with sufficient staffing to handle volume, possibly with task-shifting. Make clinic space child-friendly with addition of play space and provider training on child-friendly language and demeanor
		Space and staff numbers and attitude not conducive to child testing	
Post-test coping	Fear about child and caregiver coping with negative emotions, experiencing stigma and abandonment		Provide sessions with peer counselor or other caregivers who have tested their children; Provide

	Supportive messaging about child's future encouraging	resources (books, groups, etc.) for caregivers to initiate and complete disclosure and adherence discussions with children
	Denial can impede linkage to care	
	Communication with child about HIV status and care challenging	

Table 5: Prevalence of barriers and facilitators and association with testing choice

	Overall	
	N	n (%)
Why has the child not been tested for HIV? *(unprompted)*	116	
Child is not sick		66 (60)
Do not think child is HIV positive		55 (47)
Afraid to know child's status or fear positive		26 (22)
Disclosure or stigma concerns (Caregiver, partner, or child)		17 (15)
Never offered HIV testing for child		7 (6)
Partner or family concerns about testing child		7 (6)
Cost of transport, missing work, or childcare is prohibitive		5 (4)
Do not know where to get child tested or that children can be tested		5 (4)
Logistical issues (child lives far or caregiver has no time)		5 (4)
Are you concerned about… *(prompted)*		
Cost of transport		79 (68)
Missing work		65 (57)
Finding someone to care for other children at home		24 (21)
Cost of testing		7 (6)
Cost of HIV care if child is positive		70 (60)
Asking partner's permission to test the child	84	23 (27)
Trust in clinical staff *(prompted)*		
Staff have adequate training to test child	114	109 (96)
Staff would treat caregiver differently if child tested positive	114	5 (4)
Staff would disclose caregiver status to others	112	2 (2)
Emotional and social concerns *(prompted)*		
Concerned about being able to offer adequate care and nutrition to child if positive	112	90 (78)
Concerned child will find out HIV status (inadvertent disclosure)	115	74 (64)
Concerned child will experience stigma at school if HIV positive	116	72 (62)
Concerned child will experience stigma in the community if HIV positive	114	69 (61)
Concerned partner could be angry if child is HIV positive	79	13 (16)
Concerned partner could be violent if child is HIV positive	78	5 (6)
Someone may discover caregiver HIV status if child is tested	113	51 (45)
Positive support *(prompted)*		
Positive support about HIV status from partner	80	56 (70)
Positive support about HIV status from family	114	46 (40)
Positive support about HIV status from friends	116	26 (22)
Positive support about HIV status from support group or counselor	115	92 (81)

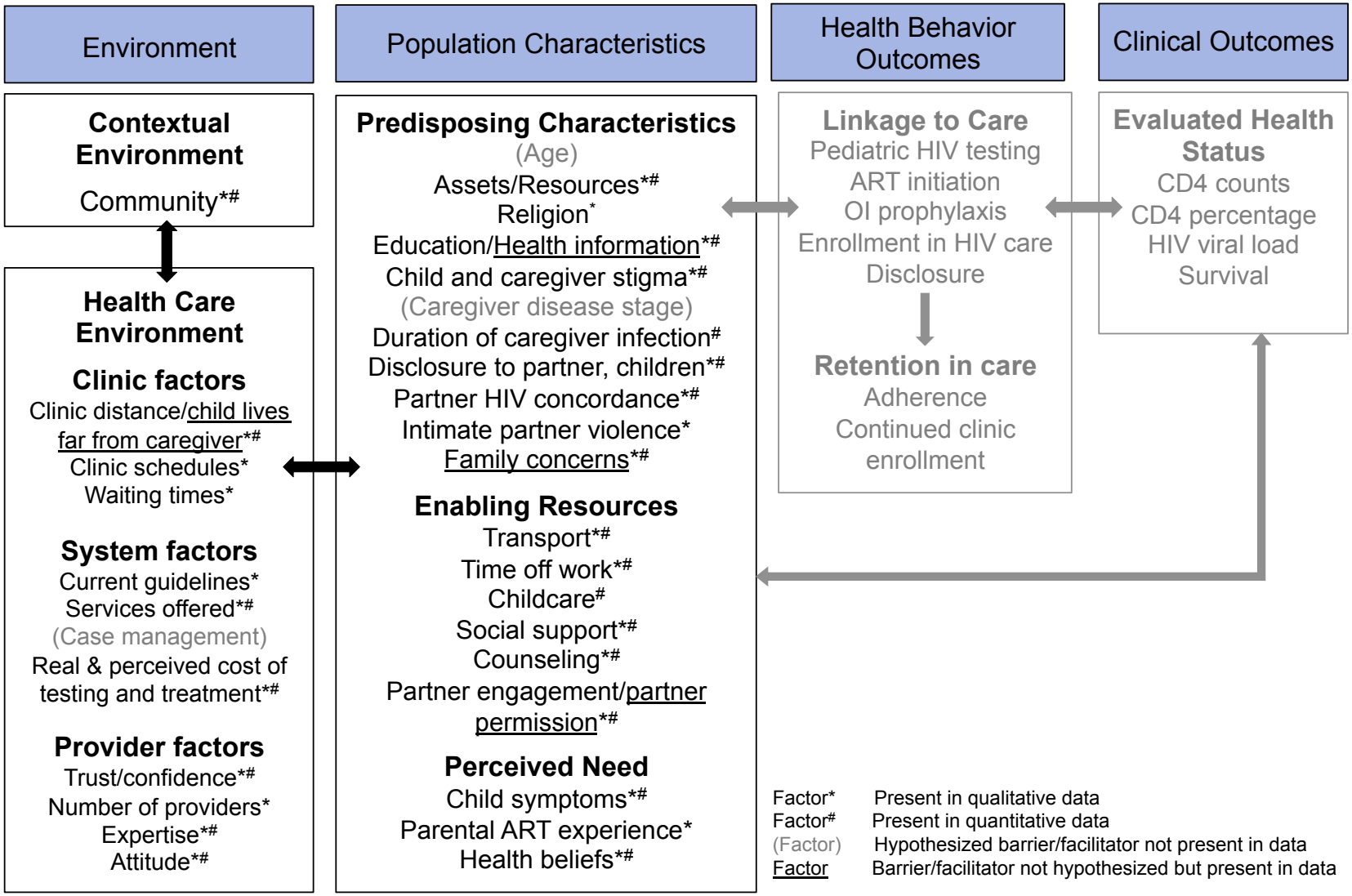

Figure 1: Conceptual model adapted from Andersen's Behavioral Model for Health Care Utilization. Barriers and facilitators

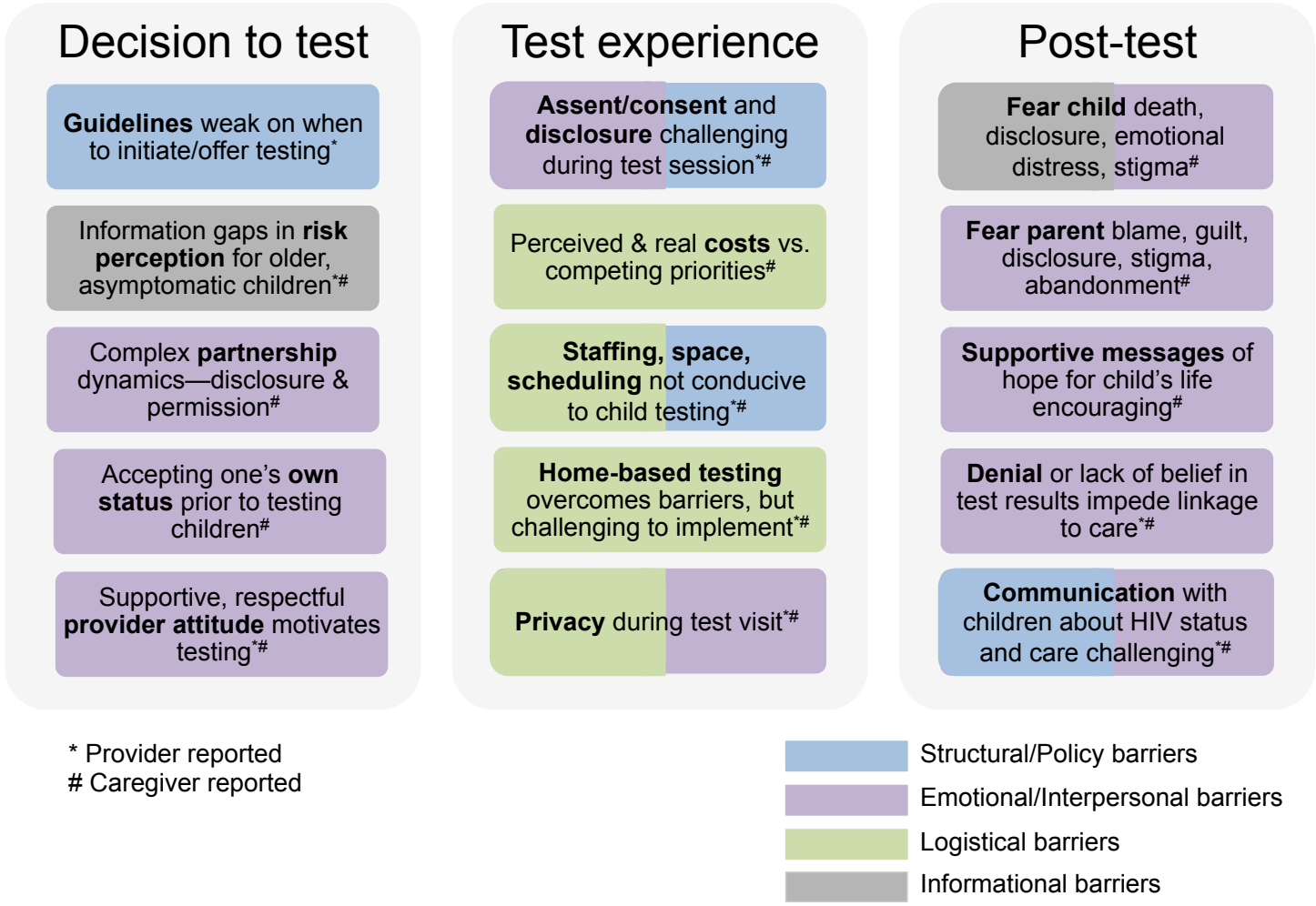

Figure 2: Barriers and facilitators to pediatric HIV testing from qualitative interviews and focus groups

CHAPTER 3: Comparison of costs and cost-effectiveness of three HIV testing models for older children of HIV-infected adults in care: passive referral, active referral, and active referral plus home-based testing

INTRODUCTION

Prevention of mother-to-child HIV transmission (PMTCT) programs have expanded coverage throughout sub-Saharan Africa with corresponding decreases in new infant HIV infections. However, older children may have become HIV-infected prior to PMTCT scale-up, and gaps in the PMTCT cascade leave some infants HIV-infected and undiagnosed [15, 36]. In the absence of a systematic testing approach, older children may not be diagnosed until they become symptomatic with HIV, at which point they tend to have poorer clinical outcomes and higher mortality [6, 9-14]. Additionally, children who remain undiagnosed until they are adolescents may reach sexual debut without knowing their status, increasing the chance of transmitting HIV to others [62, 63].

HIV care programs serve HIV-infected parents who may be willing to have their children of unknown status tested for HIV. Targeted testing of these children increases the efficiency of case detection of pediatric HIV infection compared to universal testing (Chapter 1)[16]. Reasons for not testing children for HIV have included issues of convenience and confidentiality (Chapter 2). Home-based testing (HBT), the administration of an HIV test at home, may be preferable to conventional clinic-based testing (CBT), for reasons of privacy or convenience. HBT decreases many of the critical barriers associated with traditional CBT; HBT removes client transportation costs, decreases client opportunity costs, decreases the stigma associated with testing in a setting known to be HIV-related, and allows greater flexibility with scheduling [64, 65]. Alternatively, the confidentiality of CBT may be preferable to parents who have not disclosed their status to their family.

With limited resources for HIV testing and healthcare in general, it is essential to determine the most cost-effective methods for testing children of unknown HIV status and linking HIV-infected children to care. HBT may be preferred by parents because of decreased costs to them but may cost health facilities additional funds in health care worker salaries and field transportation. Studies are needed to assess whether the increased costs of HBT in a pediatric population are associated with a greater number of children tested, and HIV-

infected children identified to merit the additional costs. Cost-effectiveness estimates comparing HBT and CBT in adult populations may not be applicable to pediatric populations infected through vertical transmission, which has a higher person-to-person HIV transmission risk and has different clinic infrastructure requirements.

In this analysis, we compare three programmatic strategies: active referral plus a choice of either home-based (HBT) or clinic-based testing (CBT) for children (referred to as "active referral + HBT"), active referral and CBT only (referred to as "active referral"), and passive referral and CBT (referred to as "standard of care"). We compare these strategies in terms of cost per child tested and cost per HIV-infected child identified.

METHODS

Model

A decision-tree model was developed to examine the cost-effectiveness of standard of care (passive referral), active referral, and active referral plus HBT for provision of HIV testing for children in Kenya over a 1-year time horizon. The decision tree model was suited to HIV testing due to the short-term nature of this outcome. Figure 1 shows a decision tree comparing the 3 models of targeted pediatric HIV testing compared in this model. The reference case was a child age 0-12 of unknown HIV status, defined as never having been tested for HIV or as having tested negative as an infant but not having confirmatory testing following the cessation of breastfeeding, whose caregiver was HIV-infected and enrolled in an HIV care clinic.

The analysis was conducted both from a Ministry of Health (MoH) perspective—which included the costs of personnel salaries, travel, test supplies—and a limited societal perspective [66]—which included all costs valued in the MoH perspective as well as costs borne by clients such as transport, lost income due to time off of work, costs of food and childcare. The MoH perspective is most relevant for Kenya because it has a national and county-wide healthcare system, but the societal perspective is most appropriate for comparison between different interventions. Additionally, the inclusion of two perspectives was critical as many of the costs averted by home-based testing are only relevant in the societal perspective. Strategies were compared on the basis of costs, children tested and HIV-infected children identified, and incremental cost-effectiveness using cost per child tested and cost per case detected to capture both coverage and efficiency. Future cost-utility analyses

are planned to estimate the cost per disability adjusted life year (DALY) averted to determine which strategies, if any, are cost-effective when compared to commonly accepted thresholds.

Strategies

Strategies are based on components of a previously completed prospective cohort study conducted between 2013-4 in Nairobi, Kenya at Kenyatta National Hospital (KNH) (Chapter 1). The CATCH study offered HIV-infected adults in care the opportunity to have their children of unknown HIV status tested for HIV in the location of their choice; either in a traditional clinic-based (CBT) or home-based (HBT) setting. Recruitment was based at the KNH Comprehensive Care Centre (CCC) HIV clinic. Each HIV-infected adult presenting for care was assessed to determine whether they had any children ages 0-12 of unknown HIV status. Caregivers with eligible children were actively referred to schedule a testing visit by either HBT or CBT; test site location was not randomized and there was no restriction on the number of children that could be tested per family. Caregivers who declined testing for their children were not contacted further.

Study staff conducting HBT visits were accompanied by a Community Health Worker (CHW) from a local HIV care clinic whose transport and time were reimbursed; all testing staff used public transportation. Children were tested by a rapid HIV testing algorithm following the Kenyan national HIV testing guidelines; children requiring PCR HIV testing submitted a venous blood sample and results were delivered during a subsequent interaction in person or by phone. Prior to each testing visit, CATCH study staff called each family as a reminder; those adults who missed their testing appointments were rescheduled a maximum of 2 more times. HIV-infected children were referred to the HIV care clinic of their caregivers' choice; study staff did not provide follow-up clinical care.

Effectiveness: We estimated the effectiveness of 3 programmatic models for testing children, based on the structure of the intervention in the CATCH study.

The **active referral + HBT model** was tested directly in the CATCH study. Under this model, all clients were assessed and clients with children of unknown status were offered the opportunity to test their children in a home or clinic setting. The numbers of children tested by HBT and CBT were estimated by adding a) the number tested in the CATCH study to b) the number of children who tested at the hospital clinic during the same time period, but outside of the study. This captured the total number of children tested during the study period at the site.

The **active referral model** was simulated based on parameters collected in the CATCH study. Under this model, all clients were assessed and clients with children of unknown status were offered the opportunity to test their children in a clinic setting. The number of children tested by CBT was estimated by adding a) the number of children observed to be tested by CBT in the study to b) the number of children whose caregivers selected HBT, but self-reported that they would have accepted CBT had HBT not been available as an option, to c) the number of children who tested at the hospital clinic during the same time period outside of the study.

The **standard of care model** was captured retrospectively from the KNH CCC using records that corresponded to the 10 months prior to the CATCH study. Under this model, adults in HIV care could spontaneously bring their children for HIV testing but assessment and referral for testing was ad hoc and not systematically implemented. The number of children tested by CBT was estimated using the number of children tested for HIV during the 10 months prior to the CATCH study.

Estimation of denominator: The number of children of unknown status who belonged to eligible caregivers was estimated using the number of adults who reported having any children of unknown status (adjusted for the possibility of incorrect reporting of eligibility among those who did not reach study staff as described in Chapter 1), multiplied by a weighted average of the number of children tested by HBT and CBT, weighted by the proportion of adults who elected each testing location.

Estimation of prevalence of HIV infection: The proportion of children infected with HIV was estimated using the overall prevalence from the CATCH study. While the prevalence of HIV infection differed in the parent study between children tested through HBT and CBT, limited power necessitated use of the full sample for a stable prevalence estimate.

Cost estimates: We estimated direct medical costs, direct non-medical costs and indirect costs associated with recruiting and testing children over a period of 10 months (Table 1). Direct medical costs—which included the costs of HIV testing materials, CBT nurse counselor, HBT nurse counselor, and community health worker reimbursements—were estimated based on study-collected program data or estimated based on market value (HIV test kits). Direct non-medical costs—which included patient and health care worker transportation costs, phone call costs, costs of food or beverage purchased outside the home by clients—were estimated based on patient report and by study-collected program data. Indirect costs—which included the opportunity costs of lost income when caregivers and spouses took time off from work, as well as childcare costs—were estimated based on patient report for paid labor and estimated based on per capita GDP for unpaid work (Table 1). The present analysis excludes potential cost savings associated with earlier identification of HIV-infected children, the additional costs of treatment for children, or the saved costs of prevented HIV transmission. All cost estimates were converted to the same base year using the consumer price index (CPI) from the Kenyan National Bureau of Statistics and converted to US dollars using the exchange rates from the Central Bank of Kenya. All cost estimates are presented in 2015 US dollars.

Baseline Analysis: We estimated the incremental costs and benefits associated with each model in both pairwise and incremental comparisons. In pairwise comparisons, we compared active referral + HBT to standard of care as well as active referral to standard of care. In incremental comparisons, we compared active referral + HBT to active referral, as well as active referral to standard of care. This enabled the estimation of an incremental cost-effectiveness ratio (ICER) in terms of cost per additional child tested and cost per additional HIV-infected child identified for each pairwise and incremental comparison. Costs included in each model are presented in Table 2. The analysis was performed using TreeAge Pro 2009

Sensitivity Analyses: Sensitivity analyses were performed to determine which parameters had meaningful impact on costs and outcomes. All parameters were varied in one-way sensitivity analyses; ranges were set using the 2.5th and 97.5th percentiles of costs from primary data, as well as 50% and 150% of the value of costs for which a distribution was not available (e.g. salaries and costs estimated from the literature) (Table 1). Probabilistic sensitivity analysis using Monte Carlo simulation was conducted using gamma distributions for cost parameters and beta distributions for probabilities.

Ethics statement: This study was approved by the University of Washington Institutional Review Board and the Kenyatta National Hospital Ethics & Research Committee. All enrolled participants provide oral informed consent and all participants who want testing for their children provided further written informed consent.

RESULTS

Probability of testing a child and probability of identifying an HIV-infected child were highest in the active referral + HBT model, followed by active referral, and was lowest in the standard of care model (19.4%, 17.5%, and 5.1% respectively for testing and 1.4%, 1.3%, and 0.4% respectively for identifying an HIV-infected child identified).

HBT had higher health care worker salary and transportation, but lower childcare and missed work costs than CBT. CBT had higher adult and child transport costs; additionally, parents missed more work and had to pay for more childcare than with HBT. The mean cost was substantially higher from the societal perspective than from the Ministry of Health perspective in all groups.

In the pairwise analysis, the incremental cost of active referral compared to standard of care was $57 from the MoH perspective and $64 from the societal perspective. The ICER was $768 per HIV-infected child identified from the MoH perspective and $868 per HIV-infected child identified from the societal perspective. The incremental cost of active referral + HBT compared to standard of care was $57 from the MoH perspective and

$61 from the societal perspective. The ICER was $780 per HIV-infected child identified from the MoH perspective and $826 per HIV-infected child identified from the societal perspective.

In the incremental analysis, the incremental cost of active referral compared to standard of care was $57 from the MoH perspective and was removed by extended dominance from the societal perspective. The ICER was $768 per HIV-infected child identified from the MoH perspective and was removed by extended dominance from the societal perspective. The incremental cost of active referral + HBT compared to active referral was $58 from the MoH perspective and removed by extended dominance in the societal perspective; the incremental cost of active referral + HBT compared to standard of care was $61 from the societal perspective. The ICER was $789 per HIV-infected child identified from the MoH perspective and removed by extended dominance from the societal perspective; the incremental cost of active referral + HBT compared to standard of care was $826 per HIV-infected child from the societal perspective. Table 3 shows MoH and societal perspective results in full detail.

One-way sensitivity analyses from the MoH perspective revealed that the ICER comparing active referral to standard of care was most sensitive to the cost of staff salaries and probabilities of testing under the two models, while the ICER comparing active referral + HBT compared to active referral was most sensitive to probabilities of testing under the two models (Figure 2 shows ICER in terms of children tested from MoH perspective).

In probabilistic sensitivity analyses from the MoH perspective, active referral was consistently more costly and more effective than standard of care (Figure 3 shows ICER in terms of children tested from MoH perspective), and the 95% confidence intervals did not cross either the cost or effectiveness axes. The ICER comparing active referral + HBT and active referral showed a high degree of variability both in costs and effectiveness, with estimates in all four quadrants of the cost-effectiveness plane (Figure 3 shows ICER in terms of children tested from MoH perspective). Standard of care was most likely to be cost-effective at lower willingness-to-pay for an additional child tested or HIV-infected child identified, but active referral + HBT became most likely to be cost-effective at willingness to pay above $60 (Figure 4).

DISCUSSION

This study compared the cost-effectiveness of three targeted pediatric HIV testing models—active referral + HBT, active referral, and standard of care. Active referral + HBT and active referral were more effective and more costly than standard of care. The ICER in terms of children tested from MoH perspective comparing active referral + HBT to active referral was highly sensitive to costs and effectiveness estimates.

The model results of cost per additional child tested and per additional HIV-infected child identified are sensitive to several assumptions about staffing; each scenario assumes the most efficient use of each health care worker's time. For example, the health care worker performing home-based testing visits is paid only for the time when s/he is in transit and performing the test visit under the assumption that either all of his/her hours are spent conducting these activities in a full-time job or that s/he is paid hourly for his/her work. This is reasonable in a scenario where one health care worker can provide coverage for several low-volume, geographically close clinics, or a single high-volume clinic. However, in cases where a health care worker is paid for a full-time position but does not spend all hours conducting home-based visits (i.e. servicing just one low-volume clinic), or in locations with longer travel distances to homes, the cost of this health care worker per child tested could rise substantially. Additionally, as the proportion of parents with children of unknown status continues to decrease with enhanced testing efforts, and the probability of a child testing positive decreases as the number of children born before effective PMTCT systems decreases, the cost of clinic-based staff salaries will also rise, increasing the cost per child tested and per HIV-infected child identified. All models assumed that staff were trained HIV testing and counseling (HTC) counselors, who have substantially higher salaries than peer counselors or other less highly trained counselors. Innovative task-sharing between HTC and peer counselors could reduce the costs of each model substantially.

The authors are not aware of any studies of the cost-effectiveness of case detection strategies for older children. Many adult HIV testing programs have been evaluated for cost per person tested, as well as a limited

number of early infant diagnosis strategies. While not directly comparable due to differences in expected prevalence and life years saved between populations, the estimated costs per person tested under adult and infant HIV testing models provide context for this study's intervention. Adult HIV testing strategies from the payer perspective have ranged in cost per person tested from $2.45-$14.37 for door-to-door approaches, $3.26-$33.54 for mobile testing, $12.91-$29.56 for hospital or VCT-based testing, $15.30 for index-based testing, and $126.48 for church-based testing [67]. Early infant diagnosis testing approaches from the payer perspective have ranged from $19.60-$63.81 [4]. This study's cost per child tested was within the ranges of both adult and infant case detection strategies per person tested (Table 5). The average cost of a year of HIV care for a child in PEPFAR supported countries is between $698-$823 [68], which is comparable to the cost per HIV-infected child identified in our testing model (Table 5). Adult HIV testing, EID, and pediatric treatment have all been scaled globally. However, as the outcomes in each of these models are not directly comparable to those for pediatric case detection for older children, further research is needed to estimate the cost-effectiveness of this model in terms of DALYs averted. Other case detection strategies for older children should conduct cost-effectiveness analyses in order to select strategies that merit scaling.

This study has several strengths: it included primary data collection for all client costs allowing detailed calculations of lost wages and transportation costs and reasonable sensitivity ranges based on observed distributions of costs, and was based on prospectively collected HIV testing data from both a research and standard clinical setting.

This analysis is limited in that effectiveness data for the active referral model was estimated based on self-report for a subset of clients, which is less reliable than observed actions and tends to overestimate effectiveness. Estimates of the number of children requiring testing were extrapolated based on the subset of clients enrolled in the study, which may be an over- or under-estimate. The prevalence of HIV infection was based on the full cohort, although previously conducted analysis suggests that the prevalence may be lower among children tested by HBT than those tested by CBT. Additionally, this analysis included data from one urban referral hospital site, which may not be generalizable to other settings in Kenya; future analyses will

include geographically diverse settings with differing travel distances, HIV prevalence among children, and costs.

In this analysis, we measured intermediate outcomes—number children tested for HIV and number of HIV-infected children identified. We are unable to estimate the impact of testing and identifying infected children on outcomes such as morbidity and mortality due to a paucity of available data on DALYs averted by early treatment in older children diagnosed with HIV; while the CEPAC-Pediatric model has been validated on a large population of children, it does not include children diagnosed over age 5 [69]. Pediatric HIV progression is notably different from adult HIV progression; within children, infant and younger children progression, where there is more readily available information, may not reflect progression among older children who have remained asymptomatic until later ages [70]. In future studies, we plan to use mathematical modeling techniques to estimate the impact of testing and identifying HIV-infected children on morbidity and mortality and to estimate cost per disability-adjusted life year (DALY) averted.

CONCLUSION

Uptake of targeted pediatric HIV testing was substantially increased by the addition of active referral and a choice of home and clinic-based testing, compared to a standard of care passive referral system. Active referral and active referral plus home-based testing are consistently more costly and more effective than standard of care, but it is unclear whether active referral or active referral + HBT is more cost-effective; additional precision is needed in estimates of effectiveness. Additional research is needed to determine whether either option is cost-effective in terms of cost per DALYs averted.

TABLES AND FIGURES:

Table 1: Model parameters

Costs per child		Value	Low	High	Distribution[#]	Data source
Direct Medical Costs	CBT personnel salary for active referral	$6.31	$3.16	$9.47	Gamma	Primary data collection
	HBT personnel salary	$13.81	$6.90	$20.71		Primary data collection (assumes 5 hours per visit for travel, testing & counseling)
	HIV test kit	$1.69	$0.85	$2.54		Estimate based on market values*
	HIV test consumables	$0.28	$0.14	$0.42		Estimate based on market values*
Direct Non-Medical Costs	Childcare or house help	$0.17	$0.00	$3.20		Primary data collection
	Communication with client (phone call reminders)	$0.50	$0.25	$0.75		Primary data collection (assume 5 mins each call, 3 KSH per minute)
	Food and beverage bought outside of the home	$1.21	$0.35	$2.43		Primary data collection
	Adult client transport, CBT group in active referral model	$1.20	$0.00	$4.00		Primary data collection
	Adult client transport, CBT group in active referral + HBT model	$1.23	$0.00	$4.27		Primary data collection
	Child client transport, CBT group in active referral model	$1.25	$0.00	$3.65		Primary data collection
	Child client transport, CBT group in active referral+ HBT model	$1.13	$0.00	$4.27		Primary data collection
	HBT nurse transport	$1.31	$0.53	$2.14		Primary data collection*
	HBT CHW transport & reimbursement	$1.57	$1.07	$3.20		Primary data collection*
Indirect Non-Medical Costs	Client and partner missed wage (paid and unpaid work) CBT group	$3.64	$0.00	$12.43		Primary data collection
	Client and partner missed wage (paid and unpaid work) HBT group in active referral + HBT model	$0.17	$0.00	$2.56		Primary data collection
Probabilities		**Value**	**Low**	**High**	**Distribution**	
Testing uptake	Proportion of children tested by any method under standard of care model	0.05109	0.03584	0.07035	Beta	Estimated based on observed historic testing rates
	Proportion of children tested by any method under active referral model	0.17518	0.14744	0.20576		Estimated based on combination of primary data observed choice and self report
	Proportion of children tested by any method under active referral + HBT model	0.19416	0.16518	0.22580		Primary data collection
	Proportion of children tested by HBT under active referral + HBT model	0.33083	0.25172	0.41766		Primary data collection
Prevalence	Proportion of HIV-infected children	0.07407	0.03252	0.14075		Primary data collection**

**Low and high values based on base value +/-50%*

***Low and high values reflect 95% confidence interval around prevalence but are similar to ranges seen in recent meta-analysis of targeted pediatric HIV testing models*

[#]Distribution assumed for probabilistic sensitivity analyses

Table 2: Costs included in each comparator by perspective

		Standard of care CBT		Active referral CBT		Active referral + HBT			
						CBT		HBT	
Costs		Societal	MoH	Societal	MoH	Societal	MoH	Societal	MoH
Direct Medical Costs	CBT personnel salary for active referral			X	X	X	X	X	X
	HBT personnel salary							X	X
	HIV test kit	X	X	X	X	X	X	X	X
	HIV test consumables	X	X	X	X	X	X	X	X
Direct Non-Medical Costs	Childcare or house help	X		X		X			
	Communication with client (phone call reminders)			X	X	X	X	X	X
	Food and beverage bought outside of the home	X		X		X			
	Adult client transport, CBT group in SoC and active referral model	X		X					
	Adult client transport, CBT group in active referral + HBT model					X			
	Child client transport, CBT group in SoC and active referral model	X		X					
	Child client transport, CBT group in active referral + HBT model					X			
	HBT nurse transport							X	X
	HBT CHW transport & reimbursement							X	X
Indirect Non-Medical Costs	Client and partner missed wage (paid and unpaid work) CBT group	X		X		X			
	Client and partner missed wage (paid and unpaid work) HBT group in active referral + HBT model							X	

Table 3: Pairwise and incremental cost-effectiveness analyses

Pairwise					**Per child tested**				**Per positive child identified**			
	Average Cost		Incremental Cost		Average Effectiveness	Incremental Effectiveness	**ICER**		Average Effectiveness	Incremental Effectiveness	**ICER**	
	Societal	MoH	Societal	MoH			**Societal**	**MoH**			**Societal**	**MoH**
Standard of Care	$0.48	$0.10	--	--	0.051	--	**--**	**--**	0.0038	--	**--**	**--**
Active Referral	$8.46	$7.16	$7.98	$7.06	0.175	0.124	**$64.32**	**$56.86**	0.0130	0.00920	**$868.37**	**$767.60**
Active Referral + HBT	$9.23	$8.27	$8.75	$8.17	0.194	0.143	**$61.18**	**$57.13**	0.0144	0.01060	**$825.96**	**$780.19**

Incremental Analysis (Societal Perspective)			**Per child tested**			**Per HIV-infected child identified**		
	Average Cost	Incremental Cost	Average Effectiveness	Incremental Effectiveness	**ICER**	Average Effectiveness	Incremental Effectiveness	**ICER**
Standard of Care	$0.48	--	0.051	--	**--**	0.0038	--	**--**
Active Referral + HBT	$9.23	$8.75	0.194	0.143	**$61.18**	0.0144	0.01060	**$825.96**

**Active referral removed by extended dominance*

Incremental Analysis (MoH Perspective)			**Per child tested**			**Per HIV-infected child identified**		
	Average Cost	Incremental Cost	Average Effectiveness	Incremental Effectiveness	**ICER**	Average Effectiveness	Incremental Effectiveness	**ICER**
Standard of Care	$0.10	--	0.051	--	**--**	0.0038	--	**--**
Active Referral	$7.16	$7.06	0.175	0.124	**$56.86**	0.0130	0.00920	**$767.60**
Active Referral + HBT	$8.27	$1.11	0.194	0.019	**$58.45**	0.0144	0.00140	**$789.03**

Table 4: Cost per child tested and cost per positive child identified

	Average cost per child tested		Average cost per child tested	
	Societal	MoH	Societal	MoH
Standard of Care	$9.43	$1.97	$127.33	$26.57
Active Referral	$48.31	$40.85	$652.23	$551.47
Active Referral + HBT	$47.31	$42.57	$642.11	$574.69

FIGURES

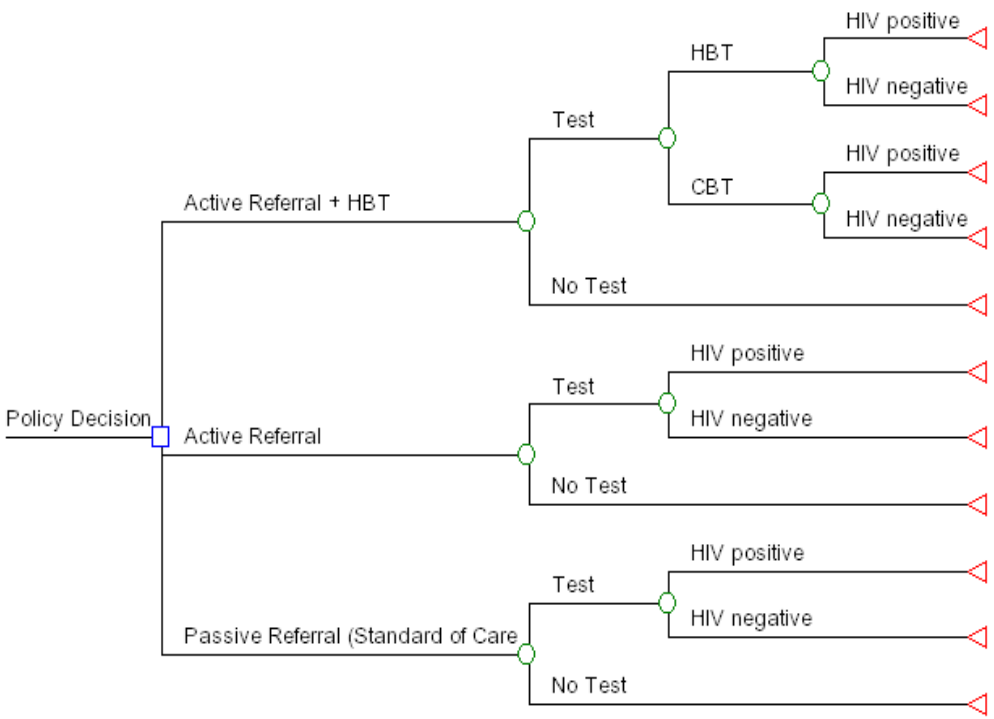

Figure 1: Simplified decision tree

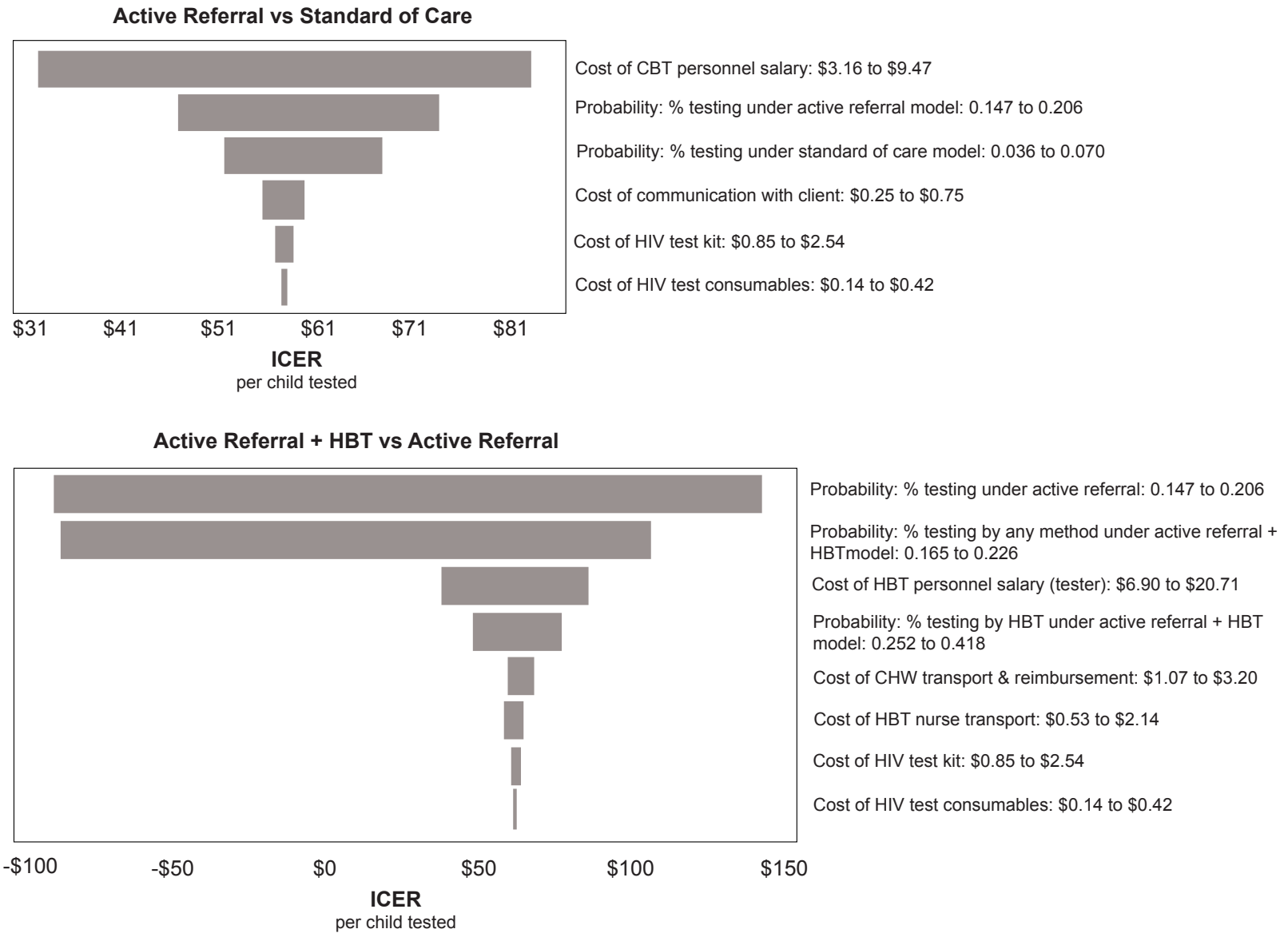

Figure 2: Tornado diagrams for one-way sensitivity analyses

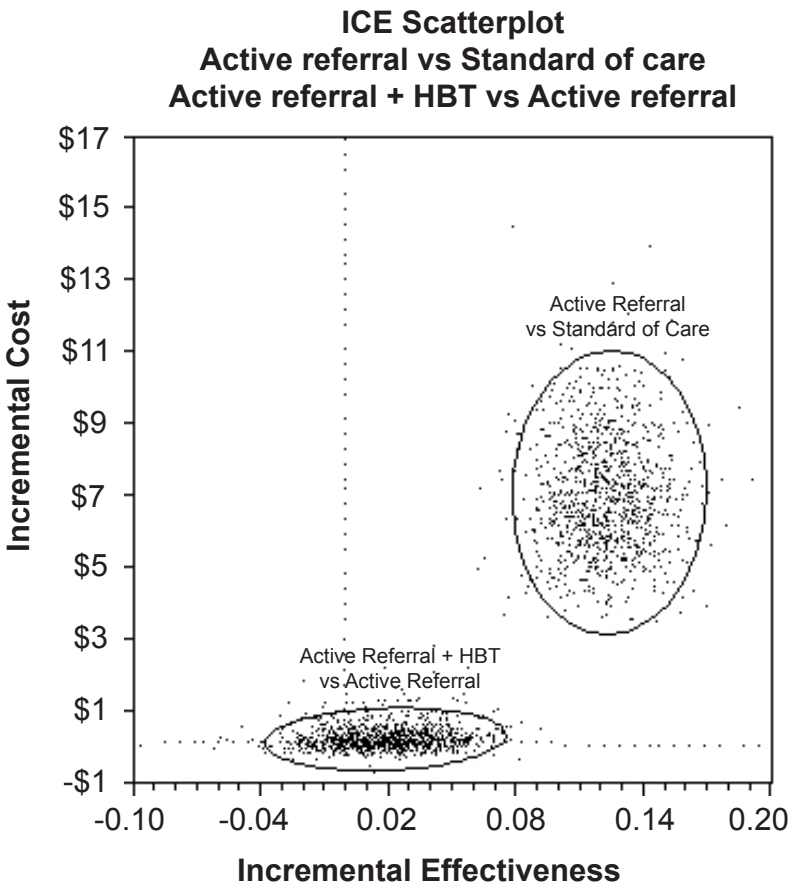

Figure 3: ICE scatterplot comparing each pairwise comparison

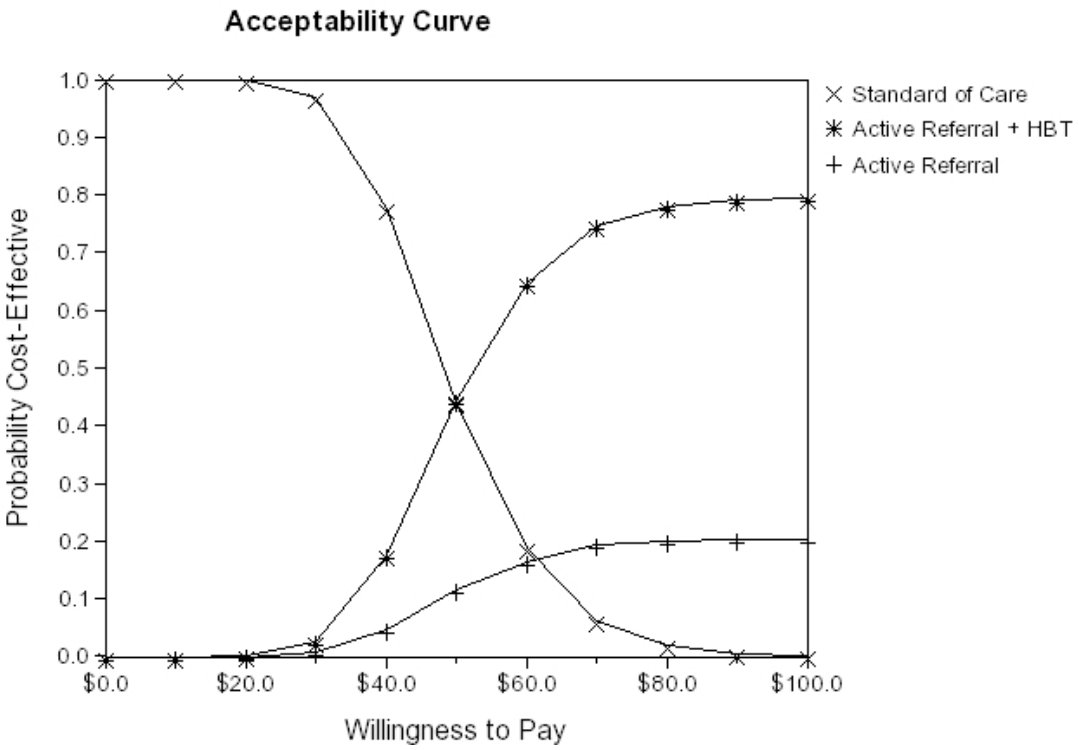

Figure 4: Cost-effectiveness acceptability curve

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