Facility and community-based index-linked HIV testing strategies for children and adolescents in Zimbabwe

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Declaration of originality

I, Chido Dziva Chikwari, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signed  …… Date: 26 /02 /2021

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Abstract

Globally over 2.8 million children aged between 0-18 years were living with HIV in 2019. ART substantially reduces mortality but the pre-requisite step for accessing treatment is HIV diagnosis. Coverage of HIV treatment in children has lagged behind when compared to adults largely because of delayed diagnosis. Children experience unique challenges to access HIV testing. Existing strategies for paediatric HIV testing, which largely are similar to those used for adults, have not been effective in addressing the HIV diagnosis gap in children. Index-linked HIV testing (HIV testing offered to household members and sexual contacts of individuals living with HIV) for children and adolescents may improve HIV testing uptake and have high HIV yield. Offering index-linked HIV testing for children and adolescents in both facility and community settings may be an effective strategy to help bridge the HIV testing gap. The aim of this research was to evaluate facility and community-based approaches for index-linked HIV testing for children and adolescents aged 2-18 years in Zimbabwe.

This PhD combined mixed methods research in the city of Bulawayo and in Matabeleland South province between January 2018 and May 2019. Overall, 2870 index patients had 6062 children who were eligible for HIV testing in their households. Indexes were offered a choice of facility-based or community-based HIV testing (either home-based HIV testing by a health provider or an oral mucosal transudate (OMT) HIV test kit given to a caregiver to test their child(ren)). HIV testing was accepted for 5326 (87.9%) children, and 3638 children were tested (60.0% HIV testing uptake). The HIV prevalence and yield were 1.1% and 0.6% respectively. Older children and adolescents were less likely

to be tested when compared to children aged 2-5 years. Children had increased odds of being tested if community-based HIV testing was chosen over facility-based HIV testing. There was inadequate emphasis on paediatric HIV in routine HIV care which had a negative impact on subsequent uptake of HIV testing for children. Once the decision to test had been made, access to facilities was sometimes challenging and alleviated by community-based HIV testing.

OMT tests, although previously validated for HIV testing in adults and widely used in HIVST for adults had not been validated for HIV testing in children <12 years. In this research, OMT sensitivity was 100% [97.5% CI: 94.9% to 100%]) and specificity was 99.9% [95% CI: 99.6% to 100.0%] among children aged 2-18 years when compared to national HIV testing algorithms. A further application of OMT testing evaluated as part of this research was caregiver's ability to test their children for HIV and interpret test results. Overall, most caregivers correctly collected oral fluid (87.1% without provider demonstrations and 96.8% with demonstrations from a provider, p=0.002).

The HIV yield was low when compared with blanket HIV testing approaches in similar settings. There is a need to improve messaging on the importance of HIV testing for children and adolescents and to provide support to caregivers and their families in order to increase HIV testing uptake. Addressing access barriers through the provision of community-based HIV testing can optimise index-linked HIV testing. Caregiver-provided testing using OMTs is a feasible and accurate HIV testing strategy for children and can also be used to improve uptake of HIV testing for children.

Acronyms and abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Care
aOR	Adjusted Odds Ratio
ART	Antiretroviral Therapy
B-GAP	Bridging the Gap in HIV testing and Care for Children in Zimbabwe Study
BBT	Blood Based Testing
BMJ	British Medical Journal
BRTI	Biomedical Research and Training Institute
cART	Combination Antiretroviral Therapy
CDC	Centres for Disease Control
CI	Confidence Interval
DRC	Democratic Republic of Congo
EID	Early Infant Diagnosis
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
HIVST	HIV Self-Testing
HLA	Human Leukocyte Antigen
HTS	HIV Testing Services
JAIDS	Journal of Acquired Immune Deficiency Syndromes
LGBQTI	Lesbian, Gay, Bisexual, Transgender, Queer and Intersex
LMIC	Low- and Middle-Income Countries
LSHTM	London School of Hygiene and Tropical Medicine
MoHCC	Ministry of Health and Child Care
MRCZ	Medical Research Council of Zimbabwe
MTCT	Mother to Child Transmission
NAC	National AIDS Council
NVP	Nevirapine
OMT	Oral Mucosal Transudate
PCR	Polymerase Chain Reaction
PEPFAR	President's Emergency Plan for AIDS Relief
POC	Point-of-Care
PWID	People Who Inject Drugs
PMTCT	Prevention of Mother to Child Transmission
SMS	Short Message Service

SSA	Sub-Saharan Africa
STI	Sexually Transmitted Infection
TB	Tuberculosis
UK	United Kingdom
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization
ZIMPHIA	Zimbabwe Population-based HIV Impact Assessment

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1. Introduction

1.1 Background

Globally over 2.8 million children aged between 0-18 years were living with HIV in 2019.[1] Prevention of Mother-to-Child Transmission (PMTCT) programmes have been rapidly scaled up over the last decade.[2] PMTCT programmes include HIV testing for pregnant mothers, provision of antiretroviral therapy (ART) and HIV testing for HIV exposed infants (early infant diagnosis (EID)). In 2010 global coverage of pregnant mothers receiving ART was only 46%, but this had increased to 92% by 2018.[2]

Although PMTCT programmes have been successful in reducing mother to child transmission of HIV (MTCT) there is geographical heterogeneity in PMTCT coverage; for example in 2018 within the Eastern and Southern Africa region ART coverage among HIV positive pregnant mothers in Angola was only 38% while coverage in Botswana was >95%.[2] Poor access and adherence to ART among pregnant and breastfeeding mothers results in continued MTCT.

Gaps in EID are substantial and result in many children with HIV not being diagnosed and starting ART until later childhood. In 2018 only 68% of infants born to mothers living with HIV were tested within 6 weeks of birth globally.[2] In 2019 global ART coverage among children aged (0-14 years) was only 53%.[3] HIV testing is the critical first step to accessing HIV treatment and the low coverage of ART among children is primarily due to delayed HIV diagnosis.

A key HIV testing strategy recommended by the World Health Organization (WHO) since 2007 is provider-initiated testing and counselling (PITC) whereby HIV testing is offered to all individuals presenting to health facilities regardless

of the reason for presentation.[4] However, this strategy has been challenging to implement. One study in Zimbabwe where the approach of PITC was optimised by moving from an opt-in to an opt-out approach, with the use of additional staff and maintaining test kit supply chains, showed 35% of children living with HIV were still undiagnosed in a community prevalence survey conducted after two years of providing PITC in the study facilities.[5]

A limitation of PITC in children is that caregivers and providers often perceive children to be at low risk of being HIV-infected if they have survived infancy. This is likely to be due to the very high rates of mortality among infants observed in the pre-ART which led to the assumption that survival beyond early childhood with HIV was exceptional. Therefore HIV testing of children who survive infancy has often not been prioritised by paediatric HIV programmes.[6-8] Furthermore, the lower HIV prevalence and subsequently the low HIV yield among children means blanket HIV testing approaches such as PITC may not be the most efficient nor cost-effective, particularly in resource-constrained settings.[6-8] Health facilities are often inaccessible to children due to opening hours that compete with school times and in addition, HIV testing for children also requires parental consent which is often difficult to navigate for health providers in settings where many children are orphaned and present to facilities with caregivers who are not their biological parents.[6-8] These limitations and challenges with facility-based PITC for children highlight the need for HIV testing strategies that are tailored for this population group.

1.2 Research starting points

Index-linked HIV testing (HIV testing offered to household members and sexual contacts of individuals living with HIV) was recommended by WHO in 2015 as an HIV testing strategy to identify sexual partners and children of people living with HIV with undiagnosed HIV.[9] For sexual contacts this targeted strategy has been proven to have higher yields of undiagnosed HIV and is more cost effective when compared to blanket HIV testing approaches.[10-12] Although evaluated for sexual contacts, there was scarce data on the uptake and yield of index-linked HIV testing for children and adolescents.[11,13]

In addition to index-linked HIV testing WHO also recommended the use of community-based HIV testing strategies to expand HIV testing access and identify more individuals living with undiagnosed HIV in high prevalence settings.[9] These community strategies include door-to-door HIV testing to reach all people in a geographical area, mobile clinics, events based HIV testing, workplace HIV testing and HIV testing campaigns.[14] Key among community-based HIV testing strategies is HIV self-testing (HIVST) whereby adults can use oral mucosal transudate tests (OMTs) to perform HIV testing on themselves.[15] These strategies have been shown to increase awareness of HIV testing and also increase the rates of people who test for the first time.[16] Notably, OMT tests were not validated for children <12 years.

1.3 Rationale of the study

Diagnosing HIV and starting ART early in children has been shown to significantly improve morbidity and mortality.[17,18] The CHER trial which was conducted in South Africa showed that early HIV diagnosis and initiation on ART

reduced early infant mortality by 76%.[17] However, a 2018 cohort analysis of data from 25 countries in SSA found the median age to start ART among children born between 1994-2005 was 7.8 years in LMIC and 7.3 years in upper-middle income countries within the region.[19]

HIV testing is the first step in the HIV cascade.[2] Children living with undiagnosed HIV continue to be missed by the current HIV testing strategies. The development and evaluation of novel and effective HIV testing strategies to optimise the identification of children with undiagnosed HIV is the first step to successful control of HIV.

Index-linked HIV testing for children and adolescents may improve HIV testing uptake and have high HIV yield. Offering index-linked HIV testing for children and adolescents in both facility and community settings may be an effective strategy to help bridge the HIV testing gap. Furthermore, investigating the barriers and facilitators of index-linked HIV testing for children and adolescents can support in improving implementation and operationalization of this strategy.

1.4 Research aims and objectives

The aim of this research was to evaluate approaches for index-linked HIV testing for children and adolescents (aged 2-18 years), through a mixed methods research.

The study objectives were to:

1. Evaluate the acceptability, uptake and yield of an index-linked HIV testing strategy (HIV testing offered to children living in households with an

individual living with HIV) offered in facility and community-based settings.

2. Explore provider and caregiver perceptions and experiences of index-linked HIV testing for children and adolescents.
3. Evaluate the diagnostic accuracy of the oral mucosal transudate HIV test for children and adolescents.
4. Assess the feasibility and accuracy of caregiver provided HIV testing for children and adolescents.

The research was conducted as part of the *Bridging the Gap in HIV testing and care for children in Zimbabwe* (B-GAP) project, which aimed to evaluating index-linked HIV testing for children as well as a community-based support intervention for children who test HIV positive. This thesis is based on the HIV testing component of the B-GAP project.

1.5 Thesis outline

This thesis follows the "research paper style" in accordance with the London School of Hygiene and Tropical Medicine (LSHTM) guidelines. As such the thesis is made up of six manuscripts that have been published. The outline of the chapters is as follows:

Chapter 1 (this chapter) contains an overview of the research background, gaps in knowledge, study rationale, the research aim and objectives and the outline of the thesis.

Chapter 2 provides a review of the literature on HIV, the epidemiology of paediatric HIV, the evolution of PMTCT programming and the barriers to HIV testing for children and adolescents. This chapter includes Research Paper 1, a

review published by Current Opinion in HIV and AIDS in 2018 summarising the barriers and strategies for HIV testing for adolescents in Sub-Saharan Africa.[20] The title of the paper is "*Barriers to, and emerging strategies for, HIV testing among adolescents in sub-Saharan Africa*". In addition, this chapter also provides an overview of the HIV epidemic in Zimbabwe.

Citation (Research Paper 1): **Chikwari CD**, Dringus S, Ferrand RA. Barriers to, and emerging strategies for, HIV testing among adolescents in sub-Saharan Africa. Curr Opin HIV AIDS 2018; 13(3): 257-64.

Chapter 3 is a published protocol paper describing the methods used in this research. The paper is titled *"Evaluating the effectiveness and cost-effectiveness of health facility-based and community-based index-linked HIV testing strategies for children: protocol for the B-GAP study"* and was published by BMJ Open.[21] In addition to this chapter the methods specific to individual studies are described in the respective chapters in which each study is included.

Citation (Research Paper 2): **Dziva Chikwari C**, Simms V, Dringus S, Kranzer K, Bandason T, Vasantharoopan A, Chikodzore R, Sibanda E, Mutseta M, Webb K, Engelsmann B, Ncube G, Mujuru H, Apollo T, Weiss HA, Ferrand R. Evaluating the effectiveness and cost-effectiveness of health facility-based and community-based index-linked HIV testing strategies for children: protocol for the B-GAP study in Zimbabwe. BMJ Open 2019;9: e029428. doi: 10.1136/bmjopen-2019-029428

Chapter 4 is a published research paper comparing uptake of facility vs community-based index-linked HIV testing strategies and the overall uptake and

yield of index-linked HIV testing for children and adolescents. The paper is titled "*Comparison of Index-linked HIV testing for children and adolescents in health facility and community-based settings in Zimbabwe: Findings from the interventional B-GAP study*" and was published in the Lancet HIV.[22]

Citation (Research Paper 3): **Dziva Chikwari C**, Simms V, Kranzer K, Dringus S, Chikodzore R, Sibanda E, Webb K, Engelsmann B, Redzo N, Bandason T, Mujuru H, Apollo T, Ncube G, Hatzold K, Weiss HA, Ferrand RA. Comparison of index-linked HIV testing for children and adolescents in health facility and community settings in Zimbabwe: findings from the interventional B-GAP study. Lancet HIV. 2020.

Chapter 5 is a published research paper in Implementation Science Communications. This manuscript evaluates the provider and caregiver perspectives of index-linked HIV testing in order to identify barriers to uptake and ways through which implementation of index-linked HIV testing can be improved. It is titled "*Addressing the challenges and relational aspects of index-linked HIV testing for children and adolescents: insights from the B-GAP study in Zimbabwe*".[23]

Citation (Research Paper 4): **Dziva Chikwari C**, Bernays S, Dringus S, Simms V, Weiss HA, Sibanda E, Kranzer K, Ncube G, Chikodzore R, Webb K, Chirimambowa T, Sithole K, Ndondo N, Apollo T, Mutseta M, Ferrand RA: Addressing the challenges and relational aspects of index-linked HIV testing for children and adolescents: insights from the B-GAP study in Zimbabwe. Implementation Science Communications 2020, 1:99

Chapter 6 is a brief report titled *"Diagnostic Accuracy of Oral Mucosal Transudate Tests Compared with Blood-Based Rapid Tests for HIV Among Children Aged 18 Months to 18 Years in Kenya and Zimbabwe".*[24] This report was published in the Journal of Acquired Immune Deficiency Syndromes (JAIDS) and assesses the sensitivity and specificity of the oral HIV test in children and adolescents when compared to the national HIV testing algorithms.

Citation (Research Paper 5): **Dziva Chikwari C**, Njuguna IN, Neary J, Rainer C, Chihota B, Slyker JA, Katz DA, Wamalwa DC, Oyiengo L, Bandason T, McHugh G, Dauya E, Mujuru H, Stewart KA, John-Stewart GC, Ferrand RA, Wagner AD. Brief Report: Diagnostic Accuracy of Oral Mucosal Transudate Tests Compared with Blood-Based Rapid Tests for HIV Among Children Aged 18 Months to 18 Years in Kenya and Zimbabwe. Journal of acquired immune deficiency syndromes (1999) 2019; 82(4): 368-72.

Chapter 7 is a manuscript also published in JAIDS and is titled, "*Feasibility and Accuracy of HIV testing of children by caregivers using oral mucosal transudate HIV tests.*" The manuscript evaluates caregiver's ability to accurately perform oral HIV testing on their children and caregiver's ability interpret the oral HIV test results either with or without prior provider demonstrations.

Citation (Research Paper 6): **Dziva Chikwari C**, Simms V, Kranzer K, Dringus S, Chikodzore R, Sibanda E, Webb K, Redzo N, Mujuru H, Apollo T, Ncube G, Hatzold K, Bernays S, Weiss HA, Ferrand RA. Feasibility and Accuracy of HIV testing of children by caregivers using oral mucosal transudate HIV tests. Journal of acquired immune deficiency syndromes (in Press).

Chapter 8 is a discussion of all the study findings, strengths and limitations of the research, the implications of this research, conclusions and recommendations for future research for the implementation of index-linked HIV testing for children and adolescents.

1.6 Contribution of the author

I was responsible for the development of the study protocol based on a 4-page grant proposal prepared by Professor Ferrand. Under the supervision of Professor Ferrand and Dr Simms, I designed the study methods, outcomes, data collection tools, topic guides and standard operating procedures. I applied for all the ethical approvals for the study in Zimbabwe and at LSHTM.

I recruited, trained and supervised all the research assistants that enrolled participants into the study and collected both the quantitative and qualitative data. The study database was managed by Tsitsi Bandason and Nicol Redzo who also did the data cleaning. I prepared the analytical plans and performed the data analysis for all the publications in this thesis with support from Dr Simms (quantitative analysis) and Dr Bernays (qualitative analysis).

I wrote the complete drafts of all the research papers included in this thesis, was responsible for submission to the journals and responding to the reviewer comments.

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2. Literature review

2.1 Introduction

The following chapter presents a narrative review of HIV among children and adolescents including HIV transmission among children, HIV testing methods, gaps and barriers to HIV testing for children and adolescents as well as a narrative of the setting in which this research was conducted, Zimbabwe. A narrative review was selected instead of a systematic literature review as it used as a background to the overall doctoral project. Chapters 2-7 of this thesis are published manuscripts and as such focus on specific components of index-linked HIV testing in relation to the research question addressed by the respective manuscript. The aim of this chapter and the narrative review which is embedded in it is to provide an overall background to the thesis. The specific aim of the narrative review is **to understand the current landscape for HIV diagnosis of children and adolescents and what strategies have been used to address HIV testing gaps for this age group**. Given that the review was conducted to describe the broad landscape around paediatric HIV testing, a systematic review approach (which would have focused on a specific outcome) was not used. The methods used in developing this narrative review included a breakdown of the review into relevant sections (subtopics) and a search of relevant literature in each subtopic on PubMed and Google Scholar. Two critical limitations of this strategy were that the search was conducted only by me, and this literature search was conducted in a non-systematic manner, which may have missed some key publications.

2.2 HIV infection

The HIV epidemic was identified in the United States in 1981. A cluster of cases of unusual tumours and opportunistic infections (Kaposi's sarcoma and Pneumocystis pneumonia) in previously well homosexual men was subsequently recognised as being due to a new form of acquired immune deficiency syndrome (AIDS).[1,2]

Epidemiological investigations indicated that the disease was sexually transmitted and could also be acquired from administration of infected blood products and exposure to contaminated needles.[3,4] HIV was identified as being the cause of AIDS in 1983, and the development of a serological test to identify HIV infection in 1984 was followed by the discovery that AIDS was not only a "western" disease but also occurring in the heterosexual population of central African countries.[5] In Kinshasa, Democratic Republic of Congo (DRC), the annual number of cases of Kaposi's sarcoma diagnosed in a large public sector hospital tripled from 1970 to 1984, and epidemic increases in the wasting syndrome (termed "Slim disease"), a sentinel marker of AIDS, were noted in the late 1970s in Uganda and DRC.[6,7] HIV is now recognised to have originated in Africa, which remains the worst affected continent.

HIV causes depletion of CD4+ T-cells, the central mediators of the human immune response, by entering and replicating within the CD4+ T-cells and consequently causing CD4+ T-cell destruction and depletion.[8,9] The depletion of CD4+ T-cells results in immune deficiency causing an increased frequency of opportunistic infections among those infected.[32] If untreated, HIV leads to AIDS, a syndrome of advanced HIV infection and ultimately results in death.[10]

The epidemiology of HIV infection is heterogeneous with substantial local, national and regional variations. Some parts of the world have experienced concentrated HIV epidemics (general population HIV prevalence <1% but HIV prevalence >5% in at least one high risk sub-population e.g., sex workers or men who have sex with men) such as in Latin America, the Middle East and Europe. Other regions such as within parts of southern and eastern Africa have experienced generalised HIV epidemics (general population HIV prevalence >1%).[11] Sub-Saharan Africa (SSA) is the epicentre of the HIV pandemic and in 2019 over 70% of the total number of people with HIV globally were living in SSA.[8,12] Additionally, in the 2017 Global Burden of Disease study, HIV was the leading cause of morbidity and mortality in SSA among children and adults.[13] Within the southern African region, in 2018 Eswatini had the highest HIV prevalence (27.4%) among adults aged 15-49 years.[14]

HIV transmission occurs in three ways; through unprotected sexual (vaginal or anal) intercourse, from blood products or from an infected mother to her child.[15] In part the disproportionally high HIV prevalence in SSA has been attributed to high prevalence of ulcerative sexually transmitted infections (STIs) and multiple concurrent sexual partnerships.[16,17] Heterosexual transmission is the predominant mode of transmission in SSA with an associated epidemic in children as result of vertical (mother-to-child) transmission in countries with generalised HIV epidemics.[16,18]

2.3 HIV diagnosis

There are two types of HIV diagnostic approaches -either using viral detection or antibody detection methods. The first HIV antibody tests were available in 1985,

which were laboratory based. Subsequently, rapid, point-of-care blood-based tests were developed with results available within 20 minutes, enabling HIV testing to be done in lower-level health facilities and in community-based settings.[19,20] The sensitivity of these tests may be improved by combining HIV antibody detection with detection of the p24 antigen, a viral protein. The p24 antigen appears in blood sooner than antibodies after infection thus resulting in a shorter window period (time after HIV infection but before it can be picked up by an HIV test).[21] These tests require a fingerprick blood sample and have mostly been performed by trained health providers. HIV antibodies can also be found in saliva, leading to the development or oral mucosal transudate (OMT) tests for HIV testing.[22] In order to optimise HIV diagnosis by balancing specific test sensitivity and specificity, HIV testing algorithms that use two or more tests for diagnosis confirmation are routinely used.[23]

Viral detection methods involve detection of viral nucleic acid using polymerase chain reaction (PCR).[19] PCR testing requires laboratory infrastructure and is mainly used for early infant diagnosis (EID) of HIV, where HIV antibody tests cannot be used due to the passive transfer of maternal antibodies to the infant.[19]

2.4 Treatment of HIV infection

HIV remains an incurable infection, but antiretroviral therapy (ART) given in combination (highly active ART (HAART) or combination ART (cART)) of three or more drugs can durably suppress viral replication.[24] Durable suppression of viral replication enables immune reconstitution, thus reducing the risk of infections and death.[10] Viral load measured in blood gives an indicator of the response to ART in an individual, with an undetectable viral load (depending on

the threshold of the viral load measurement assay) demonstrating successful treatment.[10]

Early initiation of ART, before severe immune deficiency, has substantial benefits such as reduction in HIV associated clinical events, HIV morbidity and mortality.[25,26] Treatment guidelines have evolved over time in terms of the definition of "early treatment" with initial guidance recommending treatment initiation based on WHO clinical stage (3 or 4) and also on CD4 count (<350 cells/mm^3). Evidence from three key randomised controlled trials and observational studies showed initiating ART at higher CD4 counts (>550 cells/mm^3) reduced the risk of disease progression to AIDS. Findings from the TEMPRANO trial conducted in the Ivory Coast showed among adults the risk of death and severe HIV related illness was lower for those who had initiated ART with a baseline CD4+ count >500 cells/mm^3 when compared to those with delayed initiation.[27] A multicontinental randomised controlled trial conducted by the HIV Prevention Trials Network (HPTN 052) also showed early treatment initiation (with CD4+ counts between 350-500 cells/mm^3) when compared to initiation after CD4+ count <350 cells/mm^3 was associated with a 41% reduction in HIV related clinical events.[28] Furthermore initiating ART as soon as possible after diagnosis vs after having two or more clinic visits was shown not to cause attrition in care nor detract from viral suppression.[29] Based on findings from these and other studies a "treat all" policy, regardless of clinical stage and CD4 cell count, was recommended by WHO for all individuals living with HIV from 2016.[26] Despite the lack of similar data on the impact on mortality in older children, the approach of universal treatment regardless of disease and

immunological stage was extended to all age-groups for standardising delivery programmes and on the premise that earlier treatment could facilitate better immune constitution and reduce risk of comorbidities in children such as growth failure, neurocognitive disease and organ damage.[30-32]

2.5 Mother to child transmission of HIV

While initially recognised predominantly as an adult infection primarily contracted through unprotected sexual intercourse, HIV can be transmitted from mother to child.[33] HIV transmission from mother to child can occur in utero, intra-partum (during labour or delivery) or via post-natal transmission through breastfeeding.[34] In utero transmission of HIV can occur from as early as 8 weeks gestation.[33] Intra-partum transmission is largely due to exposure of the baby to cervico-vaginal secretions.[33,35]

The generalised adult HIV epidemic in SSA was therefore followed by an epidemic of HIV in children, mirroring the adult HIV epidemic.[36] Approximately 90% of HIV infections in children occur as a result of mother to child transmission (MTCT).[33] In 2005 a survey comparing ANC and population-based HIV prevalence conducted in rural South Africa found over 38% of pregnant women attending antenatal care (ANC) clinics were HIV positive.[37] The HIV prevalence among pregnant women attending ANC clinics was much higher than among all women in the sampled general population (25%). This higher prevalence was likely due to the fact that women attending ANC are sexually active and not using contraceptives.[37] Higher prevalence of HIV among ANC attendees is consistent in many countries with generalised HIV epidemics.[38] In

2019 the global MTCT of HIV including both perinatal and postnatal HIV transmission was 9.1%.[36]

Factors that affect MTCT of HIV can be categorised as viral, maternal, obstetrical, foetal and infant.[33] High maternal viral load, prolonged rapture of membranes during labour, prematurity of pregnancy and prolonged/mixed breastfeeding have been shown to increase the risk of HIV transmissions from mother to child.[33,39,40] Elective caesarean sections were shown to decrease the risk of HIV transmission by up to 50% likely due to the fact that an elective caesarean occurs prior to the rapture of membranes and reduces contact of the foetus with secretions or blood from the mother during labour contractions and in the genital tract.[41] However, the decreased risk of HIV transmission conferred by elective caesarean section was offset by the increased risks associated with surgery and challenges with implementation in resource limited settings.[42]

The presence of HIV in cell-free and cellular portions of breast milk is responsible for postnatal transmissions through breastfeeding.[33] In SSA breastfeeding contributes significantly to perinatal HIV transmissions.[33] In a randomised controlled trial conducted in Kenya from 1992-1998 there was significantly higher HIV infection in the arm where children were breastfed (36.7%) when compared to those who were formula fed (20.5%) in the first two years of life.[39] A cohort study conducted in South Africa from 2001-2005 comparing HIV transmission among infants breastfed exclusively and those who received mixed feeding showed increased HIV transmission risk among those who received mixed breastfeeding.[43] While avoidance of breastfeeding was initially proposed

as a strategy to prevent MTCT it is not often feasible in low- and middle-income settings where clean and safe drinking water is often not accessible.[42]

2.6 Prevention of mother to child transmission of HIV

2.6.1 ART for the prevention of mother to child HIV transmission

Over the last 20 years there have been a number of approaches developed for prevention of mother-to-child HIV transmission (PMTCT).[44] Key among the PMTCT strategies adopted is the use of ART for pregnant mothers.[36] A landmark study conducted by the Paediatric AIDS Clinical Trials 076 Study Group in 1994 showed that HIV transmission rates at 18 months post-delivery were significantly lower when zidovudine prophylaxis was given to the mother and her child (8.3% compared to 25.5% among recipients of placebo).[44,45] Despite this, the zidovudine regimen was not widely implemented in resource-constrained settings due to the requirement for early engagement with care and early treatment initiation for pregnant women as well as the intravenous administration of zidovudine during labour which would not be practical in many LMIC settings.[44] Drug regimens subsequently were simplified and shortened to mitigate against these challenges e.g. the introduction of single dose nevirapine (NVP). In an HIV Prevention Trials Network randomised controlled trial (HIVNET 012) conducted in Uganda published in 2003 the prevalence of HIV at 6-8 weeks among infants who had received single dose NVP was 11.8% while that among infants receiving zidovudine was 20.0%.[44] This regimen was simple, cheap and effective, however, concerns about NVP resistance soon surfaced, and cART was recommended as a strategy for PMTCT since 2006.[44]

Current WHO guidance is that all pregnant women are to be initiated on treatment at the point of diagnosis regardless of their CD4 count in order to reduce the likelihood of HIV transmission to children.[46] This was recommended after evidence from multiple cohorts showed treatment started before pregnancy together with having an undetectable viral load can result in zero risk of HIV transmission to children.[47]

With few alternatives to breastfeeding in LMIC settings additional PMTCT strategies aimed at reducing post-natal transmission through breastfeeding were evaluated, namely the use of ART as prophylaxis for infants during the breastfeeding period.[42] Current treatment regimens recommend prophylaxis using either NVP or zidovudine among breastfed or non-breastfed infants for a duration of 4-6 weeks post-delivery with room for extension of up to 12 weeks.[44] The extension up to 12 weeks is for scenarios where the mother was diagnosed during labour or after delivery and intends to breastfeed or if the infant was identified as HIV exposed after delivery and is breastfeeding.[64] WHO recommends exclusive breastfeeding for six months.[44]

2.6.2 Coverage of the prevention of mother to child transmission of HIV programmes

The coverage of pregnant women living with HIV accessing ART has increased significantly over time. In 2010 global coverage was 17%, however, by 2019 global coverage had reached 85%.[36] However, there is substantial heterogeneity in coverage with some regions such as in West and Central Africa having under 60% coverage while some regions, such as Eastern and Southern Africa, have successfully and consistently reached almost all pregnant women with 95%

coverage in 2019.[36] Importantly, the gaps in coverage of ART within PMTCT programmes mean that new infections in children continue to occur.

2.6.3 Gaps in the prevention of mother to child transmission of HIV programmes

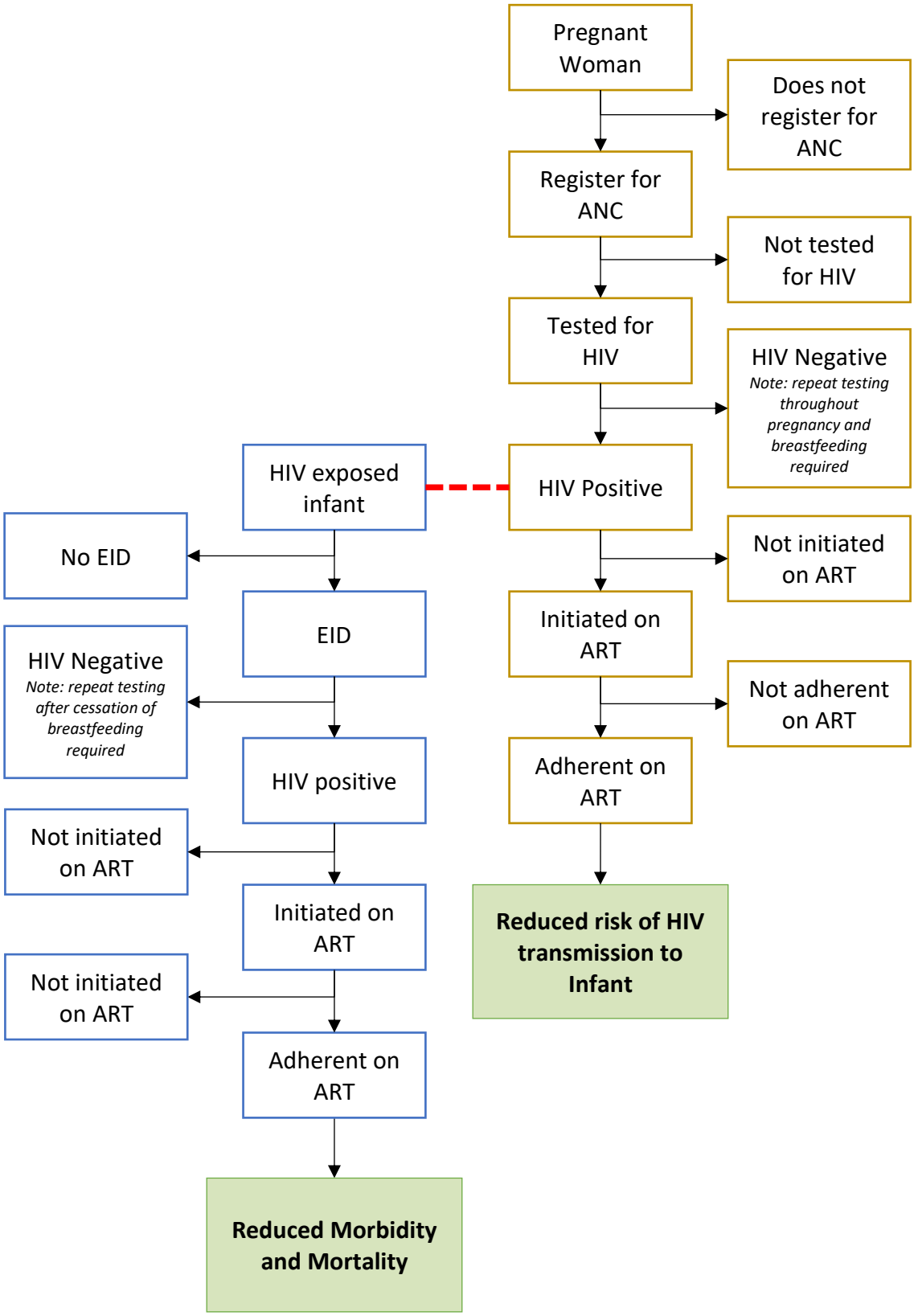
Firstly, some women do not register for ANC which means they do not access HIV testing as part of PMTCT programmes and are therefore unable to access and initiate treatment early.[36,48] HIV testing while initially offered by request in ANC, evolved into an opt-in and subsequently to an opt-out (HIV testing performed on women presenting for ANC unless they actively decline) approach which increased uptake.[36,49] In addition, women who test negative remain at risk of HIV infection, necessitating repeat HIV testing during pregnancy and breastfeeding. The early stage HIV infection is associated with a very high viral load and a particularly high risk of MTCT.[50] Uptake of HIV retesting among initially HIV negative pregnant women can be low. A study conducted in Tanzania from 2015-2016 found only 30% of pregnant women where were HIV negative at first ANC contact retested for HIV up until the postpartum period. [51]

Late or no registration for ANC has been attributed to structural barriers such as costs to access facilities, limited access to facilities due to long distances needed to be travelled to access health facilities and also long waiting times at facilities. [52,53] Furthermore, individual barriers exist such as lack of knowledge about the need to register for ANC early to access PMTCT as well as lack of partner involvement in ANC.[52,53] HIV associated barriers also exist such as HIV stigma and discrimination in the community which stops women from accessing HIV testing and subsequently HIV treatment. [52,53]

Secondly, once tested and initiated on treatment further challenges among pregnant women still prevail including poor adherence to ART during pregnancy and breastfeeding and loss to follow up (Figure 1).[50] Disrupted or poor ART adherence increases risk of MTCT of HIV and has been attributed to non-disclosure of HIV status by pregnant mothers to their partners and limited partner involvement to support with HIV treatment.[52,53]

To optimise PMTCT widespread coverage of HIV testing and ART among pregnant women together with interventions to monitor and maintain viral suppression are required.[54] Possible solutions include community sensitisation on the importance of HIV testing and treatment for pregnant mothers, improved access to HIV testing, ANC services and ART through decentralisation of services to primary care level and ensuring adequate resources to avoid test kit or drug stock outs.[33,54,55]

Figure 1: Prevention of Mother to Child Transmission of HIV Cascade



2.6.4 Early Infant Diagnosis

Infants born to HIV positive mothers are recommended to have an HIV test within 4 – 6 weeks of birth. However, according to UNAIDS, in 2019 only 60% of children eligible for HIV testing at birth had received an HIV test within 6 weeks globally.[36,56] Rapid antibody tests (tests that detect HIV antibodies in blood or oral fluid) which can be done at the POC produce results within 20 minutes but cannot be used for testing infants due to the passive transfer of maternal antibodies resulting in false positive tests.[57]

Therefore, up until 18 months of age, diagnosis of HIV requires viral detection (rather than antibody detection) methods such as DNA PCR.[40,58,59] Virological tests detecting DNA PCR are costly and require much more infrastructure and sophisticated laboratory capacity, resulting in HIV testing being restricted to central laboratories. Turnaround of test results (from laboratory to the health facility or to the patient) can often take several months meaning delayed diagnosis for infants who do return for results but also many infant-mother pairs are lost to follow up.[58] In an observational study of eight African countries 98.3% of infants who had POC tests in 2017 received their results within 30 days. In comparison only 18.7% of infants receiving virological HIV testing from 2014-2017 had received their results within 30 days.[60]

As such, strategies that have been used to try and improve uptake of EID include alignment of HIV testing with routine child health visits, use of SMS reminders and community follow up of infants who are lost to follow up.[58]

More recently, several POC HIV testing platforms for EID have been evaluated, demonstrated to be feasible and to improve rates of results return and ART initiation rates but have not been implemented widely to date.[58,61] This may be due to the costs associated with roll out of the POC EID testing platforms or their more recent introduction into the market whereby only two EID POC tests had been prequalified by WHO by January 2019.[59] In an observational study of eight African countries, over 92.3% of HIV positive infants who received POC HIV testing were initiated on ART within 60 days while only 43.3% of infants receiving conventional EID were initiated.[60] Current WHO guidance is that HIV exposed infants should also be tested for HIV again at nine months. However, often children do not return for repeat HIV testing.[23]

The suboptimal coverage of PMTCT and EID mean HIV infections in children continue to occur and those infected are not identified timely (Figure 1).

2.7 Paediatric HIV infection

HIV in children is associated with rapid disease progression and high mortality, with a 50% mortality by age two years recorded in African cohorts in the pre-ART era.[62] However, there is variation in disease progression among children with perinatal HIV infection. Some children with HIV have much slower progressing disease, and survive to older childhood even without ART.[63] A French paediatric cohort of HIV infected children published in 2007 showed that 2% of children infected in the perinatal period had no clinical nor immune disease progression by 10 years of age.[64] An Italian study from 1994 found that among 182 HIV infected children who survived beyond 5 years of age 15% had no disease symptoms.[65]

It is estimated that a third of children with perinatally-acquired HIV have slow-progressing disease, with a median survival of at least 16 years (no upward estimates available).[66] A study conducted between 2007-2008 in Zimbabwe found that 46% of the 301 adolescents aged 10-18 years admitted at two general hospitals for any reason were HIV positive, of whom only 38% were previously undiagnosed.[67] These adolescents presented with a spectrum of opportunistic infections as well as chronic co-morbidities showing evidence of long term survival with perinatally-acquired HIV.[67]

In the last twenty years, as HIV epidemics have matured in Africa, large numbers of children have been presenting to clinical services with advanced HIV infection in older childhood and adolescence. The reasons for these differences in disease progression among perinatally infected children are multi-faceted and may include clinical factors such as low CD4 count and high viral load and disease stage, of the mother, viral factors (e.g., viral subtype) or immune factors (e.g., HLA type).[68]

It is important to note that slow progression does not imply that children growing up with HIV are asymptomatic.[69] The majority commonly have recurrent minor infections such as skin and upper respiratory tract infections that are also common in children without HIV, and therefore may not prompt HIV testing because they may not be automatically associated with HIV infection.[70] HIV infection is also associated with growth failure, pubertal delay and other comorbidities such as chronic cardiorespiratory, neurocognitive disease and skin disease.[66,67,71-74] Importantly, once established, these conditions may not be reversible with ART.[73,75] In infants (aged 6-12 weeks) enrolled in the CHER trial,

immediate initiation of treatment following diagnosis reduced mortality by 76% which prompted WHO guidelines for ART in infants regardless of disease or immunological stage.[76] Such a big reduction in mortality has not been observed in other age groups, however, several studies have shown that earlier treatment is associated with faster CD4 count recovery in the first 3 months on ART and a sustained higher CD4 count.[30,76] Furthermore, ART is associated with improved growth but children who start ART later may not achieve their full growth potential.[73,77]

Many children who were born with HIV before PMTCT programmes were scaled up or continue to be infected despite availability of PMTCT programmes are presenting and will continue to present in later childhood due to the gaps in PMTCT and EID programmes discussed above. Delayed initiation on ART increases the risk of disease progression, additional end organ complication and also reduces grown potential.[66] Earlier access to treatment can prevent these complications.

There is a need to continue strengthening PMTCT programmes including EID to facilitate timely initiation of ART in infants who test HIV positive. However, as the HIV epidemic has aged, it is apparent that there is a need to focus on timely diagnosis of children and adolescents who have been missed by PMTCT programmes.

2.8 Global HIV testing models and trends

HIV testing is the entry point for access HIV treatment and care as well as for accessing HIV prevention interventions. UNAIDS has set specific targets aimed at

ending the HIV epidemic, namely the 95-95-95 targets with 95% of people living with HIV aware of their status, 95% of those aware of their status on ART and 95% of those on ART virally supressed by 2030.[78] The first target highlights the importance of HIV testing in both improving clinical outcomes (as people are able to access HIV treatment once diagnosed) and in being a key pilar for epidemic control.[78]

2.8.1 HIV testing coverage

Coverage of HIV testing uptake globally has increased over time with an estimated 70% of people living with HIV in 2015 knowing their HIV status and 79% in 2018. In 2019, an estimated 7.1 million people with HIV were undiagnosed.[78] There is significant heterogeneity among population groups, for example there is lower uptake of HIV testing among adolescents.[79] In a 2016 survey among adolescents and young adults (aged 15-24 years) in Nigeria only 24% had ever tested for HIV.[80] There is also geographic variation of HIV testing coverage with only 52% of people in the Middle East and North Africa living with HIV knowing their HIV status in 2019 while in the same year 70% of people living with HIV in eastern Europe and central Asia knew their HIV status.[78] There is therefore a need to bridge these HIV testing gaps in order to improve HIV morbidity and mortality through access to HIV treatment.

2.8.2 HIV testing models

Successes in HIV testing coverage and knowledge of HIV status have been attributed to the availability of timely and low-cost rapid diagnostic tests, and policy changes to facilitate increasing numbers of testers though lay workers and more recently HIV testing in community-based settings.[81]

HIV testing models have evolved over time: Voluntary counselling and testing (VCT) was one of the earliest HIV testing approaches used, whereby HIV testing was made available in different settings but was client-initiated and relied on individuals deciding to undergo HIV testing and attending VCT services. Uptake of HIV testing through VCT was low [23] In 2008 study from Tanzania VCT uptake among men and women was 12% and 7% respectively.[82] Similarly a cohort study published in 2007 among adults in Zimbabwe showed lifetime VCT uptake of only 11%.[83] These findings were consistent in SSA and low VCT uptake was largely attributed to individuals believing they are at low-risk for HIV infection and lack of awareness about the availability and need for HIV testing.[20,84] VCT relies largely on the individuals initiative and often results in late diagnosis.

In 2007 WHO recommended that provider-initiated testing and counselling (PITC) be offered to all patients attending health facilities in settings with generalised HIV epidemics.[20,85] PITC places the onus of HIV testing on the health provider, and requires that the provider offers HIV testing to all clients irrespective of symptoms or clinical diagnosis.[85] One application of PITC was HIV testing in ANC setting for pregnant mothers as part of PMTCT programmes, particularly to facilitate delivery of ART for reducing the risk of MTCT.[20] In a study conducted in Botswana ANC patients who knew their HIV status increased from 47% to 78% after the introduction of PITC.[86] PITC removed some barriers to HIV testing such as the need for personal motivation to test. While PITC has helped improve HIV testing uptake PITC coverage has been suboptimal in some groups such as among children where HIV testing is not offered consistently by providers.[87]

Challenges with implementation of PITC include lack of staff and overworked health providers who are then not able to prioritise HIV testing, unstable supply chains of HIV test kit supplies, lack of space to conduct HIV testing; difficulty in navigating ethical issues such as consent and confidentiality.[88,89] Client level barriers to HIV testing include lack of personal motivation to seek testing, fears of HIV positive diagnosis, fear of HIV related stigma and discrimination and not feeling ready to test.[90,91] A key limitation of PITC is that it requires individuals to present to health facilities in order to access HIV testing; for those who are living with HIV this may translate to delayed HIV diagnosis which would only occur at the onset of symptoms and therefore advanced disease stage.

Innovative HIV testing strategies are therefore needed to bridge gaps in uptake of facility-based HIV testing. HIV testing outside health facility settings including workplace-based testing, home-based testing, mobile outreach, and school-based testing have been aimed at reaching individuals who otherwise would not access health facilities. They have broadly been effective in reaching population groups where HIV testing has historically been low such as men and young people.[23,92] A systematic review of strategies to engage with HIV testing services in SSA found mobile and home-based HIV testing significantly increased HIV testing by males when compared to VCT.[93] There are several advantages to community-based HIV testing strategies such as being able to reach groups that traditionally do not engage with health facilities (e.g. men, young people, marginalised groups such as PWID, LGBQTI etc) and reduction of stigma by normalising HIV testing. However, there are several concerns associated with these approaches including lower HIV yield and therefore potentially being less

cost-effective, the requirement for additional human and infrastructural resources, concerns about privacy and confidentiality in the different test locations and onward linkage to care for those who test HIV positive.[23]

2.8.3 HIV self-testing

HIV self-testing (HIVST) is a novel HIV strategy whereby individuals are able to test themselves for HIV.[22] Individuals collect the test specimens, perform the test and interpret the test results without assistance from a provider. While routine HIV testing mainly uses rapid blood-based testing the HIVST is usually performed using an OMT test using a salivary sample. In four studies conducted between 2003-2004 where OMT tests were compared to enzyme immunoassays and western blot tests, OMT tests had a sensitivity of 99.1% and a specificity of 99.6%.[94] In a meta-analysis assessing the diagnostic performance of the Oraquick advance rapid HIV-1/2 (OraSure Technologies Inc, PA, USA) test, the pooled sensitivity was 98.0% for oral specimens and 99.7% for blood based specimens.[95] In this analysis pooled specificity was 99.7% for oral specimens while that of blood specimens was 98.5%.[95] While OMT testing is highly sensitive and specific neither study included children and OMT testing had not been validated for use in children younger than 12 years at the time of conducing this research.[96]

Current WHO guidelines are that any positive/reactive HIVST result must be confirmed by subsequent blood based tests at a health facility in order to confirm an HIV diagnosis.[22,23] This has successfully been implemented in many high HIV prevalence setting such as Malawi, Zimbabwe and Zambia.[22] High HIVST uptake has been reported among key population groups such as sex workers, men who have sex with men and also among older adolescents.[97,98] In a community-based

study conducted among adults >16 years in Malawi the crude uptake of HIVST was over 83%, however, adolescents aged 16-18 years were more likely to test.[98]

HIVST has been shown to be highly acceptable to first time testers and some population groups for several reasons including non- reliance on trained health providers. HIVST is convenient and allows testers to have autonomy about when or where HIV testing occurs and also allows them to perform the test in private. The non-invasive nature of OMT tests also makes them more accessible when compared to blood-based test.[99,100] Some potential concerns about HIVST were low literacy to read and follow instructions, concerns about being able to accurately perform the test, concerns about social harms after tests have been performed in the absence of a provider (e.g. in the community) and the costs of buying a self-test kit.[101,102] The unit cost of an OMT test is higher than that of a blood-based rapid antibody test.[103]

Successes in HIV testing coverage and knowledge of HIV status have been attributed to the availability of timely and low-cost rapid diagnostic tests and policy changes to facilitate increasing numbers of testers though lay workers and HIV testing in community-based settings.[81] Gaps in coverage and challenges with HIV testing uptake persist leaving a requirement for innovative strategies to improve HIV testing uptake and coverage.

2.8.4 HIV testing for children and adolescents

Globally HIV testing rates among children and adolescents are much lower when compared to those in adults.[104] In 2019 only 53% children <14 years living with HIV were aware of their HIV status and on treatment compared to 63% among

older adolescents and adults (>15 years).[78] Children living with HIV who are not identified in infancy are subsequently often identified when they present with advanced disease or AIDS-indicator conditions.[70,105]

HIV testing strategies for children have largely been the same as those used for adult populations.[56] As described above, PITC has been recommended by WHO since 2007.[106] Despite this, HIV testing uptake among children and adolescents also remains low. In Zimbabwe, after two years of implementing PITC for children in primary health facilities, a community prevalence survey in 2016 found 37.7% of children (8-17 years) with HIV were still undiagnosed.[107] This reflects the inadequacies of facility-based HIV testing strategies for reaching children with HIV as well as scope for the inclusion of children in community-based HIV testing approaches.

There are a number of issues that need to be considered when considering HIV testing in children and adolescents:

1. *Lower HIV prevalence in children*

   In comparison to adults children and adolescents have a lower HIV prevalence which may result in lower HIV yield with universal HIV testing strategies when compared to adults.[108] As such the resources required to identify one child living with undiagnosed HIV are higher which makes blanket HIV testing approaches less suitable.

2. *Guardians act as intermediaries*

   In many countries within SSA all children under the age of 16 years require guardian consent in order to access HIV testing services.[109] The

legal requirement for parental consent, which does not exist for adults, adds a layer of logistical complications to be navigated for HIV testing children who are sometimes orphaned and have frequent changes in guardianship in settings with generalised HIV epidemics.[109-111] In addition, the requirement for caregiver support and approval for the HIV testing of children and adolescents means children and adolescents have to navigate further social barriers such as caregiver fears surrounding HIV stigma, discrimination and fears of disclosing their own HIV status to the child or the status of the child to the child.

3. *Low perception of HIV risk*

   There is a historic assumption the children with perinatal HIV infection do not survive beyond infancy.[87] As such often older children and adolescents are believed to not have perinatal HIV infection as they have lived undiagnosed and untreated till adolescence. This impacts HIV testing as carers are less likely to suspect HIV infection in children despite the children having recurring illness.[87] Furthermore it creates institutional barriers where providers also have low perceived HIV risk and as such children and adolescents are perceived to be of lower priority and providers do not routinely offer HIV testing for children as suggested by PITC strategies.[87]

4. *Children living with HIV have a sexually transmitted disease acquired perinatally*

   A study from Zimbabwe found that providers often felt ill-equipped for navigating counselling and disclosure issues when HIV testing children

and adolescents.[87,112] The fact that children living with HIV have a diseases predominantly acquired through sexual intercourse means that the HIV testing process, in particular counselling for HIV testing is a process that requires the provision of additional information as well as provider skills in navigating the complexities of this.[112]

5. *Availability of HIV tests*

   For younger children (<18 months) the presence of maternal HIV antibodies means routinely used rapid blood-based HIV tests cannot be used in this age group.[87,113] For children <12 years the OMT tests which are increasingly being used have not yet been validated for use in this population.[87,113] The smaller pool of available HIV tests for children limits HIV testing access in this group when compared to adults.

The review paper at the end of this chapter (Research Paper 1) describes in detail the barriers and emerging strategies for HIV testing among adolescents.

2.8.5 Targeted HIV testing strategies and Index-linked HIV testing

Targeted HIV testing strategies often focus on high-risk groups such as sex workers and men who have sex with men as well as hard to reach groups who don't usually engage with health facilities and HIV testing such as men and adolescents.[22,114] They can also reduce the number of tests required to identify one HIV positive case and therefore may be more efficient and cost-effective.[114] Targeted HIV testing strategies that have been rolled out include mobile HIV testing in known hotspots, home based HIV testing, social network HIV testing and partner notification services or index-linked HIV testing.[23,114] Some of these have been highly successful such as index case HIV testing for sexual partners

which when compared to routine HIV testing services such as passive referral in a study conducted in 2009 in Malawi had significantly higher uptake (24% vs 51% respectively).[115]

Among children and adolescents, a simple four item screening tool to identify those at risk of being HIV infected and who can subsequently be targeted for HIV testing reduced the number need to test to identify one HIV-positive child by up to 50%.[116,117] In a study conducted in Zimbabwe a screening tool with four questions to identify older children (10-19 years) living with HIV in health facilities had a sensitivity of 80.4% and specificity of 66.3% to identify HIV.[116]

Another targeted strategy is index-linked HIV testing whereby children of individuals living with HIV are specifically targeted for HIV testing.[23] At the time of conducting the research for this thesis index-linked HIV testing for children had been evaluated in one study in Kenya among 2–12-year-olds and had an HIV prevalence of 7.4% which was much higher than the general population prevalence of 1%.[118]

2.9 Zimbabwe

2.9.1 The HIV epidemic in Zimbabwe

Zimbabwe has had an early onset generalised HIV epidemic, with adult HIV prevalence peaking at 29% in 1997.[119] In 2020 the HIV prevalence in Zimbabwe still remained one of the highest in Sub-Saharan Africa at 12.9% among individuals >15 years.[120] There have been minor fluctuations in prevalence in the last five years due to the widespread roll out of ART and people living longer with HIV infection. Zimbabwe is one of the few countries where HIV incidence (0.38%

in 2020 compared to 5% in 2000) has dropped.[121] An earlier drop in HIV incidence was attributed to the intensified roll out of prevention measures such as condoms distributed freely nationwide and more recently nationwide voluntary medical male circumcision campaigns, treatment as prevention and other behavioural interventions.[121]

HIV testing and treatment services in Zimbabwe are largely facility-based. Additionally, community-based HIV testing strategies such as events-based HIV testing, and mobile outreach HIV testing have been implemented though the MoHCC and partner organisations but are often not sustained. In 2016, among adults (15-64 years) 73.7% had been tested before, however, this proportion was much lower in young adults (15-24 years) at 50.4% in the same year.[122]

The early onset sustained HIV epidemic in Zimbabwe led to an associated epidemic of HIV infection among children prior to the advent and scale up of PMTCT programmes, with large numbers presenting for the first time in older childhood and adolescence as HIV epidemics matured.

In 2010 PMTCT coverage in Zimbabwe was only 29%, increasing to 94% in 2019.[14] However, MTCT continues to occur due to the gaps in PMTCT programmes and suboptimal coverage of EID means that children continue to present beyond infancy with undiagnosed HIV.[123] In 2018 Zimbabwe recorded 4800 new HIV infections among children aged 0-14 years.[14] According to a national population based survey (ZIMPHIA) the HIV prevalence among children and adolescents (0-14 years) was 1.6% in 2016.[122]

2.9.2 The economy, public health system and HIV response in Zimbabwe

Over the last 30 years the Zimbabwe has been faced with a weakened economic and political environment. This decline over time has negatively impacted the delivery of and funding for health services.[124] However, HIV programming has remained one of the top health priorities, and over 1.1 million Zimbabweans were accessing ART in 2018.[14] Funding for HIV services in Zimbabwe is largely though international donors such as PEPFAR and the Global Fund as well as domestic funding through the national AIDS Levy which was introduced by the Zimbabwean government in 1991.[14,125] The HIV response in Zimbabwe is coordinated by the National AIDS Council (NAC) in collaboration with the Ministry of Health and Child Care (MoHCC).[125]

HIV testing and treatment services are largely decentralised and provided in nurse-led primary care health facilities. HIV programmes also include primary care counsellors (who mainly provide HIV testing services) and community or village health workers who follow up clients defaulting on HIV or TB treatment, and refer clients from the community to the facility.[126] Primary care counsellors go through a 6-week training programme while village/community health workers go through an 8-week training programme with the opportunity of refresher training.[127]

It is within this landscape that my PhD project was conducted.

2.10 Summary

Early diagnosis of HIV and initiation on treatment improves morbidity and mortality. Although PMTCT programmes have been rapidly scaled up, MTCT of

HIV continues to occur, with many children only diagnosed when they present with advance disease in later childhood, and coverage of ART in children lagging behind that in adults because of the delay in diagnosis.

Children and adolescents are faced with unique barriers to access HIV testing and there is an urgent need to develop and evaluate interventions suitable for this group. This thesis will focus on the evaluation of index-linked HIV testing for children and adolescents in Zimbabwe, a country with sustained severe generalised HIV epidemic.

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2.12 Research Paper 1: Barriers to, and emerging strategies for, HIV testing among adolescents in sub-Saharan Africa

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RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	398292	**Title**	Ms
First Name(s)	Chido		
Surname/Family Name	Dziva Chikwari		
Thesis Title	Facility and community-based index-linked HIV testing strategies for children and adolescents in Zimbabwe		
Primary Supervisor	Professor Rashida A Ferrand		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Current Opinion in HIV and AIDS		
When was the work published?	March 2018		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	**No**	Was the work subject to academic peer review?	**Yes**

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	Choose an item.

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was the first author of this paper and wrote the first draft. I was responsible for the manuscript submission process and revised the manuscript in response to peer reveiwer comments.

SECTION E

Student Signature	[redacted]
Date	26/02/2021

Supervisor Signature	[redacted]
Date	26/01/2021

Barriers to, and emerging strategies for, HIV testing among adolescents in sub-Saharan Africa

Chido D. Chikwari[a,b], *Stefanie Dringus*[c], *and Rashida A. Ferrand*[a,b]

Purpose of review
HIV/AIDS is one of the leading causes of death among adolescents in sub-Saharan Africa and 40% of new HIV infections worldwide occur in this group. HIV testing and counselling (HTC) is the critical first step to accessing HIV treatment. The prevalence of undiagnosed HIV infection is substantially higher in adolescents compared with adults. We review barriers to HTC for adolescents and emerging HTC strategies appropriate to adolescents in sub-Saharan Africa.

Recent findings
There are substantial individual, health system and legal barriers to HTC among adolescents, and stigma by providers and communities remains an important obstacle. There has been progress made in recent years in developing strategies that address some of these barriers, increase uptake of HTC and yield of HIV. These include targeted approaches focused on provision of HTC among those higher risk of being infected, for example, index-linked HTC and use of screening tools to identify those at risk of HIV. Community-based HIV-testing approaches including HIV self-testing and incentives have also been shown to increase uptake of HTC.

Summary
In implementing HTC strategies, consideration must be given to scalability and cost-effectiveness. HTC approaches must be coupled with linkage to appropriate care and prevention services.

Keywords
adolescents, barriers, HIV, strategies, testing

INTRODUCTION

HIV testing and counselling (HTC) is the critical first step to accessing HIV treatment and is an opportunity to promote healthy sexual behaviour through counselling and linkage to HIV prevention and sexual reproductive health services [1,2▪▪,3]. The prevalence of undiagnosed HIV infection is substantially higher in adolescents compared with adults [4]. Population HIV Impact Assessments (PHIA) surveys conducted in Malawi, Zambia and Zimbabwe between 2015 and 2016 showed that less than 50% of young people aged between 15 and 24 years living with HIV were aware of their HIV status [5▪,6,7]. Adolescents with HIV include those who have acquired HIV vertically as well as horizontally [2▪▪]. In sub-Saharan Africa (SSA), which bears 74% of the global burden of HIV infection, large numbers of adolescents, infected vertically before interventions to prevent mother-to-child transmission were scaled up have been presenting to health services with undiagnosed HIV in recent years [8]. In addition, 40% of new HIV infections worldwide occur in adolescence and HIV infection rates in this age-group are projected to rise [5▪,9]. Delayed diagnosis is associated with an increased risk of mortality as well as onward HIV transmission [5▪]. We review barriers to HIV testing for adolescents and emerging HTC strategies appropriate to adolescents in SSA.

BARRIERS TO HIV TESTING AND COUNSELLING AMONG ADOLESCENTS

Barriers to HTC among adolescents occur at individual, health service provider and policy levels (Table 1).

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KEY POINTS

- The prevalence of undiagnosed HIV infection is higher in adolescents compared with other age-groups.
- Barriers to HTC among adolescents include need for guardian consent, negative attitudes and lack of training among healthcare workers, stigma and distance from facilities, inconvenient opening hours of facilities and long waiting times.
- Several strategies have improved uptake and yield of HTC in adolescents including HIV testing targeted at adolescents at high risk of being infected, community-based testing (campaigns, mobile testing, home-based testing), use of incentives and HIV self-testing.
- HTC strategies for adolescents must be evaluated for their potential for scalability and cost-effectiveness and should ensure linkage to appropriate treatment and prevention services after testing.

Studies have reported a lack of comprehensive HIV knowledge and of inaccurate perception of personal risk, with some adolescents considering HTC to be neither necessary nor important [19]. Other barriers to HTC reported by adolescents are fear of the consequences of having a positive test result, and stigma from peers and providers [10▪]. Adolescents, particularly younger adolescents who are more likely to be vertically infected, rely on their caregivers for accessing HTC. Many are orphaned and have changing caregivers. In addition, caregivers may have more urgent competing priorities, which mean that they only consider having their child tested whenever the child gets sick and likely develops advanced disease [13,14]. Although many caregivers suspect their adolescent may have HIV either because of the parent having died or because of chronic ill-health, there is a misplaced desire to protect their child from the stigma she or he may face in the community [13]. In the case of a vertically infected adolescent, a positive HIV test deductively discloses the HIV status of the mother (and possibly the father) and the guilt and the fear of blame from their child has been shown to be a reason why caregivers may not have their children tested [13,15,16].

Since 2007, the World Health Organization (WHO) has recommended provider-initiated HIV testing and counselling (PITC) in high HIV-prevalence settings, whereby HIV testing is offered proactively to all clients attending a healthcare facility regardless of the reason for attendance [20]. This relies on clients attending the facility and a healthcare worker (HCW) then offering HTC. Distance from health facilities, transportation costs and

Table 1. Summary of barriers to HIV testing and counselling in adolescents

Individual and societal	
Individual	Fear of HIV-positive status and stigma [10▪,11–13]
	Lack of comprehensive HIV knowledge [11]
	Perception of low risk [14,15]
Family/community	Stigma and sanctioning of sexual activity in adolescents [10▪,13,16]
	Caregiver noninvolvement [10▪]
	Parental fear of disclosure of own HIV status [15,16]
	Desire to protect children from stigma [16]
	Competing priorities among caregivers [11]
	Lack of HIV knowledge [11]
Health service provider	
Staff	Healthcare worker judgemental attitudes [10▪,12]
	Lack of confidentiality (healthcare provider disclosure of HIV status to caregivers) [10▪,12]
	Lack of HIV knowledge [14]
	Insufficient training of healthcare workers in discussing HIV, ethicolegal issues [14]
	Concern about unavailability of support services for adolescents with HIV [14]
Health facilities	Lack of staff and testing kits [14]
	Priority for HIV testing within facilities given to other services, for example, PMTCT [14]
	Accessibility of facilities; location and unsuitable working hours [12]
Health policy and legal	
	Legal age of consent [11,14,17▪]
	Discrepancies in national HIV-testing guidelines [14,18]

inconvenient opening hours are barriers for accessing health services by adolescents. Common reasons adolescents report for not accessing HTC are the stigmatizing and judgemental attitudes of healthcare providers, and lack of confidentiality [2▪▪,10▪]. In a 2013 study evaluating PITC among children aged 6–15 years attending primary healthcare clinics (PHCs) in Zimbabwe, only 54% underwent HTC, the primary reason for the low coverage being that HCWs did not offer HTC [14]. Notably, being aged more than 11 years was associated with lower odds of being offered HIV testing. From a provider perspective, inadequate knowledge and training of healthcare providers in addressing the complexities of HIV in adolescents such as ethicolegal issues, disclosure and the 'language' to discuss HIV serve as barriers to offering HTC [14]. Other barriers include lack of adequate staff, and prioritization driven by donor funding [e.g. prioritization of prevention of mother-to-child transmission (PMTCT)], concern about the availability of appropriate support services for those who test HIV-positive, and the perception of adolescents as a low-risk group (particularly younger adolescents who would not be expected to be sexually active) [8,14].

Most countries require consent from a guardian for minors to access HTC [17▪]. Many adolescents in Africa do not live with their parents but within extended family structures, either because they are orphaned or because parents migrate for work [13]. Caregiving arrangements are, therefore, unstable and guardianship is often not legally defined, leaving healthcare providers to make a difficult decision about whether the accompanying caregiver is 'suitable' to give consent [17▪,18]. In five SSA countries, the legal age of consent for HTC is 18 years or above [17▪]. There have been policy changes in some countries, for example, in South Africa, whereby a child above the age of 12 years can consent for an HIV test independently [21]. However, the legislation also stipulates that it is an offence to have consensual sex below the age of 16 years, a legal barrier for sexually active adolescents at high risk of HIV infection to seek HTC [17▪,18,21]. Policies do make provision for healthcare providers to give consent on behalf of the minor whenever a guardian is unavailable, if HTC is 'within the best interests of the minor,' or provision to consent independently by those deemed to be 'mature minors' [17▪]. However, these conditions are often subjective and rely on providers having to make decisions, which they are not always trained to do. The practical implications of legislature around consent has posed challenges for healthcare providers in terms of the conflict between maintaining confidentiality versus disclosing test results to caregivers to ensure that adolescents are supported [22].

Table 2. Summary of HIV testing strategies for adolescents

Strategy type	Delivery method
Self-testing	Self-administered self-tests
	Assisted self-testing
Use of incentives (financial/nonfinancial)	Incentives to caregivers
	Incentives to adolescents
	Incentives to facilities
Targeted testing	Index-linked testing
	Use of screening tools
Facility modifications	Extended hours
	Youth friendly services
	Routine opt-out testing
Community-based testing	Door-to-door testing
	Mobile testing
	Campaign testing
	Use of social events
	Youth centres
	School based
Technology and edutainment	Telephone-based counselling
	Simulated processes

HIV TESTING AND COUNSELLING STRATEGIES FOR ADOLESCENTS

HTC strategies have evolved over the last 10 years from client-initiated approaches such as voluntary counselling and testing (VCT) to provider-initiated testing and counselling approaches (PITC) offered routinely in health facilities, and more recently implementation of community-based strategies [7]. These have largely focused on adults and not been tailored to the needs of adolescents [23▪]. Recognizing the need to prioritize adolescents as a key population for HIV prevention and care, the WHO developed specific HTC guidelines for adolescents in 2013 [24]. Most of the WHO recommendations were based on low-quality evidence, and the guidelines highlighted the need to establish comparative effectiveness of interventions to improve access to HTC in this age-group [24]. In this section, we discuss recent approaches to HTC tailored for adolescents in SSA. These strategies are summarized in Table 2 and relevant studies are detailed in Table 3.

PITC has been shown to have a high yield (proportion of individuals who test HIV positive of those eligible for testing), but as discussed above relies on providers offering HTC to clients [34]. A study in

Table 3. Studies describing HIV testing strategies in Adolescents in sub-Saharan Africa

Lead author, year, country	Age (years)	Testing strategy	Setting	Type of HIV test	Number offered HTC	Percentage accepted HIV testing	HIV prevalence	Yield	Comments
Ahmed, 2017 Malawi [25▪▪]	1–24	Index linked	Home and facility	Not specified	461 index cases 711 children and young persons	94% index cases	4%	Not reported	95.5% of tests conducted at home. 65% of adult index cases reported having at least one biological child with an unknown HIV status
Chaila, 2017 Zambia [26]	10–14	Screening tool	Community	Not specified	17 870	51%	1%	0.4%	Among participants tested HIV prevalence was higher in those termed as 'at risk' (2.4%) compared with those not at risk (0.6%)
Daniels, 2017 South Africa [27]	Unrestricted	Technology, social marketing, telephone counselling	Community	Not specified	72 220 program participants	Not reported	Not reported	Not reported	
Kranzer, 2017 Zimbabwe [28]	8–17	Financial incentives	Facility	Blood-based rapid	2050 households	20% (no incentive) 48% (fixed incentive) 40% (lottery)	Not reported	Not reported	HTC offered to all adolescents in households
Njuguna, 2017 Kenya [29]	0–12	Index-linked HTC and Incentives	Facility	Blood-based rapid test if >18 months HIV DNA PCR if <18 months	71 (index cases)	73% of randomized index cases	2%	Not specified	Uptake of HTC was higher in the group offered incentives compared with a cohort that did not receive incentives Uptake of testing did not differ depending on incentive offered
Shanaube, 2017 Zambia [30]	15–19	Door-to-door	Home	Not specified	10 809	81%	2%	1%	Intervention was coupled with HIV prevention services
Bandason, 2016 Zimbabwe [31]	6–15	Screening tool	Facility	Blood-based rapid test	12 057	80%	5%	4%	Tool sensitivity 88.4%; specificity 66.3% in identifying children living with HIV
Fatti, 2016 South Africa [32]	10–19	Index-linked Door-to-door HTC campaign HTC	Home Home Outdoor events	Not specified	4800	99%	6%	6% 6% 9%	
Ferrand, 2016 Zimbabwe [33]	6–15	ROOT	Facility	Blood-based rapid test	7301	95%	5%	4%	Supplementation of test kits and personnel by study

HTC, HIV testing and counselling; ROOT, routine opt-out testing

Zimbabwe that compared routine opt-out testing (ROOT), whereby clients are tested unless they actively declined to test, to standard PITC among children aged 6–15 years attending in six PHCs in Zimbabwe, showed that implementation of ROOT increased the proportion of individuals who underwent HTC and the yield of undiagnosed HIV [33]. An opt-out strategy transforms HIV testing into a routine, default clinical action, which removes some decision-making from the providers and guardians. A potential concern of such an approach is that it may result in coercion of the client and reduce client autonomy, a concern that has been debated within PMTCT of HIV programmes wherever such an approach is widely used [35]. Such a concern needs to be weighed against the right to and also benefit of access to effective and life-saving treatment, and the reliance of adolescents on others to give consent on their behalf to access HTC. More recently, implementation and scale-up of HIV-prevention programmes such as voluntary medical male circumcision (VMMC) and preexposure prophylaxis (PreP) include opt-out HIV testing and serve as an opportunity for adolescents to know their HIV status [36–38].

A potential concern about blanket HTC approaches such as PITC in adolescents is that it is an inefficient strategy, given the relatively low-HIV prevalence in this age group compared with adults [33]. Thus, targeted approaches that identify those at higher risk of being HIV-infected have been proposed as potentially more cost-effective and sustainable [34]. Two studies conducted in Malawi and Kenya between 2013 to 2015 showed that 45 and 42% of adults in care, respectively, had children and adolescents of unknown HIV status [25▪▪,39]. Notably, in the Kenya study, of adults who had children of unknown HIV status, 82% reported their child being more than 13 years, suggesting that adolescents are much more likely to be undiagnosed than younger children [39]. Actively testing children of HIV-infected parents, an approach referred to as index-linked testing, showed a four-fold increase in HIV-testing rates as well as a high yield of HIV (7–15%) compared with yield in studies that have offered 'unselected' HTC [39]. Similarly, in the Malawi study, index-linked testing of children (1–15 years) and young persons (aged 15–24 years), coupled with home-based testing and tracked follow-up was highly acceptable and resulted in high uptake (94%) and yield of HIV (4%) [25▪▪].

A screening tool consisting of five items [client-reported orphan hood, past hospitalization, skin problems, a sexually transmitted infection (STI) and poor functional ability] developed in 2011 to identify adolescents (10–18 years) at risk of being HIV-positive who could then be targeted for HIV testing, reduced the numbers needed to test to identify an HIV-infected adolescent by 60% in Zimbabwe [40]. In a follow-up study in 2015 that field-tested a modified tool (four items, STI removed) in older children and adolescents (6–15 years) attending PHCs, the sensitivity and specificity in detecting HIV infection were 80.4 and 66.3%, respectively [31]. In a similar study in Zambia among 10–14 year olds, the odds of being HIV-infected was 4.3 higher among those classified at risk by the tool compared with those classified as not at risk [26]. Although both targeted approaches increase yield, they are more likely to identify vertically rather than horizontally infected adolescents.

Community-based HTC strategies including door-to-door, mobile and campaign HTC may be able to diagnose individuals at an earlier stage of infection by being more accessible and not relying on providers' discretion or on a client visiting a health facility [41]. The latter is particularly relevant as health facility usage rates among adolescents are low [42]. A prevalence survey in Zimbabwe showed that although health facility-based HTC resulted in high yield of HIV, it was insufficient to reduce community-level burden of undiagnosed HIV [43]. Nearly 40% of adolescents (8–17 years) with HIV in the community-based survey were found to be undiagnosed despite implementation of optimized PITC over 2 years in the seven study communities [43].

In Zambia, the PopART trial showed an 81% uptake of HTC among adolescents aged 15–19 years using a community-based door-to-door approach. However, within households enumerated, contact was not made with 25% of adolescents and one of the major challenges cited in this study was difficulty in obtaining consent from parents for their adolescents to undergo HTC [30]. The yield in this study was 3% among women and 1% among men. A study from Kenya and Uganda that used mobile community health campaigns wherever HTC was offered over 2 weeks, followed by door-to-door HTC reported 88% uptake of HTC among adolescents and young people aged 10–24 years [44]. This was a significant increase in HTC uptake as only 28% of respondents reported prior HIV testing [44]. Although there was high coverage of HTC, the number needed to test to identify one HIV-positive adolescent was 88 in Uganda and 23 in Kenya. A cross-sectional study in South Africa conducted between 2014 and 2015, evaluating index-linked HIV testing, campaign HTC and door-to-door testing among adolescents (10–19 years) reported uptake of 99% among adolescents who had received counselling. However, yield of HIV was highest through campaign testing (9%) followed by index-linked testing (6%) and door-to-door testing had the

lowest yield (5.9%) [32]. The HPTN043 multicountry trial (Project ACCEPT) conducted in Zimbabwe, South Africa, Tanzania and Swaziland, which combined community mobilization and mobile HTC with posttest support services for adults (≥18 years), improved rates of HIV testing by 25%, which were sustained over 36 months of continued evaluation, setting this intervention apart from traditional one-off community-based HIV-testing campaigns [45]. The increase in proportion of testers was especially pronounced in men (45% increase). However, overall incidence of HIV among young people [18–22, 23▪,24] was the same in intervention and nonintervention communities [intervention effect 0.98 confidence interval (CI) 0.80–1.22; $P = 0.86$][45].

Although community-based HTC strategies appear to have high acceptance, reduced barriers to access, and may identify those who are otherwise hard-to-reach and are asymptomatic and would, therefore, not attend health facilities, they have a low yield of HIV, and require considerable resources [30]. The cost effectiveness of these strategies must be assessed to inform the feasibility of scalability and long-term sustainability [46,47]. In addition, ensuring linkage to care may be more challenging with community-based HTC.

A study conducted among 16–24 years olds in South Africa to evaluate self-testing using a rapid blood test demonstrated that 96.4% completed the test correctly and were able to interpret the test results [48], and only 3% of participants failed to prick their finger [48]. In recent years, HIV self-testing using oral mucosal transudate (OMT) HIV tests has been shown to be highly acceptable and accurately performed by adults in SSA [37,49]. Following a large-scale evaluation of HIV self-testing in SSA, there has been a rapid scale-up of this strategy with a consequent reduction in the cost of OMT tests [50]. Self-testing provides individuals the flexibility to choose where and when to perform an HIV test without fear of judgement from a provider [51], and has the potential to bridge the gap that currently exists in access to HTC among adolescents [52]. A community-based study in Malawi that evaluated self-testing found that the highest uptake was among 16–19-year olds. [49]. This approach may, however, not be appropriate for younger adolescents [17▪,21], and an alternative may be to train guardians to test their own children.

The use of incentives may be one approach to increase uptake of HTC [53]. A recent randomized controlled trial conducted in Zimbabwe comparing a fixed incentive (US$ 2) or lottery participation (to win US$ 5 or US$ 10), both given to caregivers of 8–17-year olds, showed 3.67 and 2.66 higher odds, respectively, of adolescents accessing HTC compared with the control arm (no incentive) [28]. A pilot randomized trial in Kenya also found higher uptake of HTC in children aged 0–12 years whenever an incentive of cash or mobile money transfer (KSH500, KSH1000 and KSH1500) was offered to their female caregiver whenever compared with a similar cohort that did not offer incentives (72 versus 14%) [29]. In this study, 25% of caregivers had children of unknown HIV status who were more than 12 years and, therefore, ineligible. Concerns have been raised about the potential for scalability, the cost-effectiveness and the potential for coercion from caregivers to adolescents to test [28,29]. However, the risk of coercion is unlikely to be significant, given the small amounts of incentives given. In both studies incentives were given to caregivers suggesting that this strategy would likely be more sustainable for younger adolescents in the context of vertical HIV infection and repeated HTC would not be required until sexual debut. Further research is required to assess effectiveness of incentives offered to adolescents themselves on HTC uptake.

Organized social events (sports events and campaigns) that incorporate sexual and reproductive health services and HTC have been used to reach adolescents. 'One-stop shop' services that incorporate HTC among a broader package of health services (e.g. nutritional counselling) could decrease the stigma associated with HIV testing and be more acceptable to adolescents. Such an approach has been used in South Africa delivered through mobile services and at youth centres [54]. Grassroots Soccer, a nongovernmental organization, through their SKILLZ Street program for girls aged between 12 and 16 years in South Africa from 2011 to 2012 found that as part of their soccer-based program, 69% of girls had tested for HIV [55].

Use of mobile technology coupled with edutainment has been used to improve HTC uptake and intention to test among adolescents [27,56]. The Shout-It-Now program in South Africa used a stepwise process with a combination of technology, telephone counselling and social marketing with reports of testing uptake of 98.5% through their school program [27]. More research is required to evaluate the yield and effectiveness of this approach.

CONCLUSION

HIV testing is the critical first step to accessing HIV treatment and prevention services. In recent years, there has been progress made towards developing HTC strategies appropriate for adolescents. It is vital to consider not only the feasibility, acceptability and yield of strategies but also their potential for scalability and cost-effectiveness. Finally, linkage to

appropriate care and prevention services must be coupled with HTC approaches.

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Conflicts of interest

There are no conflicts of interest.

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3. Evaluating the effectiveness of health facility-and community-based index-linked HIV testing strategies for children and adolescents

3.1 Introduction

As detailed in the previous chapter children face significant barriers in accessing HIV testing and often reach adolescence with undiagnosed HIV infection.[6,85,88] As such, effective strategies are needed to identify children and adolescents living with undiagnosed HIV.

The aim of the B-GAP project was to evaluate the effectiveness of index-linked HIV testing in identifying children with HIV aged 2–18 years in Zimbabwe. As part of the B-GAP project people living with HIV were offered index-linked HIV testing for household members aged 2-18 years via a choice of three HIV testing methods, namely facility-based testing by a provider, community-based testing by a lay worker and provision of an HIV self-test kit to the caregiver to test their children at home.

This chapter presents the published protocol of the main B-GAP study. The paper provides a description of the formative work conducted, study setting and study procedures. Although all components of this thesis are covered in this protocol paper the hypothesis that underpinned this PhD was that **"Providing differentiated HIV-testing through the gateway of index testing is an effective and acceptable way to identify undiagnosed HIV in children".**

The methods used in the final research for this thesis are founded on the methods outlined in the protocol paper and on formative work conducted as part of the study. However, some operational adaptations were made throughout the implementation of the study and as such methodology for some components evolved. To add to information provided in this manuscript; Table 1 below

summarizes the key objectives and methods finally used in answering the research questions presented in this thesis. In addition, detailed methods are described in each subsequent chapter.

Table 1: Overview of Research Objectives and Methods used in thesis

Objective	Methods
1. Evaluate the acceptability, uptake, and yield of an index-linked HIV testing strategy (HIV testing offered to children living in households with an individual living with HIV) offered in facility and community-based settings.	**Quantitative Study** • Clinic based screening of potential indexes by research staff • Follow up and testing of children and adolescents by research staff • Quantitative data collection on tablet-based questionnaires administered and completed by research staff
2. Explore provider and caregiver perceptions and experiences of index-linked HIV testing for children and adolescents.	**Qualitative Study** • Focus Group Discussions (FDGs) with health providers and caregivers • FDGs conducted by external research staff not involved in implementation of the main study
3. Evaluate the diagnostic accuracy of the oral mucosal transudate HIV test for children and adolescents.	**Quantitative Study** • Facility based screening and testing of children and adolescents by research staff • Quantitative data collection on tablet-based questionnaires administered and completed by research staff
4. Assess the feasibility and accuracy of caregiver provided HIV testing for children and adolescents.	**Quantitative Study** • Facility based screening and community-based observations of caregivers testing their children by research staff • Quantitative data collection on tablet-based questionnaires administered and completed by research staff

3.2 Citation

Dziva Chikwari C, Simms V, Dringus S, Kranzer K, Bandason T, Vasantharoopan A, Chikodzore R, Sibanda E, Mutseta M, Webb K, et al: **Evaluating the effectiveness and cost-effectiveness of health facility-based and community-based index-linked HIV testing strategies for children: protocol for the B-GAP study in Zimbabwe.** *BMJ Open* 2019, **9:**e029428.

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3.4 Research Paper 2: Evaluating the effectiveness and cost effectiveness of health facility-based and community-based index-linked HIV testing strategies for children: protocol for the B-GAP study in Zimbabwe

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SECTION A – Student Details

Student ID Number	398292	**Title**	Ms
First Name(s)	Chido		
Surname/Family Name	Dziva Chikwari		
Thesis Title	Facility and community-based index-linked HIV testing strategies for children and adolescents in Zimbabwe		
Primary Supervisor	Professor Rashida A Ferrand		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	BMJ Open		
When was the work published?	9 July 2019		
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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was the first author of this paper. I wrote the study protocol on which this manuscript was based. I smmaried the main study protocol for this manuscript and incroporated feedback from the co-authors. I was responsible for the manuscript submission process and revised the manuscript in response to peer reveiwer comments.

SECTION E

Student Signature	[redacted]
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Evaluating the effectiveness and cost-effectiveness of health facility-based and community-based index-linked HIV testing strategies for children: protocol for the B-GAP study in Zimbabwe

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ABSTRACT

Introduction The number of new paediatric infections per year has declined in sub-Saharan Africa due to prevention-of-mother-to-child HIV transmission programmes; many children and adolescents living with HIV remain undiagnosed. In this protocol paper, we describe the methodology for evaluating an index-linked HIV testing approach for children aged 2–18 years in health facility and community settings in Zimbabwe.

Methods and analysis Individuals attending for HIV care at selected primary healthcare clinics (PHCs) will be asked if they have any children aged 2–18 years in their households who have not been tested for HIV. Three options for HIV testing for these children will be offered: testing at the PHC; home-based testing performed by community workers; or an oral mucosal HIV test given to the caregiver to test the children at home. All eligible children will be followed-up to ascertain whether HIV testing occurred. For those who did not test, reasons will be determined, and for those who tested, the HIV test result will be recorded. The primary outcome will be uptake of HIV testing. The secondary outcomes will be preferred HIV testing method, HIV yield, prevalence and proportion of those testing positive linking to care and having an undetectable viral load at 12 months. HIV test results will be stratified by sex and age group, and factors associated with uptake of HIV testing and choice of HIV testing method will be investigated.

Ethics and dissemination Ethical approval for this study was granted by the Medical Research Council of Zimbabwe, the London School of Hygiene and Tropical Medicine and the Institutional Review Board of the Biomedical Research and Training Institute. Study results will be presented at national policy meetings and national and international research conferences. Results will also be published in international peer-reviewed scientific journals and disseminated to study communities at the end of study.

Strengths and limitations of this study

- Our study will provide evidence for the effectiveness of index-linked HIV testing in facilities and communities. The strategy has the potential to be a cost-effective and efficient strategy for HIV testing in children, given the relatively low prevalence in this age group.
- Our intervention is relevant to policy questions for the implementation of HIV testing for children. This study will provide evidence for use of lower level cadres to offer and perform HIV testing as advocated by the WHO in both rural and urban settings.
- Other HIV testing interventions will be implemented by other stakeholders in the study areas during the study period. This may affect the impact assessment of this study.
- Potential challenges include low uptake of the intervention, lost-to-follow-up of clients once they have agreed to have their child tested and finding clients who have opted for home-based testing.
- Due to relatively low HIV prevalence (<4%), analysis of linkage to care will be limited to a purely descriptive analysis of the proportion of children linking to care and virologically suppressed at 12 months.

INTRODUCTION

HIV testing is the critical first step to accessing life-saving antiretroviral therapy (ART).[1] Despite this, many children living with HIV in sub-Saharan Africa, which was home to approximately 92% of the 3.2 million children below 15 years with HIV globally in 2014, remain undiagnosed.[2–4]

Children infected through mother-to-child transmission who are not diagnosed in infancy often remain undiagnosed until

they present with symptomatic HIV infection in later childhood.[5] Coverage of early infant diagnosis is suboptimal and therefore a substantial proportion of children infected through mother-to-child transmission are not diagnosed timely in infancy and are only identified in later childhood when they develop advanced disease.[6] In 2017, only 63% of HIV-exposed infants in eastern and southern Africa received an HIV test within 8 weeks of age as recommended.[6] In a study that implemented provider-initiated HIV testing and counselling (PITC) among children aged 6–16 years in primary care clinics in Zimbabwe from 2013 to 2015, the median age of HIV diagnosis was 11 years and those aged >13 years were less likely than younger children to be diagnosed.[7 8] The high proportion of undiagnosed HIV among children in sub-Saharan Africa, together with low paediatric treatment coverage, continues to be key in sustaining the epidemic.

Barriers to HIV testing of children and adolescents include the need for guardian consent in most countries in sub-Saharan Africa for children younger than 16 years, negative attitudes and lack of training among healthcare workers, stigma and long distances between homes and healthcare facilities where testing is provided, inconvenient opening hours of facilities and long waiting times.[1]

A 2011 study from Zambia assessing reasons for non-uptake of HIV testing among children aged below 15 years found that the majority (76%) with confirmed or suspected HIV infection had a primary caregiver who was also living with HIV.[9] A study from Zimbabwe testing children aged 6–16 years conducted in 2014 found that 95% of those who tested HIV positive were perinatally infected. More importantly, 65% had a caregiver or sibling known to be HIV positive or taking ART, and 20% of the accompanying caregivers also tested HIV positive.[10] Similarly, in a Malawian study including patients (15–49 years) on ART at a large ART clinic in 2006–2007, 81% of their children (0–16 years) had reportedly not been tested.[11] These studies show that children living with HIV-infected adults are at high risk for being HIV positive themselves; however, in most instances, these children have not been provided with HIV testing.

The WHO has recommended index-linked HIV testing, whereby household members, sexual contacts or children of a known HIV-infected person are offered an HIV test, as one of the approaches for addressing the gap in HIV testing.[12] Two studies that have implemented such an approach among children in Malawi and Kenya found that more than 40% of adults in HIV care were living in households with children of unknown HIV status and the prevalence of HIV in children tested through this approach was significantly higher than from other 'unselective' HIV testing approaches within Africa.[13 14]

The Bridging the GAP in HIV testing and care for Children in Zimbabwe (B-GAP) study aims to investigate the effectiveness of index-linked HIV testing among children aged 2–18 years in Zimbabwe. Testing will use both facility-based and community-based approaches to address the barriers described above. Notably, as well as offering facility-based and home-based HIV testing for untested children of index adults with HIV, this study will also investigate a novel approach whereby caregivers can test their children using an oral mucosal HIV test. We elaborate on the formative research that informed the approaches to index-linked HIV testing, study design and methodology, analysis and intended study impact. In addition, the study will also evaluate the cost-effectiveness and conduct a process evaluation to inform factors that will influence scalability of this approach in programmatic settings. This study speaks strongly to the WHO recommendations to develop innovative feasible strategies to reduce the burden of undiagnosed HIV among children.[12]

METHODS

Study objectives

The aim of the study was to evaluate the effectiveness of index-linked HIV testing in identifying children with HIV aged 2–18 years in Zimbabwe. The objectives are to

1. Evaluate the acceptability, uptake and yield of an index-linked HIV testing strategy for children and adolescents in facility-based and community-based settings.
2. Investigate factors associated with uptake of index-linked HIV testing and with choice of a certain method (clinic-based, community-based provider-delivered and community-based caregiver-delivered testing).
3. Investigate linkage to care, retention in care and virological suppression among children living with HIV who are offered community health worker (CHW) delivered support in addition to clinic-based care (the standard of care).
4. Estimate the cost and calculate the cost-effectiveness of index-linked HIV testing for children and adolescents, compared with current standard of care.
5. Conduct a process evaluation of the intervention's implementation, mechanisms of impact and local context to inform the components required for sustainability and scalability.

Patient and public involvement

Formative research and key considerations for study design

Between May and December 2017, we conducted extensive stakeholder engagement and a situational analysis to inform the intervention design with regard to the testing strategy. The specific objectives were first to understand HIV testing pathways within public healthcare facilities and their partnerships with non-governmental stakeholders; to inform selection of study sites and healthcare worker cadres to implement the intervention; and second to elicit key stakeholder views on preferences, potential limitations and foreseeable obstacles for delivery of index-linked HIV testing. Results were used to inform the intervention design and preparedness for implementation, as well as development of standard operating procedures.

Table 1 Summary of how formative research informed intervention design

Finding	Intervention design
Prevalence of undiagnosed HIV among children is heterogeneous across settings and regions.	Study sites were chosen based on an anticipated high prevalence of undiagnosed HIV.
Index-linked testing has not been fully implemented due to staff shortage at health facilities.	Research staff were hired to support implementation of intervention in facilities.
HIV testing services are provided by multiple stakeholders across the country with poor coordination between stakeholders. This results in duplication of services and failure to link individuals accessing services through community partners with health facilities.	A collaborative agreement between the research team and the MoHCC and its implementing partners conducting HIV testing in facilities and communities was established. HIV test kits will be provided by the MoHCC and all HIV testing data reported to the MoHCC.
User fees are in place for health service provision at the urban facilities including HIV testing (US$5 and US$3 depending on age of child).	For the purpose of this study, user fees will be dropped for all children and adolescents undergoing HIV testing in selected healthcare facilities
Individuals have to travel long distances to access healthcare facilities particularly in rural settings.	A novel HIV testing strategy will be introduced whereby caregivers will be given the option to test their children at home using an HIV self-test kit, thus eliminating the requirement for caregivers to bring children to the healthcare facility for testing.

MoHCC, Ministry of Health and Child Care.

Interviews were conducted with Ministry of Health and Child Care (MoHCC) officials and key informants from MoHCC partner organisations that were implementing HIV programmes in Zimbabwe. In total, 25 field observations, 19 site assessments at healthcare facilities across 2 provinces and 53 in-depth interviews (IDIs) with healthcare providers, community-based organisations, adults and adolescents living with HIV and CHWs were undertaken. These findings will be reported in detail elsewhere; however, a summary of how findings informed design is shown in table 1.

Formative work was also conducted to inform the community-based support intervention for children living with HIV delivered by CHW. The research findings, development and design of the community-based support intervention will be presented in a separate manuscript.

Study sites

Zimbabwe has the sixth highest adult HIV prevalence globally and approximately 1.3 million people were living with HIV in 2017.[6 15] The study will be conducted in six primary healthcare clinics (PHCs) in Bulawayo (urban) and three PHCs in Mangwe district (rural) in Zimbabwe. In 2016, Bulawayo had the highest adult HIV prevalence (18.7%) in an urban setting, while Mangwe in Matabeleland South Province has the highest national HIV prevalence (22.3%).[15] Clinics were purposively selected based on (1) the size of the facility so that the target sample size could be reached, and (2) their geographical locations to allow good accessibility by the study team in rural sites (figure 1). HIV clinics in hospitals were excluded due to their larger and less well-defined catchment area which would make community-based testing and follow-up difficult.

Participant recruitment: inclusion and exclusion criteria

All individuals with HIV attending for care at study clinics will be screened daily to identify attendees with children aged 2–18 living in their household (index). If the index attendee is <18 years, they will need to be accompanied by a parent or caregiver aged ≥18 years to provide consent. Indices who have children with unknown status or children who previously tested HIV negative more than 6 months ago will be offered HIV testing for their children. Being tested more than 6 months ago was included as a criterion for offering testing to account for older children who may have been horizontally infected. If the index consents to having the child or children in the household tested, three testing options will be offered: (1) testing at the clinic by a healthcare provider, (2) home-based testing performed by a healthcare provider or (3) at home by the caregiver using a self-test kit.

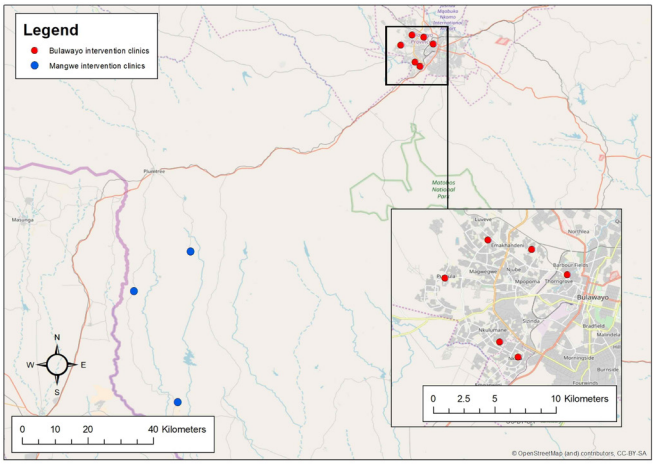

Figure 1 Map of the selected Bridging the GAP in HIV testing and care for children in Zimbabwe sites.

Demographic details of the index and the children will be recorded electronically on tablets by the research assistants using Open Data Kit.[16] Locator details of the household including mobile phone numbers and physical addresses will be collected for all consenting index cases and particularly for community-based HIV testing and to ascertain HIV test outcomes among those who opt to test their children using a self-test kit. All participants will be given a study helpline number to call for further information, counselling referrals or support.

HIV testing procedures

HIV testing will be carried out according to national guidelines using a serial testing algorithm.[17]

Clinic-based HIV testing

Caregivers who opt for clinic-based HIV testing of their children will be given referral cards on the day of screening by a research assistant. HIV testing will be performed by routine clinic staff. Research assistants will use locator information to follow-up participants who have consented to have their child(ren) tested in the clinic but have not presented to the clinic within 7 days of recruitment. They will make up to three attempts to locate the index via telephone or home visit at day 7, 14 and 21 postscreening.

Community-based HIV testing by a healthcare provider

Caregivers who opt for community-based testing will indicate a suitable date for HIV testing on the day of screening. A MoHCC implementing partner for community-based testing will visit the household to conduct an HIV test. If no contact is made on the scheduled visit date, the provider will conduct a further two visits to perform HIV testing. A test outcome will be recorded once three attempts have been made within 30 days of screening.

Community-based HIV testing by the caregiver

Caregivers who opt to use an HIV oral mucosal test (OMT) to test their children at home will undergo an assessment of guardianship status for each child. Only indices who are parents or legal guardians of eligible children will be eligible to take an OMT kit. Detailed instructions on performing an oral HIV test and interpreting the test result will be given by research assistants in the clinic using an OMT, an instruction pamphlet from the manufacturer translated to local languages and demonstration videos. The research assistant will complete a brief competency assessment including a demonstration of how to perform the test and how to interpret a set of results displayed on pictures by the caregiver. If the caregiver fails the competency assessment, they will be asked to take up either of the other two testing options. Caregivers who successfully complete the competency assessment will be provided with a test kit for each eligible child and will be instructed to conduct the test within 5 days of screening and to keep the used OMT kit. They will be instructed to bring each child who tests OMT reactive for HIV to the clinic for confirmatory HIV testing as recommended by WHO guidelines.[18] Written information about confirmatory HIV testing services will be provided. Caregivers will be followed up to ascertain HIV test outcome either by telephone call or home visit within 7 days and their used/unused OMT test kits will be collected within 21 days of screening.

The first 10–15 index cases who select caregiver testing in each clinic will undergo supervised caregiver self-testing to evaluate if there are any problems with caregivers' understanding. The parent/guardian will conduct the test while a research assistant is present at the home on the selected testing date and in parallel the research assistant will conduct a rapid blood test as per the national HIV testing algorithm.[17] During the assessment, the research assistant will note any challenges the caregiver had with completing the test and whether or not the caregiver requested assistance from the research assistant. Appropriate changes will be made to the training and demonstration practices if necessary.

Linkage to care if HIV positive

Children and adolescents will be told their HIV status according to their level of understanding and maturity as described by the national HIV testing and counselling guidelines.[17] All caregivers and children who test HIV positive will receive post-test counselling and a written referral to their nearest healthcare facility for confirmatory HIV testing and linkage to HIV care. For clinic-based testing, referrals will be made to the clinic staff responsible for initiating care on the day of testing. For community-based testing and caregiver testing, written referrals will be made to the nearest/preferred healthcare facility and all participants will be followed up by study staff to ascertain linkage to HIV care. Study staff will share all HIV testing records with the relevant healthcare facility. Caregivers of and children who test HIV positive (or are identified as known HIV positive but not linked to care) will be offered support visits from a CHW at home or at a community-based location of their choice conducted at 1, 3 and 6 months postdiagnosis.

In addition to the above-described testing procedures, partners of index cases will be offered HIV testing. This will not contribute to study outcomes but will be implemented to ensure the intervention complies with current standard of care and WHO recommendations.

Outcomes

The primary outcome will be uptake of HIV testing, defined as an eligible child having completed an HIV test and the caregiver knowing the test result within 30 days of the HIV test being offered. The HIV test result or reasons why a test is not done will be recorded. Secondary outcomes for the study will include the preferred HIV testing method, HIV yield and prevalence. HIV prevalence and yield will be stratified by age group (0–5, 6–10 and 10–18 years). Additional secondary outcomes will be linkage to HIV care and viral load suppression at 12 months postdiagnosis.

Cost-effectiveness analysis

The cost-effectiveness analysis aims to determine whether index-linked testing in children is a cost-effective strategy compared with current standard of care in Zimbabwe; passive provider-initiated testing at healthcare facilities. Both the full costs of delivering the intervention and the incremental costs will be estimated using a provider perspective through mixed methods involving a combination of primarily bottom-up micro-costing, with the use of top-down costing when necessary. Costs will be presented as follows: (1) Cost per child tested via each of the index-linked testing modalities; (2) Cost per HIV-positive child detected through each of the index-linked testing modalities; and (3) cost per new HIV initiate. The base case Cost-Effectiveness Analysis (CEA) will be conducted over a lifetime time horizon, annually discounted at the standard rate of 3%,[19] to reflect future costs and effects at current value, to estimate the incremental cost effectiveness ratio, as cost per disability-adjusted life year (DALY) averted. A dynamic transmission model will be used to estimate the DALYs averted, derived from a combination of accessing treatment and the HIV infections averted, using parameters extracted from the literature. A sensitivity analysis will be conducted to explore the impact of key variables on the results including HIV prevalence and geographical location. As there is much debate and uncertainty surrounding recommended C-E threshold values for different settings,[20] a cost-effectiveness acceptability curve will be constructed. The resulting Incremental Cost-Effectiveness Ratio (ICER) will be compared against different threshold values that are likely to be appropriate to the Zimbabwe setting. This analysis will help inform MoHCC policy around alternate forms of HIV testing and counselling.

Process evaluation

A detailed mixed-methods process evaluation will be conducted alongside the delivery of the intervention. The process evaluation will be based on the Medical Research Council Process Evaluation Framework and will explore three core evaluation functions: implementation, mechanisms of impact and context to evaluate the delivery and receipt of the intervention, in order to better understand what components of the intervention work, for whom and under what circumstances.[21] The process evaluation data will be analysed and written up in order to contribute to understanding the study results and to provide guidance for sustainable and scalable implementation of the intervention by local health authorities should it prove successful. Quantitative indicators for the process evaluation will include staff turnover, record of shortage of test kits and supplies and incident reports about facility-based and community-based testing from research assistants and the project coordinator. Descriptive statistics of these indicators will be used to help assess aspects of the intervention's fidelity, feasibility and acceptability, and to identify lessons important in informing the replication and scale-up of this approach to testing.

Focus group discussions (FGDs) with research assistants and FGDs and IDIs with a purposively selected sample of indices will be conducted to elicit provider and caregiver perceptions and experiences of index-linked HIV testing for children at baseline and end line. Sampling for FGDs will include a group of caregivers representing index age (older vs younger) and sex, HIV testing option, HIV test uptake (accepted vs did not accept testing; and whether child tested or not) and study site (rural vs urban). We will also conduct IDIs with caregivers who had a child test HIV positive through index-linked HIV testing at end line.

As testing by caregivers is a novel intervention, the acceptability of this method will be explored from providers' and caregivers' perspectives. IDIs will be held with caregivers who selected this option to understand how messaging and training for caregiver testing used in the competency and accuracy assessments can be improved, as well as how testing is performed by caregivers on their children in their homes. Interviews will also be held with index participants who did not select his method to understand their concerns.

Sample size estimates

Sample size estimations are based on precision of estimates of uptake of index-linked HIV testing. We will recruit participants from nine clinics, with an average daily adult attendance of 32 per clinic (excluding repeat attenders). Over 12 weeks per clinic, we expect to screen a total of 5184 HIV-positive index cases at nine clinics with children aged 2–18 years (assuming 5 working days a week and 30% of adults with HIV have children and adolescents living in the household). Assuming an index refusal rate of 35%, and an average of 2 children per household, we would screen approximately 6739 children and adolescents. This sample size provides ±1% precision for an estimate of 80% of screened children and adolescents taking up HIV testing, with a 95% CI of 79.0%–81.0%. Sample sizes for qualitative work will be determined on an ongoing basis by study staff until thematic saturation has been reached.

Assuming HIV prevalence of 4%, this would yield 215 children living with HIV eligible for linkage-to-care. This sample size provides good precision of ±6% around an estimated 80% linking-to-care (n=172) and precision of ±9% around an estimated 70% with viral suppression at 12 months out of 85% retained in care (n=102/146).

Data analysis

A study flowchart showing total number of index cases screened, eligibility of index cases and children in their household, proportions of index cases providing consent for collection of additional data about themselves and the children living in their households will be presented (figure 2). Demographic characteristics of index participants and children and adolescents living in their households will be summarised using proportions, means and SD. The uptake of HIV testing and HIV prevalence stratified by age group (0–5, 6–10 and 10–18 years) and sex will

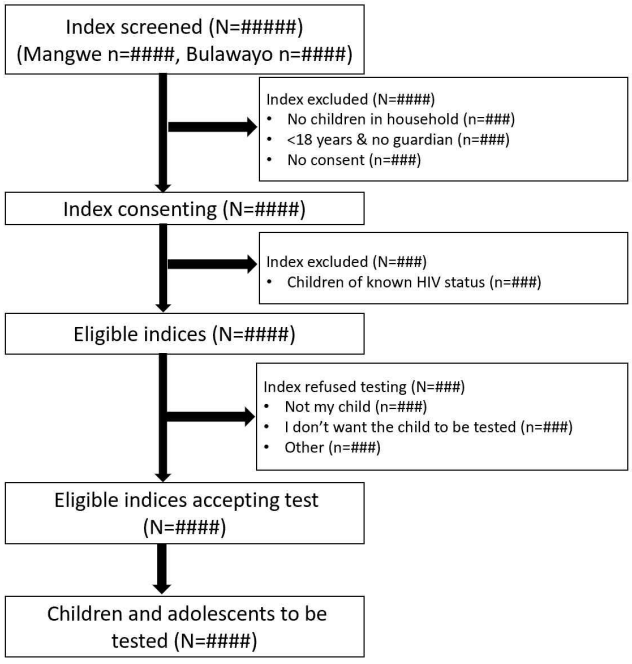

Figure 2 Index-linked HIV testing participant flow.

be calculated, and factors associated with uptake of index-linked HIV testing will be assessed using univariate analysis. A multivariate logistic regression will be conducted to assess factors predictive of uptake/non-uptake of HIV testing adjusted for clustering by index case. We will evaluate factors associated with the uptake of the preferred HIV testing method using multinomial logistic regression. The proportion of children who tested positive and linked to HIV care and the proportion with virological suppression will be calculated at 12 months.

Study status

The study began recruitment of study participants in January 2018. Recruitment is ongoing.

DISCUSSION

There has been a remarkable scale-up of prevention of mother-to-child HIV transmission (PMTCT) programmes resulting in a decline in numbers of perinatally acquired HIV infections.[2] However, many children and adolescents with HIV, acquired before PMTCT programmes were scaled-up, remain undiagnosed, with diagnosis only occurring when they present with advanced disease.[6] In addition, suboptimal coverage of early infant diagnosis within PMTCT programmes results in many HIV-exposed children not being identified.[2 6] Those who acquire HIV postnatally through breastfeeding may also present later in childhood. HIV testing is the critical step to accessing HIV treatment and high rates of undiagnosed HIV partly explain the lower coverage of HIV treatment in children and adolescents compared with adults.[22]

PITC has been recommended by the WHO since 2007.[23] However, this relies on an individual attending a health facility. Also, PITC may not be as cost-effective a strategy in children as in adults given the lower HIV prevalence among children compared with adults. Index-linked testing is a targeted strategy focusing on testing of children at higher risk of HIV infection. If effective, this strategy has the potential to be a more cost-effective and efficient HIV testing strategy in resource-limited settings. Our study will implement both community-based and health facility-based HIV testing for children and investigate a novel approach of caregivers testing their own children to increase accessibility and uptake of HIV testing.

We believe that community-based strategies in our study have the potential to eliminate many of the barriers to HIV testing for children and adolescents.[14] In a study conducted in Malawi, index-linked testing offered to children and young people (1–24 years) had higher uptake for community (95.5%) when compared with facility-based (4.5%) testing.[14] Enabling caregivers to test their children may reduce the burden of client-associated costs such as time spent in and getting to facilities for testing by clients, provider time, and maintenance and upkeep of health facilities. However, most importantly, it allows the caregivers to perform the test in the comfort and privacy of their homes and empowers them to take responsibility for the testing. Another innovation is the use of CHWs to perform HIV testing in the community. While a similar cadre termed 'primary care counsellor' is widely used to provide HIV testing in health facilities, HIV testing in communities is largely provided by nurses. The CHWs will complete a 2-week training in ethics and rapid HIV testing as well as on study procedures. If effective, our study will provide evidence for use of lower level cadres such as community health workers to offer and perform HIV testing as advocated by the WHO.[12] There is evidence to show that the use of lower level cadres can reduce cost of staffing for the government and may improve cost-effectiveness of community-based approaches when compared with traditional facility-based HIV testing.[24]

Furthermore, the study also addresses linkage to care, initiation of ART and adherence through a community-based support intervention. It is crucial that any HIV testing intervention addresses these steps in the continuum of HIV care to ensure maximum benefits (ie, reduced morbidity and onward transmission).

Potential challenges include low uptake of the intervention, lost-to-follow-up of clients once they have agreed to have their child tested and finding clients who have opted for home-based testing. Within our study, user fees for HIV testing were dropped. This has implications for the generalisability of our findings in settings where user fees are in place and may act as a barrier to uptake of HIV testing services. Similarly, our study findings may not be generalisable to other settings as contextual factors may affect uptake of the intervention. It is important to note that in parallel to evaluation of uptake and yield of index-linked HIV testing, we will conduct a detailed process evaluation to explore the implementation, mechanisms of impact and contextual factors affecting the delivery and acceptability of this intervention, which will help

inform sustainability and scale-up should it prove effective. Another limitation is that other HIV testing interventions will be implemented in our study settings at the same time. However, detailed recording of other HIV testing interventions will be part of the process evaluation. This will help with understanding how other HIV testing interventions interact with each other and index-linked testing.

Ethics and dissemination

Ethical approval was sought and granted by the Medical Research Council of Zimbabwe (MRCZ), the London School of Hygiene and Tropical Medicine ethics committee and the Institutional Review Board of the Biomedical Research and Training Institute.

Study progress and findings will be reported annually to MRCZ and feedback meetings will be held quarterly with the health directorates of the two study sites. Results of interim data analysis will be presented at national and international research meetings and conferences. Results will also be prepared for publication in international peer-reviewed scientific journals and disseminated to study communities at the end of study. A detailed dissemination plan to inform scale-up will be developed for implementation.

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Contributors RF conceptualised the project. CDC developed the study protocol and data collection tools. AV and VS contributed to the design of cost-effectiveness evaluation of the study. SD, RF and CDC designed the study process evaluation. RC, MM, BE, KW, TB and ES contributed to the formative work and development of project logistics. HAW, KK, GN, HM and TA provided technical input to the design and statistical analysis of the study. All authors have read and approved the final manuscript.

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4. Comparison of index-linked HIV testing for children and adolescents in health facility and community settings

4.1 Introduction

The aim of this chapter is to compare the uptake and yield of community and facility-based delivery of index-linked HIV testing for children and adolescents in urban and rural settings in Zimbabwe, a country with a sustained, severe generalised HIV epidemic. Indexes (defined as HIV positive individuals who had children in their households eligible for HIV testing i.e. children who had not previously been tested or had tested HIV-negative more than six months ago) were offered a choice of i) bringing the child(ren) for HIV testing at the health facility, ii) the child(ren) receiving home-based testing performed by a health provider or iii) taking an OMT test kit to test their children in the home.

The study showed that facility-based HIV testing was most frequently chosen by indexes, but children were more likely to be tested if the index chose either of the community-based HIV testing methods. Additionally, older adolescents were less likely to be tested compared to younger children, and boys were less likely to be tested than girls. In this study the yield of HIV was low when compared to other studies in similar settings.

4.2 Citation

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4.3 Research Paper 3: Comparison of index-linked HIV testing for children and adolescents in health facility and community settings in Zimbabwe: findings from the interventional B-GAP study

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Surname/Family Name	Dziva Chikwari		
Thesis Title	Facility and community-based index-linked HIV testing strategies for children and adolescents in Zimbabwe		
Primary Supervisor	Professor Rashida A Ferrand		

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SECTION B – Paper already published

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Comparison of index-linked HIV testing for children and adolescents in health facility and community settings in Zimbabwe: findings from the interventional B-GAP study

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Summary

Background Index-linked HIV testing, whereby children of individuals with HIV are targeted for testing, increases HIV yield but relies on uptake. Community-based testing might address barriers to testing access. In the Bridging the Gap in HIV testing and care for children in Zimbabwe (B-GAP) study, we investigated the uptake and yield of index-linked testing in children and the uptake of community-based *vs* facility-based HIV testing in Zimbabwe.

Methods B-GAP was an interventional study done in the city of Bulawayo and the province of Matabeleland South between Jan 29 and Dec 12, 2018. All HIV-positive attendees (index patients) at six urban and three rural primary health-care clinics were offered facility-based or community-based HIV testing for children (age 2–18 years) living in their households who had never been tested or had tested as HIV-negative more than 6 months ago. Community-based options involved testing in the home by either a trained lay worker with a blood-based rapid diagnostic test (used in facility-based testing), or by the child's caregiver with an oral HIV test. Among consenting individuals, the primary outcome was testing uptake in terms of the proportion of eligible children tested. Secondary outcomes were uptake of the different HIV testing methods, HIV yield (proportion of eligible children who tested positive), and HIV prevalence (proportion of HIV-positive children among those tested). Logistic regression adjusting for within-index clustering was used to investigate index patient and child characteristics associated with testing uptake, and the uptake of community-based versus facility-based testing.

Findings Overall, 2870 index patients were linked with 6062 eligible children (3115 [51·4%] girls [sex unknown in seven], median age 8 years [IQR 5–13]). Testing was accepted by index patients for 5326 (87·9%) children, and 3638 were tested with a known test outcome, giving an overall testing uptake among 6062 eligible children of 60·0%. 39 children tested positive for HIV, giving an HIV prevalence among the 3638 children of 1·1% and an HIV yield among 6062 eligible children of 0·6%. Uptake was positively associated with female sex in the index patient (adjusted odds ratio [aOR] 1·56 [95% CI 1·38–1·77], p<0·0001) and child (aOR 1·10 [1·03–1·19], p=0·0080), and negatively associated with any financial cost of travel to a clinic (aOR 0·86 [0·83–0·88], p<0·0001), increased child age (6–9 years: aOR 0·99 (0·89–1·09); 10–15 years: aOR 0·91 [0·83–1·00]; and 16–18 years: aOR 0·75 [0·66–0·85]; p=0·0001 *vs* 2–5 years), and unknown HIV status of the mother (aOR 0·81 [0·68–0·98], p=0·027 *vs* HIV-positive status). Additionally, children had increased odds of being tested if community-based testing was chosen over facility-based testing at screening (1320 [73·9%] children tested of 1787 *vs* 2318 [65·5%] of 3539; aOR 1·49 [1·22–1·81], p=0·0001).

Interpretation The HIV yield of index-linked testing was low compared with blanket testing approaches in similar settings. Index-linked HIV testing can improve testing uptake among children, although strategies that improve testing uptake in older children are needed. Community based testing by lay workers is a feasible strategy that can be used to improve uptake of HTS among children and adolescents.

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Introduction

The scale-up of antiretroviral therapy (ART) globally in the past 20 years has substantially reduced HIV-associated mortality across all age groups.[1] However, globally the coverage of ART in children (<15 years) was only 53% in 2019, largely due to delays in diagnosis.[2] Testing of HIV-exposed children within prevention of mother-to-child transmission (PMTCT) programmes remains suboptimal, and subsequently children with perinatally acquired HIV are often diagnosed later in childhood when they present with HIV-associated sequelae.[3,4] Late diagnosis is associated with chronic complications such as growth failure, organ damage, and increased mortality.[5–7] Effective strategies to address the barriers to HIV diagnosis in children are urgently needed.[8]

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Research in context

Evidence before this study

HIV testing rates in children exposed to HIV remains low in prevention of mother-to-child transmission programmes in sub-Saharan Africa, with many children being diagnosed late in childhood when they develop advanced disease. Due to the relatively low HIV prevalence among children and adolescents, targeted HIV testing services (HTS) approaches such as index-linked testing (HIV testing offered to children in the same household as people with HIV) might be most efficient and cost-effective. On April 1, 2020, we searched Medline for studies on index-linked HIV testing in children and adolescents, without restrictions on date, location, or language. Using the keywords "HIV testing", "index", "children", and "adolescents", we found five studies that had evaluated index-linked testing in children and adolescents (age 0–19 years). The studies were done in Cameroon, Kenya, Lesotho, and Malawi between 2016 and 2019. All of the studies reported higher HIV yield with index-linked testing than that obtained via routine HTS. Only one of the studies offered index-linked HIV testing in both rural and urban settings and only two studies offered index patients a choice of test location (facility-based or community-based). None of the five studies evaluated factors associated with uptake of testing.

Added value of this study

Our study is the first to compare the uptake of index-linked testing in children via health facility testing versus community-based testing by lay workers or caregivers in an HIV-prevalent setting. We evaluated preferred choice of HIV testing modality, and index patient and child factors associated with choice and uptake of testing. Our study shows that, although facility-based methods are more commonly chosen when initially proposed, probably because this approach is well known to the public, actual uptake of HTS is higher with community-based approaches. Community-based approaches might address some of the key barriers to facility-based testing, such as travel costs, distance to a clinic, particularly in rural areas, and suboptimal access due to restrictive opening hours of health facilities. Our study also shows that community HTS provided by lay workers and caregivers is feasible.

Implications of all the available evidence

To reach the UNAIDS 95-95-95 targets (95% of HIV-positive people aware of status, ART for 95% of those diagnosed, and viral suppression for 95% of those treated by 2030), HTS strategies will need to focus on hard-to-reach populations and address barriers that existing approaches have not been able to overcome. Community-based approaches might address such barriers but will require sensitisation and education of communities, and support for caregivers who test their children. Quality control, monitoring, and linkage to care for children who test positive will need to accompany these approaches.

Given the relatively low prevalence of HIV in children,[2,3] targeted HIV testing strategies, including the use of screening tools and index-linked testing, have been suggested to improve testing efficiency and potentially reduce costs.[9] Index-linked testing, whereby an HIV test is offered to contacts of an index case (ie, an individual living with HIV), has been shown to increase HIV yield when used in children, but as with any other testing strategy, it relies on uptake by parents and carers.[9,10] The test location (eg, health facilities *vs* community-based settings) might influence uptake.[11] Barriers to facility-based testing in children include inflexible facility working hours, user fees, distance to clinics, transport costs, and insufficient or overworked health-care providers.[12] In view of these barriers, WHO recommended the use of lay workers in community settings in 2018 to reduce costs and increase uptake of HIV testing services (HTS).[13] Index-linked testing of children, adolescents, and young adults (age 1–24 years) in community-based settings resulted in higher uptake than at health facilities in Malawi.[14] In recent years, self-testing with oral mucosal transudate (OMT) has been implemented among adults in sub-Saharan Africa,[15,16] and an extension of this approach whereby caregivers test their children might also improve accessibility.[17] Offering indexes a choice of different HTS delivery models acknowledges different preferences, and providing flexibility in the place and mode of HTS delivery might optimise uptake of index-linked HIV testing.

Zimbabwe has an early-onset, sustained, severe HIV epidemic, with an adult HIV prevalence of 13% in 2018.[3] HIV prevalence in children (age 0–14 years) was 1·6% and in young people (age 15–24 years) was 4·4% in 2016.[3,18] Although PMTCT coverage in Zimbabwe is high, with 94% of HIV-positive pregnant women receiving ART, only 63% of infants born to HIV-positive mothers were tested within the first 2 months of birth in 2019.[3]

In the Bridging the Gap in HIV testing and care for children in Zimbabwe (B-GAP) study, we evaluated index-linked testing provided in health facilities and via two community-based approaches (namely testing by a trained lay worker and HIV testing by the caregiver at home using OMT), for children aged 2–18 years in rural and urban Zimbabwe. The aim of this study was to investigate the uptake and yield of index-linked testing and factors associated with its acceptance. We also investigated the choice of testing methods (ie, community-based vs facility-based testing) and factors associated with acceptance of community-based over facility-based index-linked HIV testing. We hypothesised that offering HTS to children living in households with an HIV-positive individual will result in a high yield

of HIV diagnoses when compared with approaches that are not targeted, and that the option for community-based HTS might increase uptake compared with facility-based HTS alone.

Methods

Study design and participants

The B-GAP study was an interventional study without a control group done in Bulawayo, the second largest city in Zimbabwe, and Matabeleland South province, between Jan 29 and Dec 12, 2018. Matabeleland South borders Botswana and has the highest HIV prevalence (20·4%) in the country.[18] Three rural primary health-care clinics in Mangwe district in Matabeleland South and six urban primary health-care clinics in Bulawayo were purposively selected on the basis of the number of patients registered for HIV care and distance to another facility.[18]

At each facility, all individuals attending for HIV care, regardless of ART status and time since diagnosis, were screened over 3 months to identify index cases. The national HIV programme provides a 3 month drug supply, therefore the majority of clinic attendees were anticipated to have undergone eligibility screening for study inclusion by 3 months. After screening and inclusion, a structured questionnaire collecting sociodemographic data, the number of children in the household, and their HIV status was administered by research assistants to index patients and data was entered on electronic tablets into Open Data Kit (version 1.11.1). Index patients were defined as consenting HIV-positive individuals who had at least one child aged 2–18 years living in their household (regardless of whether or not they were a biological parent) who was eligible for HTS (ie, had never had an HIV test or had a negative HIV test more than 6 months before screening). Children who were reported to have had an HIV-negative test more than 6 months ago were eligible for testing as index patients could have over-reported testing of children, older adolescents might have been sexually active, and some children might have been victims of sexual abuse.

Written informed consent for participating in the study was obtained from all eligible index patients in either English, Shona, or Ndebele when they were approached at the health facility. Index individuals aged younger than 18 years were included in the study if accompanied by an adult who could provide consent. At the point of testing of children either at the facility or in the community, verbal consent from the child's parent or legal guardian and child assent (for children aged <16 years) or direct verbal consent from the child (for children aged ≥16 years) for HIV testing was sought.

Ethical approval for this study was obtained from the Medical Research Council of Zimbabwe, the institutional review board of the Biomedical Research and Training Institute of Zimbabwe, and the London School of Hygiene & Tropical Medicine ethics committee. The B-GAP study protocol has been published previously.[19]

Procedures

Index patients were offered three choices of HIV testing for eligible children living in their household: testing in the health facility; testing by a lay worker at home; or testing by the index caregiver at home. Testing in the facility was done by routine clinic staff or research assistants. Research assistants were the lay workers and in addition to training for the study had undergone a 2-week training course on rapid HIV testing and counselling provided by a private training institution affiliated with the Zimbabwe Ministry of Health and Child Care. The lay workers were stationed at each clinic. Index patients could only elect for caregiver testing if they were a biological parent or the legal guardian to ensure safeguarding of children who would be tested in the absence of a health-care provider. Caregiver testing was done with OMT (OraQuick ADVANCE Rapid HIV-1/2; OraSure Technologies, Bethlehem, PA, USA). Caregivers were counselled and shown how to do the test by research assistants at each facility. If assessed by the research assistant to be competent to test, they were given an OMT HIV test for each eligible child and asked to do the test within 5 days. A helpline number for counselling and support was provided. Results of caregiver-provided testing were by self-report. Index patients who chose caregiver-provided testing were told to return to the facility for confirmatory HIV testing in the event of a reactive OMT test as per WHO guidelines.[20]

Index patients who chose community testing by a lay worker were visited at home on a scheduled date. Up to two further home visits were undertaken if the child was not present on the scheduled date. For facility and caregiver-provided testing, all index patients were contacted by lay workers by phone on days 7, 14, and 21 post-screening if their children had not yet been tested. If unreachable by phone, a maximum of two home visits were undertaken and HIV testing done at home by a lay worker if the index patient and child consented. Therefore, index patients who initially chose facility-based testing could later consent to testing in the home. Similarly, index patients who initially chose community-based testing could, at a later date, switch to testing at the facility. The test method chosen by the index patient at screening and the final test location for children was recorded. Testing at the facility or community-based testing by a lay worker was done according to the national HIV testing algorithm via a blood-based rapid diagnostic test, with results available on the same day.[21] We defined community-based testing as either testing done by a lay worker at home or caregiver-provided testing.

Children were given age-appropriate explanations of the test results, determined by the age and maturity of the child and guided by the Zimbabwe Ministry of Health and Child Care guidelines for HIV testing and counselling for children.[22]

For children who were not tested, the reason was recorded. Children who tested HIV-positive were referred

to their nearest facility or the preferred facility of the child or household for onward care.

Outcomes

The primary outcome of the study was the uptake of testing, defined as the proportion of eligible children having an HIV test during the study. Secondary outcomes were the uptake of the different HIV testing methods, HIV yield, and HIV prevalence. HIV yield was defined as the proportion of HIV-positive children among all eligible children. HIV prevalence was defined as the proportion of HIV-positive children among those tested. Any children with an unknown test outcome were classed as not tested and therefore not included in the denominator for HIV prevalence.

Statistical analysis

Sample size estimations were based on precision of the estimated proportion taking up HIV testing. An average of 32 clients were anticipated to attend a clinic per day. A sample size of 6739 children would provide a 1% precision interval for an estimate of 80% of children taking up testing. An average of 32 clients were anticipated to attend a clinic per day based on routine data on attendance of each clinic in 2017. Therefore, during the 3 month study period at each clinic, in nine clinics assuming 5 working days per week, this visit rate would provide sufficient numbers of index patients assuming 30–40% of index patients had eligible children and accepted participation. Within-index clustering was not taken into account when calculating sample size due to the small numbers of children expected in each household.

All analyses were done with Stata software (version 15.0). Continuous variables were summarised as means and SDs or medians and IQRs, and categorical variables as counts and percentages. We used univariable logistic regression to investigate the association between index patient characteristics and at least one child in their household having an HIV test, and between child characteristics and a child having an HIV test. Index characteristics of interest were age, sex, health-care facility setting (rural or urban), highest level of education, time since HIV diagnosis, mode of transport to the facility, and cost of travel to the facility. Child characteristics of interest were age, sex, HIV status, relationship to index patient, orphanhood status, mother's HIV status, history of receiving ART for PMTCT, and any previous offer of HIV testing. For each model, significant index patient or child variables (at $p<0·10$) in univariable analysis were retained in multivariable logistic regression models (significance deemed at $p<0·10$). Using logistic regression we also evaluated the odds of having an HIV test by selected testing model adjusted for clustering by index. For models including child characteristics, robust standard errors or generalised estimating equations were used to allow for household-level clustering. Additionally, index patient and child characteristics associated with selection of community-based testing models versus facility-based testing at screening were evaluated in univariable and multivariable models. As sensitivity analyses, we investigated factors associated with selection of testing by a lay worker versus facility-based testing, and with selection of testing provided by a caregiver versus facility-based testing. Clustering by index patient was adjusted for in all models including child variables. An independent project steering committee met annually.

Role of the funding source

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

Results

Between Jan 29 and Dec 12, 2018, 9927 individuals were screened in the nine primary health-care clinics (427–2005 per clinic), of whom 5164 reported no children aged 2–18 years in the household and 820 declined consent to provide information about children in their household. Of the remaining 3943 individuals, 2870 had at least one child eligible for HTS in their household and were therefore classed as index patients (figure 1). The median age of index patients was 39 years (IQR 32–46) and 2259 (78·8% of 2866 with available data) were women. 1622 (56·5%) of the 2870 index patients had been diagnosed with HIV in the past 5 years. The main means of transport to the clinic was by foot (for 1874 [65·4%] of 2866 with available data; table 1). The median number of children living in the households of index patients was 1 (IQR 1–3).

8218 children (4147 [50·5%] girls [sex unknown in nine], median age 9 years [IQR 5–13]) living in the households of index patients (n=3943) were screened for eligibility (figure 1). Of these children, 6062 (73·8%) were eligible for index-linked testing (3115 [51·4%] girls [sex unknown in seven], median age 8 years [IQR 5–13]), with 2837 (34·5%) having tested HIV-negative more than 6 months ago, and 3225 (39·2%) having not previously tested. The range in eligibility prevalence by clinic was 54·4–98·6%. 500 (6·1%) children had a known HIV-positive status.

Of the 2870 index patients with at least one eligible child, 1789 (62·3%) had at least one child in their household tested, including 1012 (35·3%) who had two or more children tested. Overall, 1476 (51·4%) index patients had all eligible children in their households tested. In terms of corresponding numbers in children, HIV testing was accepted for 5326 (87·9%) of 6062 eligible children (range by clinic 61·3–98·4%). The main reason for index patients refusing testing in 736 children was that the index patient was not the biological parent of the eligible child (304 [41·3%] children). In the 5326 children with acceptance for testing, 3638 (68·3%) were subsequently tested (range by

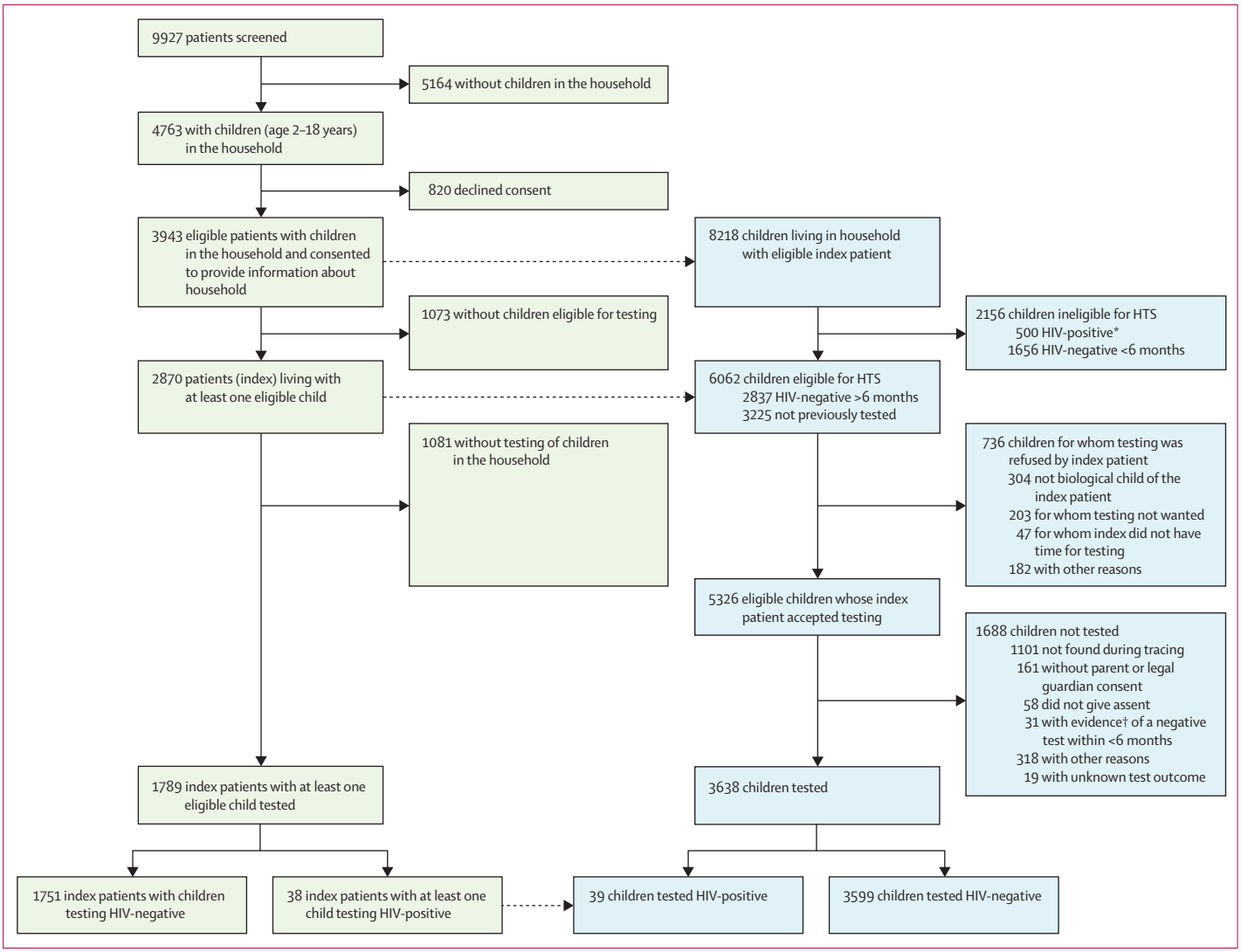

Figure 1: **Screening and HIV testing flow for HIV-positive clinic attendees (green) and children living in their households (blue)**
HTS=HIV testing services. *490 children registered in care and 10 not registered in care. †Test result slip or note in the child's medical records.

clinic 53·5–92·0%), representing an overall uptake of HTS among 6062 eligible children of 60·0% (figure 1). Among 1688 children not tested despite acceptance by the index patient, the main reasons for non-uptake were inability to contact children (1101 [65·2%]) and no consent from guardians at the point of testing (161 [9·5%]).

Of the 3638 children with an HIV test outcome, 39 were positive, giving an HIV prevalence of 1·1%, and an HIV yield among 6062 eligible children of 0·6%. HIV prevalence was 1·0% (24 of 2322 children) in urban settings and 1·1% (15 of 1316) in rural settings. The median age of children diagnosed with HIV was 11 years (IQR 8–15; range 3–18) and 28 (71·8%) were girls. 17 (43·6%) of the 39 children were single or double orphaned, 25 (64·1%) were biological children of the index patient, 28 (71·8%) had not been previously tested, and nine (23·1%) were linked to index patients who had been diagnosed within the past year. HIV was diagnosed in 26 (prevalence 1·4%) of 1916 children tested in a health-care facility and 13 (0·8%) of 1722 children tested in the community. In the community, HIV was diagnosed in 12 (0·8%) of 1522 children tested by a lay worker, and one (0·5%) of 200 tested by their caregiver using OMT and confirmed HIV-positive at their health-care facility. Of the 39 children who tested HIV-positive and received a referral, 36 (92·3%) were registered with a facility.

The proportion of index patients who had at least one child tested was similar between urban (1286 [61·7%] of 2084 index patients) and rural (504 [64·1%] of 786) sites (table 1). In our univariable analysis of index patient characteristics, female sex, cost to travel to the facility, and mode of transport were associated with HIV testing for at least one child in the household. In multivariable analysis, female sex of the index patient was associated with at least

	Index patient population		Univariable analysis		Multivariable analysis*	
	Patients with at least one eligible child (n=2870), n (%)	Patients with at least one child tested (n=1789), n (% of those with ≥1 eligible child)	OR (95% CI)	p value	aOR (95% CI)	p value
Age, years						
0–18	54 (1·9%)	36 (66·7%)	1·00 (ref)	..	..	..
19–34	892 (31·1%)	566 (63·5%)	0·87 (0·49–1·55)	..	..	..
35–59	1767 (61·6%)	1087 (61·5%)	0·80 (0·45–1·42)	..	..	..
≥60	157 (5·5%)	101 (64·3%)	0·90 (0·47–1·73)	0·63	..	..
Sex†						
Male	607 (21·2%)	329 (54·2%)	1·00 (ref)	..	1·00 (ref)	..
Female	2259 (78·8%)	1456 (64·5%)	1·53 (1·28–1·84)	<0·0001	1·56 (1·38–1·77)	<0·0001
Site						
Rural	786 (27·4%)	504 (64·1%)	1·00 (ref)	..	..	..
Urban	2084 (72·6%)	1286 (61·7%)	0·90 (0·76–1·07)	0·24	..	..
Highest level of education completed†						
None	45 (1·6%)	27 (60·0%)	1·00 (ref)	..	..	..
Primary	909 (31·7%)	571 (62·8%)	1·13 (0·61–2·08)	..	..	..
Secondary	1817 (63·4%)	1136 (62·5%)	1·11 (0·61–2·03)	..	..	..
Tertiary	95 (3·3%)	52 (54·7%)	0·77 (0·38–1·59)	0·36	..	..
Mode of transport to facility†‡						
By foot	1874 (65·4%)	1259 (67·2%)	1·00 (ref)	..	..	..
Public transport	844 (29·4%)	442 (52·4%)	0·54 (0·46–0·64)	<0·0001	..	..
By car	42 (1·5%)	20 (47·6%)	0·45 (0·24–0·82)	0·0097	..	..
Other	106 (3·7%)	65 (61·3%)	0·78 (0·52–1·16)	0·22	..	..
Cost of travel to facility‡						
No cost (0 US$)	1998 (69·6%)	1332 (66·7%)	1·00 (ref)	..	1·00 (ref)	..
Some cost (>0 US$)	872 (30·4%)	458 (52·5%)	0·86 (0·83–0·90)	<0·0001	0·86 (0·83–0·88)	<0·0001
Time since HIV diagnosis, years§						
<1	290 (10·2%)	174 (60·0%)	1·00 (ref)	..	..	..
1–5	1332 (46·6%)	820 (61·6%)	1·06 (0·82–1·38)	..	..	..
6–10	990 (34·7%)	618 (62·4%)	1·10 (0·85–1·45)	..	..	..
>10	245 (8·6%)	168 (68·6%)	1·45 (1·02–2·08)	0·16	..	..

Tested children were classed as all those who received a test and had a known test outcome. OR=odds ratio. aOR=adjusted OR. *Significant index patient variables (at p<0·10) in univariable analysis were retained in multivariable logistic regression. †Missing data for four index patients. ‡Only cost of travel to facility included in multivariate analysis due to collinearity with mode of transport to facility. §Missing data for 13 index patients.

Table 1: **Index patient characteristics associated with HIV testing in at least one child**

one child in the household having an HIV test (adjusted odds ratio [aOR] 1·56 [95% CI 1·38–1·77], p<0·0001). Additionally, children were less likely to be tested if the index patient reported any financial cost for them to travel to the facility (aOR 0·86 [0·83–0·88], p<0·0001; table 1).

In our univariable analysis of child characteristics, having an HIV test was associated with sex, age, HIV status, relationship to the index patient, and mother's HIV status. In multivariable analysis, female sex of the child was associated with having an HIV test (aOR 1·10 [95% CI 1·03–1·19], p=0·0080). Increased age of the child (6–9 years: aOR 0·99 (0·89–1·09); 10–15 years: aOR 0·91 [0·83–1·00]; and 16–18 years: aOR 0·75 [0·66–0·85]; p=0·0001 *vs* 2–5 years) and unknown HIV status of the mother (aOR 0·81 [0·68–0·98], p=0·027 *vs* HIV-positive status) were associated with reduced odds of having an HIV test (table 2).

Of the 5326 eligible children whose index patient accepted testing at screening, facility-based testing was chosen for 3539 (66·4%) children and community-based testing for 1787 (33·6%; figure 2). Per clinic, the proportion of children whose index patients opted for community-based testing ranged from 8·9% to 81·1%. In univariable analysis adjusting for clustering by index patient, the odds of the child being tested were higher if the index patient selected community-based testing versus facility-based testing (1320 [73·9%] children tested of 1787 *vs* 2318 [65·5%] of 3539; aOR 1·49 [95% CI 1·22–1·81], p=0·0001).

Regardless of initial choice, similar proportions of eligible children were tested by facility-based and community-based approaches (of 3638 children with a known test outcome overall, 1916 [52·7%] were tested at a facility *vs* 1722 [47·3%] in the community). 2318 children with initial acceptance for facility-based testing went on

	Child population		Univariable analysis*		Multivariable analysis (n=5043)*†	
	Eligible children (n=6062), n (%)	Children tested (n=3638), n (% of those eligible)	aOR (95% CI)	p value	aOR (95% CI)	p value
Sex‡						
Male	2940 (48·6%)	1720 (58·5%)	1·00 (ref)	..	1·00 (ref)	..
Female	3115 (51·4%)	1911 (61·3%)	1·07 (1·01–1·15)	0·032	1·10 (1·03–1·19)	0·0080
Age, years‡						
2–5	1801 (29·7%)	1159 (64·4%)	1·00 (ref)	..	1·00 (ref)	..
6–9	1586 (26·2%)	956 (60·3%)	0·97 (0·89–1·06)	..	0·99 (0·89–1·09)	
10–15	1981 (32·7%)	1174 (59·3%)	0·89 (0·82–0·97)	..	0·91 (0·83–1·00)	
16–18	687 (11·3%)	342 (49·8%)	0·73 (0·65–0·82)	<0·0001	0·75 (0·66–0·85)	0·0001
HIV status§						
Never tested	3224 (53·2%)	1930 (59·9%)	1·00 (ref)	..	1·00 (ref)	..
Known negative >6 months	2837 (46·8%)	1708 (60·2%)	1·10 (1·02–1·20)	0·021	1·06 (0·96–1·17)	0·28
Relationship to index patient‡						
Non-biological child	2482 (41·0%)	1466 (59·1%)	1·00 (ref)	..	1·00 (ref)	..
Biological child	3573 (59·0%)	2165 (60·6%)	1·22 (1·11–1·33)	<0·0001	1·12 (0·96–1·32)	0·16
Orphanhood status‡						
Not orphaned	4728 (78·1%)	2796 (59·1%)	1·00 (ref)	..	..	..
Paternal orphan	960 (15·9%)	613 (63·9%)	1·00 (0·90–1·12)	0·98	..	..
Maternal orphan	190 (3·1%)	101 (53·2%)	0·98 (0·79–1·23)	0·88	..	..
Double orphan	177 (2·9%)	121 (68·4%)	1·15 (0·91–1·46)	0·23	..	..
Mother's HIV status¶						
HIV-positive	3223 (63·9%)	2048 (63·5%)	1·00 (ref)	..	1·00 (ref)	..
HIV-negative	901 (17·9%)	585 (64·9%)	0·83 (0·74–0·94)	0·0037	0·90 (0·76–1·07)	0·24
Unknown to index patient	920 (18·2%)	475 (51·6%)	0·73 (0·64–0·83)	<0·0001	0·81 (0·68–0·98)	0·027
Prevention of mother-to-child transmission treatment history‖						
No	1839 (55·4%)	1147 (62·4%)	1·00 (ref)	..	..	..
Yes	1284 (38·7%)	758 (59·0%)	1·07 (0·97–1·18)	0·20	..	..
Unknown to index patient	196 (5·9%)	115 (58·7%)	1·05 (0·83–1·33)	0·67	..	..
Previous offer for HIV testing‖						
No	1191 (35·9%)	715 (60·0%)	1·00 (ref)	..	..	..
Yes	1999 (60·2%)	1216 (60·8%)	1·05 (0·95–1·17)	0·36	..	..
Unknown to index patient	136 (4·1%)	96 (70·6%)	1·10 (0·82–1·49)	0·52	..	..

Tested children were classed as all those who received a test and had a known test outcome. aOR=adjusted odds ratio (with adjustment for clustering by index patient). *Logistic regression with generalised estimating equations. †Significant child variables (at p<0·10) in univariable analysis were retained in multivariable logistic regression; n reflects children tested minus those with data missing on model variables. ‡Missing data for seven children. §Missing data for one child. ¶Missing data for 1018 children as question was introduced into the study after March 1, 2018. ‖Question only asked if the child was the biological child of the index patient (n=3319).

Table 2: **Child characteristics associated with having an HIV test**

to be tested, 473 (20·4%) of whom were tested in the community. By contrast, 1320 children with acceptance for community-based testing went on to be tested, of whom 71 (5·4%) were tested in a facility (figure 2).

In univariate analysis adjusted for clustering by index, factors associated with uptake of community-based HIV testing were site type (urban or rural), index patient age, cost of travel to a facility, time since diagnosis in the index patient, child age, child HIV status, PMTCT treatment history, and a previous offer of HIV testing. On multivariable analysis, urban residence (aOR 2·29 [95% CI 1·80–2·91], p<0·0001), any travel cost to the facility (aOR 1·21 [1·15–1·28], p<0·0001), and time since HIV diagnosis in the index patient (1–5 years since diagnosis: aOR 1·58 [1·07–2·31]; and ≥6 years since diagnosis, aOR 1·59 [1·07–2·35]; p=0·070 *vs* diagnosis <1 year ago) were associated with selection of community-based testing compared with facility-based testing at screening (table 3). Increased child age (6–9 years: aOR 1·20 [1·02–1·41]; and 10–15 years: aOR 1·35 [1·14–1·59]; p=0·0020 *vs* 2–5 years) and unknown HIV status in the child (aOR 1·33 [1·12–1·59], p=0·0013) were also associated with selection of community-based testing at screening. Results were similar in our sensitivity analysis, in which the outcome was defined as testing delivered by a community lay worker (n=1487 children) compared with

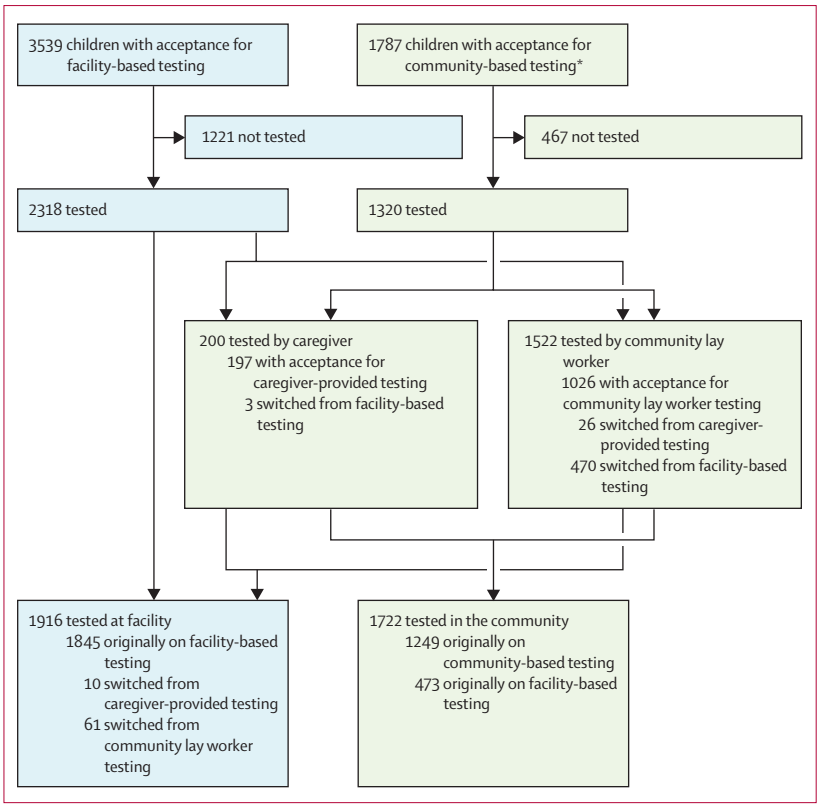

Figure 2: Selection of facility-based (blue) and community-based (green) HIV testing for eligible children whose index patient accepted testing

*1487 children with acceptance for testing by a lay worker and 300 for testing by a caregiver at screening.

See Online for appendix

facility-based testing (appendix pp 1, 2). Selection of caregiver-provided testing (n=300 children) versus facility-based testing at screening was associated with urban residence, the cost of transport, unknown HIV status in the child, and, additionally, female sex of the index patient (appendix pp 3, 4). No adverse events were reported in our study.

Discussion

We found an overall uptake of index-linked HIV testing of 60% after offering index patients a choice of facility-based or community-based HTS. A greater proportion of index patients chose facility-based testing over community-based testing; however, children were more likely to be tested if the index chose community-based testing. Index patients who had to pay to get to the clinic were less likely to have children in their households tested, and older children were less likely to be tested. Some index patients refused testing for children because they were not the biological parents of children living in their households. This finding highlights the challenges of identifying children with HIV, who are disproportionately likely to be orphaned.[23] Although being a biological child was associated with having a test in univariable analysis, this effect was not significant in multivariate analysis. We also found that female index patients were more likely to have at least one child tested and female children were more likely to be tested than their male counterparts. Poor health-seeking behaviour is commonly reported among men and our study highlights the need for further work to engage men, to inform the development of acceptable HTS.[24]

The yield of HIV was lower than anticipated when compared with blanket approaches such as outpatient and inpatient provider-initiated testing and counselling in Zimbabwe and within sub-Saharan Africa, in which HIV yield among children and adolescents ranged from 7·4% to 12·2%.[11] This finding might be due to the scale-up of the PMTCT programme in Zimbabwe, where coverage was 94% in 2018.[3,25] Although index-linked testing implemented in Kenya and Malawi detected high prevalence of HIV (7·4% among children aged <12 years in Kenya and 4·0% among individuals aged 1–24 years in Malawi), their PMTCT coverage was similar at 91% and 95%, indicating the possibility of missed diagnoses before the scale-up of PMTCT.[3,14,26] Alternatively, low yield could also imply that even index-linked HTS is an insufficient strategy to address the gap in HIV testing for children in Zimbabwe. Some index patients refused testing or did not complete testing for eligible children in their households. Further studies evaluating reasons or risk factors for non-uptake of testing are therefore warranted. However, we do note that while 500 children living in households with an index patient were known to be HIV-positive before the study, 39 (7·2%) of 539 children (500 who were known HI-positive and 39 newly diagnosed in this study) had been missed by existing services.

The median age of children diagnosed with HIV in our study was 11 years. Older children are at particularly high risk of living with undiagnosed HIV as they have missed HIV testing within PMTCT programmes[27] and were less likely to be tested in our study. A misplaced assumption might be that an older child who is not ill is unlikely to have perinatally acquired HIV infection, particularly when the mother's status is not known. In addition, adolescents are a challenging group to engage within health services. In our study, older children and children whose mother's HIV status was not known had lower odds of being tested. Our findings highlight the need for continued efforts to expand HTS particularly among older adolescents. Notably, this age group is also at risk of horizontal transmission and index-linked testing might need to be combined with other approaches.

Facility-based index-linked testing has been recommended in WHO guidelines and in Zimbabwean national guidelines.[19,28] Our study found that similar proportions of children were tested by facility-based or community-based index-linked HIV testing, despite substantially more index patients choosing facility-based testing at screening. Community-based testing potentially addresses some of the barriers to HTS, such as costs of travel to health facilities and the time taken

by index patients to bring children to facilities. Children were less likely to be tested if the index patient had to pay for travel (eg, via public transport or a car) rather than walk to a health facility. In addition, paying for travel to a health facility was associated with selection of community-based rather than facility-based HIV testing by the index patient. Community-based index-linked testing might identify children who are particularly hard to reach with currently available approaches. Indeed, index patients who had been diagnosed with HIV for a long period of time, increased age of the child, and no history of previous testing of the child, all of which are indicators of a lack of engagement with HTS for children, were independently associated with selection of community-based HIV testing.

Although WHO has recommended community-based HIV testing by lay workers,[13] in many countries including Zimbabwe, HTS in the community is done by nurses. In the B-GAP study, lay workers underwent 2 weeks of training on study processes and rapid HIV testing and caregivers were also able to test their children using an oral HIV test after brief demonstrations within the health facility. Our study shows the feasibility of lay individuals with minimal training implementing community-based HTS. HIV self-testing for adults has had high uptake among groups such as men, older adolescents (age 16–18 years), sex workers, and men who have sex with men.[13,15,16] This high uptake is often attributed to ease, privacy, and confidentiality, and the non-invasiveness of the test compared with blood-based testing.[13,15,29] We identified a low uptake of caregiver-provided testing, probably due to poor awareness of self-testing among our study population, for whom HIV self-testing is not yet routinely or widely available. In our study, female index patients were more likely to take up caregiver-provided testing, which might reflect the potential usefulness of this strategy within PMTCT programmes.

Community-based testing by lay workers or caregivers could reduce workload for facility-based health workers and has potential to be cost-effective.[30] Additionally, community-based testing could be used as a back-up mechanism for children who do not present for facility-based index-linked testing. Many children in our study were subsequently tested in the community, as lay workers visited children at home who did not attend facilities for testing as per the protocol procedures.[22] Notably, 20% of children whose index patients initially opted for facility-based testing were subsequently tested by a community-based approach, but only 5% whose index patients opted for community-based testing were ultimately tested in a health facility.

The strengths of this study include a large sample size and comprehensive ascertainment of outcomes. The inclusion criteria were not restricted to biological children of index patients to ensure that children who might have been orphaned were not excluded. The study was done in public sector clinics and in both urban and rural settings,

	Community-based testing chosen (n=1787 children)	Univariable analysis		Multivariable analysis (n=5262)*	
		aOR (95% CI)	p value	aOR (95% CI)	p value
Index patient variables					
Age, years					
0–18	29 (1·6%)	1·00 (ref)	..	1·00 (ref)	..
19–34	480 (26·9%)	1·48 (0·63–3·47)	..	1·07 (0·46–2·45)	..
35–59	1146 (64·1%)	1·99 (0·86–4·60)	..	1·27 (0·56–2·89)	..
≥60	132 (7·4%)	2·32 (0·92–5·88)	0·02	1·64 (0·65–4·12)	0.22
Sex					
Male	363 (20·3%)	1·00 (ref)	..	..	..
Female	1424 (79·7%)	1·00 (0·79–1·27)	0·98	..	..
Site					
Rural	448 (25·1%)	1·00 (ref)	..	1·00 (ref)	..
Urban	1339 (74·9%)	2·51 (1·99–3·17)	<0·0001	2·29 (1·80–2·91)	<0·0001
Highest level of education					
None	33 (1·9%)	1·00 (ref)	..	..	..
Primary	538 (30·1%)	0·74 (0·33–1·63)	0·45	..	..
Secondary	1143 (64·0%)	1·19 (0·54–2·58)	0·67	..	..
Tertiary	73 (4·1%)	1·90 (0·76–4·70)	0·17	..	..
Mode of transport to facility†					
By foot	1003 (56·1%)	1·00 (ref)	..	..	..
Public transport	691 (38·7%)	2·42 (1·95–3·00)	<0·0001	..	..
By car	12 (0·7%)	0·64 (0·25–1·65)	0·35	..	..
Other	81 (4·5%)	1·01 (0·60–1·68)	0·98	..	..
Cost of travel to facility, US$†					
No cost (0 US$)	1090 (61·0%)	1·00 (ref)	..	1·00 (ref)	..
Some cost (>0 US$)	697 (39·0%)	1·24 (1·18–1·31)	<0·0001	1·21 (1·15–1·28)	<0·0001
Time since HIV diagnosis, years‡					
<1	132 (7·5%)	1·00 (ref)	..	1·00 (ref)	..
1–5	815 (46·5%)	1·53 (1·07–2·20)	..	1·58 (1·07–2·31)	..
≥6	804 (45·9%)	1·48 (1·03–2·13)	0·066	1·59 (1·07–2·35)	0·070
Child variables					
Sex§					
Male	884 (49·5%)	1·00 (ref)	..	..	..
Female	902 (50·5%)	0·95 (0·84–1·07)	0·42	..	..
Age, years§					
2–5	472 (26·4%)	1·00 (ref)	..	1·00 (ref)	..
6–9	474 (26·5%)	1·26 (1·09–1·47)	..	1·20 (1·02–1·41)	..
10–15	645 (36·1%)	1·41 (1·21–1·63)	..	1·35 (1·14–1·59)	..
16–18	195 (10·9%)	1·23 (0·99–1·53)	0·0001	1·08 (0·86–1·38)	0·0020
HIV status§¶					
Known HIV negative >6 months	1028 (57·6%)	1·00 (ref)	..	1·00	..
Unknown	758 (42·4%)	1·32 (1·17–1·48)	<0·0001	1·33 (1·12–1·59)	0·0013
Relationship to index§					
Non-biological child	672 (37·6%)	1·00 (ref)	..	..	..
Biological child	1114 (62·4%)	1·09 (0·94–1·26)	0·24	..	..

(Table 3 continues on next page)

	Community-based testing chosen (n=1787 children)	Univariable analysis		Multivariable analysis* (n=5262)	
		aOR (95% CI)	p value	aOR (95% CI)	p value
(Continued from previous page)					
Orphanhood status§					
Not orphaned	1387 (77·7%)	1·00 (ref)	..	..	..
Paternal orphan	288 (16·1%)	0·96 (0·78–1·19)	0·71	..	..
Maternal orphan	45 (2·5%)	0·77 (0·48–1·23)	0·28	..	..
Double orphan	66 (3·7%)	1·28 (0·86–1·93)	0·23	..	..
Mother's HIV status‖					
HIV-positive	985 (65·9%)	1·00 (ref)	..	..	..
HIV-negative	247 (16·5%)	0·81 (0·63–1·05)	0·11	..	..
Unknown to index	262 (17·5%)	1·14 (0·88–1·48)	0·31	..	..
Prevention of mother-to-child transmission treatment history**††					
Yes	344 (32·2%)	1·00 (ref)	..	..	..
No	646 (60·4%)	1·26 (1·05–1·52)	0·015	..	..
Unknown to index	80 (7·5%)	2·32 (1·50–3·59)	0·0002	..	..
Previous offer for HIV testing¶**					
Yes	577 (53·9%)	1·00 (ref)	..	..	..
No	443 (41·4%)	1·48 (1·21–1·81)	0·0002	..	..
Unknown to index	50 (4·7%)	1·40 (0·84–2·33)	0·20	..	..

aOR=adjusted odds ratio (with adjustment for clustering by index patient). *Significant index patient variables (at p<0·10) in univariable analysis were retained in multivariable logistic regression; n reflects children tested minus those with data missing on model variables. †Only cost of travel to facility included in multivariate analysis due to collinearity with mode of transport to facility. ‡Missing data for 36 index patients. §Missing data for one child. ¶Only HIV status included in multivariable analysis due to collinearity with previous offer for HIV testing. ||Missing data for 293 children as question was introduced into the study after March 1, 2018. **Question only asked if the child was the biological child of the index patient (n=1070). ††Excluded in multivariable model due to high number of missing data.

Table 3: **Factors associated with uptake of community-based testing options at screening**

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making the findings generalisable to similar settings within Zimbabwe and the sub-Saharan Africa region. A limitation of our approach, whereby the starting point of offering testing is at the facility level, is that it excludes index patients who are disengaged from care and whose children might be HIV-positive but without a confirmed diagnosis. Additionally, contacting participants to ascertain outcomes might have indirectly increased uptake. Furthermore, oral testing results were obtained by self-report. We did a substudy to investigate accuracy of caregiver testing and findings will be reported separately. A further limitation was that the study was not aimed or powered to investigate index patient factors associated with an HIV-positive child diagnosis. If completed, a study focused on index factors associated with HIV-positive child status would allow health service providers to further target index-linked testing in children and adolescents, and we therefore recommend future studies on this aspect.

Evaluation of the affordability of index-linked approaches is crucial to inform scalability. Previous studies have shown that community-based HTS strategies among adults, including HIV self-testing, are cost-effective compared with facility based HTS in South Africa and Malawi.[31,32] However, cost-effectiveness of any approach will depend on HIV yield and uptake of HTS. A cost evaluation of the HTS approaches in the B-GAP study is underway and will be reported separately.

Substantial progress has been made in reducing the incidence of HIV infection, due to the scale-up of PMTCT programmes and improved coverage of ART in children. However, implementing strategies to identify hard-to-reach groups of children is imperative if the UNAIDS 95-95-95 targets (95% of HIV-positive people aware of status, ART for 95% of those diagnosed, and viral suppression for 95% of those treated by 2030) are to be met. Increasing the reach of testing will require strategies that target residual barriers to accessing HIV testing, which approaches to date have not been able to overcome. Although a targeted approach such as index-linked testing is an efficient approach in children in whom HIV prevalence is low, coverage to date has not been optimal. Our study provides evidence for the effectiveness of community-based approaches via lay health workers and caregivers for the testing of children at risk of HIV. Community-based testing might reduce burden on health facilities and address barriers to HTS access. Combined approaches and providing index patients with choice and flexibility might further improve uptake.

Contributors

RAF and CDC conceived the study. CDC developed the study protocol, data collection tools and methods, and standard operating procedures, and coordinated the study. NR and TB were responsible for data management. VS, KK, SD, KW, BE, HM, TA, GN, KH, HAW, and RAF contributed to study design and reviewed final drafts of the paper. ES and RC contributed to study logistics. All authors have read and approved the final manuscript.

Declaration of interests

We declare no competing interests.

Data sharing

The B-GAP dataset is publicly available from the London School of Hygiene & Tropical Medicine repository, Data Compass.

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5. The challenges and relational aspects of index-linked HIV testing for children and adolescents

5.1 Introduction

Chapter 4 presented the uptake and yield of index-linked HIV testing for children and adolescents and found that HIV yield was low when compared to other studies in similar settings using the same index-linked strategy.[22] The study showed that older adolescents were less likely to be tested when compared to younger children. Additionally, while most indexes chose facility-based HIV testing for their children, children were more likely to be tested if the indexes chose HIV testing in the community.

In this chapter the factors that influence and affect uptake of index-linked HIV testing for children and adolescents are evaluated.[9] Using data from five focus group discussions, this manuscript builds on the findings from Chapter 4 by exploring the factors that affect uptake of HIV testing, from both the health providers and caregivers' perspectives.

The study found that caregivers viewed HIV testing of children not as a "one-off" event but as a process with potential consequences on multiple people and relationships. Hence, as well as providing information about the need to test children for HIV, discussions about HIV testing with caregivers should be tailored to enable caregivers to engage with HIV testing in their individual context.

While programmes often adopt a broad policy based on improving "health outcomes", this study highlights the importance of considering the context of the individuals targeted in public health programmes. The findings from this study inform how implementation of index-linked HIV testing for children and adolescents can be strengthened to optimise the success of this approach.

5.2 Citation

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5.4 Research Paper 4: Addressing the challenges and relational aspects of index-linked HIV testing for children and adolescents: insights from the B-GAP study in Zimbabwe

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Surname/Family Name	Dziva Chikwari		
Thesis Title	Facility and community-based index-linked HIV testing strategies for children and adolescents in Zimbabwe		
Primary Supervisor	Professor Rashida A Ferrand		

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RESEARCH Open Access

Addressing the challenges and relational aspects of index-linked HIV testing for children and adolescents: insights from the B-GAP study in Zimbabwe

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Abstract

Introduction: Index-linked HIV testing, targeted at sexual contacts or children of individuals with HIV, may improve yield and efficiency. The B-GAP study evaluated index-linked testing approaches in health facility and community-based settings. This paper reports on a qualitative study to understand factors that affect uptake of index-linked HIV testing for children and adolescents.

Methods: We conducted four focus group discussions (FGDs) with caregivers who had their children tested through B-GAP and one FGD with providers who offered index-linked HIV testing to indexes. We aimed to understand enabling and inhibiting factors in the decision-making process. Translated and transcribed transcripts were read for familiarisation. Following initial coding, analytical memos were written to identify emerging key themes across the data.

Results: Our findings showed there was inadequate emphasis on paediatric HIV in routine care which had a negative impact on subsequent uptake of testing for children. Once the decision to test had been made, access to facilities was sometimes challenging and alleviated by community-based testing. A key finding was that HIV testing is not a discrete event but a process that was influenced by relationships with other family members and children themselves. These relationships raised complex issues that could prevent or delay the testing process.

Conclusion: There is a need to improve messaging on the importance of HIV testing for children and adolescents and to provide support to caregivers and their families in order to improve testing uptake. Addressing access barriers through the provision of community-based testing and implementing a family-centred approach can optimise index-linked testing.

Keywords: HIV testing, Index-linked testing, Barriers, Children, Adolescents

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Contributions to the literature

- Although promoted and recommended by the World Health Organization, index-linked HIV testing for children has not been a standard practice in routine HIV care for many countries including Zimbabwe.
- Prior this study, no study has evaluated the factors that influence and affect uptake of index-linked HIV testing for children and adolescents as reported in our manuscript.
- Our findings have the potential to bridge the HIV testing gap for children and optimise index-linked testing. This strategy has been shown to result in higher yield of HIV when compared to universal HIV testing; however, index-linked testing uptake remains suboptimal.

Introduction

Globally, 2.8 million children aged 0–19 years were living with HIV in 2018 [1, 2]. While coverage of prevention of mother to child transmission programmes (PMTCT) has increased (82% in 2018 compared to 43% in 2013), corresponding coverage of early infant diagnosis of HIV remains low (59% in 2018) [3]. Therefore, many children living with HIV are only diagnosed in later childhood, with a consequent increased risk of mortality and morbidity [4].

The World Health Organization (WHO) has recommended targeted HIV testing strategies such as index-linked HIV testing to improve efficiency and reduce costs of HIV testing [5]. Index-linked HIV testing (i.e. HIV testing offered to children or sexual contacts of individuals living with HIV) is anticipated to have higher uptake and yield compared to universal HIV testing approaches. When implemented in Malawi, Kenya, Lesotho and Cameroon, index-linked testing for children did result in a higher yield of HIV (proportion of eligible children who test positive) compared to universal testing, but uptake of testing (proportion of eligible children tested) remained suboptimal, ranging from 14 to 71% [6–8].

Children and adolescents face specific barriers to accessing HIV testing in facilities, including the requirement for parental consent, perceived low risk in this age group by healthcare providers who then do not offer testing, and lack of personal resources to independently access HIV testing [9]. Index-linked HIV testing may mitigate some of these barriers by targeting and follow up of children and adolescents at risk of HIV. However, index-linked testing initially requires uptake by a parent or caregiver, and there are a number of factors that influence the decision-making process by individuals when considering HIV testing for their children. HIV remains a deeply stigmatised infection and therefore a diagnosis of HIV is associated with risk of social harms [10]. HIV infection also requires lifelong treatment which may have a significant impact on children as well as their caregivers' lives [11]. Therefore, when implementing index-linked HIV testing, it is important to understand the lived experiences of indexes which will influence their ability to engage with HIV testing and care services [12].

The Bridging the Gap in HIV testing and care for children in Zimbabwe (B-GAP) study evaluated uptake and yield of index-linked HIV testing for children and adolescents aged 2–18 years in rural and urban communities in Zimbabwe [13]. Testing in facility and community-based settings was offered to children of individuals living with HIV already accessing treatment. In this paper, we report on the lived experiences of caregivers who went through index-linked HIV testing for children in their households and providers who offered index-linked testing to the caregivers in order to further understand the decision-making process for testing. We aimed to understand enabling and inhibiting factors for testing, which are critical to inform how this testing strategy should be implemented to optimise uptake.

Methods

Study setting

Zimbabwe has experienced an early onset, severe and sustained HIV epidemic with antenatal HIV prevalence peaking at 35% in 1998 [14] and current adult HIV prevalence of 14% [2]. In 2016, an estimated 24% of households had at least one HIV-positive household member, and HIV prevalence among children aged 0–14 years in Zimbabwe was 2% [1, 2]; 39% were undiagnosed and only 26% of children born to mothers with HIV received an HIV test within 1 year of birth [2].

The B-GAP study was conducted in three rural and six urban facilities from January to December 2018. Individuals attending for HIV care who had children aged 2–18 years of unknown HIV status in their households (indexes) were offered three options for having their children tested for HIV: health facility-based testing, community-based testing by a provider or provision of an oral HIV test kit to the index to test their child at a location of their choice (Fig. 1). Indexes were followed up by telephone or home visits at specified intervals over 21 days to ascertain test outcomes.

Qualitative study procedures

We conducted one focus group discussion (FGD) with providers who offered index-linked HIV testing to indexes in the health facility, and four FGDs with indexes who had their children tested for HIV through B-GAP (caregivers). No qualitative data collection was conducted with indexes who did not take up HIV testing for

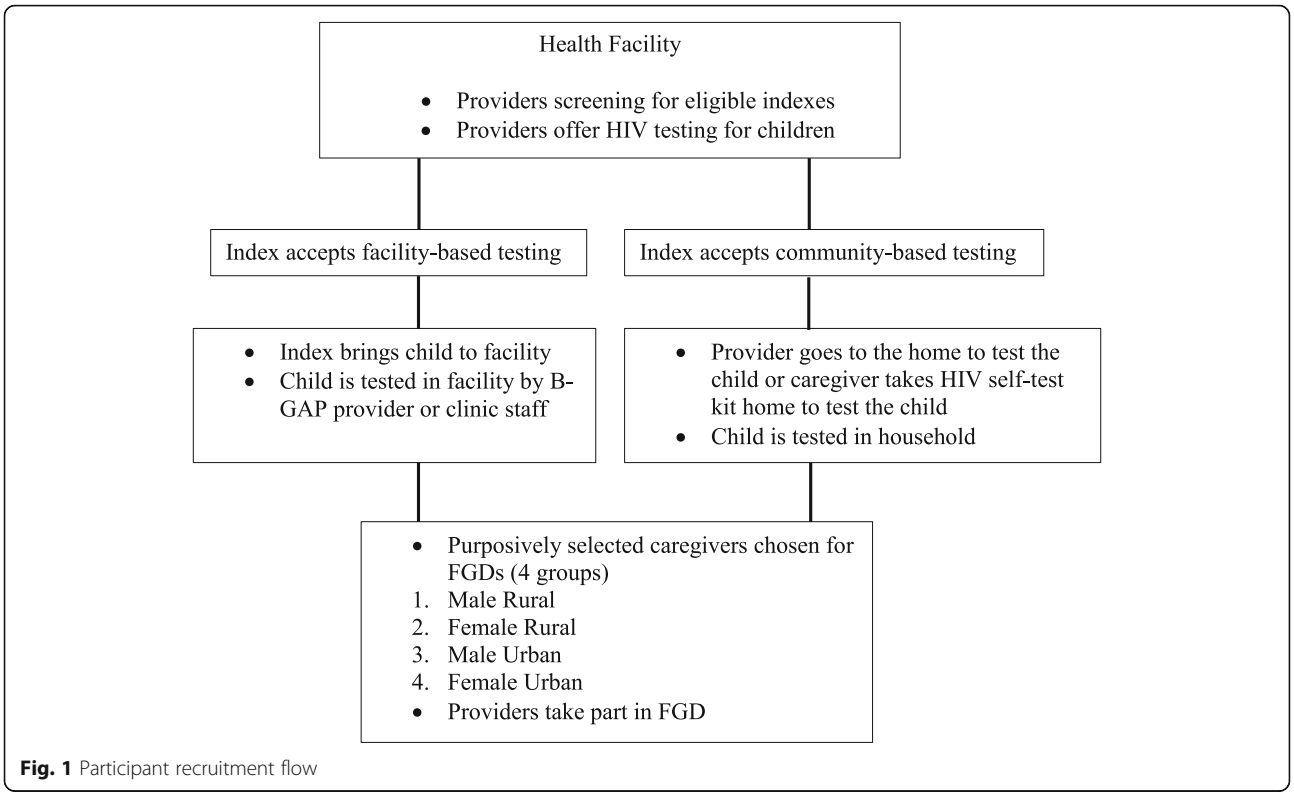

Fig. 1 Participant recruitment flow

their children due to anticipated difficulties in engaging this group. FGDs with caregivers were conducted up to 4 months after being approached to have their child(ren) tested. The four caregiver FGDs were grouped according to gender and site (Figure 1).

Caregivers were purposively selected from the study sites to represent a mix of those who took up the different test location options. Open invitations were made via telephone call to selected B-GAP participants, and those who were available on the scheduled day were recruited. All the B-GAP providers participated in the provider FGD. All of the caregiver FGDs were conducted in a private room at the health facility and the provider FGD was conducted at the study office. They were facilitated by two Zimbabwean research assistants (one male and one female) who were not involved in the recruitment of caregivers for index-linked testing, in order to minimise the risk of interviewer bias. The researchers (NN and KS) were experienced in qualitative research and had at least Bachelors level education. They both received a 1-day refresher training in qualitative data collection prior to conducting the FGDs. Neither NN nor KS had prior relationships with the participants and introduced themselves and the purpose of the research.

Caregivers selected for the FGDs were purposively selected to represent an equal mix of caregivers who had taken up each of the three testing approaches offered through B-GAP. Facilitators used topic guides (Additional files 1 and 2) to generate discussion focused on understanding the caregiver's experiences of testing for their children, their preferences for how and where index-linked testing should be conducted as well as to gain insights from both the caregivers and the providers about the enabling and inhibiting factors in the decision-making process around index-linked testing. Given the specificity of the sample inclusion criteria, the topic guides were not piloted but in line with best qualitative practice, iterative data collection and analyses allowed for the guides to be refined after each FG D[15]. All FGDs were face-to face and were conducted in either English or one of the local languages (Ndebele and Shona) depending on the participants preferences. Some participants used the local languages interchangeably as is common practice in this setting. NN and KS took field notes during each FGD.

Data analysis

FGDs were audio recorded and translated from Shona and Ndebele and transcribed into English by NN and KS. Translation was a discursive process to allow for the identification of correct English words for vernacular terms or to decide on words with equivalent meanings where this was not obvious. The translators provided interview summaries to CDC and were involved in discussing the content of the interviews. Transcripts were read by CDC for familiarisation and open coding.

Constant case comparisons were made between the coded caregiver transcripts to identify overarching patterns and differences. Caregiver and provider FGD transcripts were analysed separately then compared for similarity and contrast. Following initial coding, analytical memos were written to identify emerging key themes. Content thematic analysis was done collaboratively by the first two authors (CDC and SB), and recurring themes were noted in the later FGDs [15–17]. The coded data was organised using Microsoft Word and Excel. Refined coding was undertaken to further develop thematic areas and to explore case comparisons across the dataset, including considering the learning from any deviant cases.

Ethics

Ethical approval was obtained from the Medical Research Council of Zimbabwe, the Institutional Review Board of the Biomedical Research and Training Institute, and the London School of Hygiene and Tropical Medicine ethics committee. Written informed consent was obtained from all study participants (caregivers and providers). As part of the consent process and prior to commencing the FGD, participants were made aware that their HIV status would be implicitly disclosed to others in the group and that they could withdraw participation at any point. Participants were not incentivised for participation but reimbursed transport costs. Due to confidentiality concerns surrounding deductive disclosure in the home, FGD transcripts were not given to participants. A dissemination meeting with participants is scheduled at the end of the B-GAP study.

Results

We conducted five FGDs with 30 caregivers and seven providers between December 2018 and February 2019. The number of participants in each caregiver FGD ranged from 4 to 11. The caregiver FGDs lasted over 2 h on average, and the provider FGD was conducted over 5 h in two sessions. The median age of caregivers was 37 years (IQR 32–45) and 21 (70%) were female (Table 1). Most caregivers (68%) interviewed were biological parents of the children tested. In the main B-GAP study (89%) of indexes offered testing for children in their households had been diagnosed with HIV over a year prior to being offered testing and only 9% had not initiated antiretroviral therapy (ART).

Three key themes were identified that explain caregivers' uptake of testing and the decision-making process around index-linked testing: (i) inadequate emphasis on paediatric HIV information in routine adult care, (ii) the relational nature of index-linked HIV testing of children and (iii) limited access to facilities once the decision to test has been made. Additional provider perspectives that were unique to those voiced by the caregivers included logistical challenges in locating homes for community testing, follow-up and indirect refusals through the provision of wrong addresses and phone numbers.

Table 1 Participant demographics

	Caregivers ***N* = 30**	
		n (%)
Age category[a]	18–25	2 (6.7)
	25–50	20 (99.7)
	> 50	7 (23.3)
Sex	Male	9 (30.0)
	Female	21 (70.0)
Site	Rural	15 (50.0)
	Urban	15 (50.0%)
Test location	Facility-based	11 (36.7)
	Community-based by provider	15 (50.0)
	Caregiver-provided self-test	4 (13.3)
Relation to child [b] N = 78	Biological parent	53 (67.9)
	Grandparent	18 (23.1)
	Other relation	5 (6.4)
	Non-relation	2 (2.6)
	Providers ***N* = 7**	
		n (%)
Age category	18–25	1 (14.3)
	25–50	6 (85.7)
	> 50	0 (0.0)
Sex	Male	2 (28.6)
	Female	5 (71.4)
Site	Urban	4 (57.1)
	Rural	3 (4.3)

[a]Missing data for 1 caregiver
[b]Caregivers had different relationships to children that were tested in their households

Inadequate emphasis on paediatric HIV in routine adult care

Caregivers felt confident about understanding the implications of their own HIV infection, but not how HIV infection would affect their children. Although they had children in their care, for some caregivers, literacy about paediatric HIV was poor, particularly understanding of perinatal HIV and testing for children. This information was not given much emphasis in their routine care, and some caregivers only became meaningfully aware of the need for testing children and the possibility and benefits of testing through their involvement in the B-GAP study. Caregivers reported that the way information was

provided in B-GAP enabled them to understand the need to test.

> We had only seen posters about free testing and if you are infected, you start on your medication. However, we had not heard about taking your children for testing, we heard this for the first time from B-GAP. (Caregiver #26, Male, 54)

Participants reported that while information about paediatric HIV testing in routine care is an important first step in encouraging the testing of children, information alone is insufficient. A critical step to encourage caregivers to take up testing was being able to apply the pertinence of this information to one's personal situation. This required more nuanced and individualised information that would enable caregivers to accurately assess their child's risk.

> With younger children, the ones that you are talking about, maybe those who are 7 and below, their parents were a bit hesitant because they would say; 'Where would they have gotten the HIV from?' (Provider#1, Female, 30)

Without adequately tailored information, testing is often not taken up, with delays justified by an incorrect assumption that it is unnecessary. In such situations, testing tends to be done reactively only once illness has developed.

> As for me, I had never really heard it as such, that children can get tested. But…. my child was constantly sick. So, I thought to myself that it would be best if I brought in my child for testing. (Caregiver #13, Female, 31)

As such, the provision of tailored information provided within the B-GAP intervention was influential in encouraging the uptake of testing. Many caregivers noted that the B-GAP providers explaining the rationale for testing reassured them and resulted in the caregivers having courage to take up testing. Caregivers valued the time that the providers took to convey information and to help them apply it to their individual context. Caregivers emphasised the benefits of allowing time to discuss and listen to their concerns. For some, these conversations extended over more than one encounter.

> I would say that the B-GAP team were an experienced team, who were well taught about their program because they would approach you in a way that make you feel free. One person will approach you and explain what they are doing in a good way that helps you to open up and tell them your status and the team was well trained and open. (Caregiver #22, Male, 52)

The relational nature of index-linked HIV testing of children

Participants illuminated the complex relational webs that HIV so perniciously affects. Caregivers viewed HIV testing of children not as a "one-off" event but as a *process* with potential consequences on multiple people and relationships.

They described living with HIV as a lifelong burden which the child experienced from a young age. Index-linked testing would also inadvertently reveal their own status to other family members, and they would have to confront this both with the child and others. Many caregivers who had kept their HIV status a secret from others in their household feared that they might lose the control they had exercised over disclosing their own status.

> I still remember, there was this case uh, of this particular lady who said; 'Living with HIV is already a burden to me. It's quite difficult. So, if you come into my home and test these children, and they come out positive, the assumption will be that I am the one who infected them and that will certainly disturb my family; the makeup of my own particular family'. (Provider #4, Male, 34)

Other reported concerns that would follow a positive HIV test were having to support the medication-taking throughout childhood and disruption of care for other children. Caregivers were living with HIV themselves and for many the potential additional responsibility involved in managing their child's HIV care alongside their own was undesirable, but testing would at least facilitate access to care. Often caregivers would take time to make this decision and reach a point where they are willing and ready.

> This one lady; she had initially refused, then I had shown her my office because I usually screen them where she was. So, she came in later, she said; 'I realised that in as much as I do not want my child to be tested, but I am already on ART, and it is really helping me. I have seen other people die when they are not taking ART. So… I would rather have my child tested so that we know the way forward than to stay in the oblivion age where he/she doesn't know what is going on'. (Provider#6, Female, 24)

Caregivers stated that these factors would impede uptake of HIV testing for children but, importantly, they

emphasised that they needed both time and support to work through these concerns and reported that feeling under pressure to quickly move to testing was not conducive to uptake.

The relational dynamics between caregivers were an important determinant of uptake of index-linked HIV testing for children. Caregivers demonstrated that index-linked HIV testing for children requires negotiation with, and the involvement of, different individuals. In some instances, the decision to test had to be a joint decision between two caregivers such as biological parents. In the B-GAP study, most indexes were women, who sometimes sought the permission of their husbands for testing of their children. Beyond the relational nature of the decision, there are extensive ramifications that could follow a positive HIV test result, including who is deemed responsible for HIV transmission as well as for supporting treatment.

> Where the father lives in South Africa, those mothers may not accept the idea of testing the child on their own in the absence of the father of the children because when he returns, he may want answers about where the child got HIV. (Caregiver #11, Female, 37)

While indexes may have been the primary caregiver, they were not always the biological parent of the children living in their households. Caregivers, who were not the biological parents, expressed concern about their right to link a child to testing and care and the negative impact that HIV testing of the child would have on their relations with the biological parents.

> If my brother receives a call from me telling him that his child got tested and is now on ARVs, the next time we meet he will certainly kill you. (Caregiver #23, Male, 58)

Regardless of relation to the child, the issue of bearing the additional emotional and financial cost of supporting someone who was not their biological child was raised. However, while acknowledging these issues, many caregivers felt they were liable to make the final decision because they provided day to day care of children. There was variation in how caregivers handled the decision-making, a process which would likely take time to resolve sometimes together with biological parents.

> If you are saying that if the children are under your care you would first need to inform a parent in South Africa, what if the child gets sick and needs to be admitted in hospital? What would you do then? In my view, whether the biological parent wants or not I will get the child tested! (Caregiver #19, Female, 42)

> I live with my grandchildren; my child lives in South Africa. If anything happens to those children, I am responsible. But I am expected to first inform my child, and if she refuses… I would rather tell her after the fact that I did this and that. (Caregiver #14, Female, 53)

> Sometimes we have to take a stand and make the effort to have an open discussion with the biological parents so that it does not become a problem in future. Because it is also a burden to have this opportunity and yet decline to have those non-biological children tested. It is also difficult. So, I need to discuss with the biological parents and inform them of their children's statuses. I need to be open about it. (Caregiver #10, Female, 65)

In addition to needing to inform biological parents about testing for their children, caregivers who were not the biological parents of the children to be tested noted that the inadvertent disclosure of the HIV status of biological parents was a critical factor to consider in the testing process for non-biological children. Caregivers had to weigh up the importance of testing the child versus the unwelcome risk of doing so potentially revealing the mother's HIV status, which she may not have wanted to share.

> I feared that if the child who isn't mine biologically tested HIV positive, I was going to struggle to inform the child's real mother. Perhaps the mother is positive, and she has not disclosed this to me. Initially it used to bother me, but I resolved that I would tell her since she is my younger sister and I tested the child because the child lives under my care. (Caregiver #11, Female, 37)

Caregivers highlighted the need to engage children themselves in the HIV testing process, particularly older children who were often reluctant to go to the clinic. In these cases, caregivers expressed a preference for community health workers to go to the household and speak to older children directly about HIV testing.

> This option (home based testing) was very helpful to me because I have an older child who always used to refuse to go with me to the clinic, every time I would ask him to go and get tested at the clinic he would refuse. However, when they arrived,

> they summoned him, and he could not refuse. And they spoke to him in their way and before I knew it, they were holding hands and they seemed to really click. (Caregiver #2, Female, 36)

For older adolescents, caregivers repeatedly mentioned the need to consider sexual risk rather than solely the perinatal HIV infection assumed by index-linked HIV testing. Caregivers mentioned the fears that adolescents may have about disclosing their sexual behaviour by ways of an HIV test. Older adolescents were felt to be old enough to consent independently.

> It's because they will be afraid, young people indulge and experiment on a lot of things, then that brings in the fear that leads one to decide not to accept this kind of testing. (Caregiver #30, Male, Age-unknown)

Addressing limited access: provision of community-based HIV testing options

Once the decision to test has been made caregivers often need to bring their children to a health facility. As has been reported in other studies, this leads to out-of-pocket expenditure and loss of income by taking time off work to make the journey.

> I had always wanted my children to get tested but I didn't have the time to take the children to the clinic. (Caregiver #29, Male, 25)

To address these barriers, the B-GAP study provided two options for testing in the community, which participants noted was helpful in increasing accessibility of testing for their children.

> We were happy that B-GAP would come home. Taking the children to the clinic using a taxi will be costly since I had 4 children that needed to be tested, so it meant us filling the whole taxi as a family to the clinic and back home, this was going to be too costly and that money would be money that we can use at home for a month, this is what was good about B-GAP. (Caregiver #28, Male, 39)

Provider perspectives: follow-up, logistics and indirect refusals

Explicit contributions from providers included challenges surrounding community testing by providers and follow-up for caregivers who chose facility testing. Providers noted that sometimes they had difficulty locating households due to inaccurate or wrong addresses and phone numbers provided by the caregivers.

> When you are asking about directions then someone says you turn to the left and in actual fact they mean turn to the right, so until you are now in the road and you call and you ask you said I should turn left and they say yes turn to the left but you realize the actual turn is to the right. (Provider#7, Female, 40)

The providers did highlight that in some instances they felt these could be indirect refusals from caregivers who did not want to have the children in their households tested. While the study protocol was that caregivers be followed up at least 3 times in order to complete testing, some caregivers would provide false phone numbers and fake addresses.

> I don't know now because if the number doesn't go through at all, at all! And the number doesn't go through, you try for the whole month. You don't know if this number is some number that belongs to him, but is no longer in use, you know? (Provider#3, Female, 33)

> I don't think there is anything that could have been done, why I say so is because someone lies and tells you that I stay at this address and they do not stay there. (Provider#1, Female, 30)

Despite this, however, there were some caregivers who appreciated the follow-up from providers to facilitate testing for the children in their households. This follow-up allowed caregivers who were indecisive more time to make the decision to test as well as act as a reminder to caregivers who may have forgotten.

> It is very good to follow up because when you sign up with B-GAP people, they will call you, I was called, and they asked when they should come. And I told them I was in the village, when I got back, I never got back to them, but they called me again. And they asked when they should come and I appreciated that because I had forgotten about it, so I think that the follow ups are good. If they had gone stealth, I also would have forgotten about it. So, the follow ups are good, some need scolding. (Caregiver #14, Female, 53)

> I think it is a good idea to follow up because at times you just agree to be part of the program because you will in a certain state of mind then you set an appointment but then that fear, on the

appointment date you decide not to go to the clinic and the clinic staff sees that someone missed their appointment so I think it is good for them to phone you and it will actually give you the confidence that you are dealing with people who are genuine who remembers to call you for a follow up and at times you would just completed a form so that the person does not continue to bother you and in actual essence you were not serious about it, so if they call you it's now confirmation that whatever the results these people might actually help since they would have made that follow up. (Caregiver #29, Male, 25)

Discussion

Our study highlights inadequate emphasis on paediatric HIV for adults living with HIV and accessing routine care. Emphasis on testing children has traditionally been confined to PMTCT in most programs and not part of general adult care [18]. Additionally, in general, standard of care focuses more on individual treatment and partner testing rather than for children [19]. Clients receiving HIV care had not been given adequate information about the need to test children in ways that they could satisfactorily engage with. This results in missed opportunities for diagnosis of children who only present once they develop HIV-associated illness. This can be reversed by directly addressing the issue of low-risk perception [20]. B-GAP staff provided tailored information so that caregivers grasped the pertinence of testing their children, which increased uptake of testing.

While many caregivers may be aware of the benefits of HIV testing, they are confronted with a myriad of issues when offered index-linked HIV testing including the prospect of lifelong treatment for their children and automatic disclosure of the HIV status of the index and that of biological parents (if the index is not the biological parent). These issues may have enormous implications on the relationships within a family unit and beyond.

Other studies have also highlighted the difficulties both caregivers and health care providers face in discussing parent-to-child HIV transmission with children, and this can be a substantial barrier to children being tested for HIV [21–24]. HIV status disclosure and potential social harms, such as gender-based violence, are consistent concerns for HIV testing [25, 26]. Support for disclosure to both other family members and to children, where wanted, should be an integral component of index-linked testing. This is likely to have longer-term benefits in terms of promoting psychological well-being and adherence to treatment should the child test HIV-positive [27].

The multiple relationships which may be affected by an HIV test result substantially influence decision-making about testing of children. If uptake of paediatric HIV testing is to be improved, providers need to recognise and more actively engage with these relational dimensions to HIV testing. Our findings illustrate the centrality of relationships in decision-making, which can potentially impede the uptake of testing for children as well as prolonging the process of testing. However, uptake can be improved if providers recognise and engage with individual concerns regarding the complex and potentially wide-ranging consequences of caregivers having their children tested for HIV.

Testing programmes are often focused on the clinical urgency of testing and on achieving targets such as the UNAIDS 90-90-90 targets, without considering social and relational issues [28]. Notably, there has been much more attention paid to these issues for supporting adherence to treatment in children and adolescents through the provision of social and community-based psychosocial support [29, 30]. We argue that a similar approach must be adopted for improving uptake of HIV testing, and HIV testing must be regarded as a *process* rather than a discrete event [31].

Although recommended by WHO, index-linked testing was not a standard practice in routine HIV care for children in Zimbabwe when B-GAP started. The B-GAP study implemented screening of individuals living with HIV and rigorous follow-up by telephone and home visits for caregivers who initially accepted testing for their children. This facilitated tailored conversations between the caregivers and providers, often within the household, with those who would not otherwise have attended healthcare facilities with their children despite agreeing to test [13]. This follow-up may have given caregivers more time and support to make a decision and subsequently led to increased uptake of testing. We note that some participants only took up testing after follow-up and after having received support from B-GAP providers.

In B-GAP, we found that older adolescents (16–18 years) were less likely to be tested when compared to children aged 2–5 years (under review). As highlighted by this and previous studies, engaging adolescents is challenging and index-linked testing may expose sexual activity of adolescents to their caregivers [32, 33]. As highlighted by caregivers, respecting adolescents' autonomy and approaching them directly and then their caregivers for consent may be more appropriate.

Our study shows that overcoming barriers to access is vital to increase uptake of HIV testing. In B-GAP, the provision of testing in community settings, such as testing at home by a provider or the provision of an oral HIV self-test kit to the caregiver, mitigated against barriers such as transportation costs and loss of income when caregivers have to take time off work to bring children to health facilities. Offering alternative testing approaches can improve uptake of index-linked testing and

this has also been demonstrated in Malawi where community testing had higher uptake than facility-based testing [6]. These community-based strategies should be included as part of routine care if we are to identify hard to reach children and adolescents living with undiagnosed HIV. We did note, however, some logistical barriers with uptake of community testing whereby some caregivers gave inaccurate or false addresses or phone numbers. In some instances, providers felt this was indicative of indirect refusals which would be expected where caregivers are not ready to test children in their households.

A key strength of our study was the provision of index-linked HIV testing by trained and dedicated staff. Health facilities in low-income settings are often understaffed and have overworked personnel who may not have the time to offer the support and detailed communication or information that was offered by providers in this study. The B-GAP study facilities are run by nurses. This highlights the limited ability for the study providers and caregivers who are part of this system to influence longstanding change. However, key learnings from this study can be integrated into large-scale implementation. A limitation of our study is that FGDs were held only with caregivers who took up index-linked testing and providers. While it may have been beneficial to include caregivers who refused or did not take up testing for children in their households, this group is difficult to engage as it may be uncomfortable for individuals to justify not acting on health recommendations. However, exploring the decision-making process of caregivers who took up testing provides an insight into the enablers to testing and the issues indexes struggle with. Providers who offered testing to all caregivers (those that took up testing and those that did not) were able to indirectly provide perspectives on both groups through their experiences.

We did not conduct in-depth interviews in our study. FGDs aim to capture social norms around index-linked HIV testing rather than focus on individual stories. However, as participants in each FGD were aware that everyone had engaged in the intervention, it was common for participants to choose to reflect on their own experiences, as well as to consider more common trends within the community. Both sexes and caregivers from both rural and urban settings were represented to allow for the breadth of contextual diversity to be explored.

Conclusion

In conclusion, this study provides a novel perspective into the lived experiences of providers and caregivers who have offered and accepted index-linked HIV testing in rural and urban settings in Zimbabwe. It demonstrates that the testing gap in children can be bridged by improving paediatric HIV literacy, recognising the relational aspects of HIV testing that caregivers are confronted with when offered HIV testing for their children, and the need for providing time for caregivers to navigate these aspects.

Panel of recommendations

- Paediatric HIV literacy should be strengthened as part of standard HIV care.
- Discussions about paediatric HIV testing should be individualised and include discussions on HIV risk in children and the benefits of testing.
- Index-linked HIV testing should be coupled with robust support for indexes.
- Offering community-based follow-up and/or an option for community-based HTC may improve access and uptake.
- A family- and process-centred approach should also be adopted to improve uptake of testing
- Adolescents should be directly engaged, and their autonomy respected for HIV testing.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s43058-020-00091-9.

Additional file 1:. Caregiver FGD Topic Guide

Additional file 2:. Provider FGD Topic Guide

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Authors' contributions

CDC developed the data collection tools, supervised data collection and led the data analysis and paper write up. KS and NN conducted the FGDs. SB supported the data analysis and write up. SD provided support in the development of data collection tools. VS, HAW, KK, KW, TA and MM contributed to the study design and reviewed final drafts of the paper. ES, GN and RC contributed to the study logistics. The authors have read and approved the final manuscript.

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Availability of data and materials

The datasets used and tools for this study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical approval was obtained from the Medical Research Council of Zimbabwe, the Institutional Review Board of the Biomedical Research and Training Institute, and the London School of Hygiene and Tropical Medicine ethics committee. Written informed consent was obtained from all study participants. As part of the consent process and prior to commencing, the

FDG participants were made aware that by participating in an FGD their HIV status would be implicitly disclosed to others in the group and that they could withdraw participation at any point. Participants were not incentivised for participation but provided with transport money and teas during the FDGs.

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

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Publisher's Note

6. Diagnostic accuracy of oral mucosal transudate tests compared with blood-based rapid tests for HIV among children aged 18 months to 18 years

6.1 Introduction

One of the index-linked HIV testing strategies evaluated as part of the B-GAP project was HIV testing performed by caregivers using OMT tests.[21] OMT tests have been shown to have high sensitivity and specificity for the diagnosis of HIV in adults but had not previously been validated against routinely used rapid blood-based HIV tests in children.[112]

In this chapter performance of OMT tests was compared to that of blood-based rapid HIV tests that are currently used as standard of care in national algorithms. The validation was done in Kenya and Zimbabwe among ART naïve children aged 18 months – 18 years. Children on ART were excluded from this study as among ART experienced individuals (including children) OMT tests have been shown to produce false negative results.[143]

In this study the OMT test was 100% sensitive and 99.9% specific. This manuscript is the first validation of OMT tests in ART naïve children and demonstrates that OMT tests can be used for HIV testing among children and adolescents, as in adults.[9] For adults, currently, OMT tests are recommended for use as a screening tests with confirmatory HIV testing using blood-based tests.[9]

6.2 Citation

Dziva Chikwari C, Njuguna IN, Neary J, Rainer C, Chihota B, Slyker JA, et al. Brief Report: **Diagnostic Accuracy of Oral Mucosal Transudate Tests Compared with Blood-Based Rapid Tests for HIV Among Children Aged 18 Months to**

18 Years in Kenya and Zimbabwe. Journal of acquired immune deficiency syndromes (1999). 2019;82(4):368-72.

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6.4 Research Paper 5: Diagnostic Accuracy of Oral Mucosal Transudate Tests Compared with Blood-Based Rapid Tests for HIV Among Children Aged 18 Months to 18 Years in Kenya and Zimbabwe

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If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Journal of Acquired Immune Deficiency Syndrome		
When was the work published?	1 December 2019		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	Choose an item.

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I developed the study protocol for the procedures used in this study. The study was later replicated by collegues in Kenya who co-authored this paper. Due to low numbers of children data was combined with the study in Kenya for this paper. I was joint first author of this paper. I wrote the first draft and led on the data analysis for the manuscript with support from IN. I incorporated all the feedback from co-authors and led on the submision of the manuscript to the journal. Together with IN, we were responsible for responding to all the reveiwer comments and resubmission after peer review.

SECTION E

Student Signature	[redacted]
Date	26/02/2021

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OPEN

Diagnostic Accuracy of Oral Mucosal Transudate Tests Compared with Blood-Based Rapid Tests for HIV Among Children Aged 18 Months to 18 Years in Kenya and Zimbabwe

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Background: Gaps persist in HIV testing for children who were not tested in prevention of mother-to-child HIV transmission programs. Oral mucosal transudate (OMT) rapid HIV tests have been shown to be highly sensitive in adults, but their performance has not been established in children.

Methods: Antiretroviral therapy-naive children aged 18 months to 18 years in Kenya and Zimbabwe were tested for HIV using rapid OraQuick ADVANCE Rapid HIV-1/2 Antibody test on oral fluids (OMT) and blood-based rapid diagnostic testing (BBT). BBT followed Kenyan and Zimbabwean national algorithms. Sensitivity and specificity were calculated using the national algorithms as the reference standard.

Results: A total of 1776 children were enrolled; median age was 7.3 years (interquartile range: 4.7–11.6). Among 71 children positive by BBT, all 71 were positive by OMT (sensitivity: 100% [97.5% confidence interval (CI): 94.9% to 100%]). Among the 1705 children negative by BBT, 1703 were negative by OMT (specificity: 99.9% [95% CI: 99.6% to 100.0%]). Due to discrepant BBT and OMT results, 2 children who initially tested BBT-negative and OMT-positive were subsequently confirmed positive within 1 week by further tests. Excluding these 2 children, the sensitivity and specificity of OMT compared with those of BBT were each 100% (97.5% CI: 94.9% to 100% and 99.8% to 100%, respectively).

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C.D.C., I.N.N., and A.D.W. developed the first draft of the manuscript and conducted the data analysis. Zimbabwe: C.R. developed the study protocol and was assisted by B.C. who developed data collection tools and standard operating procedures. R.A.F., H.M., G.M. and K.A.S. supervised C.R. and provided support in the design of the study. T.B. managed the dataset. G.M., C.D.C., B.C., and E.D. supervised field staff. Kenya: A.D.W., I.N.N., J. N., G.C.J.-S., J.A.S., D.A.K. and D.C.W. developed the protocol. A.D.W. and I.N.N. obtained grant funding. A.D.W., I.N.N. and J.N. developed study material and supervised data collection. All co-authors revised and approved the final draft of this manuscript.

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A donation of 3000 test kits was received from OraSure technologies for the Zimbabwe site.

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Conclusions: Compared to national algorithms, OMT did not miss any HIV-positive children. These data suggest that OMTs are valid in this age range. Future research should explore the acceptability and uptake of OMT by caregivers and health workers to increase pediatric HIV testing coverage.

Key Words: HIV, children, pediatric, oral HIV testing, diagnostic, saliva HIV testing

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INTRODUCTION

The HIV pandemic has heavily affected children with over 1.8 million children (<15 years) living with HIV and 180,000 newly infected in 2017.[1] Prompt diagnosis and initiation on antiretroviral therapy (ART) is associated with decreased morbidity and mortality[2,3] and improved developmental outcomes[4,5]; however, gaps remain in diagnosis, particularly among older children and adolescents.[6]

World Health Organization (WHO) recommendations endorse rapid antibody-based HIV tests for diagnosis of individuals >18 months.[7] Blood-based HIV tests (BBT) are used globally. In addition, oral mucosal transudate (OMT) rapid HIV tests allow for sample collection that is less invasive, are more acceptable to clients, poses fewer risks to health care workers (HCW), and may increase testing uptake.[8–10]

The Food and Drug Administration approved the OraQuick OMT in 2004 for testing by health providers for individuals >12 years.[11] In 2016, the OraQuick HIV Self-Test received WHO prequalification and it is now recommended by WHO as a screening test for HIV.[12] OMT has high sensitivity and specificity in detecting HIV antibodies in adults and older adolescents.[7,10] A meta-analysis comparing OMT with BBT in adults reported a pooled sensitivity of 98.0% and specificity of 99.7% for OMT.[10] OMT has not been validated in children.

We evaluated the diagnostic performance of OMT compared with routine BBT in children and adolescents aged 18 months to 18 years in Kenya and Zimbabwe.

METHODS

Setting and Participants

This analysis includes pooled data from 2 studies in Kenya and Zimbabwe that include parallel point-of-care diagnostic OMT and BBT to assess sensitivity and specificity of OMT among children and adolescents. Data were combined to increase precision of sensitivity and specificity estimates, as the number of newly diagnosed HIV-positive children in both settings has reduced with the scale-up of pediatric HIV prevention and treatment programs.

Zimbabwe

This analysis was nested within the "Bridging the Gap in HIV Testing and Care for Children in Zimbabwe" (B-GAP Project) whose aim is to evaluate index-linked testing for pediatric case detection. Study participants were children and adolescents of unknown HIV status, aged 2–18 years, attending any health services in the participating hospitals and primary health care clinics.

Kenya

The "Saliva Testing and Video Information to Expand Uptake of Pediatric HIV Testing" (STEP-UP) study enrolled children aged 18 months to 12 years. Two recruitment streams were used. First, children of HIV-positive adults attending HIV clinics who were tested for HIV within a randomized controlled trial of financial incentives for index case testing (FIT trial; NCT03049917[13]) were recruited after determining HIV status using BBT within the trial. Second, children from outpatient clinics were recruited after HIV testing using BBT within routine testing; here children who tested BBT positive were oversampled.

Procedures

Zimbabwe

Testing followed the national algorithm[14]: first, BBT by Determine (Alere Determine HIV-1/2 Ag/Ab Combo; Abbott, Chicago, IL) (fourth generation), followed by First Response (First Response HIV-1-2; Premier Medical Corporation Ltd, Kachigam, India) (third generation), if Determine was reactive. In the case of 2 reactive BBTs, the same 2 BBTs were performed by a different provider to confirm a positive diagnosis. In the case of discordant BBTs, both tests were repeated. If discordance persisted, a third test, CHEMBIO was performed (CHEMBIO HIV 1/2 STAT-PAK Assay; CHEMBIO Diagnostic Systems, Inc., New York, NY). If this third test was positive, the result was reported as inconclusive and a retest conducted in 14 days. OMT was conducted by clinic staff blinded to BBT results.

Kenya

The national algorithm mirrored that in Zimbabwe with the following exceptions: the Determine HIV test was third instead of fourth generation and DNA PCR from dry blood spot specimens was the third test and was considered conclusive.[14–16] In addition BBT was conducted by research staff for those enrolled in the FIT trial and non-research staff for those enrolled from routine testing points. Research staff performed OMT and were not blinded to BBT results.

The reference standard used for our study was the HIV status as per the national algorithim of each country.

OMT

In Zimbabwe and Kenya, OMT sample collection and processing was performed bedside by qualified HIV testing lay providers who are typically lower than nurse level providers and are responsible for HIV testing in both countries. The qualification for these providers is a standard national training for HIV services conducted over 2 weeks. Testing was conducted according to manufacturer details (OraQuick ADVANCE Rapid HIV-1/2 Antibody Test; OraSure Technologies, Inc., Bethlehem, PA), whereby the research staff collected an oral fluid sample from the participants by running the test device between the lips and outer gums of the client once on top and once at the bottom

and then place the test device pad directly into the reaction fluid immediately after collection.[17] OMT results were read once between 20 and 40 minutes in Zimbabwe, and twice in Kenya at both 20 and 40 minutes to assess test performance at the lower and upper recommended times. OMT results were not shared with caregivers, because the test was undergoing validation.

Statistical Analysis

Data were analyzed using STATA 14 (StataCorp, College Station, TX). Sensitivity was calculated by dividing the number of OMT and BBT-positive children by the number of BBT-positive children. Specificity was calculated by dividing the number of OMT and BBT-negative children by the number of BBT-negative children. Positive predictive value (PPV) and negative predictive value (NPV) were calculated in the Zimbabwean cohort by dividing the number with both positive OMT and BBT by all the positive OMT tests (PPV) and by dividing the number with both negative OMT and BBT results by the total negative by OMT (NPV). PPV and NPV were not calculated in the Kenyan cohort, because positive children were oversampled. Ninety-five percent (95%) or 97.5% (when the estimate was 100%) confidence intervals (CIs) were calculated using a binomial distribution. Stability of the test results using result interpretation pictures from the manufacturer was described in Kenya.

Ethics

Adolescents ≥16 gave independent written informed consent without parental/guardian consent. Parents/guardians of children aged 18 months–15 years provided written consent; adolescents 13–15 years signed a paragraph within the parental consent form to give their assent, whereas children 7–12 years signed a separate assent document, which was optional in Kenya. B-GAP received approval from the Biomedical Research and Training Institute, the Medical Research Council of Zimbabwe and institutional review boards at Duke University and the London School of Hygiene and Tropical Medicine. The Kenyan study received approval from the Kenyatta National Hospital Ethics and Research Committee and the University of Washington Institutional Review Board.

RESULTS

Demographics

Overall, 1776 children were enrolled; 1570 (88%) from Zimbabwe and 206 (12%) from Kenya. The median age was 7.3 years (IQR: 4.7–11.6); 2 (0.1%) were 18 months −2 years; 512 (29%) were >2–5 years; 845 (48%) were >5–12 years; and 417 (23%) were >12–18 years. Overall, 918 (52%) were female. Among Kenyan children, 169 (82%) were identified via index case testing and 37 (18%) in outpatient clinics and inpatient wards (Table 1).

TABLE 1. Sociodemographic Characteristics

Child characteristics	All, N = 1776 n (%) or Median (IQR)	BBT HIV Positive, n = 71 n (%) or Median (IQR)	BBT HIV Negative, n = 1705 n (%) or Median (IQR)
Age group			
18 mo–2 yrs	2 (0.1)	1 (1)	1 (0.1)
>2–5 yrs	512 (29)	21 (30)	491 (29)
>5–12 yrs	845 (48)	34 (48)	811 (48)
>12–18 yrs	417 (23)	15 (21)	402 (24)
Female	918 (52)	46 (65)	872 (51)
Recruitment country			
Zimbabwe	1570 (88)	28 (39)	1542 (90)
Kenya	206 (12)	43 (61)	163 (10)
Index case testing	169 (82)	7 (16)	162 (99)
Inpatient/ outpatient	37 (18)	36 (84)	1 (1)

Child characteristics	All, n = 189 n (%)	BBT HIV positive, n = 43 n (%)	BBT HIV negative, n = 146 n (%)
PMTCT history (Kenya)			
Tested positive in pregnancy	8 (4)	5 (12)	3 (2)
Any maternal ARVs	4 (50)	2 (40)	2 (67)
Any infant prophylaxis	4 (50)	2 (40)	2 (67)

OMT Sensitivity and Specificity

Among 71 children positive by BBT, 71/71 (sensitivity: 100.0% [97.5% CI: 94.9% to 100.0%]) were positive by OMT. Among 1705 children negative by BBT, 1703/1705 (specificity: 99.9% [95% CI: 99.6% to 100.0%]) were negative by OMT. In the 1570 Zimbabwean participants, the PPV was 93.3% (95% CI: 77.9% to 99.2%) and the NPV was 100.0% (97.5% CI: 99.8% to 100.0%).

In Zimbabwe, 2 children who initially tested BBT-negative and OMT-positive were retested within 1 week to confirm HIV status because of suggestive clinical presentation and history; both were confirmed positive. A 9-year-old was confirmed positive by ELISA. A 2-year-old was confirmed positive by First Response and CHEMBIO. Excluding these 2 children, the sensitivity and specificity of OMT compared with those of BBT were each 100% (97.5% CI: 94.9% to 100% and 99.8% to 100%, respectively) (Table 2).

Stability of Visual Results (Kenya)

Among 43 children with positive OMT at 20 minutes, 43 (100%) had positive OMT at 40 minutes. Among the 163 children with negative OMT at 20 minutes, 163 (100%) had a negative OMT at 40 minutes. Using result interpretation pictures from the manufacturer, among 43 positive OMT results, 26 (60%) and 29 (67%) were strongly positive at 20 and 40 minutes, respectively. Three reads that were weakly positive at 20 minutes were strongly positive by 40 minutes; the remaining 14 (33%) were weakly positive at both 20 and 40 minutes.

TABLE 2. Performance of OMT vs BBT for HIV Diagnosis Overall and Stratified by Site

	BBT		
	Positive	**Negative**	**N**
Panel A: Overall			
Results			
OMT			
Positive	71	2*	73
Negative	0	1703	1703
Total	71	1705	1776
Sensitivity			100% (97.5% CI: 94.9 to 100)
Specificity (including 2 discrepants)			99.9% (95% CI: 99.6 to 100)
Specificity (excluding 2 discrepants)			100% (97.5% CI: 99.8 to 100)
Panel B: Zimbabwe			
OMT			
Positive	28	2*	30
Negative	0	1540	1540
Total	28	1542	1570
Sensitivity			100% (97.5% CI: 87.7 to 100)
Specificity (including 2 discrepants)			99.9% (95% CI: 99.5 to 100)
Specificity (excluding 2 discrepants)			100% (97.5% CI: 99.8 to 100)
Panel C: Kenya			
OMT			
Positive	43	0	43
Negative	0	163	163
Total	43	163	206
Sensitivity			100% (97.5% CI: 91.8 to 100)
Specificity (excluding 2 discrepants)			100% (97.5% CI: 97.8 to 100)

*Subsequently confirmed as HIV-positive using additional tests within 1 week of initial testing.

DISCUSSION

In this cross-sectional study of children aged 18 months to 18 years, we found that OMT had excellent sensitivity and specificity. When compared to the Kenyan and Zimbabwean national algorithms, OMT did not miss any positive children. These data suggest that OMT is valid for HIV diagnosis in this age range.

As with other antibody tests, OMT is inappropriate as a diagnostic test for children under 18 months due to the presence of maternal antibodies.[18] In adults, antibody-based tests have limitations due to a long window period, which may lead to failure in detecting recent HIV infection.[19] However, this is less of a concern among older children and younger adolescents who, if infected, are likely to have long-standing HIV, acquired perinatally.

Our results provide evidence for wider use of OMT for pediatric testing. Current testing approaches to identify children include index-linked testing, provider-initiated testing and counseling, targeted testing in health facilities, and community-based testing.[6,7,20–26] Outpatient provider-initiated testing and counseling can identify children earlier in disease progression[27]; however, achieving high coverage is challenging[21] because of high client volume and workload for limited numbers of HCWs.[28] In resource-limited settings, scaling up testing will require simultaneously increasing coverage and minimizing costly components of testing, including HCW time.[29,30] The ease and safety of OMT presents a potential opportunity for task-shifting from HCWs to lay providers, as was done in this study, or to caregivers to overcome human resource constraints. It is also important to note that the time to perform OMT is also similar to that required for BBT. Future research is needed to explore the acceptability and feasibility of OMT by caregivers and HCWs in facility and community settings.

A 2012 systematic review comparing OMT with whole blood specimens reported a pooled sensitivity of 98.0% and specificity of 99.7% for OMT.[10] Despite this, the concentration of antibodies in oral fluid is lower than in blood and typically wanes during HIV treatment.[31,32] Previous studies in Zimbabwe have confirmed that OMT has suboptimal sensitivity in ART-experienced children.[29,33] WHO has issued warnings, advocating that rapid diagnostic tests not be used among ART-experienced adults; similar warnings seem warranted in children. Therefore, it is critical to avoid use of OMT by ART-experienced patients, either to confirm being "cured" of HIV or when reinitiating HIV care.[34] Our study included an entirely ART-naive pediatric population and observed no false-negative results. In 2 cases, children were negative by BBT and positive by OMT and were confirmed HIV-positive upon repeat testing. This suggests slightly better detection by OMT than BBT in our study; it is unclear why we observed this counterintuitive finding.

Our study's strengths include a large sample of ART-naive, HIV-positive children to inform precise estimates of sensitivity. In addition, data from Kenya and Zimbabwe provided similar results. OMT results were compared with routine, field-based BBT according to national algorithms, which provides an apt comparison with standard-of-care tests and provides useful public health information. Limitations include that OMT result interpretation was not blinded in Kenya, which may have influenced result interpretation. National algorithms between the 2 countries differed slightly, so the "reference standard" was not the same in both countries. However, in both cases, the algorithms are those used for national guidelines. Consequently, our findings demonstrate the performance of OMT against the standard-of-care and are therefore generalizable in these settings. Although the BBT in this study was not ELISA or polymerase chain reaction (PCR) based, OMT has previously been compared with these more sensitive lab-based tests to inform Food and Drug Administration approval and WHO

endorsement for use in adults.[11,31] An additional limitation is that in our study we did not have any inconclusive test results. Procedures on how to report and manage inconclusive test results must be put in place.

CONCLUSIONS

OMT is highly sensitive and specific in children and adolescents. This is consistent with findings from studies in adult populations. Policymakers and regulators should consider expanding the age at which OMT may be used to include children over 18 months.

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7. Feasibility and accuracy of HIV testing of children by caregivers using oral mucosal transudate HIV tests

7.1 Introduction

The study conducted in Chapter 6 showed that OMT tests were highly sensitive and specific in identifying HIV among children and adolescents.[1] Several studies have shown that adults are able to accurately perform HIV self-testing using OMT tests and this approach has been endorsed by the WHO.[2,3] However, the feasibility of testing of children by their adult caregivers has not previously been assessed. One of the three index-linked HIV testing approaches offered as part of the B-GAP study was HIV testing by caregivers using OMT tests in the community.

This chapter is an evaluation of how well caregivers perform the OMT on their children and whether they can correctly interpret the test results. This is the first ever study to evaluate the feasibility of caregivers testing their children for HIV. In phase one of the study caregivers were shown how to perform the test on their children and subsequently observed by research assistants while performing the test on their children. In phase two of the study caregivers were not shown how to perform the test but were also observed by research assistants. The majority of caregivers could correctly perform OMT testing on their children and interpret HIV test results with or without prior demonstration.

This study shows that this HIV testing strategy can be used by caregivers and could potentially increase access to HIV testing for children who have limited access to health facilities. In Chapter 4 where the uptake of the three HIV testing approaches is compared HIV testing by caregivers had the lowest uptake.

7.2 Citation

Dziva Chikwari C, Simms V, Kranzer K, et al. Feasibility and Accuracy of HIV testing of children by caregivers using oral mucosal transudate HIV tests. Journal of acquired immune deficiency syndromes (*in Press*).

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7.4 Research Paper 6: Feasibility and Accuracy of HIV testing of children by caregivers using oral mucosal transudate HIV tests

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SECTION A – Student Details

Student ID Number	398292	**Title**	Ms
First Name(s)	Chido		
Surname/Family Name	Dziva Chikwari		
Thesis Title	Facility and community-based index-linked HIV testing strategies for children and adolescents in Zimbabwe		
Primary Supervisor	Professor Rashida A Ferrand		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Journal of Acquired Immune Deficiency Syndromes (JAIDS)		
When was the work published?	2021		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I was first author of this paper. I wrote the first draft and did led on the data analysis for the manuscript. I incorporated all the feedback from co-authors and led on the submision of the manuscript to the journal. I was responsible for responding to all the reveiwer comments and resubmission after peer review.

SECTION E

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Feasibility and Accuracy of HIV Testing of Children by Caregivers Using Oral Mucosal Transudate HIV Tests

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Background: Children encounter multiple barriers in accessing facilities. HIV self-testing using oral mucosal transudate (OMT) tests has been shown to be effective in reaching hard-to-reach populations. We evaluated the feasibility and accuracy of caregivers conducting HIV testing using OMTs in children in Zimbabwe.

Methods: We offered OMTs to caregivers (>18 years) living with HIV to test children (2–18 years) living in their households. All caregivers were provided with manufacturer instructions. In Phase 1 (January–December 2018, 9 clinics), caregivers additionally received a demonstration by a provider using a test kit and video. In Phase 2 (January–May 2019, 3 clinics), caregivers did not receive a demonstration. We collected demographic data and assessed caregiver's ability to perform the test and interpret results. Caregiver performance was assessed by direct observation and scored using a predefined checklist. Factors associated with obtaining a full score were analyzed using logistic regression.

Results: Overall 400 caregivers (83.0% female, median age 38 years) who were observed tested 786 children (54.6% female, median age 8 years). For most tests, caregivers correctly collected oral fluid [87.1% without provider demonstrations (n = 629) and 96.8% with demonstrations (n = 157), $P = 0.002$]. The majority correctly used a timer (90.3% without demonstrations and 96.8% with demonstrations, $P = 0.02$). In multivariate logistic regression caregivers who obtained a full score for performance were more likely to have received a demonstration (odds ratio 4.14, 95% confidence interval: 2.01 to 8.50).

Conclusions: Caregiver-provided testing using OMTs is a feasible and accurate HIV testing strategy for children. We recommend operational research to support implementation at scale.

Key Words: HIV, self-testing, children, adolescents, caregiver

(*J Acquir Immune Defic Syndr* 2021;87:781–788)

INTRODUCTION

Globally, 1.8 million children (0–14 years) were estimated to be living with HIV in 2019, but over 845,000 of these were either undiagnosed or diagnosed but not on treatment.[1] Although coverage of prevention of mother-to-child transmission programs has risen substantially in the last decade, only 50% of exposed infants underwent HIV testing within the first 2 weeks of birth in 2019, and postnatal transmission continues to occur.[2] Thus, children continue to be infected (150,000 infections in 2019), with many children not presenting to health care until older childhood when they have developed advanced HIV disease.[1,3–5]

Facility-based HIV testing is routinely implemented in most high prevalence settings. However, children encounter multiple unique barriers in accessing facility-based HIV testing services including reliance on caregivers to take them, guardian consent, distance to and costs incurred to access facilities, and inconvenient opening times coinciding with school hours.[6,7]

HIV self-testing (HIVST) using oral mucosal transudate (OMT) tests has been shown to be effective in reaching previously hard-to-reach populations including men, adolescents, sex workers, and men who have sex with men.[8–10] Benefits of HIVST include privacy and autonomy, decreased workload for health care workers, and improved access through community distribution.[11]

The World Health Organization[12] (WHO) already recommends community-based HIV testing using OMT tests by lower cadre health care workers, and an extension of this

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would be HIV testing of children performed by caregivers using OMT. HIV testing for children provided by a caregiver, if feasible and acceptable, could address the barriers to testing children,[13] thus potentially increasing coverage of HIV testing among children, and decrease the demands on health care provider time and potentially be more cost-effective.[14]

Qualitative studies show that caregivers are willing to perform HIV testing on their children and believe that this form of testing has several advantages including privacy, convenience, control over who knows the child's status, and lower costs.[13,15] However, some caregivers expressed uncertainty about their ability to test children without assistance and support from a health care worker.[13] Before recommending HIV testing by caregivers at scale, there is a need to understand whether HIV testing by caregivers is performed correctly.

In this study, we evaluated the feasibility and accuracy of caregivers conducting HIV tests using OMT in children aged 2–18 years in Zimbabwe.

METHODS

The study was embedded within the Bridging the Gap in HIV Testing and Care for Children in Zimbabwe (B-GAP) project conducted between January 2018–May 2019 in 12 primary care clinics: 9 in Bulawayo (urban) and 3 in Matebeleland South province (rural).[16] Adult (aged 15–64) HIV prevalence is 18% in Bulawayo and 22% in Matebeleland South.[17]

The B-GAP project aimed to investigate different approaches for index-linked testing for children. Index-linked HIV testing is a strategy whereby an HIV test is offered to contacts of individuals living with HIV. B-GAP evaluated 3 approaches for index-linked HIV testing for children, namely, facility-based testing, home-based testing performed by a lay worker, or testing performed by a caregiver using an OMT test.[18] This study evaluates testing performed by caregivers.

Study Participants and Procedures

Study participants were consenting individuals (age ≥ 18 years) living with HIV attending the study clinics for HIV care who had children (2–18 years) in their household of unknown HIV status and who selected the caregiver-provided HIV testing option to test their children. Caregivers had to be biological parents or caregivers (where parents were not available). The unknown HIV status was defined as never having had an HIV test or having a negative test result more than 6 months previously. Caregivers were provided with HIV self-test OMT kits (OraQuick ADVANCE Rapid HIV 1/2, OraSure Technologies Inc.) for each eligible child.[19] Each kit included manufacturer's instructions in English and the 2 main local languages, Shona and Ndebele. Caregivers were explicitly told that the HIV OMT test is a screening test and that a reactive result would require confirmation by a blood test at the health care facility as per national guidelines.[20] Caregivers were also provided with a hotline number to contact should they have any questions or concerns during the testing process. All caregivers who took up caregiver testing were followed up (in person or by telephone).

The study was conducted in 2 phases initially as part of the main B-GAP study in 2018 (Phase 1) and as an extension of B-GAP in 2019 to evaluate caregiver testing without demonstrations (Phase 2).

Phase 1: Caregivers Received Demonstrations

Recruitment in this phase was in 6 urban clinics and 3 rural clinics. From January–December 2018, caregivers who consented to participate in the study and chose to test their children using OMT received a demonstration by research assistants in the clinic of how to perform the HIV self-test (see Fig. 1, Supplemental Digital Content 1, http://links.lww.com/QAI/B607). To demonstrate, the research assistants used the OMT test instruction pamphlets, a dummy test kit, and a 4-minute video on a handheld mobile device. After the demonstration, caregivers were asked to show the research assistant how to perform the test using a dummy kit to check their understanding.

A home visit was scheduled within 5 days for the first 15 caregivers enrolled in each of the 9 facilities. During the home visit, a member of the research team observed the caregiver performing the test (direct observation) on each child. No further demonstrations were provided on the testing day unless the caregiver asked for assistance. If requested to do so, the research assistants could provide assistance to caregivers. All other caregivers were followed up by telephone on day 5 after they had been given the OMT tests to ascertain the test outcome. If not reachable by telephone, caregivers were followed up by home visit (up to 2 home visits).

Phase 2: Caregivers Did Not Receive Demonstrations

As most caregivers were able to correctly preform the test in Phase 1; from January to May 2019, caregivers did not receive a demonstration in person or by video in the clinic. Direct observation of the caregiver conducting the test on their child at home was scheduled for all caregivers. During this phase, caregivers were discouraged from asking for assistance from the research assistants but would be assisted if they requested assistance. Recruitment was in 3 urban clinics. No rural clinics were included because of budget constraints.

Direct Observation

Direct observation of caregiver testing was performed by research assistants during the scheduled home visits. Using a tablet-based form, research assistants collected data on a predefined checklist assessing the testing process. The checklist evaluated caregiver performance for each step including whether or not the caregiver looked at the instruction pamphlet, collection of oral fluid from the child's mouth, and handling of test kit components such as the buffer and use of a timer when performing the test. Caregivers were asked to interpret the OMT test result. For all directly observed tests, data on whether or not the caregivers interpreted the test result correctly (according to the manufacturer's guidance) were collected. The research assistants

also collected data on whether or not the caregivers asked for assistance, what the assistance was for, and when assistance was provided.

After preliminarily data analysis, from March 2019, the research team introduced a more detailed questions asking for the OMT result interpretation by the caregiver and the OMT result interpretation by the research assistant (see Fig. 1, Supplemental Digital Content 1, http://links.lww.com/QAI/B607). In the initial questionnaire, only the caregiver interpretation was captured followed by a question about whether or not this interpretation was correct according to the research assistant. After March 2019, the questionnaire captured caregivers' interpretation of the OMT test result and in addition the interpretation by the research assistant (considered the gold standard). For the entire duration of the study, all children of caregivers who were directly observed when testing the children had a blood-based rapid HIV test performed on the child by the research assistant to confirm the OMT result. All children who tested HIV positive were referred to their preferred health facility for onward care.

Caregiver performance of conducting the HIV test was evaluated using 4 indicators which are part of the steps described in the manufacturer's instructions[19]: (1) Correct collection of oral fluid from the child's mouth ie, gently swab completely around the outer gums, both upper and lower, one time around, using the flat pad; (2) Complete insertion of the flat pad into the buffer solution ie, making sure that the flat pad touches the bottom of the vial; (3) Use of a timer during the test; (4) Correct interpretation of the test result

Each indicator was given a score of 1 if conducted correctly or 0 if incorrect, with a maximum score of 4. In both phases, direct observations and data collection were conducted for all tests conducted in the household that is for each child in the household.

Data Analysis

Analyses were conducted using STATA v15·0 software (StataCorp, TX). Categorical variables were summarized as counts (percentages), and continuous variables were summarized as medians (interquartile range: IQR). Only tests performed by caregivers who received direct observation were included in the analysis. These caregivers were grouped as those who received a demonstration and those who did not receive a demonstration. We compared 3 key caregiver characteristics (sex, age, and education level) between those who received a demonstration and those who did not, using χ^2 tests. Similarly, we compared child characteristics (age, sex, and relationship to the caregiver) by whether the caregiver received a demonstration or not, using logistic regression adjusting for clustering by caregiver with robust standard errors.

Univariable and multivariable logistic regression at the child level was used to assess factors associated with obtaining a full score for performance. We adjusted for clustering by caregiver using robust standard errors.

Ethical Considerations

Ethical approval for this study was obtained from the Medical Research Council of Zimbabwe and the Institutional Review Boards of the Biomedical Research and Training Institute and the London School of Hygiene and Tropical Medicine. Written informed consent was obtained from all caregivers. Verbal assent was obtained from children aged 2–7 years. Written assent was obtained from children aged 7–12 years, and adolescents aged 13–18 years provided signed consent.

RESULTS

Demographics and Flow

Between January 2018 and May 2019, 867 children (54.1% female, median age 8 years, IQR 5–12 years) were to be tested by 443 caregivers (81.9% female, median age 38 years, IQR 32–45) (Fig. 1). Of the 443 caregivers, 30 (6.8%) received a demonstration and were not directly observed, 77 (17.4%) received a demonstration and were directly observed, and 336 (75.8%) did not receive a demonstration and were directly observed (Fig. 1). Among the 107 caregivers in Phase 1, 10 (9.3%) were from the rural sites. As planned, all 336 caregivers in Phase 2 were from urban clinics, did not receive demonstrations from the research assistants, and were all directly observed. Overall, 413 caregivers received direct observation, and 400 caregivers (96.9%) performed the test on the children themselves (Fig. 1).

Most of the 400 caregivers who tested their children were female (83.0%), had secondary level education (75.0%), and were the biological parents of the children they tested (70.8%) (Table 1). The median age of these caregivers was 38 years (IQR 32, 45). Receiving a demonstration was associated with caregiver having less education ($P = 0.06$) and caregiver age category ($P = 0.06$) (Table 1).

Among 808 tests where caregivers were observed, caregivers performed 786 tests themselves (97.3%) (157 who received demonstration and 629 who did not receive demonstrations) (Table 2).

The reasons for not performing the test on the remaining 22 children included the child wanted to perform the test themselves (n = 6), at the point of testing the caregiver said they could not perform the test (n = 7), and that the child wanted the research assistant to perform the test (n = 3). Most of the caregivers who did not perform the test themselves (18/22, 81.8%) had not received a demonstration. Of the 786 children tested, 54.6% were female, and the median age was 8 years (IQR 5, 12). No child characteristics were associated with test demonstration (Table 1).

The subsequent analyses focus on the 786 tests performed by caregivers who were directly observed and performed the test themselves (Fig. 1).

Performance

For the 786 tests performed by caregivers, caregivers correctly collected oral fluid for most tests, and this was associated with receiving a demonstration (87.1% among

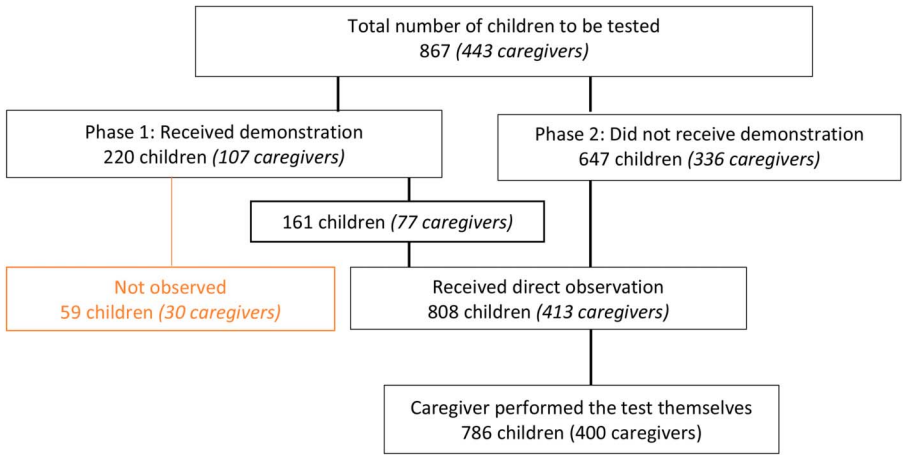

FIGURE 1. Participant flow chart. full color online

those without a demonstration and 96.8% with a demonstration, $P = 0.002$). Among 86 caregivers who did not correctly collect oral fluid, 35 (40.7%) swabbed either the lower or the upper gum alone, scrubbed the gums rather than swabbing, or swabbed both the upper and lower gums more than once. Other caregiver inconsistencies included swabbing front gums alone, brushing teeth rather than swabbing, and placing the flat pad on the tongue or gums. Most caregivers inserted

TABLE 1. Demographic Characteristics of Caregivers and Children Who Received Direct Observation and Performed the Test Themselves, Comparing Caregivers Who Received Demonstrations and Those Who Did Not

	Characteristics of Caregivers Who Performed the Test			
	Total, N = 400 (%)	**Received Demonstration, N = 74 (%)**	**Did Not Receive Demonstration, N = 326 (%)**	***P****
Sex				
Male	68 (17.0)	10 (13.5)	58 (17.9)	0.38
Female	332 (83.0)	64 (86.5)	268 (82.2)	
Age				
18–30	78 (19.5)	10 (13.5)	68 (20.9)	0.06
31–50	267 (66.8)	58 (78.3)	209 (64.1)	
>50	55 (13.8)	6 (8.1)	49 (15.0)	
Education†				
Primary	59 (14.8)	17 (23.3)	42 (12.9)	0.06
Secondary	298 (74.7)	51 (69.9)	247 (75.8)	
Tertiary	42 (10.5)	5 (6.9)	37 (11.4)	
	Characteristics of Children Tested by Caregivers			
	Total, N = 786 (%)	**Caregiver Received Demonstration,N = 157 (%)**	**Caregiver Did Not Receive Demonstration, N = 629 (%)**	***P*‡**
Sex§				
Male	356 (45.4)	70 (44.9)	286 (45.5)	0.89
Female	428 (54.6)	86 (55.1)	342 (54.5)	
Age§				
2–5	214 (27.3)	38 (24.4)	176 (28.0)	0.17
6–9	244 (31.1)	43 (27.6)	201 (32.0)	
10–15	278 (34.2)	62 (39.7)	206 (32.8)	
16–18	58 (7.4)	13 (8.3)	45 (7.2)	
Relationship to index§				
Biological child	556 (70.8)	99 (63.5)	457 (72.7)	0.12
Nonbiological child	228 (29.0)	57 (36.5)	171 (27.2)	

*P-value obtained for χ^2 tests.
†Education data missing for 1 caregiver.
‡P-value for the child characteristics were obtained from logistic regression adjusting for clustering by a caregiver using robust standard errors.
§Missing data for 2 children.

TABLE 2. Performance of Caregivers on Each Test Comparing Those Who Received a Demonstration and Those Who Did Not

N = 786	Did Not Receive Demonstration 629 (%)	Received Demonstration 157 (%)	*P**
1. Caregiver correctly collected oral fluid	548 (87.1)	152 (96.8)	0.002
2. Caregiver inserted the flat pad all the way	612 (97.3)	156 (99.4)	0.157
3. Caregiver used a timer	568 (90.3)	152 (96.8)	0.019
4. Caregiver correctly interpreted the test result	612 (97.3)	153 (97.5)	0.843
5. Caregiver received a score of 4/4	490 (77.9)	145 (92.4)	<0.001

**P*-value obtained from logistic regression adjusting for clustering by a caregiver using robust standard errors.

the flat pad all the way into the test fluid (97.3% without a demonstration and 99.4% with a demonstration, $P = 0.16$). Most caregivers used a timer during the test. Caregivers who had received a demonstration were more likely to use a timer (96.8% with and 90.3% without provider demonstrations, $P = 0.02$). Interpretation of the test result was correct in almost all instances (97.3% without a demonstration and 97.5% with a demonstration, $P = 0.84$) (Table 2).

Overall, 635/786 (80.8%) tests were performed correctly on all 4 indicators (490/629–77.9% among those without a demonstration and 145/157–92.4% among those with a demonstration) (Table 2). In univariate analysis adjusting for clustering by a caregiver, having received a demonstration was associated with performing all 4 indicators correctly (Table 3). In multivariable analysis adjusting for clustering by a caregiver, higher level of education when compared with primary level [secondary odds ratio (OR) 2.51; 95% confidence interval (CI): 1.26 to 4.99 and tertiary OR 2.82; 95% CI: 0.91 to 8.79; $P = 0.06$] and receiving a demonstration (OR = 4.14; 95% CI: 2.01 to 8.50; $P < 0.001$) was associated with a full score of 4. Because of their association with having a demonstration, level of education and caregiver age category were included in multivariable analysis. Site (rural vs urban) was not included in this analysis because no rural clinics were included in Phase 2 of the study.

Test Results and Caregiver Interpretation

All the caregivers with more detailed interpretation data presented here had not received a demonstration, and interpretation data were available for 587/786 tests. When the 587 OMT tests were compared with blood-based test results, the sensitivity and specificity of the OMT interpretation by research assistants was 100%. All invalid tests (n = 7) were HIV negative using blood-based testing. Of the 567 OMT tests deemed nonreactive by the research assistant (ie, the gold standard), all were identified as nonreactive by the caregivers (specificity = 100%, 95% CI: 99.4% to 100%; Table 4). Of the 13 OMT tests deemed reactive by the caregiver, 4 OMT tests were identified as reactive by the research assistant (sensitivity 30.8%, 95% CI: 9.1% to 61.4%). In addition, one caregiver read a nonreactive test as invalid.

Most tests were performed with no assistance from the research assistants, 608/647 (94.0%) among those who did not receive any demonstration and 123/161 (76.4%) among children whose caregiver received demonstrations ($P < 0.001$). Most caregivers who asked for assistance did so when collecting the swab on the child followed by how to maneuver the packaging and test equipment then reading the instructions.

All 30 caregivers who did not have direct observation reported nonreactive results for the 59 children tested.

Ease of Performing the Test

When caregivers who did not receive a demonstration were asked to score the ease of performing the test from 1 to 5 (1 = very easy to 5 = very difficult), most caregivers reported that performing the test was very easy (41.2%) or easy (34.1%). Only 1.6% of caregivers said that performing the test was difficult. Most caregivers who performed the test used the manufacturer's instructions in vernacular (Shona or Ndebele) (74.9%).

DISCUSSION

Our study findings show that caregivers can perform oral HIV tests appropriately on their children. Most caregivers in our study were able to accurately collect oral fluid, maneuver test kit components, and correctly interpret test results. We found that prior demonstration of OMT testing by a provider did improve performance, particularly caregiver's ability to correctly swab the child's mouth and also the use of a timer while conducting the test. We also found that most caregivers in our study, who did not receive prior demonstration from providers on how to perform the test, felt that performing the test on their children was easy and usually did not ask for assistance from a health care worker who was present to observe them performing the test. Caregivers were more likely to ask for assistance when they were explicitly told they could ask for assistance. When discouraged from asking for assistance most caregivers were able to perform the test without asking for help. These findings are consistent with other studies where individual's ability to perform the OMT test on themselves has been evaluated in different settings including in South Africa and Zimbabwe, with over 90% of users being able to correctly interpret their HIV test result.[21,22]

Although most caregivers could correctly interpret the oral HIV test result, some caregivers incorrectly interpreted a nonreactive OMT test result as reactive, and there were some invalid test results, likely because of poor performance of the caregivers in conducting the test. No caregivers incorrectly interpreted a reactive OMT test result, although it is important to note that the number of reactive OMT test results was low. Most errors (incorrectly identifying a nonreactive test as reactive) would have been picked up in subsequent

TABLE 3. Factors Associated With Obtaining a Full Score for Caregiver-Provided Testing (N = 786)

	Obtained a Full Score, n = 635	Univariate Analysis*		Multivariate Analysis†	
Characteristic	**n (%)**	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Index level variables					
Caregiver's age					
18–30	118 (81.9)	1.42 (0.61 to 3.26)	0.63	1.06 (0.45 to 2.53)	0.81
31–50	424 (81.5)	1.37 (0.68 to 2.76)		0.93 (0.44 to 1.97)	
>50	93 (76.2)	1	—	1	—
Caregiver's sex					
Male	101 (80.8)	1	—		
Female	534 (80.8)	1.00 (0.52 to 1.93)	1.00		
Caregiver's highest level of education‡					
Primary	82 (70.7)	1	—	1	—
Secondary	479 (82.3)	1.93 (1.00 to 3.71)	0.12	2.51 (1.26 to 4.99)	0.06
Tertiary	73 (83.9)	2.16 (0.70 to 6.66)		2.82 (0.91 to 8.79)	
Received demonstration					
No	490 (77.9)	1	—	1	—
Yes	145 (92.4)	3.43 (1.79 to 6.58)	<0.001	4.14 (2.01 to 8.50)	<0.001
Child level variables					
Child' sex§					
Male	288 (80.9)	1	—		
Female	345 (80.6)	0.98 (0.69 to 1.40)	0.92		
Child's age,§ yrs					
2–5	176 (82.2)	1	—		
6–9	192 (78.7)	0.80 (0.51 to 1.23)	0.56		
10–15	223 (83.2)	1.06 (0.66 to 1.74)			
16–18	42 (72.4)	0.56 (0.29 to 1.11)			
Child's relationship to index§					
Nonbiological child	447 (80.4)	1	—		
Biological child	186 (81.6)	0.93 (0.54 to 1.60)	0.78		

*Univariate analysis adjusted for clustering by a caregiver.
†Multivariate analysis adjusting for clustering by a caregiver, caregiver level of education, and caregiver age category.
‡Missing data for 1 caregiver.
§Missing data for 2 children.

confirmatory HIV testing at a health care facility according to WHO HIVST guidelines.[23] This, however, requires the guardian and child to present to a health care facility for confirmatory testing which may not always be the case. It is also important to consider the emotional impact of believing the test result is reactive on the caregiver and their child. This can be investigated further in operational studies of caregiver-provided HIV testing. We do note, however, that in Phase 1 of our study, we did have caregivers who took OMT kits home to test their children and were not observed as would happen in routine implementation.

OMT testing for HIV is accurate in children and is now recommended by WHO and international implementing partners, such as PEPFAR, as a screening test for individuals aged 2 years and above.[14,24] Caregiver-provided HIV testing, such as self-testing, if rolled out is likely to be performed independently at home without any providers present. In a previous qualitative work from our group caregivers have expressed fears about making a mistake while performing the test and concerns about not having a health care provider present to support them; however, all package inserts from the OMT manufacturer do contain local hotline numbers for remote assistance.[13] This study shows that the most caregivers can perform the test independently without support from providers and also without prior demonstrations.

In our formative work, caregivers were also worried about dealing with negative reactions to an HIV positive result.[13] As with HIVST in adults, concerns about social harms in the form of intimate partner violence or gender-based violence are warranted. In HIVST studies among adults' social harm reports were infrequent in Malawi.[9,25] Our study had a very low HIV prevalence, however, among

TABLE 4. Interpretation of Oral HIV Test Results (N = 587)

	Caregiver Interpretation			
	Reactive	**Nonreactive**	**Invalid**	**Total**
Research assistant interpretation				
Reactive	4	0	0	**4**
Nonreactive	8	567	1	**576**
Invalid	1	0	6	**7**
Total	**13**	**567**	**7**	**587**

the children tested and those who were diagnosed with HIV no social harms were reported.

Key limitations of our study design are that demonstration was not allocated at random, and hence, the 2 groups that received and did not receive test demonstration may not have been comparable. This was due to the sampling strategy whereby the study was conducted in 2 phases, and an urban population was oversampled for the group that did not receive demonstrations. Another limitation of our study is possible observer bias. Caregivers may have performed the test better or more confidently because they knew they were observed. We also note the low number of HIV-positive children in our study as a limitation precluding any firm conclusion of interpretation of reactive results. Although our study does provide the first evidence for this testing strategy, we recommend further evaluations of caregiver-provided testing to facilitate collection of good surveillance and operational data to assess when, if, how, and where to roll out large scale caregiver-provided testing.

This study shows that task shifting from highly skilled health workers such as nurses in health facilities to caregiver may be a feasible strategy for earlier diagnosis of HIV in children.[12] This is a timely approach in the context of the ongoing COVID-19 pandemic where lockdowns have made it more difficult to access health facilities for any service including HIV testing.[26] In addition to collection from health facilities, OMT kits can be distributed in the community as was piloted in another study in Malawi.[27] Another key consideration for caregiver-provided testing is rapid and effective home linkage to HIV care for children who test HIV positive. Concerns about linkage to care in the context of adult HIVST programs have been raised; however, linkage to care can be supported in multiple ways including telephone or community follow-up and provision of incentives.[27,28] Evidence is limited, and further studies to assess linkage to and retention in care for children diagnosed through caregiver provider testing are warranted.

Acceptability of caregiver-provided testing must also be assessed. This testing strategy may not be acceptable for all caregivers because of its novelty which may require sensitization efforts before scale up. In addition, caregiver-provided testing may not be suitable for testing older adolescents who may not want to disclose their own sexual activity to caregivers.[18] Further evaluations of which user groups to target such as female caregivers reiving antenatal care in facilities, individuals already receiving care but with untested children, or individuals newly diagnosed with HIV as is performed with sexual partner testing may be useful.

The cost-effectiveness of caregiver-provided testing should also be assessed and should include assessments of the potential cost savings through reduced skilled health care worker time in facilities. At scale, health worker time may involve only distribution of OMT tests to caregivers from facilities and time to demonstrate OMT test use as was performed in Phase 1 of our study. In our study, lay workers with 3 weeks training on HIV testing and HIV self-testing through the Ministry of Health and Child Care in Zimbabwe conducted the demonstration thus indicating feasibility for this to be performed by lower cadre health workers.

We conclude that caregiver-provided testing is a feasible HIV testing strategy for children and recommend further operational research to support implementation at scale.

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8. Discussion

8.1 Research aims and studies conducted

The aim of this research was to evaluate the approaches for index-linked HIV testing for children and adolescents (aged 2-18 years). The following studies were undertaken:

1. Investigation of the acceptability, uptake and yield of index-linked HIV testing for children and adolescents offered in facility and community-based settings.
2. Exploration of provider and caregiver perceptions and experiences of index-linked HIV testing for children.
3. Evaluation of the diagnostic accuracy of the oral mucosal transudate HIV test for children and adolescents
4. Assessment of the feasibility and accuracy of caregiver provided HIV testing for children and adolescents.

In this chapter, the key findings, the strengths and limitations and the implications of the research findings are discussed. The chapter also includes a description of how the findings have been disseminated and opportunities for future research.

8.2 Discussion of findings

8.2.1 Index-linked HIV testing for children and adolescents

This research showed that almost 40% of children living in the households of indexes had not previously been tested indicating an unmet need for HIV testing for children. Index-linked HIV testing was an acceptable HIV testing strategy with over 87% of indexes accepting HIV testing for their children. These findings are

comparable to a study conducted in Malawi in 2014 -2015 that showed that 64.7% of indexes had a child or a young person (1-24 years) who had not been tested living in their household and uptake of HIV testing was also high at 93.5%.[1] Therefore, a targeted HIV testing strategy such as index-linked HIV testing is a suitable strategy to reach children living with individuals already in HIV care.

Only 60% of eligible children were tested in this research; 2424 eligible children were not tested during the study for various reasons including refusals from indexes and children not found during tracing despite multiple attempts to follow up over 21 days from the day HIV testing was offered. As such despite targeted efforts, many children and adolescents in this study still remained untested possibly due to index fears about an HIV positive diagnosis for their child(ren), stigma or feeling that they are not yet ready for the child(ren) to test. It was difficult to trace some indexes during follow up as they had given false phone numbers and addresses which may have been indicative of indirect refusals for the reasons noted previously. It is likely that as HIV testing strategies are scaled up, the residual individuals who are not tested are likely to be those that are the "hardest to reach" and will require concerted and more resource-intensive efforts. One potential strategy is the use of incentives in tandem with index-linked HIV testing whereby indexes can be offered incentives to bring their children for HIV testing. Incentivisation has been used to encourage uptake of other public health interventions e.g., immunisation, but does raise ethical concerns about coercion.[2,3] The considerable risk of leaving a child undiagnosed vs the risk of coercion needs to be considered. Also, in the context, of HIV infection in children (most likely acquired perinatally and therefore no ongoing

risk via sexual transmission until they reach adulthood) incentivisation would be a one-off event. Two studies conducted in Kenya and Zimbabwe among children and adolescents showed higher HIV testing uptake in groups where an incentive for HIV testing was offered.[4,5] In the study from Kenya the provision of USD5, USD10 and USD15 incentives to mothers for HIV testing of their children younger than 12 years of age increased uptake of HIV testing to 73% compared to 14% in similar settings with no incentives.[5]

8.2.1.1 Facility vs community-based HIV testing approaches

Facility-based HIV testing was the most preferred method (66% of indexes chose facility-based HIV testing) when compared to community-based HIV testing. However, many children were later tested in the community (in this study indexes who initially chose facility HIV testing but did not present at the facility were followed up in the community). 13% of children whose indexes had initially chosen facility-based HIV testing were later tested in the community. This highlights the benefits of flexibility in test location and offering both facility and community-based HIV testing to improve HIV testing uptake. Community-based strategies can bring HIV testing closer to the individual, and this study showed that this approach is feasible and could be used as a supplementary tool to help in improving completion of the HIV testing process. A review of studies evaluating index-linked HIV testing e showed there is variation in uptake of community vs facility-based HIV testing in different geographical contexts. In contrast to this research where the majority (66%) of indexes preferred for their children to be tested at the facility, over 95% of tests conducted in Malawi were done in the indexes home while in Cameroon 94% of indexes preferred facility-

based HIV testing and subsequently 82% of children tested were tested in the facility.[1,6]

This variation may be due to a number of factors including social, cultural and contextual factors unique to each country. These factors may include the stigma associated with HIV in the country and access barriers such as the distance to the nearest health facility in each study setting which were not captured by these studies. The quantitative and qualitative findings of this research show that the distance and costs an individual needs to travel to access a facility can influence test uptake and also their decision to either come to the facility to have their children tested or have a provider come to their household to provide HIV testing.[7] In this study, indexes who had to pay anything to travel to access the health facilities were less likely to have a child in their home tested. Furthermore, indexes who lived in urban settings, those who had to pay to access a facility and those who had been on treatment for longer were more likely to choose community HIV testing for the children in their households. Individuals who have been on treatment for longer may have already disclosed their HIV status to others living in their households and were therefore more comfortable with having their child tested in their home. Furthermore, community-based HIV testing means that caregivers do not have to bear the additional cost of transporting their children to the health facility. An economic modelling analysis of the cost-effectiveness of community-based HIV testing in South Africa found home-based HIV testing could reduce HIV associated morbidity and HIV infections and was subsequently cost-effective.[8] A modelling study among pregnant women and their male partners in Kenya, also found home based HIV

testing to be cost effective.[9] However, none of these evaluations have included young children.

The findings of this study and the variation observed in the uptake of community and facility-based HIV testing highlight both the potential of community-based HIV testing strategies to increase uptake of HIV testing for children and adolescents but also the need for flexibility and choice to be built into HIV testing approaches in relation to the local and individuals' context.

8.2.1.2 Barriers and facilitators of index-linked HIV testing

Costs to travel and distance to facilities remain barriers to HIV testing. However, these can be mitigated by the provision of community-based HIV testing strategies which have also been shown to be effective in identifying some hard-to-reach populations such as men in other settings.[10] As noted above, offering a combination of HIV testing strategies such as facility and community-based HIV testing as was done in this research can further increase reach of HIV testing.

This study showed that female indexes were more likely to have children tested, a finding similar to that from a Cameroonian study on index-linked HIV testing (60% in Cameroon and 56% in Zimbabwe).[6,11] Generally, it is well-recognised that men have poorer engagement with health services than women, but they are often the gatekeepers in African contexts and have the ability to influence uptake of HIV testing for the household, and therefore engaging and targeting men is important if HIV testing rates in children are to be improved .[12]

Public health programmes often undervalue the human context in which they are delivered. The research described in this thesis sought to explore ways through

which this targeted strategy can be enhanced to further improve the uptake of index-linked HIV testing for children and adolescents by gathering provider and index perspectives of the strategy. The findings show that HIV testing for children is not a one-off event and should be approached as a process using a family centred focus for it to be more acceptable.[7] Many caregivers stressed the need to consult with other family members and often the adolescents themselves, a process which takes time, before having an HIV test. Several studies have previously shown that social factors such as the inadvertent disclosure of the parents' HIV status when a child tests positive, concerns about disclosure of the child's status to the wider family or to those outside the family or parental guilt about having infected their child impact the decisions of guardians to have their children tested. Active discussion and support to navigate these issues by providers is crucial to help individuals make a decision.[12,13] Our study shows that an approach which incorporates support and counselling is important in the context of index-linked HIV testing for children.

This study showed that there is a need to improve the quality and content of messaging currently provided on the importance of HIV testing for children and adolescents. This research showed that in routine HIV care, indexes are not aware of the need for testing their children despite constant exposure to facilities and being in care themselves. Often HIV testing for children is not offered. Many caregivers in care were not aware that HIV testing for children was available and important. Messaging about HIV testing provided in health facilities was not specific to children and adolescents and as such caregivers did not engage with HIV testing for their children. As such HIV testing for children is not emphasised

as an integral part of HIV care for indexes, although it should be. Once caregivers became aware of the need for having their children tested, they stressed that the "way" in which the providers (study staff) engaged with them and provided support to caregivers and their families facilitated them to take up HIV testing for their children. In busy HIV programmes, frequent training of health workers to focus on the HIV testing of children and facilitate this by supporting caregivers needs to be emphasised if index-linked HIV testing is to be effective. Although index-linked HIV testing has been recommended in the Zimbabwe National HIV Testing Guidelines since 2014 and the procedures defined in the 2015 Zimbabwe Operational and Service Delivery Manual for HIV, over 40% of children living with an index had not previously been tested.[14,15]

8.2.1.3 HIV Testing in older children and adolescents

Notably, older children and adolescents were also less likely to be tested when compared to the younger age groups.[6,11] Qualitative research highlighted HIV testing barriers specific to older adolescents. Indexes noted that older adolescents are also at risk of horizontal HIV transmission but may not have disclosed their own sexual activity to their parents or caregivers. As such an index-linked HIV testing strategy, whose premise is that the children of individuals who are HIV-infected will be at higher risk of perinatal HIV (due to MTCT), indirectly excludes the isosexual sexual risk and is not an ideal strategy for identifying adolescents who are at risk of also being infected horizontally. This study however adopted a broader approach to the traditional index-linked HIV testing in that any child aged between 2-18 years living in the household but not necessarily the biological child of an index was eligible. The rationale for this

approach was that there may be a clustering of factors that go beyond biological risk (i.e. risk of mother-to-child transmission) that may put children living in households with individuals who have HIV at greater risk such as poverty, level of education and lack of social capital which have previously been identified as determinants of health in the context of HIV.[16,17] In addition, testing all children in the household circumvents the potential stigma and issues such as inadvertent disclosure of HIV status of parents when using a strategy that doesn't completely rely on HIV testing of biological children of individuals with HIV.

In this research some indexes felt that adolescents should be approached directly rather than through their caregivers, in order to respect their autonomy.[18] As noted above some adolescents may not be disclosing their sexual activity to their parents and may fear indirect disclosure of this through the HIV testing process. Additional strategies tailored specifically for adolescents, who may be at risk of both sexually and perinatally acquired HIV infection, should be evaluated. A study conducted in Malawi in 2012 showed that adolescents aged 16-18 years where more likely to self-test in the community when compared to older age groups which may highlight the adolescent needs and desire for autonomy in the HIV testing process.[19] The PopART study in Zambia found that community-based HIV testing using a door to door approach improved knowledge of HIV status from 27.6% to 88.5% among adolescents aged 15-19 years at the end of the intervention.[20] There is significant social, biological, cognitive heterogeneity across childhood and no one size fits all strategy for HIV testing for different age groups. HIV testing strategies developed for adults may not be suitable for testing

children. Similarly, HIV testing strategies effective for younger adolescents may not be effective for older adolescents.

8.2.1.4 Yield of HIV testing

The HIV yield was low (0.6%) when compared to other studies of index-linked HIV testing in SSA. In Kenya, the HIV yield among children aged 0-14 years who had undergone index-linked HIV testing in 2015/2016 was 4.5% and significantly higher than that from children tested through PITC (1.6% yield).[21] Similarly in Lesotho index-linked HIV testing yield for children aged 2-14 years was 1.4%, again much higher than that observed in other HIV testing models (0.4%).[22] The findings from Kenya and Lesotho are similar to those from studies on index-linked HIV testing in children in Malawi and Cameroon.[1,6] The lower than anticipated yield among children and adolescents in this study may be due to the high coverage of PMTCT programmes in Zimbabwe. In 2018 the proportion of pregnant women with HIV accessing ART in Zimbabwe was 94%, compared to 80% in Cameroon and 77% in Lesotho, which may mean there is a higher prevalence of children with HIV, including those who may not have been identified by EID in the PMTCT programmes, in those settings.[23] Additionally, the low HIV yield may potentially be indicative of further barriers in the index-linked HIV testing approach .

8.2.1.5 Linkage to care and treatment

While HIV testing is the first step in the HIV care cascade it is followed by the important requisite of linkage to care, retention in care and also viral suppression for those who test HIV positive.[24] Although my thesis was focused specifically on HIV testing I evaluated the rest of the HIV care cascade as part of the main B-GAP

study. Among the 39 children who tested HIV positive in this research, 36 (92.3%) were registered with a facility and initiated on treatment within 12 months of diagnosis. According to UNAIDS, globally only 53% of children (0-14 years) living with HIV were accessing ART in 2019.[25] Therefore, linkage to care in this study was much higher than global estimates for ART among children. This may be due to a home visit intervention delivered to children who tested HIV positive as part of the B-GAP study.

8.2.2 Caregiver provided HIV testing using OMT tests

This research showed that the OMT test had high sensitivity and specificity (100% and 99.9% respectively) when compared to national HIV testing algorithms in children aged 2-18 years. This head-to-head comparison of the OMT test with rapid blood-based tests used in routine care in ART-naïve children had not previously been conducted. Preceding studies evaluating OMT tests use were conducted among children on ART or used an enzyme-linked immunosorbent assay (ELISA) as the gold standard against which OMT tests were compared, which is not used for routine HIV testing. While comparison with the ELISA test can evaluate internal validity, comparison of the OMT tests with the rapid blood-based tests that are used for routine HIV testing enables evaluation in operational settings. A 2011 study compared the performance of oral specimens to direct blood spot specimens in 1274 children of unknown HIV status using ELISA tests; the sensitivity of the oral specimens was only 48.8% and the specificity was 98.5%.[26] Since 2011, improved OMT tests have been developed with better performance and with results available within 20 minutes

and subsequently received WHO prequalification as rapid HIV testing device in 2017.

Several studies have shown that false negative tests can occur if the OMT test is used in those taking ART. A 2016 study from Zimbabwe in 126 children aged 7-18 years who were known HIV positive and on ART and underwent OMT testing found that there was a negative result in 11 (8.5%) of children and was indeterminant result for 2 (1.6%) children while the blood-based test was negative for only one child.[27] Thus further highlighting the potential for false negative results in children that are already on ART.

By July 2017 there was only one OMT test that had received WHO prequalification, and only for individuals >12 years.[28,29] OMT testing is less invasive than blood-based testing and therefore may be more acceptable for testing children. It is also easier to administer in community-based settings by lay individuals including caregivers.[30]

Validation of the OMT test meant this was an additional tool which could be used for the diagnosis of HIV in children and younger adolescents. However, the performance of the OMT test is also dependent on correct sample collection, following correct test procedures and correct test interpretation. The research (described in chapter 7) showed that caregivers were able to accurately collect the sample and perform the OMT test on their children. Additionally, most caregivers were able to correctly interpret the OMT test result although eight caregivers incorrectly interpreted non-reactive tests as reactive. These findings build on findings from studies which show that adults can reliably and accurately self-test for HIV.[31] In addition, this research showed that prior demonstrations

from providers of how to perform the test can improve performance of HIV testing by caregivers. It is important to note that if rolled out at scale, demonstrations by providers may not be possible.

Potential benefits of caregiver provided HIV testing for children and adolescents include the privacy and autonomy for caregivers to find out the HIV status of their child(ren) first as well as the added convenience whereby HIV testing can be conducted in the home and caregivers do not have to travel long distances or pay for transportation costs to get their children to a health facility for HIV testing. Possible harms include the lack of provider support in the HIV testing process particularly if a child has a reactive OMT test in the home.[32] A qualitative study conducted in Zimbabwe found that caregivers had concerns about their ability to perform the test without assistance and were anxious about having a reactive test alone. However, they felt counselling and assistance from health providers would help in alleviating these concerns.[32]

There have been concerns about possible social harms should children be tested outside facilities where caregivers (who are often women) do not have the additional support during the HIV testing process from health providers.[33] Gender-based violence is well documented and often blame for a child testing HIV-positive may be placed on the mother.[34,35] In this research no adverse events were reported. This is similar to other studies of HIV self-testing among adults where minimal adverse events nor major social harms were associated with HIV self-testing.[33,36] There is a possibility that subtle harms, which may not be easy to detect, could occur. These include inadvertent disclosure of the status of the parent to a partner or other household/family members who may not know,

matrimonial disharmony where either parent can be blamed for the positive HIV status of the child, feelings of isolation and stigma within households to the HIV positive child.[33]

As with any other HIV testing methods, there is also a need to consider the onward linkage to care for children who may have reactive OMT results and require confirmatory HIV testing and subsequent linkage to care if HIV positive. It was not possible to evaluate this in this research due to the low number of children who tested HIV positive using this testing strategy. However, as discussed above onward linkage to care is an important part of the HIV cascade and caregiver testing leaves the responsibility of linkage to care in the hands of the caregiver who at the point of HIV testing would not have any provider support. Factors such as time to linkage in comparison to facility-based HIV testing or any of the other community-based HIV testing approaches needs to be assesses as timely linkage to care and ART initiation has significant treatment benefits.[37]

Another consideration for the scale up of this HIV testing method is the cost effectiveness of OMT testing in comparison to routinely used blood-based HIV testing. A study from 2016 in Malawi reported that the costs of the OMT test makes HIV self-testing a more costly intervention when compared to blood-based HIV testing.[38,39] No cost effectiveness evaluations have been done in the context of caregiver provided testing for children and adolescents. This strategy may reduce the HIV testing burden on health providers and also reduce costs to caregivers who do would not need to incur costs to access health facilities. Research on the costs and cost effectiveness of caregiver provided testing in

comparison to routinely provided facility and community-based HIV is in progress.

8.3 Strengths and limitations of this research

The key strengths were that the study was conducted in public sector settings, had large sample sizes and included both rural and urban populations. For the validation of the OMT test in children data was combined from both Zimbabwe and Kenya to increase the power of the study. The research used both quantitative and qualitative methods which enabled exploration of context, caregiver and provider perceptions of index-linked HIV testing and exploration of individual experiences with the HIV testing strategies.

Limitations of this study were that although all the research was carried out in routine healthcare settings, the intervention was implemented by research staff. These staff were trained and dedicated to implementing study procedures and protocols. It is likely that this would not be the case in real life settings in Zimbabwe where health facilities are often understaffed and the staff that are present have a heavy workload and multiple roles. This could potentially affect their ability to offer index-linked HIV testing or to provide demonstrations of OMT tests to caregivers. At protocol design stage, it was proposed that screening and HIV testing be provided by clinic staff as well as partner organizations working in the community. However, during the formative work it became apparent that there were competing priorities for clinic staff and partner organizations who were driven by funders' targets to achieve high HIV yields and therefore HIV testing of children was not a priority, with greater efforts being towards actively seeking sexual partners of indexes due to the much higher yields

of HIV. These operational challenges are likely to persist in routine settings and highlight a potential limitation of generalising research findings that evaluate public health interventions to routine settings.

This research was conducted in the Matebeleland region of Zimbabwe which in addition to having the highest HIV prevalence nationally in also predominantly of the Ndebele tribal group, with distinct sociocultural norms from the Shona tribe which may have an impact on health-seeking behaviours and subsequently uptake of index-linked HIV testing.[40] Factors, such as the highly mobile population in the Matebeleland region could have affected uptake of HIV testing with many of the biological parents of children living and working in South Africa and Botswana, two countries bordering this region where better economic opportunities are available. This means that children in this region are often left in the care of grandparents or other relatives who sometimes felt they could not provide consent for these children to be tested. This is reflected in the quantitative data in Research Paper 3 and reiterated in the qualitative findings in Research Paper 4.

Other factors that could limit generalizability include structural factors such as configuration of health systems including availability of systems to deliver healthcare in community-based settings. Other cultural and social factors such as the HIV stigma and discrimination in different settings may affect acceptability of these HIV testing strategies.

8.4 Contribution of the thesis to improving HIV testing for children and adolescents

This study provides evidence that HIV testing for children in community settings can improve HIV testing uptake and that there is an added benefit from the provision of both facility and community-based HIV testing strategies. The editors of Lancet HIV commissioned an article (Appendix 1) based on Research Paper 3 titled, *"Rethinking the challenges of paediatric HIV diagnosis"*. The article highlighted that significant progress should have been made for the diagnosis of HIV in infants and children by now but continued efforts are still required to improve HIV testing for children and adolescents.[41]

The findings from this research show that in this setting facility-based HIV testing strategies are preferred but among other groups the provision of and availability of community-based HIV testing can improve access and remove cost barriers. While HIV testing by lay workers is recommended by WHO, many programmes have continued to use only nurses. This study shows that HIV testing by lay workers in community-based settings is feasible. Facility-based HIV testing should be strengthened as should the provision of index-linked HIV testing for children as part of routine HIV care. This will require investment in human resource capacity, improved messaging about the importance of HIV testing for children as part of routine HIV service provision and prioritisation of HIV testing for children as well as training and retraining of providers.

The finding of the robust performance of OMT tests in children resulted in WHO prequalification of OMT tests for HIV screening of children aged 2 -12 years by health providers in 2019 (Appendix 2). Findings from Chapter 7 demonstrate the

potential for of caregiver-provided HIV testing.[42] The Covid-19 pandemic has increased the load on health providers, shifted healthcare priorities and made access to health facilities for services such as HIV testing difficult due to prolonged and restrictive lockdowns.[43,44] In this context, the use of OMT tests by caregivers to test their children may help maintain and potentially improve HIV testing for children. In April 2020, in response to the COVID-19 pandemic, the President's Emergency Plan for AIDS Relief (PEPFAR) released guidance for countries to implement caregiver provided testing so that HIV testing for children could continue to be provided in the context of disruptions in health service delivery during the pandemic (Appendix 3).

This research shows that while index-linked HIV testing had high uptake, a proportion of children and adolescents still remained untested. There is need for ongoing and concerted efforts to ensure that children and adolescents with HIV, a vulnerable and hard to reach group, are not left behind if we are to realise our collective vision of an "AIDS-free" world.

8.5 Dissemination

The findings of this research have been disseminated at local and international platforms that included various stakeholders including researchers, study participants, national and international policy makers, programmers and donor organisations. Summarized below are key fora where I have presented the research findings.

8.5.1 Academic conferences and meetings

I presented oral and poster presentations during the course of my PhD at the following academic conferences and meetings:

1. Royal Society of Tropical Medicine and Hygiene, Research in Progress Meeting: London 2017
2. Institute of Continuing Health Education and University of Zimbabwe Medical Research Day: Harare 2018
3. International AIDS Society, HIV Adolescence Workshop: Cape Town 2018
4. Wellcome Trust Bloomsbury Centre for Global Health Research Scientific Meeting: Gambia 2019
5. International Conference on AIDS and STIs in AFRICA: Rwanda 2019
6. Conference on Retroviruses and Opportunistic Infections: Seattle 2019
7. Research Council of Zimbabwe International Symposium: Harare 2019
8. INTEREST Conference: (Virtual) 2020
9. London School of Hygiene and Tropical Medicine MRC International Statistics and Epidemiology Group (ISEG) meeting: (Virtual) 2021

8.5.2 Dissemination meetings

During the course of my PhD, I disseminated the preliminary and final research findings at the following meetings and directly to the following organizations:

1. Matebeleland South Provincial Health Team Meeting: Masvingo 2017
2. Harare Research Group Meeting: Harare 2017
3. National AIDS Council HIV research meeting: Harare 2018
4. Médecins Sans Frontières International : (Virtual) 2019
5. B-GAP Dissemination Meeting: Bulawayo 2020
6. Zimbabwe – LSHTM Research Partnership Dissemination Meeting: Harare 2020

7. Organization for Public Health Interventions and Development: (Virtual) 2020
8. World Health Organization, Catholic Relief Services, PEPFAR: (Virtual) 2020

In addition, I shared my PhD experiences on the University of London blog and the social media platforms of the British Embassy in Zimbabwe where this work was spotlighted.

The findings of my PhD have all been published in peer -reviewed journals (which form the basis of this thesis) and a policy brief has also been developed (Appendix 4). The policy brief on the topic of caregiver assisted oral HIV screening for children will be shared with the Ministry of Health and Child Care in Zimbabwe, WHO, CDC, USAID, the Office of the US Global AIDS Coordinator (OGAC), and Catholic Relief Services among others.

8.6 Opportunities for future research

Opportunities for future research include evaluation of the implementation of caregiver provided HIV testing in routine settings. Operational research to assess acceptability, feasibility and uptake of this strategy in routine settings and also in the absence of a provider will be useful in order to better inform implementation at scale and to understand how this strategy can be further targeted, adapted or improved. Potential adaptations could include targeting caregiver provided HIV testing to mothers receiving antenatal or postnatal care or targeting this strategy only for indexes who are newly diagnosed in settings where index-linked HIV testing has already been provided over long periods of time. Furthermore, when

implemented as part of future research, components such as linkage to care among children who test HIV positive and the rate of social harms through community testing by caregivers should be evaluated.

Studies that evaluate which HIV testing strategies are most acceptable to older adolescents as well as studies evaluating how to optimize the current HIV testing strategies for adolescents are warranted.

While index-linked HIV testing can improve uptake of HIV testing the costs of HIV testing are a critical consideration for developing policy and programmes. The cost implications of using oral HIV test kits which are more expensive when compared to rapid blood-based tests, need to be weighed against the cost of health provider time.[38,39] The costs and cost effectiveness of caregiver provided HIV testing for children and adolescents in comparison to routinely provided facility and community-based HIV testing by health providers should be evaluated.

8.7 Conclusion

This thesis has provided evidence for the uptake and yield of index-linked HIV testing for children and adolescents in facility and community-based settings in Zimbabwe. It has also provided evidence of the diagnostic accuracy of OMT tests for children as well a novel HIV testing approach whereby caregivers can accurately test their own children for HIV and interpret test results. Additionally, this thesis provided an in-depth exploration of some of the barriers and facilitators of index linked HIV testing for children which can be used to further

improve HIV testing uptake for children and adolescents using this HIV testing strategy.

The research provides timely evidence to guide HIV testing policy makers as well as implementers of index-linked HIV testing for a group which currently lags behind in terms of HIV testing uptake and where a concerted effort to target and improve HIV testing is required.

8.8 References

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9. Appendices

9.1 Appendix 1: Rethinking the challenges of paediatric HIV diagnosis

Rethinking the challenges of paediatric HIV diagnosis

Lancet HIV 2020
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For the **UNAIDS data on trends in antiretroviral and testing coverage for 2019** see http://aidsinfo.unaids.org/

Diagnosing infants and children with HIV was supposed to have been made easier. Several contact points now exist that create opportunities to complete the paediatric diagnosis process, including routine postnatal care visits and childhood vaccinations. However, achieving early infant diagnosis in the first few months of life has remained one of the lowest global HIV programme metrics. In 2019, antiretrovirals were delivered to 85% of pregnant women living with HIV worldwide, but only 60% of their infants were diagnosed at an age early enough to reduce the high rates of morbidity and mortality from perinatally acquired HIV.[1] Chido Dziva Chikwari and colleagues[2] sought to address this perennial challenge in their study, Bridging the Gap in HIV testing and care for children in Zimbabwe (B-GAP), on the uptake of facility-based and community-based index-linked HIV testing.

The research team developed the study after an extensive formal stakeholder engagement process to optimise the identification and testing of children and adolescents (age 2–18 years) at risk of having undiagnosed HIV.[3] Their strategy was to focus on households with caregivers living with HIV and in HIV care in both urban and rural settings, as the index patients of the programme. Families were offered three ways for their children to be tested: at a formal primary health-care facility by a health-care provider; in their homes by a community health worker; or in their homes by the caregivers themselves using an oral fluid test. The option to change the method of testing was available throughout the study.

Even in the context of this thoughtfully implemented study with a well resourced and experienced research team, only 1789 (62·3%) of the 2870 eligible index patients had at least one child in their household tested for HIV. The main challenge in two-thirds of cases was not being able to make contact with the children and adolescents, regardless of where or how the testing was to take place. The investigators identified factors associated with increased rates of acceptance and completion of testing that will be useful in guiding future efforts. Most notably, families were more likely to have their child tested if they chose a community-based option. However, their 0·6% testing yield (39 children testing positive of 6062 eligible children) by index-linked testing was lower than expected in comparison with other studies. This outcome might reflect bias in their tested population or the cumulative effect of increasingly successful maternal HIV prevention interventions in the country. However, these results should not take away from the linkage of 36 (92%) children who tested positive for HIV in the study to HIV care, representing a triple dividend of healthier adolescents who will become adults and future parents. Furthermore, we should take note that the median age of children testing positive was 11 years (IQR 8–15), which shows that the majority were adolescents with perinatally acquired HIV who were previously missed by the health care system.[4]

The B-GAP study shows that a differentiated HIV testing approach and task-shifting model (between health-care providers, lay health workers, and caregivers) can be successfully used to diagnose children and adolescents who were lost in the traditional health-care system. In addition, to reach UNAIDS targets for paediatric HIV testing and care,[5] we can and should allow for increased patient-driven flexibilities at several decision points. As informed by the study findings, we must become more comfortable as health-care providers, implementers, and policy makers with what is essentially self-testing in the context of paediatric HIV, in which a caregiver can administer a HIV test to their child in their home. The findings of Dziva Chikwari and colleagues are valuable clues to closing the gaps in the global paediatric prevention and treatment cascade.

Untested HIV-exposed children and adolescents represent some of the hardest to reach at-risk populations in low-income and middle-income country settings.[6] The B-GAP study reminds us that any intervention to improve paediatric HIV testing needs to appreciate the complex dynamics around parent-to-child HIV transmission, the consequences of orphanhood, and the financial burdens associated with accessing health care. To achieve an AIDS-free future for children, we must work from both ends of the paediatric age spectrum; by focusing on early infant diagnosis around the perinatal period, and by redoubling our efforts to find older children and adolescents who have been hidden from the usual HIV testing approaches for far too long.

AHS has received grant funding to her institution from ViiV Healthcare. L-GB declares no competing interests.

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1 Violari A, Cotton MF, Gibb DM, et al. Early antiretroviral therapy and mortality among HIV-infected infants. *N Engl J Med* 2008; **359:** 2233–44.

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9.2 Appendix 2: WHO Prequalification of In Vitro Diagnostics Public Report

WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: OraQuick HIV Self-Test
WHO reference number: PQDx 0159-055-01

OraQuick HIV Self-Test with product codes **5X4-1000, 5X4-1001 and 5X4-2001** manufactured in Thailand for **OraSure Technologies, Inc.**, **rest-of-world regulatory version**, was accepted for the WHO list of prequalified in vitro diagnostics and was listed 20 July 2017.

Summary of WHO prequalification assessment for OraQuick HIV 1/2 Self-Test[1]

	Date	Outcome
PQ listing	8-Apr-2016	listed
Dossier review	26-Jan-2016	MR
Site inspection(s) of quality management system	3 -5-Nov-2014	MR
Laboratory evaluation of performance and operational characteristics	28-Jan-2016	MR

MR: Meets requirements

Report amendments and/or product changes

This public report has since been amended. Amendments may have arisen because of changes to the prequalified product for which WHO has been notified and has undertaken a review. Amendments to the report are summarized in the following table, and details of each amendment are provided below.

Public report amendment	Summary of amendment	Date of report amendment
2.0	Introduction of a new configuration with an intended use specific for HIV self-testing (OraQuick HIV Self-Test). The new configuration (OraQuick HIV Self-Test) was adapted from their professional use product (OraQuick HIV 1/2 Rapid Antibody Test)	14-Jun-2016

[1] Dossier assessment and laboratory evaluation for the INSTI HIV Self-Test were adapted from the professional use product, OraQuick HIV 1/2 Rapid Antibody Test prequalified in 2016. Please refer to the WHO Prequalification of Diagnostics Programme PUBLIC REPORT for OraQuick HIV 1/2 Rapid Antibody Test https://www.who.int/diagnostics_laboratory/evaluations/pq-list/hiv-rdts/public_report/en/

	for which a WHO prequalification assessment had already taken place. Additional data was generated to meet requirements set out in the WHO Technical Specifications Series document TSS-1 Human Immunodeficiency Virus (HIV) rapid diagnostic tests for professional use and/or self-testing[2].	
3.0	Inclusion of a pharmacy distribution variant (5X4-2001) in addition to the existing community version (5X4-1000 and 5X4-1001)	8-May-2018
4.0	Inclusion of latest labelling and Correction of a typographical error.	20-Jun-2018
5.0	1. Add 1 IFU to the labelling on the pouched device and implement the use of a blank inner and outer pouch to allow for customization of country specific information on the pouch. Added a statement to the Public Report for PQDx-0159-055-01 indicating that country specific variations are documented through a suffix "###" to the product code. 2. Revision of the IFU from a double-sided single page to a single-sided single page. Added a limitation of the test in the IFU as follows "*This product has not been evaluated for use in self-testing for individuals younger than 12 years of age. For children ages 2-11, testing must be performed by a trained health care worker*". Revision of the inner pouch to utilize ISO 15223 compliant symbols and addition of a disposal bag to both the community and pharmacy versions of the test kit.	29-Nov-2019

Intended use[3]:

According to the claim of the manufacturer, "*OraQuick HIV Self-Test is an in-vitro diagnostic medical device (IVD) that is used for self-testing of antibodies for HIV-1 and HIV-2 in oral fluid. This test is intended as an aid to detect antibodies to HIV-1 and HIV-2 from infected individuals".*

Assay description:

[2] http://apps.who.int/iris/bitstream/handle/10665/251857/9789241511742-eng.pdf;jsessionid=E2718EC36EFD314EFE87E902244528E1?sequence=1

[3] This product is one that uses Protein A to detect human IgG antibodies. Protein A is also able to detect other classes of human antibody (IgA, IgD, IgE and IgM) but not as reliably as it does IgG. This product has been prequalified with respect to its ability to detect human IgG antibodies. Any claim to detect other types of antibodies on this kind of product has not been validated based on WHO prequalification requirements.

Assay description:

According to the claim of manufacturer, "*OraQuick HIV-1/2 is a visually read, qualitative immunochromatographic test for the detection of IgG antibodies to HIV-1 and HIV-2. The flat pad that contacts the gums is treated with a mild surfactant, and no materials of viral origin are used in the manufacture of the test. One cannot become infected with HIV by taking this test. The device is placed into the subject's mouth, so that the flat pad is between the cheek and the outer gums, then swabbed across the outer gum line. The device is then placed into a vial containing a premeasured amount of developer solution, and allowed to develop. Use only the stand provided to hold the developer vial. Fluid from the surface of the gums enters the device through the flat pad, then flows onto a test strip. As it migrates across the strip, it hydrates and mixes with a red-colored reagent (protein A bound to colloidal gold). IgG antibodies in the specimen bind to the reagent. If in turn the bound IgG antibody recognizes synthetic HIV-1 or HIV-2 antigen immobilized on the strip enclosed in the housing, a colored line forms in the 'T' (test) area of the result window. If not, no line forms there.*

Further up the strip, the colored reagent encounters an immobilized biochemical that recognizes human antibodies. The line that forms in this 'C' area of the result window is the control line. It demonstrates assay validity, indicating that the oral fluid contains IgG, that the strip is functioning properly, and that fluid is migrating appropriately through the device".

Test kit contents:

<table>
<tr><th colspan="2">OraQuick HIV Self-Test (community version)</th></tr>
<tr><th>50 pouched kits (product code 5X4-1000)</th><th>250 pouched kits (product code 5X4-1001)</th></tr>
<tr><td>Each pouched kit contains:
1 divided pouch with
- a single use test device; and
- a desiccant; and
- a developer solution vial
containing 1ml of phosphate buffer saline solution containing polymers and an antimicrobial agent
1 test stand
1 instructions for use
1 disposal bag</td><td>Each pouched kit contains:
1 divided pouch with
- a single use test device; and
- a desiccant; and
- a developer solution vial
containing 1ml of phosphate buffer saline solution containing polymers and an antimicrobial agent
1 test stand
1 instructions for use (IFU)
1 disposal bag</td></tr>
<tr><th colspan="2">OraQuick HIV Self-Test (pharmacy version)</th></tr>
<tr><th colspan="2">110 pouched kits (product codes 5X4-2001)</th></tr>
<tr><td colspan="2">Each pouch kit contains the same pouched device configuration as the community version, except the entire pouched device (containing inner pouch, test stand, and an IFU) will be folded and placed into a carton.</td></tr>
</table>

NOTE:
The inner pouch's product code is REF 5X4-0004 and suffix XXX is the designation for different versions of the IFU that are country specific due to required languages.

The outer pouch of the product has the suffix (i.e. numbers .001, .002, …). The inner pouch does not have a suffix because that is not country specific.

Product codes are listed as 5x4-1000, 5x4-1001 and 5x4-2001 are for the entire kit boxes, i.e. different sizes, configurations (pharmacy pack or community pack).

Items required but not provided:

Item
Clock, watch or timing device

Storage:

- Store and perform this test in a cool area.
- DO NOT use this test if it has been stored outside the acceptable temperature of 2 to 30 °C (36 °- 86 °F).
- This test should be performed at temperatures in the range of 15 to 37 °C (59 °- 99 °F).

Shelf-life upon manufacture:
30 months.

Warnings:
- Refer to current version of manufacturer's instructions for use.

Limitations:
- Refer to current version of manufacturer's instructions for use.

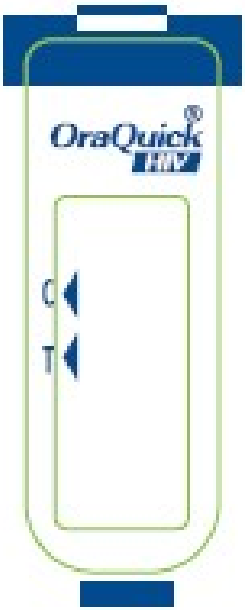
Commitments:
Final report of shipping stability to demonstrate the acceptable performance of the unit box and the device after shipping stressors, report due 31 March 2018. The commitment was closed.

Labelling

1. **Labels**
2. **Instructions for use**

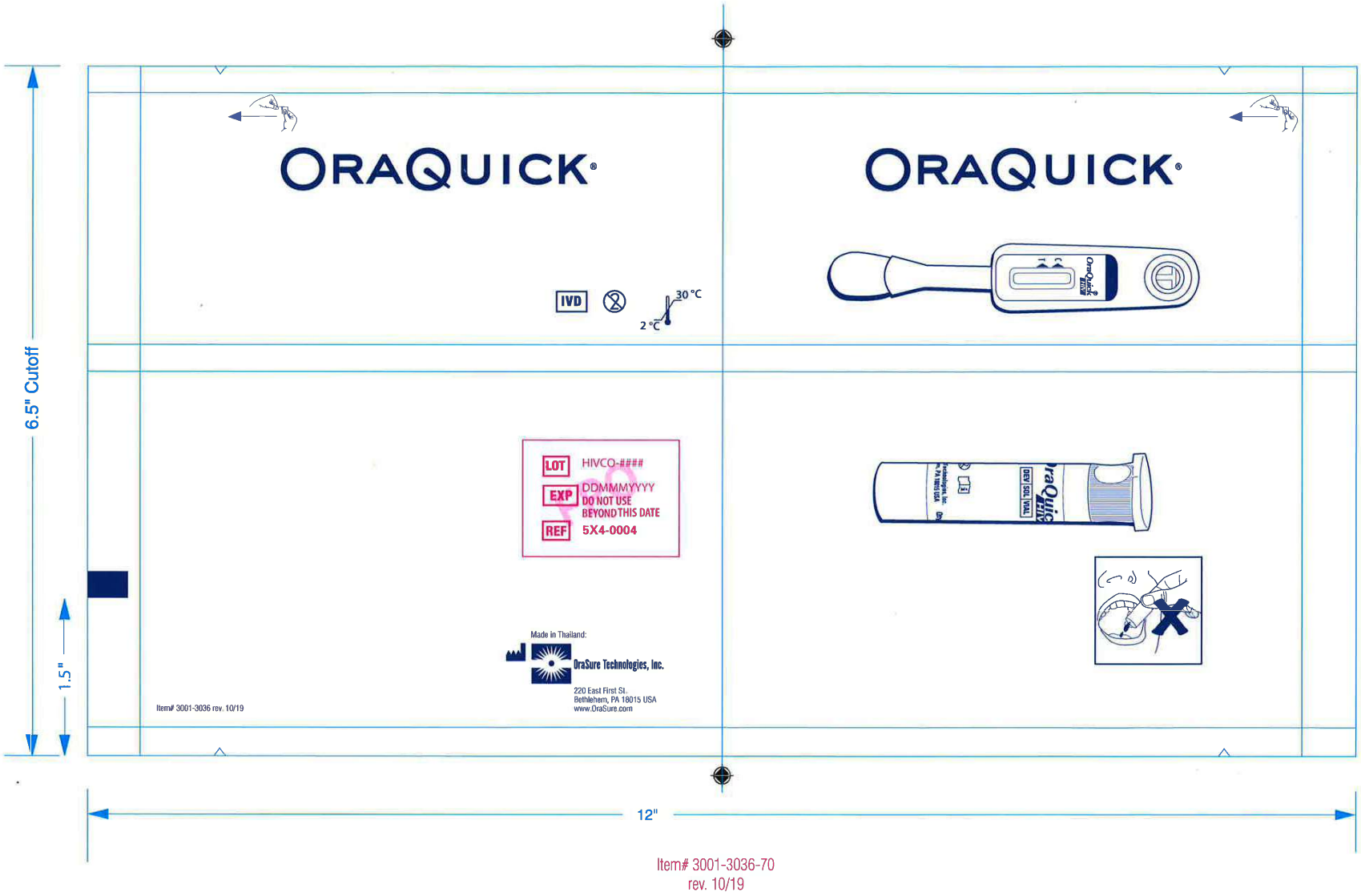
I. Community version

1. Device Label 3001-3035 rev 03/17



2. Developer Vial Label 3001-3034 rev 03/17

3. Inner Pouch 3001-3036 revision 10/19



Item# 3001-3036-70
rev. 10/19

PMS 288

4. Outer Pouch 3001-2824, revision 05/18

8″

5″

SCAN

VIEW INSTRUCTIONS

www.oraquickhivselftest.com

ORAQUICK®
HIV SELF-TEST

REFER TO TESTING DIRECTIONS INSIDE PACK

CONTENTS:

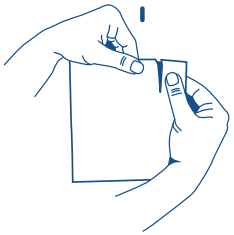
1 Instructions for Use
1 Test Device
1 Preservative
1 Developer Vial
1 Test Stand

IVD
IN VITRO DIAGNOSTIC USE

USE ONLY ONCE

30 °C
2 °C
STORE IN A COOL PLACE

TEAR HERE



TEAR HERE

Manufactured in Thailand for:

OraSure Technologies, Inc.

220 East First St.
Bethlehem, PA 18015 USA
www.OraSure.com

Item# 3001-2824 rev. 05/18

LOT HIVCO-####
BATCH CODE

DOM DDMMMYYYY
DATE OF MANUFACTURING

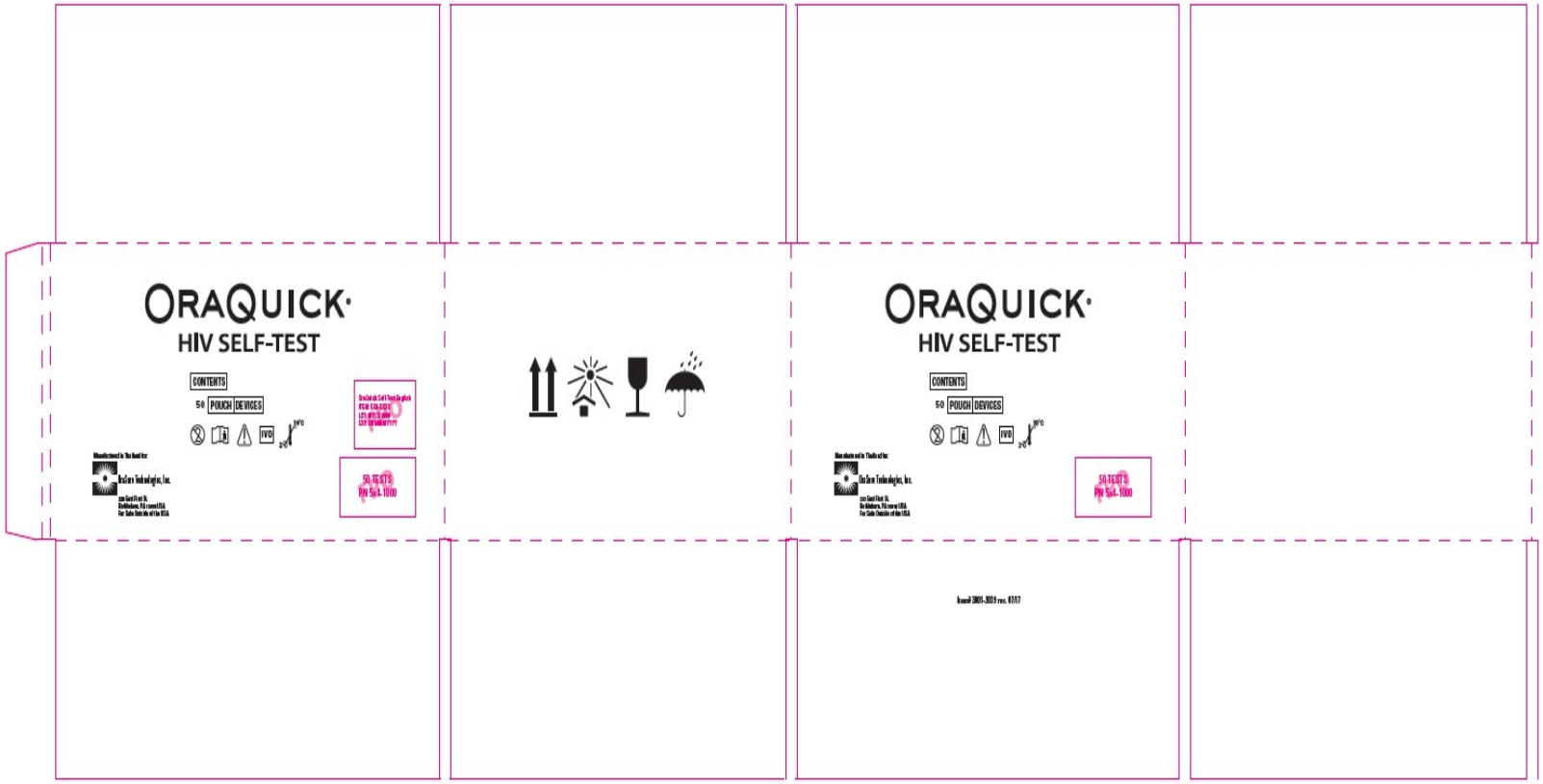
EXP DDMMMYYYY
DATE OF EXPIRATION

REF 5X4-0004.XXX
REFERENCE

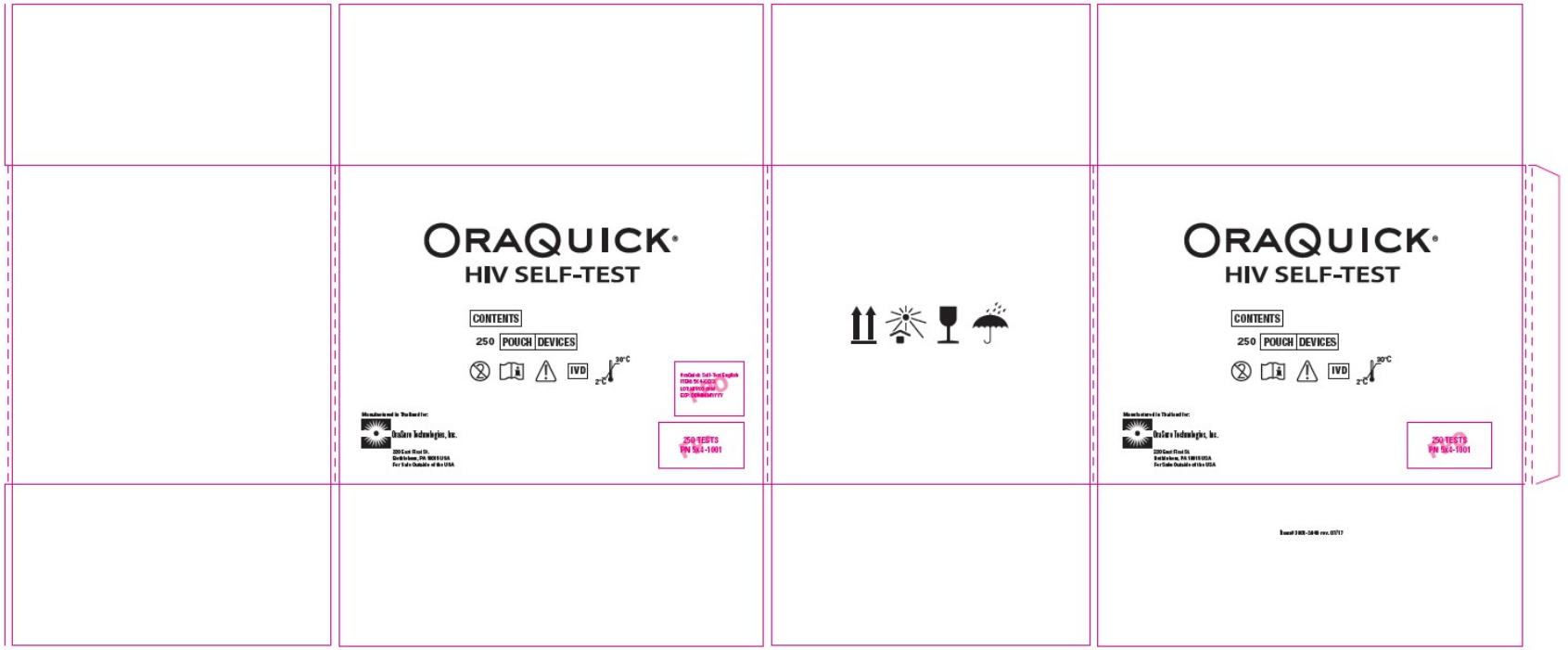
Item# 3001-2824-70
rev. 05/18

PMS 288

5. 50 Count Shipper Box 3001-3039 rev 07/17



6. 250 Count Shipper 3001-3040 rev 07/17



II. Pharmacy version

1. **Outer carton 3001-3042, revision 05/19**

ORAQUICK®
HIV SELF-TEST

For more information visit:
www.oraquickhivselftest.com

What is this test for?

OraQuick® is an Oral HIV Self-Test. HIV cannot be transmitted by saliva. This test works by detecting your body's natural antibodies that help you fight infection. Use only as an oral test. Use this test only as described in the instructions for use.

When should I use this test?

You should use this test if you want to know your HIV status. If you are infected by HIV, OraQuick® will detect antibodies and your test will be **POSITIVE**. If you are NOT infected by HIV, these antibodies will not be present and your test will be **NEGATIVE**. If you have been recently infected with the HIV virus, your body may not be making antibodies yet. **If you are using this test earlier than 3 months since a risk event and your test is NEGATIVE, you should test again 3 months after the risk event.** A 'risk event' is defined by any of the list of activities below:

- Sex (vaginal, oral or anal) with multiple sex partners.
- Sex with someone who is HIV positive or whose HIV status you don't know.
- Sex between a man and another man.
- Using illegal injected drugs or steroids.
- Shared needles or syringes.
- Exchanged sex for money.
- Having been diagnosed or treated for hepatitis, tuberculosis or a sexually transmitted disease like syphilis.

You can also use this test:

✓ If you are pregnant, test anytime.

When should I NOT use this test?

- Most people feel a little bit nervous when taking an HIV test. If you feel very nervous about taking the test, you may want to wait to take it, or get tested at a local clinic or testing center.
- If the box seal is broken or if any of the package contents are missing, broken, or open.
- If you are HIV positive.
- If today is after the use by date on the side of the box.
- If you are age 11 or younger.

ORAQUICK®
HIV SELF-TEST

FPO (Label)

Magenta box does not print

Label legend:

- IVD *In vitro* diagnostic medical device
- Do not reuse
- Consult instructions for use
- Caution, consult accompanying documents
- Temperature limitation
- LOT Batch code
- Use by
- REF Catalog number
- PN Part number
- Manufacturer
- Age restriction

Manufactured in Thailand for

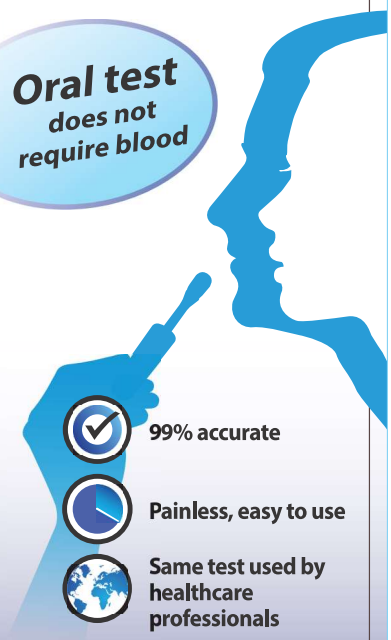
OraSure Technologies, Inc.

220 East First Street
Bethlehem, PA 18015 USA
(001) 610-882-1820
www.OraSure.com

Item# 3001-3042 rev. 05/19

ORAQUICK®
HIV SELF-TEST

Oral test does not require blood



99% accurate

Painless, easy to use

Same test used by healthcare professionals

For more information visit:
www.oraquickhivselftest.com

For *in-vitro* diagnostic use

Limitations of the test:

If you are on HIV treatment (ARVs) you may get a false result.

This test may not detect HIV infections that have occurred within 3 months of a risk event.

This product has not been evaluated for use in self-testing for individuals younger than 12 years of age. For children ages 2-11, testing must be performed by a trained health care worker.

See instructions for use and product Information for additional information.

OraQuick® provides an easy way to self-test for HIV. Testing on a regular basis is important to help stop the spread of HIV and AIDS.

OraQuick® is an oral swab-based test that does not require blood.

1 Single use test device

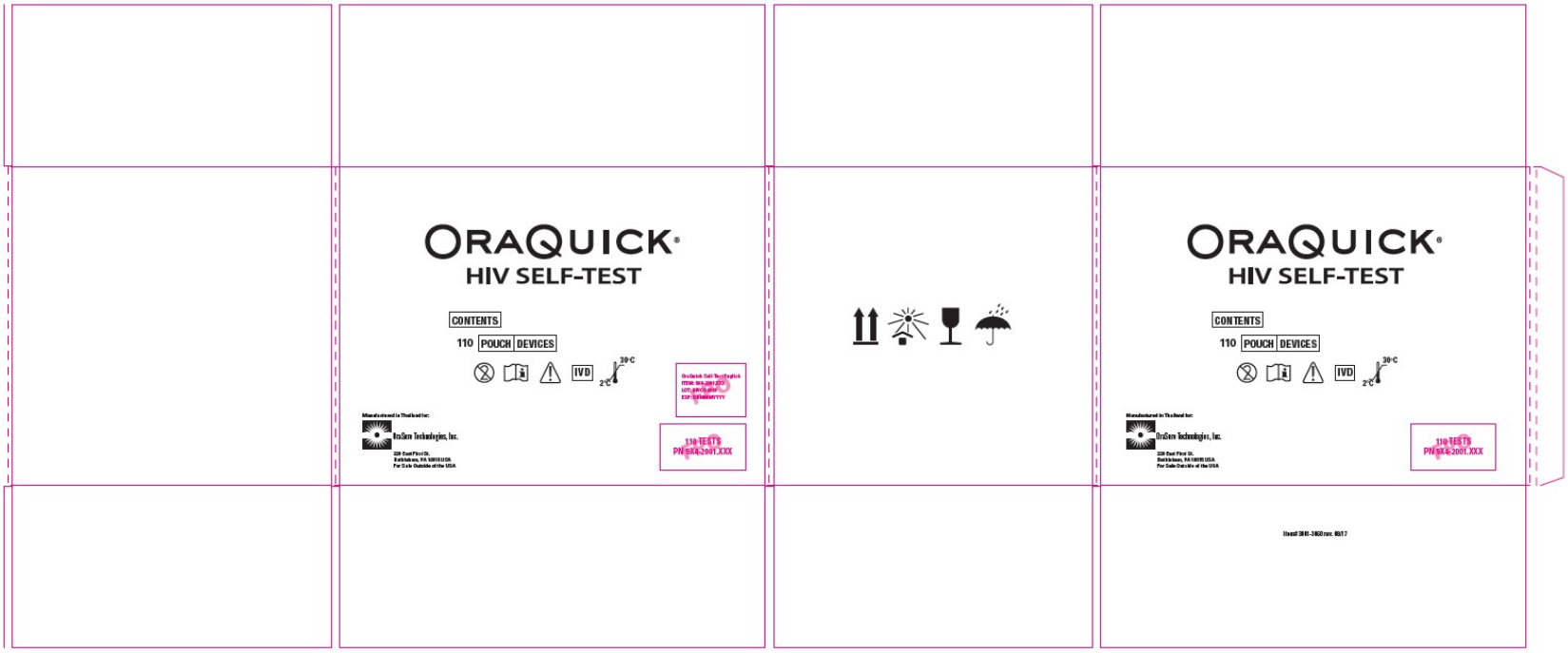
Contents

Single use self-test kit:
Test device, test tube (containing 1 mL of fluid), test stand, disposal bag, and instructions for use.

Not for Resale

Item# 3001-3042-70
rev. 05/19

2. Count shipper box (item # 3001-3060-70 rev. 08/17)



Item# 3001-3060-70
rev.08/17

7. Instructions for use [4]

[4] English version of the IFU was the one that was assessed by WHO. It is the responsibility of the manufacturer to ensure correct translation into other languages

For Outside USA Use Only • *In Vitro* Diagnostic Use • Do Not Reuse

ENGLISH
FRENCH

ORAQUICK®
HIV SELF-TEST

INSTRUCTIONS FOR USE

The OraQuick® HIV Self-Test is an *in-vitro* diagnostic medical device (IVD) that is used for self-testing of antibodies for HIV-1 and HIV-2 in oral fluid. This test is intended as an aid to detect antibodies to HIV-1 and HIV-2 from infected individuals. **You must follow the test directions carefully to get an accurate result.**

WARNING: If you are on HIV treatment you may get a false result. Clinical data has not been collected to demonstrate the performance of OraQuick® HIV Self-Test in individuals that are undergoing PrEP. **Do not eat or drink for at least 15 minutes before you start the test or use mouth cleaning products 30 minutes before you start the test.**

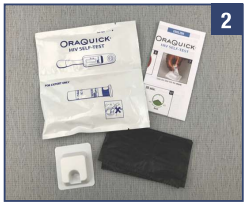
VIEW INSTRUCTIONS
www.oraquickhivselftest.com

HOW TO USE THE ORAQUICK® HIV SELF-TEST KIT

1

YOU WILL NEED A WAY TO TIME THE TEST

2

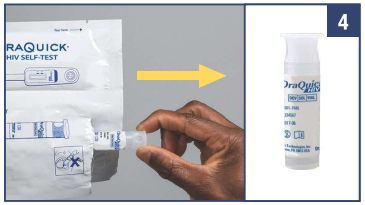


Kit contains: **test kit, test stand, instructions for use** and **disposal bag.** Remove these items to begin testing.

3

Your test kit contains two pouches.

4



Tear open the pouch containing the **tube.**

5

Remove the cap.

6

DO NOT pour out the liquid. **DO NOT** drink.

7

Slide the tube into the **stand.**

8

Tear open pouch containing the **test device** and remove. **DO NOT** touch the flat pad with your fingers. **DO NOT** eat or swallow the preservative.

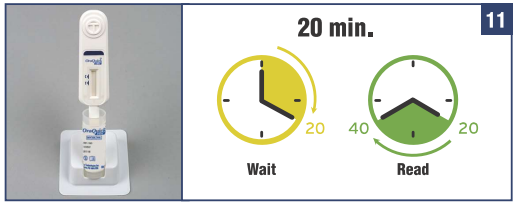
9

Press the **Flat Pad** firmly against your gum and swab it along your **upper gum once** (fig. 1) and **your lower gum once** (fig. 2).

10

Put the **flat pad** all the way into the tube until it touches the bottom.

11



LEAVE IT THERE for 20 MINUTES before reading the results. DO NOT read the result after 40 minutes.

INTERPRETING RESULTS — Read test results in a well-lit area

HIV POSITIVE RESULT

Two complete lines, even if the line is faint, means you may be HIV POSITIVE and you need to seek additional testing by a trained professional to confirm an HIV diagnosis.

99.4% of people (152 out of 153) correctly reported their result as positive. This means that 1 out of 153 people infected with HIV reported a negative test result. This is called a false negative.

As soon as possible . . .

Visit your nearest HIV Testing Centre or Health Facility

HIV NEGATIVE RESULT

IF READ BEFORE 20 MINUTES, RESULT MAY NOT BE CORRECT

ONE LINE next to the "C" and NO line next to the "T", your result is HIV NEGATIVE.

99.0% of people (717/724) correctly reported their result as negative. This means that 7 out of 724 people not infected with HIV reported a positive test result. This is called a false positive.

Seek regular testing. If you may have been exposed to HIV, test again in 3 months.

INVALID RESULT

If there is no line next to the "C" (even when there is a line next to the "T"), the test line or control line are not complete (all the way across the window), or a red background makes it impossible to read the test, the test is not working and should be repeated. **You will need to obtain another test.**

1.8% of study subjects (16 out of 900) failed to obtain a test result.

The test did not work properly.

Visit your nearest HIV Testing Centre or Health Facility to test again.

NOT SURE OF RESULT

You do not know your result or you are unsure of your result. Visit your nearest HIV Testing Centre or Health Facility to test again.

DISPOSE

Remove the test stick, put the cap on the test tube, place in the disposal bag provided and throw away all contents in the normal trash.

PRODUCT INFORMATION

REF 5X4-1000, 5X4-1001, 5X4-2001

WARNINGS AND PRECAUTIONS

- **DO NOT** use the test if you are HIV positive.
- **DO NOT** use the test if it has been exposed to household cleaning products (i.e. bleach).
- Remove dental products such as dentures or any other products that cover your gums prior to the oral fluid collection.
- If you have participated in a HIV vaccine clinical trial, you may get a positive result using this test, but it may not mean that you are infected with HIV. You should seek follow-up with your health facility.
- **DO NOT** use if any of the package contents are missing, broken, or open.
- If today is after the 'Use By' on the outside of the pouch, do not use this test.

LIMITATIONS OF THE TEST

- Oral bleeding may result in an invalid result. If the test result is invalid, visit your nearest testing center or healthcare facility.
- The OraQuick® HIV Self-Test may not detect HIV infections that have occurred within the last 3 months.
- For a positive result, the intensity of the test line does not necessarily equal the amount of antibody in the specimen.
- This product has not been evaluated for use in self-testing for individuals younger than 12 years of age. For children ages 2-11, testing must be performed by a trained health care worker.

INTERFERING SUBSTANCES AND UNRELATED MEDICAL CONDITIONS

If you are HBV, HCV or HTLV (I/II) positive, you may get a false result. It is recommended that users observe a 15 minute wait period after food and drink and a 30 minute wait period after using oral care products.

EXPLANATION OF SYMBOLS

LOT Batch Code	REF Catalog Number	Caution, Consult Accompanying Documents	Consult Instructions for Use
Do Not Reuse	IVD *In Vitro* Diagnostic Medical Device	Manufacture	EXP Date of Expiration
Temperature Limitation	Use By	Age Restriction	Date of Manufacturing

in Thailand for
OraSure Technologies, Inc.
220 East First Street, Bethlehem, PA 18015 USA
(+1) 610-882-1820 • www.OraSure.com

Item# 3001-3187 rev. 05/19

For Outside USA Use Only • *In Vitro* Diagnostic Use • Do Not Reuse

ENGLISH
KISWAHILI

ORAQUICK® HIV SELF-TEST

INSTRUCTIONS FOR USE

The OraQuick® HIV Self-Test is an *in-vitro* diagnostic medical device (IVD) that is used for self-testing of antibodies for HIV-1 and HIV-2 in oral fluid. This test is intended as an aid to detect antibodies to HIV-1 and HIV-2 from infected individuals. **You must follow the test directions carefully to get an accurate result.**

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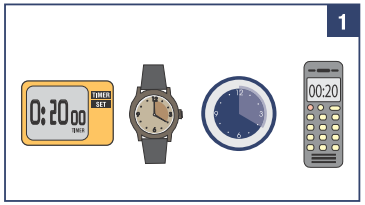
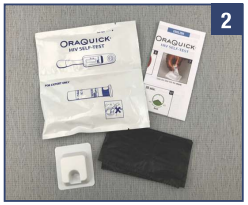
VIEW INSTRUCTIONS
www.oraquickhivselftest.com

HOW TO USE THE ORAQUICK® HIV SELF-TEST KIT



YOU WILL NEED A WAY TO TIME THE TEST



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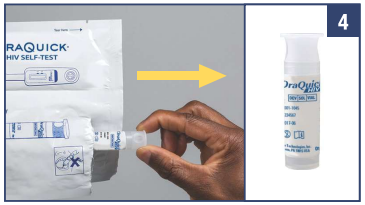


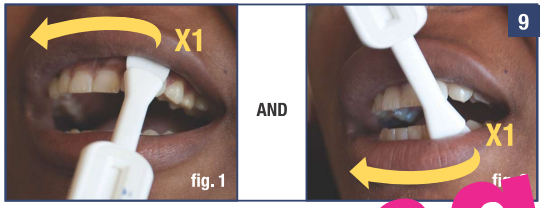
Tear open the pouch containing the **tube.**

Remove the cap.

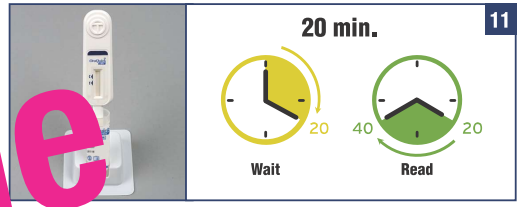
DO NOT pour out the liquid. **DO NOT** drink.

Slide the tube into the **stand.**

Tear open pouch containing the **test device** and remove. **DO NOT** touch the flat pad with your fingers. **DO NOT** eat or swallow the preservative.



Press the **Flat Pad** firmly against your gum and swab it along your **lower gum** (fig. 2).



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PRODUCT INFORMATION

REF 5X4-1000, 5X4-1001, 5X4-2001

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- **DO NOT** use the test if it has been exposed to household cleaning products (i.e. bleach).
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- This product has not been evaluated for use in self-testing for individuals younger than 12 years of age. For children ages 2-11, testing must be performed by a trained health care worker.

INTERFERING SUBSTANCES AND UNRELATED MEDICAL CONDITIONS

If you are HBV, HCV or HTLV (I/II) positive, you may get a false result. It is recommended that users observe a 15 minute wait period after food and drink and a 30 minute wait period after using oral care products.

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LOT Batch Code	REF Catalog Number	Caution, Consult Accompanying Documents	Consult Instructions for Use
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in Thailand for
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Item# 3001-3187 rev. 05/19

2nd Language

9.3 Appendix 3: PEPFAR Technical Guidance in Context of COVID-19 Pandemic

PEPFAR Technical Guidance in Context of COVID-19 Pandemic

In January 2020, a novel coronavirus, SARS-CoV-2, was identified as the causative agent of an outbreak of viral pneumonia centered in Wuhan, Hubei, China. The disease caused by this virus is called COVID-19. The disease is now widespread, and nearly every country in the world has reported cases. *https://who.sprinklr.com/*.

Widespread disturbances of international travel and shortages of medical supplies have led to challenges in the provision of medical care. In the areas hardest hit, medical facilities have been overwhelmed by large numbers of COVID-19 patients, and stay-at-home orders and staff illness provide additional challenges. During the COVID-19 pandemic, PEPFAR remains committed to continuing essential HIV prevention and treatment services, while maintaining a safe healthcare environment for clients and staff. In order to meet our commitment to uninterrupted care and treatment for PLHIV and the prevention of deaths among PLHIV due to HIV associated co-morbidities, PEPFAR is committed to adapting HIV services, so that PLHIV have the best possible outcomes within the context of stretched healthcare systems.

The evidence on the impact of COVID-19 amongst PLHIV is still scarce. There is currently no direct evidence that people with HIV are at higher risk of COVID-19, or of severe disease if affected. As more data becomes available from regions of high prevalence, we will continue to update the field on the effect of COVID-19 on PLHIV. HIV virological suppression is a critical intervention that improves the health of all PLHIV, and PEPFAR is committed to ensuring that PLHIV have uninterrupted care. Currently, there is no known effective treatment for COVID-19. We discourage the use of experimental therapies outside of registered clinical trials, as they may be dangerous. Drug-drug interactions with ART and other HIV related therapies may pose risks for our PLHIV clients.

Technical guidance is provided here for a variety of PEPFAR issues and will be updated routinely as the situation evolves.

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4. **HIV Treatment** 7
5. **HIV Testing Services** 12
6. **TB Services** 14
7. **Integrated Women's Health** 17
8. **Maternal Child Health (MCH)** 18
9. **HIV Prevention – General** 19
10. **HIV Prevention - PrEP** 20
11. **HIV Prevention – VMMC** 21
12. **Orphans and Vulnerable Children (OVC)** 22
13. **DREAMS** 24
14. **Key Populations (KP) Services During the COVID-19 Pandemic** 25
15. **Gender-Based Violence (GBV) & Child Protection (CP)** 26
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1. Guiding principles for the provision of services in PEPFAR-supported countries during COVID- 19 Pandemic

- ***Protect the gains in the HIV response:***
  Continuity of treatment for PLHIV is the foundation of PEPFAR programs during the COVID-19 pandemic. Several strategies are available and detailed in this document. Multi-month dispensing and decentralized delivery of medication form the basis of the PEPFAR strategy to maintain PLHIV on ART.

- ***The safety of PEPFAR-supported staff must be assured. If client services cannot be adapted to be performed safely, they should not be performed.***

- ***Reduce risk of transmission of COVID-19 among clients served by PEPFAR and PEPFAR-supported staff:***
  - All PEPFAR programs are under Chief of Mission authority; therefore, country teams and implementing partners should follow Embassy Front Office direction on all programming that requires personnel movement.
  - Minimizing patient contact with health facilities reduces risk to recipients of care and reduces the burden on these facilities. Health care facility visits should be limited to those that are medically essential.
  - Community programming should support social distancing and the use of alternative methods of communication to maintain contact and provide support to enrollees. These methods include virtual and digital platforms such as calls, SMS, social media, WhatsApp. Plans should be in place to adapt programming should service be disrupted.
  - Group-based activities should follow local guidelines for mass gatherings, and in-person group-based activities may need to be paused.

- ***In consultation with host governments, PEPFAR Operating Units (OUs) have flexibility to determine how best to continue to serve clients with HIV prevention and treatment services in areas affected by COVID-19 using the FAQs as a guide.***

2. Today's Updates

April 24, 2020

- ***Telehealth***– see Human Resources for Health pg.6
- ***Adolescents/Youth Living With HIV (A/YLHIV) Support Groups*** – see HIV Treatment pg.9
- ***Faith and Communities Initiative Justice for Children update*** – see Faith and Community Organizations pg.28

3. Human Resources for Health (HRH)

PEPFAR-supported cadres should follow host government guidance on home visits and avoid unnecessary in-person interactions with clients in facilities and communities to reduce exposure to, and spread of, COVID-19.

How should PEPFAR-supported healthcare worker (HCW) staffing be modified to maintain essential HIV services?

- Reconfiguration of service delivery teams
- Task shifting/sharing
- Redeployment

PEPFAR programs should be prepared to manage staff through these challenging times, which could include quarantine, infection, increased caregiving responsibilities at home, absenteeism or social disruption. PEPFAR programs should stay abreast of health worker challenges and constraints and should track and report all changes made to HCW staffing due to COVID-19 to PEPFAR country staff.

PEPFAR-supported HCWs should be prepared to deliver the essential HIV services using service delivery teams that may be rapidly and regularly reconfigured in response to staffing shortages. Staff should be prepared for task-sharing of essential services where allowed, and work with MOH and policy makers to allow emergency task-shifting where formal task-shifting policies are not in place. PEPFAR staff whose regular services may have been temporarily paused or delayed (e.g., VMMC, roving TA) should be repurposed and redeployed to support essential HIV services (e.g., treatment services). Refresh or build capacity in the new role through rapid training as necessary. Every effort should be made to retain the health workforce that PEPFAR supports, including repurposing into new roles to support HIV services for the duration of the pandemic and redesigning how services are delivered to make it safe for PEPFAR-supported staff to continue to work.

A critical element of the PEPFAR response to COVID is decentralized services. To this end staff may be temporarily repurposed to move services out of the facility and into the community wherever possible and safe. Staff may be reallocated to community-based ARV distribution for example. Where possible, digital applications or telehealth technologies should be utilized to remotely provide services. HCWs should be supported with the tools, airtime and data required, as well as training and scripts to use the technologies effectively and protect confidentiality and privacy. PEPFAR Technical Assistance (TA) providers should provide TA through telephone or digital applications in lieu of site visits.

What training is required to prepare PEPFAR HCW to respond to HIV in the context of COVID-19?

PEPFAR-supported HCWs should receive refresher training in Infection Prevention and Control (IPC) to protect themselves and HIV patients from COVID-19. While delivering HIV services, all HCWs should be equipped to provide COVID-19 risk communications to at-risk populations and PLHIV. As appropriate to their HIV service delivery role, HCWs should be trained to screen HIV patients for COVID-19 and refer as required for testing and treatment. HCW should be provided with in-country COVID guidance and case referral information (hotlines, facilities, etc.).

All training should be provided virtually using online platforms or printed job aids. Use international and national sources whenever possible. WHO is regularly updating available COVID-19 trainings at:

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/training/online-training. Utilize digital applications such as WhatsApp, Facebook Messenger groups or the ECHO platform for regular and routine information sharing with HCW staff.

What actions should be taken to safeguard PEPFAR HCW, beyond PPE?

PEPFAR programs should follow host country and WHO guidance on minimizing HCW risk of contracting or spreading COVID-19. Identify every opportunity to support HCWs to do their jobs in a different, safer way. PEPFAR programs should report all concerns regarding HCW staff safety and movement in communities to PEPFAR country staff.

- Support HCW safety within the communities they serve by securing authorization from local authorities for continued work, and work with local governments and civil society to raise awareness in the community, in particular for lay workers such as community health workers or social workers responding to violence against children. Consider introducing a uniform, bag, or other marker to aide law enforcement/community in readily identifying CHWs on official duties and provide CHWs with documentation of their role and authorization to continue work.
- Support HCW staff to use transportation methods that reduce risk of exposure while traveling to and from work, and when delivering services in the community (i.e. refrain from public transport). Consider introducing a transport stipend or arranging transport.
- Be aware and sensitive that HCWs may have underlying conditions that may affect their outcomes if they contract COVID-19, consider offering opportunities to staff to safely and discretely transition to roles away from the front line if they are concerned.
- Provide clear guidance to HCWs on OU national policies and applicable international policies that provide for workplace rights for safety, self-quarantine, and time off for caregiving of sick family members.
- Reduce in-person contact for routine administrative tasks, such as using digital payment mechanisms to ensure continuity of salary and stipend payments.
- Support HCW staff wellness through coaching or provision of psychosocial support to manage stress and avoid burnout.
- Ensure that HCW staff are kept abreast of relevant technical updates on COVID-19.

How should PEPFAR-supported cadres work with children and families in households?

Home visits, when necessary, can still achieve important objectives. Key considerations include:

- Home visitors should help to ensure that all PLHIV have access to six months MMD, ideally through community-based distribution points, to maintain adequate supply of ARVs at home.
- To protect home visitors and beneficiaries, every effort should be made to use phone calls and/or text messages to communicate and avoid making a home visit.
- Home visitors who are at higher risk for severe COVID-19 (e.g., elderly, diabetic, or have other chronic conditions) should avoid conducting home visits. Home visitors should NOT visit beneficiaries if the visitor has any symptoms of acute illness, especially fever, cough, or shortness of

breath, even if the symptoms are mild. Home visitors should NOT visit beneficiaries known to have a recent exposure to a person who tested positive for COVID-19 or is suspected of having COVID-19.

- To ensure safety and well-being of both home visitors and families, program staff should determine whether a home visit is absolutely essential.
- Many issues can be managed through counseling by phone. If unable to communicate via phone, situations that may warrant a visit include: 1) a critically ill beneficiary that urgently needs transport assistance to the clinic or hospital, 2) a child or adult exposed to physical harm, abuse or neglect requiring urgent attention, 3) CLHIV (or adult due to disability or other limitation) who cannot access ART and is in danger of treatment interruption.
- If the visit is deemed essential, ensure appropriate measures, including personal protective equipment (PPE) if available, are in place before, during, and after the visit and that both OVC staff and the client(s) consent to a visit. Once the family is stabilized, focus should then be to assist with 6mo MMD and/or drug pick-up from a community-based distribution point to ensure adequate supply of ARVs at home.

Telehealth

How should PEPFAR-supported cadres protect client confidentiality and privacy when using digital applications or telehealth technologies?

PEPFAR programs are encouraged to use digital applications or telehealth technologies to enable HCWs to continue providing support to clients while minimizing in-person contact during the COVID-19 pandemic. As programs increase their use of technology for virtual/remote patient contact, they are encouraged to develop standard processes to safeguard the confidentiality and privacy of clients. Key considerations for standard operating procedures include:

- Use of virtual technology is consistent with National Guidelines
- Develop guidelines for the HCW's environment at the time of the conversation in order to ensure client privacy.
- Confirm clients their individual preferences (in advance, when possible) on receiving calls, receiving voicemails, and receiving SMS messages.
- Before initiating a voice call, always confirm whether the client is in safe/comfortable environments to discuss their health care before initiating conversations about sensitive health issues.
- Verify identity and receive client permission before discussing any health information.
- Develop guidelines for the HCW's environment at the time of the conversation in order to ensure client privacy.
- Develop guidelines regarding management of audio/video content (e.g. advising HCWs not to record/capture any content and developing safe channels for sharing client information).
- Develop guidelines for what content can be left in voicemails/sent via SMS to clients.

4. HIV Treatment

What is most important for PEPFAR teams to implement at this time?

Key principles for the PEPFAR response to COVID include continuity of ART therapy and accelerated decongestion of health facilities to minimize transmission of COVID-19 and protect PLHIV. The critical intervention for all programs and individuals is to accelerate and complete scale-up of 3-6 multi-month dispensing (MMD) of ART and decentralized distribution for all PLHIV including PBFW and children. If there are any barriers to MMD (such as sufficient ARV availability) implementation, programs should alert their S/GAC Chair and PPM and USAID immediately for advice and assistance and should immediately quantify the increased ARV needs to scale up MMD. USAID is working with PSM to consider the additional quantities that may be required beyond the amount budgeted in COPs; and additional PEPFAR funding to roll out MMD at a broader scale will need to be considered by S/GAC before additional TLD is procured to support a rapid implementation of MMD

How will clinical services for PLHIV be affected?

Guidance for continuation of essential medical service may be found here https://www.who.int/publications-detail/responding-to-community-spread-of-covid-19. Ensuring and maintaining HIV viral load suppression should be considered an essential medical service for PLHIV. Please see laboratory section for suggested prioritization of viral load testing. Routine viral load monitoring in stable patients may be delayed based on local circumstances.

Can clients initiating ART receive multi-month dispensing?

PEPFAR recommends that ALL PLHIV who are starting ART receive at least 3 but preferably 6 months of drugs. Phone or electronic follow-up may be helpful to assess and support adherence and to assess and manage side effects. Evidence from cohort studies indicate that <5% of clients initiating ART will require a change in ARV regimen in the first 6 months of treatment. Two forms of contact, as recommended in the COP 20 guidance, should be obtained in all PLHIV, especially in ART initiators.

What should I do about individuals who are on our books but have not accessed meds in in the last 3 to 6 months?

Every effort should be made **now** to trace individuals who have been lost to follow-up and provide them with the package of care and treatment that they require before COVID-19 disruptions worsen. This is a core principle of COP 20 and section 6.1.2 of the COP 20 guidance contains tools for tracking and tracing which may be adapted for use in the current environment. The HRH section of this document provides additional considerations for ensuring home visits are safe.

What about individuals who have been out of care for more than a year?

These individuals should have a CD4 performed to assess eligibility for the advanced disease package of care. If clinically unwell, these individuals should at least receive cotrimoxazole. If TB screen is negative, TPT may be provided if appropriate.

What if PEPFAR's recommendations for adapting HIV services in the context of COVID- 19 do not align with local policy?

PEPFAR operates in partnership with the host government, and under Chief of Mission authority. PEPFAR country teams are urged to work promptly and closely with national governments to effect temporary changes in policy that will allow uninterrupted essential HIV services to children, adolescents, pregnant and breastfeeding women, and adults while minimizing the recipients of care's interactions with health care facilities and health care workers during COVID-19.

Can clients still be counted as "TX_CURR" they are getting ARVs delivered but only having phone (or other virtual) contact with program staff instead of clinic visits?

Programs can continue to count clients on ART towards TX_CURR if the client is not more than 28 days from when, based on the last delivery, their ARVs would be expected to run out. Programs should continue to be available to serve clients on ART, but the interaction does not have to include in-person contact. Please see MER guide for definitions of TX_CURR and TX_ML.

We have stock of TLE in country. TLD rollout is underway, but we are having issues with supply. We also have EFV 200 in country. LPV/r pellet and granule rollout is underway but supply has been challenging. How should we prioritize treatment?

PEPFAR prioritizes continuity of therapy for recipients of care. Countries should carefully evaluate stock on hand and projected availability to determine the best options for all PLHIV, either transitioning to newer regimens or maintaining on current regimens. If an individual is stable on the current regimen and stock is available, irrespective of bottle size, it may be reasonable to continue the current regimen, with a plan to transition to optimized regimens (TLD, ped LPVr) in the future where appropriate.

How can the impact of COVID-19 be minimized for PLHIV supported by PEPFAR?

The critical intervention for all programs and individuals is to accelerate and complete scale-up of 3 to 6-month dispensing of ART and decentralized distribution.

What changes should be considered for adjusting the model of service provisions for PLHIV?

- The overarching goal is to minimize patient contact with health facilities and reduce the burden on these facilities.
- Health facilities should optimize clinic spaces in order to minimize potential exposure to COVID-19. Individuals with proven or suspected COVID-19 should be separated from where care is provided to other clients. Dedicated HIV clinic spaces where they do not already exist may be useful in accomplishing this goal.
- Through phone calls or SMS, facilities staff should proactively communicate with HIV clients using positive messaging about the need to stay healthy.
- Please see below on plans for MMD. Facilities should maximize convenient six-month refills where stock is available in the country pipeline. Supply plans should be reviewed immediately to ensure any changes to scale 6MMD rapidly are immediately placed as orders.
- Clients should preferentially receive their drug supplies outside of the health facility. These options could be used for dispensing ARV for any duration (for 1 month, 3 month or 6 month

pick-ups), PrEP, HIV self-tests and other medicines already being supplied for chronic conditions (including drugs for hypertension, diabetes, etc.). Decentralized distribution approaches include:

  - Home deliveries: through peer-run groups OR private delivery mechanisms that maximize social distancing and respect client's privacy.
  - Community or private pharmacies: with scheduled pick-up times to maximize social distancing.
  - Pop-up pharmacy: that provide additional infrastructure in remote areas outside hospital or clinic settings with pick-up windows that are configured to ensure social distancing.
  - Automated lockers: provide additional infrastructure outside hospital or clinic settings for drug pick-ups.
  - Community pickup: through community structures such as schools, churches/FBOs, post offices or KP-focused sites

- Where countries are moving towards limiting movement, due to COVID-19, countries will need to work with law enforcement, national militaries, and other officials to:
  - Ensure importation and transport of health commodities isn't interrupted
  - Designate health commodity logistics, warehousing, and distribution (e.g. last mile delivery) operations - including private sector providers - as exempted activity and related personnel as essential personnel
  - Ensure that decentralized distribution approaches are permitted
- If OUs have significant movement restriction and/or high absenteeism amongst HCW, alternatives to face-to-face care provision should be considered, including the use of phone consultations.

Given the priority on reducing non-essential visits to health facilities to limit COVID-2 exposure among PLHIV coupled with known adherence challenges among Adolescent and Youth living with HIV (A/YLHIV), what are the recommendations for peer support groups and mentoring for A/YLHIV?

To the extent possible, and in line with host country guidelines, please ensure that peer support groups, one-on-one peer support, and treatment literacy activities are maintained virtually and ideally at the same frequency that they would normally meet. Adherence group meetings and one-on-one peer support can convene over the phone, SMS, through WhatsApp, or through other social media platforms that adolescents find acceptable, accessible, and can protect confidentiality. One-on-one virtual check-ins should be conducted for appointments and ART/MMD pick-up scheduling.

If staff/resources are limited, the highest risk A/YLHIV should be prioritized, including those with high viral load, newly initiated on ART, that are pregnant and breastfeeding, at risk for treatment disruption (running out of ARVs at home), and those with mental health or psychosocial challenges. Adolescents without personal phones can consent for their caregivers to be engaged and are encouraged to identify an accessible phone when possible. To the extent possible, incorporate COVID-19 prevention messaging per host country MOH guidelines and resources into the adherence group meetings and one-on-one check-ins.

Please ensure that youth peer leaders and facilitators have adequate resources, including airtime and/or data, to continue performing these functions.

What is the role of ARVs in the treatment of COVID-19?

There is no evidence that DTG- and EFV-based regimens which account for >90% of all ART in PEPFAR-supported program, have any activity or role in treating COVID-19 infections. Lopinavir/r has been investigated for treatment COVID-19 because of in vitro activity, but there is no evidence supporting its efficacy. A recent clinical trial failed to show a benefit[1]. Accurate messaging to prevent diversion of ARVs should be provided.

How can the most vulnerable patients be protected?

Older age and presence of uncontrolled comorbidities such as hypertension, diabetes and heart disease pose a higher risk for COVID-19 morbidity and mortality. All efforts should be made to streamline health services for older individuals living with HIV (>age 50), PLHIV with advanced disease, and those with co-morbidities. Programs should be sensitive to the medication needs of these individuals, seek methods to reduce the number of times these individuals require visiting health care facilities.

What changes in the clinic flow should be made to protect patients and HCW?

Waiting rooms can be a source of transmission for respiratory illness. Despite measures to maximally reduce the number of PLHIV coming for in-person facility visits, some visits will still be necessary.

Consider staggering clinical appointments to avoid crowding and streamlining clinic flow so PLHIV do not interact with multiple HCW (e.g. avoiding multiple points of contact between PLHIV and HCW).

Optimizing space to reduce close contact may be helpful. HIV patients should be seen in clinics that are dedicated spaces for HIV treatment services.

PLHIV with advanced HIV disease

Should evaluation of newly diagnosed clients for advanced disease continue during the COVID-19 pandemic?

Yes. Extant activities for the evaluation and management of advanced disease in clients newly diagnosed during the COVID-19 pandemic should continue.

Should individuals with advanced disease stay away from health care facilities?

Individuals with advanced disease represent a subset of PLHIV who require more intensive care, but they should still minimize health facility visits during COVID-19. All efforts should be made to maintain phone contact and to ensure that this group of individuals is seen when required.

When should individuals with advanced disease be evaluated in person?

Concerning symptoms include but are not limited to fever, persistent cough, shortness of breath, intractable headache and inability to walk unaided. For children other concerning signs and symptoms

[1] Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G et al. A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. 2020. doi:10.1056/NEJMoa2001282.

include fever, lethargy, convulsions, poor oral intake, and persistent vomiting or diarrhea. Note: all CLHIV under age 5 years who are NOT taking ART are classified as having advanced disease.

Should PLHIV with advanced disease be given MMD?

Absolutely. Extra effort should be taken to ensure that these fragile patients have sufficient medications to avoid unnecessary trips to the health facility. In addition they should be provided with all of the other medicines that they may need, such as cotrimoxazole and TPT.

Pediatric ARVs

PEPFAR COP19 guidance was to phase out NVP-based ART regimens by now. What should be done with current supply of NVP-based ART regimens?

Due to high rates of resistance to NVP, PEPFAR recommends against the use of NVP-based ART regimens even during the COVID-19 response. PEPFAR funds cannot be used to procure NVP-based ART regimens. Continuity of treatment for C/ALHIV is essential. Please urgently reach out to your Chair, PPM, and HQ supply chain and ***pediatric clinical ISMEs if the only option is to provide NVP-based ART regimens.***

Our host country requires documented virological failure before optimizing a pediatric or adolescent ART regimen. What should we do if routine VL monitoring has been impacted by COVID-19 (i.e., unreliable sample transport, lengthened turnaround time due to competing needs with SARS-CoV-2 testing, etc.)?

Please see HIV Treatment FAQ "*What if PEPFAR's recommendations for adapting HIV services in the context of COVID- 19 do not align with local policy?*" In addition, WHO recommends that viral load monitoring should not be a rate limiting step to optimizing ART. CLHIV who weigh < 20 kg should be on a LPV/r regimen (or continued on an EFV-based regimen if last viral load was < 1000 copies/mL) and C/ALHIV who weigh 20+kg can be transitioned to DTG-based therapy. Transitioning C/ALHIV who weigh 20+ kg to DTG-based regimens can help spare the supply of pediatric LPV/r formulations for younger CLHIV. Please also see previous FAQ responses below.

What are the recommendations for pediatric MMD in the setting of COVID-19?

Programs should make every effort to supply children and adolescents living with HIV (CLHIV/ALHIV) initiating and refilling ART with a 3-month supply of ARVs for those who weigh < 20 kg and a 6-month supply for those who weigh 20+ kg. The caregiver should be allowed to pick up the child's medication without bringing the child, unless the child needs a clinical visit. For children requiring Cotrimoxazole, a 3-6-month supply should be provided at the same time as ARV pickup. For children starting a new medication, administration of the first dose should be demonstrated and administered in clinic, particularly LPV/r-based formulations (liquids, pellets, granules, and 100/25mg tablets). Phone or electronic follow-up for pediatric clients (within 3-4 weeks) should be emphasized and include assessment of medication dosing and administration.

HIV-exposed infants should be given the greatest quantity of infant prophylaxis, both ART and cotrimoxazole as possible to last until the next immunization or EID testing appointment.

Our stock of LPV/r 40/10 pellets and granules is inadequate for monthly dispensing; will we have enough supply to provide 3-month dispensing?

Programs should evaluate current stock (including buffer stock) to determine when replenishment stock is needed to provide MMD. This information should be communicated to interagency pediatric and supply chain ISMEs and to the OU's S/GAC Chair and PPM. PEPFAR-funded orders required for the remainder of CY 2020 should be made now.

In light of the shortage of LPVr 100/25 tablets, how can our program employ MMD for patients that require this product?

CLHIV who receive **LPVr 100/25** tablets can 1) be transitioned to a LPV/r 200/50mg formulation as soon as safely possible, or 2) receive a one month supply of LPV/r 100/25mg, or 3) depending on in-country supply, receive a 3-month supply of LPV/r 40/10mg pellets or granules. OUs are encouraged to reach out to HQ clinical and supply chain ISMEs with questions.

In the face of COVID-19 disruptions to PEPFAR-supported treatment programs, what is PEPFAR's guidance for children who are receiving EFV based regimens?

CLHIV who are already 20kg and receiving EFV should immediately transition to a DTG-based regimen. CLHIV who are <20kg and stable on EFV with virologic suppression can continue to receive EFV temporarily (during program disruption by COVID-19) but should be transitioned to DTG 50mg once they reach 20 kg.

5. HIV Testing Services

Should all people being evaluated for COVID-19 also be tested for HIV?

It is unknown whether patients with HIV are at increased risk for COVID-19. There is overlap in COVID-19 symptoms with TB (see TB-HIV FAQ guidance) and other respiratory infections, which may be more common in PLHIV.

We recommend application of the usual criteria for determining eligibility for HIV testing when patients with unknown HIV status present with symptoms consistent with COVID-19.

How will HIV testing activities be affected?

See guiding principles. All efforts should be made to support community social distancing and reduce contact of well persons with health care settings during COVID-19 period of risk. Plans should be in place to adapt programming should service be disrupted. We acknowledge that everyone who needs an HIV test may not get tested and target achievement may be impacted by COVID-19.

Potential issues/responses include:

- Adapting HTS programming to government directives or policies on social distancing.
- Maximizing use of self-testing outside of the clinic setting (including providing self-tests through decentralized distribution approaches such as: peer home delivery, private or community pharmacies, etc.)
- Prioritizing clinical-based HTS for those most in need:
    - Testing in ANC

  - Diagnostic testing for individuals presenting (or admitted) to facilities with illness suspicious for HIV infection (Diagnostictesting)
  - Individuals with TB, STIs, malnutrition
  - Early infant diagnosis (EID) detection
  - Partner/index/family testing may be offered for individuals presenting at facilities (passive testing),
  - Testing in KP programs if ongoing and not facility based.
- HRH (including lay counselors/testers) may be impacted, reducing capacity from those affected by COVID-19
- HTS should not take place where routine adequate PPE is not available, (e.g. gloves)
- For RTK implications, please see Supply Chain/Commodities section

Can community testing for HIV continue?

Programs should adapt provision of active index testing services (also referred to as provider assisted notification) and community-based HIV testing accordingly to ensure the safety and security of testing staff and other health personnel. In some settings, it may be appropriate to continue to distribute HIV self-testing kits for KP, DREAMS, OVC, and partner testing. Any changes to guidance should be reviewed with the Chair/PPM and be in accordance with Chief of Mission directives.

Can active index testing for HIV, facility or community-based, continue?

Programs should adapt provision of active index testing services (also referred to as provider assisted notification) accordingly to ensure the safety and security of testing and other health personnel. Newly diagnosed individuals should be counseled on the importance of partner testing. Client-referral should be offered as an approach for index testing. However, in the context of COVID-19, programs are encouraged to distribute HIVST kits to index clients so that partners can screen themselves prior to coming to the facility. This will ensure that only partners who are most likely to have HIV will come to the facility for confirmatory HIV testing (see FAQ about role of HIV self-testing). National policies may limit the feasibility of active index testing and country teams should review guidance with the Chair/PPM.

What is the role of HIV Self-testing in the context of COVID-19 planning?

To alleviate congestion at the facility level and reduce the need for in-person testing services, countries may consider accelerating their plans for scaling HIV self-testing distribution for those with increased risk of HIV infection. Programs may need to develop alternate workflows to ensure that patients can receive for confirmatory testing. Please discuss with your Chair/PPM to ensure there is adequate supply of HIV self-testing kits. Please see the FAQ on testing in children for additional guidance on the role of HIV self-testing in the context of COVID-19 for children.

How should partners and field staff approach HTS for children and adolescents during the COVID-19 response?

Per previous guidance, we recommend maximizing use of self-testing outside of the clinic setting and prioritizing clinical-based HTS for those children most in need

HIV Oral Screening in Children

WHO Prequalification Department approved the use of OraQuick oral HIV testing kits for use in children 2-11 years of age in November 2019. To promote HIV screening in children during the COVID-19 response, PEPFAR Programs, in collaboration with Ministries of Health, may consider providing parents with HIV **(index clients)** with oral screening kits to screen their biological children >2 years of age for HIV at home. This temporary adaptation is intended to mitigate the effects of COVID-19 on identifying children with HIV before disease progression. Children with a positive oral HIV screening require prompt confirmatory HIV testing and, if infection is confirmed, immediate ART initiation.

HIV Recency Testing

Should recency testing continue if staff and client health care setting exposure is being minimized due to COVID-19?

Due to restrictions in group gatherings and travel associated with COVID-19, trainings and site visits for activation, monitoring, and quality assurance activities for recency testing have been postponed. Recency testing adds time to the provider-client interaction and overall clinic visit, specifically for pre-test counseling to explain procedures, consent process, specimen collection, and (if applicable) return of test results. Further, recency testing does not affect the overall clinical care of patients. PEPFAR guidance recommends that "health care facilities visits should be limited to those that are medically essential." **For these reasons, it is recommended that recency testing be paused temporarily at all health facilities and laboratories, in order to reduce potential risks of COVID-19 to clients, health care workers, project staff, and clinic population**. It is further recommended that each country, in collaboration with MoH, resume recency testing and the associated public health response as soon as feasible as COVID-19 restrictions are lifted.

6. TB Services

How can we distinguish COVID-19 from tuberculosis (TB) in PLHIV?

TB and COVID-19 symptoms may overlap, and patients may be co-infected. Whether COVID-19 presents differently in HIV patients is unknown. COVID-19 typically presents more acutely. The cough for COVID- 19 is not usually productive and fever is prominent. In contrast, patients with TB usually have a persistent cough of two weeks or more. Other TB-HIV associated symptoms include weight loss or persistent night sweats.

Programs should continue to screen, test, and think TB in high prevalence areas and consider testing for both TB and COVID-19 in PLHIV, especially in people presenting with fever and cough.

COVID-19 screening is a more urgent screening and represents a higher risk to health care workers. COVID-19 screening should be performed first if indicated and available.

How will COVID-19 affect contact tracing and case-finding for TB?

Contact identification should be conducted at the first visit and patients should inform their identified contacts of their TB diagnosis and the importance of informing health care workers of their contact status should they present to a health facility for symptoms. Contact tracing may need to be deferred in the setting of COVID-19.

Community-based testing and active TB case finding strategies should follow local guidance on movement restriction and social distance measures to preserve the safety of healthcare workers and should be consistent with TB Programs' continuity of operations in setting of COVID.

How can we ensure continuity of services for TB-HIV treatment and TB Preventive Treatment (TPT) in the context of COVID-19 disruptions?

- PLHIV on TB treatment should continue their treatment and avoid potential exposures to COVID-19 at health facilities.
- TB screening algorithms should incorporate COVID-19 evaluation pathways. PLHIV screened for COVID-19 should be screened for TB. PLHIV screened for TB should be screened for COVID-19.
- Patients should be provided the full or remaining course of their drugs for TB-HIV or TPT at the next scheduled visit or sooner, if possible.
- Where possible, we recommend adhering to the usual schedule of evaluations for PLHIV with TB substituting telephonic consultations for in-person evaluations.
    - Specimen collection should adhere to national guidelines. Individuals should be provided with materials and instructions for sample self-collection in an outdoor or well-ventilated space.
    - Telephonic consultation during the intensive phase of TB treatment is critical and should focus on screening for signs of deterioration that would warrant a visit to a healthcare facility and on counseling regarding medication adherence.
    - At the end of the intensive phase of therapy a clinical visit may be warranted based on the clinical course.
- Further guidance may be found here: https://www.who.int/tb/COVID_19considerations_tuberculosis_services.pdf

How will COVID-19 epidemic affect HIV testing of individuals with presumptive TB?

All patients with suspected or confirmed TB should continue to receive HIV testing (see March 20, 2020 FAQ). Please refer to testing guidance for strategies and guidance for HIV testing in the setting of COVID-19.

How do we manage people with TB newly diagnosed with HIV in context of COVID-19 epidemic?

ART is usually started after TB therapy is underway. Consideration may be given to dispensing ART at the same time as the initial TB therapy with close telephonic consultation on when to start ART and for clinical follow-up to detect potential adverse events (e.g., IRIS-related symptoms). ART visits should be aligned with TB visits.

How will the COVID-19 epidemic affect TB testing of PLHIV with presumptive TB?

All PLHIV should be screened for both TB and COVID-19 symptoms at every visit, and if screen-positive for either or both diseases, appropriate respiratory specimen(s) collected for molecular diagnostic testing according to local policies and guidance. Note that presence of COVID-19 symptoms does not eliminate the need for TB testing, which should proceed according to current country and PEPFAR guidance. COVID-19 testing should take place according to local guidance and may be conducted concurrently with TB testing.

What about TB/HIV patients who become unwell at home?

TB-HIV patients who become unwell at home, should first contact the health facility by telephone to determine whether it is necessary to come into the facility. COVID-19 screening should be performed on the phone. Where an in-person visit is necessary, ensure understanding of procedures on arrival which should include a screen for COVID-19 and COVID-19 isolation where appropriate.

How will the COVID-19 epidemic affect people undergoing direct observed therapy (DOT)?

Individuals providing DOT should follow local guidance on social distance measures and restrictions on movement. The benefits of DOT must be balanced against the potential unintended exposure of healthcare workers. Telephone and/or video-assisted visits can help ensure adherence while abiding by social distance measures.

What infection control precautions should healthcare workers caring for TB-HIV patients take in the setting of COVID-19?

Programs should refer to WHO's Technical Guidance on Infection Control Measures in the setting of COVID-19: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance

Addressing the triple risk of stigma & discrimination for patients with TB, HIV, and COVID-19

Stigma, discrimination, and social isolation are relevant for COVID-19, TB, and HIV. Programs should use lessons learned and ongoing efforts to reduce stigma for HIV and TB to also address and reduce the potential impacts of stigma and discrimination against patients with COVID-19.

What should be done with TPT programs?

Tuberculosis preventive therapy remains a core HIV service and countries may continue their scale- up. A full course of TPT (INH or 3HP) should be dispensed. For those already on TPT, the remaining course of their TPT regimen should be given. Programs should ensure that systems are in place for adverse event monitoring whether via telephone, SMS, or electronically. Differentiated service delivery models may be helpful in this setting; adherence to infection control procedures is required.

How will TB and TPT services be affected?

For individuals already on TB or TPT regimens, please ensure they have the remaining doses needed to complete a full course of treatment. Ensure that side effect monitoring can be done via telephone, SMS, or electronically. DSD models, if in place may be utilized for community distribution and adherence support as long as they adhere to social distancing policies and guidance within the country/district.

7. Integrated Women's Health

What changes for integrated women's health services are needed for women living with HIV (WLHV) need during the COVID-19 response?

During the COVID-19 pandemic, voluntary family planning (FP) services continue to be an essential service for women of reproductive age, per country guidance. Principles of voluntarism and informed choice guide USG health service efforts.

HIV services which are integrated with contraceptive services should be optimized and streamlined to avoid unnecessary patient visits to health facilities and to efficiently use client and provider time when clinic visits are necessary. Attention should be focused on facility-based service delivery, including the following approaches:

- PEPFAR funds cannot be used to procure contraceptives, however, multi-month provision of oral contraceptive pills (OCPs) and condoms should be provided to clients who choose to use/continue use one of those methods;
- Client centered FP counseling that proactively addresses possible side effect concerns related to hormonal contraceptive use to help minimize need for revisits;
- Coordination of client FP revisits with other individual and family follow-up services to streamline and/or integrate revisit appointments;
- Voluntary long acting contraception as needed for users, develop and disseminate a schedule of service provision to ensure that clients have continued access during periods of limited facility operations/provider availability.

How will programs ensure an adequate supply of FP commodities are available for WLHIV in PEPFAR integrated programming during COVID-19?

Although PEPFAR funds cannot be used to procure contraceptives, they are made available to PEPFAR supported programs through coordination and collaboration with national FP programs and through USAID and other donor funded FP activities. Due to ongoing and newly emerging challenges with global contraceptive supply chains, it is possible that some countries may experience problems with procuring certain contraceptives. Country teams are advised to keep in close contact with their national contraceptive coordination team to get updates and report contraceptive supply problems. Contraceptives to be included in the list of essential drugs that are allowed entry into countries while shipments are restricted. Integrating FP and HIV supply chain management and distribution may also help ensure that contraceptives are available for HIV affected populations.

How will cervical cancer screening services be affected?

Cervical cancer screenings conducted outside of same-day and same-site ART clinical service visits should be limited to decrease exposure to health centers. Screening done as part of a routine ART visit may continue. Women undergoing evaluation and treatment for high grade lesions should continue with their recommended medical management. This will be reviewed in June.

8. Maternal Child Health (MCH)

How will maternal and child health (MCH) services change within the context of COVID-19?

Please defer to local government regulations for specific guidance on clinic operations. When MCH clinics are operational, please encourage or enable HIV testing for pregnant/breastfeeding women (PBFW) and treatment services for women living with HIV (WLHIV) and their HIV-exposed infants to be included within essential services, including prioritizing maternal HIV testing and treatment and early infant diagnosis. PBFW on treatment should receive MMD (see HIV Treatment FAQ). Consider options to limit or reduce time spent in clinical settings, such as providing services in community settings, bundling services, or providing them in separate mother and baby fast track areas.

Should the frequency of ANC visits be adjusted, given the current COVID-19 context?

Women should follow local and national guidelines for ANC testing.

- Regular retesting for HIV is still encouraged if feasible, especially in high burden areas, at the already-scheduled visits and at delivery;
- Women should be encouraged to leave children and other family members at home during their clinic visits. While at the clinic, all consideration should be made to allow patients to wait in uncrowded areas for their visits and to streamline visits by integration with other essential services;
- Consider operational adjustments to improve flow of patients through the clinic and to reduce amount of time spent in clinical settings;
- Consider dispersing some services to community settings when possible.

Should we continue offering PrEP to PBFW during this time?

Absolutely. PrEP is a critical HIV prevention tool. Consider multi-month dispensing of PrEP.

If safety concerns related to COVID-19 result in WLHIV giving birth outside facilities, should they be offered newborn prophylaxis to take home in case they deliver at home/in a community setting?

Yes, this can be supported through PEPFAR programming.

- Consider providing infant ARVs with dosing instructions to women who will not be able to return to the facility for delivery. Please ensure that women are offered the correct regimens and dosages pursuant to local guidelines and provide supply for as long as necessary. The weight of the unborn infant will need to be estimated by the provider in order to determine the correct dosing. It may be useful to estimate if the baby will be small, medium, or large to determine which weight band to use.
- In some countries, mother-baby packs have been used to package ARVs for mother-infant pairs together. Clinic staff can actively follow up with WLHIV by phone to check in on accurate dosing. Retention and adherence support can also be reinforced by phone through community cadres, such as M2M, Mentor Mothers and/or OVC community caseworkers.
- If a woman has been given drugs to keep at home for newborn prophylaxis and she comes to a facility for delivery, she should bring the drugs with her for her newborn.

Should EID continue during the COVID-19 pandemic?

Yes, EID is an essential service. There is high mortality associated with untreated HIV among infants. HIV-exposed infants should continue to receive an EID test and clinical assessment as close to the recommended algorithm timing as possible. Fears of COVID-19 may make women reluctant to attend postnatal visits with their infants.

Consider options for timing and location that allow for social distancing such as reducing wait times and crowded waiting rooms through scheduling and staggering appointments, streamlining clinic flow so that patients do not interact with multiple clinic providers, and providing EID and immunizations in community settings if possible.

Consider creating an area for postpartum/well-baby checkups that is near to but separated from the health care facility to reduce contact/exposure for PBFW and their infants. Every effort should be taken to minimize stigma by integrating HIV services for HIV-exposed infants and mothers with postpartum/well-child services including immunizations. If mobile testing or point of care services are available at the community level please consider expanding those options.

Women are not returning with their infants for follow up visits or HIV testing. Most mass immunization campaigns have been suspended. How can we improve services for PBFW during the COVID-19 pandemic?

Retention and adherence support to pregnant and breastfeeding women is still crucial to prevent MTCT. Consider expanding phone/SMS support to mothers and infants through existing support mechanisms (e.g. community health workers, peer navigators, M2M, mentor mothers) to align with ANC and PNC clinical touchpoints, as well as identifying transport methods to bring women or infants who are high risk or in need of clinical support to the facility.

9. HIV Prevention – General

Can implementing partners who work on HIV prevention activities continue operations during the COVID-19 pandemic?

HIV prevention activities can and should continue. The safety of staff members, volunteers and clients must be prioritized, and person-to-person interactions should be limited whenever possible – but PEPFAR is not stepping away from the life saving measures that HIV prevention services bring to people around the world. Alternate methods of communication such as phone calls, WhatsApp and text messaging services should be utilized in order to minimize individual visits, meetings or counseling sessions related to HIV prevention.

Why are we concerned about HIV acquisition rates increasing during periods of confinement/social isolation/self-quarantines?

Physical confinement measures are critical to contain the spread of COVID-19, but as these periods of confinement are extended, there is growing potential for increasing rates of sexual exposure for many people. Interpersonal violence, including sexual violence and violence against women and children may increase. Agencies need to work with IPs and Government to ensure that information about Gender Based

Violence (GBV) is provided. Please see GBV specific FAQs. Sharing local contact options of responders who can address GBV related concerns may be initial options in some PEPFAR contexts.

What are some HIV prevention services that can be kept operational within the physical distancing parameters of COVID-19?

Some examples such as the following should be considered based on populations at risk and budget availability:

- As PEPFAR teams prepare supply chain forecasts early, they should ensure that condom and lubricant supplies are also increased both to account for the increase in need, and because bulk packaging/delivery will be necessary once shipments arrive (i.e. clients will no longer be able to take 1 or 2 condoms at a time during a clinic visit or from a volunteer health care worker at a community gathering);
- Packaging of condoms and lubricants should be made in larger than normal quantities (akin to multi-month dispensing of ARVs) so that clients can obtain necessary supplies in sufficient quantities that allow them to minimize the number of collection visits they might need to make to a collection point. Distribution points or displays should be modified in order to allow clients to pick up these products without touching or handling products for other clients (e.g. avoid bowls). Clients are also encouraged to clean anything they pick up from collection points.

10. HIV Prevention - PrEP

Should PrEP be considered an essential prevention intervention during the COVID response?

PrEP is an essential component of PEPFAR HIV programming. Strong advocacy for PrEP service delivery should continue as part of comprehensive combination prevention including counseling (by phone), condoms, and lubricants, or as outlined in country guidelines.

Can multiple months of PrEP be given on the first/initiation visit? What happens to the currently standard one-month check in visit?

This should be assessed and decided by the client and provider together according to the client's needs. If a client is committed to taking several months of PrEP from initiation, then it should be allowed. Many clients express interest in taking PrEP but either don't start or don't follow-up at the one month visit. Follow-up one month after starting PrEP remains important but can be conducted through other available modalities, such as over the phone, or somewhere outside of the clinic space, in order to decrease facility congestion and adhere to social distancing guidance.

With some reductions of direct hire staff in some countries due to evacuations and/or competing priorities because of COVID-19, how can we ensure PrEP services are properly supported?

PEPFAR staff who have evacuated post continue to work from remote settings. Teams should address how IPs can make a determination how best to provide PrEP services and to provide USG agency oversight. As services are decentralized from clinics to lessen congestion, it will be important to communicate to clients where services can be accessed and provide a contact for continued communication, as needed.

Are there innovations or programmatic solutions that implementing partners (IPs) can utilize to keep PrEP services going during COVID-19?

PEPFAR recommends moving PrEP services away from and out of clinics as much as possible, using virtual options for client initiations, refills and check-ins, decentralizing dispensing of PrEP through community delivery, and moving to multi-month dispensing (MMD) as much as possible. We recommend using SMS for refill and for adherence reminders, for example. Solutions for how some IPs have shifted to decentralized and/or virtual platforms will be shared in the coming weeks through PEPFAR and the PrEP Community of Practice.

Should demand creation for PrEP continue?

Demand creation based on larger social gatherings, or social mobilization, should be paused for the duration of COVID-19 until social distancing requirements are relaxed in the specific community. However, other demand creation based on no-contact or limited-contact platforms such as radio, printed materials or virtual platforms such as videos, internet banners or podcasts should continue. With increased attention to social platforms (WhatsApp, Facebook, Instagram) to encourage community cohesion during physical isolation periods, community leaders and mentors can continue to encourage PrEP uptake safely from these settings.

How will PrEP be affected?

For individuals already on PrEP, a 3-month supply of PreP medication should be given. Any interim or follow up visits to assess side effects should be done by telephone, SMS, internet, or e-mail if possible (with agreement of clients). Teams are encouraged to immediately calculate any increase in PrEP that would be required to dispense 3 months' worth of PrEP.

Community distribution and adherence support in small groups (less than 10 people present at a time) for PrEP may help support people and would not be a burden on the health care system. Adherence group meetings over the phone and use of SMS to send reminders is suggested as well. It is suggested that decentralized drug distribution approaches be considered for PrEP that include peer home delivery, scheduled community or private pharmacy pick-ups, distribution through pop-up pharmacies (that dispense other products such as products for hypertension, diabetes, HIV self tests, etc.).

Decentralized approaches can be used whether dispensing a monthly or 3-month supply. Note that it is up to the provider and client to decide how many months to dispense according to the needs of the client, and this can be done at any visit, including the first. As multi-month dispensing of PrEP occurs, it will be important to notify supply chain colleagues to ensure adequate supply planning.

11. HIV Prevention – VMMC

How will VMMC services be affected?

New VMMCs may be delayed or paused if guidance around mass gatherings renders them impractical. Post-operative follow-up should continue for circumcisions that have already occurred with consideration given for telephonic consultation as an initial screening, before an in-person visit. We acknowledge that prevention services for men may be impacted by COVID-19.

Should country teams continue reporting VMMC Notifiable Adverse Events and conducting investigations?

Teams should continue reporting NAEs as they normally would. If guidance around travel/stay-at-home orders makes the investigation of NAEs impossible, please include that information in the initial notification email to VMMC_AE@state.gov. **Investigations of any cases involving the death of a client should continue as normal to the extent possible**. Country teams should reach out to VMMC_AE@state.gov for any further guidance as needed.

What age considerations should be followed for VMMC once services are resumed?

Due to increased risk of severe AEs in boys 10-14 years of age, PEPFAR's COP20 guidance changed the lower age limit for VMMC to 15 years. Countries were encouraged to prepare for this change in COP19 with full transition at the start of COP20. However, severe AEs have continued to occur among boys 10-14 and VMMC services are currently partially or fully paused due to the COVID-19 pandemic.

When VMMC services resume following the COVID-19 related pause, programs should:

1. Not circumcise boys age 10-14
2. For boys under 15 presenting for VMMC, provide other age-appropriate prevention services as outlined in COP20 guidance, counsel the client/parents on additional risks identified in boys 10-14 and encourage them to return for VMMC when the boy is 15 years or older.
3. Further information about use of the Shang ring will be provided when appropriate.

12. Orphans and Vulnerable Children (OVC)

Per MER 2.4 guidance, OVC "active" beneficiaries are required to have a case plan and must be monitored at least quarterly. Due to "stay at home" restrictions imposed by host country governments during COVID-19, OVC frontline workers are in many cases unable to monitor children via direct contact. Can OVC continue to be counted as "active" if contact is not made in person?

Yes. While direct contact is preferred in order to observe the status of the child and family, the MER guidance states that monitoring can occur "virtually where needed." During the COVID-19 period, it is expected that virtual contact may be the only option until operations return to normal. To be counted as "active," all OVC_SERV requirements must be met, which includes: having a case plan that has been developed (or updated) in the last 12 months; at least quarterly monitoring; and delivery of at least one of the OVC services (listed in MER Guidance Appendix E) in each of the past two quarters. Documentation of any virtual contact should be recorded in the child's case plan.

As many OVC programs shift to providing temporary virtual support to children and families via remote case management, which services may be counted under OVC_SERV?

Any OVC service included in MER Guidance (Appendix E: Illustrative eligible services for active OVC beneficiaries) that can be delivered or facilitated via remote/virtual support, in line with host country government social distancing policies and guidelines, can be counted. For example, adaptations may include providing treatment literacy and adherence support, through routine phone, SMS, and/or WhatsApp

communications and support. Remote case management can facilitate linkage to local food supplementation, hygiene supplies, social grants, and distance learning opportunities. IPs are also encouraged to incorporate COVID-19 prevention messaging per host county MOH guidelines and resources into their virtual support to households.

HIV Risk Screening in OVC

If OVC case management shifts to a phone-based virtual approach, consider including HIV risk screening of OVC with unknown HIV status in the list of phone-based services. Implementing partners can develop a list of children who warrant HIV testing to ensure children in need of testing be identified for HIV testing as soon as feasible.

OVC Enrollment in the Context of COVID-19

Should enrollment in OVC programs continue in the context of the COVID -19 epidemic?

The safety and wellbeing of OVC workers and potential beneficiaries are of the utmost importance and should be prioritized when assessing whether to continue enrollment during COVID-19. PEPFAR-supported cadres should follow host government guidance as it relates to new enrollments and avoid unnecessary interactions with potential beneficiaries in facilities and communities to reduce exposure to and spread of COVID-19. National approaches and sub-national unit operations to prevent COVID-19 transmission may vary within a given country or region.

If enrollment is not allowed nor feasible, programs should create a waiting list or tracking system to ensure that eligible beneficiaries who were not able to be enrolled due to COVID-19 can be rapidly enrolled when normal operations return.

If enrollments into OVC programs are feasible, which infants, children, and adolescents should be prioritized?

OVC programming should follow current COP guidance. Populations to be prioritized for enrollment include:

- Children and adolescents living with HIV (C/ALHIV)
- HIV-exposed infants (especially those of adolescent mothers and newly diagnosed women)
- All infants, children, or adolescents who are exposed to abuse, harm, or violence

If OVC enrollment is allowed/feasible, how should enrollments of priority sub-populations take place?

As previously discussed, OVC programs should explore the temporary use of telephone-based enrollment and referrals. In select cases (e.g. critically ill child/child failing treatment, child abuse), in-person referrals, enrollment, and immediate linkage to emergency services may be required (see PEPFAR FAQs regarding home visits and GBV/CP). Key steps for enrolling priority OVC sub-populations in the COVID-19 operating context include:

- Update program MOUs, SOPs, and/or referral protocols between OVC and accredited clinical, child protection/social service, and law enforcement service providers to include an option for routine

telephone-based referrals to the OVC program. Referrals to OVC should include accurate telephone contact information for each child's parent/primary caregiver.

- Designate relevant OVC case workers to serve as points of contact for phone-based referrals; ensure that the service providers mentioned above have case workers' current contact information; and ensure the provision of sufficient airtime for OVC case workers processing referrals via phone.
- Based on receiving a phone referral from a service provider, the OVC case worker contacts the child's parent/primary caregiver via phone; provides key information about the OVC program and the types of support provided; and offers OVC program enrollment to the family.
- If the parent/primary caregiver accepts OVC program enrollment, the OVC case worker proceeds to request additional child and family information via phone in order to complete the program enrollment form.
- The OVC case worker and parent/primary caregiver arrange an appropriate date and time for a follow-up call to conduct a broader assessment of the child and family in order to complete the OVC needs assessment form.
- The OVC case worker opens a new child and family OVC case file and initiates remote case management (including care plan development, relevant counseling, service linkage where feasible, and monitoring) via routine telephone checks-ins with the parent/primary caregiver.

Please see the FAQ on testing children under HIV Testing, and cadres working with children and families under HRH for further relevant information.

13. DREAMS

Given the inability to gather in groups, or in some cases in person, how should DREAMS IPs stay engaged with AGYW?

A major priority during this time is to maintain contact with DREAMS AGYW in the most practical and cost effective way possible. Depending on the country and local context, this might be via SMS, phone calls, or other digital platforms such as WhatsApp. Please ensure that mentors and facilitators have adequate airtime and/or data to perform these functions. Ideally, mentors would maintain contact with AGYW in their cohorts and at the same frequency they would normally meet. Digital contact should be made both individually and as a group if possible. Partners should choose the best way to stay in touch based on their context.

Contact should focus on keeping AGYW engaged with her mentor and peers, providing referrals for time sensitive services, e.g. GBV response, FP, and PrEP, and reinforcing content that was already conveyed during in-person sessions. Delivery of new sessions from DREAMS curriculum should not be delivered over SMS or digitally.

How will the key population and DREAMS activities be affected?

With respect to prevention activities for KP and DREAMS beneficiaries, planning for smaller gatherings should begin. Group-based activities should follow local guidelines for mass gatherings (e.g. community

mobilization and norms change sessions, parenting sessions, and 'safe space' sessions) and in-person group-based activities may need to be paused. If multiple groups are meeting concurrently in a shared space, teams/partners should be sure that there is enough time and space between groups so that they are still adhering to the local mass gathering guidance. For DREAMS specifically, if possible, country teams should consider temporarily moving safe spaces that are currently held in facilities into community spaces identified by AGYW and mentors. If this is not possible, teams/partners may need to consider postponing safe spaces meetings until guidance allows for them to begin again.

Additionally, where feasible and appropriate, facility-based DREAMS services should be offered in the community with appropriate social distancing.

14. Key Populations (KP) Services During the COVID-19 Pandemic

Depending on how COVID-19 impacts your country, there may be significant interruptions in access to HIV services for key populations. This may lead to economic uncertainty, increased risk-taking behavior, further experience of stigma and personal violence. Community outreach and traditional peer outreach approaches will likely be disrupted and will need to be adapted based on the client's needs.

Prioritize Uninterrupted HIV Treatment Access, Clinical Care, and Support for Key Populations

- Services should be modified and decentralized so that all KPs can continue to access treatment, PrEP and viral load testing and other care through community platforms.
- Continued coordination and collaboration among community case management teams prioritizing virtual platforms to determine appropriate and needed differentiated services for KPLHIV

Testing, Prevention and PrEP Services

- Prioritize differentiated service delivery through community initiation and refill of PrEP and delivery of HIV testing including self-testing via mobile clinics, drop-in centers (DICs), and other community platforms or alternative arrangements for pickup or delivery of services
- Ensure peer outreach workers have enough supply of commodities and/or there are also community distribution points for commodities like condoms, lubricant and self-test kits.
- **Leverage Virtual Approaches**: Use of social media, phone, SMS, and alternative methods of communication by health care and peer workers may ensure critical services are continued.

Ensure Safety of Key Populations

- Programs should track reports of barriers to service delivery
- Work with IPs and engage KP community-based organizations to provide basic communications materials including infection prevention
- Programs should ensure violence prevention mechanisms and referrals are functioning to track and link clients to needed services

Is there an update on index testing for key populations?

The evolving situation with COVID-19 may have implications for HTS implementation, monitoring and achieving HTS results, and teams are expected to operate under any COVID-19 related country guidelines as well as KP and HTS programming considerations below. However, given the progress made in recent months on ensuring HTS minimum standards through multiple processes, at this time, the previous halt on active index testing among key populations has been lifted. PEPFAR will work with country teams to ensure that either: (1) existing data confirm that current HTS provision at sites meets minimum standards or (2) sites are brought up to standards and assessed using vetted and valid tools. PEPFAR remains committed to ensuring all sites providing index testing services do so in a manner that meets established standards. Consult your S/GAC chair or PPM if needed.

15. Gender-Based Violence (GBV) & Child Protection (CP)

What should all PEPFAR teams be aware of regarding violence during the COVID-19 pandemic?

Domestic violence has sharply increased since the COVID-19 outbreak (Godin, 2020). Violence, particularly intimate partner violence (IPV), increases risk of HIV acquisition (WHO, 2013) and can negatively impact an individual's adherence, retention, and viral suppression (Hatcher, 2015), PEPFAR programs must respond to violence in order to maintain achievements in retention and viral suppression during the COVID-19 outbreak.

All PEPFAR programs (both clinical & community) can respond to GBV and CP by:

1. Advocating with host governments to designate child protection and GBV responders (and their organizations and government agencies) as essential and operational during lockdowns. This also includes child helplines and other remote services.
2. Working with local governments, community partners, local organizations, and other donors to continuously update lists/directories (e.g. contact information, opening hours) of all local GBV/CP response services and national hotlines that are functional, including both clinical and non-clinical supportive services.
3. Specific considerations for clinical and community partners are noted in the following FAQs. Additional resources can be found here: https://gbvguidelines.org/en/knowledgehub/covid-19/

If there is immediate concern for a child being exposed to physical harm, abuse or neglect that requires urgent attention, this should be reported to the appropriate accredited authorities. Please see FAQs on home visits.

How can clinical partners respond to GBV and CP issues during the COVID-19 pandemic?

1. Ensure that all staff have access to an updated list of local GBV/CP responses services and national hotlines for referrals.
2. Facilities should have printed material that provides information on functioning local GBV/CP services and national hotlines that providers can discreetly give to clients. Community partners and local organizations may already have materials available for distribution.

3. Providers should deliver age-appropriate first-line support (LIVES) to all clients who disclose violence and provide or refer clients to appropriate, functioning GBV response services.
4. Providers should help clients make a plan to stay safe at home while living in quarantine or isolation, including tips on how to safely access support. Ensuring privacy is critical (e.g., using a safety/code word if disclosing violence in proximity of the perpetrator). It is important to do no harm.
5. Providers should help clients find ways to discreetly and safely take their ARVs while in quarantine or isolation. This is important for people who have not disclosed their status or use of ART or PrEP to their partner/family.
6. Ensure PEPFAR-supported specialized GBV/CP facilities or one-stop-centers have enough phone/internet credit to provide virtual psychosocial support and safety planning services.

How can community partners respond to GBV and CP issues during the COVID-19 pandemic?

Maintain and adjust communication

- Implementing partners (IPs) should use calls, SMS, social media, and/or work with Governments to provide information about GBV/CP and COVID-19, including contact information for functioning GBV/CP response services.
- IPs with access to media such as radio, internet, or television can provide information on the risk for increased interpersonal violence during COVID-19 and resources available to those who need support.

Keep in contact with those at elevated risk for GBV or child abuse/neglect

- For participants who have disclosed experiences with violence or are potentially at higher risk for violence, staff (e.g., counselors, social workers, gender leads) may proactively reach out and discretely offer support, including developing a safety plan in the case of quarantine or social isolation and ensuring those in need know how to safely access support. Ensuring privacy is critical (e.g., using a safety/code word if disclosing violence in proximity of the perpetrator). It is important to do no harm.
- Programs that have existing relationships with individuals and families (e.g., OVC, DREAMS) should maintain communication using virtual platforms as possible. Please refer to the DREAMS FAQ on maintaining contact with AGYW.

Support frontline staff

- IPs should ensure their field staff, mentors, and community health workers have the resources (e.g., internet connection, airtime) to reach out to PEPFAR participants to provide support, safety planning, and linkage to services as necessary.
- IPs should promote self-care and prioritize safety of staff, being cognizant of potential trauma during emergency situations.

Ensure appropriate response services are in-place and known

- Ensure that all staff have access to an updated list of local GBV/CP responses services and national hotlines for referrals.

16. Faith and Community Based Organizations

How can Faith and Community leaders help with the multiplicity of challenges countries are facing due to the co-occurrence of HIV and a COVID-19 pandemic?

- Provide accurate and timely information from reliable sources about practical considerations and recommendations for religious leaders and faith communities in the context of COVID-19. Example: https://www.who.int/publications-detail/practical-considerations-and-recommendations-for-religious-leaders-and-faith-based-communities-in-the-context-of-covid-19
- Encourage PLHIV in and/or known to their congregations, to maintain an adequate supply of ART

What changes in the 'Faith and Community Initiative' activities are needed during the COVID-19 response?

In the context of COVID-19, PEPFAR-supported staff working on priority #1 of the FCI: "Engaging faith communities to reach men and children living with HIV, and to link and retain them in care", should be focused on supporting, maintaining, and extending continuity of HIV treatment for men, youth, and children, by:

- Leveraging functioning religious structures to use weekly virtual Facebook Live/YouTube® religious services for congregations and men's, women's, and youth groups, as well as congregational WhatsApp groups, to disseminate HIV Messages of Hope, prioritizing messages that use FCI message prototypes (SMS messages, video clips, etc.) to support adherence for PLHIV; leveraging these religious structures to integrate COVID-19 risk prevention communications for at-risk populations and PLHIV.
- Expanding engagement of Religious Leaders Affected by and Infected with HIV, in reducing HIV-associated stigma, to include stigma associated with TB and COVID-19
- Expanding client base of faith-engaged neighborhood Community Posts to increase convenient access to ARV pick-ups and MMD, among index clients and contacts,
- Expanding FCI models that link highly targeted HIV self-testing to treatment and retention support
- PEPFAR-supported FCI staff providing psychosocial support to boost adherence should avoid home visits and should provide such support remotely using phone, text, or WhatsApp.

PEPFAR-supported staff working on priority #2 of the FCI: "Strengthening Justice for Children" will need to adjust the 4 required activities to align with local "stay at home" orders and guidance regarding mass gatherings.

- Educational sessions and trainings for implementing partners, community leaders, and community members will need to be delayed or paused if restrictions on mass gatherings are in place, unless these can be conducted virtually. This includes: delivery of the Sexual Violence 101 module to community leaders; training of implementing partners on and delivery of evidence-based interventions such as Coaching Boys into Men and No Means No; training of implementing partners (primes and subs) on child safeguarding policies; and, trainings on justice sector responses to sexual violence against children.

- Country teams and IPs should continue planning for future trainings and education modules as well as who the target audience(s) will be and appropriate venues for when restrictions are lifted.
- If already part of implementation plans, efforts focused on Justice Sector systems change should continue and be finalized, with government entities using conference calls and video platforms, if available.
- Justice for Children implementing partners should review the technical guidance on Child Protection and GBV (see section 15) to ensure that they can provide appropriate assistance regarding post-violence care for survivors of violence.

17. Infection Prevention and Control

What measures should be implemented to reduce COVID-19 exposures in the healthcare setting?

- The basic principles of IPC and standard precautions should be applied in all health care facilities and are critical to containment of SARS CoV-2.
- Health care facilities visits should be limited to those that are medically essential
- All facilities should have a designated focal point to oversee and monitor infection prevention activities; this individual should be supported to provide the basic principles according to WHO guidance which include:
    - Written procedures for identifying and managing clients and staff with potential COVID- 19 exposures or illness;
    - Systematic triage to identify ill persons;
    - Strict adherence to hand hygiene and respiratory hygiene;
    - Medical masks to be used by patients with respiratory symptoms;
    - Prioritization of care of symptomatic patients
    - When symptomatic patients are required to wait for services; ensure they are placed in a separate waiting area.
    - Appropriate supplies to allow implementation of contact and droplet precautions for all suspected COVID-19 cases;
    - Strict protocols for routine cleaning and disinfection of medical equipment and environmental (especially “high touch”) surfaces
    - Education and training of staff regarding IC precautions for COVID-19
    - Airborne precautions are recommended only for staff performing aerosol generating procedures. These procedures include tracheal intubation, non-invasive ventilation, tracheotomy, cardiopulmonary resuscitation, manual ventilation before intubation, and bronchoscopy

Details can be found here:

https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care- when-novel-coronavirus-(ncov)-infection-is-suspected-20200125

Non-medical (or Homemade) Masks

Should IPs promote the use of non-medical (or homemade) masks as Personal protective equipment (PPE) in PEPFAR-supported health clinics/facilities?

No. Non-medical or homemade facemasks are not considered PPE because they have unknown protective capabilities. This is consistent with both CDC guidance and WHO guidance.

Should IPs promote the informal production and use of non-medical (or homemade) masks to prevent community spread of COVID-19?

- As of April 6, CDC recommends the use of cloth face coverings to lessen transmission of COVID-19 in public settings where other social distancing measures are difficult to maintain (e.g., grocery stores and pharmacies) particularly in areas impacted by COVID-19. Under no circumstances should cloth face masks replace or substitute for the approved PPE recommended for frontline workers (e.g., healthcare workers, community workers) to protect themselves from coronavirus acquisition in health facilities.
- As of April 6, WHO guidance takes a more cautious approach for non-medical masks used by the general public in community settings, citing the lack of evidence on effectiveness but also outlining a decision-making framework for policymakers.
- IPs should only consider this action if official policy, normative guidance, and/or agreement is obtained from host country governments. IPs should communicate at all times that non-medical masks are distinctly different from PPE.
- Community-based production of homemade face masks can also be integrated into current economic strengthening or income-generation activities, where such activities are already taking place and able to continue. Examples can include supplying raw materials along with training activities that are prudently adapted to ensure proper social distancing (e.g., virtual training through WhatsApp and other accessible technology).
- IP efforts should follow normative guidelines and standardized practices (such as the CDC guidance) and coordinate closely with promotional campaigns (which may or may not be implemented directly by the IP) to ensure public sensitization on proper use, re-use, and disposal as well as limitations on personal protection.

18. Laboratory Services

How has COVID-19 affected the supply chain of laboratory products and what measures should be taken to minimize its impact?

There are current delays for rapid test kits (RTKs) either manufactured in China or relying on key starting materials from China, and Asia, more broadly. Delays or pricing increases are being tracked and

communicated as they arise. Current guidance is to place orders for laboratory commodities and RTKs **one month** earlier than normal, to account for potential shipping delays.

What is the overlap between viral load testing and SARS-CoV-2 testing, since they are both PCR- based?

At present, most laboratories in the Africa region are using instruments and reagents for SARS-CoV- 2 testing that are different from those used for HIV viral load and EID testing; however, SARS-CoV-2 testing options are evolving rapidly and commonly used HIV viral load and EID instruments are anticipated to be coming online for SARS-CoV-2 in the short to medium term.

How will SARS-CoV-2 testing impact HIV VL testing?

OUs should anticipate increased use of common consumables and PPE for COVID-19 and HIV-related testing in laboratories and anticipate and plan for diversion of or reductions in laboratory staff and other HRH available for HIV (VL/EID) testing due to COVID-19. Laboratories should prioritize testing based on local requirements. For HIV laboratory testing, EID and viral load services for children, PBFW, and adults with documented non-suppression on their last VL result should be prioritized.

What measures should be taken to ensure stocks of laboratory supplies?

OUs should update current stock counts at national and subnational levels and forecast for additional consumable needs to accommodate increases in COVID-19 testing. It is recommended that orders be places at least one month in advance to reduce the risk of shipping delays resulting in stock outs.

Is there a plan to use HIV VL/EID platforms for SARS-CoV-2 testing?

On Friday, March 13, the Roche SARS-CoV-2 Test received FDA emergency use authorization (EUA) and other manufacturers are developing COVID-19 tests that may be run on existing HIV VL/EID instruments.

What procedures should be carried out If testing for SARS-CoV-2 and HIV VL/EID are conducted in the same laboratories?

In PEPFAR supported laboratories running COVID-19 and HIV-related testing on the same instrument, SOPs should be developed to account for prioritization of testing (e.g., COVID-19, EID, VL).

19. Supply Chain/Commodities

Decentralized Drug Delivery

Decentralized drug delivery systems offer the opportunity to reduce risk in the health care setting and are recommended for all programs.

Supply Chain for ARVs

We don't currently have enough stock to supply each recipient with six months of therapy. What should we do?

PEPFAR advises country programs to access the current total stock on-hand in-country and develop a distribution plan to replenish all facilities and patient dispensing sites. If sufficient ARV stock is not available for 6 month dispensing for adults and adolescents and 3 month dispensing for children, countries should distribute the available drug supply with a goal that all clients have enough drug on hand to last for the

next 3 months. This will require a change in procedure related to the maintenance of the minimum stock levels and buffer stock levels. Replenishment orders should be placed as soon as possible. Following this strategy will ensure that recipients of care will have sufficient ARVs in the coming months should there be additional disruptions in clinical operations or restrictions in distribution. PEPFAR is actively working to ensure supply security of HIV/AIDS commodities and will continue to provide timely updates using the USAID Supply Chain Activities Managers weekly call. USAID is also coordinating with Global Fund to ensure that ARVs are imported to prevent overstock and stock-outs. PEPFAR Country teams should work with Ministries of Health to ensure that multi-month dispensing policies are communicated to all HIV/AIDS providers, facilities, pharmacies, and supply chain to ensure continuity of services are assured. For recipients of care due for refills within the next 3 months, consideration should be given to providing additional supply early, and distributing stock to clinics rather than holding large quantities at central medical stores or provincial stores, in case local transportation and access to the clinics becomes restricted.

Should we expect delays in ARV drug orders?

A median delay of about 25 days is anticipated for adult and pediatric ARVs. Buffer stocks available in central warehouses should be sufficient to cover shortages caused by this delay. Deliveries of orders for antiretrovirals are delayed, because the majority of the US-FDA approved ARV manufacturers are based in India, which has been experiencing a lockdown in response to COVID-19. Originally planned for 21 days, the lockdown in India has now been extended until May 3, 2020.

Although pharmaceutical manufacturing is exempt from the lockdown, it is hampered by lockdown impacts on public transport and other logistics. Consequently, suppliers report operating at approximately 30 to 50 percent normal manufacturing capacity, and at least one manufacturer has completely shut down. Fortunately, in recent weeks, there has been an increase in manufacturing capacity and an improvement with in-country logistics (movement of truckers between states) as the lockdown continues. USAID, through GHSC-PSM, is actively pursuing other sources of ARVs.

Are there also delays expected for orders of non-ARV drugs?

Non-ARV medications: Most orders for essential medicines (non-ARVs) have not been significantly impacted by COVID-19 disruptions in logistics. Chinese pharmaceutical and diagnostics suppliers are operating at nearly 90% capacity. Other essential medicines, including medicines used for TPT, are mainly sourced through USAID International Wholesalers based in the Netherlands and Denmark.

What changes may be anticipated for the supply chain of drugs?

As the COVID-19 pandemic continues to evolve S/GAC, USAID, CDC and GHSC-PSM have taken steps to monitor the situation as it pertains to availability of ARVs and other drugs essential to the HIV response. Because of anticipated delays USAID has instructed the Missions to place orders one month earlier than normal lead times would suggest. As mentioned above, additional stock may be required to activate 6MMD at a wider scale and commodity needs above COP19 and COP20 plans should be discussed with USAID and PSM immediately.

What should be done to prevent country-level drug shortages?

Consider the following interventions:

- Substituting products/formulations where necessary.

- Ongoing supply plan and inventory data (PPM/R) review to identify and respond to urgent need
- Decentralized distribution approaches (as highlighted above) that include: Home deliveries, community or private pharmacies, pharmacy in a box and automated lockers.
- Order staggering to prevent delivery delays
- Prioritization exercises across Task Order and as feasible across procurers to ensure that the most urgent need is met (across products, across countries)
- Reallocation of urgently needed orders to less impacted suppliers, as warranted and feasible

Tracking Supply Chain Impact

How will supply chain for COVID-19 be tracked?

GHSC-PSM is in the process of developing a **COVID 19 Impact Dashboard**, which will allow Mission supply chain staff to track the impact of COVID-19 on their orders. Additionally, GHSC-PSM is developing a **Market Risk Map** by commodity portfolio to assess the long-term impact commodity portfolio to assess severity of the risk, probability of the risk, and timing of the potential risk to help inform our short and long-term mitigation strategies

How will USAID and GHSC-PSM Mitigate Risk?

- Early Identification of Delayed and At-Risk Orders
- Bi-weekly order status reports from all suppliers with supplemental calls as needed
- Ongoing monitoring of key raw material export data
- Ongoing market assessments to identify capacity constraints
- Ongoing updates on sampling restrictions and communications with QA labs
- Exploring alternate shipment modes to reduce delays
- Coordination meetings with WHO Access to Medicines and Health Products, and the Global Fund

Supply Chain for Personal Protective Equipment (PPE)

What about personal protective equipment?

There is currently a world-wide shortage of personal protective equipment (PPE). PEPFAR has not procured PPE in large quantities in the past and cannot currently ensure appropriate or adequate supply. We are therefore asking teams to seek alternative sources at this time. It is important that health workers providing ART services in areas impacted by COVID-19 use PPE to protect against self-exposure and transmitting to our highly vulnerable population. PEPFAR will work to gather and disseminate information about alternative sources or solutions for PPE as they become available.

Requirements for PPE can be found here:

https://apps.who.int/iris/bitstream/handle/10665/331215/WHO-2019-nCov-IPCPPE_use-2020.1- eng.pdf

20. Operations

How will operations at PEPFAR be affected and what measures should be taken to prevent disruptions?

- Social distancing measures including quarantine have resulted in disrupted operations due to evacuations, travel restrictions and fragile communications networks outside of the larger cities. PEPFAR country teams should make all efforts to stay in communication with headquarters, and with implementing partners who may be most affected.
- Requests to utilize resources that support HIV services but also respond to COVID-19 should follow budget guidance that has been provided in a separate document. Agencies at Post must, in turn, consult with the S/GAC Chair with copy to **SGAC_M&B@state.gov** ahead of granting approval for such activities.

21. Reporting and SIMS

Is the PEPFAR Quarter 2 reporting deadline still the same?

Recognizing challenges with site-level access in countries across the world, the PEPFAR Quarter 2 reporting deadline has been moved to **Friday, June 5th**. Detailed guidance is forthcoming from SGAC_SI. We will closely monitor PEPFAR program implementation in the ensuing weeks and provide updated guidance as needed for Quarter 3 reporting.

Are we expected to continue SIMS implementation and reporting?

All PEPFAR programs are under Chief of Mission authority therefore country teams and implementing partners should follow Embassy Front Office direction on all programing that requires personnel movement. There are updated WHO guidelines and public health recommendations regarding personal safety to determine the feasibility of in-person site monitoring visits during the COVID-19 response. Please also refer to the Operational Issues and Infection Prevention and Control sub-sections of this guidance document. We recognize that SIMS implementation and reporting has, and will continue to be, affected during this time. Similar to guidance issued regarding MER, the SIMS Q2 reporting deadline has also been extended. **The SIMS FY20 Q2 import deadline is extended to May 29, 2020** (as per usual, this is one week prior to the quarterly DATIM data entry close deadline; now June 5 for FY20 Q2). Additional SIMS reporting guidance is forthcoming from SGAC_SIMS@state.gov

Budget Guidance

Please coordinate with your agency financial POCs for how to address any budget implications of implementing this guidance.

Feedback/Question Submission: As is feasible given your country situation, PEPFAR programs are requested to share new MoH guidance for HIV services in the COVID-19 context, incoming technical questions, as well as any solutions for PEPFAR programs in the context of COVID-19. Guidance that has already been issued should be shared for awareness; PEPFAR HQ would be happy to provide rapid input on guidance that is still in draft form. Please send these new MoH guidance documents directly to S/GAC by

emailing them to Dr. Katy Godfrey qea0@cdc.gov, Teri Wingate gza2@cdc.gov, and Helina Meri MeriHD@state.gov, copying your Chair and PPM.

22. Information and Resources

Resources on GBV and Child Protection:

- Health care for women subjected to intimate partner violence or sexual violence: A clinical handbook – WHO, 2014
  - Job aids can be found on pages 11 (how to ask about violence) and 14-32 (LIVES, including safety planning and referrals)
- Caring for women subjected to violence: A WHO curriculum for training health-care providers - WHO, 2019
- Integrating Violence Against Children Prevention and Response into HIV Service
  - Job aids can be found in the Participants Manual on pages 48-53 (LIVES) and 72 (referrals).

Training Resources:

- The Strengthening Interprofessional Education for HIV (STRIPE) program offers trainings specific to COVID-19 for HIV care providers at: https://stripe-website-dev.globalhealthapp.net/module-material/.

9.4 Appendix 4: Accuracy, Acceptability, Feasibility, and Safety of Caregiver-Administered HIV Testing of Children Using Oral Mucosal Transudate (OMT) Tests

TO: [*INSERT PRIMARY STAKEHOLDER, i.e. PEPFAR, WHO, CDC, etc.]*
FROM: Irene Njuguna (MBChB, MSc, MPH, PhD), Anjuli Wagner (MPH, PhD) & Chido Dziva Chikwari (BSc, MSc, PhDc)

Accuracy, Acceptability, Feasibility, and Safety of Caregiver-Administered HIV Testing of Children Using Oral Mucosal Transudate (OMT) Tests

Executive Summary:
COVID-19 presents many barriers to clinic-based, health worker administered HIV testing. Caregiver-administered OMT testing may be a useful alternative to test children for HIV during this critical time. Our studies show that caregivers can administer tests accurately without additional health workers' support. We believe this approach is timely because it supports compliance to social distancing recommendations, defrays costs of travel to a healthcare facility, and maintains momentum in pediatric HIV testing. This policy memo draws evidence from a series of studies about the accuracy, acceptability, and feasibility of health worker and caregiver-administered testing, and safety of OMT testing for children outside of PMTCT settings, like in the STEP-UP study for Kenyan children (Dziva Chikwari & Njuguna et al 2019) and B-GAP study for Zimbabwean children (Dziva Chikwari et al 2019).

Key Findings

1. OMT tests are **accurate** among children >18 months
2. Even with variable yield, HIV testing benefits **all children**
3. Caregivers are **willing** to test their children at home using OMT with concerns that can be mitigated
4. Caregivers can **accurately** test their children, and performance improves with demonstrations
5. Social harm concerns **may exist,** so assessments must be made to understand and mitigate them

Key Finding: OMT is accurate among children

OMT is highly sensitive (100%) and specific (99%) in children 18 months to 18 years (Dziva Chikwari & Njuguna et al 2019).

Key Finding: Testing has benefits for all children

Caregivers avoid seeking care for minor illnesses for their untested children; 22% of caregivers avoided seeking care for their child's minor illness due to fear of HIV testing. Caregivers who predicted a child was HIV positive were 8 times more likely to avoid seeking care. After testing, 82% of caregivers who avoided care for their children in the past were more likely to seek care. Overall, testing provides emotional relief for both caregivers of HIV positive and negative children (Mugo et al 2019).

Image Source: The Sunday Mail, 2016

Acknowledgements

Thanks to the B-GAP and STEP-UP study participants.

STEP-UP team: Grace John-Stewart, Dalton Wamalwa, Jennifer Slyker, Gabrielle O'Malley, David Katz, Laura Oyiengo, Jillian Neary, Michelle Bulterys, Cyrus Mugo, Xinyi Zhai, Yu Wang, Verlinda Anyango, Vincent Omondi, Lukio Agalo, Pamela Agola, Anita Orimba, Anne Auma, Joseph Orondo, and the Kenya Pediatric Studies Staff

B-GAP team: Rashida A Ferrand, Vicky Simms, Helen Weiss, Stefanie Dringus, Sarah Bernays, Tsitsi Bandason, Nicol Redzo, Crissi Rainer, Belinda Chihota, Kearsly Stewart, Collaborating institutions and the B-GAP Research Assistants.

Key Finding: Caregivers are willing to test their children at home using OMT

There are potential advantages and disadvantages for caregiver-administered OMT. Overall, caregiver-administered OMT is acceptable with minor concerns that can be mitigated (Neary et al 2020; Rainer et al 2020).

Potential Advantages	Potential Disadvantages
• Shorter time • Convenience • Privacy* • Control over who knows child status** • Lower cost* • Increased child testing • Reduced provider workload • Easier administration • Child comfort of familiar setting • Caregiver belief of results	• Not receiving pre-test and post-test counseling • Not trusting results • Disagreements with partners or child neglect • Need for HCW support for positive screening result • Uncertainty in the ability to test without assistance or unable to read**

*Kenyan and Zimbabwean setting; **Zimbabwean setting alone; remainder is Kenyan setting alone

Key Finding: Caregivers can accurately test their children

In the B-GAP study, caregivers were able to accurately collect a sample, manipulate the test kit, and interpret the test results. Without additional provider demonstrations, 87% of caregivers (N=629) correctly swabbed both the upper and lower gum for fluid, 97% inserted the flat pad all the way into the reaction fluid, 90% used a timer, and 97% interpreted the test results correctly. With additional provider demonstration, 97% of caregivers (N=157) swabbed both the upper and lower gum for fluid, 99% inserted the flat pad all the way into the reaction fluid, 97% used a timer, and 98% interpreted the test result correctly (Dziva Chikwari et al, manuscript in preparation). Overall, gaps existed in swabbing both gums and using a timer, but both were overcome with demonstrations. Caregivers can accurately interpret test results, even without any additional demonstrations.

Key Finding: Concerns about social harms exist but limited observational data note low frequency

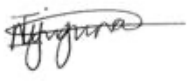
Concerns exist about social harm (child neglect, abuse, and abandonment) associated with caregiver-administered OMT testing. There are few unique risks, which are largely theoretical, and the existing evidence, though minimal, does not indicate increased harm.

Policy Recommendations

1. Caregiver-administered OMT testing can be used as an **alternative** to testing children during the COVID-19 pandemic as it supports compliance to the social distancing recommendations, defrays costs of travel to a healthcare facility, and maintains gains in pediatric HIV testing
2. Implementers may focus on **mitigating social harms** by using available resources, such as focusing on counseling messages and offering health worker support for testing/linkage through mHealth
3. Implementers may **monitor social harms** through routine questions to screen for and assess incident social harms

Our team would be happy to discuss our work with you and consult on pediatric HIV testing strategies during this challenging time to ensure gains continue to be made in pediatric HIV testing and treatment.

Sincerely,



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